THÈSE

En vue de l'obtention du

DOCTORAT DE L'UNIVERSITÉ DE TOULOUSE

Délivré par :

Institut National Polytechnique de Toulouse (Toulouse INP)

Discipline ou spécialité :

Sciences des Agroressources

Présentée et soutenue par :

Mme NYDIA ILEANA GUZMAN BARRERA

le jeudi 14 juin 2018

Titre :

Eco-compatible syntheses of bio-based solvents for the paint and coating industry

---

Ecole doctorale :

Sciences de la Matière (SDM)

Unité de recherche :

Laboratoire de Chimie Agro-Industrielle (L.C.A.)

Directeur(s) de Thèse :

MME SOPHIE THIEBAUD-ROUX
MME EMELINE VEDRENNE

Rapporteurs :

M. BRUNO ANDRIOLETTI, UNIVERSITE LYON 1
Mme ANNE-SYLVIE FABIANO-TIXIER, UNIVERSITE D'AVIGNON

Membre(s) du jury :

Mme MARTINE URRUTIGOITY, INP TOULOUSE, Président
M. JORGE ARTURO ABURTO ANELL, INSTITUTO MEXICANO DEL PETROLEO, Membre
Mme EMELINE VEDRENNE, INP TOULOUSE, Membre
Mme SOPHIE THIEBAUD-ROUX, INP TOULOUSE, Membre

REMERCIEMENTS

J'ai une grande liste de personnes à remercier, des personnes qui m'ont aidé, scientifiquement ou moralement, pendant ces années de thèse et qui m'ont permis de terminer ce doctorat avec succès.

Tout d'abord, je voudrais remercier Carlos Vaca García, directeur du Laboratoire Chimie Agro-industrielle, de m'avoir rencontré au Mexique et de m'avoir accueilli au laboratoire.

Je tiens à remercier les membres de mon jury d'avoir accepté d'examiner mon manuscrit et pour leurs discussions critiques qui ont su enrichir mon travail. Merci à Mme Martine URRUTIGOITY, pour avoir accepté de présider le jury de thèse. Merci à mes rapporteurs Mme Anne-Sylvie TIXIER et M. Bruno ANDRIOLETTI pour avoir évalué mon travail, leurs rapports m'ont vraiment donné beaucoup de confiance à présenter ma thèse. Merci à Idoia ETXEBERRIA, coordinatrice du projet ECOBIOFOR, pour avoir accepté de participer à ce jury et pour toute son aide et son soutien pendant le développement de mes travaux de recherche. Je tiens également à remercier M. Jorge ABURTO, qui a également fait son doctorat au LCA et qui m'a recommandé de faire le mien ici, étant ainsi à l'origine de cette aventure. Merci d'avoir fait confiance à mon travail depuis mes études d'ingénieur et d'avoir toujours inspiré mon travail avec ton grand dévouement à l'enseignement et à la science.

Je tiens à remercier mes directrices de thèse, Sophie THIEBAUD-ROUX et Emeline VEDRENNE. Merci de votre confiance et de m'avoir permis de développer ce projet librement, mais toujours avec vos conseils, votre aide et votre soutien. Merci d'avoir été toujours à l'écoute et disponible quand j'avais besoin de votre expertise scientifique. Je vous suis également reconnaissante de m'avoir permis de participer librement à des cours, congrès, écoles d'été, etc. qui ont grandement enrichi ma formation. Ce fut un véritable plaisir de travailler avec vous au cours des ces années.

Merci à Mme Caroline SABLAYROLLES, co-encadrante de cette thèse, pour m'avoir accompagné et aidé dans la partie dédiée à l'analyse du cycle de vie. Merci pour ta disponibilité et ton soutien durant ce travail. Comme je t'ai toujours dit, j'aurais aimé travailler plus avec toi et en apprendre davantage sur ton expérience en ACV.

Je tiens également à remercier Jérôme PEYDECASTAING, qui m’a donné des conseils scientifiques lors de cette thèse. Merci beaucoup, ce travail n'aurait pas été le même sans toi. Je te remercie d'avoir toujours été disponible, de m’avoir accompagné tout au long de mes recherches et pour la réalisation et la planification des expériences. Merci pour ta bonne humeur, pour les discussions scientifiques, mais aussi pour les discussions philosophiques.

Je voudrais également remercier tous les membres du projet ECOBIOFOR qui ont rendu ce travail possible : Idoia Etxeberria, Izaskun Garmendia, Ingemar Svensson, Pilar Caro, Beatriz Palomo, Sara Monteiro, Cathy Kroll, Claudio Pagella, Jan Van der Meulen, Philippe Marechal, Jon Begiristain, Laura Castañeda, Carles Estevez, Lucas Misset, Samuel Scholler. Ce fut un plaisir de vous rencontrer et de travailler avec vous.

Je tiens maintenant à remercier à l'ensemble du personnel du laboratoire. Merci à tous pour votre sourire échangés au détour des couloirs, les discussions et moments agréables à la cafétéria et vos encouragements.
Je tiens à remercier spécialement à :
Cécile BORIES (alias patin del diablo), un grand merci pour ton aide dans le projet ECOBIOFOR. Merci d'être toujours disponible pour m'aider dans les expériences et dans la réalisation du cycle de vie de nos super solvants. Merci pour tous les moments de plaisir au fil des ces années.

Philippe BEHRA, merci pour votre aide dans l'analyse des phases solides nécessaire à la compréhension du mécanisme de réaction de la synthèse de la méthyl éthyl cétone, ce qui a été un défi dans ce travail. Merci aussi à Brigitte DUBREUIL pour m'avoir aidé pour les analyses Raman de mes échantillons, pour m'avoir enseigné cette technique intéressante et pour les discussions constructives que nous avons eues. Merci à Joël ALBET pour son aide dans la modélisation de la MEK en PROSIM. Merci a Yannick COPPEL du LCC pour son aide en RMN solide et a Jérôme ESVAN du CIRIMAT pour son aide en XPS.
Merci à Romain, Didier, Ingrid, Emmanuelle, Karine et Christina pour leur aide logistique. Merci aussi à Céline et Dominique pour leur aide en analytique.

Ces années de thèse n'auraient pas été les mêmes sans les collègues et amis doctorants, elles auraient sûrement été beaucoup moins amusantes.
Je tiens tout d'abord à remercier mes collègues de bureau, qui sont devenus des amis et m'ont beaucoup aidé à faire face aux moments de stress et de désespoir pendant ma thèse ☺. Merci Rémi, Etienne et Nico, pour nos moments de musique pour se détendre, nos discussions sur la politique et la société et tous les rires que nous avons eus. Merci Rémi et Etiennecito, pour m'avoir forcé à vous parler jajaja, sans vous je n'aurais jamais enlevé mes écouteurs pour devenir sociable. Merci pour votre amitié sincère et votre bonne humeur. Merci Etiennecito ce fut un plaisir d'être ta voisine de bureau, merci d'être toujours disponible pour m'écouter sur n'importe quel sujet, j'ai trouvé en toi un grand ami, tu fais partie des gens extraordinaires que j'ai eu le plaisir de rencontrer dans cette expérience transatlantique. Merci beaucoup Kevin pour ton aide et ton regard critique sur mon

travail, pour ton temps dédié à lire ma publication et tes conseils et suggestions très pertinents pour améliorer mon travail, merci aussi pour toutes les discussions intéressantes et amusantes que nous avons eues, pour ton bonne humeur et pour m'avoir fait connaître mon nouvel endroit préféré.

Gracias a mis amigos latinos, Monica, Lucero (las espero en Bordeaux para probar nuestro Pessac favorito!!), Pablo, Alejandra, Jesus, Francisco, c'était génial de partager ces années avec vous, de pouvoir parler en espagnol pendant la pause café, et pour les moments de plaisir toujours nécessaires pour survivre pendant la thèse.

Merci à tous les anciens thésards, Jéremy, Jean-Baptiste, Hien, Evelien et Assad. Merci à Evelien, les premières années de thèse ont été géniales grâce a toi. Merci à Assad, qui m'a beaucoup aidé dans ma première année au laboratoire, surtout avec son grand talent pour faire des discours, mon français s’est beaucoup amélioré grâce à toi , merci aussi pour les soirée salsa y bachata.

A tous les nouveaux et pas si nouveaux doctorants, Margaux, Pauline, Huy, Clement, Douaa, Niki, Alice, Mathieu, Lonn, je leur souhaite un parcours de réussite, courage !! la fin donne beaucoup de joie.

Je tiens également à remercier à Benjamin pour m'avoir soutenu et aidé au cours des derniers années de thèse. Gracias por tu resistencia a mi estrés y un poco mal humor en los últimos meses de redacción, por alimentarme, obligarme a dormir y por tener siempre palabras de aliento y réconfort. Merci aussi à ta famille, de m’avoir permis de me sentir chez moi et pour son soutien.

Agradezco enormemente a mis padres, Gustavo y Cony, y a mis hermanos, Ariel, Hiram y Abril, por ayudarme y apoyarme en la distancia, no fue nada fácil estar lejos de ustedes y mi amado país, pero siempre tuvieron las palabras perfectas para impulsarme a continuar. Éste logro es suyo y sin su apoyo y esfuerzo no habría llegado hasta aquí!!.

Gracias a mis amigos: Omar, Claudia, Yatzil, Elayne, Jessica, Natalia, Fernanda, Abraham e Iliana por sus palabras reconfortantes, por creer en mí y por siempre echarme porras del otro lado del teléfono.

Y finalmente, gracias a todo el pueblo mexicano, que sin estar completamente consiente, me permitió realizar mis estudios de doctorado a través de una beca CONACyT del gobierno Mexicano. Orgullosamente hecha en México!!!

Abstract

Global solvent production accounts for about 28 million tonnes, including 5 million tonnes in Europe. The paint and coating industry is the main consumer (46% of the solvents produced). In this sector, the most used solvents are ethyl acetate, butyl acetate and methyl ethyl ketone. These molecules are currently synthesized industrially from petrochemical substrates in the presence of homogeneous catalysts and under energy-consuming conditions.

In order to reduce the environmental impact of paints and coatings, the substitution of these fossil-based solvents by their bio-based equivalents has been studied in the framework of the European project ECOBIOFOR (FP7/2007-2013/Grant Agreement n^{o} 605215), in which this thesis work was inscribed. Thus, the objective of this thesis was to develop production processes for these three solvents that would start from renewable synthons and would be simple to implement, inexpensive and respectful of the principles of green chemistry.

For the production of ethyl and butyl acetates, two synthetic routes have been studied in the presence of an ion exchange resin as a heterogeneous catalyst. The first route uses acetic acid and the corresponding bio-based alcohol (ethanol or butan-1-ol); the second involves acetic anhydride instead of acetic acid. Kinetic and thermodynamic studies have led to select the most efficient resin and the most suitable reaction conditions. This study has finally allowed to propose an efficient and innovative coproduction process for the two targeted acetates in which their purification is facilitated, the production of waste and co-products is reduced and the recycling of the resin is possible. The evaluation of the performance of the synthesized acetates in nitrocellulose lacquer and polyurethane varnish formulations has shown that these molecules meet the specifications in terms of drying, viscosity, film formation, gloss and adhesion. Finally, the environmental benefit of the co-production process was highlighted by the calculation of green metrics and the life cycle assessment (LCA) of the produced esters. Furthermore, the influence of the origin of alcohols (bio-based or petrochemical) on the environmental impact was evaluated. The impact on climate change is reduced through the use of bio-sourced synthons.

For the synthesis of methyl ethyl ketone, we decided to study the decarboxylation reaction of levulinic acid, which is a bio-based platform molecule available and inexpensive. Unlike the main industrial process, which relies on the dehydrogenation of butan-2-ol from fossil origin, the method developed in this work uses conditions that are more respectful of the environment since the reaction is carried out in water in the presence of potassium persulfate and a silver salt at a moderate temperature (100°C). The evaluation of the role of each of the reagents allowed us to propose a complex reaction mechanism for this reaction. The study of the evolution of the solid phase species carried out through various spectroscopic analyzes (SSNMR, XRD, XPS, AES and SEM) made it possible to highlight the species involved in the decarboxylation and finally to propose a method to obtain high conversions and yields.

Résumé

La production mondiale de solvants représente environ 28 millions de tonnes, dont 5 millions en Europe. L'industrie des peintures et des revêtements en est la principale consommatrice (46 % des solvants produits). Dans ce domaine, les solvants les plus utilisés sont l'acétate d'éthyle, l'acétate de butyle et la méthyl éthyl cétone. Ces molécules sont actuellement synthétisées industriellement à partir de substrats d'origine pétrochimique en présence de catalyseurs homogènes et dans des conditions énergivores. Afin de réduire l'impact environnemental des peintures et revêtements, la substitution de ces solvants issus du pétrole par leurs équivalents bio-sourcés a été étudiée dans le cadre du projet européen ECOBIOFOR (FP7/2007-2013/Grant Agreement n° 605215), dans lequel se sont inscrits ces travaux de thèse. Ainsi, l'objectif de cette thèse a été de développer, à partir de synthons renouvelables, des procédés de production de ces trois solvants simples à mettre en œuvre, peu coûteux et respectueux des principes de la chimie verte.

Pour la production des acétates d'éthyle et de butyle, deux voies de synthèse ont été étudiées en présence d'une résine échangeuse d'ions comme catalyseur hétérogène. La première voie utilise de l'acide acétique et l'alcool biosourcé correspondant (éthanol ou le butan-1-ol); la seconde met en jeu l'anhydride acétique à la place de l'acide acétique. Dans ces synthèses, quatre résines ont été testées. Des études cinétiques et thermodynamiques ont permis de choisir la résine la plus performante et les conditions de réaction les plus adaptées. Cette étude a finalement permis de proposer un procédé de coproduction des deux acétates efficace et innovant dans lequel la purification des acétates est facilitée, la production de déchets et coproduits est réduite et le recyclage de la résine est possible. L'évaluation des performances des acétates synthétisés dans des formulations de laques nitrocellulosiques et de vernis polyuréthanes a permis de montrer que ces molécules répondent au cahier des charges en terme de séchage, viscosité, formation de film, brillance et adhérence. Enfin, le bénéfice environnemental du processus de coproduction a été mis en évidence par le calcul des métriques de la chimie verte et l'analyse du cycle de vie des esters produits. De plus, l'influence de l'origine des alcools, bio-sourcés ou pétrochimiques, sur l'impact environnemental a été évaluée. L'impact sur le changement climatique est réduit avec l'utilisation des synthons bio-sourcés.

Pour la synthèse de la méthyl éthyl cétone, nous avons décidé d'étudier la réaction de décarboxylation de l'acide lévulinique, molécule plateforme biosourcée disponible et peu coûteuse. Contrairement au principal procédé industriel qui repose sur la déshydrogénation du butan-2-ol d'origine fossile, la méthode développée dans ces travaux utilise des conditions plus respectueuses de l'environnement puisqu'elle est réalisée dans l'eau en présence de persulfate de potassium et d'un sel d'argent à une température raisonnable (100°C). L'évaluation du rôle de chacun des réactifs a permis de proposer un mécanisme réactionnel complexe de cette synthèse. L'étude de l'évolution des espèces en phase solide réalisés par diverses analyses spectroscopiques (RMN du solide, DRX, XPS, AES et MEB) a permis de mettre en évidence les espèces impliquées dans la décarboxylation et finalement de proposer une méthode permettant d'obtenir des conversions et des rendements élevés.

CONTENTS

INTRODUCTION

Solvents are liquids capable of dissolving, suspending or extracting other materials. They are principally used in extraction processes, in chemical syntheses, in cleaning procedures and in the formulation of commercial products, such as adhesives, household products, paints and coatings.

In the paint and coating industry, solvents are essential as they allow the dissolution and the dispersion of pigments, binder and additives. Thus, thanks to the solvent, a homogenous solution of adequate viscosity is formed for an efficient application of the paint. Once the paint or coating is applied, the solvent evaporates to produce a continuous film on the surface.

Traditional solvents are currently produced from petrochemical sources. In an attempt to reduce the petroleum dependence and to offer alternatives to fossil solvents, economic and political concerns have arisen. Accordingly, the European Union has encouraged the replacement of these solvents by greener alternatives. Thus, in the last years, interest in biomass as feedstock for the production of chemicals has increased. The use of biomass, as a raw material for the production of solvents, offers an alternative resource, with a lower carbon footprint and could have a positive impact on the economy in the long term.

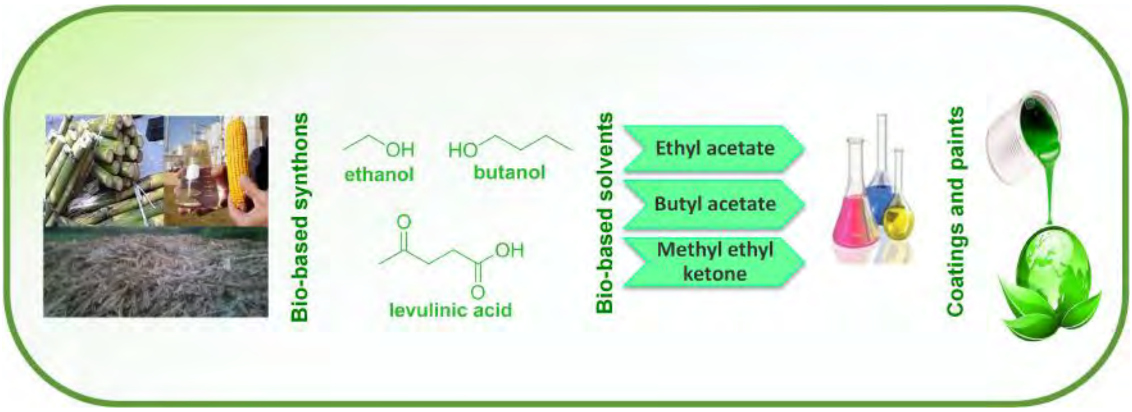
This thesis work has been developed within the framework of the European ECOBIOFOR project (ECOpaint BIO-based FORmulations; FP7/2007-2013) [Grant Agreement n° 605215]). “The ECOBIOFOR project focuses on the development and production of bio-based solvents, by the easiest chemical and biotech production way. The new Ecopaint Bio-based Formulations will include renewable versions of the traditional organic solvents (with a lower carbon footprint), bearing the same chemical structure and physical properties and a brand new alternative of reactive solvent, not emitting VOCs” (http://ecobiofor.eu/Home).
In order to achieve the objectives of the European project, a multidisciplinary consortium was created. It was formed by:

- 5- Small and Medium-sized Enterprises (SME): Asociación Española de Bioempresas (ASEBIO, Spain), Associação Portuguesa de Bioindústrias (APBIO, Portugal), Swiss Biotech Association (SBA, Switzerland), Consorzio per la Promozione dei Prodotti Vernicianti e Ricopenti (PROCOAT, Italy), Conseil Européen de l'Industrie des Peintures, Encres d’Imprimerie et des Couleurs d’Art (CEPE, Belgium),

- 3 other enterprises or end-users: Stéarinerie Dubois Fils (France), Castellano Peintures (France), Industrias Químicas Irurena (Spain),
- 3 Research, Technology & Development performers (RTD): Fundación Tecnalia Research & Innovation (Spain, coordinator), Institut Universitari De Cienca i Tecnologia (IUCT, Spain), Institut National Polytechnique de Toulouse (Laboratoire de Chimie Agro-industrielle, LCA, France).

A part of the investigations was carried out in the Laboratoire de Chimie Agro-industrielle (Toulouse INP-LCA), whose role was to develop new green synthesis pathways of ethyl acetate, butyl acetate and methyl ethyl ketone, starting from biomass. Indeed, these selected solvents are considered among the least toxic solvents and present the lowest risk to health, according to the Food and Drug Administration (FDA agency).[1] In addition, these solvents are considered as readily biodegradable by the European Chemical Agency (ECHA).[2–4]

The synthesized bio-based solvents will meet the criteria required to replace the traditional petrochemical solvents in paint and coating formulations, since they will have the same physicochemical properties.



In this thesis work, we have set as main objectives:

- To synthesize ethyl acetate, butyl acetate and methyl ethyl ketone from bio-based building blocks.
- To produce these solvents according to an eco-compatible process, using mild reaction conditions and respecting as far as possible the principles of green chemistry, considering: the atom economy, the reduction of the number of reaction steps, the use of catalysts easy to separate and recycle and the reduction of waste production.

This manuscript is composed of 4 chapters:

The first chapter presents an overview of the use of solvents in the paint and coating industry and the properties that these solvents have to match to be incorporated in formulations. As most of the used solvents have negative effects on the environment and health, measures have been taken to regulate their use and alternative solvents, such as bio-based solvents, have been developed to replace them. In this context, we propose in this chapter, the bio-based synthons from which ethyl and butyl acetates and methyl ethyl ketone have been synthesized.

The second chapter consists in the development of the syntheses of ethyl and butyl acetates according to the principles of green chemistry. This work has been published in an article in *Green and Sustainable Chemistry*. This research allowed the development of an innovative coproduction process of the targeted esters. Additionally, in this section the synthesized acetates are characterized and tested in two coating formulations of nitrocellulose lacquers and polyurethane varnishes.

In chapter three, the evaluation of the developed syntheses of acetates from an environmental point of view is carried out. Two approaches are considered: the calculation of green metrics and the life cycle assessment (LCA). This work has been published in *The International Journal of Life Cycle Assessment.* Furthermore, the benefit of the use of bio-based alcohols as starting material, instead of the petrochemical corresponding molecules, is evaluated.

The last chapter consists in the study of the synthesis of methyl ethyl ketone from bio-based levulinic acid. A system silver species/potassium persulfate is used to decarboxylate levulinic acid. The evolution of the silver species involved in the reaction is analysed through several spectroscopic techniques (SSNMR, XRD, XPS, AES and SEM-EDX) in order to gain more insight into the mechanism of this reaction and to improve the conversion and reaction yield. This work has been submitted to the *Journal of American Chemical Society*.

CHAPTER I. The paint and coating industry: from petrochemical to bio-based solvents

1.1 Paints and Coatings

1.1.1 History of paints: evolution of the use of solvents in paint formulations

Paints are present in daily life since the prehistoric era, as they were used to create graphic representations or decoration in caves. The earliest paintings made by the primitive men are from Europe and Australia, they date approximately from 25000 years ago. The paints found in caves in Altamira (Spain) and Lascaux (France) were composed of iron and manganese oxides, with which the colors black, red, yellow and their intermediate colors were obtained.[5] During this period, other natural pigments such as chalk, charcoal and green earth were used. The powdered pigments were probably mixed with water, animal fats, blood, egg whites and yolks (as binders) to make the paints.

Many centuries later, from 3000 to 600 BCE, the Egyptians also used natural pigments. They have developed a wide range of colors: blue from the lapis lazuli rock, red from iron oxide, yellow from arsenic trisulfide, green malachite from basic copper carbonate, and the white pigment gypsum from the calcium sulfate. Besides, the Egyptians were the first to develop a synthetic pigment, the Egyptian blue, which was obtained by calcining lime, sodium carbonate, soda ash, copper oxides and silica between 800 and 1000 °C. They employed a variety of organic and inorganic materials as binders, such as gum arabic, gelatin and beeswax.[6]

Later, the Greek and Roman civilizations used paints to decorate buildings, statues and other objects. Besides the pigments exploited by the Egyptians, the Romans developed other synthetic colors from white lead (vapor acid), yellow lead oxide (oxidation at high temperatures), red lead (calcination of yellow lead oxide), verdigris (acetic acid and copper) and bone black. They have also used carmine dye obtained from a secretion produced by the *Kermes* insect. Their paints were still composed of natural binders: gelatin, starch, beeswax, charcoal and various clays and minerals. Resins and oils were employed in paint formulations but only for liniments.[6–8]

In Mexico and Central America, the Mayan civilization (250-950 CE) developed their paints only with organic pigments, from a wide variety of insects and plants, which made their pigments unique in the world. The color white was obtained from the mixture of lime with the juice of the “chichebe” plant (scientific name: *Sida acuta*). Some natural earths gave the color brown and were used to darken the color red; the red pigment was produced from the cochineal insect, which was one of the most lucrative products that was brought to Europe by the Spanish.[9] The blue color was obtained from plants containing aniline compounds, such the “añil” plant or “xiuhquilitl” in Mayan language; yellow was made from the achiote fruit; and black color was prepared by carbonizing the resinous tree "chaka" in Mayan language (scientific name: *bursera simaruba)*. Finally, paints were formulated by Mayans using binders such as the mucilage found in the bark of trees like "chichebe" and a kind of gel that has been suggested was obtained from the bulb of orchids[10] or from the sap of the *Opuntia* species.[11]

Although cedar oil-based resins were already used in Egyptians time to paint buildings, sculptures and mummification coffins, it was in the 11th century that the use of oleoresins was expanded, and new coatings were developed, based on natural resins, such as amber. During the Renaissance (14-16th century), painters such as Leonardo da Vinci and Rembrand made their own paint formulations, in which they mixed different pigments with amber, rosin and sandarac resins dissolved in hot linseed oil without the use of any volatile compound. However, the turpentine, a resinous liquid exuded from conifers, was found in some paintings. This unusual diluent used by Leonardo da Vinci became the first reported solvent in paints.[12,13] Its principally function was to reduce the viscosity of paints and coatings, allowing the painters to employ the varnishes at ambient temperature.[8]

In 1773, a detailed technical preparation of paints and varnishes reported by Watin showed that copal and amber continued to be the principal resins and turpentine the diluent. Varnishes factories began to operate throughout Europe, starting the booming of the paint industry. Turpentine was chemically analyzed for the first time in 1818 and was attributed the empirical formula C_5H_8. Later, other studies were carried out from 1858 to 1863, allowing the identification of camphene and pinene as the main components of turpentine.

In the 19th century, the use of turpentine was greatly extended, specially for the naval sector since it was necessary to use large amounts of paint to protect the boats from the corrosion caused by water. This involved a rapid increase in demand and consequently in the production of turpentine, making this solvent the second product of naval stores.[14] Its production was one of the most profitable activities in the United States, even better than the production of cotton. However, at the end of the century, an interest in solvents of petrochemical origin began to arise due to the difficulties to provide turpentine. Finally, in the 20th century, the cost of petrochemical solvents became very competitive and in the 40's years, the turpentine was completely replaced in paint formulations by a petroleum distillate, white spirits, which emits a more pleasant smell than the turpentine.

Currently, the growing interest in replacing solvents of petrochemical origin by bio-based solvents in the paint and coatings industry has led to the exploration of new alternatives and, of course, the resurgence of the use of turpentine as a solvent.[15,16]

1.1.2 Current composition of paints and coatings

Paints and coatings are liquids, pastes or powders that are applied to a surface through different methods and equipment and have principally a decorative or protective function.[17] They are mainly constituted by four elements: binders, pigments, additives and solvents.[18,19]

- **Binders**

The binder or resin is the most important ingredient of paints, because it forms the matrix of the coating in which other components will be incorporated. The resin is the film-forming agent of the paint and its density is responsible of the permeability as well as the chemical and ultraviolet resistance of the coating. Binders are divided into several categories according to how they form the film and how they cure or dry: solid thermoplastic film formers, lacquer-type film formers, oxidizing film formers, room-temperature catalyzed film formers, heat-cured film formers and emulsion-type film formers.[6] The most commonly used binders are alkyd, acrylic, phenolic, urethane and epoxy resins, latex and chlorinated rubber.[20]

- **Pigment**

The pigments are solids that are scattered in the paints and coatings to give them color and opacity. This is their main function. The color pigments also provide the esthetic value and gloss. Furthermore, they can contribute to the structure and the impermeability of the film.[21] In order to obtain good performance, pigments should be compatible and resistant to the environmental conditions. The addition of pigments provides not only the color to the coating system but also protects the surface from the corrosion and the UV-light.[17]

The anticorrosion pigments protect the substrate by corroding themselves or by passivating the surface. Among these kind of pigments, we can quote: the blocking pigments, the galvanic pigments and the passivating pigments.[22] The blocking pigments are absorbed in metal surfaces reducing the corrosion area; they form a transport barrier for ionic species to and from the substrate.[23] Galvanic pigments are metallic particles that corrode themselves to prevent the metal surface from oxidizing: here, only the cathodic reaction takes place on the metal surface. In the case of the passivating pigments, they are capable of forming a layer on the anodic surface (area susceptible to oxidation) thus passivating the surface, leading to its protection.[24]

- **Additives**

Additives are generally added to paint formulations in trace amounts to provide specific functions, increasing the performance of the paint. They can, for example, provide faster drying (driers) or retard the deterioration of the resin by heat or sunlight (ultraviolet stabilizers). Other additives, such as coalescing aids are used to promote the formation of homogeneous films. Surfactants and emulsion stabilizers are used to improve the affinity between paint components. They can, for example, lead to the dispersion of pulverulent pigments in paint and coating formulations.[17,25]

- **Solvents**

The objective of the use of solvents in paints is to dissolve or disperse the different components (binder, pigments and additives) and to reduce the viscosity of the resin solution in order to obtain a homogeneous formulation with a satisfying consistency. The role of the solvent before and after paint and coating application is different. Before application, solvents form a homogeneous liquid coating or paint, facilitating its application. On the contrary, after paint or coating application, the solvent should reduce its interactions with the components to form the film while evaporating.[22,26]

After having exposed the history of painting, its composition and the function of each of its components, herein we are particularly interested in solvents. Therefore, the rest of this work will focus on them.

1.1.3 Solvent market: the domination of the paint and coating industry

The global consumption of solvents is significant, with almost 28 millions metric tons consumed in 2012.[27] The reported global market size is around USD 20 billions and it is expected to reach USD 28.25 billion by 2021 at a Compound Annual Growth Rate (CAGR) of 7.9 from 2016 to 2021.[28] Europe, the solvent production represents approximately 5 millions tons.[29]

Solvents play a major role in many processes and products. They are typically used for:

- Formulation of products such as adhesive, paint and household products
- Extractions and purifications
- Chemical syntheses
- Cleaning procedures

The most important consumers of solvents are the producers of paints and coatings, which dominate the world market of solvents (Figure 1), with a consumption that has increased from 46 % in 2009 to 60.6 % in 2011.[30] An increase in the solvents demand from this sector of 2.9 % per year until 2019 has been predicted.[31] The high demand of solvents by the paint industry is due to the paint formulations in which solvents represent:

- more than 50 % of the total composition for conventional solvent-based paints.[32]

- between 25 % and 35 % of the high solid coatings.
- between 5 % and 20 % of the total composition of water-based coatings.

For the other alternative paints such as powder paints and radiation-cured coatings, no solvent is needed.

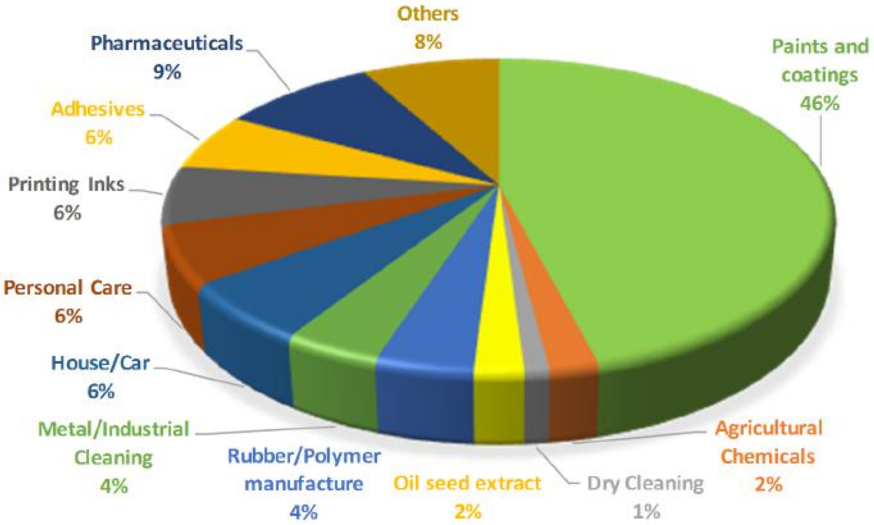


Figure 1. Industrial use of solvents in Europe (Cited by Pereira et al. 2011)[33].

1.1.4 Definition of solvents in the paint and coating industry

Chemically a solvent can be defined as a liquid, a solid or a gas capable of dissolving a solute to form a homogeneous or semi-homogeneous solution. Conventional organic solvents mainly consist of hydrocarbons, esters, alcohols, chlorinated organic compounds, ketones and glycol ethers.

In the paint and coating industry, a solvent is defined as a liquid consisting of one or more component(s), which is able to dissolve other substances (binder, pigments and additives) to produce a homogeneous solution without reacting. Thus, the role of the solvent is to dissolve/disperse the solid or semisolid compounds in order to reduce the viscosity, facilitating the application of the paint.[22,34] The first reported solvents used in paints and coatings were natural oils such as linseed oil, and the turpentine, as previously mentioned. Then, these solvents were replaced by petrochemical ones that provide a faster drying to the paint. Nowadays, different mixtures of solvents have been developed and studied to improve the drying and to optimize the application of the paint.[17]

There are three major uses of solvent in the paint industry, as:[35]

- an integral part of a paint formulation
- paint thinner, in order to dilute paint.
- cleaning agent of the equipment used for paint formulation or during its application.

Although the solvent is not part of the paints and coatings after their application, since it evaporates during the film formation, it has the capacity to affect their physical characteristics, their resistance and their durability. Once the coating has been applied, the solvent has to be completely evaporated to allow the drying and to produce a continuous film on the surface. In the coating sector, the systems based on organic solvents dry up to 10 times faster at room temperature than water-based systems, which presents the advantages of keeping production rates up, minimizing cost and energy consumption.[18,36]

1.1.5 Solvent classification in the paint and coating industry

Solvents can be classified according to their function into: active, latent and diluent, or they can be classified chemically into: hydrocarbons, oxygenated, and others.[22]

1.1.5.1 Classification by function

- **Active Solvents**

The active solvents, commonly known as "true solvents", are responsible for dissolving resins and other film formers to reduce the viscosity of paints, varnishes and lacquers. They have usually the strongest solvent power, such as ketones, esters and glycol ethers.

- **Latent Solvents**

The latent solvents are described as poor solvents or non-solvents of most resins. However, they have a hidden or latent solvency that can be evidenced when they are combined with an active solvent. The synergism created between the two types of solvents makes it possible to obtain results equivalent to those of the active solvents. They are principally used in nitrocellulose and lacquer formulations. Some examples are alcohols such as ethanol, propanol and butanol.[22,37]

- **Diluents**

Diluents are commonly solvents used to thin lacquers and paints, reducing their viscosity and facilitating their application. They are generally considered as non-solvents of binders. They are incorporated during paint manufacture or added at the time of use to achieve the required application characteristics without causing disruption (binder precipitation for example).

1.1.5.2 *Classification by chemical families*

In addition to the classification by function, the solvents can also be classified by chemical type into three categories (Figure 2):[17]

- Hydrocarbon solvents
- Oxygenated solvents
- Other solvents

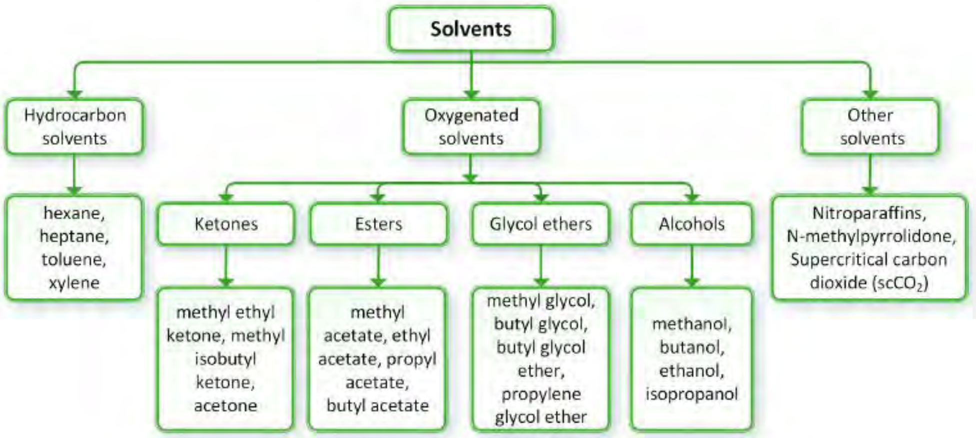


Figure 2. Chemical classification of solvents in the paint industry

- **Hydrocarbon solvents**

The hydrocarbon solvents are organic solvents that are composed of only hydrogen and carbon atoms. They are classified as aromatic or aliphatic hydrocarbon solvents. The first group, as the name suggests, has an aromatic (benzene) ring structure. These solvents present a high dissolving power, which makes them capable of dissolving the binders that are most difficult to solubilize, such as alkyd and saturated polyester resins, polyacrylates and vinyl copolymers. In coatings, toluene and xylene are the most representative solvents of this category.[34] In the case of the aliphatic hydrocarbon solvents, they consist of a mixture of saturated paraffins with straight chain, branched chain or cycling chains that do not contain a benzene ring in their structure. The most common aliphatic hydrocarbons used in paints and coatings are hexane, heptane and odourless mineral spirits.[22,25]

- **Oxygenated solvents**

The oxygenated solvents are the most consumed solvents, composed of hydrogen, carbon and oxygen atoms. They are used as active solvents in paint and coating formulations to dissolve resins due to their strong solvency, to reduce the viscosity of paints, varnishes and lacquers and to facilitate their application. The oxygenated solvents can be divided in 4 subcategories: ketones, esters, glycol ethers and alcohols (Figure 2).[38]

Esters and ketones are the most consumed solvents of this category. They are used for the manufacture of paints and coatings, because they are good hydrogen acceptors thanks to their carbonyl group, which bring them a high solvent power. The mainly used esters in coatings are acetates, such as ethyl acetate, isopropyl acetate, butyl acetate and butyl cellosolve acetate (2-butoxyethyl acetate). The most frequently used ketones are methyl ethyl ketone (MEK), methyl isobutyl ketone (MIBK) and methyl amyl ketone (MAK).[17,22,25]

Alcohols can be divided into lower and higher alcohols. The lower alcohols, such as methanol and ethanol, are good solvents for highly polar binders, such as phenolic resins, amino resins, cellulose nitrate, ethyl cellulose and polyvinyl acetate. The higher alcohols such as propanol are mainly used as diluents.[5,17,39]

The glycol ethers based on alkyl ethers of ethylene glycol, have the functionality of an ether and an alcohol, which is why they are widely used in coating formulations; some examples are ethylene glycol ethyl ether and ethylene glycol *n*-butyl ether.[20,22,40]

- **Other solvents**

The group of other solvents are defined as the organic solvents composed of hydrogen, carbon, oxygen (or not), and other atoms such as chlorine or nitrogen (nitroparaffins and *n*-methylpyrrolidone). Water and supercritical carbon dioxide ($scCO_2$) are also included in this category (Figure 2). Supercritical carbon dioxide is, for example, used in spray-applied coatings (for example UNICARB® spray solution that contains between 10 and 50% of dissolved CO_2).[22,41]

1.1.6 Solvent properties required for paints and coatings

Several specifications are required for solvents in paints and coatings in order to guarantee the formulation performance in terms of aesthetics and applicability on various substrates. They include:

- the technical specifications of the solvent such as its flash point to prevent safety hazards, its solvency, its evaporation rate and other physicochemical properties such as its color, its refractive index, its boiling point, its vapour pressure and its viscosity,[22,25,26,39]
- the toxicological properties of the solvent,
- the solvent behaviour in the environment
- and the solvent cost: it depends on its production process and the used raw materials. This cost is in the order of one to few euros per kilogram for a paint and coating solvent. For example, ethyl acetate, butyl acetate and methyl ethyl ketone were estimated between 0.8

and 1.1 €/kg in 2016 (data provided by ECOBIOFOR industrial partners Irurena, Castellano and Stéarine Dubois).

1.1.6.1 Physicochemical properties

Although many physicochemical properties (density, color, refractive index, relative polarity, acidity, vapor pressure, surface tension, viscosity, melting point, boiling point and flash point) can be evaluated for a solvent, we will only detail, in this section, the properties considered necessary to obtain a high quality paint formulation. These properties are presented below:

1.1.6.1.a Density, color and refractive Index

Density, color and refractive index are useful parameters for solvents quality control. These two parameters can be affected by the presence of impurities. Modification of solvents color due to the presence of impurities and bad storage conditions can be determined by UV-Visible spectroscopy.[42,43] On the other hand, solvent density can be measured using a pycnometer. As density varies with temperature, the ISO 758 Standards "liquid chemical products for industrial use" impose to evaluate density at 20 °C.[44] In order to check the solvent purity before its use in manufacture of paints and coatings, its refractive index can also be measured. The refractive index is the ratio of the speed of light through a vacuum to the speed of light through the sample.[43]

1.1.6.1.b Flash point

The flash point of a liquid is the lowest temperature at which the liquid emits sufficient vapour to form an ignitable mixture with air, producing a flame when a source of ignition is used close to the surface of the liquid. Evaluation of flash point has to be carried out under control-test conditions at a standard barometric pressure of 760mmHg. This parameter is an indicator of the relative flammability hazard of a solvent.[22,25] Solvents can be classified in 3 categories according to their flash point (Table 1).

Category	Criteria
1: Extremely flammable liquid and vapour	Flash point < 23°C and initial boiling point ≤ 35°C
2: Highly flammable liquid and vapour	Flash point < 23°C and initial boiling point > 35°C
3: Flammable liquid and vapour	Flash point ≥ 23°C and ≤ 60°C

Table 1. Classification of flammable liquids according with the CPL regulations[45]

The European CLP regulation (Classification, Labelling and Packaging) recommends a flash point above 61°C to work in safety conditions. Similarly, the US National Fire Protection Agency (NFPA) has changed its definition of flammable liquids by increasing the flashpoint limit to 60.5°C.[45]

Unfortunately, solvents with flash points higher than 60-61°C are rarely used in paints and coatings as their evaporation rate are generally not sufficient to get a fast drying.

1.1.6.1.c Boiling point

The boiling point (b.p) of a liquid is the temperature at which vapor pressure of the liquid is equal to atmospheric pressure. This property is determined at atmospheric pressure (760 mm Hg).

The boiling point is usually used in the paint industry as a guide to select a solvent, since it is known that liquids with a low boiling point evaporate more quickly than those with a high boiling point.

In the paint and coating industry, solvents are classified according to their boiling point into: low boilers that have a boiling point below to 100°C, medium boilers with b.p. between 100 and 150°C and high boilers with a b.p higher than 150°C. This classification helps painters to select the method of paint application. For example, low boilers are used in spraying methods, whereas high boilers are preferred in brushing techniques.[21]

1.1.6.1.d Vapor pressure

Vapor pressure for a solvent is defined as the pressure at which the gas phase is in equilibrium with its liquid (condensed) phase at a given temperature in a closed system. Liquids with high vapor pressures are known as volatile liquids. This property can be measured by controlling the solvent pressure and measuring its boiling temperature. At the boiling temperature, the vapor pressure is equal to the applied external pressure.[43]

This is a parameter used to define the organic volatile solvents (VOC's) in Europe. Any solvent that has a pressure vapor greater than 10 Pa at 25°C is considered as VOC.[46]

1.1.6.1.e Evaporation Rate

The evaporation rate is an important parameter to be determined as the solvent vaporizes from the paint during and after its application, increasing the solid content and the viscosity. The evaporation rate of a solvent has to be in accordance with the method of paint application. This means that in case of manual use, the solvent must evaporate slowly to allow the film to remain fluid during its application. On the contrary, if a spraying technique is used, the solvent needs to evaporate very quickly so that the viscosity of the film increases to avoid excessive flow. Choosing the right solvent with desired evaporation properties is very important to prevent problems, such as blistering and cratering during the film forming process.[5,17,22,36]

The evaporation rate can be evaluated by two methods: i) the determination of evaporation time of the studied solvent compared with a reference such as *n*-butyl acetate or diethyl ether and ii) the measurement of the weight loss of the solvent with an electrobalance.

- **Determination of evaporation rate relative to *n*-butyl acetate or diethyl ether**

Solvent evaporation rate is a relative value as it depends on the experimental conditions (temperature, humidity, nature of the solute, surface area in contact with the air, etc.). In practice, evaporation rate is expressed relative to *n*-butyl acetate or diethyl ether as references.

The NFT 30 301:1969 standard "Paints-Determination of the volatility index of a solvent" defines the evaporation rate as follows:[47]

$$evaporation\ rate = \frac{evaporation\ time\ of\ butyl\ acetate}{evaporation\ time\ of\ the\ studied\ solvent} \qquad \text{Eq. I-1}$$

Solvents that evaporate faster than *n*-butyl acetate have higher values of evaporation rate and vice versa.[22] Solvents that evaporate rapidly are known as fast or hot solvents (evaporation rate higher than 3), while those that evaporate slowly are called slow solvents (evaporation rate lower than 0.8).

Diethyl ether can also be used to evaluate the evaporation rate of a solvent. It is usually used as standard to evaluate fast-evaporating solvents. According with the DIN 53 170 standard "Solvents for paints, varnishes an similar coating materials; determination of the evaporation rate", evaporation rate can be calculated as follow: [47]

$$evaporation\ rate = \frac{evaporation\ time\ of\ the\ studied\ solvent}{evaporation\ time\ of\ diethyl\ ether} \qquad \text{Eq. I-2}$$

Thus, the solvents that evaporate faster than ethyl ether have lower evaporation rate values.[48,49]

- **Evaporation rate by electrobalance**

Solvent evaporation rate can also be determined according to the standard method ASTM D3539 "Test Methods for Evaporation Rates of volatile Liquids by Shell Thin-Film Evaporometer" which measures the loss in weight or volume of the solvent as a function of time. This test consists of adding and distributing a determined volume (0.7 mL) of solvent with a syringe to a known area of filter paper (0.9 cm diameter). The filter paper is placed in an electrobalance. The test is carried out at 25 °C, at a relative humidity of 5%. The weight loss of the paper, due to the evaporation of the solvent, is measured as function of the time during which the solvent evaporates.[43]

1.1.6.1.f Solvency

One of the most controlled property of a solvent is the solvency, which is the ability of a solvent to dissolve resins, to stabilize them in solution when diluents (considered as non-solvents of resins in paints, such as water) are used and to reduce the viscosity of the resin solutions, lacquers and paints. The relative solvency can be indirectly measured from the determination of the compatibility of a specific resin with the solvent. This property can be detected visually from the observation of the lack of miscibility that causes a cloudy solution due to the presence of two phases: liquid/liquid or liquid/solid.[50,51] However, other methods can be employed to better characterize the solvent power. They are detailed below.

- **Indirect determination of solvency**

Three indirect tests can be used to measure the relative "strength" of a solvent: the determinations of the Kauri-Butanol value (KB), the aniline point and the diluent dilution *ratio* (Table 2).[22]

Test	Measure	Definition	Method
Kauri-Butanol value (KB)	Solvent power of hydrocarbon solvents	Maximum solvent volume that is added at 25 °C to a standard solution of Kauri Gum in *n*-butanol without causing cloudiness.	ASTM Method D 1133
Aniline Point	Solvent power of hydrocarbon solvents	Minimum equilibrium solution temperature for equal volumes of aniline and solvent. It is the temperature at which aniline and the solvent become immiscible	ASTM Method D 611
Diluent dilution ratio	Solvent power of oxygenated active solvents	Maximum number of unit volumes of a diluent (generally toluene) that can be added to a unit of solvent to cause the first persistent heterogeneity in a solution of nitrocellulose	ASTM Method D 1720

Table 2. Indirect methods for the solvency determination

- **Hansen Solubility parameters**

One of the best strategies for facilitating the choice of the adequate solvent for a given resin is the determination of the Hansen solubility parameters. This useful method predicts the solubility capacity of a solvent and helps to select solvent combinations for the formulations of coatings, paints, cosmetics, printing inks, cleaners.[22]

The solubility parameters are generally considered to be a measure of the attractive forces between molecules such as dispersive forces (London forces), polar forces (Keesom and Debye forces) and hydrogen bonding interactions, which can also have influence on other solvent properties such as boiling point, surface tension and latent heat.[26] These parameters are useful and an easy tool to establish in which solvent the resin would be more easily dissolved or would be more compatible. A solvent is predicted to be an appropriate solvent for the resin if its solubility parameters are close to the solubility parameters of the resin itself.[25]

The concept of solubility parameter was introduced for the first time by Hildebrand and Scott in 1950, focused on its application to non-polar liquid mixtures. It was calculated from the energy of association of molecules in the liquid phase, in terms of cohesive energy density (CED) defined as the *ratio* of the energy required to vaporize 1 mL of liquid with respect to its molar volume. The solubility parameters were defined as the square root of the cohesive energy density of the liquid (Eq. I-3),[51]

$$\delta = \sqrt{CED} = \sqrt{\frac{\Delta E_v}{V_m}} \qquad \text{Eq. I-3}$$

where: δ=Hildebrand parameter, ΔE_v= energy of vaporization and V_m= molar volume.

In this way, it is possible to determine that two liquids are miscible when they have similar δ values. On the contrary, they are immiscible if their δ values are significantly different. For many years, the paint technologists have used this method to select an adequate solvent, compatible with the resins, from the wide range of solvents, polar and non-polar. However, as this concept took only into account a single parameter, it rapidly became insufficient to characterize all the variety of solvents that was used in the paint industry.

Burrell (1955) was the first to use the concept of solubility parameter and hydrogen bonding parameter to predict the solubility of resins.[52,53] Firstly, he classified the solvents in three categories according to their hydrogen bonding power in poorly, moderately, and strongly. Then, the resin solubility was evaluated in different solvents from each hydrogen bonding power category. Finally, the solubility parameter range of the resin was considered as the range of solubility parameters of the solvents that dissolved the resin.[40]

In 1966, Hansen evaluated the concept of solubility parameters and proposed three-dimensional solubility parameters that relate the three types of intermolecular forces: dispersion forces, polar forces, and hydrogen bonding.[5] The three-dimensional solubility parameters were applied in the paint and coating industry not only to characterize solvents and resins, but also plasticizers, polymers, emulsifiers, pigments and dyes. In all the cases, the solubility of the different materials has been calculated to determine the mutual solubility and compatibility of solvents with polymers, resins and pigments.[51]

In order to calculate the solubility parameters, Hansen has determined the dispersion forces (*d*) of a molecule by comparing it to an alkane of similar structure (homomorphism). Besides, the polarity (*p*) was determined by measuring the molecular dipole moments, which was compared with similar functional groups in smaller molecules. Finally, the contribution of the hydrogen bonding (*h*) to the overall polarity was also determined. The relative contribution of the independent values was then calculated as fractions of the unique Hildebrand value.[54] In this way, Hansen proposed that the cohesive energy density of a solvent results from all the volatilization energies arising from all the intermolecular attractions present in the liquid (Equation I-4).

$$\frac{\Delta E_t^v}{V_m} = \frac{\Delta E_d^v}{V_m} + \frac{\Delta E_p^v}{V_m} + \frac{\Delta E_h^v}{V_m} \qquad \text{Eq. I-4}$$

where: $\frac{\Delta E^v}{V_m}$= cohesive energy density of *t*=total, *d*=dispersion forces, *p*=polarity and *h*=hydrogen bonding

The cohesive energy can be expressed in terms of the solubility parameter δ as follows:[55]

$$\delta_t^2 = \delta_d^2 + \delta_p^2 + \delta_h^2 \qquad \text{Eq. I-5}$$

where $\delta^2 = \frac{\Delta E^v}{V_m}$ and the subscripts δ_d, δ_p and δ_h represent the individual solubility parameter for dispersion (London forces), polar (Keesom forces) and hydrogen bonding forces.[51]

If it is considered that the solubility parameter of a given solvent is a vector with components δ_d, δ_p and δ_h, then each solvent can be located in a three dimensional system as a fixed point whose coordinates are δ_d, δ_p and δ_h.

The basic principle of the application of the Hansen solubility parameters (HSP) consists of the postulate that when the value of HSP of a solvent falls within the HSP range of a polymer, the polymer is then soluble in that solvent.[56]

The determination of Hansen solubility parameters of a polymer, a resin or a solvent can be an experimental evaluation where this compound is added to 40-45 well-chosen solvents from different families, with known and well-distributed partial solubility parameters in the Hansen space. Once both substances have been mixed in similar proportions, the mixtures are observed to check the satisfying solubility or miscibility or to identify changes such as formation of phase layers, solution turbidity, polymer surface attack or polymer swelling.

According to these observations, solvents can be classified in two categories: “good” for the acceptable solutions and “bad” when the polymer is not solubilized as expected or when the two solvents are not immiscible. Then, the qualifications are transformed into 1 (good) and 0 (bad) to facilitate the computational data processing, which will finally give the Hansen Solubility Parameters (HSP) values and the corresponding sphere of solubility.[50,57] Thus, the solubility sphere of the polymer, resin or solvent according to its relative position with respect to the three axes can be defined by the coordinates of its centre and its radius R. Solvents capable of solubilizing the given polymer, resin or solvent are represented as points in planes having as coordinates (0, δp, δh), (2δd, 0, δh), (2δd, δp, 0), and lying within the circle of radius R (Figure 3).[58] Hansen established a simple way to interpret and solve the practical problems related to the solubility parameters with the postulate "like dissolves like", which means that the more similar the solubility parameters of two materials, the more affinity they have.[50,55]

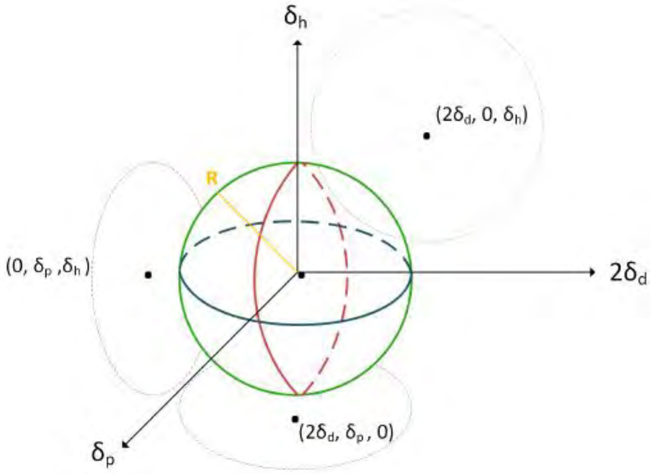


Figure 3. Hansen’s sphere representation based on Hansen solubility parameters (Modified from Lambourne and Strivens[5] and F. Gharagheizi and M. T. Angaji[58]).

- **Computational Polarity Modelling: COnductor-like Screening MOdel for Real Solvents (COSMO-RS)**

In 1995, Klamt established the method of prediction for thermodynamic properties of fluids and mixtures of liquids: COSMOS-RS.[59] It describes the liquid-phase interactions such as contact interactions between molecular surfaces, allowing representations of the molecule and providing solubility predictions. This technique considers a statistical thermodynamic approach and a quantum chemistry method.[60] It does not need experimental data to predict the polarity of a substance and its solubility. This method can be used with all type of systems formed by a solute and an organic solvent.

In the COSMO-RS approach, the solute is embedded in a cavity surrounded by a virtual medium, called COSMO. The COSMOS-RS tool generates a charge density surface (σ-surface) that shows the most stable state of the molecule in a perfect conductor. The color of the σ-surface provides the value of the charge density at each point of the molecule. For example, the green corresponds to very low charge density (carbon skeleton), the blue corresponds to high positive charge density (δ^+; hydrogen atoms), and the red describes high negative charge density (δ^-; oxygenated or nitrogenous groups).[61]

Charge distribution is segmented and reduced to a histogram called σ-profile that translates the information of the 3D density surface into a 2D profile. This profile allows to predict the solubility of a solute in a solvent when calculating the σ-potential ($\mu_s(\sigma)$) of a specie in solution. The σ-potential describes the affinity of the liquid system for a molecular surface.[62,63] For example, the 3D σ-surface, σ-profile and σ-potential of methanol, ethyl acetate and hexane are shown in figure 4.

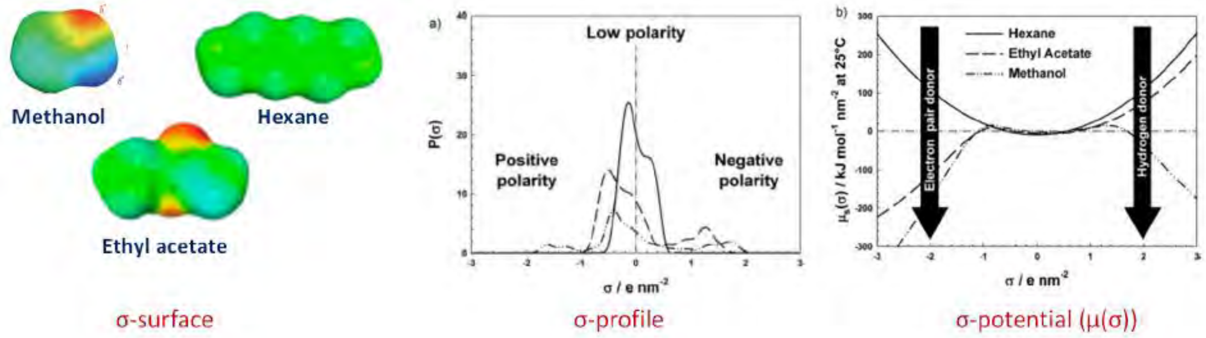


Figure 4. σ-Surface, σ-profile and σ-potential of hexane (apolar), ethyl acetate (hydrogen bond acceptor) and methanol (amphiprotic solvent; adapted from Durant et *al*.[63] and Breil et *al*.[64])

1.1.6.2 Impact of solvents on health and environment

- **Solvents as sources of VOC emissions**

Organic solvents in paints and coatings are usually volatile organic compounds (VOC) as they have specific physicochemical properties, such as vapour pressure greater than 10 Pa at 25 °C and boiling point equal or lower than 250 °C at a standard pressure of 101.3 kPa.[46]

Note that the European definition is different to that of the United States where a VOC is defined as an organic compound that participates in photochemical reactions in the atmosphere (with the exception of some solvents described in a list of exempt compounds such as acetone, dichloromethane and *tert*-butyl acetate.[65,66] If the European definition is unequivocal since sanctioned by a measurable value, the American definition is much less precise since the photochemical activity is not easily demonstrated.

In addition to odour nuisances of solvents due to the VOC emissions, they are important sources of atmospheric pollution and have a direct effect on human health.

- **Solvent impact on health**

Some volatile solvents have short- and long-term negative effects on health even at low concentrations. The principal effects that have been detected on health are: irritation of eyes, nose and throat, headaches, nausea, and in more critical cases, damages in kidney, liver and central nervous system. In addition, some VOCs (*i.g*. benzene, ethylbenzene, carbon tetrachloride and tetrachloroethylene) have been reported to cause cancer in animals and they are suspected to cause cancer in humans.[67–70]

The toxicity of solvents can be predicted or evaluated experimentally, *in vivo* on different organisms or *in vitro* on cells. These different forms of toxicity are distinguished by the rapid onset of symptoms, their severity, their duration or the rapid absorption of the toxic substance. Among these toxicity categories, we can mentioned: acute toxicity (single exposure at a high dose), chronic toxicity (repeated exposures over long periods-more than 90 days), subacute toxicity (prolonged exposure over a short period-maximum 28 days), subchronic toxicity (frequent and repeated exposures for more than 28 days and less than 90 days), skin sensitization or skin irritation, and carcinogenic, mutagenic and reprotoxic properties.

To quantify the toxicity or the toxic dose, the median lethal dose (LD_{50}) or the median lethal concentration (LC_{50}) can be determined in the air or in the aquatic environment. The chemical substances are qualified as non-toxic if the LC_{50} exceeds the non-toxicity thresholds shown in Table 3. Some of the oral LD_{50} for commonly used solvents, tested in rats, are for example: ethyl acetate=5620-10200mg/kg,[71] butyl acetate=10760-12789mg/kg,[3] methyl ethyl ketone=2737 mg/kg[72] and ethanol=7060 mg/kg.[73]

	Oral LD$_{50}$ (Single dose to rats) mg/kg	Inhalation LC$_{50}$ rats (Exposure for 4h) ppm	Dermal LD$_{50}$ (Single application to rabbits skin) mg/kg	Eco-toxicity-Fish LC$_{50}$ (Exposure for 48 or 96h in water concentration) mg/mL
Extremely toxic	1 or less	10 or less	5 or less	0.1 or less
Highly toxic	1-50	10-100	5-53	0.1-1
Moderately toxic	50-500	100-1000	44-340	1-10
Slightly toxic	500-5000	1000-10000	350-2810	10-100
Practically non-toxic	5000-15000	10000-100000	2820-22590	100
Relatively Harmless	15000 or more	100000	22600 or more	100 or more

Table 3. Classification of acute toxicity by the oral, dermal (LD50) and inhalation *via* [74,75]

Workers involved in painting and coating activities are the most exposed to the negative effects of the VOC emissions depending on the manufacturing methods of the paint, but especially its application method. Indeed, solvents can be easily absorbed *via* the respiratory system and the toxic effect would depend on the type of solvent, its concentration and the exposure time. In this way, when spraying application method is used, the principal effects are the inhalation of solvent in aerosols form and the contact of the solvent with the skin causing irritations. On the other hand, the damage by solvent contact is higher when manual application is used.

More generally, VOC emissions from the paint and coating sector come either from the production plants, where the paint or the coating are formulated, or from their application on the substrate. The first mentioned source represents only the 5% of the VOC emissions, while the second one is the largest contribution representing the remaining 95 % of emissions (Figure 5).[76,77]

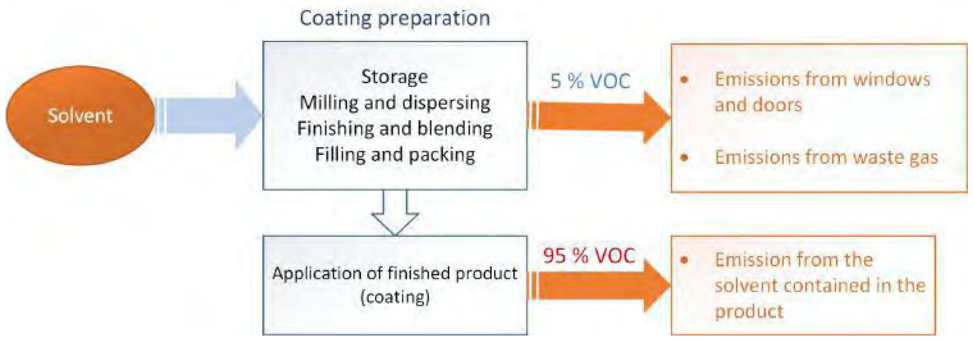


Figure 5. VOC emissions from coating industry

1.1.6.3 Environmental properties

When solvents evaporate into the atmosphere, they participate in photochemical reactions influenced by sunlight or traces of other substances present in the air.[78] These reactions are responsible of the production of ozone (O_3), which is a greenhouse gas and the principal compound of the smog.[17]

To characterize the environmental impact of a chemical compound on the environment, some parameters such as biodegradability and bioaccumulation can be evaluated.[79]

- **Biodegradability**

Two approaches can be considered for the evaluation of the biodegradability of a compound: i) the microbiological approach, based on a test with pure bacterial cultures under optimum conditions and ii) the environmental approach, which is based on the compound biodegradability in water and soil obtained from recipients of solid wastes (like water treatment plants).[80] The organisation for Economic Cooperation and Development (OECD) has determined 6 biodegradation forms: half-life, disappearance time 50, ultimate, primary, inherent and readily biodegradation. This last classification is usually used for chemical compounds that have passed specific tests from which it can be assumed that the compound will be rapidly and completely biodegradable in an aquatic environment under aerobic conditions.[81] For example, ethyl acetate, butyl acetate and methyl ethyl ketone are considered as readily biodegradable.[2–4]

- **Bioaccumulation**

Bioaccumulation refers to the process by which a chemical substance is absorbed by an organism from its natural environment. Bioaccumulation is caused by the imbalance between the consumption (water or food) and depuration (excretion) of toxic compounds, which causes their accumulation in the organism.[82] Bioaccumulation can be expressed in terms of bioaccumulation factor (BAF) or by the partition coefficient *n*-octanol-water (Kow):

Bioaccumulation factor (BAF)

The degree to which bioaccumulation occurs is determined by the bioaccumulation factor (BAF), which is defined as the *ratio* of the toxic compound concentration in the organism (at equilibrium) and that of the environment.[83–85]

Partition Coefficient *n*-octanol-water (Kow)

Bioaccumulation is generally related to the lipophilicity of a compound, and thus it can be measured as the partition coefficient between *n*-octanol and water. It is an important property because it provides a measure to evaluate the bioaccumulation potential of a toxic compound.[83–85]

To conclude about the solvents properties used in the chemical industry, many of them such as toxicity, flammability, volatility, bioaccumulation and persistence, represent risks for human health and environment. In order to assess these hazards and limit the use of toxic solvents, different classifications have been created. For example, the Center for Drug Evaluation and Research (CDER) of the USA Food and Drug Administration (FDA) has proposed four categories of solvents according to their impact on health and the environment (Table 4).[1]

Class	Toxicity	Solvent
Class I	Highly undesirable. Unacceptable toxicity or deleterious environmental impacts. Carcinogen, toxic or/and hazard to environment	Benzene
		1,2-dichloroethane
		Carbon tetrachloride
Class II	Use should be limited in pharmaceutical products. Inherent toxicity	Acetonitrile
		Toluene
		Tetrahydrofuran
Class III	Considered as less toxic and of lower risk to human health. No known human health hazards at solvent levels normally accepted in pharmaceuticals	Acetic acid
		Ethyl acetate
		1-butanol
		Ethanol
Class IV	Solvents with insufficient toxicological data	Isooctane
		2-Methyltetrahydrofuran

Table 4. Solvent classification according to the FDA

In Europe, the use of chemical substances is controlled by the REACH regulation in order to prevent and reduce human health and environmental risks. For example, the use of solvents such as 1-methyl-2-pyrrolidone, 1,2,3-trichloropropane, 2-ethoxyethanol, 2-ethoxyethyl acetate and 2-methoxyethanol has been restricted in paint and coating formulations by REACH due to their toxicological risk (reprotoxicity).[86,87]

1.2 Solvent Regulations

In order to reduce the negative effect on the environment and on the animal and human health, legislation and voluntary control measures have been implemented during the recent years. Here, it will be presented the legislation changes that have been adopted by China, the European Union and the United States.

1.2.1 Legislation in China

China is the largest producer and consumer of coatings since 2009. As a result, solvent concerns in the coating Chinese industry have increased and compulsory standards have been applied. In order to create, manage and revise the standards that regulate the use of toxic substances in paints, various committees have been created, such as the SAC/TC (National Technical Committee of Standardization Administration of China). In this committee was created the division SAC/TC5, whose complete name is “the National Technical Committee 5 on Paints & Pigments of Standardization Administration of China”. This division is in charge of controlling the coatings standards. Thanks to this commission, the standards GB18581-2009 and GB18582-2008 were created with the objective of controlling the harmful substances of indoor decorating and refurbishing materials, including solvent-based wood coatings, interior coatings, coatings for toys and automotive coatings. In addition, another standard GB/T23994-2009 was also created to limit certain harmful elements of coatings for consumer products in contact with humans, such as sport equipment, household appliances, mobile phones, machine tools, bicycles and motorcycles.[88] Besides, VOCs emissions of benzene, toluene, ethylbenzene and xylene are controlled in solvent-based coatings and the emission limits differ by products. As a consequence, it is possible to find in the current China market “zero-VOC” coatings *i.e.* free of benzene, toluene, ethylbenzene and xylene. In addition to those measures, a tax on the price of any solvent-based coating that generates levels greater than 420 g/L of VOC has been imposed.[89]

1.2.2 Legislation in the United States of America

In the United States of America, the VOCs emissions are regulated by the Environmental Protection Agency (EPA). The regulations implemented by the Agency are primarily aimed at limiting the amount of VOCs that could be present in paint products. There are few exceptions to the rule since manufacturers have the option of paying the excess fees for products that exceed the imposed limits. The VOC limits were established at 250 grams per liter (g/L) for flat paints and 380 g/L for others.[90] Thanks to these measures, a reduction of 80% of VOC emissions from the paint and coating sector was achieved in the United States between 1990 and 2014.[91]

1.2.3 Legislation in the European Union

In the European Union, the production, utilization and commercialization of all chemical substances are controlled by the regulation REACH (Registration, Evaluation, Authorization and Restriction of Chemicals). This regulation is responsible for taking measures for the protection of human health and the environment, *e.g.* prohibits the use of substances that are considered dangerous.[92] The REACH regulation favours industrial competitiveness and encourages companies to develop safer alternatives for health and environment.

The reduction of air pollution has also become one of the priorities of the European Union: a Thematic Strategy on Air Pollution was adopted whose objective is the reduction of 51% of VOC emissions from 2005 to 2020.[93]

The limitation of VOC emissions is specially imposed by two European Directives in order to prevent and reduce air pollution:

- The Directive 2004/42/CE sets out the limit values for the VOC content in decorative paints and varnishes and vehicle refinishing products and supports the Directive 2001/81/EC on national emissions ceilings for certain atmospheric pollutants including VOC, SO_2, NH_3 and NO_x. It prohibits to sale or purchase any product that has a VOC content that exceeds specified limits and that do not have the corresponding labelling.[46] This Directive 2004/42/CE has amended the VOC emissions Directive 1999/13/EC through its article 13 by removing a sub-activity of "vehicle refinishing" from the scope of the VOC Solvents Directive mentioned below.

- The Directive 2010/75/EU on industrial emissions (integrated pollution prevention and control), replacing the Directive 1999/13/EC, sets out provisions to prevent, reduce and eliminate the emissions into air, water and land produced from many industrial activities (manufactures of chemicals, paper, textiles, food, etc.).[94]

In order to meet the requirements related to the European legislation, the paint and coating industry have considered several ways to reduce its generated VOC emissions like waste air treatments, low-solvents or solvent-free products, and the development of new paint application technologies (Figure 6).[8,17,95]

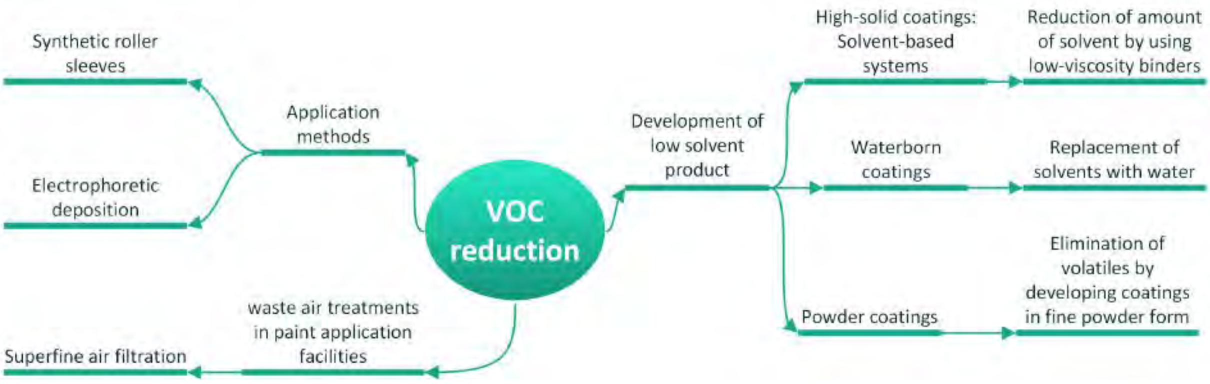


Figure 6. Actions for the reduction of VOC in the paint and coatings industry

Furthermore, in order to shift the market towards a sustainable industry, the European Union has created mandates such as M/491 to promote the development of bio-surfactants and bio-solvents.[96] These initiatives have resulted in the launch of several European projects, dedicated to the production of greener solvents, or more generally to the development of greener alternatives processes or new types of solvents.[97–99]

As many conventional solvents generally present risks and hazards and are responsible for about 20% of VOC emissions, the chemical industry, encouraged by these regulations, is looking for solutions to substitute them. It also tends to replace petrochemical solvents by green alternatives because of the fossil depletion, the growing of consumers demand for safer and healthier products and because it is an opportunity for companies to set themselves apart from the competition.

1.3 Green solvents

1.3.1 What is a “green solvent”?

Several criteria have to be taken in account to consider a solvent as “green”.[79,100,101] Inspired by the principles of the green chemistry of Anastas and Warner[102] and to facilitate the identification and classification of a green solvent, Gu and Jérome have proposed a criteria list that green solvents have to meet:[103]

1) Availability: the availability of a green solvent in the market has to be ensured.
2) Price: the production process of the solvent has to be sustainable in order to guarantee competitive prices respects to fossil solvents.
3) Recyclability: green solvents should be able to be recycled in all chemical processes, to make them eco-compatible. Besides, the catalyst used for the synthesis of a green solvent should be able to be reused.

4) Grade: production of green solvents with technical grade is fundamental in order to avoid exhaustive purification processes.
5) Synthesis: the solvents have to be synthesized by environmental-friendly processes reducing energy consumption. The production processes have to be easy to handle, and the synthetic reactions should have a high atom economy.
6) Toxicity: the raw materials for the synthesis of the solvents and the solvents themselves should have low or negligible toxicity in order to reduce damage in human health and in the environment during the production process or their application.
7) Biodegradability: solvents should be biodegradable and should not produce toxic metabolites.
8) Performance: the synthesized green solvents must have similar or better physicochemical properties (viscosity, polarity, density, solvency, boiling point, etc.) compared to the fossil-ones for replacing them in various applications and processes.
9) Stability: a green solvent has to be thermally and electrochemically stable to be used in chemical processes and reactions.
10) Flammability: green solvents should not be flammable during manipulation (safety conditions).
11) Storage: a green solvent should be easy to store and fulfill all transport legislations.
12) Renewability: the use of renewable raw materials for the synthesis of green solvents is more suitable in order to participate in the CO_2 balance.

Considering these criteria, a bio-based solvent or a petrochemical solvent that is non-toxic and/or biodegradable and that is produced through an eco-friendly process can be called “green solvent”.
Many green solvents have been developed since the late nineties to replace solvents harmful for health and environment. They can be classified into: water, eco-friendly solvents, supercritical fluids, ionic liquids/eutectic mixtures, liquid polymers, fluorinated solvents, and solvents derived from biomass.[104]

1.3.2 Water

Water is considered as a green solvent, because it is non-flammable, non-toxic, and relatively inexpensive. Nevertheless, the use of water in some processes can lead to high environmental impacts, which makes the water “lose its green character”. For example, a separation process using water can be less efficient than a process involving an organic solvent, which results in higher energy costs. It is the same when water used as solvent for the reaction leads to lower yields than with an organic solvent.[101,103,105] On the contrary, water is considered as a green solvent in cases where enhancement in the reaction was observed. For example, good results have been reported with water when used as solvent in the case of some biphasic reactions (hydroformylations and carbonylations)[106] or in biocatalysis (*e.g.* for enzymatic cleavage of penicillin G, a precursor of semi-synthetic antibiotics).[106]

1.3.3 Eco-friendly solvents

Solvents can be also considered as eco-friendly when they have good Environment, Health and Safety (EHS) profiles. Consequently, ethanol, and methyl acetate are classified in this category from an EHS perspective.[79] In this category it is also possible to find petrochemical-based solvents that are non-toxic and biodegradable like the 3-methoxy-3-methylbutan-1-ol (MMB), which is also a non-VOC solvent, commonly used in household and industrial cleaner formulations. Furthermore, it is possible to consider in the classification of "eco-friendly" solvents those that are co-products of industrial processes, such as dimethyl, diethyl and dibutyl esters of glutaric, succinic and adipic acid, co-products from nylon 66 fabrication.[62,101]

1.3.4 Supercritical fluids (SCF)

A supercritical fluid is any substance that does not have different phases of liquid and gas when it is placed under a temperature and a pressure higher than those of its critical point. Hence, the critical point of a supercritical fluid is defined as the highest temperature and pressure at which the substance can exist as vapour-liquid in equilibrium. Its principal characteristic is that it presents properties such a liquid-like density and gas-like diffusivity, surface tension and viscosity.

The most popular of the supercritical solvents is the liquid carbon dioxide ($scCO_2$), due to its moderate critical constants ($Tc = 31.3°C$, $Pc = 72.9$ atm).[107] Moreover, $scCO_2$ has other advantageous features: it is inert, non-toxic, inexpensive, non-flammable and it can be obtained as by-product of fermentation and combustion. The $scCO_2$ has been reported to be a very suitable solvent in chemical syntheses where air or O_2 are used due to its stability. It is also inert to free-radicals and easily removed from products to avoid solvent residues.[108,109] In organic chemistry, $scCO_2$ can be used in hydrogenations, hydroformylations, Dies-Alder cycloadditions, oxidations, palladium mediated couplings, bio-transformations and photochemical and radical reactions.[110] Other common supercritical fluids are methane, ethylene, ethane, propylene, propane, acetone, methanol, ethanol and water.[111]

1.3.5 Ionic liquids and eutectic solvents

Ionic liquids (ILs) are organic salts that are liquid at room temperature and have melting points below 100°C. They are considered as green solvents because they have a low volatility, which means they do not produce VOC emissions. Furthermore, thanks to their low vapour pressures, the reaction products can be easily separated from them by distillation. Moreover, they have good thermal stability, and their physicochemical properties can be modified by varying the anion and cation.[112]

The deep eutectic solvents are alternatives to ionic liquids as they are mixtures of Lewis or Brønsted acids or bases that contain in their structure a variety of either anions and/or cations. Usually, they are based on bio-based choline chloride, polyols, esters, amides, carboxylic acids or urea. The bio-deep eutectic mixtures can have the advantage of being produced from biomass and are generally less toxic and more biodegradable than conventional ionic liquids,[113] because they have sites that can potentially be attacked by oxygenases or hydrolases, such as the ammonium ILs prepared with choline.[114]

Despite the advantages of ionic liquids and eutectic mixtures, they have a main drawback which is their expensive and complex methods of preparation,[115] which call into question their greenness. Additionally, their toxicity cannot always be determined due to their complicated structure.

1.3.6 Liquids polymers

A liquid polymer can be considered as a solvent when it is a low molecular weight polymer or a polymer having a low glass-transition temperature (temperature below which it becomes hard and brittle like glass).[116]

Liquid polymers are considered as “green solvents” due to their non-volatility, biodegradability and biocompatibility. They generally have a low or negligible toxicity to marine life. Besides, they can be easily separated from the products and recycled in further reactions.[117] The most representative solvents of this category are the poly(tetrahydrofuran) (PTHF), poly(methylphenylsiloxane) (PMPS), poly(ethylene glycols) (PEG), poly(propylene glycols) (PPG) and also variations of these molecules with ether or ester end-capping groups. PEG is the most interesting of the liquid polymers due to its toxicological properties, biodegradability and short- and long-term hazards that are well established and known. For these reasons, PEG has been recognized by the FDA as GRAS (General Recognized as Safe) and has been approved for consumption as food ingredient.

Liquid polymers can be used in a wide range of applications: immunology, culture media, extractions, homogeneous and phase-transfer catalyses, organic reactions and enzymatic reactions.[117,118]

1.3.7 Fluorinated solvents

Fluorinated solvents are composed of fluorocarbon groups attached to the organic main chain as showed in Table 5. They are not soluble in water and they typically show temperature-dependant miscibility with organic phases. The high fluorinated molecules, as perflurocyclohexane, are only soluble in fluorous media.[119] They can be described as fluorous biphase systems (FBS), presenting a fluorous and an organic phase.[120] This behaviour allows the recycling of valuable catalyst and other chemicals and offers the advantages of working with a heterogeneous or homogeneous system by adjusting external parameters such as the temperature.

The fluorinated solvents have the advantages of being chemically unreactive and non-flammable; they have a low toxicity, high stability and good oxygen and carbon dioxide dissolving power.[121] Nevertheless, they present negative impacts on the environment because of their long persistence and volatility.[122]

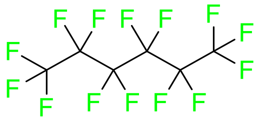
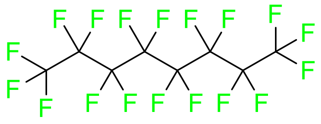
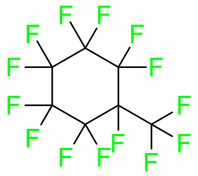
 Perfluorohexane (FC-72) b.p. 57.1°C	 Perfluorooctane (FC-77) b.p. 103-105°C	 Perfluoro(methylcyclohexane) (PFMC) b.p. 75.1°C

Table 5. Fluorous solvents and boiling point

1.3.8 Solvents derived from biomass

Today, increasing energy security by reducing our dependence on oil and the environmental sustainability are the main drivers of bio-based products development. As the bio-based products sector has become a priority area with a high potential, various European policies have been adopted to increase the participation of the industrial sector in developing and/or optimizing the infrastructures that could use biomass as feedstock for the production of bio-based products.[123,124]

In the chemicals market, the production of bio-based products, which can be principally divided into plastics, lubricants, solvents and surfactants, tend to increase. The interest for this sector has become so important that an increase from $ 6474 million in 2016 to $ 23,976 million in 2025 is expected.[125] Of course, this is related to the benefit that the use of bio-based products implies in different categories:[126]

- Lower environmental impact: by reducing the production of chemicals wastes and toxic products
- Economic independence: by developing alternative energy sources to the fossil-ones
- Jobs creation: the increase of jobs is expected, as a result of the chemical industry rise, and also because of the participation of farmers to provide sources of bio-based feedstock
- Reduction of expenses: due to the reduction of handling hazardous chemicals, disposal of wastes and treatment of undesirable by-products

One of the most explored areas of the bio-based market is the bio-solvents sector, that was the second largest consumers in 2008 as it can be seen in Figure 7 and with the greatest potential according to forecasts for 2020. The main actors in the market who are interested in bio-solvents are the industry of cleaning formulations, adhesives, printing inks, pharmaceuticals, cosmetics, paints and coatings. The latter industry consumed most of the bio-solvents in 2016, with 40% of the market, which was valued at USD 6.01 billion.[127,128]

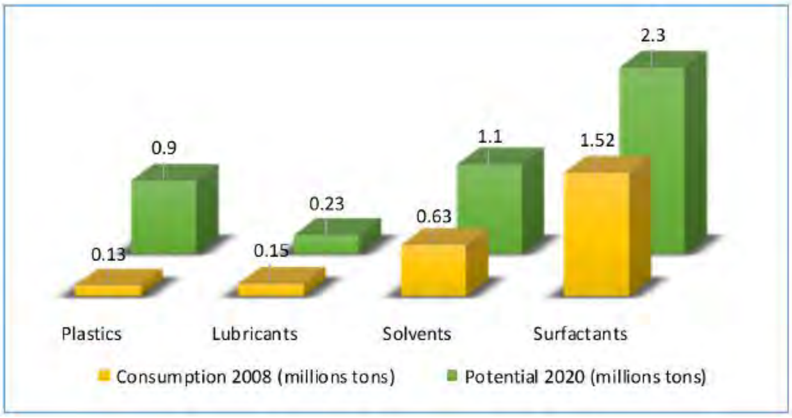


Figure 7. Estimated EU production volumes of bio-based products (data taken from Europe Innova Report)[129]

As explained above, many studies are currently focusing on the replacement of hazardous solvents with more environment-friendly alternatives.[130] Consequently, the manufacture of solvents from renewable resources offers a good alternative to reduce our dependence on petroleum and to improve the positive environmental balance due to the reduction of CO_2 emissions.[131] Besides, the use of bio-solvents can offer many other advantages, depending on the solvent: they can be easy to recycle, non-carcinogenic, biodegradable and can have very low volatility and high solvency power.[132]

However, it is not because a solvent is from bio-based origin that it has low toxicity and environmental impact. For example, although *N*-methylpyrrolidone (NMP) can be produced from glutamic acid *via* 4-aminobutyric acid,[133] this solvent is part of the REACH substances of Very High

Concern list because of its toxicity and problematic waste disposal. It is classified as serious health hazard (GHS08) and especially toxic for reproduction. Tetrahydrofuran (THF) and dimethylsulfoxide (DMSO) can also be synthesized from biomass, THF *vía* succinates hydrogenation[134] and DMSO as by-product of kraft pulping.[135] Nevertheless, these solvents were also classified as problematic in the (IMI)-CHEM21 guide (Innovative Medicines Initiative), proposed by a European consortium conformed by pharmaceutical industries, universities and SMEs.[104,136] DMSO's concern as a solvent is that when it gets into the skin, it absorbs everything on the skin. THF is suspected of causing cancer, and is identified as harmful by the European Chemical Agency (ECHA).[137]
Therefore, the European Committee for Standardization has established some requirements to define bio-based solvents in order to guarantee some characteristics (Standard EN 16766:2017 - Bio-based solvents - Requirements and test methods).[138]

For the development of renewable solvents, two alternative processes can be presented (Figure 8). The first one is to apply known technologies, currently used on petrochemical derivatives, on molecules derived from the biomass to produce the same molecules. In that case, existing infrastructures can be used as only the starting material changes. The second alternative is to develop new processes using renewable synthons to produce innovative molecules. Novel industrial installations have thus to be constructed.[133,139,140]

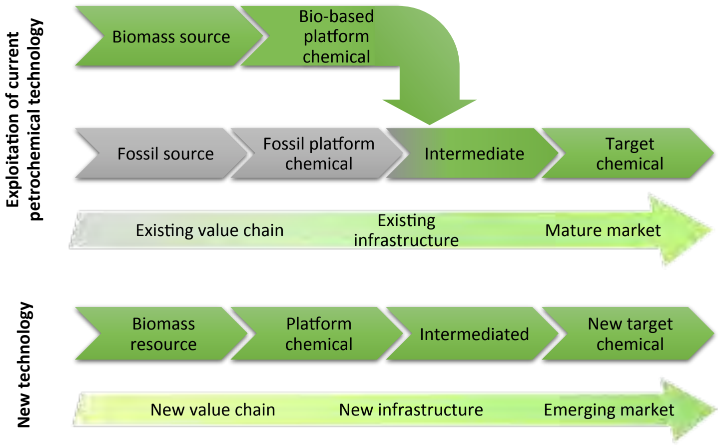


Figure 8. Alternatives to develop renewable chemical products (modified from Vennestrom et al.).[139]

The biomass currently used for the production of bio-based solvents is principally composed of carbohydrates/sugars, lignin, lipids and terpenes. Their content in biomass depends on the feedstock and growth conditions. Pre-treatment of the lignocellulosic biomass is, for example, necessary to increase access to the internal structure and to allow its fractionation into sugars, lipids, lignin[141] and proteins.[142] Although proteins represent a good source for the synthesis of bio-based products,[143]

their use in the production of solvents are limited and less described in the state of art. Only the synthesis of N-methylpyrrolidone (NMP) from glutamic acid has been well studied.[144,145]
In this work, bio-based solvents derived from carbohydrates/sugars, vegetable oils, terpenes and lignin will be presented.

1.3.8.1 Solvents derived from carbohydrate-biomass

The biomass feedstock and their derived products can be divided into first and second generation. The first generation products are obtained from biomass rich in sugars or starch-rich crops, such as sugarcane and corn. For example, 1st generation chemicals can be produced from the sugar solution obtained through the enzymatic hydrolysis of starch-based biomass or by extraction from sugarcane. The simplest and more known transformation of the obtained sugar solution is its fermentation into ethanol. Although ethanol is a solvent by itself, it can also be used as a building block for the synthesis of other solvents.

The use of first generation raw materials for the production of chemicals has been subjected to discussions and doubts related to the competition of their use in the food chain. Therefore, a great interest has arisen in developing alternative routes for obtaining bio-based products from second-generation feedstock, such as lignocellulosic biomass including agricultural and forestry wastes, grasses and woody materials. The lignocellulosic biomass is generally composed of lignin (10-15 %), hemicellulose (20-30 %) and cellulose (40-50 %).[146] The interest in this type of biomass is due to the fact that cellulose and hemicellulose are potential sources of sugars. Although cellulose is the most abundant polysaccharide on earth, the complex structure of the lignocellulosic biomass limits the access and digestibility of both cellulose and hemicellulose. Accordingly, the conversion of biomass to fermentable sugars requires a pre-treatment, whose principal action is to break the lignin structure and modify the crystalline structure of cellulose to make it more accessible for its hydrolysis into sugars.[147,148]

From the state of art, a wide variety of solvents can be produced from carbohydrates as shown in Figure 9. Among them, classical solvents such as methanol, acetic acid, ethanol, acetaldehyde, ethyl acetate, levulinic acid, 2-butanone, *n*-butanol, isobutanol, butyl acetate can be found, but also “neoteric” solvents. The development of these new solvents was prompted by the need to produce solvents with low impact on health and environment. These “neoteric” solvents have the main characteristic of having a chemical structure different from that of the classical solvents, which avoids the prevalent problem such as the toxicity, generally associated with the structure.[103,133,142,149–154]

The following list presents the biomass-derived solvents considered as "neoteric", offering benefits principally related to the toxicity, biodegradability and the reduction of the negative effects on the environment.

Lactic acid can be produced through the fermentation of glucose, maltose, sucrose or lactose.[134,155] It is an interesting solvent due to its non-toxicity, biodegradability, recyclability and low production cost.[156] The use of lactic acid as solvent has not been well explored as much as its derivative ethyl lactate. Yang et *al*. showed that lactic acid is efficient to replace acetic acid in organic reactions such as the condensation of salicylaldehyde with diethyl acetylenedicarboxylate and the synthesis of substituted quinones. The use of lactic acid in these reactions increased yields, enhanced reaction rates and facilitated product purification.[157] This study opens the door to investigate the use of lactic acid in other reactions.

Ethyl lactate is synthesized by esterification of lactic acid with ethanol. It presents many advantages such as its biodegradability, non-toxicity, water solubility and its low cost production and environmental impact. It can be used as flavouring, perfume ingredient and as solvent in coating formulations. For example, it is an interesting alternative solvent to replace toluene in magnetic tape coatings.[158]

Fusel oil is a neoteric solvent, by-product of the distillation of fermented agricultural products.[159] It is particularly obtained from the bioethanol distillation. The principal constituents of fusel oil are isoamyl, isobutyl and *n*-amyl alcohols. *N*-Butyl and isopropyl alcohols are also present in lesser amounts.[160] Noteworthy, the composition of fusel oil will depend on the fermentation conditions and on the type of the *inoculum* used.[161]

γ-valerolactone (GVL) can be produced through the hydrogenation of levulinic acid using a metal catalyst, such as Ru-based catalyst.[162] γ-Valerolactone has very good solvent properties, low melting point (-31°C), high boiling and flash points (207°C and 96°C, respectively) and high solubility in water.[163] The environmental advantages of this solvent are its biodegradability and low toxicity. GVL has been used with water (in a 9/1 weight *ratio*) for the production of furfural from hemicellulose.[164] Furthermore, Duan and Hu (2012) reported for the first time the use of GVL in bio-catalysis for the synthesis of phosphatidylserine, achieving a yield of 95%.[165]

2-Methyltetrahydrofuran (2-MeTHF) is produced by catalytic hydrogenation of furfural or γ-valerolactone.[134] Despite of the fact that the toxicological profile of 2-MeTHF has not been determined, this solvent does not present problems related to genotoxicity and mutagenicity. In addition to its bio-based origin, it presents advantages such as its biodegradability and its stability under basic and acid conditions.[103] 2-MeTHF has been used to replace THF and toluene in the extraction of polar organic compounds from aqueous systems. Besides, it can also be an alternative to replace *n*-hexane in aroma compounds extraction[158] and dichloromethane in biphasic reactions like amidations, alkylations and nucleophilic aromatic substitutions.[103] 2-MeTHF is also an interesting solvent in enzymatic, organo- or organomellatic-catalysed reactions.[150]

Di-methyl isosorbide (DMI) is the methyl ether of isosorbide, a sorbitol derivative. Its greenest production process is based on the methylation of isosorbide with dimethyl carbonate.[166] It has been proposed as a viable substitute of some toxic solvents such as dimethyl sulfoxide (DMSO), dimethylformamide (DMF) and dimethylacetamide (DMAc) in the pharmaceutical industry.[151,166] For example, DMI was used to replace DMSO as pharmaceutical excipient for topical administration of non-adhesive liquid embolic agents.[167]

Dimethyl ether (DME) is a gas that can be easily liquefied under pressure conditions. DME is mainly produced *via* dehydration of methanol, but its synthesis from syngas in a single step has been also studied.[168,169] Liquified DME has become attractive as green solvent in extraction methods.[170] It is used in protein extractions for the meat industry and considered as safe by the European Food Safety Authority (EFSA).[171] It was evaluated in the extraction of lipids from microalgae *Botryococcus braunii* Race B. paste, showing similar results than hexane Soxhlet extraction.[172] Additionally it was used in the extraction of capsaicine from ground chilli,[173] caffeine from green tea[174] and carotenoids from microalgae.[175]

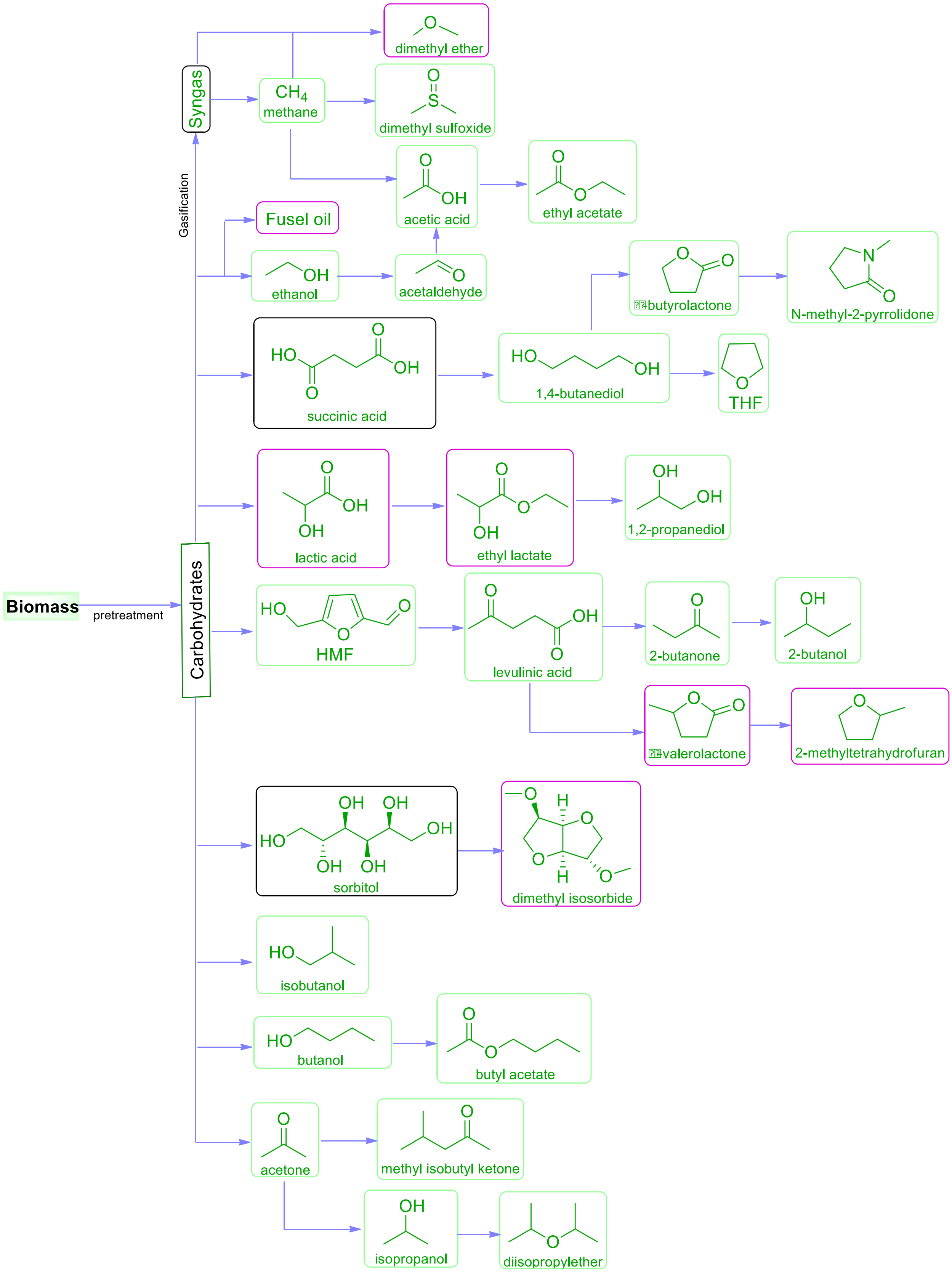


Figure 9. Solvents produced from carbohydrates. Pink=neoteric solvents, Green=bio-based conventional solvents, Black=building block.

1.3.8.2 Solvents derived from lipid-biomass

Vegetable oils, such as linseed, castor, soybean, sunflower, argemone, corn, canola, palm, coconut, jatropha, safflower oils, are extracted from the seeds of plants. They are composed of 95 wt.% of triglycerides, which are esters of saturated or unsaturated fatty acids and glycerol. Phospholipids, free sterols and sterol esters, tocols, triterpene alcohols, hydrocarbons and fat-soluble vitamins can also be found in their compositions.[176,177] Vegetable oils are non-volatile but unstable in the case of unsaturated oils whose double bond(s) can be oxidized.[178]

The main solvents that can be obtained from lipid-rich biomass are fatty acid methyl esters, glycerol and its derivatives as summarized in Figure 10.

The fatty acid methyl esters (FAMEs), known as biodiesel, are obtained from the trans-esterification of vegetable oil with methanol, giving glycerol as by-product. Both of them can be considered as green solvents due to their high biodegradability and low toxicity.[179] FAMEs have been used as solvent in polymerization reactions starting from methyl methacrylate, vinyl acetate, butyl acrylate and styrene.[41] They can also be suitable for the solubilisation of epoxy resin pre-polymers.[180] One of the main FAMEs is the methyl soyate produced from the esterification of soybean oil and methanol. It is used as solvent in the preparation of household and industrial cleaners, printing ink cleaners, in the formulation of adhesives- and graffiti-removers and as diluent in paints, stains and anti-corrosion coverings. In paint formulations, methyl soyate is usually mixed with a co-solvent like ethyl lactate to increase solvent evaporation rate.[41,181]

Glycerol and its derivatives are considered as "neoteric" solvents. It has the advantages of being cheap, non-toxic, biodegradable, easy to recycle and sustainable.[182] It is a polar solvent capable to dissolve organic salts, acids, bases and enzymes. Besides, glycerol has been described to increase the rate of various reactions, such as the reduction of ketones using *Saccharomyces cerevisiae*, the electrophilic activation of aromatic aldehydes with indoles, the aza-Michael reaction of *p*-anisidine with *n*-butyl acrylate and the enzymatic transesterification of 2-methylheptanoate.[183,184] Furthermore, glycerol derivatives have been identified as good solvents in several applications: triacetin have shown good potential in caffeine extraction from coffee and tea;[185] glycerol formal, solketal and 4-hydroxymethyl-1,3-dioxolane are used as solvent in paint and ink formulations and in cleaning agents.[186] Glycerol carbonate was evaluated as solvent in enzymatic transesterifications[187] and in epoxy and polyurethane formulations.[41]

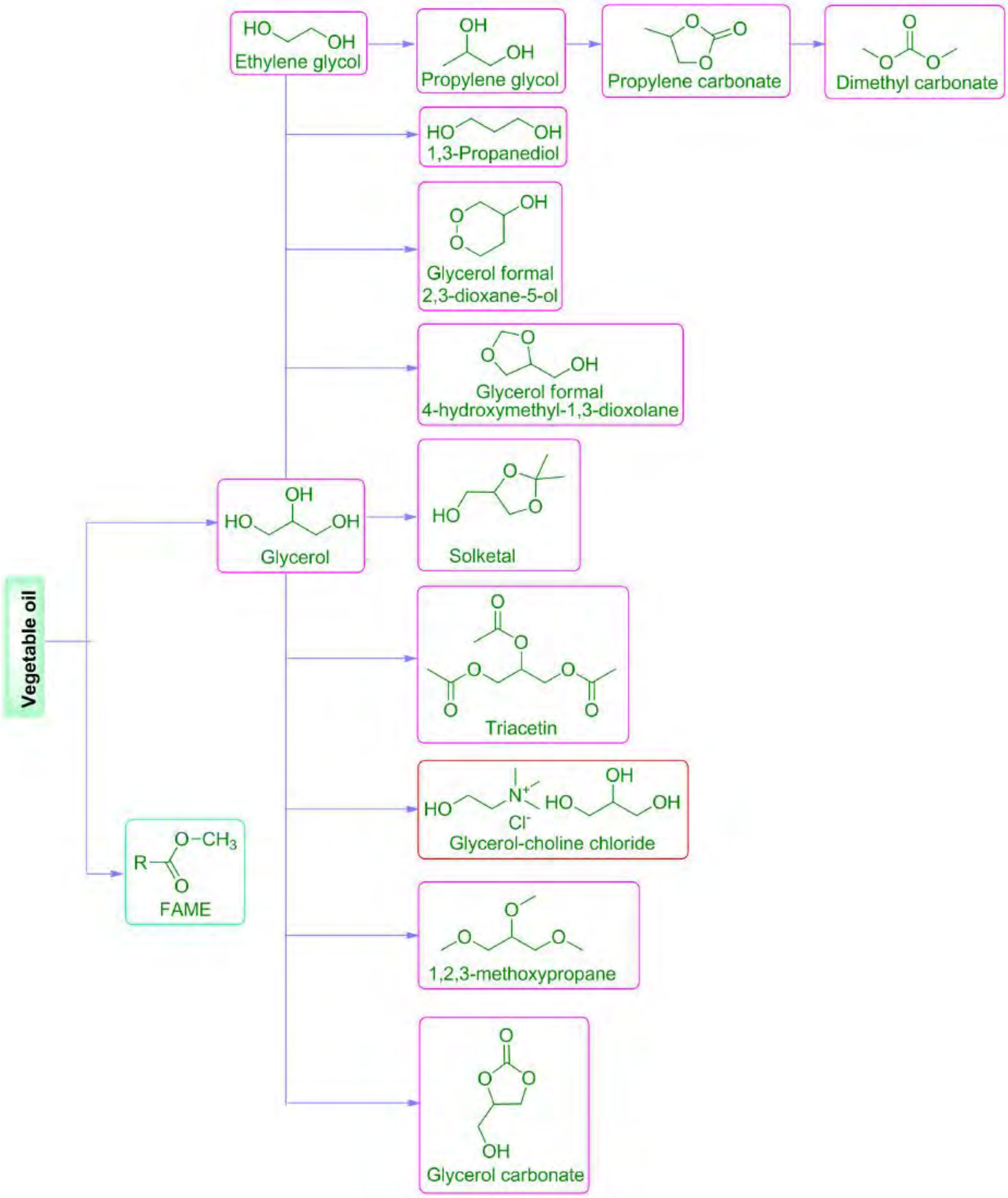


Figure 10. Solvents produced from lipid-biomass. Green=bio-based conventional solvents, Pink=neoteric solvent, Red=deep eutectic solvent

1.3.8.3 Solvents derives from terpenes

Terpenes are natural hydrocarbons, whose basic unit is isopropene (C_5H_8). Monoterpenes ($C_{10}H_{16}$), formed by two isopropene units, are the most abundant terpenes.[188] They are the principal components of essential oils and resins of various biomass feedstocks. They can also be obtained from citrus peels and pine resin wastes.[151] Pinene (principal constituent of turpentine) and limonene are the most representative monoterpenes. They are shown in Figure 11.

The **turpentine**, as it was previously mentioned, began to be used as the main solvent for paintings and varnishes during the nineteenth century. Turpentine is the volatile fraction of tree resins and can be obtained by distillation. It is a mixture of mainly α-pinene and β-pinene, with lesser amounts of camphene, carene, limonene, terpinolene, menthane and eucalyptol.[151] Its composition depends of the tree species, geographic location and the method used for its extraction.[188] There are four types of turpentine depending of its extraction and isolation: 1) the gum spirits of turpentine, which are obtained from the distillation of the oleoresin from wounded pine trees; 2) the sulphate wood turpentine, which is the condensate steam produced during the Kraft pulping process; 3) the wood turpentine obtained from the distillation of heartwood chips of pine stumps; and 4) destructively distilled wood turpentine, obtained from the destructively distillation of pinewood stumps.[180]
The turpentine has physical properties similar to toluene and methylene chloride,[154] and its use as replacement of *n*-hexane in the extraction of bioactive compound was recently reported.[189]

Pinane is produced from the hydrogenation of α-pinene and β-pinene. It is a stable molecule that cannot be oxidized as it does not have any double bond. Pinane can be used as solvent in the extraction of bioactive compounds like carotenoids and aromas. Recently, the use of pinane in carotenoids extraction showed better results than *n*-hexane.[189]

D-Limonene can be obtained from citrus peels (orange, lemon, mandarin, grapefruit and lime) by hydrodistillation with a Clevenger apparatus. Limonene has a low toxicity and is considered as GRAS (generally recognized as safe) by the FDA.[190] This bio-based solvent, which has a low polarity, is mostly used for replacing non-polar petrochemical solvents.[103] It is also able to substitute solvents such as MEK, acetone, toluene, glycol ethers, dichloromethane and *n*-hexane. Moreover, it can be used as an essential oil in cleaning (including degreasing), cosmetic, food and pharmaceutical industries.
Terpineol is one of the principal monocyclic monoterpenoid alcohols found in the nature. It can be obtained from flowers such as narcissus and freesia, herbs such as sage, marjoram, oregano and

rosemary and from cajuput, pine and lemon peel oil, as a mixture of *α*-, *β*-, *δ*-terpineol and terpinen-4-ol.[191] It is used as solvent in the solubilization of single-wall carbon nanotubes,[192] and in the preparation of TiO_2 thin-film photocatalyst,[193] paints formulations, cleaning agents and degreasers.[194]

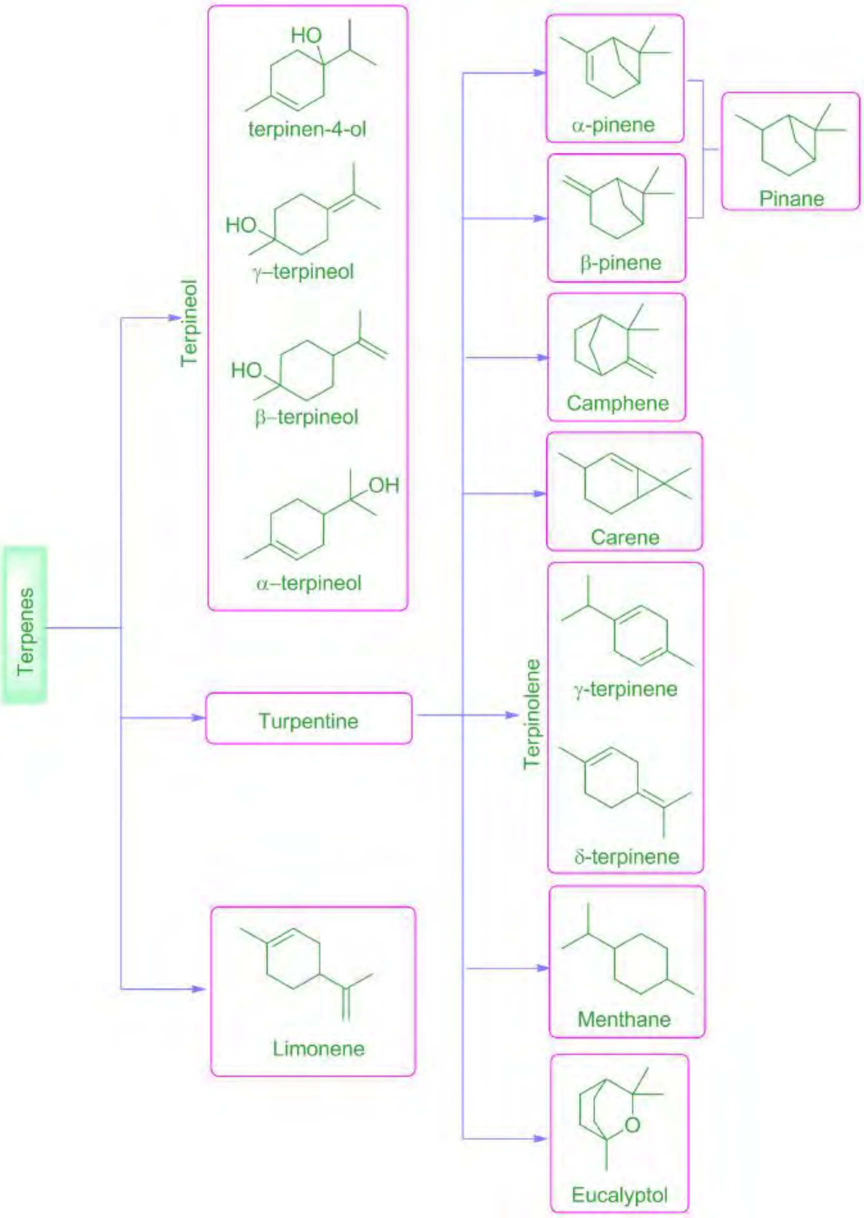


Figure 11. Solvents derived from terpenes. Pink=neoteric solvent

1.3.8.4 Solvents derived from lignin-biomass

The lignin is the second most abundant natural polymer on earth after cellulose. It is formed by the polymerization of cinnamyl alcohols or monolignols, depending on the type of plant. *p*-Coumaryl alcohol, coniferyl alcohol and sinapyl alcohol are the main monolignols (Figure 12).[195,196] The only difference between these precursors is the number of methoxy groups (-OCH_3) present in the aromatic ring.[197]

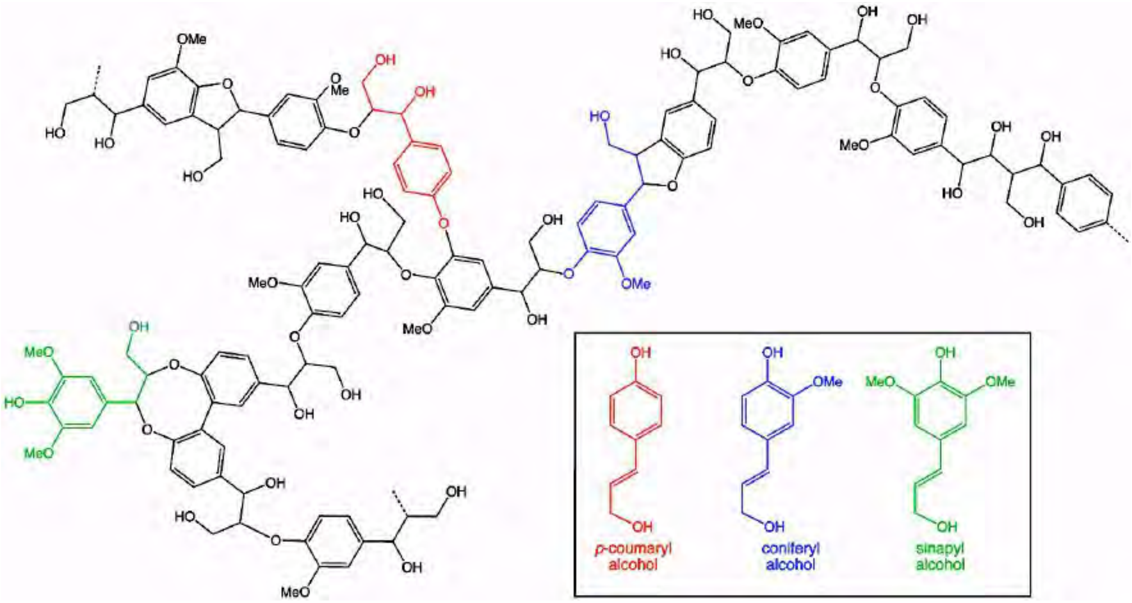


Figure 12. Structure of lignin[198]

Lignin represents an interesting source of fuels and aromatic chemicals due to its composition. Different methods of fractionation and isolation of lignin have been studied. Nevertheless, few studies in literature have described the synthesis of solvents from lignin. It has been reported that the pyrolysis of lignin can produce an oil, that after methylation with dimethyl carbonate and purification under supercritical CO_2, results in an ester that can be used as solvent, called "**lignin pyrolysis oil methyl ethers (LOME)".**[185] Besides, the research group of Dumesic has reported the synthesis of a solvent called "**lignin-derived solvent (LDS)"**, which is produced from the catalytic depolymerisation of lignin using a metallic catalyst (*i.e.* Pd/C, Rh/C and platinum black). This lignin-derived solvent is mainly composed of propyl guaiacol (PG) and propyl syringol (PS) (Figure 13). This phenolic solvent was effectively used in the conversion of cellulose and hemicellulose into 5-hydroxymethyl-furfural (HMF), levulinic acid (LA) and γ-valerolactone (GVL). The obtained results were similar to those obtained using 2-*sec*-butylphenol.[199]

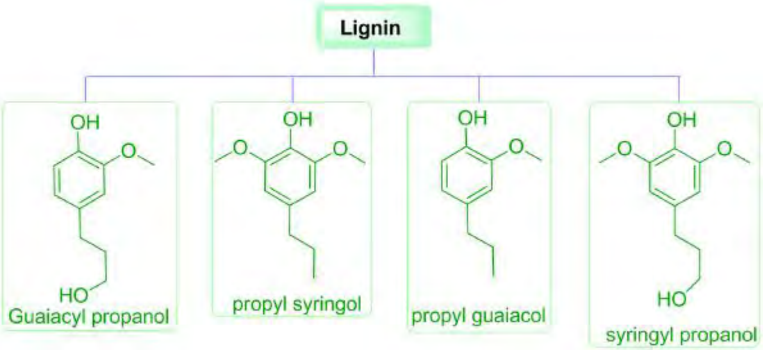


Figure 13. Solvents derived from lignin-biomass

1.4 Solvents substitution methodologies

To cope with the need of environmental-friendly and healthy solvents, a few substitution methodologies and tools have been developed. Indeed, the selection of alternative solvents is a complex task since the substitution by a solvent with a better HSE (health, safety and environmental) profile must not be accompanied by an alteration of technical performance. In this context, different substitution methodologies can be employed such as the use of solvent guides as selection tools, the test and error approach, the predictive methodology and the reverse formulation.

1.4.1 Solvent selection guides

The guidelines for the selection of solvents for chemical processes allow the identification of less toxic solvents with similar performance to that of conventional ones. These guides classify solvents according to their toxicity and their impact on the environment.[100] Among these guides can be found the one developed by the Pfizer,[200] GlaxoSmithKline (GSK),[201,202] Sanofi[135] and AstraZeneca[203] companies. Some of the most common solvents to be replaced and the substitutes recommended by the Pfizer guide are, for example, shown in Table 6.[100]

Undesirable solvent	Issues	Alternative solvent
Pentane	Lower flash point than other similar solvents	Heptane
Di-isopropyl ether	Powerful peroxide formation compared to similar solvents	2-MeTHF
Hexane	More toxic than other similar solvents	Heptane
Chloroform	Carcinogen	Dichloromethane
Pyridine	Carcinogenicity	Triethylamine
NMP	Reproductive toxicity	Acetonitrile

Table 6. Pfizer guide for solvent replacement

1.4.2 The test and error methodology

Based on the work of Goldschmidt (1993),[204] the test and error methodology was proposed by Bégin and Gérin in 2001.[205] In order to eliminate hazardous solvents used in work place and find less dangerous substituents with similar performances, they proposed a nine-step solvent substitution methodology:

1. Problem identification
2. Drafting an action plan
3. Collecting process information
4. Proposal for solvent alternatives, based on existing solvent classifications (dipole moment, dielectric constant, protic or aprotic character, Hansen parameters) and previously described guides
5. Evaluation of the consequences of each option
6. Comparison of options
7. Test of the proposed solvents and selection
8. Implantation
9. Evaluation

Although this methodology allows to propose alternative solvents for a specific industrial use, it results in an exhaustive and time-consuming study since all the proposed solvents must be tested. In addition, it may be possible that the selected molecule is not the best substitution alternative.[181] That is why other methodologies, described below, have been developed.

1.4.3 Predictive methodology

The predictive methodology is based on the prediction of the properties of alternative solvents. It consists in four general steps:

1. Identification of the solvent to be replaced
2. Definition of specifications, depending on application
3. Prediction of properties of the solvents envisaged for the substitution with reliable property models
4. Selection of the best alternative and validation in application conditions

This technique is very useful because it enables to eliminate the proposed molecules whose properties do not meet the specifications. Different computer predictive tools can be used (Table 7). These tools can focus on the prediction of physicochemical properties, such as the boiling point, melting point, vapor pressure, viscosity and solubility. They can also predict certain toxicity and eco-toxicity properties, such as persistence, bioaccumulation, toxicity, LD50, mutagenicity or carcinogenicity.[206]

Tool	Description
IBSS	Reverse design and prediction of physicochemical and toxicological properties
HSPiP	Hansen Solubility Parameters
COSMO-RS	COnductor like Screening MOdel for Real Solvents
PBT	Persistence, Bioaccumulation, Toxicity
Epi Suite	Estimation Program Interface
Caesar	Computer Assisted Evaluation of industrial chemical Substances According to Regulations
VEGA	Virtual Models for Evaluating the properties of chemicals within a Global Architecture
Tox predict	Estimate toxicological hazard of a chemical structure

Table 7. Property prediction tools for solvent substitution[207]

The predictive methodology is very useful for the replacement of petrochemical solvents with bio-based molecules.

The main advantage of this technique is that only the molecules that meet the requirements have to be synthesized (if it does not exist commercially) and tested, which results in savings of time, energy, raw materials and costs.[181]

1.4.4 Reverse design

The methodology of reverse design is based on chemical knowledge and the use of a Computer-Aided Molecular Design tool (CAMD). This methodology consists in identifying the molecules that meet a set of requirements (*a priori* defined). The software produces the chemical structures, predicts their properties thanks to models and compares them with the target specifications. The suggested molecules are classified according to their compatibility with the requirements. Finally, the most suitable molecules are selected according to the feasibility of their synthesis as well.

An example of CAMD tool is InBioSynSolv (IBSS), that has been created by the laboratory of Chemical Engineering (LGC) from Toulouse INP in collaboration with the Laboratory of Agro-industrial Chemistry (LCA from Toulouse INP) for the creation of solvents from biomass origin.[208,209] It helped to design bio-based solvents, derived from furfural, to replace conventional solvents used for the solubilisation of phytosanitary and resin active principles (Figure 14).[207]

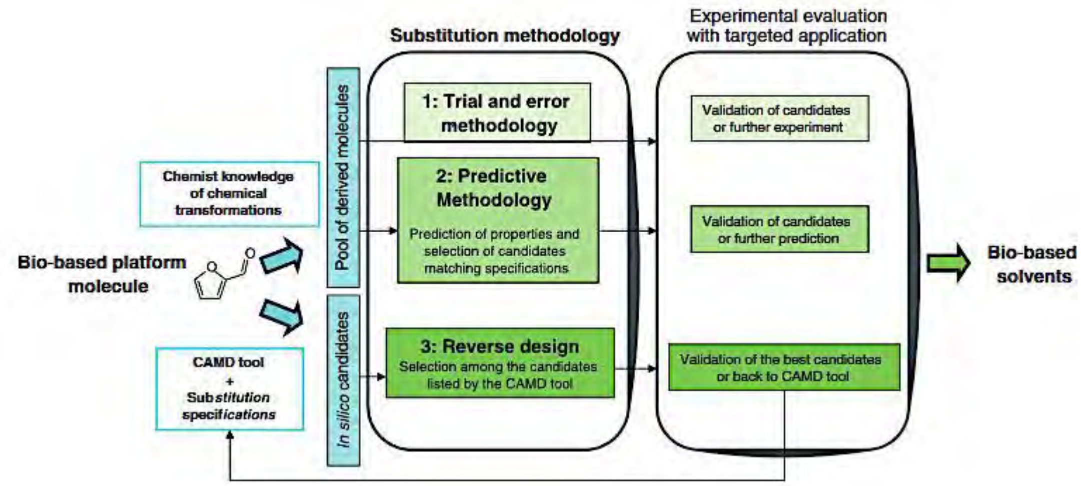


Figure 14. Solvents substitution methodologies[206]

1.4.5 Substitution of a fossil-based product by its bio-based counterpart

In order to be close to the applications and properties of the solvents currently used in the industry, another substitution strategy is the replacement of fossil molecules by bio-based ones, thanks to the use of building blocks obtained from biomass. This approach is interesting from an industrial point of view because the development of new factory infrastructure is not necessary.[134] It is therefore appropriate to develop new eco-friendly catalytic processes to obtain lower negative impacts on health and environment. However, this methodology is not relevant if the fossil-based solvent (to be substituted) has not a good HSE profile, since the incorporation of bio-based atoms in the molecule does not change its properties.

As examples of this approach, known bio-based synthons, such as bio-ethanol, bio-*n*-butanol and bio-acetone, have been used as starting material, instead of the corresponding fossil molecule, for the syntheses of several solvents, as shown in Figure 15. In the current market, various suppliers of these common bio-solvents can be found.[210,211]

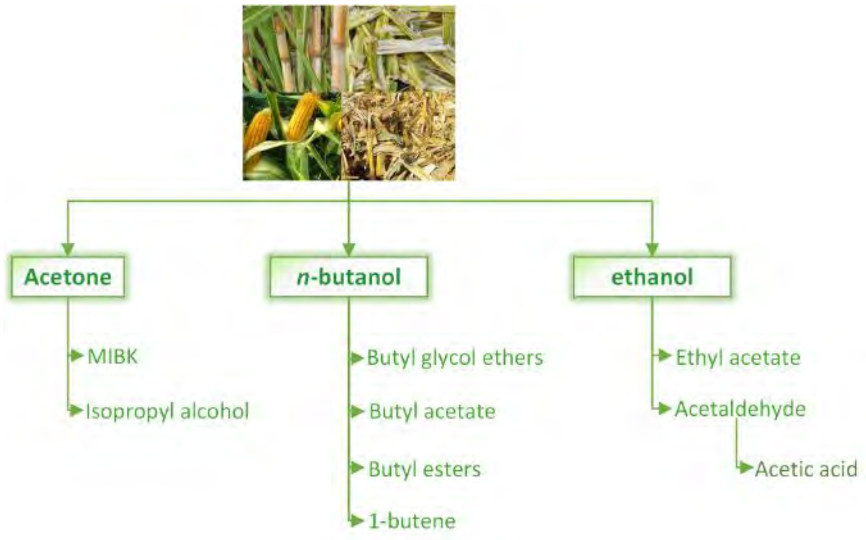


Figure 15. Bio-based solvents equivalent to the petrochemicals ones

1.5 Strategy chosen for the substitution of some conventional fossil-based solvents used in paint and coating industry

The solvent-borne and the waterborne coatings are the two types of formulations in paint and coating industry. In this work, we were focused on the first category, where the organic solvents or combinations of organic solvents are used.

For solvent-borne formulations, the most commonly used solvents are acetates and ketones, such as ethyl acetate (IUPAC: ethyl ethanoate, CAS: 141-78-6), butyl acetate (IUPAC: butyl ethanoate, CAS: 123-86-4) and methyl ethyl ketone (IUPAC: butan-2-one, CAS: 78-93-39).

Although these solvents are considered as VOC, they have the advantage of presenting low toxicity and low risk on health according to the FDA. Short-term toxicity studies have shown non genotoxicity-risk.[1] Moreover, these solvents were classified according to their HSE profile as "preferred" in the GlaxoSmithKline solvent guide, which considers the impacts of the solvent on health and environment, its risk of flammability/explosion, its reactivity/stability and its life cycle. Furthermore, as mentioned before, these solvents were determined as readily biodegradable by the ECHA.[2–4]

However, these solvents are nowadays produced from petrochemical sources through industrial processes that have many disadvantages such as the use of homogeneous acid catalysts that make the separation-purification steps difficult and that generate environmental damages due to waste production. This is why in the European project ECOBIOFOR, it has been proposed to replace these molecules from petrochemical origin with identical molecules but produced from biomass. This option has been guided by the industrial partners of the project, who did not want to invest in the registration of new molecules in REACH. Accordingly, the objective of this project was to study synthesis processes, starting from bio-base building blocks, alternatives to those currently available for the production of petrochemical solvents. It has then become crucial to identify new synthetic routes that guarantee the development of greener processes. This can be accomplished, either by using milder process conditions and/or by replacing the classic homogeneous catalysts by heterogeneous ones, which will, among other advantages, facilitate the separation step and reduce waste production (thanks to the reuse of catalysts after filtration).

In this project, we have thus decided to develop new syntheses of the principal solvents used in the paint and coating industry: **ethyl acetate (EAc), *n*-butyl acetate (BAc) and methyl ethyl ketone (MEK**). These syntheses will start from bio-based synthons and respect, as far as possible, the principles of green chemistry.

1.5.1 Selection of bio-based synthons:

One simple way to identify the possible bio-based synthons that can be used in the syntheses of the desired molecules is to carry out a retrosynthesis analysis: the target molecule is decomposed into less complex structures that will allow the identification of the initial reactants.[212–214]

For the case of ethyl acetate, three possible options were identified as shown in Figure 16.

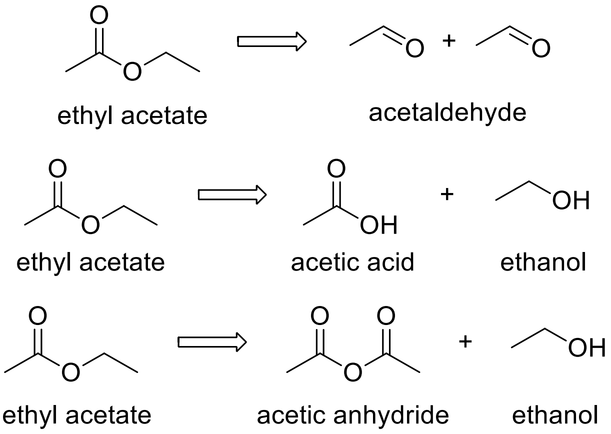


Figure 16. Identified chemical pathways for ethyl acetate production by retrosynthesis

The first one (using acetaldehyde) was discarded since this substance is highly toxic. Indeed, it is considered as carcinogenic. The two other synthesis proposals, starting from non-toxic ethanol and acetic acid or acetic anhydride, were finally chosen. Noteworthy, bio-based acetic acid can be found in the current market and bio-acetic anhydride can be produced from bio-acetic acid.

For the synthesis of butyl acetate, two chemical pathways were also identified, starting from *n*-butanol and acetic acid or acetic anhydride, as shown in Figure 17.

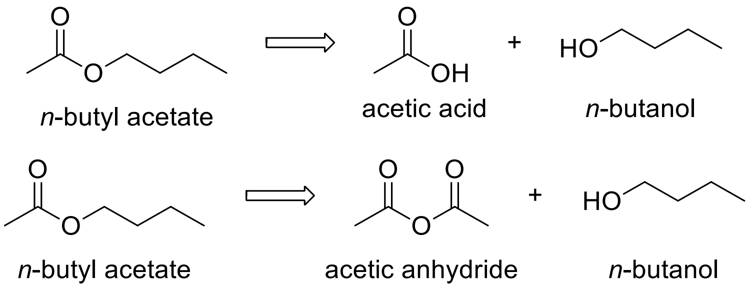


Figure 17. Identified chemical pathways for butyl acetate production by retrosynthesis

Concerning methyl ethyl ketone (MEK), syntheses starting from bio-based levulinic acid or *n*-butene *via* butan-2-ol as reaction intermediate can be proposed (Figure 18). Nevertheless, as the synthesis pathway involving *n*-butene requires more reaction steps, we decided to study the decarboxylation of levulinic acid. A one-step reaction is indeed preferred for solvent production as it is expected to be less expensive (between 1 €/kg and 6 €/kg for high value added product). Furthermore, levulinic acid is a key building block that has been identified among the 12 strategic synthons selected by the US Department of Energy for industrial development.[215]

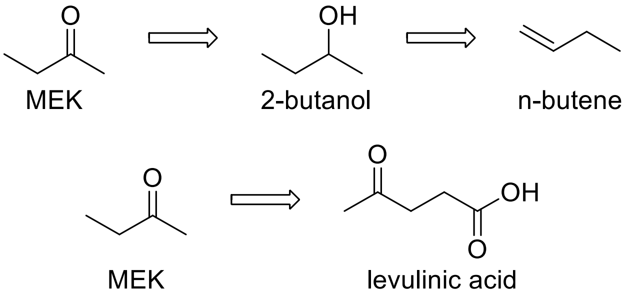


Figure 18. Identified chemical pathways for MEK synthesis

To summarize, the following synthons (Table 8) were proposed for the syntheses of the selected bio-based solvents:

Targeted Bio-solvent	Building-block
Ethyl acetate (EAc)	Ethanol
	Acetic acid
	Acetic anhydride
Butyl acetate (BAc)	Butanol
	Acetic acid
	Acetic anhydride
Methyl ethyl ketone (MEK)	Levulinic acid

Table 8. Building-blocks selected for the synthesis of bio-based solvents

Some of the selected synthons can be found on the current market in bio-based version: acetic acid, butanol, ethanol, and levulinic acid.

Our attention was not only focused on the renewable feedstock but also on their production processes that can have impacts on the environment and human health. We found that most of the selected synthons are synthesized through biochemical methods, avoiding the use of hazardous catalyst. They are considered as both 1st and 2nd generation products as they are produced from starch and lignocellulosic biomass such as hardwood, switchgrass, corn residues, and forestry residues, as shown in Table 9. This table also indicates the companies declaring to produce these bio-based molecules.

Building blocks	Industries	Raw materials	Technology
Acetic acid	SEKAB[210]	Agricultural and forestry residues	Catalytic oxidation
	ZEACHEM [216]	Forestry and agricultural wastes, grains, sugarcane	Fermentation
	Lanza Tech [217]	CO_2	Gas fermentation
Butanol	ZEACHEM[216]	Hardwood, softwood, switch grass and corn stover	Fermentation
	Green Biologics [211]	Corn, sugar, woody and agricultural residues	Fermentation
	ABENGOA [218]	Bioethanol from plant biomass, agricultural and forestry residues	Catalytic dehydration
Ethanol	ABENGOA[218]	Plant biomass, agricultural and forestry residues	Fermentation
	Beta Renewables [219]	Agricultural wastes	Fermentation
	Green Plains[220]	Corn, wheat, sorghum. Agricultural wastes (rice hulls, cheese whey, potato wastes), brewery and beverage wastes and forestry and paper wastes	Fermentation
	Shell Global[221]	Sugar cane and sugar cane wastes	Fermentation
	Pacific ethanol Inc.[222]	Corn	Fermentation
	Petrobras[223]	Sugarcane	Fermentation
	The Andersons[224]	Corn and other feedstocks	Fermentation
Levulinic acid	GFBiochemicals[225]	Cellulosic wastes	Atlas technology

Table 9. Producers of the selected bio-based synthons

By choosing building blocks produced from renewable sources and developing greener chemical pathways (for example using heterogeneous catalyst), the principles of the green chemistry, proposed by Anastas and Warner (Figure 19),[226] will be respected as far as possible. In particular, our work will be in accordance with the 7th principle concerning the bio-based origin of the building blocks and the 2nd, 3rd, 5th, 8th and 9th principles that are mainly related to the use of less toxic and safer raw materials (reactants and solvents if necessary), through the easiest transformation pathways.

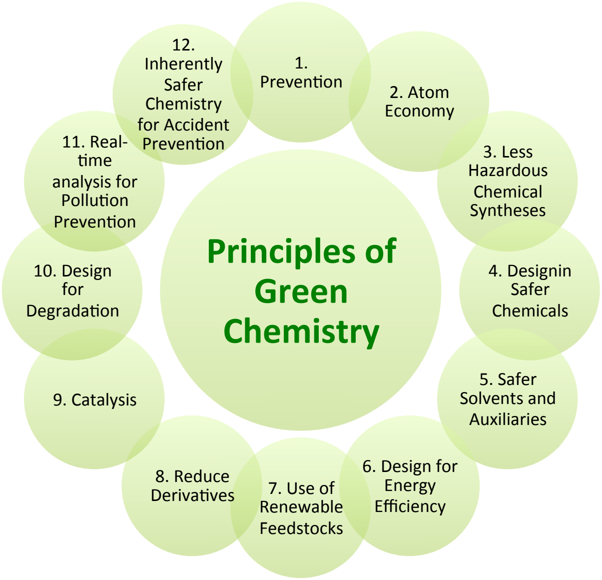


Figure 19. The 12 Principles of Green Chemistry[102]

1.6 Conclusions

For a long time, from prehistory to middle age, solvents were not used and 100% natural paints were prepared. Gradually, the use of solvents appeared necessary to facilitate the paint application. The first solvent used was turpentine, which was produced from conifers. Although this solvent provided adequate paint formulations, it was rapidly replaced by petrochemical solvents, which were economically more competitive.

Today, the paints and coatings sector is the main consumer of solvents since they are widely used, not only in solvent-borne formulations, but also in high solid coatings and in water-borne formulations, where the solvent can make up to 20% of the formulation.

The use of solvents in paints and coatings allows to obtain homogeneous formulations having drying times and viscosity suitable for the application method of the paint. The evaluation of other physicochemical properties of solvents (refractive index, color, density, boiling point, vapor pressure, evaporation rate and solvency) is also very important to guarantee the good performance of the paint. In addition, the HSE-relevant properties are evaluated in order to determine the hazardous nature of the solvent and its impact on the environment.

Otherwise, solvents are an important source of VOC emissions, which cause a negative impact on health and the environment (since they contribute to the formation of ozone). As consequence, legislation has been updated to regulate the use of solvents (REACH, Directive 2010/75/EU and Directive 2004/42/CE in Europe). It does not only limit the amount of VOCs that can be emitted by industrial installations and the solvent content in some paints, but also prohibits the use of solvents considered problematic for health. These measures have clearly driven companies to look for alternative solvents that are friendlier for the environment and health. As a result, a great door has been opened towards the research and development of greener solvents, such as supercritical fluids, ionic liquids, deep eutectic solvents, liquid polymers, fluorinated solvents and solvents derived from biomass.

Ethyl and butyl acetates and methyl ethyl ketone are among the most commonly used solvents in the paint and coating industry, as they are weakly toxic and readily biodegradable. These solvents are industrially produced from fossil sources using homogeneous catalysis (source of waste generation) and energy consuming conditions. An easy alternative to apply for the replacement of these solvents, which does not require the development of new paint formulations, is to substitute these petrochemical molecules by their bio-based equivalents. It will thus be essential to develop new processes starting from bio-based synthons, using milder synthesis conditions. Heterogeneous catalysts can, for example, replace homogeneous catalysts in these reactions, as they are easy to separate from the reaction medium and can be recycled.

We undertook this study to develop new syntheses of ethyl acetate, butyl acetate and methyl ethyl ketone starting from bio-based synthons. In this chapter, thanks to retrosynthetic analyses, we have identified and selected the bio-based starting materials to synthesize these desired solvents:

- Ethyl acetate can be obtained from ethanol and acetic acid or acetic anhydride by esterification reaction

- Butyl acetate can be synthesized from *n*-butanol and acetic acid or acetic anhydride

- Methyl ethyl ketone can be produced from bio-based levulinic acid through a decarboxylation reaction

In the next chapters, we will thus be interested in the development of new green processes for the production of these targeted solvents, their optimization and the study of their greenness.

CHAPTER II. Development of eco-compatible syntheses of ethyl and butyl acetates

2.1 Introduction

Ethyl and butyl acetates are widely used solvents in the pharmaceutical, food, perfume, printing, and paint and coating industries. These solvents have qualities that make them attractive for the paint and coating sector, among which we can quote their ability to evaporate quickly, their soft smell and their low toxicity.

Ethyl and butyl acetates are mainly produced from petrochemical sources. Their production processes currently used, involve the use of sulphuric acid or *p*-toluenesulfonic acid as catalysts. The use of these homogeneous catalysts makes the separation of the product and the catalyst difficult, produces equipment corrosion and generates waste related to their treatment.

In order to overcome these problems, the first objective of this work was to develop greener syntheses of acetates from alcohols that can be bio-based building blocks.

Thus, this chapter focuses on the study of the syntheses of ethyl and butyl acetates, in which the homogeneous catalyst is replaced by a heterogeneous one. Two synthetic routes were studied for each of the acetates: the first one using acetic acid and the second one using acetic anhydride, in the presence of ethanol and butanol for the production of ethyl acetate and butyl acetate, respectively. In each of the syntheses, four ion exchange resins were tested. Kinetic and thermodynamic studies allowed the selection of the best resin.

This chapter is divided into three parts. In the first part, the generalities related to the physicochemical properties of the acetates and their industrial productions are presented. To justify the substitution of homogeneous catalysts with ion exchange resins, the advantageous characteristics of the latter were also specified.

In the second part of the chapter, a complete study of the aforementioned syntheses is described. This study allowed us to propose an interesting co-production process of acetates. Thanks to this innovative process, the purification of the studied molecules is facilitated and the production of waste and co-products avoided. This work resulted in a first scientific publication. This paper submitted to the “Green and Sustainable Chemistry” journal was accepted on the 14th Avril 2018. Here we present a different formatted version that contains the same information as the publication.

The third part of this chapter focuses on the evaluation of the performance of the synthesized solvents in two types of coating formulations: nitrocellulose lacquers and polyurethane varnishes.

Different properties were evaluated and the results were compared with those obtained from commercial formulations. This study was carried out jointly with two of the partners of the ECOBIOFOR project: TECNALIA (Technology Centre, Spain) and Industrias Químicas IRURENA (SME, SPAIN, experts in wood coatings).

2.2 Generalities: Transition between the petrochemical acetates to greener alternatives

2.2.1 Ethyl acetate: Properties, Applications and Industrial Production

2.2.1.1 Properties and applications

Ethyl acetate (CAS number: 141-78-6), also called ethyl ethanoate according to the IUPAC nomenclature, is an oxygenated, colourless organic ester, which has a slight characteristic fruit-like odour. Ethyl acetate is considered as a moderately polar solvent with a high volatility, low toxicity and non-hygroscopic character. It is classified in the category of lowest toxic solvent, called "preferred", in the Pfizer solvent guide.[200] This classification takes into account different criteria, such as the worker safety, carcinogenicity, mutagenicity, reprotoxicity, skin absorption/sensitization, odour and environmental and regulatory concerns.[104,136] Its physicochemical and toxicological properties are summarized in the following table (Table 10).

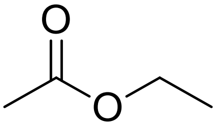
Structure	Properties	Value
 CAS: 141-78-6	Molecular formula	$C_4H_8O_2$
	Molecular weight	88.1 g/mol
	Flash point	-4 °C
	Boiling point	77.1 °C
	Melting point	-83.6 °C
	Evaporation rate (relative to butyl acetate)	4.5
	Density	0.903 Kg/L
	Solubility in water, 20 °C	80 g/L
	Viscosity, 25 °C	0.426 cP
	Specific gravity D_{20}^{20}	0.902
	Refractive Index n_D^{20}	1.3719
	DL_{50} (oral in rat)	5620-10200 mg/kg
	Biodegradability	Readily biodegradable
	Partition coefficient (log Kow)	3 (low potential for bioaccumulation)

Table 10. Physicochemical and toxicological properties of ethyl acetate[2,71,227,228]

Ethyl acetate has a wide variety of applications as a solvent and thanks to its low toxicity, it can replace some more toxic solvents that causes serious damage to human health and the environment. Due to its sweet smell, it is widely used as a synthetic flavouring in the food industry.[229] It is also used as an ingredient in perfumes, inks and adhesives.[230] Besides, it is incorporated into nail polish removers, replacing acetone and thus avoiding the negative effects caused by its strong smell and by the dryness it provokes to the nails.[231]

This acetate is also a common solvent used in extraction processes, such as the decaffeination process of coffee and tea.[232,233] It was efficient to replace hexane in the extraction of carotenoids.[234] Moreover, as ethyl acetate is classified in the list of solvents with the lowest toxic impact on health, according with FDA and the Pfizer solvent guide,[1,136] it is used in pharmaceutical syntheses (sertratiline as anti-depressant)[235] and extractions of bioactive compounds (phenolics and anthocyanins)[236] to replace ethyl ether and chlorinated solvents that are more toxic.

Ethyl acetate is widely used in the paint and coating industry, as it quickly evaporates due to its high vapour pressure (9.7 kPa at 20°C). In addition, thanks to its great solvent power, it is effective to dissolve nitrocellulose, cellulose ethers, natural and synthetic resins such as polyvinyl acetates, polyacrylates, polystyrene and alkyd resins, which makes it adequate for the preparation of nitrocellulose and cellulose acetate lacquers and for alkyd, acrylic, and polyurethane varnishes.[34,228]

2.2.1.2 Current industrial production processes

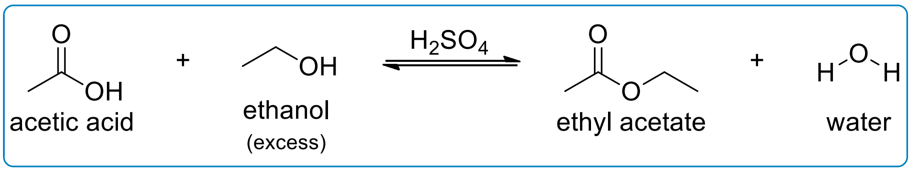
The worldwide production of ethyl acetate showed an increase of 80 % from 2004 to 2011 to reach more than 3 million tonnes. In 2012, a total world production of ethyl acetate of 3.12 million tonnes was reported and an annual increase of 4.5% until 2018 was predicted.[237]

Nowadays, ethyl acetate is synthesized using petrochemical feedstocks. It is industrially produced through three different processes:

1. the Fischer esterification reaction of acetic acid
2. the Tishchenko reaction by combination of two acetaldehyde molecules
3. the addition of acetic acid to ethylene

2.2.1.2.a The Fischer esterification reaction of acetic acid

The production of ethyl acetate by the Fischer reaction[238] consists in the esterification of the acetic acid with an excess of ethanol in the presence of a homogeneous catalyst, generally sulphuric acid or *p*-toluenesulfonic acid. This method is the principal production way of ethyl acetate in Western Europe (Scheme 1).



Scheme 1. Fischer esterification reaction for ethyl acetate synthesis

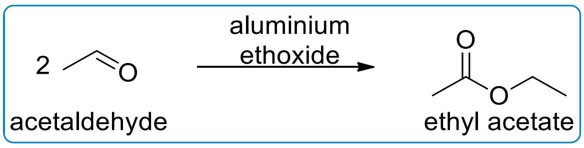
In this process, the homogeneous catalyst is added to the mixture of acetic acid and ethanol. The molar ratio acetic acid:sulphuric acid used in this reaction is 1:1.1.[239] As in the overall classic esterification reactions, the yield in ethyl acetate is only of 65% due to the equilibrium of the reaction. However, it can be shifted to the right if the water is constantly removed.[240] The reaction is thus carried out using an azeotropic distillation column; in this way, the reaction products can be distilled to be then collected in a decanter. They are subsequently conducted to a second distillation column. A ternary azeotropic mixture of ethyl acetate-water-ethanol consisting of 85% ethyl acetate is obtained. A third distillation needs to be carried out to finally obtain 95 % of ethyl acetate.[227,241,242] The treatment of aqueous effluents containing the acid catalyst can be carried out according to different neutralization techniques: by passing the acid wastes through limestone beds, by using lime slurries or by the addition of caustic soda or sodium carbonate.[243] Otherwise, for the recovery of the acid, a distillation is required but needs very high temperature as the boiling point of H_2SO_4 is 337°C at atmospheric pressure. Under lower pressures (less than 20mm Hg), temperature can be reduced to 200°C.[244,245] It is clear that the treatment of homogeneous acid catalyst involves an additional cost or greater energy consumption to recover the acid.

Thus, the principal disadvantages of this process are: i) the use of sulphuric acid or *p*-toluenesulfonic acid as homogeneous catalyst, which requires corrosion resistant equipment and treatment of the aqueous waste, and ii) the production of a ternary azeotrope, ethyl acetate-water-ethanol (10.7-60.7-28.6 %mol), which needs energy-intensive processes, such as several stages of distillation, to purify ethyl acetate.

2.2.1.2.b Tishchenko reaction of acetaldehyde

The Tishchenko method for the production of ethyl acetate has been developed in countries where the price of ethanol is high (making the Fischer process uncompetitive) or where acetaldehyde is produced in high amount quantities as in Japan and Germany.[246]

In the Tishchenko reaction, two equivalents of acetaldehyde are used in the presence of an alkoxide base as catalyst (Scheme 2). The catalyst is prepared by dissolving aluminium ethoxide in an ethanol/ethyl acetate mixture.



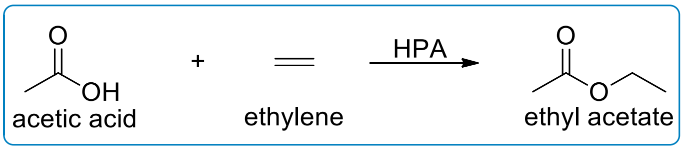
Scheme 2. Tishchenko reaction for the ethyl acetate synthesis

As the Tishchenko reaction is highly exothermic, it needs to be carried out at -20 °C during 1h. Under those conditions, an acetaldehyde conversion of 98 % is reached with an ethyl acetate yield around 61 % and acetaldol (3-hydroxybutanal) as by-product.[246] Finally, the reaction mixture is distilled to obtain ethyl acetate with a purity of 99.8%.[185]

Among the drawbacks of this production process, the main one is the use of acetaldehyde, which is considered as highly toxic, mutagenic and carcinogenic.[247] It is especially classified in the "group 1 carcinogen to humans" according to the International Agency of Research on Cancer (IARC).[248] Besides, the catalyst can be deactivated by the water produced from the dehydration of the by-product acetaldol (secondary reaction), generating a large amount of catalyst waste that requires to be treated.[246] Furthermore, it is important to consider the high-energy consumption due to the intensive cooling needed to carry out the reaction.

2.2.1.2.c The addition of acetic acid to ethylene

Ethyl acetate can also be produced from ethylene and acetic acid. This method has been adopted by different industries. This is the case of BP Chemicals who has developed a new technology for the production of ethyl acetate: the Advanced Acetates by Direct Addition of acetic acid to ethylene (AVADA process).[249] In this AVADA process, ethyl acetate is produced by reaction of ethylene with acetic acid in the presence of water, using a silica-supported phosphotungstic heteropolyacid as catalyst (HPA, Schema 3).[250]



Scheme 3. Reaction of the addition of acetic acid to ethylene for the synthesis of ethyl acetate

The use of a small amount of water (ranged from 1 to 10 %mol relative to the total quantity of ethylene and acetic acid) leads to the reduction of the amount of undesired by-products such as 2-butanone and acetaldehyde that can be formed during the reaction. The reaction is carried out at a temperature between 160 and 195°C and at a pressure between 1200 kPa and 1500 kPa. In the AVADA process, ethyl acetate is obtained with a purity of 99.9%.

The AVADA process was launched in 2001 at Hull, UK. This is the world largest ethyl acetate plant with a production capacity of 220,000 metric ton of EAc/year. In 2011, the AVADA process has produced the 56% of ethyl acetate in Europe. [251]

This process is characterized by its high atom efficiency because there is no formation of co-products, if the amount of water and the conditions of temperature and pressure are adequately controlled.[252]

The disadvantages of the process are principally the use of high temperature (until 195°C) and the catalyst deactivation, which can affect the quality of the product.

2.2.2 *n*-butyl acetate (BAc): properties, applications and industrial production

2.2.2.1 Properties and applications

n-butyl acetate (CAS number: 123-86-4; IUPAC systematic name: butyl ethanoate) is a colorless solvent with a fruity aroma. It is a very used organic solvent, miscible with other solvents such as alcohols, ketones, aldehydes, ethers, glycols, glycol ethers, aromatic hydrocarbons and aliphatic hydrocarbons.[253] The physicochemical and toxicological properties of *n*-butyl acetate are summarized in the following Table 11.

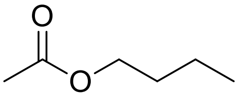
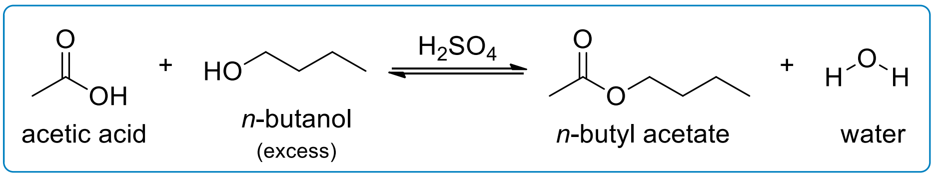
Structure	Properties	Value
 CAS: 123-86-4	Molecular formula	$C_6H_{12}O_2$
	Molecular weight	116.16 g/mol
	Flash point	27 °C
	Boiling point	126.1 °C
	Melting point	-78.0 °C
	Evaporation rate (relative to butyl acetate)	1
	Density	0.883 Kg/L
	Solubility in water, 20 °C	68 g/L
	Viscosity, 25 °C	0.685 cP
	Specific gravity D_{20}^{20}	0.882
	Refractive Index n_D^{20}	1.3941
	DL$_{50}$ (oral in rat)	10760-12789 mg/kg[3]
	Biodegradability	Readily biodegradable
	Partition coefficient (log Kow)	2.3 (low potential for bioaccumulation)

Table 11. The physicochemical properties of *n*-butyl acetate[3,227]

n-butyl acetate is used as solvent in the food industry due to its sweet aroma. Also, it is widely employed in extractions in the pharmaceutical industry. The principal use of *n*-butyl acetate is in the paint and coating industry, where thanks to its versatility, it is usually employed to reduce the viscosity of formulation and to improve the film formation of coating films. Besides, it has a good solvent power that make it excellent to dissolve polymers, resins, oils and cellulose nitrate, which explains its main use in the preparation of coatings based on nitrocellulose and synthetic resins.[20]

2.2.2.2 *Current industrial production process*

Butyl acetate is industrially synthesized only through the Fisher esterification reaction between glacial acetic acid and *n*-butanol, using concentrated sulfuric acid as homogeneous catalyst (Schema 4).



Scheme 4. Esterification reaction for the synthesis of *n*-butyl acetate

The synthesis of *n*-butyl acetate by esterification is an equilibrium-limited reversible reaction (around 65 % for the BAc yield). Butyl acetate is produced with a purity of 98 wt% after distillation steps.[254 255] This production process shows main drawbacks such as the complex process of butyl acetate purification because of the presence of multiple azeotropes and the separation of unreacted butanol to be recycled. Furthermore, low acetate yields are obtained due to water formation that limits the reaction.

As in the case of ethyl acetate, the homogeneous acid catalyst treatment consists in neutralization with a basic reagent (limestone beds, lime slurries, caustic soda or sodium carbonate). Then the generated aqueous effluents needs a subsequent treatment in a sewage treatment plant, increasing operational costs.[243]

In order to overcome these problems, reactive distillation has become an interesting alternative and was described in some patents for butyl acetate production. For example, a patent described the reactive distillation by using an ion exchange resin packed in the distillation column.[254] In this process, the esterification reaction was performed in the reaction zone that is located in the middle of the column, while the separation of products was carried out in the lower and upper parts of the separation zone. Butyl acetate was obtained as the bottom product of the distillation with a purity of 95-99 wt%.

The production of butyl acetate using reactive distillation has been the subject of many simulations[256–260] and only a few cases of experimental studies due to the complexity of the process.[261–263]

2.2.3 Strategy for the development of eco-compatible syntheses of ethyl and butyl acetates

As we have mentioned above, the current industrial processes for the production of ethyl and butyl acetates presents various disadvantages, principally related with the toxicity of the reactants, the use of homogeneous catalyst, high temperatures or pressures, and the requirement of several distillation steps for an efficient purification to separate the esters from the various azeotropes they formed. Accordingly, it is necessary to develop syntheses that could be carried out under milder conditions and in the presence of heterogeneous catalyst to avoid the waste production and facilitate the purification of the products. The use of greener starting materials could also offer environment-friendly molecules that can substitute the corresponding fossil derivatives.

2.2.3.1 Ion exchange resins: a greener alternative to homogeneous catalyst in the syntheses of acetates

The currently running esterification processes for the syntheses of acetates involve the use of sulfuric acid or *p*-toluenesulfonic acid (PTSA) as catalysts.[264] However, the use of these homogeneous catalysts has many disadvantages, such as the complicated post-treatment procedures for catalyst separation and purification of the desired products and the equipment corrosion. These processes also generate a significant amount of waste resulting in a negative impact on the environment.[265]

In order to avoid these problems due to the use of homogeneous catalysts, a possible alternative is their replacement by heterogeneous catalysts such as acidic ion exchange resins.

2.2.3.1.a Structure of Ion exchange resins

An ion exchange material can be defined as an insoluble matrix containing labile ions capable of exchanging with the ions in the surrounding medium without major physical changes in its structure. The catalysis by ion exchangers can be explained in terms of the catalytic activity of the exchanging ions, which can act as insoluble acids or bases. Reactions can be carried out in aqueous and non-aqueous solvent solutions.[266]

In general, ion exchange resins consist of a base matrix made of polystyrene copolymers between which is a divinylbenzene cross-linker (DVB), that made them insoluble in aqueous and non-aqueous systems.

An important aspect in resins is the degree of cross-linking of the three-dimensional matrix, since the structure of the internal pores of the resins will depend on it and will affect the internal movement of the exchanging ions.[267] These resins are divided according to their structure into: i) gel resins, which are microporous structures that present a dense internal structure with no discrete pores, and ii) macroporous or macroreticular resins, which are porous multichannelled structures.

Gel type resins are three-dimensional polymeric structures that possess a homogeneous matrix without discontinuities. They have generally a content of DVB below 10 % and a pore size between 0.05 and 5 nm. The gel beads have negligible catalytic activity when they are totally dry. Nevertheless, they have the ability to swell in the presence of solvents, creating spaces in their structure that facilitate the diffusion of the reactants. The swelling property of the resins is advantageous when used in reactions where water is produced, as the esterification reactions: water can be easily adsorbed by the resin provoking a greater swelling that results in an effective catalysis, in some cases better than with macroporous resins.[268,269]

Macroporous resins, on the contrary to gel resins, have a multichannel structure with a content of DVB greater than 10 % and in which pore diameters are ranged from 0 to 200 nm. The three-dimensional matrix of the resins provides a higher surface allowing the exchange of larger ions, which enables their use with a wide variety of reactants and non-aqueous systems. Contrary to gel resins, macroporous resins are rather suitable in water-free reactions because it has been observed that water can compete with the reactant for the active sites, decreasing the rate of the reaction.[266] Macroporous resins can be used in reactions where water is a by-product. Nevertheless, water should be removed continuously from the reaction medium in order to avoid the decrease of the resin catalytic activity. Macroporous resins are rigid offering less fragility, which facilitates their removal from the systems and avoids the use of special handling care.

The differences between gel type resin and macroporous one are presented in Figure 20.

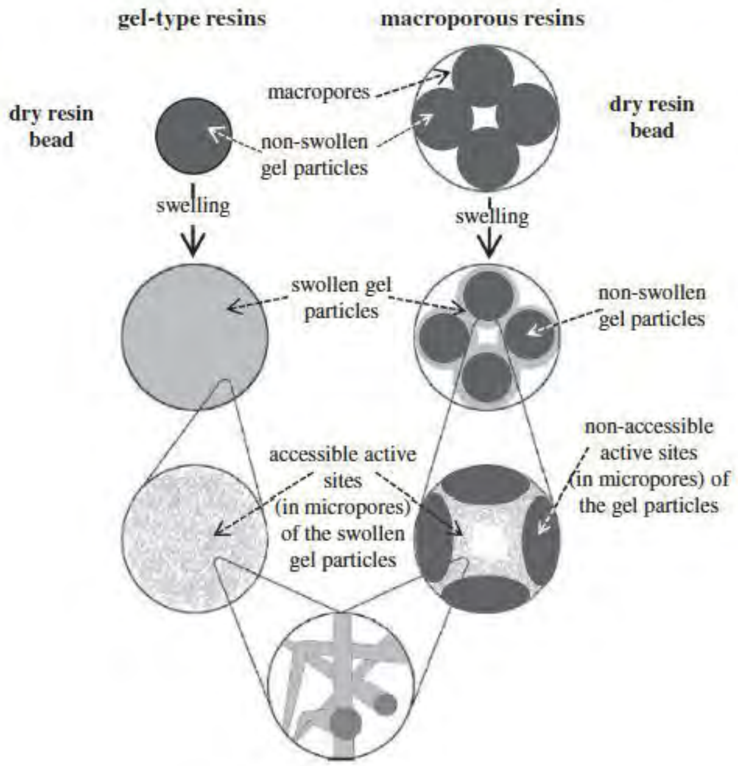


Figure 20. Structure of gel type resins and macroporous resins[270]

2.2.3.1.b Nature of ion exchange resins

Ion exchange resins can be classified depending on the type of the functional group grafted to them. They can be strongly acidic, weakly acidic or strongly basic materials as shown in table 12.

Resin type	Functional group	
Strong acid cation	Sulfonate	$-SO_3^-H^+$
Weak acid cation	Carboxylate	$-COO^-H^+$
Strong base anion	Type 1: benzyltrimethylammonium Type 2: benzyldimethylethanolammonium	$-C_6H_4-CH_2N^+(CH_3)_3$ $-C_6H_4-CH_2N^+(CH_3)_2(CH_2CH_2OH^-)$

Table 12. Classification of resins by nature of the functional group[271]

The functional group determines whether cations or anions are exchanged, acting in a similar way to conventional acids and bases.[267] The styrene-divinylbenzene matrix can for example be treated with a sulfonating agent for the production of a strong acid cation-exchange resins or through the chloroethylation and amination for the production of anion-exchange resins.[272]

2.2.3.1.c Use and advantages of ion exchange resins

The use of an ion exchange resin as catalyst is an interesting alternative due to the multiple advantages it offers: 1) side reactions are minimized,[273] 2) the separation of the catalyst from the reaction medium is easy by simple filtration,[274,275] 3) the resin recycling is possible,[266,276–278] 4) continuous reactions can be performed, 5) post-reaction treatments of the catalyst are not necessary reducing waste production,[279] and 6) special corrosion resistant equipment is not needed. Due to these advantages, resins have been widely employed in reactions, such as esterification, ester hydrolysis, alcoholysis, acetal condensation and sugar inversions, where they have shown a catalytic behaviour similar to the soluble acids.[280] For example, the dehydration of *tert*-butanol was reported to be more effective when Dowex 50WX was used instead of *p*-toluenesulfonic acid (*p*-TSA).[281] The same was reported when Amberlyst 15 replaced *p*-TSA in the addition of alcohols to olefins.[282] Also, the etherification of ethylene and propylene glycols with isobutylene was enhanced when Amberlyst 15 were used instead of *p*-TSA.[283]

2.2.3.2 Proposition of alternative syntheses for ethyl and butyl acetates

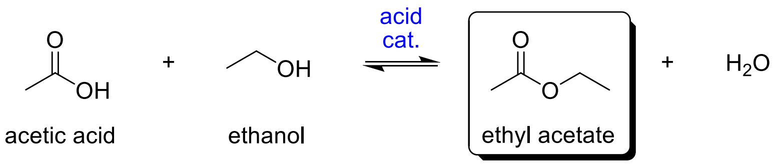
In order to develop greener syntheses of ethyl and butyl acetates in comparison with the current ones, we proposed in this work, to replace the homogeneous acid catalyst by heterogeneous ion exchange resins that, as stated above, have several advantages summarized in Table 13. This operation will meet the 1st (waste prevention), 3rd (use of less hazardous chemicals) and 12th (safer chemicals) principles of the green chemistry proposed by Anastas and Warner.[102,226]

Current production process	Alternative proposal
• Catalyst: acid sulphuric or *p*-toluenesulfonic acid (*p*-TSA)	• Heterogeneous catalyst: ion exchange resins.
• Difficult catalyst-product separation: during the reaction, products and reagents are in the same homogenous phase and the separation of the products requires distillation process	• Catalyst free products can be obtained by simple filtration
• Complicated post-treatment procedures: waste disposal includes dilution of the acid and neutralization of the acid-aqueous effluent	• Catalyst can be easy recovered by simple filtration
• Complicated catalyst recovery/recycling: the recovery of the acid involves a great energetic expenditure, distillation at high temperatures are required	• Recycling: the ion exchange can be reused in several cycles of reaction without regeneration. Then their regeneration is possible
• Equipment corrosion	• Special corrosion resistant equipment is not necessary

Table 13. Advantages of ion exchange resins over classical catalyst

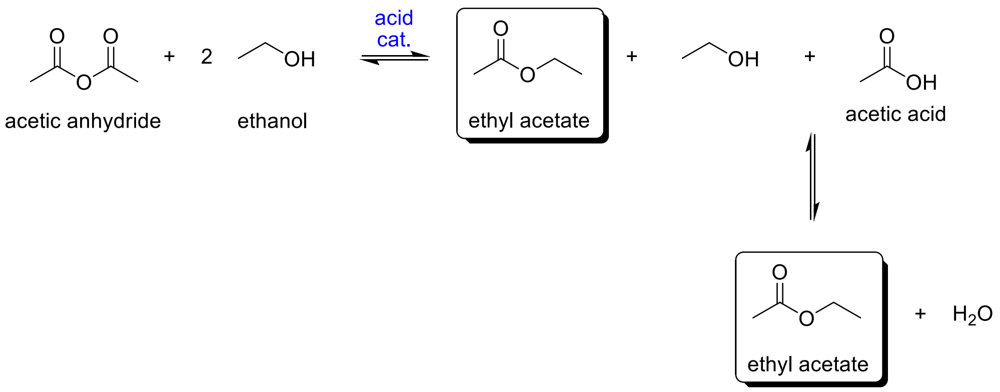
For this study, four resins have been selected to be tested as catalysts in the acetates syntheses: Amberlyst 15 (A15), Amberlyst 16 (A16), Amberlyst 36 (A36) as macroporous resins and Dowex 50WX8 (D50) as a gel-type resin.

For the production of ethyl acetate, two synthetic chemical pathways have been studied. The first one uses acetic acid and ethanol (which can be bio-sourced), as starting materials in the presence of an acidic resin (Scheme 5).



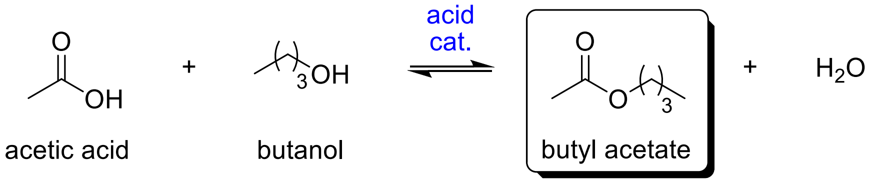
Scheme 5. Synthesis of ethyl acetate starting from ethanol and acetic acid.

The second method uses acetic anhydride instead of acetic acid (Scheme 6).

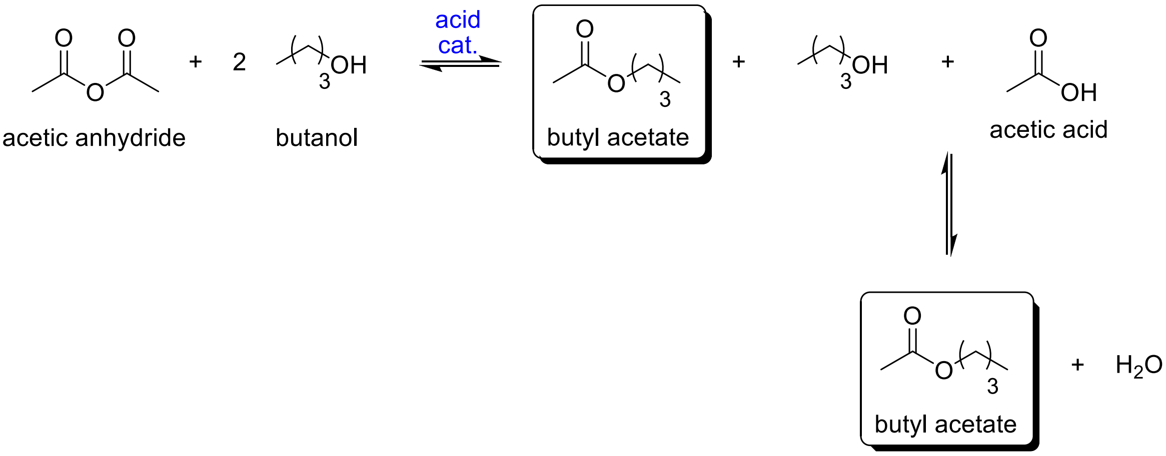


Scheme 6. Synthesis of ethyl acetate from ethanol and acetic anhydride

For the production of *n*-butyl acetate, the same methodology was applied replacing ethanol by butanol (Schemes 7 and 8).



Scheme 7. Synthesis of butyl acetate from *n*-butanol and acetic acid.



Scheme 8. Synthesis of butyl acetate from *n*-butanol and acetic anhydride.

Then, an innovative process of coproduction of ethyl and butyl acetates was developed, as it is described in the paper below.

2.3 A novel process using ion exchange resins for the coproduction of ethyl and butyl acetates

Nydia Ileana Guzman Barrera, Cécile Bories[a], Jérôme Peydecastain, Caroline Sablayrolles, Emeline Vedrenne, Carlos Vaca-Garcia, Sophie Thiebaud-Roux

Laboratoire de Chimie Agro-industrielle (LCA), Université de Toulouse, INRA, INPT, Toulouse, 31030, France

This paper has been accepted in Green and Sustainable Chemistry

ABSTRACT: Before proposing an innovative process for the coproduction of ethyl and butyl acetates, the individual syntheses of ethyl acetate and butyl acetate by two different routes were first studied. These syntheses involved the reaction of ethanol or *n*-butanol with acetic acid or acetic anhydride in the presence of ion exchange resins: Amberlyst 15, Amberlyst 16, Amberlyst 36 and Dowex 50WX8. Kinetic and thermodynamic studies were performed with all resins. The lowest activation energy (E_a) value was obtained with Dowex 50WX8, which was identified as the best-performing resin, able to be reused at least in four runs without regeneration.

The presence of water-azeotropes during the synthesis of ethyl acetate makes its purification difficult. A new strategy was adopted here, involving the use of ethanol and acetic anhydride as the starting material. In order to minimize acetic acid as co-product of this reaction, a novel two-step process for the coproduction of ethyl and butyl acetates was developed. The first step involves the production of ethyl acetate and its purification. Butyl acetate was produced in the second step: *n*-butanol was added to the mixture of acetic acid and the resin remaining after the first-step distillation. This process yields ethyl acetate and butyl acetate at high purity and shows an environmental benefit over the independent syntheses by green metrics calculation and life cycle assessment.

Keywords

Ion exchange resins, esterification, ethyl acetate, butyl acetate, coproduction, life cycle assessment

2.3.1 Introduction

Ethyl acetate (EAc) and butyl acetate (BAc) are among the solvents most frequently used in the coating, adhesive, ink and cosmetic industries [227]. They are conventionally produced by the esterification of acetic acid (AcOH) with excess alcohol (ethanol (EtOH) and *n*-butanol (BuOH), respectively) in the presence of homogeneous acid catalysts. Strong liquid mineral acids, such as sulfuric acid, p-toluenesulfonic acid (PTSA) and hydrochloric acid, are the most effective catalysts for achieving high esterification yields. [264,284,285] However, these processes require the use of alkaline salt solutions for catalyst neutralization, resulting in the generation of aqueous waste [265].

The use of ion-exchange resins bearing sulfonic acid (-SO_3H) groups as heterogeneous catalysts in esterification reactions is well documented.[286–292] These resins generally give results similar to those obtained with homogeneous acid catalysts.[280] The use of a heterogeneous ion exchange resin as a catalyst is advantageous in a number of ways. In particular, by contrast to processes involving the use of homogeneous acid catalysts, there is no need to neutralize the medium. This limits waste production [279]. Side reactions are also limited, resulting in higher reaction yield and higher product purity.[273] The resin is easy to remove from the reaction medium by filtration or decantation.[274,275] The recovered resin can be reused without regeneration, but can also be regenerated for further use.[266,276–278]

Esterification reactions are known to be equilibrium-limited. The equilibrium is often shifted by adding an excess of one of the reactants or by removing one of the products (i.e. water) during the reaction (Le Chatelier's principle). However, the presence of azeotropes makes purification more difficult, due to the need for energy-intensive processes. Ethyl acetate is generally purified by rectification, in several distillation steps. However, each step reduces the yield and additional recycling is required. It can also be extracted through extractive distillation with an agent containing DMSO,[255] polyethylene glycol or dipropylene glycol[293] or using ionic liquids (ILs).[294,295] More recently, pressure-swing distillation has been explored.[296–298] Reactive distillation (RD) has also been studied as a method for producing this ester, to avoid azeotropic limitation and to increase yield and purity.[256,299–304]

In this study, a novel coproduction process for ethyl acetate and butyl acetate was studied, with the aim of rendering the syntheses of these two molecules greener and easier to perform in terms of ester purification. Firstly, we studied the individual syntheses of ethyl acetate and butyl acetate by two different routes, using acetic acid or acetic anhydride with the corresponding alcohols (ethanol or *n*-butanol). Four ion exchange resins were compared: Amberlyst 15 (A15), Amberlyst 16 (A16), Amberlyst 36 (A36) and Dowex 50WX8 (D50). Kinetic studies were performed for all reactions, for both syntheses and routes, to ensure the selection of the best resin for the coproduction process. The recycling of the most effective resin was also evaluated by studying its activity over several production cycles.

The coproduction of ethyl and butyl acetates has already been reported by Tian and coworkers.[256,257] They studied the feasibility of coproduction with the Aspen Plus® simulation tool and then checked the simulated model experimentally. However, the process described requires two reactive distillation columns: one for the synthesis of ethyl acetate and the other for butyl acetate.

The coproduction process proposed here consists of two steps. The first consists of the production of ethyl acetate from ethanol and acetic anhydride in the presence of the ion exchange resin selected in preliminary studies of the catalytic effects of resins on the separate syntheses of the two acetates. In this synthetic route, acetic acid is produced, and water formation is limited, making it possible to purify ethyl acetate by simple distillation. In the second step, *n*-butanol is added to the residual mixture of acetic acid and resin remaining after distillation to purify the product of the first esterification. Finally, the butyl acetate obtained is purified by distilling the heteroazeotrope formed after the addition of a selective entrainer facilitating the liquid/liquid separation of water in the decanter.

2.3.2 Experimental methods

2.3.2.1 Chemicals

Ethanol, *n*-butanol, acetic anhydride, acetic acid, cyclohexane and methyl isobutyl ketone, all analytical grade, were purchased from Sigma Aldrich Co. (France).

2.3.2.2 Catalyst

Heterogeneous ion exchange resins: Amberlyst 15, Amberlyst 16, Amberlyst 36 and Dowex 50WX8 were supplied by Sigma Aldrich Co. (France). They were used as catalysts for the esterification reactions, after washing in water, filtration and drying to constant weight in an oven at 50°C to eliminate any moisture.

2.3.2.3 Synthesis of ethyl acetate (EAc): Selection of catalyst and reaction conditions

In a typical run, a mixture of 0.20 g ethanol (4.4 mmol, 1 equiv.) and 0.26 g acetic acid (4.4 mmol, 1 equiv.) was stirred at 80°C in the presence of the resin (5% w/w relative to ethanol). The reaction was also carried out with 0.25 g ethanol (5.4 mmol, 1 equiv.) and 0.28 g acetic anhydride (2.7 mmol, 0.5 equiv.) or 0.56 g acetic anhydride (5.5 mmol, 1 equiv.). The ethyl acetate obtained was then purified by simple distillation.

2.3.2.4 *Synthesis of butyl acetate (BAc)*

Butyl acetate was produced in a 2 L jacketed glass reactor equipped with a Dean-Stark apparatus. A solution of 800 g *n*-butanol (10.8 mol, 1 equiv.), 648 g acetic acid (10.8 mol, 1 equiv.) and 80 mL cyclohexane (as an entrainer, to remove water from the reaction medium) was stirred in the presence of the resin (5% w/w relative to *n*-butanol) at 105°C for 4 h. The cyclohexane was then removed from the reaction mixture by distillation. The butyl acetate was recovered by filtration of the resin.

2.3.2.5 *Coproduction of ethyl acetate and butyl acetate*

A mixture of 400 g ethanol (8.7 mol, 1 equiv.) and 889 g acetic anhydride (8.7 mol, 1 equiv.) was stirred in the presence of the resin (5% w/w relative to ethanol) in a 2 L jacketed glass reactor at room temperature for 4 h. The ethyl acetate formed was then distilled off from the reaction medium. We then added 400 g *n*-butanol (5.4 mol, 1 equiv.) and 45 mL cyclohexane (5% v/v relative to the reaction mixture) to the reactor containing the remaining acetic acid and resin mixture. The reactor was equipped with a Dean-Stark apparatus (to remove water from the reaction medium). The resulting medium was stirred at 105°C for 4 h. At the end of the reaction, cyclohexane was removed by simple distillation and the butyl acetate was recovered after catalyst filtration.

2.3.2.6 *Analysis methods*

The reaction products were analyzed with a gas chromatograph (VARIAN 3600) equipped with a flame ionization detector. A DB-624 column (AGILENT, 0.25 mm x 30 m, df = 1.4 µm) was used for the analyses. The oven temperature was maintained at 50°C for 2 min, then gradually increased to 100°C at a rate of 5°C/min and then to 190°C at a rate of 25°C/min. The temperature of the detector and the injector was fixed at 300°C. The injection volume of samples was 1 µL, with a 1:100 split. Methyl isobutyl ketone (MIBK) was used as the internal standard. Water content was determined by Karl Fisher titration (SCHOTT Titroline).

2.3.2.7 *Statistical analyses*

Statistical analyses were performed with Minitab 16 software. Data were analyzed by analysis of variance (ANOVA) and with Tukey’s test, with an alpha risk of 0.05 ($p<0.05$).

2.3.3 Results and discussion

2.3.3.1 Study of the synthesis of ethyl acetate with different ion exchange resins

2.3.3.1.a Synthesis of ethyl acetate starting from ethanol and acetic acid

The main industrial process for ethyl acetate (EAc) production involves the esterification of acetic acid (AcOH) with ethanol (EtOH) in the presence of a homogeneous catalyst, generally sulfuric acid. We decided to circumvent the problems relating to the use of homogeneous catalysts, such waste production and separation, and to use a greener approach. We therefore replaced the acid catalyst with a heterogeneous ion exchange resin.

Experiments were carried out with different ion exchange resins, to evaluate the efficiency of conversion of ethanol and *n*-butanol into ethyl acetate and n-butyl acetate (BAc), respectively. Four ion exchange resins were used: Amberlyst 15 (A15), Amberlyst 16 (A16), Amberlyst 36 (A36) and Dowex 50WX8 (D50). The beads of these resins consist of styrene-divinylbenzene copolymers. A15, A16 and A36 are macroporous resins with multichannel structures, whereas Dowex 50WX8 is a gel resin. The properties of these resins are presented in Table 14.

Catalyst	Physical form	Concentration of acid sites	Shipping weight	Fine content	Coarse beads	Surface area	Mean pore diameter	*Ion exchange capacity (meq/g)
Amberlyst 15	Opaque beads	≥1.7 eq/L ≥4.7 eq/kg	610 g/L	< 0.300 mm: 0.5 % max	> 1.180 mm: 5 % max	53 m^2/g	300 Å	4.9
Amberlyst 16	Opaque beads	≥1.7 eq/L ≥4.7 eq/kg	780 g/L	< 0.355 mm: 1 % max	> 1.180 mm: 5 % max	52 m^2/g	300 Å	6.1
Amberlyst 36	Opaque beads	≥1.95 eq/L ≥5.4 eq/kg	800 g/L	< 0.425 mm: 0.5 % max	> 1.180 mm: 4 % max	33 m^2/g	240 Å	4.9
Dowex 50WX8 200-400	Crystalline powder or powder	≥1.7 eq/L	802 g/L	NA	NA	NA	10-20 Å	4.8

Table 14. Characteristics of the resins used for the synthesis of ethyl and butyl acetates. *Ion exchange capacity of resins determined in this work. Standard deviation=0.2 meq/g.

The capacity of each resin was determined in terms of exchangeable counterions per unit dry weight, with a 0.2 M solution of NaOH. Ion exchange capacity is expressed in milliequivalents per gram of resin. The highest resin capacity was obtained with Amberlyst 16 (Table 14). The other resins had similar capacities.

We therefore began by studying the synthesis of ethyl acetate starting from ethanol and acetic acid in a 1:1 molar ratio (Eq. II-1), replacing the homogeneous catalyst with each of the ion exchange resins described in Table 14.

$$CH_3COOH + CH_3CH_2OH \rightleftharpoons CH_3COOCH_2CH_3 + H_2O \qquad \text{Eq. II-1}$$

The reactions were carried out at 80°C and the final composition of the reaction medium was analysed by gas chromatography. The changes in the ethanol, acetic acid and ethyl acetate contents of the reaction medium are reported in Figure 21.

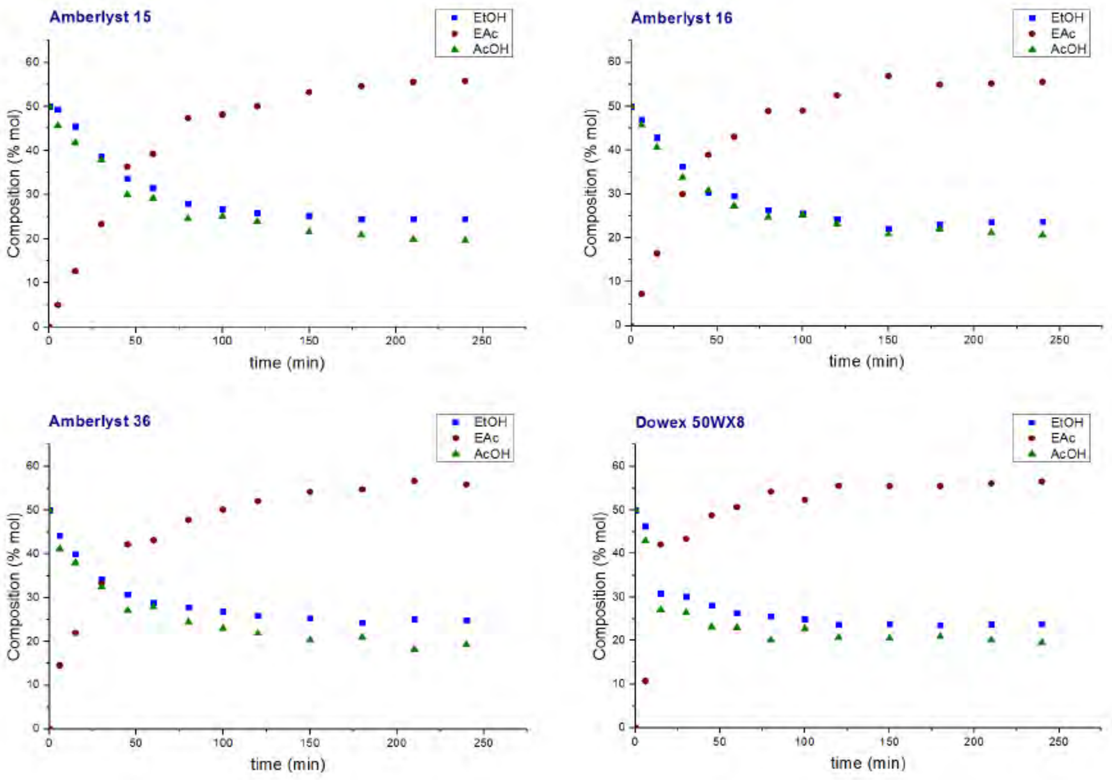


Figure 21. Kinetic study of the synthesis of ethyl acetate from ethanol and acetic acid (molar ratio 1:1) at 80°C, in the presence of the various ion exchange resins: A15, A16, A36 and D50 (catalyst loading: 5% w/w relative to ethanol).

Equilibrium was reached more rapidly with Dowex 50WX8than with the macroporous resins A15, A16 and A36 (90 mins versus 180 minutes). These results are consistent with the report from Lee et al. of a greater efficiency for the gel-type Dowex 50WX8 than for the macroreticular resin Amberlyst 15 in the esterification of acetic acid and amyl alcohol.[268] Similarly, better conversion of 2-propanol with acetic acid was obtained with a gel-type resin (Dowex 50) than with a macroreticular catalyst (Ali et *al*.). The authors suggested that the water formed during the reaction affects gel-type and macroreticular catalysts in different ways, decreasing the activity of macroreticular, but not gel-type catalysts.[290] Indeed, water influences the swelling of Dowex 50WX8, enhancing the exposure of its acid sites and, thus, its activity.[285,287] By contrast, greater cross-linking, as in macromolecular resins, such as Amberlyst 15, decreases water absorption,[305] limiting mass transfer within the polymer beads. Gel-type resins have thus been recommended for reactions in which water is one of the products.[266]

The conversion of ethanol and the yield of ethyl acetate were then determined at equilibrium (Table 15). Similar results were obtained for all the resins tested. The low ethanol conversion can be attributed to the formation of water, which shifts the equilibrium toward the reactants, thereby limiting ethyl acetate production.

Ion exchange resins	Conversion of ethanol (%)	Yield of EAc (%)	Composition of reaction media (%mol)			
			AcOH	Ethanol	EAc	Water[a]
Amberlyst 15	71	69	17	14	35	34
Amberlyst 16	71	69	16	14	34	36
Amberlyst 36	71	69	16	14	35	35
Dowex 50WX8	70	68	16	15	34	35

Table 15. Comparison of the various resins in terms of their ethanol conversion and ethyl acetate yields, for reactions starting from ethanol and acetic acid (molar ratio 1:1). Conditions: resin loading 5% w/w relative to EtOH, 80°C, 4 h. [a]: determined by Karl Fisher titration. SD: ± 2.

2.3.3.1.b *Effect of reaction temperature*

The effect of temperature on ethanol conversion was assessed by setting the temperature to 90, 80, 65, 50 and 40°C. The ethanol conversion plots as a function of reaction temperature are presented in Figure 22. Similar profiles were obtained with all the resins tested (data shown only for Dowex 50WX8). The reaction rate increased with temperature. For the esterification of ethanol and acetic acid, reaction equilibrium was reached after 60 minutes at 90°C, but after 5 h at 50°C.

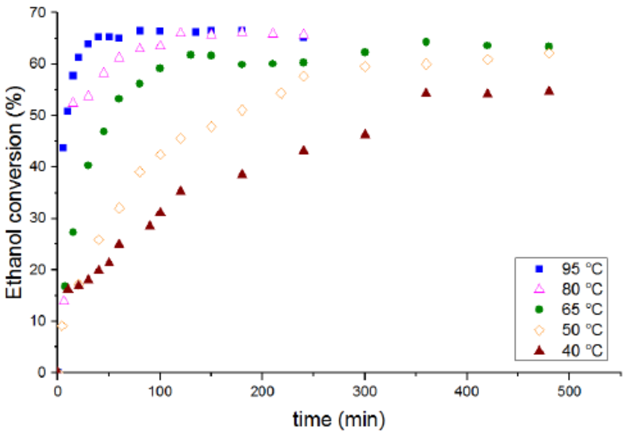


Figure 22. Effect of temperature on ethanol conversion with Dowex 50WX8 as the catalyst. Reaction starting from ethanol and acetic acid (1:1). Catalyst loading: 5% w/w relative to EtOH.

The effect of temperature on the reaction rate was investigated by setting the temperature to 40, 50, 65 and 80°C. The molar ratio of ethanol and acetic acid was kept at 1:1, with a catalyst loading of 5% dry w/w relative to ethanol. Assuming that the esterification reaction is a second-order reaction, the apparent activation energy (E_a) was determined for all resins, by applying the Arrhenius equation to the early part of the reaction. The k value was calculated by plotting ln [EtOH] against time. The k value was obtained from the slope of the tangent to the curve at the origin, which was calculated from the second-degree polynomial equation (Figure 23).

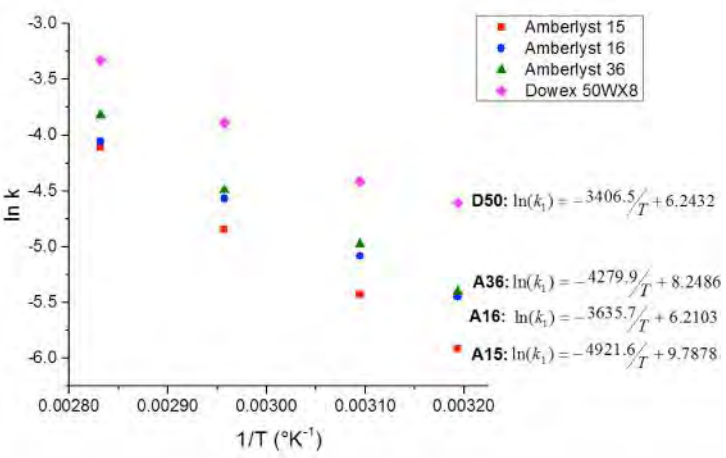


Figure 23. Activation energy determination, natural logarithm of the equilibrium constant as a function of the inverse of temperature.

The activation energy (E_a) was higher for the macroporous resins: it was highest for Amberlyst 15 (40.9 kJ·mol^{-1}), followed by Amberlyst 36 (35.5 kJ·mol^{-1}) and Amberlyst 16 (30.1 kJ·mol^{-1}). The lowest value obtained was that for Dowex 50WX8: 28.3 kJ·mol^{-1}. These values are considerably lower than published values for this reaction catalysed with 5% sulphuric acid (65.6 kJ·mol^{-1})[306] or 0.38 wt% H_2SO_4 (57 kJ·mol^{-1}).[307] Higher E_a values have also been reported for various macroporous resins as catalysts of the esterification of acetic acid and alcohols, such as methanol (SAC 13: 51.8 kJ/mol,[285] Indion 30: 38.13 kJ·mol^{-1},[276] A15: 58.5 kJ·mol^{-1});[308] isobutanol (Amberlite IR120: 49 kJ·mol^{-1}),[273] isoamyl alcohol (Purolite CT175: 47 kJ·mol^{-1})[288] and amyl alcohol (Dowex 50WX8: 47.9 kJ·mol^{-1}).[268] Our results confirm that Dowex 50WX8 catalyses the esterification of ethanol and acetic acid more efficiently than the macromolecular resins A36, A16 and A15. This higher efficiency can be attributed to greater accessibility of the active sites to reagents, thanks to the swelling and low levels of cross-linking (8% divinylbenzene) of the resin.

2.3.3.1.c Synthesis of ethyl acetate starting from ethanol and acetic anhydride

We tried to increase reaction yield and to shift the equilibrium towards ester formation, by testing the resins in another synthetic route, starting from ethanol and acetic anhydride (Eq. II-2)

$$\mathrm{(CH_3CO)_2O + 2CH_3CH_2OH \rightleftharpoons 2CH_3COOCH_2CH_3 + H_2O} \qquad \text{(Eq. II-2)}$$

There are fewer published descriptions of the synthesis of esters from an anhydride. Kolena et *al*. patented a method for synthesizing ethyl acetate by reactive distillation, using a mixture of acetic acid and acetic anhydride.[309] The synthesis of methyl acetate by this route has also been reported.[310,311] This reaction has the advantage of decreasing water formation due to the reaction stoichiometry and partial consumption for the hydrolysis of acetic anhydride into acetic acid.

The esterification reaction starting from ethanol and acetic anhydride (Eq. II-2) is best summarized by the following steps:

$$\mathrm{(CH_3CO)_2O + CH_3CH_2OH \rightleftharpoons CH_3COOCH_2CH_3 + CH_3COOH} \qquad \text{(Eq. II-2.1)}$$

$$\mathrm{CH_3COOH + CH_3CH_2OH \rightleftharpoons CH_3COOCH_2CH_3 + H_2O} \qquad \text{(Eq. II-2.2)}$$

$$\mathrm{(CH_3CO)_2O + H_2O \rightleftharpoons 2CH_3COOH} \qquad \text{(Eq. II-2.3)}$$

We checked our findings suggesting a greater efficiency of Dowex 50WX8, by testing all the resins for catalysis of the esterification of acetic anhydride with ethanol. The reactions were carried out with an ethanol:acetic anhydride molar ratio of 2:1, at 80°C, with A 15, A16, A36 or Dowex 50WX8 as the catalyst. The course of the reactions was followed over a period of 180 min (Figure 24).

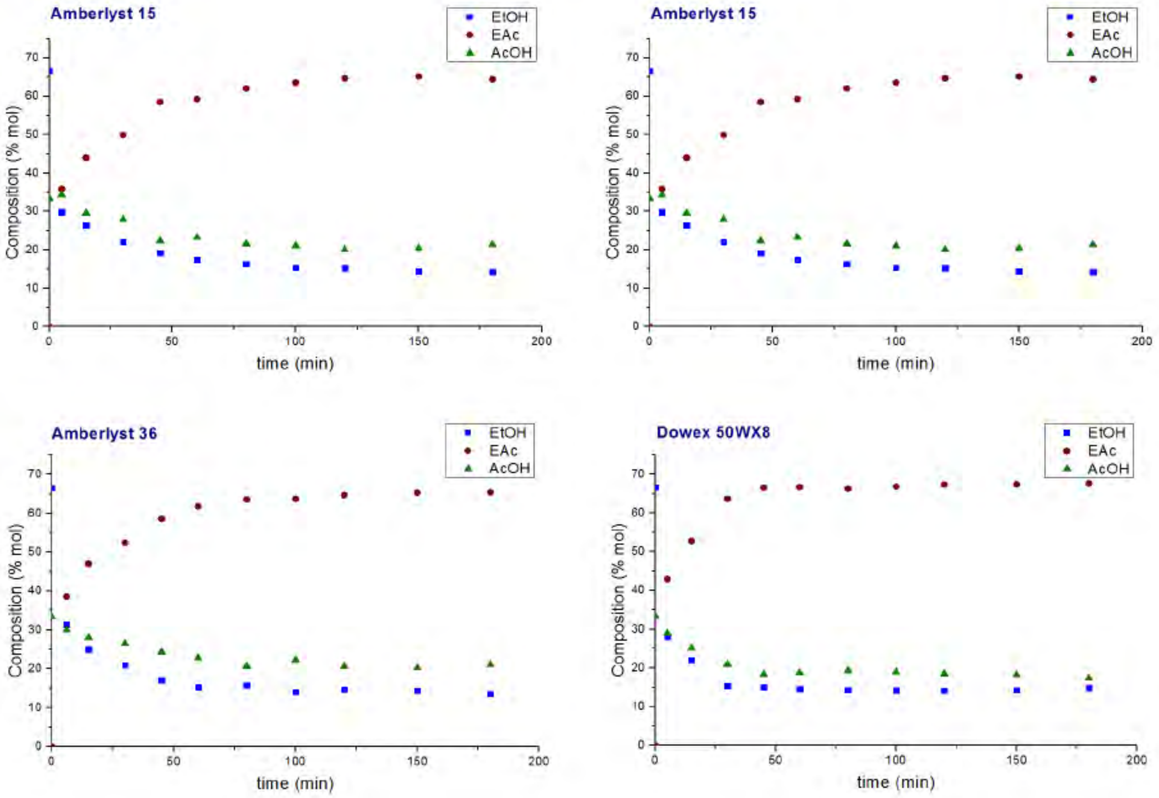


Figure 24. Kinetic study of the synthesis of ethyl acetate from ethanol and acetic anhydride (molar ratio 2:1) at 80°C, in the presence of different ion exchange resins: A15, A16, A36 or D50 (catalyst loading: 5% w/w relative to ethanol).

The equilibrium of the reaction was reached more rapidly if acetic anhydride was used in place of acetic acid. For the macroporous resins A15, A16 and A36, equilibrium was reached after 90 min with acetic anhydride, and 180 min with acetic acid (Figure 24). The reaction performed with acetic anhydride in the presence of Dowex 50WX8 was also slightly faster, reaching equilibrium at 60 min, versus 90 min with acetic acid (Figure 21 vs 24).

The ethanol conversion and the yield of ethyl acetate were determined by GC and similar values were obtained for all four resins at equilibrium. Higher conversion and yields were obtained for reactions starting from acetic anhydride rather than acetic acid (10% increase in conversion; Table 15 vs 16). This may be due to the smaller amount of water in the medium (from 34 to 20%mol, with acetic acid and acetic anhydride, respectively) due to its consumption in the hydrolysis of acetic anhydride into acetic acid, as described in equation 2.1-2.3, shifting the equilibrium to the right.

Ion exchange resin	Conversion of ethanol (%)	Yield of EAc (%)	Composition of reaction media (%mol)			
			AcOH	Ethanol	EAc	Water[a]
Amberlyst 15	81	78	15	13	53	19
Amberlyst 16	80	83	15	13	53	18
Amberlyst 36	80	80	15	13	54	18
Dowex 50WX8	79	83	15	14	54	17

Table 16. Comparison of the different ion-exchange resins in terms of their ethanol conversion and ethyl acetate yields, for the reaction starting from ethanol and acetic anhydride (2:1). Conditions: resin loading 5% w/w relative to EtOH, 80°C, 4 h. [a:] determined by Karl Fisher titration. SD: ± 2.

Based on these kinetic results, Dowex 50WX8 was considered to be the most efficient acidic ion exchange resin for the rapid production of high yields of ethyl acetate. Higher ethanol conversion and reaction yields were also obtained for the reaction starting from ethanol and acetic anhydride. We therefore decided to use these reactants as the starting materials, with Dowex 50WX8 as the catalyst, in subsequent studies.

2.3.3.1.d Evaluation of Dowex 50WX8: catalyst loading and reusability

The influence of catalyst loading on the ethyl acetate yield obtained at equilibrium was evaluated with a 2:1 molar ratio of ethanol:acetic anhydride. The reaction was carried out at 80°C for 4 h, with a catalyst loading of 2.5%, 5% and 10% dry weight relative to the weight of ethanol. Ethyl acetate yield increased with resin loading (Figure 25). Nevertheless, for confirmation of the positive effect of the increase in catalyst loading on ethyl acetate yield, an analysis of variance (ANOVA) was performed. Ethyl acetate yield differed significantly between resin loadings (α=0.05, p=0.041). Nevertheless, a Tukey test showed that there was no significant difference between catalyst loadings of 5% and 10%. We therefore considered a catalyst loading of 5% to be sufficient to obtain the maximum yield of ethyl acetate.

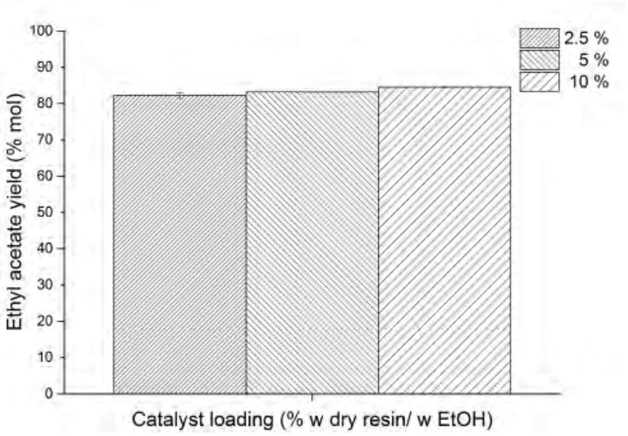


Figure 25. Evaluation of the effect of catalyst loading on EAc yield

The reusability of Dowex 50WX8 was then assessed by evaluating ethyl acetate yield after several recycling runs (Figure 26). The test was performed with the same catalyst for four consecutive runs, under the same conditions; the catalyst was filtered and washed with water between runs. The analysis of variance (ANOVA) showed that there was no significant difference in ethyl acetate yield between the runs on reused resin (α=0.05, p=0.073). The catalyst is thus reusable and resin reactivation is not required, at least in these conditions.

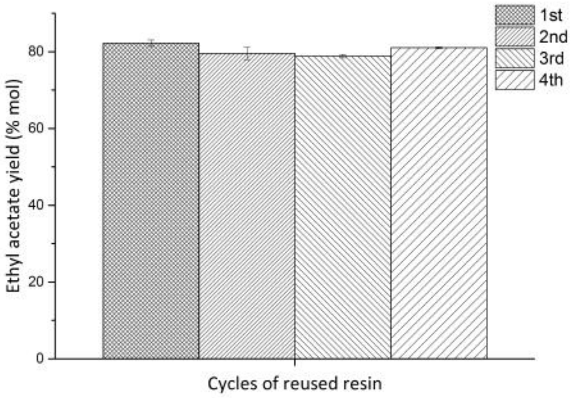


Figure 26. Effect of the reused resin on EAc yield

2.3.3.1.e Purification of ethyl acetate

In the ethyl acetate reaction system, there are three binary azeotropes and one ternary azeotrope. As the boiling point of the pure components (ethyl acetate 77.2°C, ethanol 78.3°C, water 100°C, acetic acid 118°C) and the azeotropes they form are very similar, it is difficult to achieve efficient purification by distillation. The composition and boiling points of the azeotropes are shown in Table 17.

Azeotropes	Boiling Point (°C)	Molar fractions		
		EtOH	EAc	H_2O
EtOH/EAc/H_2O	70.09	0.1069	0.6073	0.2858
EAc/H_2O	70.37	-	0.6869	0.3131
EtOH/EAc	71.81	0.4572	0.5428	-
EtOH/H_2O	78.18	0.9016	-	0.0984

Table 17. Boiling points and molar fractions of the various azeotropes in the ethyl acetate system[312]

The use of extractive methods for ethyl acetate purification is also limited because this compound forms azeotropes with conventional solvents used for water removal, such as benzene (bp=102.45°C), cyclohexene (bp=100.87°C), cyclohexane (bp=102.45°C), 1-hexene (bp=91.47°C) and hexane (bp=101.32°C).[313]

The yield and purity of ethyl acetate (limitation of water formation) can be improved by reactive distillation (RD), to shift the chemical equilibrium and overcome azeotropic limitations.[300,314,315] Pervaporation (PV) has been proposed for the separation of azeotropes or the dehydration of organic compounds.[301,316,317] Hybrid processes, combining pervaporation with other separation techniques, for example, have also been described,[301,318,319] but these techniques involve a complex analysis of the configuration of the columns and require special equipment. We therefore developed an alternative strategy for improving yield and facilitating ethyl acetate purification with conventional laboratory equipment (Section 2.3.3.3).

2.3.3.2 Study of the synthesis of n-butyl acetate with various ion exchange resins

2.3.3.2.a Synthesis of butyl acetate starting from n-butanol and acetic acid

After studying the synthesis of ethyl acetate, we decided to evaluate Dowex 50WX8 as a catalyst for the production of butyl acetate (BAc). The synthesis of butyl acetate starting from a 1:1 molar ratio of *n*-butanol and acetic acid (Eq. II-3) was first studied, with each of the four ion exchange resins tested for ethyl acetate synthesis as the catalyst (A15, A16, A36 and D50).

$$\mathrm{CH_3(CH_2)_3OH + CH_3COOH \rightleftharpoons CH_3COO(CH_2)_3CH_3 + H_2O} \qquad \text{(Eq. II-3)}$$

The reactions were performed at 100°C, and changes in the composition of the reaction medium were followed for 4 h (Figure 27).

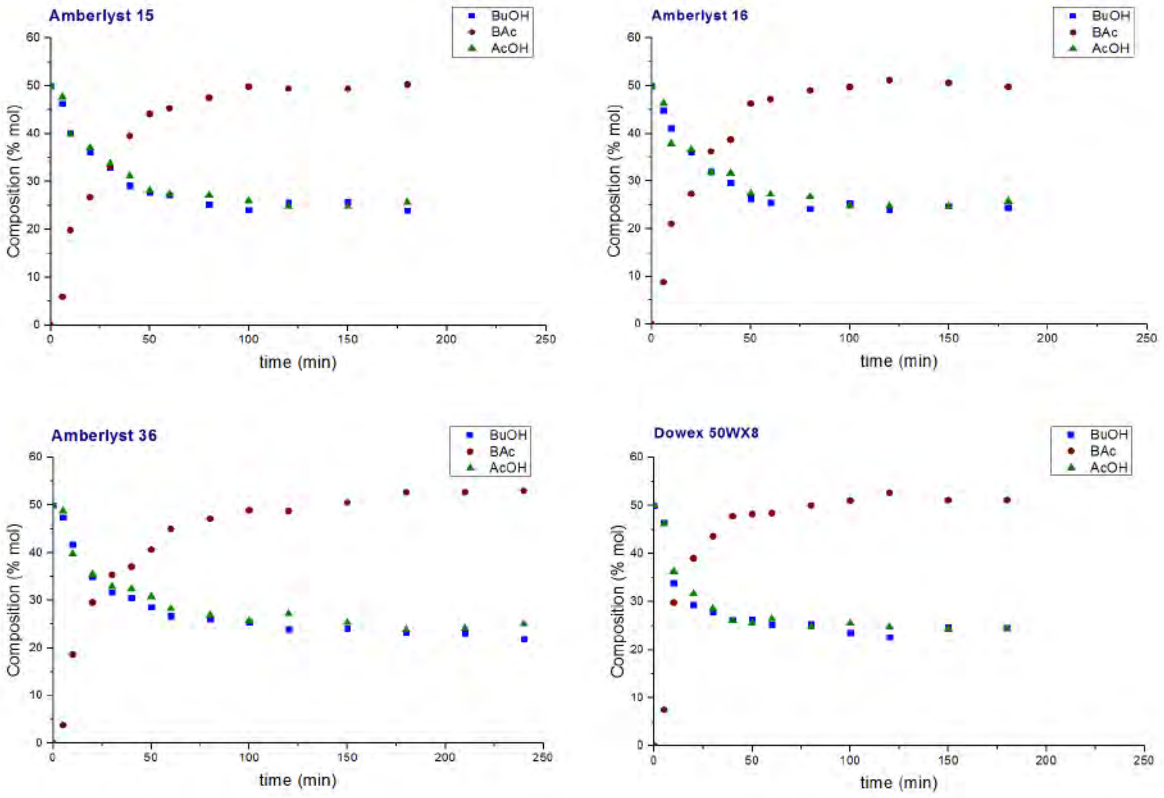


Figure 27. Kinetic study of the synthesis of butyl acetate from *n*-butanol and acetic acid (molar ratio 1:1) at 100°C in the presence of different ion exchange resins: A15, A16, A36 and D50 (catalyst loading: 5% w/w relative to *n*-butanol).

Equilibrium was reached after about 50 minutes with Dowex 50WX8. A similar profile was obtained with A16, whereas it took 100 minutes to reach equilibrium with A15 and A36.

The *n*-butanol conversion and the yield in n-butyl acetate were determined at equilibrium, by GC analyses (Table 18).

Ion exchange resins	Butanol conversion (%)	Yield of BAc (%)	Composition of reaction media (%mol)			
			AcOH	Butanol	BAc	Water[a]
Amberlyst 15	68	74	17	16	38	29
Amberlyst 16	71	61	17	16	35	32
Amberlyst 36	72	68	18	16	37	29
Dowex 50WX8	71	66	17	16	36	31

Table 18. Comparison of the various ion exchange resins in terms of *n*-butanol conversion and butyl acetate yield, for reactions starting from *n*-butanol and acetic acid (1:1). Conditions: resin loading 5%w/w BuOH, 100°C, 4 h. [a]: determined by Karl Fisher titration. Standard deviation: ± 2%.

The *n*-butanol conversion and the yield of BAc were similar for all four resins. As for ethyl acetate, the low conversion was attributed to the formation of water, shifting the equilibrium towards the reactant side.

2.3.3.2.b Effect of reaction temperature

The effect of temperature on the conversion of *n*-butanol and the esterification of butanol and acetic acid was also studied, by setting the temperature at 100°C, 80°C, 70°C, 60°C and 50°C. Butanol conversion was plotted as a function of temperature (Figure 28). The reaction rate increased with increasing temperature, with the fastest conversion of butanol observed at 100°C. Equilibrium was reached after about 80-100 min at this temperature, whereas it took 180 minutes at 60°C.

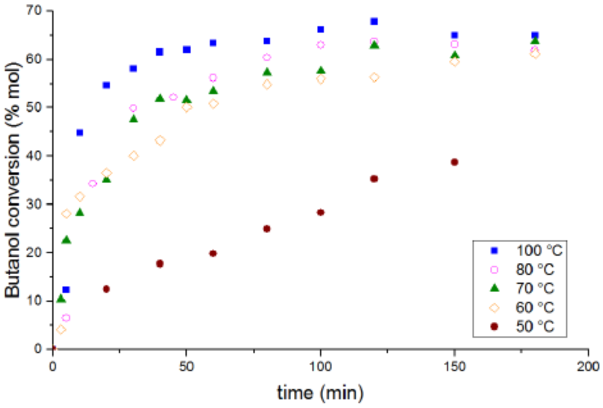


Figure 28. Effect of temperature on the conversion of n-butanol.

The activation energy (E_a) was determined from the Arrhenius plot between ln(k) and 1/T, at 80°C, 70°C, 60°C and 50°C. The molar ratio of *n*-butanol:acetic acid was maintained at 1:1, with a catalyst loading of 5% w/w BuOH. The k value was calculated from the slope of the tangent to the curve at the initial time point, for the second-degree polynomial equation. The values of E_a were: A15, 59.5 $kJ \cdot mol^{-1}$; A16, 32.2 $kJ \cdot mol^{-1}$; A36, 67.7 $kJ \cdot mol^{-1}$ and Dowex 50WX8, 47.6 $kJ \cdot mol^{-1}$. Similar values have been reported for Dowex 50WX8 for the esterification of isobutanol/acetic acid at a molar ratio of 1:1 (59.3 $kJ \cdot mol^{-1}$).[286]

2.3.3.2.c Synthesis of butyl acetate starting from n-butanol and acetic anhydride

Following the same route as for ethyl acetate, and to increase butyl acetate yield, *n*-butanol and acetic anhydride were used as the starting reactants, at a molar ratio of 2:1.

$$2CH_3(CH_2)_3OH + (CH_3CO)_2O \rightleftharpoons 2CH_3COO(CH_2)_3CH_3 + H_2O \qquad \text{(Eq. II-4)}$$

The reactions were carried out in the same conditions as for acetic acid: 100°C, for 4 h, with a catalyst loading of 5% w/w relative to butanol. The changes in n-butanol, acetic acid and butyl acetate content were plotted over time (Figure 29).

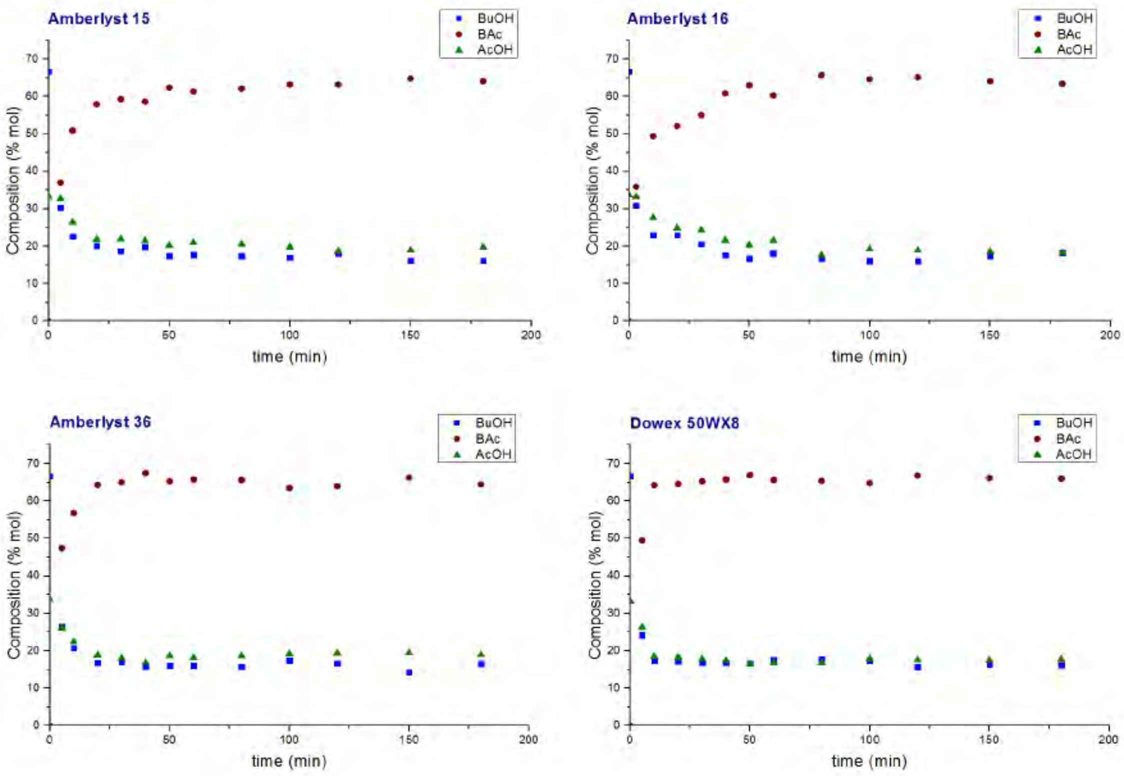


Figure 29. Kinetic study of the synthesis of butyl acetate with n-butanol and acetic anhydride (molar ratio 2:1) as the starting materials, at 100°C, in the presence of various ion exchange resins. A15, A16, A36 and D50 (catalyst loading: 5% w/w relative to butanol weight).

Equilibrium was reached more rapidly with Dowex 50WX8 (10 min) than with the other resins. For the macroporous resins A15, A16 and A36, butyl acetate content reached a maximum after 50 min. These results are consistent with those for ethyl acetate production, for which Dowex also had the most rapid kinetics.

Butanol conversion and butyl acetate yield increased by 10% (from 70% to 80%) when acetic acid was replaced with acetic anhydride (Table 18 & 19). Water content was reduced from 30% to 15% if acetic anhydride was used as the starting material. This decrease in the water content of the reaction medium displaced the equilibrium to the right, enhancing butyl acetate production.

Resin	Butanol conversion (%)	Yield of BAc (%)	Composition of reaction media (mol%)			
			AcOH	Butanol	BAc	Water[a]
Amberlyst 15	79	68	17	16	51	17
Amberlyst 16	81	82	16	13	55	16
Amberlyst 36	81	81	14	13	57	16
Dowex 50wx8	81	83	15	13	57	15

Table 19. Comparison of the various ion exchange resins in terms of n-butanol conversion and butyl acetate yield, starting from n-butanol and acetic anhydride (2:1). Conditions: catalyst loading of 5% w/w relative to BuOH, 100°C, 4 h. [a]: determined by Karl Fisher titration. Standard deviation: ± 2.

The best results were obtained with n-butanol and acetic anhydride as the starting materials, and Dowex 50WX8 as catalyst.

2.3.3.2.d Purification of butyl acetate

In the synthesis of butyl acetate (bp=126.1°C) from *n*-butanol (bp=117.7°C) and acetic acid (bp=118.1°C), three binary azeotropes and one ternary azeotrope are present (Table 20).[313,320]

Azeotrope	Boiling point (°C)	Molar fractions		
		BuOH	BAc	H_2O
BAc/H_2O	90.2	-	0.2876	0.7134
BuOH/BAc	117.6	0.7329	0.2671	-
BuOH/H_2O	93.0	0.2218	-	0.7782
BuOH/BAc/H_2O	90.7	0.0551	0.24	0.7049

Table 20. Boiling points and molar fractions of the various azeotropes in the butyl acetate system.[227,320,321]

For butyl acetate production, an entrainer, such as cyclohexane (80.74°C), can be used to remove the water produced during the reaction, shifting the equilibrium and increasing both butanol conversion and butyl acetate yield. A Dean Stark apparatus was used (in the reaction from acetic acid) to produce an azeotropic mixture of cyclohexane and water (69.5°C), and the azeotrope was distilled out of the reaction mixture. The composition of the reaction medium after butyl acetate purification is presented in Table 21.

BuOH conversion (%)	Yield of BAc (%) after distillation	Composition of the reaction media			
		AcOH	BuOH	BAc	H_2O
99	76	(mol%)			
		0.8	1.7	91.2	6.4
		(%w/w)			
		0.4	1.1	97.4	1.1

Table 21. Composition of the purified butyl acetate obtained by the esterification of butanol and acetic acid in a molar ratio of 1:1. Conditions: loading of 5% w/w Dowex 50wx8/BuOH, 100°C, 4 h. [a:] determined by Karl Fisher titration. SD: ±2.

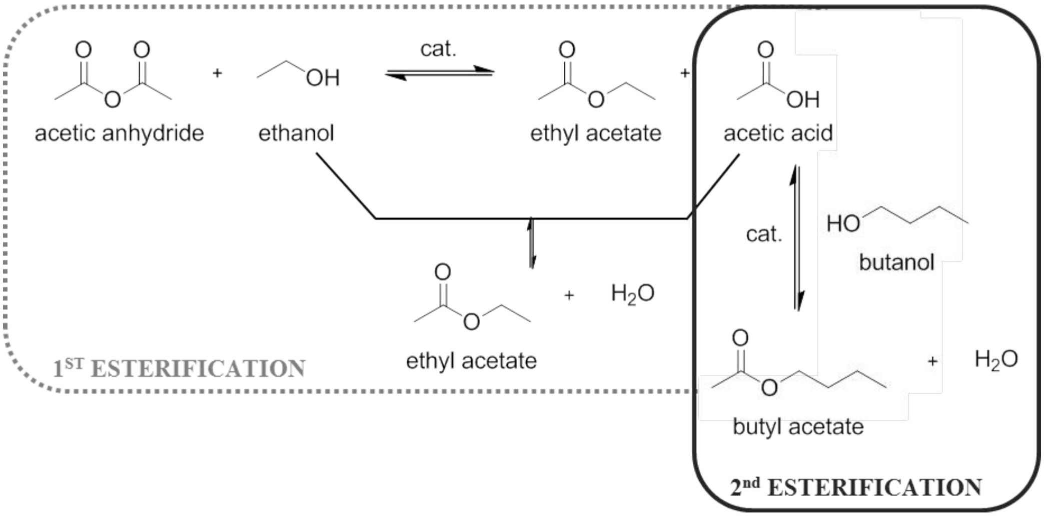
After separation, *n*-butyl acetate was obtained at a purity of 97.4%, with only very small amounts of *n*-butanol and acetic acid that did not react and a small amount of residual water in the mixture. Butanol conversion was increased from 70 to 99% by removing water during the reaction but the yield of butyl acetate increased by only 10% (from 66% to 76%; table 18 vs. 21). A larger increase might have been expected given the improvement in conversion. This relatively low yield after distillation, even with the removal of water, may be due to the double distillation required to remove first water, and then cyclohexane from the medium.

The purity of the butyl acetate obtained was further increased by removing the 1.1% of water remaining in the medium by adding molecular sieves (3A) in distilled BAc. The water content measured 24 hours later was 0.002% (Karl Fisher titration).

These studies of the esterification of ethanol or butanol with acetic acid or acetic anhydride show that alcohol conversion and reaction yields are higher if acetic anhydride is used (rather than acetic acid), but the use of this starting material leads to the generation of acetic acid as waste. Thus, to meet the requirements of a circular economy, we decided to use co-product of the reaction in a second esterification, as described below.

2.3.3.3 Coproduction of ethyl acetate and n-butyl acetate

As previously stated, ethyl acetate is difficult to purify due to the formation of azeotropes with water. Thus, to facilitate the purification of ethyl acetate and to avoid the production of waste when acetic anhydride is used as a reactant (instead of acetic acid), an acetate coproduction strategy was adopted (Scheme 9):



Scheme 9. Coproduction of ethyl acetate and n-butyl acetate

In the first step, the esterification of ethanol and acetic anhydride at an equimolar ratio generates ethyl acetate and acetic acid in the presence of the ion exchange resin Dowex 50WX8. Ethyl acetate is easily removed from the reaction mixture by simple distillation.

The second step involves a second esterification reaction between the acetic acid generated in the first reaction and n-butanol, which is added to the reactor to produce butyl acetate (Figure 30).

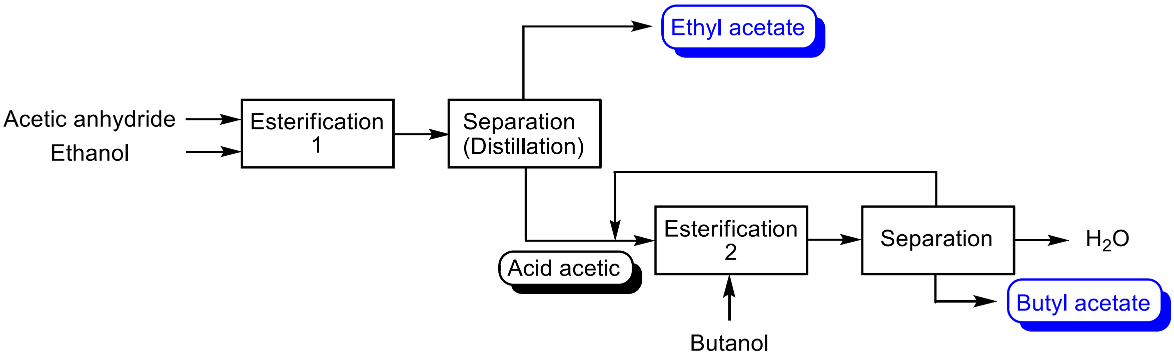
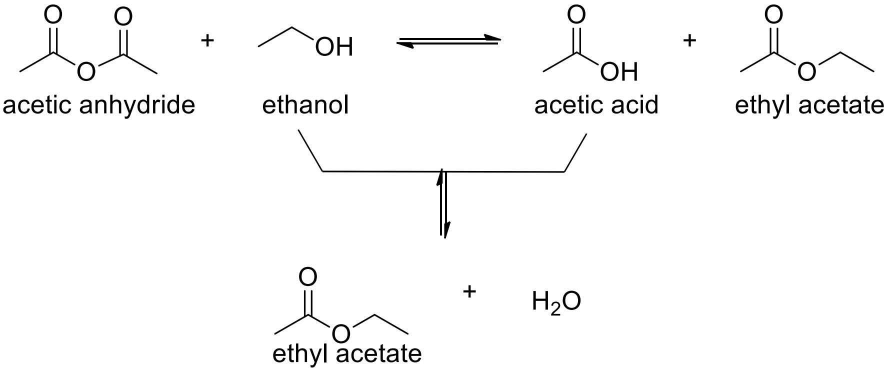


Figure 30. Coproduction process for ethyl and butyl acetates

2.3.3.3.a First step: synthesis of ethyl acetate and production of acetic acid

In the synthesis of ethyl acetate from ethanol and acetic anhydride (molar ratio of 1:1), acetic acid is also produced (Scheme 10). The reaction is exothermic and no heating is required.



Scheme 10. First step in the coproduction process: synthesis of ethyl acetate from acetic anhydride and ethanol at a molar ratio of 1/1.

As shown in table 22, water content was reduced from 20 to 3% (molar percentage) by using an equimolar ratio of acetic anhydride and ethanol (Table 16 vs 22). The stoichiometry of the reaction is consistent with a total absence of water formation, but the presence of this small amount of water can be explained by a slower competitive esterification between the acetic acid generated in the first reaction and the remaining ethanol (Scheme 10). The water generated in this way can also be consumed in the hydrolysis of acetic anhydride to generate acetic acid, with the release of heat. The use of an equimolar ratio of ethanol and acetic anhydride thus gave very high yields of ethyl acetate (98%) and a high ethanol conversion (99.4%) at the end of the reaction (Table 22).

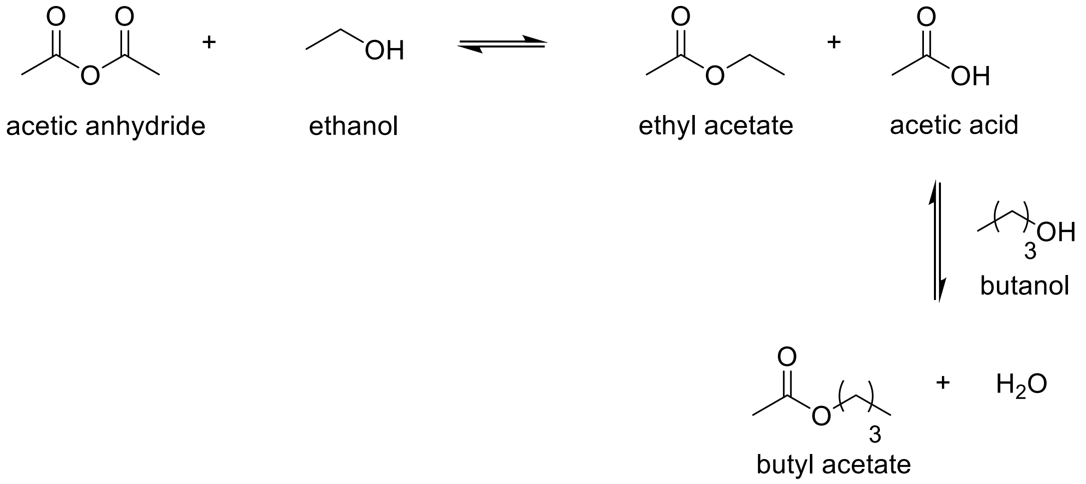
The low water content of the crude mixture facilitates the purification of ethyl acetate. Simple distillation yields a mixture composed principally of ethyl acetate and small amounts of acetic acid and water (Table 22).

	Conversion of EtOH (%)	Yield of EAc (%)	Composition of the reaction medium				
			%	AcOH	EtOH	EAc	H_2O
At the end of reaction	99.4	98	mol	48.4	0.3	48.5	2.8
			w/w	40.1	0.2	59.0	0.7
After distillation	100	87	mol	9.1	0.0	85.4	5.4
			w/w	6.7	0.0	92.1	1.2

Table 22. Composition of the crude reaction mixture and of the distilled ethyl acetate obtained from ethanol and acetic anhydride, at a molar ratio of 1/1, at room temperature for 4 h.

2.3.3.3.b Second step: synthesis of n-butyl acetate

From the reaction of ethanol and acetic anhydride at a molar ratio of 1:1, a mixture of acetic acid and ethyl acetate (77.5% and 22.5% w/w, respectively) remains in the reactor in large amounts, together with the resin, after the removal, by distillation, of most of the ethyl acetate. With a view to preventing waste and recycling this mixture, we propose the addition of *n*-butanol to the reactor for a second esterification reaction to produce *n*-butyl acetate (Scheme 11).



Scheme 11. Coproduction of ethyl acetate and butyl acetate

The use of the acetic acid/ethyl acetate mixture generated by the first esterification had no influence on the synthesis of butyl acetate. As in the individual synthesis of this molecule, the reaction was carried out with a Dean Stark apparatus and the addition to the mixture of a small amount of cyclohexane to remove water from the reaction. Similar butanol conversion was obtained for both the individual and coproduction syntheses (99% and 94%, respectively). After the purification of butyl acetate, a mixture consisting principally of butyl acetate was obtained (97.1% w/w). Traces of acetic acid, butanol, ethyl acetate and water were detected (Table 23).

Conversion of BuOH (%)	Yield of BuAc (%)	Composition of the reaction media						
		%	AcOH	BuOH	EtOH	BAc	EAc	H_2O
94	69	mol	0.2	2.9	0.0	92.7	0.2	3.9
		w/w	0.1	1.9	0.0	97.1	0.2	0.6

Table 23. Composition of the purified butyl acetate obtained with the coproduction process.

The proposed novel coproduction process is an interesting way to produce ethyl acetate and butyl acetate, as it generates no waste, and all the reactants are consumed in the reaction, resulting in high yields of the desired esters. Recycling of the resin is also possible.

2.3.4 Conclusions

We propose here a sustainable and innovative process for the coproduction of ethyl acetate and butyl acetate that respects the principles of green chemistry. Ion exchange resins were used to replace homogeneous catalysts, to reduce waste generation. The gel-type resin Dowex 50WX8 outperformed the other macroporous resins tested, for the production of ethyl and butyl acetates.

The first step in the coproduction process was the synthesis of EAc from ethanol and acetic anhydride at a 1:1 molar ratio. This reaction produces EAc and acetic acid and decreases water production, thereby facilitating the purification of ethyl acetate. In the second step, the acetic acid generated by the first reaction is used as a starting material for a second esterification to produce butyl acetate.

This innovative process prevents waste, facilitates the purification of the desired acetates and reuses by-products and the catalyst.

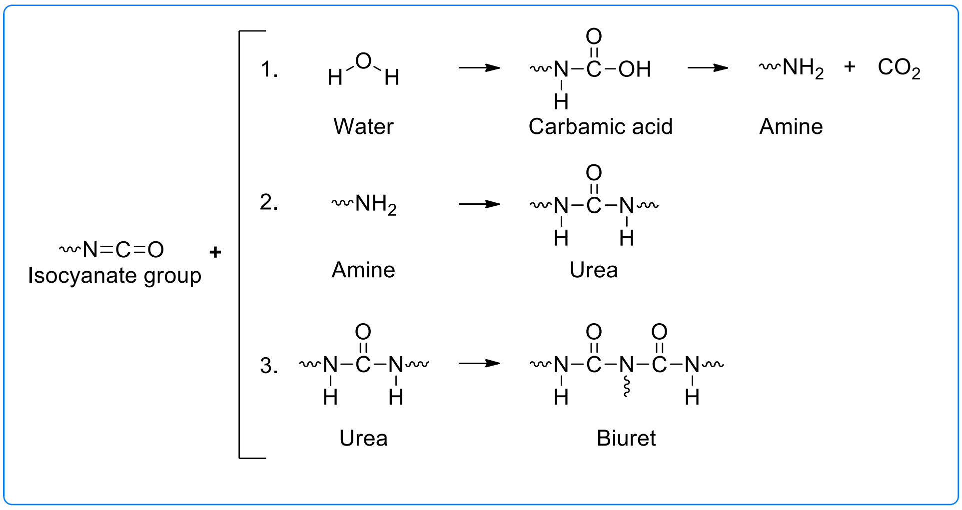
2.4 Characterization of the synthesized ethyl and butyl acetates

Ethyl acetate and butyl acetate were synthesized using the developed co-production process (previously described in §2.3.3.3. Ethyl acetate was manufactured using bio-ethanol provided by the Spanish company ABENGOA. Butyl acetate was produced from conventional butanol since none of the companies declaring its bio-based production were in a position to provide it.
These esters were subsequently purified in order to meet two criteria (mentioned below) required for the coating preparation. Then, they were characterized to verify that they can be used as solvents in paint and coating formulations.

2.4.1 Solvent specifications for its use in paint and coating formulations: problem solving due to the presence of water and acetic acid

Before carrying out the characterization of the synthesized acetates, some considerations related to the water and acetic acid contents had to be taken into account. The presence of these molecules can indeed be a problem in the paint and coating formulations:

- Regarding the presence of water, it can reduce the transparency and gloss in paints, lacquers and varnishes, and can also react with some components of coatings such as the isocyanates (used in the preparation of hardeners in polyurethane systems), involving the presence of solid in the hardener formulation. Indeed, isocyanate groups react with water producing primary amines that crosslink with the isocyanate excess forming symmetric urea, which in turn can react with isocyanate, producing isocyanate-biuret[322,323] (white solid; Scheme 12).



Scheme 12. Side reactions provoked by water[323,324]

Therefore, maximum water residual content of 0.5 % is tolerated in solvent-borne formulations, according with our project partner **Industrias Quimicas IRURENA** (SME from SPAIN, experts in wood coatings).

- The presence of acetic acid (AcOH) in the solvents could cause instability in urethane and epoxy-amine coating-systems.[325] Indeed, the acetic acid can diffuse into the film and forms ammonium acetate salts with the amine groups. This hydrophilic salt increase the solubility of water in the film, increasing thus water permeability and making the film more sensible to damages. [326] Besides, acetic acid can react with pigments provoking color modifications.[22]

Considering the problems that water and acetic acid can cause in paint and coating formulations, we decided then to neutralize the acetic acid from the solvents using potassium hydroxide, in equimolar amount respect to the acid. Thus, there was no more acetic acid in the solvent (Table 24).

In addition, we used molecular sieves 3A (20 %w/v respect to the solvent) during 48 h to reduce the water content. It was efficiently decreased from 1.2 to 0.07 %w/w.

Composition of ethyl acetate (EAc)	AcOH (% w/w)	EtOH (% w/w)	EAc (% w/w)	H_2O (% w/w)
After distillation	6.7	0.0	92.1	1.2
After neutralization and drying	0.0	0.0	99.93	0.07

Table 24. Composition of ethyl acetate (%w/w) after neutralization by KOH and drying with molecular sieves 3A

In the case of BAc, the addition of potassium hydroxide used for the acetic acid neutralization slightly hydrolysed the butyl acetate, increasing of the BuOH content (Table 25 and 26). Fortunately, butanol should not represent a problem in the formulations because it is usually added to butyl acetate to increase its solvency.[327]

Composition of butyl acetate (BAc)	AcOH (% w/w)	BuOH (% w/w)	BAc (% w/w)	H_2O (% w/w)
After distillation	0.4	1.1	97.4	1.1
After neutralization and drying	0.0	1.5	98.1	0.4

Table 25. Composition of butyl acetate from the individual synthesis (%w/w) after neutralization by KOH and drying with molecular sieves 3A

Composition of butyl acetate from the co-production	AcOH (% w/w)	BuOH (% w/w)	EtOH (% w/w)	BAc (% w/w)	EAc (% w/w)	H_2O (% w/w)
After distillation	0.1	1.9	0.0	97.1	0.2	0.6
After neutralization and drying	0.0	5.5	0.0	94.2	0.2	0.03

Table 26. Composition of butyl acetate from the co-production process (%w/w) after neutralization by KOH and drying with molecular sieves 3A

The addition of KOH and the molecular sieves to the synthesized acetates was thus a successfully strategy to make the solvents purer thanks to the elimination of acetic acid and water from them. In this way the solvents achieve the requirements for their use in paint and coating formulations.

2.4.2 Physicochemical characterization of the “purified” acetates

Once the synthesized acetates were “purified” by removing water and acetic acid, the physicochemical characterizations were determined and compared with those of the commercial fossil-based versions of these esters in order to check if these molecules produced according to a greener pathway can be used in paint and coating formulations without properties change.

Structural analyses of ^{1}H NMR and FTIR were thus carried out and the Hansen solubility parameters were determined.

2.4.2.1 Nuclear Magnetic Resonance (NMR) analyses

The nuclear magnetic resonance spectra of the “purified” acetates (obtained from the individual syntheses and the co-production process after neutralization and drying) were acquired with a FOURIER 300 spectrometer from BRUKER CORPORATION (300 MHz). The temperature probes were set at 300°C. Samples were dissolved in deuterated chloroform ($CDCl_3$). Standard pulse sequences were used for ^{1}H. The multiplicity of signals is denoted by singlet (s), doublet (d), triplet (t), quadruplet (q) and multiplet (m).

- **Ethyl acetate (EAc):**

In the case of ethyl acetate, only the characteristic signals of this ester are observed, confirming its high purity determined by GC analysis (99.93 %w/w).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.10 (q, J = 7.1 Hz, 2H, CH_2CH_3), 2.02 (s, 3H, CH_3CO), 1.24 (t, J = 7.1 Hz, 3H, CH_2CH_3).

- ***n*-Butyl acetate individual synthesis (BAc):**

In the NMR analysis of the butyl acetate produced in the individual synthesis, only the characteristic signals of BAc are observed. The amount of butanol (1.1 %w/w determined by GC analysis) present in the sample is too small to be observed on the NMR spectrum.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.04 (t, J = 6.7 Hz, 2H, OCH_2), 2.02 (s, 3H, CH_3CO), 1.69 – 1.50 (m, 2H, OCH_2CH_2), 1.45 – 1.27 (m, 2H, CH_2CH_3), 0.91 (t, J = 7.3 Hz, 3H, CH_2CH_3).

- ***n*-Butyl acetate (Bac) of the coproduction process:**

In the NMR analysis of butyl acetate obtained from the coproduction process, the characteristic signals of butyl acetate are observed, as well as those of butanol since its concentration is higher (5.5 %w/w) than in the BAc produced individually (1.1 %w/w).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.06 (t, J = 6.7 Hz, 2H, **BAc**), 3.67-3.62 (m, 0.22H, BuOH), 2.04 (s, 2.97H, **BAc**), 1.62 – 1.51 (m, 2.48H, **BAc**, BuOH), 1.45-1.32 (m, 2.19H, **BAc** + BuOH), 0.93 (t, J = 7.3 Hz, 3.24H, **BAc**, BuOH).

2.4.2.2 Infrared (FTIR) analysis

Infrared spectra of the ethyl acetate and *n*-butyl acetate prepared from the individual syntheses and the co-production process were obtained with a spectrophotometer Spectrum 65 (PERKIN ELMER), used in ATR mode (Attenuated Total Reflection) with a spectral range of the wavenumber between 700 and 4000 cm^{-1} and a resolution of 2 cm^{-1}.

- **Ethyl acetate:**

In the FTIR spectrum of ethyl acetate, only the characteristic bands of the ester (corresponding to C=O and C-O vibrations) and alkyl (corresponding to C-H vibrations) groups are observed, which again highlights the high purity of the compound (99.93 % w/w). The main IR bands for ethyl acetate are show in table 27.

Characteristic IR bands	Wavenumber (cm^{-1})
C=O saturated stretch from EAc	1737
Alkyl C-H stretch from EAc	3022-2872
C-O stretch from EAc	1235 and 1045

Table 27. Characteristic IR bands of ethyl acetate

- **Butyl acetate (BAc) from the individual synthesis and the coproduction process:**

The FTIR spectra of butyl acetate from the individual synthesis and the co-production show the characteristic vibration bands of ester and alkyl groups. However, the O-H band due to the presence of butanol is only observed in the IR spectrum of BAc from the coproduction, as its amount is higher than in the BAc from the individual synthesis (0.8 % w/w *vs* 5.5 %w/w).

These results are consistent with the NMR analyses. The main IR bands for both BAc from individual and co-production are shown in table 28.

Characteristic IR bands	BAc (individual)	BAc (co-production)
	Wavenumber (cm^{-1})	
C=O stretch saturated from BAc	1739	1741
Alkyl C-H stretch from BAc	2938-2961	2935-2961
C-O stretch from BAc	1229 and 1031	1244 and 1031
O-H stretch from butanol	----	3200-2718

Table 28. Characteristic IR bands of butyl acetate from the individual synthesis and the co-production process

2.4.2.3 Experimental determination of Hansen solubility parameters

To determine experimentally the Hansen solubility parameters (HSP) of the synthesized acetates, 49 solvents were selected based on their own solubility parameters to cover the whole Hansen space with an optimal solvent distribution of solvents (Table 29).

The solubility of the synthesized ethyl and butyl acetates in the selected solvents were then tested by preparing mixtures (50:50 for the volume ratio) with 0.5 mL of acetate and 0.5 mL of the selected solvent at room temperature. The binary mixtures were homogenized into an ultrasonic bath during 5 min and then allowed to stand for 10 minutes. Visual observations were directly made in order to determine if the liquids were miscible or immiscible. Immiscibility was evidenced by the presence of two distinct phases or by the presence of turbidity. These observations were then translated into ratings: 1 if miscible or 0 if immiscible (Table 29).

#	Solvents	δd $(MPa)^{1/2}$	δp $(MPa)^{1/2}$	δh $(MPa)^{1/2}$	[a]Ratings (1=miscible, 0=immiscible)		
					EAc	[b]BAc (Ind)	[c]BAc (Copr)
1	Glycerol-water (70:30)	16,8	12,7	31,7	0	0	0
2	Acetone	15,5	10,4	7	1	1	1
3	Acetonitrile	15,3	18	6,1	1	1	1
4	Acetophenone	18,8	9	4	1	1	1
5	Anisole	17,8	4,4	6,9	1	1	1
6	Benzyl alcohol	18,4	6,3	13,7	1	1	1
7	1-Butanol	16	5,7	15,8	1	1	1
8	Carbon disulfide	20,2	0	0,6	1	1	1
9	Chlorobenzene	19	4,3	2	1	1	1
10	1-Chlorobutane	16,2	5,5	2	1	1	1
11	Chloroform	17,8	3,1	5,7	1	1	1
12	Cyclohexane	16,8	0	0,2	1	1	1
13	Cyclohexanone	7,8	8,4	5,1	1	1	1
14	Decane	15,7	0	0	1	1	1
15	o-Diclorobenzene	19,2	6,3	3,3	1	1	1
16	Diethyl carbonate	15,1	6,3	3,5	1	1	1
17	Diethyl ether	14,5	2,9	4,6	1	1	1
18	Dimethyl carbonate	15,5	8,6	9,7	1	1	1
19	Dimethyl sulfoxide (DMSO)	18,4	16,4	10,2	1	1	1
20	1,4-Dioxane	17,5	1,8	9	1	1	1
21	Ethanol	15,8	8,8	19,4	1	1	1
22	Ethyl acetate	15,8	5,3	7,2	1	1	1
23	Ethyl benzene	17,8	0,6	1,4	1	1	1
24	Ethyl lactate	16	7,6	12,5	1	1	1
25	2-Ethylhexanol	15,9	3,3	11,8	1	1	1
26	Heptane	15,3	1	0	1	1	1
27	Isoamyl acetate	15,3	3,1	7	1	1	1
28	Isobutyl isobutyrate	15,1	2,8	5,8	1	1	1
29	Isophorone	17	8	5	1	1	1
30	Isopropyl acetate	14,9	4,5	8,2	1	1	1
31	Methyl cyclohexane	16	0	1	1	1	1
32	Methyl ethyl ketone (MEK)	16	9	5,1	1	1	1
33	Methyl isobutyl ketone (MIBK)	15,3	6,1	4,1	1	1	1
34	N-Methyl-2-Pyrrolidone	18	12,3	7,2	1	1	1
35	Methylene dichloride	17	7,3	7,1	1	1	1
36	Morpholine	18	4,9	11	1	1	1
37	N,N-Dimethylacetamide	16,8	11,5	9,4	1	1	1
38	Nitroethane	16	15,5	4,5	1	1	1
39	2-Nitropropane	16,2	12,1	4,1	1	1	1
40	Octane	15,5	0	0	1	1	1
41	Pentane	14,5	0	0	1	1	1
42	Propylene Carbonate	20	18	4,1	1	1	1
43	Tetrachloroethylene	18,3	5,7	0	1	1	1
44	Tetrahydrofuran (THF)	16,8	5,7	8	1	1	1
45	Tetrahydronaphthalene	19,6	2	2,9	1	1	1
46	Toluene	18	1,4	2	1	1	1
47	2,2,4-Trimethylpentane	14,1	0	0	1	1	1
48	Water	15,5	16	42,3	0	0	0
49	o-Xylene	17,8	1	3,1	1	1	1

Table 29. Hansen Solubility Parameters (HSP) of the 49 solvents used for the determination of the HSP of the synthesized acetates. [a] Solubility ratings of the acetates in each solvent. [b]Ind: Individual synthesis. [c]Copr: Co-production process

As shown in table 29, the three acetates: EAc, BAc (from individual syntheses) and BAc (from coproduction) were miscible in the same solvents.

The data were input into the **HSPiP software**, developed by S. Abbott, C. Hansen and H. Yamamoto.[57] Each solvent is represented in three-dimensional space by a point with its Hansen solubility parameters as coordinates. The software plots the Hansen solubility sphere including the maximum of miscible solvents (1=blue points) and excluding the immiscible ones (0=red points). Then it calculates the HSP of the studied solvent (EAc and BAc) that are the coordinates of the sphere centre and its radius.

As the synthesized and "purified" acetates are miscible with the same solvents, these 3 esters present the same experimental HSP, solubility spheres and radius. The experimental Hansen solubility parameters of the synthesized acetates were compared also with the theoretical values reported in the HSP Handbook in tables 30 and 31.[50]

- **Ethyl acetate:**

In the case of the synthesized ethyl acetate, the experimental HSP were found to be identical to those of fossil-based acetate and close to the theoretical parameters reported in the HSP Handbook (Table 30). Indeed, the HSP distance (called Ra) between the experimental data and the theoretical ones, calculated from equation II-5, is quite small (3.6), significantly lower than the radius of the sphere. Note that Ra is generally calculated to check the compatibility between two molecules. The smaller Ra, the more likely they are to be compatible and thus miscible. The Hansen solubility sphere of EAc is shown in figure 31.

$$Ra^2 = 4\,(\delta D_A - \delta D_B)^2 + (\delta P_A - \delta P_B)^2 + (\delta H_A - \delta H_B)^2 \qquad \text{Eq. II-5}$$

HSP	EAc (HSP Handbook)	Experimental HSP of synthesized EAc
δD ($MPa^{1/2}$)	15.8	17
δP ($MPa^{1/2}$)	5.3	8.0
δH ($MPa^{1/2}$)	7.2	7.4
Radius ($MPa^{1/2}$)		12.3

Table 30. Experimental Hansen solubility parameters of the isolated ethyl acetate (by using HSPiP software and simple algorithm sphere fit, with n=10)

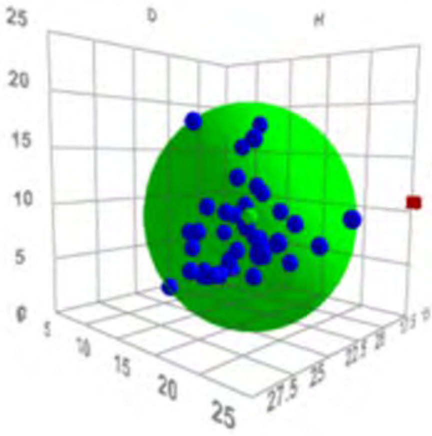


Figure 31. Hansen solubility sphere of ethyl acetate

- ***n*-Butyl acetate (BAc) from the individual synthesis and the coproduction process:**

In this case, we can observe that the experimental values of δD and δH are close to the theoretical ones, but the experimental value of δP is twice the theoretical (Table 31). This difference may be related to the presence of butanol, which has higher HSP than BAc (δD=16, δP=5.7, δH=15.8). However, the calculated distance Ra between experimental HSP and theoretical HSP of BAc is 4.99. The obtained value leads us to suggest the compatibility between the synthesized BAc and the fossil version. Figure 32 shows the Hansen solubility sphere of butyl acetate obtained experimentally.

Hansen solubility parameters	BAc (HSP Handbook)	Experimental HSP of BAc (Individual synthesis)	Experimental HSP of BAc (coproduction)
δD ($MPa^{1/2}$)	15.8	17.0	17.0
δP ($MPa^{1/2}$)	3.7	8.0	8.0
δH ($MPa^{1/2}$)	6.3	7.4	7.4
Radius ($MPa^{1/2}$)		12.3	12.3

Table 31. Experimental Hansen solubility parameters of the butyl acetates from the individual synthesis and the co-production process (by using HSPiP software and simple algorithm sphere fit, with n=10)

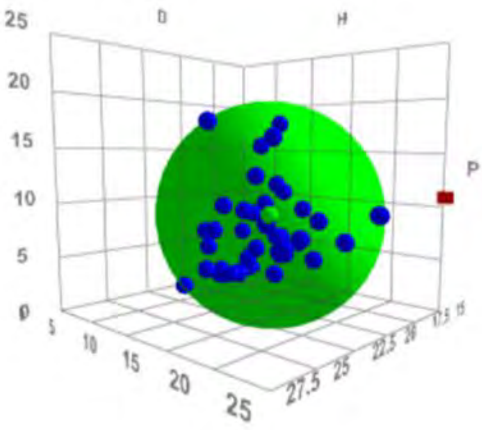


Figure 32. Solubility sphere of butyl acetate. The same spheres were obtained for individual and coproduction syntheses

Despite the differences found between the experimental and theoretical HSP for both acetates, the distance between them were not significant, which means that they could dissolve the same substances.

From these observations, we can suggest that there will be no problem of solubility when the synthesized molecules will be used in paints and coatings. However, their validation is essential to verify that they do not cause changes in these formulations and that they can therefore effectively replace the corresponding petrochemical solvents.

2.5 Validation of the synthesized ethyl and butyl acetates in solvent-borne coating formulations

As we previously demonstrated that the physicochemical properties of the synthesized acetates are close to the commercial version made from petrochemical starting materials through a homogeneous catalysis process, we were then interested in their use in solvent-borne formulations. We chose to only evaluate the esters obtained through the coproduction process, as they are the most industrially relevant. The acetates produced in the coproduction were thus used and evaluated in nitrocellulose lacquers and polyurethane varnishes prepared by **TECNALIA (Technology Centre, Spain)**, as the coordinator of the European project ECOBIOFOR. These formulations were compared with their respective commercial formulations provided by **Industrias Quimicas Irurena, SA (Spain)**. Different properties were determined, such as the viscosity, the film formation behaviour and the performance that includes the hardness, gloss and the adhesion to the substrate.

2.5.1 Evaluation of synthesized ethyl and butyl acetates in nitrocellulose (NC) formulations

The distinctive characteristics of fruity-like odour and fast drying of ethyl and butyl acetates make them ideal in preparation of nitrocellulose formulations. Besides, the use of ethyl acetate confers low viscosity to nitrocellulose solutions. On the other hand, butyl acetate has a great solvent power that makes it suitable for dissolving natural and synthetic resins. Its moderately evaporation rate (1.0, considered medium) avoids moisture condensation providing good flow and blush resistance to nitrocellulose lacquers.[328]

2.5.1.1 Preparation of nitrocellulose lacquers

The formulation used for the preparation of nitrocellulose (NC) lacquers is shown in the following table 32 (data provided by IRURENA).

#	Component	Composition in weight (%w/w)
1	Alkyd resin binder	20
2	NC solution I in ethyl acetate	13
3	NC solution II in butyl acetate	27
4	Aromatic solvent	19
5	Other organic solvent (alcohol)	20
6	Additives	1
	Total	100

Table 32. Formulation of Nitro-cellulose lacquers

The production of the nitrocellulose lacquers proceeds in three main steps:

1) Step 1: preparation of the nitrocellulose (NC) solutions:

   NC solution I: consist in 10 % of the NC resin dissolved in 90 % ethyl acetate.

   NC solution II: consist in 30 % of the NC resin dissolved in 70 % of butyl acetate.
2) Step 2: dissolution of the alkyd resin binder (#1) in aromatic solvent (#4) and the organic solvent (#5).
3) Step 3: mixture of the NC solution I and II (#2 and #3), the prepared resin binder and the additives (#6).

For the validation, the NC-formulation prepared with the synthesized acetates (called in this work: ECOBIOFOR formulation) was compared with the commercial formulations provided by IRURENA, which were prepared with the commercial acetates.

2.5.1.2 Viscosity

The viscosity is one of the most important parameters in coating and paint formulations as it determines the success of a coating application. The viscosity determines the flow, levelling properties of the coating and the solids content that will affect the dry film thickness. Besides, the selection of the application method of the coating will depend on the viscosity. A very simple way to measure the viscosity is to use the viscosity flow cups, which are anodized aluminium devices that have a stainless steel hole through which a liquid can flow. In this technique, the cup is filled with the coating formulation and the time it takes for the entire coating to flow through the cup until the first cut in the flow occurs is measured.[329] According to the ASTM International D1200 standard, we decided to use the Ford No4 Efflux Cup, a specific standard cup suitable for low viscosity liquids.

The following table 33 shows the viscosity results of the NC-formulation prepared with the synthesized acetates (NC-ECOBIOFOR formulation) and those obtained with the commercial formulation.

NC-formulation	NC-ECOBIOFOR formulation	NC-Commercial formulation
Viscosity in seconds (Ford No4. Efflux Cup)	70	63

Table 33. Viscosity of NC-formulations

The viscosity of NC-ECOBIOFOR prepared with the synthesized solvents was slight higher than the value of the commercial formulation. Nevertheless, the specification for the viscosity of this NC-lacquer formulations is 65±5 s (data provided by IRURENA). Thus the ECOBIOFOR formulation is in accordance with this specification.

2.5.1.3 Film formation and levelling

Film formation is the conversion of a coating film from a liquid or fluid into a solid form.[330] Uniform film thickness of a coating is important because it affects the appearance and the protection of the surfaces where the coating is applied. The levelling is the process of smoothing the initial rough surface.

The NC lacquer formulated with the synthesized ethyl and *n*-butyl acetates (NC-ECOBIOFOR) was applied over glass, wood, plastic and metal. In all the cases, the substrates have shown good film formation and appearance when using both the NC-ECOBIOFOR and the NC-commercial formulations (results only shown for Sapelly wood; Table 34).

NC-ECOBIOFOR formulation	NC-Commercial formulation
	

Table 34. Film formation and levelling from NC-formulations applied to Sapelly wood surface

2.5.1.4 Drying time

The control of the drying process is necessary to ensure the best performance of the coating when applied on the substrate. The drying time of paints and coatings is affected by their formulation composition, coating thickness and the environmental conditions such as temperature, relative humidity and circulation of air and light. Besides, the drying time is important because it would affect the time and method of application of the coating.[20,26] The control of drying conditions is required to determine the drying time of a coating. The typical standard conditions are temperature at 23±2 °C and relative humidity at 55±5 %.[22]

In our case, the drying tests were carried out at room temperature and consist of determining the time in which the film is dry to touch (no damage is done when applying pressure) and when no stain is produced after applying white powder. For this test, a first coat of NC-ECOBIOFOR formulation was applied, which dried in 45 min. Then, a second coat was applied and final drying was obtained after 24 hours. The drying of the NC-ECOBIOFOR formulation was similar to that obtained with the NC-commercial formulation. Therefore we can conclude that the formulation based on synthesized acetates is as effective as the commercial one (Table 35).

Coating application	Drying time NC-ECOBIOFOR formulation	Drying time NC-Commercial formulation
1st coat	✓ 45 min	✓ 45 min
2nd coat	✓ 24 h	✓ 24 h

Table 35. Validation of drying time for the NC-formulations

2.5.1.5 Gloss

Nitrocellulose lacquers are principally used in finishes, such as in automobile, decoration material and furniture finishes. Besides it is used in decorative house paint. This is why gloss is an important aesthetic property in both clear and pigmented lacquers.[331,332] Gloss is measured using a glossmeter by analysing the amount of light reflected at a given intensity and angle. The higher the reflectance value is, the higher the gloss is.

For measuring the gloss level of coating, a reflectometer ("Micro-TRI-gloss" from BYK-GARDNER GmbH) was used. The light emitted by the reflectometer is directed to the surface of the sample at a defined angle and the reflected light is measured photo-electrically. According to the ISO 2813:2014 standards (Determination of the specular gloss index at 20°, 60° and 85°),[333] the measurement of the gloss is based on the measurement of the reflected light in a directional manner when light is applied to the surface with a given geometric angle. The index of specular gloss is not measured according to the intensity of the incident light but according to the reflection properties of a black glass standard with a gloss corresponding to 100 GU with a refraction index of 1.567. The intensity of the reflected light depends on the material surface and the geometric angle at which the light is incident. Table 36 shows the measurement angles specified to coatings (20°, 60° and 85°) and the gloss range for each gloss surface category.

Gloss	Geometric angle	Gloss Units (GU)
Highly reflective surfaces	20	>70
Semi-gloss surfaces	60	10-70
Matte surfaces	85	< 10

Table 36. Angles of incidence for gloss determination

The gloss of the NC-ECOBIOFOR applied on glass and wood was determined at 60° and 85°. It was not measured at 20° because this angle is considered only for high gloss surfaces and lacquers are classified from matte to semi-gloss surfaces.

As we can observed in table 37, when the gloss measurements were carried out at 85°, the gloss values were higher than 10 % (in both cases glass and wood), so the NC-ECOBIOFOR lacquers cannot be classified as matte. On the other hand, when the gloss values were measured at 60°, the gloss percentages were ranged from 10 to 70 %, which allow us to classify the NC-ECOBIOFOR formulation as a semi-gloss coating when applying in both glass and wood.

Reflectometer angle	Type of coated material	Gloss (GU)	
		NC-ECOBIOFOR formulation	NC-Commercial formulation
60°	glass	70	60°
85°	glass	90	85°
60°	wood	37-39	60°
85 °	wood	48-50	85 °

Table 37. Gloss percentage of NC-ECOBIOFOR formulations

The same classification was obtained with the NC-Commercial formulation, which validates that the replacement of the commercial esters by our synthesized acetates does not change the gloss of the nitrocellulose lacquers (Table 37).

2.5.1.6 *Wetting and adhesion*

Wetting can be described as the spreading and contact of a liquid (the coating in this case) on a solid surface. When a great contact between the liquid and the solid is obtained, the liquid adheres perfectly to the surface, causing the elimination of the air and thus minimizing the interfacial defects of the coating.[334]

A good adhesion of the coating would depend of the wettability of the surface. The adhesion of the coating can be validated using a cross-cut tester, which is a multi-cut 6 cutting edges over a flexible cutter head to facilitate the ease-of-handling and to guarantee the reproducibility of the cross cuts. The classifications of wetting according to the ISO 2409 standards are shown in the following table (Table 38).[335]

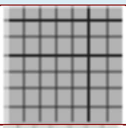
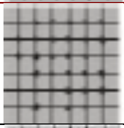
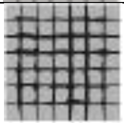
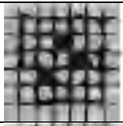
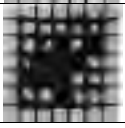
Cross-Cut assessment	Classification ISO 2409 standards	
	Class 0	Edges of cut are completely smooth None of the squares of coating is detached
	Class 1	Detachment of small flakes at the intersection of the cuts Max. 5 % of the cross cut area is affected
	Class 2	Flaked along the edges and/or intersection of the cuts Affected cross-cut area: 5-15 %
	Class 3	Squares are partially/wholly damaged Affected cross-cut area: 15-35 %
	Class 4	Square partly/wholly detached Affected cross-cut area: 35-65 %
	Class 5	Any flacking worse than Class 4 Affected cross-cut area > 65 %

Table 38. Classification of cross-cut test results

The cross-cut test was applied to different substrates, such as wood, metal and plastic, after being coated with the NC-ECOBIOFOR formulation. The results were compared to those obtained with the NC-commercial formulation. After visual analyses of the substrates submitted to the test, the NC-formulations were classified according with the ISO 2409 standards. The classification of the NC-ECOBIOFOR and NC-commercial formulations are shown in Table 39.

	NC-ECOBIOFOR formulation	NC-Commercial formulation
Wood (Sapelly)	 **Class 0-1**	 **Class 0-1**
Metal (steel/carbon)	 **Class 0**	 **Class 0**
Plastic (PVC)	 **Class 0**	 **Class 0**

Table 39. Adhesion cross-cut test on substrates coated with NC-ECOBIOFOR formulation and NC-Commercial formulation

The same classification was obtained for the two formulations applied to the three substrates, confirming the good performance of the formulations prepared with the synthesized acetates. Values of 0 were determined as any of the squares were detached after the cross-coating.

2.5.1.7 Conclusions concerning nitrocellulose-ECOBIOFOR lacquer

A nitrocellulose (NC) lacquer formulation was prepared according to a conventional industrial protocol but using ethyl and butyl acetates synthesized from the co-production process instead of the commercial acetates. Various parameters of this NC-formulation were checked as the viscosity, the drying and the film formation. In addition, its performance properties (gloss, adhesion) when applying on different substrates (wood, glass, plastic, metal) were also evaluated. The results were compared with those of commercial nitrocellulose lacquer.

As observed throughout the study, similar results were obtained with the ECOBIOFOR formulation and with the commercial one, which confirms that the synthesized solvents can effectively replace the petrochemical commercial ones in the production of nitrocellulose lacquers without changing their properties. The traces of water present in synthesized ethyl and butyl acetates did not affect to obtain a homogeneous formulation and did not have consequences on the film properties. As expected, the small amount of butanol (5.5% in BAc) had no negative effect on NC-coatings because this alcohol can be used as one of the components of the NC-formulation among alcohol compounds. No secondary reaction can occur in NC-formulation from these impurities contained in both acetates. To complete this validation study of the use of synthesized acetates in solvent-borne coatings, polyurethane formulations prepared with these solvents were also evaluated and described in the next section.

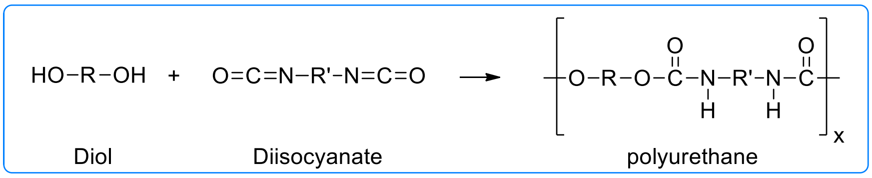
2.5.2 Evaluation of synthesized ethyl and butyl acetates in polyurethane varnishes

The polyurethane varnish (PU) is a clear, waterproof, durable gloss varnish that contains polyurethane as binder.[336] Polyurethane varnishes show a good combination of properties such as toughness, chemical and abrasion resistance, and durability. Solvent-borne polyurethane varnishes have a wide range of application on wood products.[337] Ethyl and butyl acetates are the most commonly used solvents in the preparation of polyurethane varnishes due to their fairly rapid evaporation (necessary for a fast drying) and their high solvent power for dissolving alkyd resins.

2.5.2.1 Preparation Polyurethane varnishes

The polyurethane varnish selected in this work is a two component-system called 2K coating system,[32] because it is obtained from a reaction between two parts, the part A (containing the alkyd resins binder) and the part B ("hardener" agent, containing di- and poly-isocyanates). The polyurethane varnishes are prepared in three general steps:

1) Step 1: preparation of the alkyd resin binder (part A).
2) Step 2: preparation of the "hardener" agent (part B).
3) Step 3: chemical reaction between the alkyd resin binder containing alcohol groups (part A) and the di- or poly-isocyanates compounds present in the hardener (part B; Schema 13).



Scheme 13. General reaction between alcohol groups and diisocyanates to produce polyurethane coatings[338]

Although acetates are used in the formulation of alkyd resin binder (part A) and in the hardener agent (part B), it is in the preparation of the hardening agent that they are in higher amounts.

Therefore, the synthesized ethyl and butyl acetates were only used for the preparation of the hardener agent, using the following formulation (Table 40):

#	Component	Composition in weight (%w/w)
1	Toluene diisocyanate (TDI)	14.5
2	Hexamethylene diisocyanate (HDI)	35.0
3	Ethyl acetate	35.0
4	Butyl acetate	15.5
	Total (Part B)	100

Table 40. Formulation of the hardener agent for polyurethane varnish.

In this work, the polyurethane varnish formulation prepared with synthesized acetates was called: PU-ECOBIOFOR formulation, and was compared with the commercial formulation provided by IRURENA (Spain).

The validation of the PU-ECOBIOFOR formulation includes the same tests than those made for the validation of nitrocellulose formulations: viscosity, film formation and levelling, drying time, smoothness, wetting and adhesion.

2.5.2.2 *Viscosity*

The viscosity were determined according to the international standard ASTM D1200. Similar viscosity values were obtained for both the PU-ECOBIOFOR formulation and the PU-Commercial formulation (Table 41). Based on values of viscosity required for polyurethane varnishes provided by IRURENA (25±5s), the two formulations comply with the specification values.

PU-formulation	PU-ECOBIOFOR formulation	PU-Commercial formulation
Viscosity in seconds (Ford No4. Efflux Cup)	23±2	25±2

Table 41. Viscosity of PU-formulations

2.5.2.3 *Film formation and levelling*

For the evaluation of the film formation and levelling, the PU-formulations were applied on two wood substrates, Sapelly and Oak. On both substrates, a homogeneous film formation, good appearance and high transparency were obtained with the ECOBIOFOR and the commercial formulations (Table 42). Once again the good performance of synthesized solvents has been demonstrated.

Noteworthy, the wood colour was enhanced with the PU-ECOBIOFOR formulation compared with the commercial one.

Substrate	PU-ECOBIOFOR formulation	PU-Commercial formulation
Sapelly		
Oak		

Table 42. Film formation and levelling from the PU-formulations applied to sapelly and oak wood surfaces.

2.5.2.4 Drying time

The solvent-borne polyurethane varnishes have the characteristic of a fast drying. Herein, a first coat of the PU-ECOBIOFOR formulation was dried after 10 min. Then, a second coat was applied, which was dried after 2 hours. The same drying time were observed for the PU-commercial formulation, indicating that our solvents offer the same drying properties as the commercial varnishes (Table 43).

Coating application	Drying time PU-ECOBIOFOR formulation	Drying time PU-Commercial formulation
1st coat	✓ 10 min	✓ 10 min
2nd coat	✓ 2-3 hours	✓ 2-3 hours

Table 43. Validation of drying time for the PU–formulations

2.5.2.5 Smoothness

As the prepared PU-formulation is not used as a "top coat" but as a primer coat, the gloss is irrelevant. Thus, in the case of PU-formulation, the smoothness and the good formation of the thickness film on the wood was evaluated by determining the roughness of the coat using sandpaper.

The results have shown satisfactory properties in both cases, with the PU-ECOBIOFOR formulation and with the commercial one. A smooth surface that did not clog the sandpaper was obtained. The great finish of the coating was obtained thanks to the fast drying of the varnishes (Table 44).

Smooth surface on wood	
PU-ECOBIOFOR formulation	PU-Commercial formulation
✓	✓

Table 44. Determination of the smoothness of the surface

2.5.2.6 *Wetting and adhesion*

The wetting of the two PU-formulations was determined on Sapelly and Oak substrates as previously described (§ 2.5.1.6). In both cases, good wetting and adhesion were obtained. The PU-ECOBIOFOR formulation was classified according to the ISO 2409 standards[335] in a class between 0-1 because the cut edges were not completely smooth after the cross-cut test. Similar results were obtained with the commercial formulation, which ensure the quality of the PU-ECOBIOFOR formulation (Table 45).

	PU-ECOBIOFOR formulation	PU-commercial formulation
Sapelly	 **Class 0-1**	 **Class 0-1**
Oak	 **Class 0-1**	 **Class 0-1**

Table 45. Adhesion cross-cut test on substrates coated with PU-ECOBIOFOR and PU-Commercial formulations

2.5.2.7 *Conclusions of polyurethane-ECOBIOFOR varnish*

For the European project ECOBIOFOR, one hardener used in the preparation of the polyurethane varnish was prepared with the ethyl and butyl acetates produced from the co-production process. As in the case of the nitrocellulose lacquer formulations, we have obtained herein equivalent results for the PU-ECOBIOFOR and commercial formulations. The properties obtained with both formulations were always in agreement with the specifications provided by IRURENA (expert in wood coatings).

Fortunately, the presence of butanol and water in traces did not affect the varnish properties although water can provoke secondary reactions with isocyanate producing urea that can form isocyanate-biurets.

Through this study, we have been able to verify that the synthesized solvents have the same properties in the coatings systems as the conventional ones, which allows us to ensure the feasibility of the replacement of the classic petrochemical solvents by the acetates synthesized in this work.

2.6 Conclusion

As mentioned at the beginning of this chapter, ethyl acetate and butyl acetate are the most important solvents in the paint and coating industry. In addition, they are also strongly used for extractions in other industries such as pharmaceutical and food industries. These solvents are currently produced from petrochemical synthons using harsh conditions and/or homogeneous catalysis that could be at the origin of waste production. In order to offer greener alternatives compared to existing ones, the objective of this work was to develop production processes that comply as far as possible with the principles of the green chemistry.

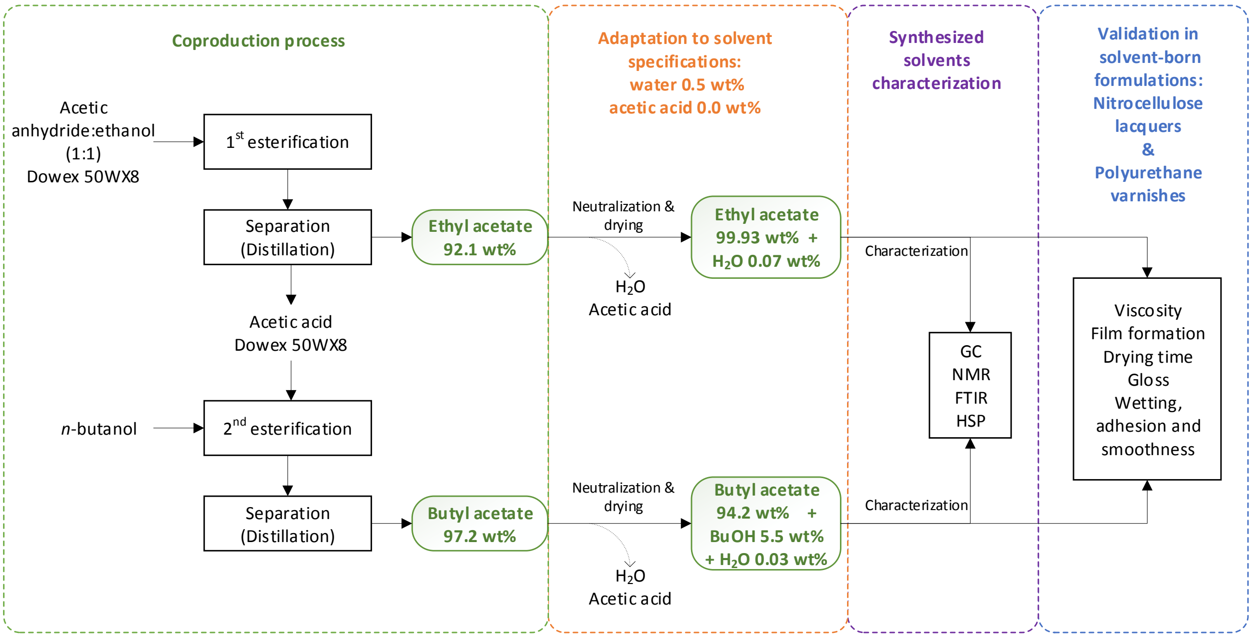
In this chapter, two different pathways were studied for the syntheses of ethyl acetate and *n*-butyl acetates: the reactions of acetic acid and acetic anhydride with ethanol and butanol, respectively. In these studies, we replaced the homogeneous catalyst currently used in industrial processes by heterogeneous ion exchange resins.

Although esterification with ionic resins has been widely described in the literature, a complete kinetic and thermodynamic study of these resins had still not been carried out. That is why in this work, we decided to perform these studies with 4 different resins (A15, A16, A36, D50WX8) in the two proposed chemical pathways. Herein, the determination of activation energy for each resin was useful to select Dowex 50WX8 as the best resin for the syntheses of acetates. In addition, the parametric study allowed us to choose the best operational conditions and the most suitable reagents for synthesizing the target solvents.

The purification of these acetates is complex because water is produced during the esterification forming several azeotropic mixtures with the acetates and the remaining alcohols. To obtain the solvents with a high purity, several distillations are thus required, which are energetically demanding. In order to face this problem, we have proposed an innovative process of co-production of acetates that consists basically in two steps: i) the synthesis of ethyl acetate from acetic anhydride and ethanol in a 1:1 molar ratio, in which the production of water was avoided facilitating the separation of ethyl acetate through a simple distillation, and ii) in the second step, the acetic acid obtained as co-product during the synthesis of ethyl acetate is used in the synthesis of butyl acetate. Besides, the resin involved in the first esterification is re-used in the second esterification.

This process of co-production is interesting because it avoids the use of intensive processes of distillation and reduces the production of waste related to the acetic acid produced. With this process, we were able to produce, after distillation, ethyl acetate and butyl acetate in a high purity, 92.1 and 97.1 wt%, respectively.

The development of greener acetates was thought to respond to the need of the ECOBIOFOR project partners dedicated to the production of paints and coatings. The evaluation of the behaviour of the synthesized solvents in nitrocellulose lacquers and polyurethane varnishes allowed us to validate that these molecules perfectly meet the required criteria (drying, viscosity, film formation, gloss, smoothness wetting and adhesion) to substitute the conventional petrochemical solvents in paints and coatings. It means that the strategy we implemented (neutralization and drying) to eliminate the acetic acid and water remaining in the synthesized acetates after distillation was successful. After that treatment, no more acetic acid was present and water content was reduced to 0.07 wt% for EAc and 0.03 wt% for BAc. The final purities of ethyl and butyl acetates were 99.93wt% and 94.2 wt%, respectively. Although traces of water were still present in the synthesized acetates, no problem due to water-isocyanate side reactions was identified during the preparation of the polyurethane coating and therefore did not affect its performance.



Scheme 14. Graphical summary of coproduction process of acetates, "purification" to meet solvent specifications for using in coatings, characterization and validation of synthesized solvents.

CHAPTER III. Environmental assessment of ethyl and *n*-butyl acetates production and coproduction: green metrics and Life Cycle Assessment (LCA)

Chapter III. Environmental assessment of ethyl and *n*-butyl acetates production and coproduction: green metrics and Life Cycle Assessment (LCA)

Chapter III. Environmental assessment of ethyl and *n*-butyl acetates production and coproduction: green metrics and Life Cycle Assessment (LCA)

3.1 Introduction

One of the most important aspects of green chemistry is the evaluation of the greenness of a chemical process, since in this way, it is easier to choose the greenest option among the different synthetic pathways proposed.[339]

The first approach that we considered to evaluate and compare in an easy way the two developed synthetic pathways for acetates, the individual routes and the co-production process (presented in the Chapter II), was through green metrics calculations. However, green metrics only give information about the process itself, without taking into account the total impact of the whole life cycle, that is, the contributions of origin and preparation of reagents, the energy used during the process, or the final disposal of the product. Therefore, to obtain further in-depth information about the environmental impact of the syntheses, life cycle assessments of the individual and coproduction process were performed.

In the first part of this chapter, we present the generalities on green metrics calculations and life cycle assessment methodology.

In the second part, in order to determine which of the syntheses is the greenest, complying better with the principles of green chemistry, the life cycle assessment and green metrics of the individual syntheses and the coproduction process were performed. This work was published in the International Journal of Life Cycle Assessment.

The last section of this chapter is dedicated to the comparison of the life cycle assessments of the individual syntheses and the coproduction of acetates using bio-based starting materials, bio-ethanol and bio-butanol for ethyl and butyl acetate syntheses, respectively. In addition, the production of bio-acetates through the developed syntheses was compared with the industrial petrochemical current ones.

Chapter III. Environmental assessment of ethyl and *n*-butyl acetates production and coproduction: green metrics and Life Cycle Assessment (LCA)

3.2 Generalities: Sustainability evaluation of the synthesized ethyl and butyl acetates

3.2.1 Green metrics

Green metrics are a simple way to obtain concrete, complete and quantitative information about the efficiency in terms of materials and energy, the individual chemical reactions and the complete processes.[340] The purpose of the analysis of the green metrics is basically to determine between different synthetic routes, which is the chemical synthesis that better achieves the definition of green chemistry. It is for this reason, that the green metrics have to be clearly defined, simple, measurable, and objective.[341] Among the list of green metrics, the most studied are the atom economy, the E-factor, and the percentage from renewable sources that can be considered when petrochemical sources are replaced by bio-based ones.

3.2.1.1 Atom Economy

The second principle of the green chemistry is related to the atom economy, which is considered as the fundamental green chemistry metric and the basis for all the other green metrics.

The efficiency of a chemical reaction is commonly evaluated according to the yield of the reaction. When the yield of a reaction is closer to 100 %, the reaction is consider as an efficient reaction. Nevertheless, the production of wastes is not taken into account in this kind of calculation, and reactions with a high percentage yield can also produce a high amount of wastes. With the aim of overcoming this lack, Barry M. Trost (1991) introduced the concept of **Atom economy (AE).**[342]

In simple words, the atom economy is the calculation of the amount of reactant that remains in the final product. Therefore, the perfect atom economy in a chemical reaction or in a process is that in which all the reactive atoms are in the final desired product.[343]

The percentage of atom economy of a generic stoichiometric chemical reaction A + B → C is calculated by dividing the molecular weight of the final product by the sum of all reactants (Eq. III-1).

$$AE = \left(\frac{m.w.of\ product\ C}{m.w.of\ reactant\ A + m.w.of\ reactant\ B}\right) x\ 100 \qquad \text{Eq. III-1}$$

where $m.w.$ is the molecular weight of products or reactants

This simple calculation only considers the reactions where the intermediate products that are formed in one step are consumed in another and therefore are neglected. Additionally, it is supposed that the chemical equations of the reaction are correctly balanced.

The determination of the atom economy of a full process is also possible,[341,343] but it is important to identify the intermediates produced in a step and that are not consumed in further ones. For a linear process:

$$1)\ \ A + B \rightarrow C$$

$$2)\ \ C + D \rightarrow E$$

$$3)\ \ E + F \rightarrow G$$

The atom economy is calculated as presented in equation III-2:

$$AE = \left(\frac{m.w.of\ product\ G}{m.w.of\ A + m.w.of\ B + m.w.of\ D + m.w.of\ F}\right)\ x\ 100 \qquad \text{Eq. III-2}$$

Where $m.w.$ is molecular weight of products (G) or reactants (*i.e.* A, B, D and F)

In conclusion, the processes that have a high atom economy are efficient processes because they need the use of less reagents to obtain the same amount of product, thus decreasing waste production with the potential reduction of the operational cost.

3.2.1.2 Environmental impact factor (E-factor)

Another simple ways to evaluate a process is by determining the production of wastes, whereby In 1992, Roger Sheldon considered this problem and introduced the concept of the environmental impact factor (E-factor).[343] The objective of the E-factor is to measure the mass of generated waste per mass of final product. In this context, the mass of wastes generated from a process is considered as the sum of the masses of unreacted reagents, by-products, side products, reaction solvents and purification materials, all of those involved in the production of the desired product.

The E-factor is expressed in the equation III-3.

$$E - factor = \frac{\sum mass\ of\ wastes\ (g)}{mass\ of\ product\ (g)} \qquad \text{Eq. III-3}$$

The way to interpret the result of the E-factor is: when the value of the E-factor is closer to zero, so the process is more sustainable and green, which indicates a less generation of wastes. On the contrary, higher E-factor value means more wastes, and thus greater negative impacts on the environment. The E-factor can be applied to an individual step, but also is easily applied to a multi-step process to facilitate the assessment of the full process.

The limitation of this metric in industrial processes is the lack of clarity of the definition of waste. Indeed, it becomes difficult to determine for example, if the water used in a process is a waste or not. Sheldon has proposed an easy definition of waste: "everything but the desired product", except water.[344] However, depending on the process, water is considered as waste such as in pharmaceutical industry and in bio-catalytic processes.

The advantage of the E-factor is that it can be used to evaluate and obtain specific information about the process or its emissions on air or water. Besides, the environmental impact factor is useful to select the starting material for a chemical reaction that would reduce waste generation. The prevention of waste can be achieved if the reagents and solvents are recycled. In this case, heterogeneous catalysts result interesting from this point of view because they can be used in continuous processes where the desired product is constantly removed (Figure 33).

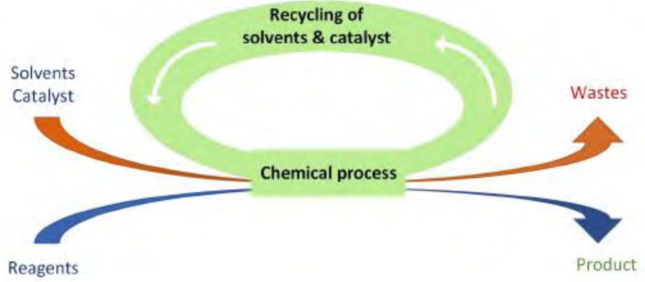


Figure 33. Prevention of wastes by recycling solvents and catalyst[345]

3.2.1.3 Percentage from renewable sources

The development of chemical pathways that allow the used of starting materials derived from bio-based resources has become an essential requirement. This is reflected in the 7th principle of the green chemistry that address to the use of renewable feedstocks, and for which it has been necessary to implement a green metrics dedicated to the bio-based origin of a product: the percentage from renewable sources.

The percentage from renewable sources (PRS) expresses, as the name implies, the percentage of material from biological sources used in the chemical synthesis that is at the final product. It is represented in equation III-4:[346]

$$PRS = \frac{\sum Mass\ of\ all\ renewable\ raw\ material\ (g)}{Mass\ of\ final\ product\ (g)}\ x\ 100 \qquad \text{Eq. III-4}$$

The need to evaluate the sustainability of a chemical process has led to the development of different green metrics that determine the toxicity, eco-toxicity (metrics: TRACI health and ecotoxicity impacts) and biodegradability of a product, as well as the maximization of energy efficiency in the synthesis (metric: total energy demand) and the use of local raw material (metric: feedstock distance). Nevertheless, the green metrics consider only the environmental contribution of the chemical syntheses, without taking into account the contributions of the whole life cycle.

Sometimes when talking about the development of more sustainable chemical products, we immediately think of using renewable sources that replace fossil-ones. However, this is not enough to achieve a positive and complete transition towards a cleaner and more sustainable industry.[347] Therefore, it is important to remember that the sustainability of the products derived from the biomass will also depend on the use of the sources and of course on the transformation process that is employed.[348] In this context, the Life Cycle Assessment (LCA) method is a useful tool to evaluate the environmental impacts not only of the transformation step itself (as in the case of the green metrics), but also the impacts relate to the origin and sources of the biomass and the product end of life (Figure 34).

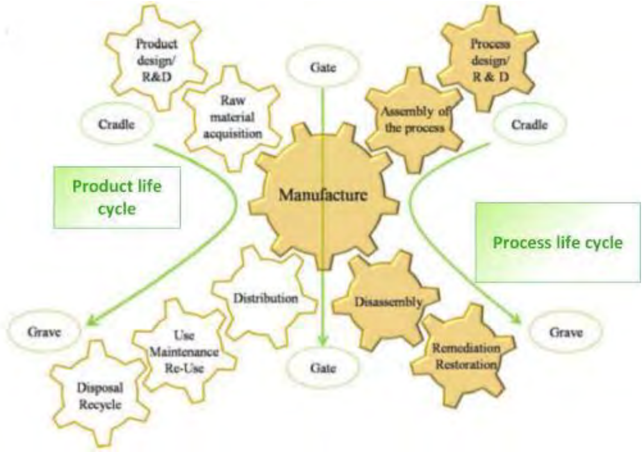


Figure 34. Life cycle approaches of process and products (Jacquemin et *al.*)[349]

3.2.2 Life cycle assessment (LCA) methodology

The life cycle assessment (LCA) has been defined in the international standard ISO 14040 as a method that allows determining the environmental aspects and the impacts to human health and environment, caused by a product's life from its raw material to its disposal.[350,351] In other words, the LCA method is useful to determine the environmental impacts associated with a product. To carry out this type of analysis in an appropriate way, it is necessary to follow the next basically steps (Figure 35):

- The definition of the system;

- The compilation of an inventory with the important inputs and outputs of a product system;
- The evaluation of the potential environmental impacts associated with the entire life cycle;
- The interpretation of the results obtained from the inventory analysis and the impact assessment phases related to the objectives of the study.

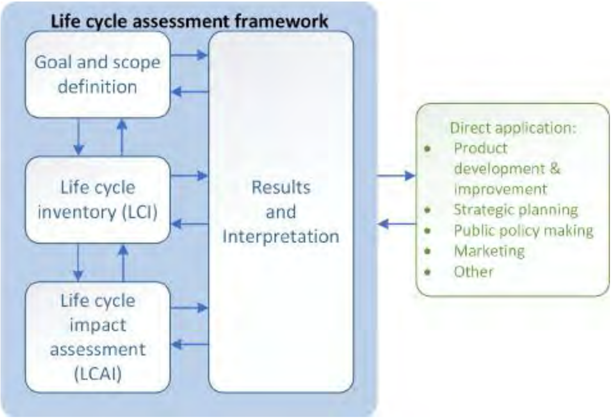


Figure 35. General framework of LCA according to ISO 14040:1997/2006

3.2.2.1 Life cycle of a product

The entire life cycle of a product is considered from the extraction of the raw material (cradle) to the end product, this means the use and disposal phase (grave). The LCA will allow designing or modifying the product in order to develop the safest process.

Three main approach of life cycle assessment can be considered, according to the depth with which the product system needs to be studied: cradle-to-gate, cradle to grave and cradle-to-cradle (Figure 36).

The most conspicuous of the approaches is the **cradle-to-gate** analysis, which depending on the requirements, could be performed only considering a partial part of the entire life cycle of a product. This means that the product would be studied from the extraction of the source (cradle) to the final production of the product (gate), without taking into account the phase of use and disposal. This approach is considered in cases where a new synthesis process wants to be evaluated, and thus it is considered that the stages following the production are not important because they remain the same.[352]

A more extensive analysis is the **cradle-to-grave** analysis, which considers all the different steps of the life cycle of a product, that is, from the resource extraction to the final disposal phase of the product. This approach takes into account the production stages, the intermediates and waste production, and the transport, use, and disposal of the product.

The last of the approache is the **cradle-to-cradle** analysis, which includes the environmental impact analysis associated from the extraction of raw materials until the disposal of the product. The difference between this analysis and the cradle-to-grave analysis is that the disposal of the product in this case is the recycling or reuse, which means that there is a closed cycle of the life cycle of the product, which would not generate negative impacts on the environment.[353]

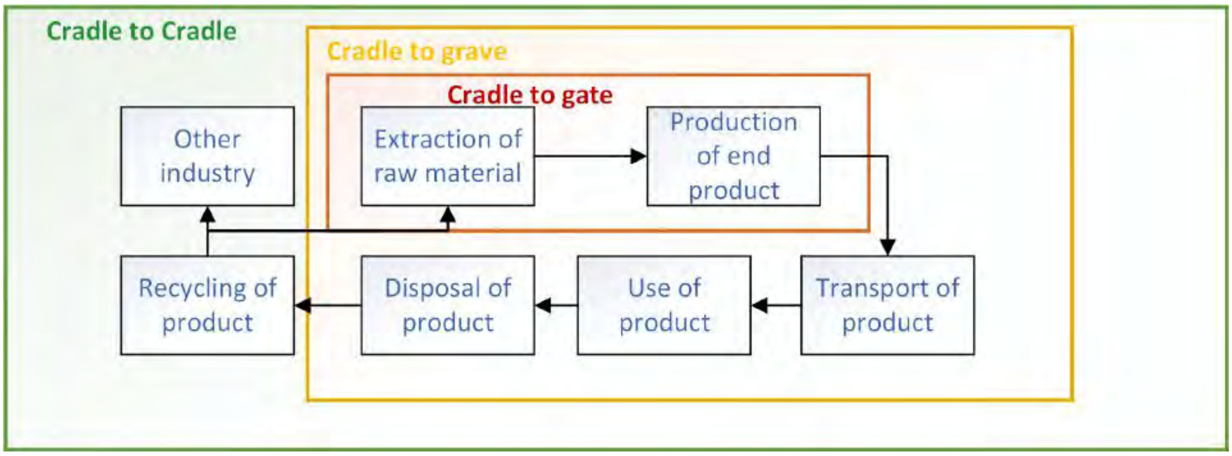


Figure 36. Principal types of Life Cycle Analysis of a product

3.2.2.2 Goal, functional unit and scope

- **Goal**

The international Standard 14044 determined “*that the goal and the scope of an LCA shall be clearly defined and shall be consistent with the intended application. Due to the iterative nature of LCA, the scope may have to be refined during the study”.*[350] The clearly definition of the LCA goal will help in turn to define the scope and the system boundaries. The ISO 14040:2006 mentioned that “the scope of the study have to be well defined to ensure that the breadth, depth and detail of the study are compatible and sufficient to address the stated goal”. In addition, the clear and concise definition of the objective is important since the collection data for the inventory analysis will also depend on it.[354] The answer to some questions about the study that will be carried out can be a way to easily define the goal of the analysis:[352]

- What is the objective of the study?
- Why is an LCA study conducted?
- For whom will an LCA study be addressed?

- The LCA study will be used to compare different products?

- **Functional unit**

In order to perform an adequate LCA it is necessary to determine a quantified description of the performance requirements that the product system must meet, and that will help to define the product system, this is known as the **"functional unit"** of the product system.[355,356] The selection of the functional unit is closely related to the definition of the goal.

The functional unit is not only the quantified description of the product system, but also enables the comparison and analysis between products. For example, in the case of our syntheses, the functional unit could be the production of 1 L of solvents.

- **System boundaries**

The definition of the goal of the study is also related to the establishment of the system boundaries, which will depend on the comparisons that want to be carried out in the study. The system boundaries will determine which unit process would be included in the LCA study. Therefore, the inputs and outputs necessary for the study of a product, which are within the limits of the system, should be followed upstream and downstream (Figure 37).[357]

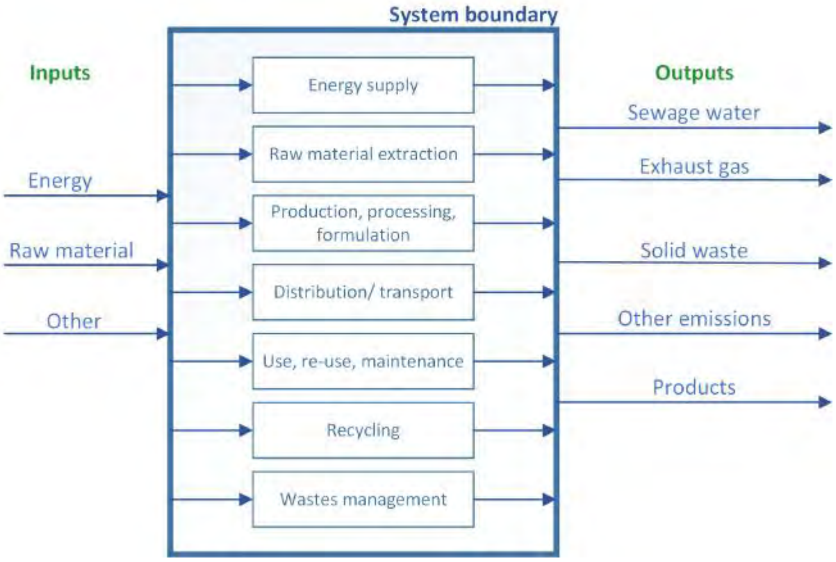


Figure 37. System boundary. (Modified from SETAC, 1991. Life Cycle Assesment, Klöppfer).[352]

The system boundaries have to be clearly specified in order to clearly answer to a specified problem. Thus, system boundaries can be determined in different dimensions:[357]

- **Boundaries between the technological system and the nature**: The life cycle starts with the acquisition of raw materials or energy carriers or the extraction of the natural resource. All the necessary activities in each process need to be taken in account. The end of the cycle is when heat or waste are realised on the environment (soil, water or air). For example, the waste treatment infrastructures are considered in the technological system.
- **Geographical area:** Depending on the economic context and the definition of the product, there are some considerations that must be taken into account when defining the geographical limits. Among these it can be found the place of production of the product, the type of infrastructure (electricity, waste management, transport system) according to the region, and the effects of pollution on the environment that can vary from one area to another (additionally, the global effects are considered for some categories: climate change / greenhouse effect).
- **Temporal system/Time horizon:** The period for the data acquisition has to be defined in order to evaluate the present and future environmental impacts caused by the production and consumption of the product along the time.

3.2.2.3 Life Cycle Inventory Analysis (LCI)

The second phase of LCA is the life cycle inventory analysis, which is defined in the ISO standard 14040:2006 as:[350]

> *"The phase of life cycle assessment involving the compilation and quantification of inputs and outputs for a product throughout it entire life cycle"*

The life cycle inventory (LCI) can be described as a systematic procedure that aims to quantify the energy and raw materials needed in a process, as well as the emissions that are generated to the environment. All of this considering the entire life cycle of the product. In other words, the LCI is the process of collecting and calculations to quantify the inputs (materials, energy) and outputs (including the environmental releases) for a specific product.[358] In order to facilitate the LCI, there are some steps that were proposed by Babu,[359] and that are exposed in the following list:

1. **Development of a flow chart**, which is a diagram of the studied product system that consists of small boxes representing the "unit process" where the processes involved are specified and their mutual dependencies are indicated by one or two-sided arrows. The unit process has to be exactly defined for a specific process. Each unit process can be aggregated into larger units and

be successively averaged. This makes the conduction of an iterative inventory analysis because when a data is collected the requirement of new data arises, which provokes a change in the data collection in order to accomplish the goal of the study.

2. **Development of an LCI data collection plan**. This step includes the clear definition of the data quality goals. Therefore, it is necessary the identification of data quality indicators, data sources and types. Besides, the development of a data collection spread sheet will facilitate the good management of the collected data.

3. **Data collection**. This step of the LCI can be divided in two principal parts: i) all the inputs: energy, energy sources, water and ii) the outputs of the product: atmospheric emissions, waterborne wastes, solid wastes, products, transportation, co-product allocations, industrial scrap, data-time period, specific data versus composite data, geographic specificity, routine/fugitive/accidental release, and economic input-output approach to LCAI.

   The qualitative and quantitative data of the inventory should be collected for each unit process foreseen in the study. The most used tool to facilitate the collection of data is the process flow diagram, which is a useful tool to ensure that the system boundaries are properly described; it is also useful to organize the data modules in relation to one another during the data collection.

   The data collection used to be the most difficult part of an LCA because sometimes there is a lack of information about a material, chemical or process. This problem could be solved if the information can be obtained from the industry. Otherwise, it can be omitted the step that lacks information or adequate estimations can be made, which despite of the uncertainty of the data is preferable to the omission of these. LCI databases contain data for all flows of several unit processes. Many of the databases are already included in LCA software systems.

4. **Evaluation and documentation of the LCI results**: The best way to document the LCI results is to list the quantified elementary flows of sources and emissions.[360] The LCI results can be documented as a table format for each unit process in order to provide a clear view of the names and quantities of all flows (materials, energy, resources, products, waste and emissions).

5. **Interpretation data:** The LCI results are the compilation of elementary flows over all the processes considering the defined flow of the functional unit. The final LCI result will be the sum of each resources and emissions (from each unit processes) in the overall process. In this phase

it is important to verify that the inventory is complete in relation with the goal and the scope of the study and of course if all the results are within the boundaries of the system.

3.2.2.4 Life Cycle Impact Assessment (LCIA)

The ISO 14044 describes the Life Cycle Impact Assessment (LCIA) as the:

> *"Phase of life cycle assessment aimed at understanding and evaluating the magnitude and significance of the potential environmental impacts for a product system throughout the life cycle of the product"*[350]

This is the third phase of a life cycle assessment and its objective is to evaluate the impacts on different categories provoke by the emissions and extractions that were previously determined during the Life Cycle Inventory (LCI).

The LCIA involves: i) the selection of the category indicators and the characterization of the models, ii) the assignment of the inventory results (classification), and iii) the calculation of category indicator results (characterization). In this phase, the results of the inventory analysis are assigned to an impact category (mid-point category: climate change, ozone depletion, human toxicity, etc.) that will affect a final category (endpoint category: coral reefs, forest, crop harvests) from a specific area (human health, quality of ecosystems, climate change, and resources) (Figure 38).[361]

The selection of the impact categories shall be in agreement with the goal and the scope defined to the study. Furthermore, during the classification the emissions and extractions determined in the inventory can be assigned to one or more impact categories. *i.e.* SO_2 emissions can contribute to acidification and eutrophication. Then, in the stage of characterisation the results obtained during the inventory analysis are converted to a common unit within the same impact category, this is possible using a characterization factor.

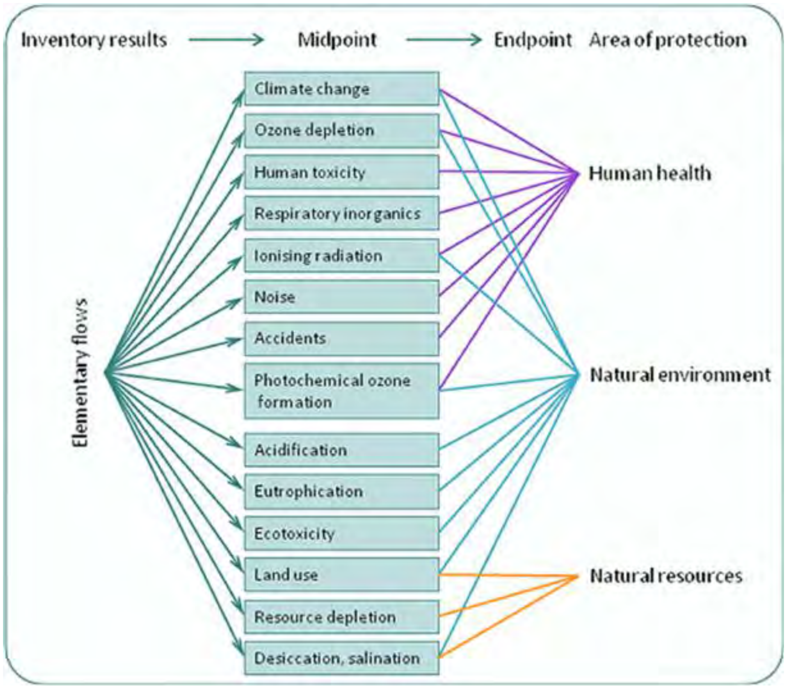


Figure 38. General structure of the life cycle impact assessment.[361]

In life cycle analyses of ethyl and butyl acetates synthetized in this work, we decided to use the intermediary characterization, called "midpoint". Herein, we used a derivative of the ILCD 2011 1.05 method to characterize the contribution of the various flows of inventory emissions and extractions in each impact category. The description of categories is developed in section 3.3 of this chapter.

3.2.2.5 Life Cycle Interpretation

The interpretation phase consists in making the pertinent conclusions and recommendations based on the results of the inventory and the impact assessment. During this phase, it is possible to identify the most important stage of the life cycle assessment that could be modified to reduce the environmental impacts produced by the system of study. Additionally, during this step, the critical points of the life cycle should be determined and also it is necessary to evaluate the quality and robustness of the results.

The ISO 14040 (2006) defined the life cycle interpretation stage as follows:

> *"Interpretation is the phase of LCA in which the findings from the inventory analysis and the impact assessment are considered together or, in the case of LCI studies, the findings of the inventory analysis only. The interpretation phase should deliver results that are consistent with the defined goal and scope and which reach conclusions, explain limitations and provide recommendations"*[350,352]

In the ISO 14044 have been defined three steps to interpret the results of the inventory analysis and the impact assessment:[350]

1) Identification of the significant issues based on the results of the LCI and LCIA stages of the Life Cycle Assessment,
2) An evaluation that considers completeness, sensitivity and consistency checks,
3) Conclusions, limitations and recommendations.

The identification of significant issues allows determining the data elements that contribute most to the results of the LCA from both LCI and LCIA, helping to prevent over-and misinterpretations. Then, the evaluation establishes confidence and reliability in the results of an LCA, thanks to a completeness, sensitivity and consistency check (Figure 39). Finally, the last part of the LCA is the conclusions in which the alternatives that have the overall least impact to the human health and the environment are defined. The results of the last phase of the LCA shall be reported in a clear and complete report.[362]

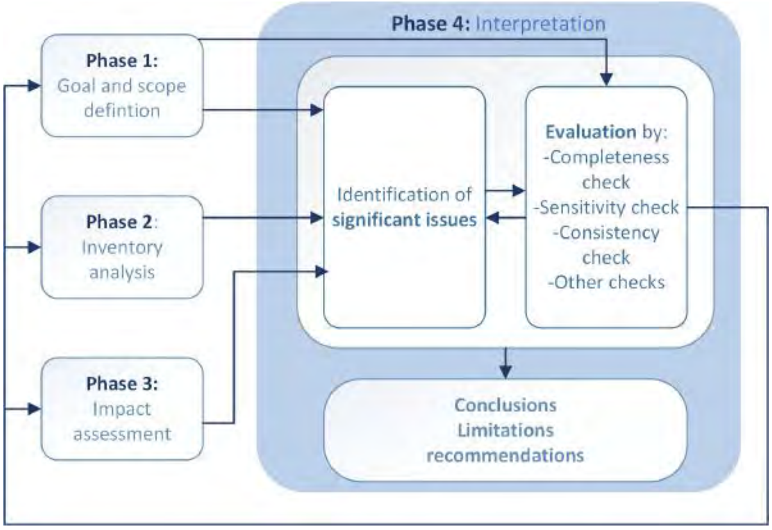


Figure 39. General overview of the relation between the phases 1,2 and 3 with the interpretation phase.

For the studied chemical processes, the evaluation of several indicators related to their environmental impacts and the implementation of green chemistry principles are a way to guide the choice of the greener process among different alternatives. In order to verify that the new coproduction process developed in this work for the syntheses of ethyl and butyl acetates is more eco-friendly than the two independent syntheses, two approaches have been considered: Green metrics and life cycle assessment (LCA).

3.3 LCA case study: Comparison between independent and coproduction pathways for the production of ethyl and *n*-butyl acetates

Cecile Bories, Nydia Ileana Guzman Barrera, Jerome Peydecastaing, Emeline Vedrenne, Carlos Vaca Garcia, Sophie Thiebaud-Roux, Caroline Sablayrolles

Laboratoire de Chimie Agro-industrielle (LCA), Université de Toulouse, INRA, INPT, Toulouse, France

This paper has been accepted and published in the International Journal of Life Cycle Assessment

DOI 10.1007/s11367-017-1317-8

Abstract: The production of ethyl acetate and *n*-butyl acetate was investigated through two different pathways: either by independent reactions or by coproduction. In the coproduction pathway, the *n*-butyl acetate was produced by reusing the by-products of the synthesis of ethyl acetate.

This study provides a comparison of the environmental impacts of these two pathways using a Life Cycle Assessment (LCA). A discussion about the use of LCA on chemicals and its challenges was also developed.

Keywords: coproduction, esterification, ethanol, *n*-butanol, green chemistry, life cycle assessment, sustainability

3.3.1 Introduction

Nowadays, the global consumption of solvents is significant, with almost 28 million metric tons consumed in 2012.[363] The most important users are the producers of paints and coatings (60.6 % in 2011 of the total consumption). This demand is predicted to increase by 2.9 % per year until 2019.[364] Solvents in the paint industry can be used as integral part of the formulation for homogenization or adjustment of the viscosity, as paint thinner by post-addition to adjust application properties or even as cleaning agent for equipment for example.

Ethyl acetate (EtAc) and *n*-butyl acetate (*n*-BuAc) are one of the most used solvents.[261,365] They have been commonly synthesized through direct esterification of acetic acid with the corresponding alcohol (ethanol for ethyl acetate and *n*-butanol for *n*-butyl acetate), in the presence of a homogeneous acid catalyst, usually sulfuric acid or *p*-toluenesulfonic acid (PTSA).[277,366,367] The use of these homogeneous catalysts presents many disadvantages such as the production of by-products due to multiple side reactions, the difficult product/catalyst separation and the equipment corrosion. In order to avoid these problems and in a context of sustainable development, the use of heterogeneous catalysts for esterification such as ion exchange resins,[261,263,287] montmorillonite[368] or even sulfated zirconia[365,369] has been studied.

However, as the esterification is an equilibrium-limited reversible reaction, the yield and conversion of the reactants are generally quite low (limited to 66 %), due to thermodynamics limitations.[263,370] In order to increase the ester formation, either the alcohol can be introduced in excess or one product, usually water, can be removed from the reactive medium all along the reaction. The equilibrium will be thus shifted to the products formation. In the literature, the most reported technique to achieve this goal is to use reactive distillation process.[371,254,259,300,303] Indeed, in the case of the synthesis of acetates using acetic acid, the reaction is rather complicated to handle as the esterification leads to the formation of an important quantity of water that will be difficult to separate from the acetate due to azeotropes formation.[372] The reactive distillation process, where chemical reaction and distillation are combined in a single unit, helps this separation. Nevertheless, it presents many drawbacks: the process is complex, expensive and not easily transposable at different scales and several disadvantages were observed, linked to the experiment itself (volatility requirement, temperature and pressure compatibility, long catalyst lifetime).[373]

In this project, in order to avoid these problematic while maximizing the reaction yield, it was decided to replace the reactive distillation process by a simple esterification. Moreover, acetic acid was replaced by acetic anhydride. The use of anhydride avoids azeotropes formation and thus enhances the products separation through distillation. A coproduction pathway to produce both ethyl and *n*-butyl acetates was thus investigated (Fig 1): the use of acetic anhydride for the ethanol esterification led to the production of ethyl acetate and acetic acid (AcOH) that can be reused for *n*-butanol esterification; the same catalyst being also reused for the second reaction. This process can minimize reaction steps and so waste production.

A coproduction of EtAc and *n*-BuAc, through reactive distillation, has already been presented by Tian *et al.*, but only by simulation, with acetic acid as starting material.[257] In our case, these consecutive syntheses were carried out, through experiments, in the simplest reactor that can be easily adapted either at laboratory or industrial scale and abiding by the principles of green chemistry (use of heterogeneous catalyst, soft reaction conditions).

In order to evaluate from an environmental point of view the chemical pathway developed, Life Cycle Assessment (LCA) was used as a decision tool. Indeed, this standardized and accurate method consists in measuring and comparing the potential environmental impacts of these production processes on their entire life cycle, *ie.* from cradle to the laboratory gate (in our case).

In this study, both independent syntheses of the esters (scenario 1) and coproduction (scenario 2) were modeled, after a complete inventory at laboratory scale. The results were compared to highlight the interest of this new coproduction pathway on an environmental point of view.

3.3.2 Methods and materials

3.3.2.1 Chemicals

Ethanol, *n*-butanol, acetic anhydride, acetic acid, cyclohexane and methyl isobutyl ketone, all at analytical grade, were purchased from Sigma Aldrich Co (France). Sodium chloride and Dowex 50wx8 resin was also obtained from Sigma Aldrich Co (France).

3.3.2.2 Scenario 1 (Sc1): Independent syntheses of acetates

Both esterifications were carried out in a 2 L glass jacketed stirred reactor.

For the production of ethyl acetate, ethanol (EtOH, 400 g) and acetic anhydride (AnAc, 889 g) were added into the reactor, followed by the incorporation of the dried heterogeneous catalyst, Dowex 50wx8 (20 g, i.e., 5 wt.% respect of the mass of ethanol). The reagent amounts were calculated according to the desired molar ratio (1:1 EtOH – AnAc).

The system was left at room temperature for 4 h, the reaction being highly exothermic, under mechanical stirring. After the reaction, the produced ethyl acetate (665 g) was recovered through distillation in order to improve the purity of the desired ester (yield= 87%, purity=92.1 %*w/w*).

For the production of *n*-butyl acetate, *n*-butanol (BuOH, 800 g) and acetic acid (AcOH, 648 g) were added into the reactor in the appropriate amount (molar ratio 1:1 alcohol-acid). The catalyst, previously dried, was then incorporated to the reactor (40 g, *i.e.*, 5 wt.% respect of the mass of butanol). A Dean-Stark apparatus was used, in the presence of a small amount of cyclohexane (80 mL, *i.e.*, 5 %*v/v* respect of the volume of the reaction mixture), in order to remove the produced water and so improve the yield of esterification. The reaction was carried out at 105 °C, under mechanical stirring, until all the water was distilled out (approximately 8 hours). The remaining cyclohexane was then removed from the system through a simple distillation. The *n*-butyl acetate (953 g) was finally collected after catalyst separation (yield = 76 %, purity = 97.4 %*w/w*).

3.3.2.3 Scenario 2 (Sc 2): Co-production of ethyl and n-butyl acetates

In the coproduction scenario, ethyl acetate was synthesized following the protocol described in Scenario 1.

After ethyl acetate distillation, the remaining media, containing the acetic acid formed during the EtAc synthesis and the catalyst Dowex 50wx8, was respectively used as reagent and catalyst for the production of *n*-butyl acetate. *n*-Butanol (BuOH, 498 g) was then added into the reactor in an equimolar amount compared to the acetic acid.

On the reactor, a Dean-Stark apparatus was used, in the presence of a small amount of cyclohexane (50 mL, *ie*. 5 %v/v respect of the volume of the reaction mixture), in order to eliminate the produced water and so improve the esterification yield. The reaction was carried out at 105 °C, under mechanical stirring, until all the water was distilled out (approximately 8 hours). The remaining cyclohexane was then removed from the system through a simple distillation. The *n*-butyl acetate (538 g), obtained by coproduction, was collected after catalyst filtration (yield = 69 %, purity = 97.1 %*w/w*).

3.3.2.4 Life Cycle Assessment (LCA)

The Life Cycle Assessment was undertaken using the ISO 14040[374] and 1044[375] standards: the first one defining the principles and the framework and the second one describing the different stages of the analysis.

3.3.2.4.a Goal and scope definition

The Life Cycle Assessment was conducted on the solvent production process in order to analyze the environmental impacts of the developed synthetic pathways and identify the process unit that presents the strongest impacts through a hot spot analysis. The comparison between the two scenarios (independent or coproduction syntheses) was also investigated.

In order to build the inventory of production, it was necessary to define the functional unit. The functional unit chosen was the production of 1 kg of solvent, with a purity determined experimentally, as presented typically in the literature.[376–378]

To focus only on the impacts related to the production of these solvents in the laboratory, it was decided to carry out a "cradle to gate" analysis centered on the raw material acquisition and on the production step (Figure 40).

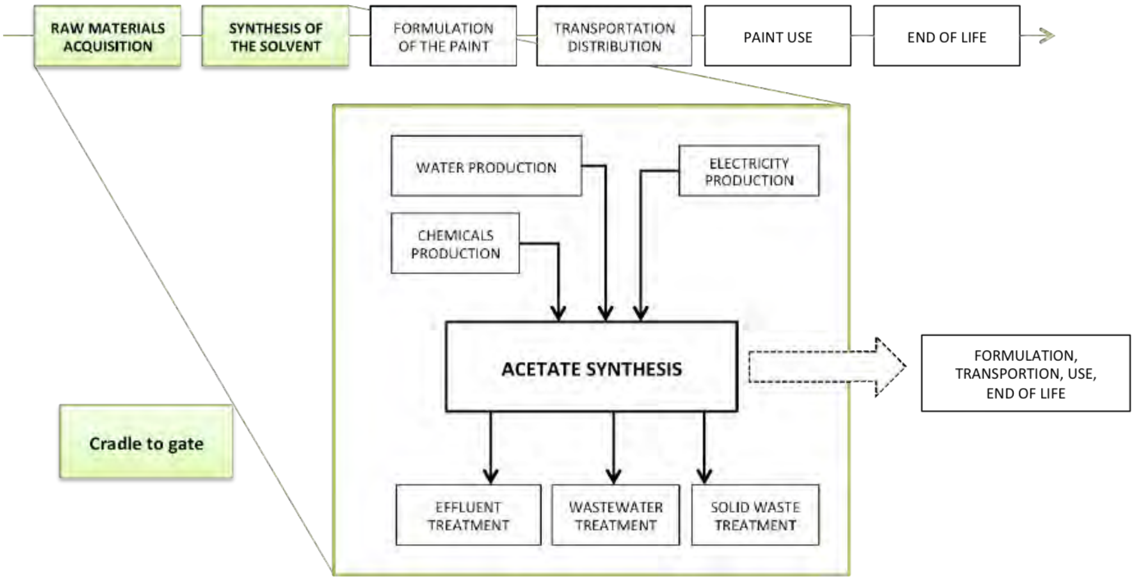


Figure 40. System boundaries of the Life Cycle Assessment of this study

For the modeling, initial hypotheses were defined as follows:

- The energy used was considered as a French energy mix.
- The cleaning of all the devices is neglected.
- The transportation of the chemicals is estimated as follows: 600 km by train followed by 100 km by lorry with a capacity greater than 32 tons.[379]
- The depreciation of the infrastructures is estimated to be equal to $4{\cdot}10^{-10}$ p/kg of product (value based on a production of 50.000 tons of products over 50 years) (estimation as described in the Ecoinvent database).
- 0.2 % of the mass of the used chemicals is emitted directly into the air (estimation as described in the Ecoinvent database).
- The whole wastes and emissions are fully treated by the sewage plant, *ie.* the sewage plant is considered with an efficiency of 100 %.

3.3.2.4.b Life Cycle Inventory

The most important task in a LCA study is the data collection. Two types of data have to be distinguished: the foreground data and the background data.

The foreground data, on the one hand, refer to specific data needed to model the system. They include all the measurements collected directly on experimental devices and all the estimated data that are not directly available. On the other hand, the background data are usually related to energy, transport and waste materials. They are mostly available in databases (in our case Ecoinvent 3.1) or in the literature.

- **System description**

For the Life Cycle Inventory, all the inputs and outputs of the system were listed for the different stages of the syntheses, either for the independent pathways (scenario 1) or for the coproduction (scenario 2).

The flowcharts, showing the different steps of the processes with the associated flows, are presented in figure 41 for the independent esterifications and in figure 42 for the coproduction.

Noteworthy, all the foreground data detailed in Figure 41 and 42 present their own life cycle that are taken into account for modeling the global life cycle of the ester syntheses.

Some differences between the two flowcharts (Figure 41 and 42) can be highlighted. Indeed, the aim of the coproduction is to recycle the remaining mixture after ethyl acetate distillation. These wastes are used, without any treatment, as reagents for the second esterification performed in series. The catalyst that is in the remaining mixture is still active after the first cycle. Indeed, the value of the ion-exchange resin capacity was not modified after the synthesis of ethyl acetate (4.8 meq/g).

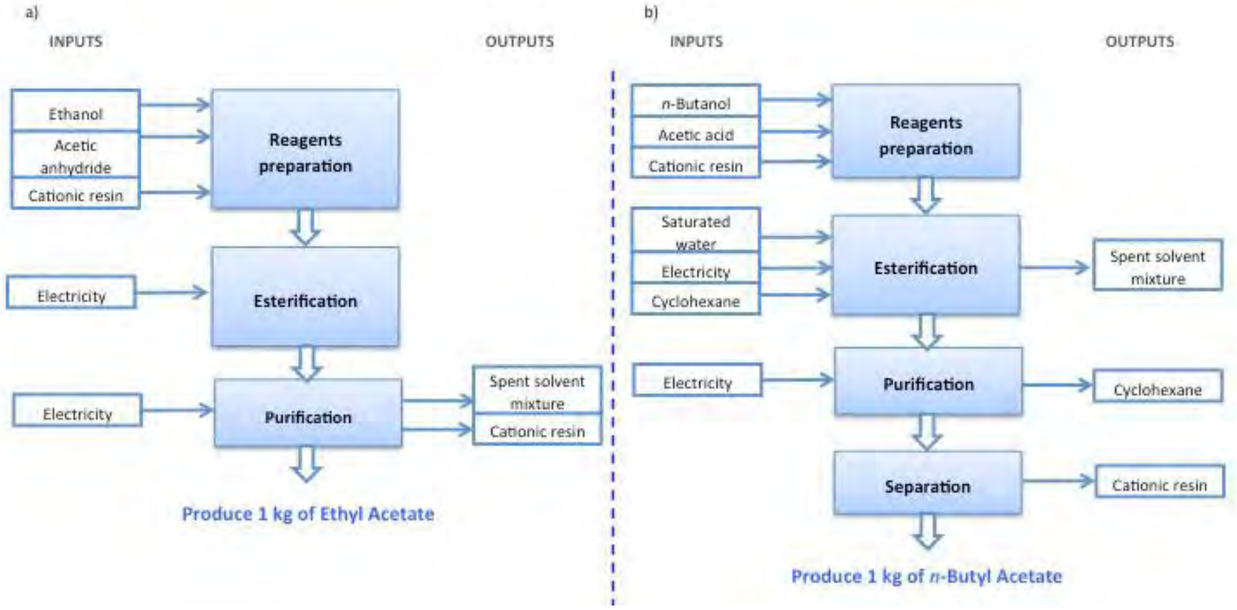


Fig 41: Process flowchart of the independent syntheses of ethyl acetate (a) and *n*-butyl acetate (b)

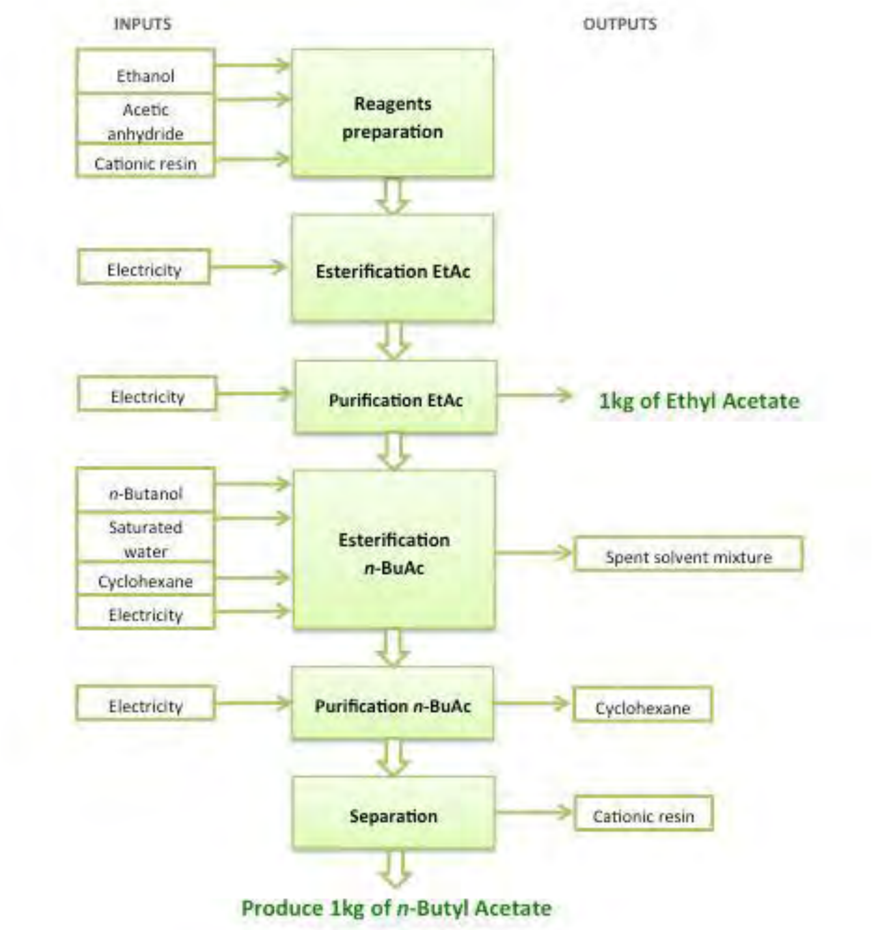


Fig 42: Process flowchart of the coproduction of ethyl acetate and *n*-butyl acetate

- **Data collection**

The inventory data, also called foreground data, were collected directly in the laboratory by the experiments. They were considered relatively reliable compared to those from the literature.

The emission and extractions data, or background data, were obtained from the Ecoinvent 3.1 database. If possible, the French (FR) or even the European (RER) data were used in order to be consistent on the geographic point. In other cases, the data from the global market (GLO) were considered.

Unfortunately, all the chemicals were not available in the used database. In order to overcome this problem, that could affect the modeling of the environmental performance of the syntheses, proxys and bibliographic study were used.

The data used in the analyses and their sources are presented in Table 46.

Data	Source
Ethanol without water in 99.7% solution slate, from ethylene {GLO} / market for	Ecoinvent 3.1
1-Butanol {GLO} / market for	Ecoinvent 3.1
Acetic anhydride {RER} / market for	Ecoinvent 3.1
Acetic acid, without water, in 98% solution slate {GLO} / market for	Ecoinvent 3.1
Cationic resin {GLO} / market for	Proxy
Cyclohexane {GLO} / market for	Ecoinvent 3.1
Sodium chloride, powder {GLO} / market for	Ecoinvent 3.1
Water, deionized, from tap water, at user {GLO} / market for	Ecoinvent 3.1
Transport, freight train {CH} / market for	Ecoinvent 3.1
Transport, freight, lorry <32 metric ton, EURO 3 {GLO} / market for	Ecoinvent 3.1
Chemical factory, organics {GLO} / market for	Ecoinvent 3.1
Electricity, medium voltage {FR} / market for	Ecoinvent 3.1
Spent solvent mixture {CH} / treatment of hazardous waste incineration	Ecoinvent 3.1

Table 46. Source of the data used in the LCA

Before any modeling, the quality of the data needed to be estimated in order to guarantee the value and reliability of the data used in the Life Cycle Assessment. In this study, all the data were not of equivalent accuracy and uncertainty existed between them. It was thus necessary to evaluate this uncertainty that could affect the interpretation of the results. For this, the quality indicators developed by Weidema and Wesnaes were used.[380]

Table 47 summarizes the reliability ratings of each type of data (the reliability being assessed by a score from 1 for the maximum to 5 for the minimum).

Data	Comments	Quality rating (reliability)
INPUTS		
Chemicals mass	The mass of chemicals has been precisely measured during the synthesis, directly in the laboratory.	1
Energy	The quantity of energy needed for the synthesis have been estimated by calculation, by using the operation time of each device and their technical characteristics. These data could not have been measured.	3
Transportation distances	The transportation distances, either by lorry or train, have been determined through hypothesis. This is an estimate of average distance for the transport of chemicals.	3
Infrastructure depreciation	The depreciation of the infrastructure (regarded as a chemical plant) is estimated from the mean values over the entire life of the plant.	3
OUTPUTS		
Emissions into air	Emissions to air are derived from assumptions.	3
Byproducts masses (avoided products)	The masses of avoided products that can be recycled or recovered are measured precisely during the synthesis.	1
Masses of waste and emissions treatment	The masses of waste treatment and emissions are measured precisely during the synthesis.	1

Table 47. Evaluation of the reliability of the inputs and outputs (with score from 1 being the best and 5 the worst)

3.3.2.4.c Impact assessment

To characterize the different environmental impacts, a derivative of the ILCD 2011 1.05 method was used. Indeed, in the existing method, indicators of resource depletion (water and mineral, fossil or renewable resources) were not sufficiently reliable.[379] These indicators have thus been replaced by a water flow indicator (corresponding to the "water depletion" indicator of the ReCiPe method) and an energy consumption indicator, based on the Cumulative Energy Demand method. The 17 midpoint impact categories used are presented in Table 48.

The inventory and the impact calculations were performed on SimaPro 8.1.1 software.

Midpoint impact categories	Description	Unit
Climate change	Emissions of greenhouse gases that cause an increase in temperature of the lower atmospheric layers (for example CO_2, CH_4, N_2O, CFC, CO)	kg CO_2 eq
Ozone depletion	Air emissions of substances that destroy the stratospheric ozone layer (for example CFC, HCFC, CCl_4)	kg CFC -11 eq
Human toxicity, cancer effects	Emissions to soil, water and air of substances that harm human health (for example heavy metals, dioxins, VOC, NOx, SO_2, particulates...) with carcinogenic effects	CTUh
Human toxicity, non-cancer effects	Emissions to soil, water and air of substances that harm human health (for example heavy metals, dioxins, VOC, NOx, SO_2, particulates) with non-carcinogenic effects	CTUh
Particulate matter	Air emissions of particulate matter less than 2.5 microns	kg PM2.5 eq
Ionizing Radiation, Human Health	Ionising radiation or radioactive, with impacts on human health	kgBq ^{235}U eq
Ionizing Radiation, Ecosystems	Ionising radiation or radioactive, with impacts on ecosystems	CTUe
Photochemical ozone formation	Air emissions of substances that cause the production of tropospheric ozone or smog (for example NOx, VOC, CH_4, CO)	kg NMVOC eq
Acidification	Air emissions of substances that cause acid rain (for example NOx, SO_2, NH_3, VOC, HCl)	molc H^+ eq
Terrestrial eutrophication	Emissions to air and water of substances that cause an excess of nutrients (for example components containing N and P)	molc N eq
Freshwater eutrophication	Emissions to air and water of substances that cause an excess of nutrients in lakes, rivers and oceans (for example components containing N and P)	kg P eq
Marine eutrophication	Emissions to air and water of substances that cause an excess of nutrients in marine water (for example components containing N and P)	kg N eq
Freshwater ecotoxicity	Emissions to water and air of substances that damage the ecosystems (flora and fauna) in fresh water (for example heavy metals, acids, pesticides...)	CTUe
Land Use	The occupation by men of a certain area of agricultural land for a certain period for agriculture and the landscape changes or space resulting	kg C deficit
Mineral, fossil, renewable resources depletion	Environmental depletion of mineral, fossil and renewable resources. The calculation performed is based on the remaining stocks and on the current consumption rates	kg Sb eq
Water flow	Environmental depletion of water. The calculation performed is based on the remaining stocks and on the current consumption rates	m3
Non renewable energy consumption	Quantification of the energy content of non-renewable energy resources (fossil, nuclear and biomass)	MJ

Table 48. Midpoint impact categories used for the evaluation method (a derivative of the ILCD 2011 1.05 method)

3.3.3 Results and discussion

3.3.3.1 Syntheses of ethyl and n-butyl acetates

3.3.3.1.a Independent synthesis of ethyl acetate

The strategy to use ethanol and acetic anhydride, instead of acetic acid used mostly in the literature for the production of ethyl acetate,[303,368] was developed in order to avoid the formation of water during the synthesis.

Indeed, starting from ethanol and acetic acid, for one mole of ethanol, one mole of water is produced. At the end of the esterification, this production of water lead to difficulties in purification, as the ethyl acetate forms azeotropes with water and also with the remaining ethanol.[381] One promising solution to break this azeotrope water-ethanol-ethyl acetate is the pervaporation.[382–384] In our case, starting with a mixture of ethanol and acetic anhydride at an equimolar *ratio* leads to the formation of ethyl acetate and acetic acid, easily separable by distillation. Noteworthy, as the reaction is highly exothermic, there is a competition between the reaction of ethanol with acetic anhydride and the acetic acid that was formed during this reaction. The acetic acid reacts with the remaining ethanol, all along the synthesis and thus led to a nearly total conversion of the ethanol and the formation of a small amount of water that will not disrupt the purification of the acetate. In order to separate and purify ethyl acetate, a distillation was carried out.

The compositions of the obtained reaction medium before and after distillation are presented in Table 49.

	Conversion of EtOH (%)	Yield of EtAc (%)	Composition of the reaction medium				
			%	AAc	EtOH	EtAc	H_2O
At the end of reaction	99.4	98	mol	48.4	0.3	48.5	2.8
			w/w	40.1	0.2	59.0	0.7
After distillation	100	87	mol	9.1	0.0	85.4	5.4
			w/w	6.7	0.0	92.1	1.2

Table 49. Quantitative analyses of the reaction medium before purification and the isolated ethyl acetate after purification

After the laboratory distillation, ethyl acetate was obtained at a purity of 92.1 %w/w, acetic acid and water still being present in the distillate.

When the distillation was stopped, 43.8 %w/w of the medium still remained in the reactor, with a composition of 77.5 %w/w of acetic acid and 22.5 %w/w of ethyl acetate. Thus, a way of recycling needed to be considered.

3.3.3.1.b Independent synthesis of n-butyl acetate

In the case of *n*-butyl acetate, the use of *n*-butanol and acetic acid at a molar *ratio* of 1:1, in the presence of a heterogeneous catalyst, led to the formation of one mole of water per mole of *n*-butyl acetate. It is thus mandatory to remove continuously the produced water in order to shift the equilibrium and so enhance the ester formation. The use of a Dean Stark apparatus, in the presence of a small amount of cyclohexane, was decided in order to produce and remove the azeotropic mixture cyclohexane/water and so increase the reaction yield. The composition of the medium obtained after the separation was presented in the Table 50.

Conversion of BuOH (%)	Yield of BAc (%)	Composition of the reaction media				
		%	AAc	BuOH	BAc	H_2O
99	76	mol	0.8	1.7	91.2	6.4
		w/w	0.4	1.1	97.4	1.1

Table 50. Quantitative analysis of the isolated n-butyl acetate after purification

After distillation, *n*-butyl acetate was obtained at a purity of 97.1% w/w, containing very small amounts of butanol, acetic acid, and water. The yield of formation of *n*-butyl acetate is a bit lower than the one of ethyl acetate (76% compared to 87%) as two successive distillations are needed to recover the desired acetate (water elimination followed by cyclohexane distillation). In each distilled fractions, traces of n-butyl acetate were revealed

3.3.3.1.c Co-production of ethyl acetate and n-butyl acetate

After studying both ethyl acetate and *n*-butyl acetate separately, their coproduction was investigated. The wastes of the ethyl acetate purification, *ie.* a mixture composed of 77.5 %w/w of acetic acid and 22.5 %w/w of ethyl acetate, were reused as reactants for the *n*-butyl acetate production. The heterogeneous catalyst was also recycled in the second esterification. The composition of the distilled *n*-butyl acetate after the coproduction process is presented in Table 51.

Conversion of BuOH (%)	Yield of BAc (%)	Composition of the reaction media						
		%	AAc	BuOH	EtOH	BAc	EAc	H_2O
94	69	mol	0.2	2.9	0.0	92.7	0.2	3.9
		w/w	0.1	1.9	0.0	97.1	0.2	0.6

Table 51. Quantitative analysis of the distilled butyl acetate, obtained by co-production

The use of acetic acid mixed with ethyl acetate, recycled from the first esterification, did not affect the production of the desired ester as a mixture highly enriched in *n*-butyl acetate (97.1 %w/w of purity after coproduction *vs* 97.4 %w/w after the independent esterification) was obtained. It is thus an interesting way of production of *n*-butyl acetate that minimizes waste production and so treatment by sewage plants.

3.3.3.2 Life cycle assessment

After characterizing the products obtained either by independent esterifications or by coproduction, the feasibility of using them as part of paint formulation was evaluated by TECNALIA (See section 2.5).

As both solvents presented interesting properties, their processes were compared through a life cycle analysis. The environmental impacts of the chemical reactions were assessed according the functional unit (FU) defined previously as the production of 1 kg of purified solvent. Only the purified esters (ethyl acetate and *n*-butyl acetate) were considered for this study.

In this study, the acetates were only produced at laboratory scale: the scale-up optimization was not investigated. Therefore, the developed processes were not compared to the industrial ones, available in the databases, as this comparison would not be relevant.

3.3.3.2.a Life cycle assessment of the independent syntheses (scenario 1): ethyl acetate

According to the process flowchart of the ethyl acetate production through Sc 1 (Figure 41a) and the experimental analysis of the obtained medium (Table 49), the inventory data (Table 52) have been collected *via* experiments and by using the hypotheses described in part 3.3.2.4a.

	Reagents preparation	Esterification	Purification
INPUTS			
Ethanol (kg/UF)	0.601	-	-
Acetic anhydride (kg/UF)	1.332	-	-
Cationic resin (kg/UF)	0.030	-	-
Transport, train (kgkm/UF)	1177.7	-	-
Transport, lorry (kgkm/UF)	196.3	-	-
Chemical factory (p/UF)	4.10^{-10}	-	-
Electricity (kWh/UF)	-	1.4	18.8
OUTPUTS			
Ethanol – *into air* (kg/UF)	$1.202.10^{-3}$	-	-
Acetic anhydride – *into air* (kg/UF)	$2.664.10^{-3}$	-	-
Cationic resin – *avoided product* (kg/UF)	-	-	0.030
Spent solvent (kg/UF)	-	-	0.847

Table 52. Inventory data for the ethyl acetate esterification

The results of the assessment of the ethyl acetate production are presented in Figure 43.

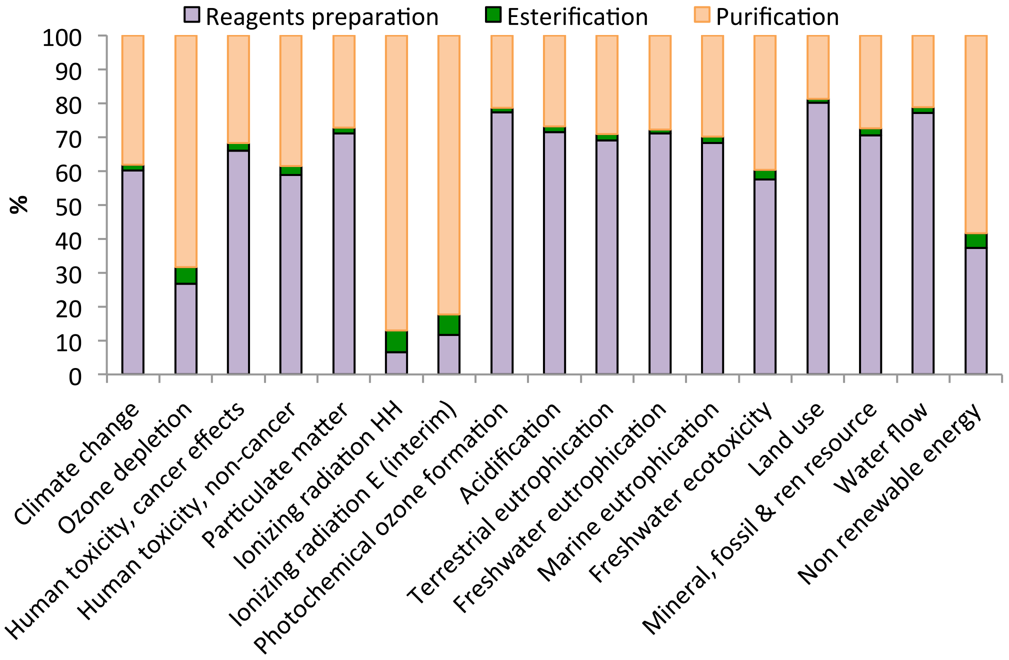


Figure 43. Hot spot identification of the ethyl acetate production – Impact characterization by a derivative of the ILCD 2011 1.05 method

It clearly appears that the reagents preparation step presents the most significant environmental impacts (between 53 % and 84 %) for 13 of the 17 impact categories. These results can be explained by the strong impacts generated by the production of acetic anhydride involving in particular the use of acetic acid. In the case of the four other impact categories (ozone depletion, ionizing radiation HH, ionizing radiation E and non renewable energy consumption), the purification step has the greatest impact on the environment, due to a large consumption of electricity during 8 hours.

For example, the potential “human toxicity, cancer effects” impact was $3.85{\cdot}10^{-7}$ CTUh, with a contribution of the reagents preparation step of $2.53{\cdot}10^{-7}$ CTUh and of acetic anhydride itself of $1.98{\cdot}10^{7}$ CTUh, corresponding to 51.5 % of the total impact. These results are in line with those presented in the works of Domènech et al.,[385] Wang et al.,[378] and Groslambert and Léonard.[386] They highlighted that the main environmental impacts came from the burdens associated with the production of reactants. One way for improving these LCA results could be the use of greener reactants produced either from biomass or with a greener and more direct process.

3.3.3.2.b Life cycle assessment of the independent syntheses (scenario 1): n-butyl acetate

Before modeling the chemical production of *n*-BuAc, the inventory data were collected in the laboratory and reported in the Table 53.

	Reagents preparation	Esterification	Purification	Separation
INPUTS				
1-Butanol (kg/UF)	0.840	-	-	-
Acetic acid (kg/UF)	0.680	-	-	-
Cationic resin (kg/UF)	0.042	-	-	-
Cyclohexane (kg/UF)	-	0.050	-	-
Sodium chloride (kg/UF)	-	0.010	-	-
Water, deionised (kg/UF)	-	0.010	-	-
Transport, train (kgkm/UF)	937.1	36	-	-
Transport, lorry (kgkm/UF)	156.2	6	-	-
Chemical factory (p/UF)	4×10^{-10}	-	-	-
Electricity (kWh/UF)	-	18.8	9.4	-
OUTPUTS				
1-Butanol – *into air* (kg/UF)	1.68×10^{-3}	-	-	-
Acetic acid – *into air* (kg/UF)	1.34×10^{-3}	-	-	-
Cyclohexane – *into air* (kg/UF)	-	$0.1.10^{-3}$	-	-
Cyclohexane – *avoided product* (kg/UF)	-	-	0.050	-
Cationic resin – *avoided product* (kg/UF)	-	-	-	0.042
Spent solvent (kg/UF)	-	0.493	-	-

Table 53. Inventory data for the *n*-butyl acetate production.

The results of the assessment of the butyl acetate production are presented in figure 44.

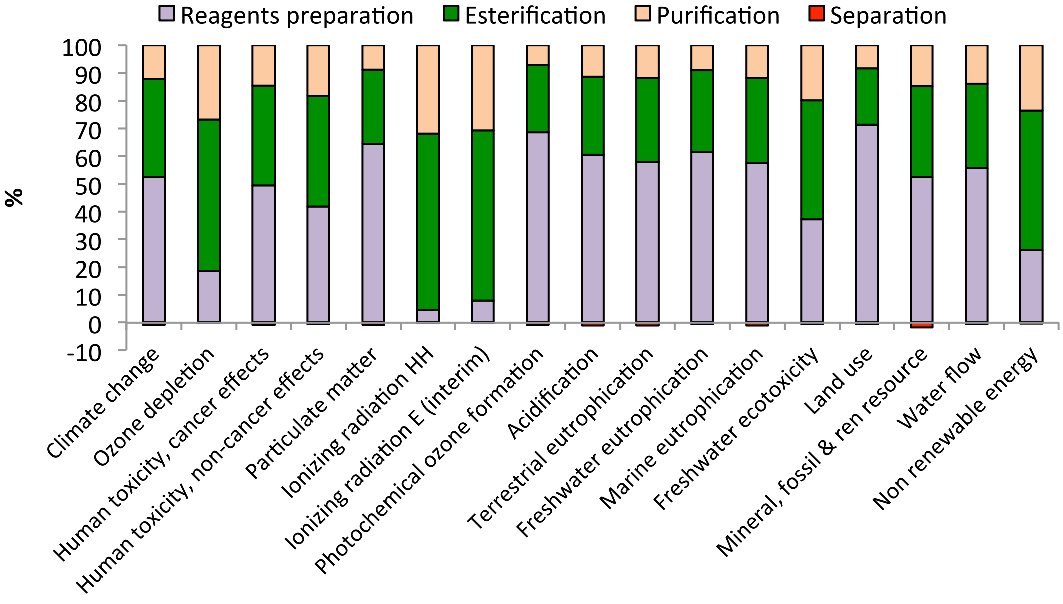


Figure 44. Hot spot identification of the *n*-butyl acetate esterification – Impact characterization by a derivative of the ILCD 2011 1.05 method

As for the ethyl acetate production, the reagents preparation step is responsible of the majority of the environmental impacts (12 impact categories out of 17). This observation can be explained by the use of *n*-butanol as a reactant and especially the use of propylene related to its production. For the five other impact categories (ozone depletion, ionizing radiation HH, ionizing radiation E, freshwater ecotoxicity and non-renewable energy consumption), the impact of the electricity consumption can be highlighted, with a major role for the esterification and purification steps. Noteworthy, as the cyclohexane was recovered after distillation and recycled, it does not contribute to environmental impacts in the esterification step.

These conclusions (high quantity of reactants and energy intensive processes such as distillation) are also presented in Jödicke et al.'s work as important contributors on the LCA.[387]

3.3.3.2.c Life cycle assessment of the co-production of acetates (scenario 2)

After studying both esterifications separately (scenario 1), they were investigated according to a coproduction process (scenario 2) where the co-products of the first synthesis were recycled in the second one. As presented in the process tree detailed in figure 42, the functional unit of this coproduction is the production of 1 kg of *n*-BuAc, using the acetic acid from the synthesis of EtAc. It is thus needed to determine the quantity of initial reactants to obtain the sufficient amount of acetic acid to produce 1 kg of *n*-BuAc, knowing the characteristics of the esterifications (Table 50 and Table 51). According to our calculation, 1.141 kg of EtAc must be synthesized in order to recover the 0.749 kg of acetic acid needed for the production of 1 kg of *n*-BuAc.

The inventory data of this coproduction were collected directly through our experiments at laboratory scale (Table 54).

Noteworthy, the spent solvent mixture considered as wasted from the "Esterification *n*-BuAc" step (as presented figure 42) was composed of a mixture of reagents and products (*n*-butanol, acetic acid, ethyl acetate, n-butyl acetate and water).

	Reagents preparation	Esterification EtAc	Purification EtAc	Esterification *n*-BuAc	Purification *n*-BuAc	Separation
INPUTS						
Ethanol (kg/UF)	0.686	-	-	-	-	-
Acetic anhydride (kg/UF)	1.520	-	-	-	-	-
Cationic resin (kg/UF)	0.034	-	-	0.012	-	-
1-Butanol (kg/UF)	-	-	-	0.925	-	-
Cyclohexane (kg/UF)	-	-	-	0.050	-	-
Sodium chloride (kg/UF)	-	-	-	0.010	-	-
Water, deionised (kg/UF)	-	-	-	0.010	-	-
Transport, train (kgkm/UF)	1343.7	-	-	598.0	-	-
Transport, lorry (kgkm/UF)	224.0	-	-	99.7	-	-
Chemical factory (p/UF)	$4\cdot10^{-10}$	-	-	-	-	-
Electricity (kWh/UF)	-	1.4	18.8	18.8	9.4	-
OUTPUTS						
Ethanol – *into air* (kg/UF)	$1.371\cdot10^{-3}$	-	-	-	-	-
Acetic anhydride – *into air* (kg/UF)	$3.039\cdot10^{-3}$	-	-	-	-	-
1-Butanol – *into air* (kg/UF)	-	-	-	$1.85\cdot10^{-3}$	-	-
Cyclohexane – *into air* (kg/UF)	-	-	-	$0.1\cdot10^{-3}$	-	-
Cyclohexane – *avoided product* (kg/UF)	-	-	-	-	0.050	-
Cationic resin – *avoided product* (kg/UF)	-	-	-	-	-	0.046
Spent solvent (kg/UF)	-	-	-	0.664	-	-

Table 54. Inventory data for the coproduction of ethyl and *n*-butyl acetate – scenario 2

These inventory data were then connected to the environmental damages caused by the substances inventoried, as presented in Fig. 45.

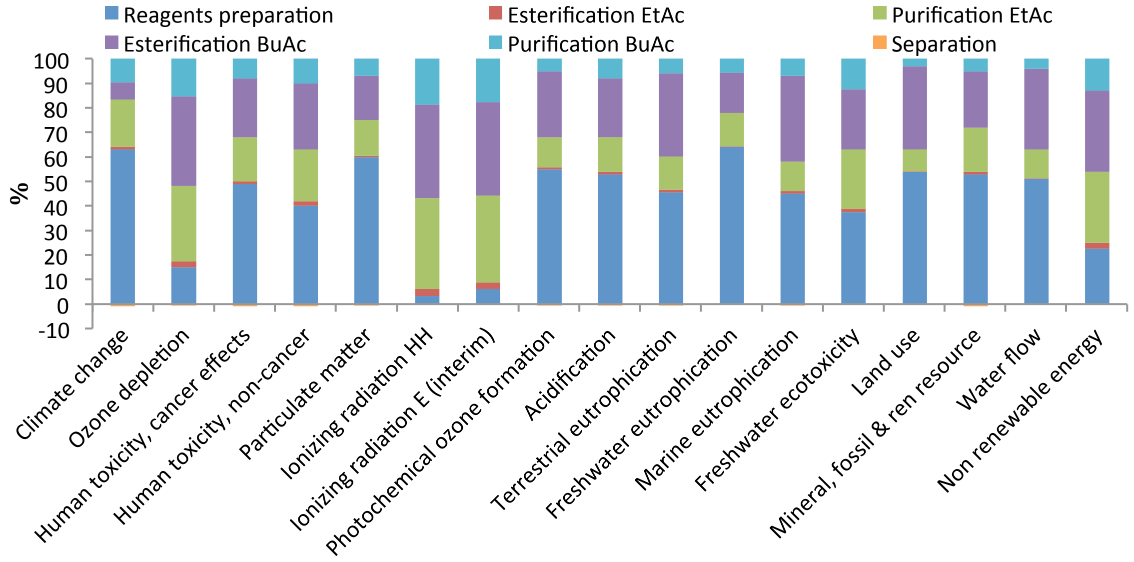


Figure 45. Hot spot identification of the coproduction process (scenario 2). Impact characterization by a derivative of the ILCD 2011 1.05 method.

The results obtained through LCA, for the coproduction (scenario 2), seem to be quite similar to those obtained for independent esterifications (scenario 1): the reagents preparation step is still the one responsible of the majority of the environmental impacts for 13 impact categories.

A deeper comparison between both scenarios has been made. Noteworthy, as the scenario 2 generates 1.141 kg of ethyl acetate and 1 kg of *n*-butyl acetate; the same factors were used for the scenario 1, i.e., the impacts caused by the synthesis of the ethyl acetate were multiplied by 1.141. Actually, by studying these results deeper and comparing in more details those two different processes, it appears that the coproduction presents lowest impacts on the environment (Fig. 46).

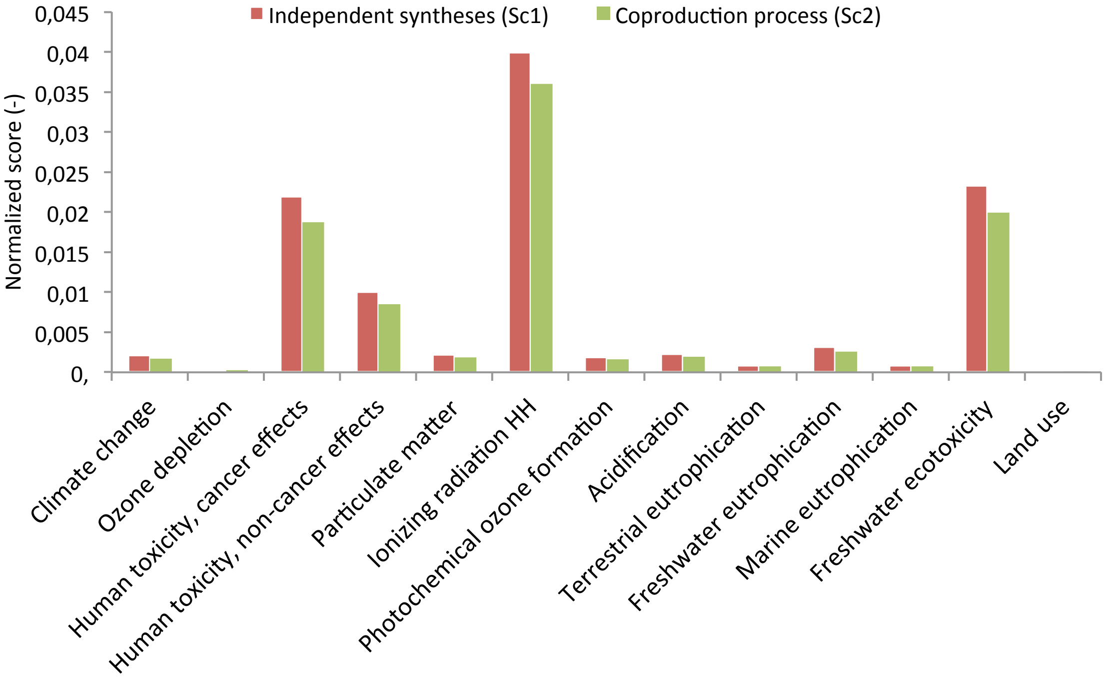


Figure 46. Comparison between the independent synthesis (Sc1) and the co-production process (Sc2). Normalization of the impacts by derivative of the ILCD 2011 1.05 method.

These results have been confirmed by a Monte Carlo analysis, over 5000 iterations (Figure 47). Indeed, for all the 17 impact categories evaluated in the method, processing the ethyl acetate and *n*-butyl acetate syntheses in parallel (Sc 1) had a higher probability of occurrence than the coproduction (Sc 2), that is to say that there is more chance that Sc 1 creates more impacts on the environment than Sc 2. These results can essentially be explained by the recycling of the acetic acid produced through the ethyl acetate esterification, by using acetic anhydride. This recycling also led to a reduction of the quantity of spent solvent to be treated by incineration or wastewater treatment plant, and so the substances emitted by these treatments. Moreover, as the ion exchange resin was also recycled; it avoided effluent consumption needed for potential treatment.

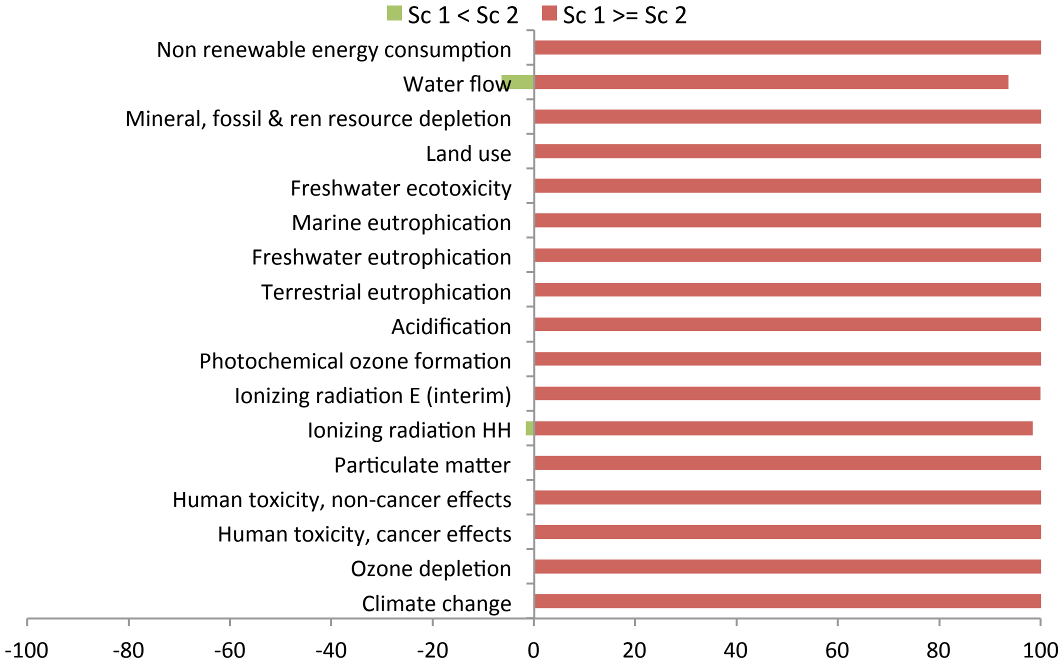


Figure 47. Comparison between the independent reactions (Sc1) and the coproduction (Sc2) through a Monte Carlo analysis. Impact characterization by a derivative of the ILCD 2011 1.05 method

3.3.3.3 Challenges for Life Cycle Assessment of chemical syntheses

In this study, we have faced several problems due to the lack of LCA perspective in the chemical field.

3.3.3.3.a Problematic of the data collection

Only few LCAs have been carried out on chemicals and syntheses.[385,388,389] An important lack of data has been highlighted: nowadays, about 84,000 substances are used but only 1,500 are available in Life Cycle Inventory (LCI) databases, such as Ecoinvent, Agribalyse or GaBi.[390] This lack of data can be explained by the fact that collecting data is complex, time consuming and expensive. When possible, data were directly collected in laboratories or chemical industries such as BASF[391] or GlaxoSmithKline[392] but due to confidentiality issues, the results of the assessment were barely published. The scarcity of the data availability is problematic to correctly determine the potential environmental impacts of these chemicals.

To overcome this lack of data, the inventories are mostly estimated. Different techniques exist to fill these gaps such as an estimation of the inputs/outputs derived from heuristics and on-site data on chemical production processes,[393] the use of stoichiometric equations from technical literature,[394] the use of chemical engineering process design[392] or even the use of substitutes or proxys.[390] For all, uncertainty analysis must be undertaken to avoid under or overestimations of the potential environmental impacts, especially in product comparisons.

In our case study, all the chemicals needed were not available in the database used (Ecoinvent 3.1). To overcome this problem, proxys and bibliographic study were used. For example, the ion-exchange resin used in our experiments, Dowex 50wx8, is not presented in Ecoinvent 3.1. It was thus decided to substitute this chemical by the data “Cationic resin {GLO}, market for” that considers the production of 1 kg of moist resin, containing 50 wt.% of moist and with 6-8 wt.% divinylbenzene (DVB) crosslinking. It was also mentioned that the production process of the resin contained lots of uncertainty, leading to a low quality of the data.

3.3.3.3.b Problematic of the functional unit description

The definition of the functional unit has to be done carefully as the results of LCA strongly depend on this choice.[395]

In this study, we decided to consider, in a cradle to gate approach, the production of 1 kg of the desired solvent, at a purity determined experimentally. The knowledge of the purity of the solvent to be assessed, and furthermore the presence of potential by-products, is essential to correctly estimated the inputs and outputs of the study. Indeed, in the case of the ethyl acetate presented in the part 3.1.1.1, producing 1 kg of ethyl acetate at 92.1 %w/w, really means the production of 1.086 kg of mixture including 1 kg of acetate, 0.072 of acetic acid and 0.014 of water, according to the composition of the final reaction mixture (Table 49).

To compare different syntheses, it was essential to use the same functional unit, as reference, *ie*. the production of 1 kg of desired solvent (ethyl or butyl acetate).

In our study, the limits of this statement were faced. Indeed, for the coproduction process developed, two syntheses were made consecutively. If we studied the production of 1 kg of ethyl acetate followed by the production of 1 kg of *n*-butyl acetate, there will not be enough acetic acid produced in the first process to be used in the synthesis of *n*-butyl acetate (process presented in figure 37). It is thus necessary to adapt the functional unit to the study.

Another important point could have been observed if the study was focused on a cradle to gate approach, up to the formulation of the paint and its application. Indeed, in this case, the functional unit could have been to cover a wall with a determined opacity. Changing the degree of opacity could completely change the calculations of the LCA.

3.3.4 Contribution of LCA *vs* green metrics

As we have previously mentioned, green metrics provide a quantitative analysis of the efficiency and the environmental performance of chemical reactions and processes.[340] In this way, calculation of green metrics, of the individual syntheses and the coproduction process of acetates, is an easy and fast way to get information for the selection of the most environmental-friendly chemical route.

The principal metrics used in the evaluation of new chemical pathways are the atom economy (AE), the environmental factor (E-factor), and the percentage from renewable sources (PRS). This green metrics can be related to the principles of green chemistry proposed by Anastas and Warner.[102] For example, prevention, atom economy, use of renewable feedstocks and use of safe solvent and auxiliaries (Figure 48).

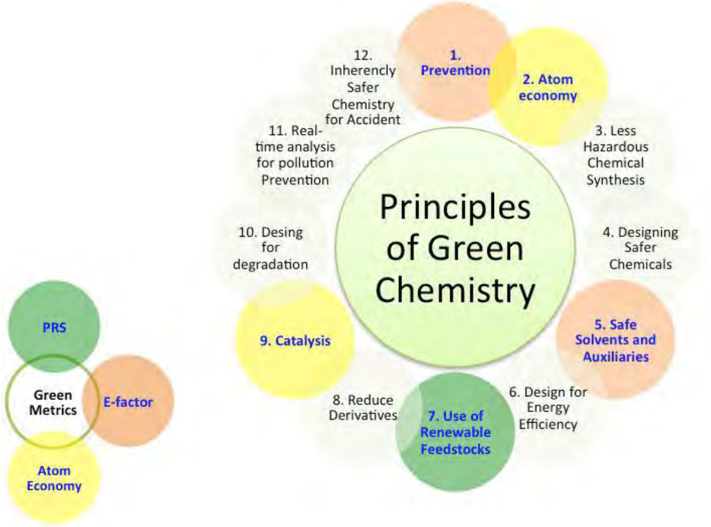


Figure 48. Relation between the principles of the green chemistry and the green metrics.

In the development of the co-production process of acetates using ion exchange resins as catalyst we were able to respect several of the principles of the green chemistry proposed by Anastas and Warner:[226] the 1st, 2nd, 3rd, 5th, 7th, 9th and 12th. It is important to highlight that the toxicity (3rd principles) and the chemicals handling hazards (12th principle) were reduced in the developed co-production process, thanks to the replacement of the sulfuric acid (H314, H318, R35; related to burns risk), used in the current industrial process, by the ion exchange resin Dowex 50WX8 as catalyst. It is noteworthy that 7th principle related to the use of renewable feedstock was taken into account because ethanol and *n*-butanol can be from bio-based origin. Indeed, nowadays several companies supply bio-ethanol and bio-butanol (for example GreenBiologics, ZeaChem, Abengoa, Shell Global and Pacific ethanol Inc.) in the current market.

The atom economy (AE), the environmental (E-factor) and the percentage from renewable sources (PRS) were calculated for (Table 55):

- The individual syntheses starting from i) acetic anhydride and ethanol (1:1) for the production of ethyl acetate and ii) acetic acid and butanol (1:1) for the preparation of butyl acetate.
- The co-production process of ethyl and butyl acetates.

Process	% AE	E-factor	% PRS
Ethyl and butyl acetates through individual syntheses	72.4	0.68	57.90[a]
Ethyl and butyl acetates through coproduction process	**91.9**	**0.31**	57.90[a]

Table 55. Green metrics for the classical individual syntheses and the co-production process developed in this work. [a]Percentage from renewable sources calculated considering that ethanol and butanol are from bio-based feedstock.

According to the green metrics gathered in the table 55, the developed co-production pathway resulted in a more efficient process compared to the individual syntheses.

The atom economy was higher with the co-production process thanks to the recycling of the acetic acid produced in the first esterification as it was used as reagent in the second one for the synthesis of butyl acetate.

As it was expected, the environmental factor (E-factor) of the co-production process was also better than the obtained with the individual syntheses, 0.31 *vs* 0.68, respectively. These results are not surprising, since as we have discussed, the production of wastes was considerably reduced during the co-production process.

Considering the percentage of renewable sources, same PRS values were obtained with both the individual syntheses and the co-production process when bio-based ethanol and *n*-butanol were used.

Green metrics method, atom economy and E-Factor, demonstrates that acetates co-production process is more environmental friendly and sustainable than the individual syntheses, due to the reduction of wastes and by-products. Nevertheless, this approach only evaluate the synthesis it self. In this way, life cycle assessment (LCA) offers more accurate information about the impact to the environment generated not only by the syntheses, but also by the whole processes, considering for example, the production of starting materials, the energetic consumption during the process, the production and treatment of wastes and the final use of the product.

3.3.5 Conclusions

As the solvent market is still going to increase, it is essential to focus on different manners to improve their way of production, especially from an environmental point of view. Even with the petrochemical resource depletion, temporary solution could be investigated to reduce the environmental impacts of the chemical synthesis. This study was focused on the production of two common esters particularly used in paints and coatings: ethyl and *n*-butyl acetate.

The two developed esterifications were coupled in order to simplify and make greener the global process: no water is produced during the first step that forms ethyl acetate and acetic acid. This acid was thus recycled for the synthesis of *n*-butyl acetate, after its separation with ethyl acetate. With the proposed process of coproduction, the objectives were completed with an efficient production of acetates in the presence of heterogeneous acidic resin (Dowex 50wx8).

The environmental impacts of this new process were thus evaluated through a Life Cycle Assessment (LCA) and compared to those of the both esterifications, realized in parallel. Using a derivative of the ILCD 2011 1.05 method, it appeared that, for all the 17 midpoint impact categories taken into account, the coproduction presents lowest impacts on the environment. Indeed, as the by-products of the ethyl acetate esterification, *ie* a mixture of acetic acid and ethyl acetate, were recycled in the second synthesis, the impact of the substances was reduced up to 23 %.

In a context of sustainable chemistry, this new way of production of acetates presents many advantages such as comparable results on a technical point of view and above all, a clear improvement of the environmental impacts.

This case study also allowed us to raise the issue of the lack of perspective on the LCA of chemicals, whether in terms of data collection or for the definition of the functional unit. The interest of LCA compared with green metrics was also discussed.

3.4 Bio-ethyl and bio-butyl acetates synthesized thought the individual and the coproduction process: green metrics and Life Cycle Assessment

In the previous section, we studied the environmental impact of acetates syntheses using commercial ethanol and butanol (from petrochemical origin), which is found in the Ecoivent 3.1 database. However, it is interesting to analyse the environmental impact of these syntheses, but this time considering their production from bio-ethanol and bio-butanol (for ethyl acetate and butyl acetate, respectively).

3.4.1 Effect of the use of bio-ethanol and bio-butanol for ethyl and butyl acetates syntheses on environmental impacts

3.4.1.1 Functional unit and system boundaries

As in the cases described in section 3.4, the production of 1Kg of solvent as functional unit was defined. The purity of the solvents was obtained experimentally at laboratory scale (see section 3.3, table 49 and 50). To analyse the impacts related to the syntheses of the molecules from bio-based feedstocks (bioethanol and bio-butanol), an analysis type "cradle to gate" was carried out, from the acquisition of the raw material to the production stage.

3.4.1.2 Life cycle inventory

For the life cycle inventory, the inputs and outputs of the system were identified for each stage of both syntheses, the independent pathways and the coproduction process. Here, the unique difference with the flowcharts of the section 3.4 is the replacement of ethanol by bio-ethanol and butanol by bio-butanol (Figure 49 and 50).

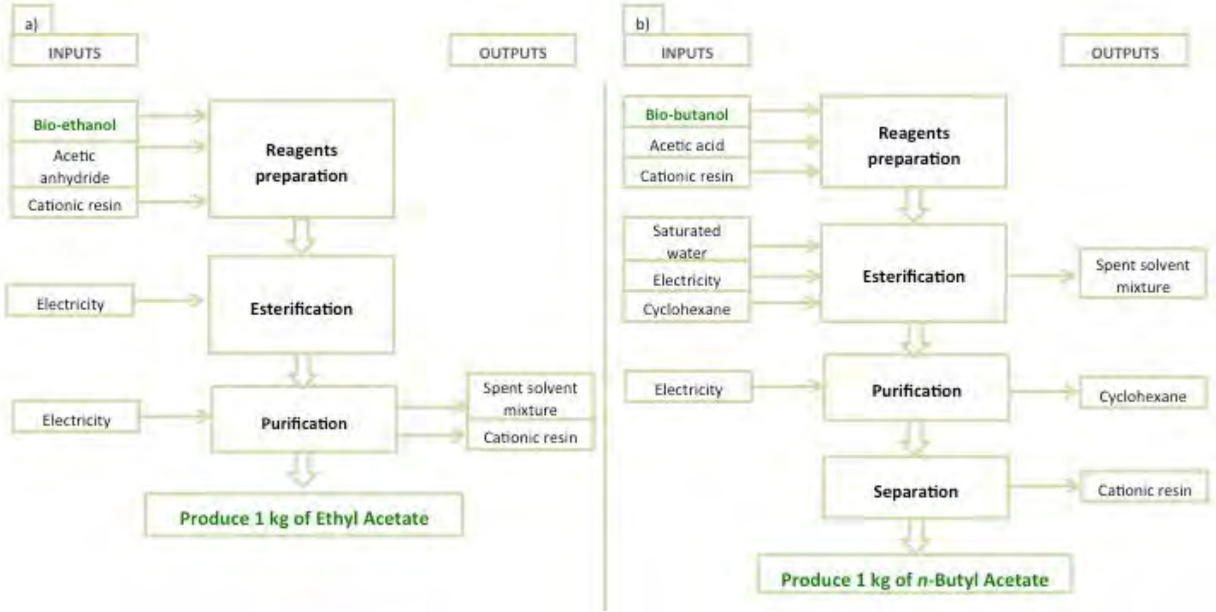


Figure 49. Process flowchart of the synthesis of ethyl and butyl acetates using bioethanol and bio-butanol, respectively

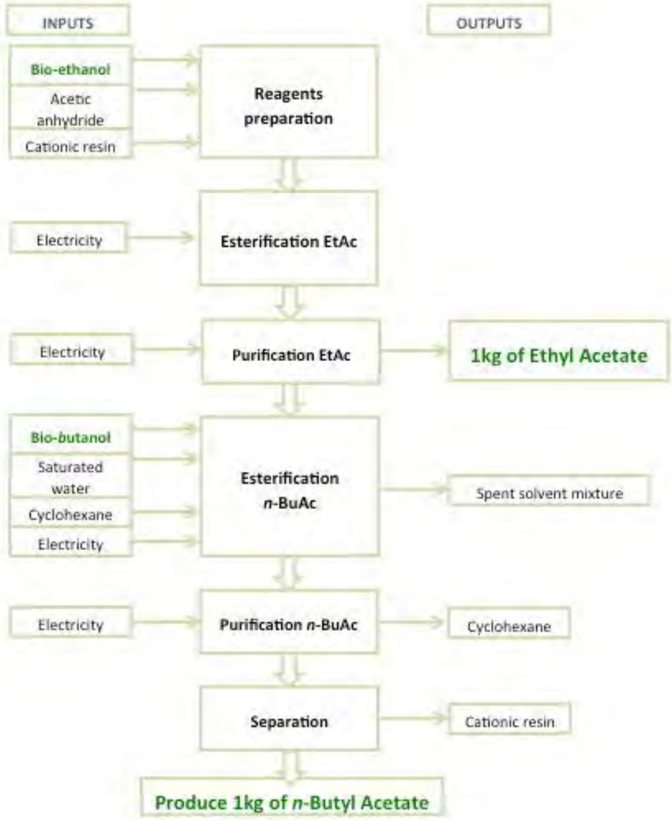


Figure 50. Flowchart of the coproduction process using bioethanol and bio-butanol

3.4.1.3 Life cycle assessment of the independent syntheses (Scenario 1): bio-ethyl acetate

The inventory data for the production of bio-ethyl acetate were collected according to the process flowchart of the figure 49a and with the experimental results obtained in the laboratory (Table 56).

Functional Unit = 1 kg of Ethyl Acetate		Reagents preparation	Esterification	Purification
INPUTS				
Bio-based ethanol (kg/FU)	Ecoinvent 3.1 "maize"	0.601	-	-
Acetic anhydride (kg/FU)	Ecoinvent 3.1	1.332	-	-
Cationic resin (kg/FU)	Proxy	0.030	-	-
Transport, train (kgkm/FU)	Ecoinvent 3.1	1177.7	-	-
Transport, lorry (kgkm/FU)	Ecoinvent 3.1	196.3	-	-
Chemical factory (p/FU)	Ecoinvent 3.1	4.10^{-10}	-	-
Electricity (kWh/FU)	Ecoinvent 3.1	-	1.4	18.8
OUTPUTS				
Ethanol – into air (kg/FU)		$1.202.10^{-3}$	-	-
Acetic anhydride – into air (kg/FU)		$2.664.10^{-3}$	-	-
Cationic resin – avoided product (kg/FU)		-	-	0.030
Spent solvent (kg/FU)		-	-	0.847

Table 56. Inventory data for the ethyl acetate production

In this synthesis, we considered the use of bio-ethanol. In the Ecoinvent database are proposed several sources of bio-ethanol: maize, sugarcane and wood. We decided to work with the bio-based ethanol produced from maize since it is the most representative worldwide. Indeed, 51% of bioethanol worldwide comes from the United States,[396] where it is produced mainly from corn (94%).[397]

As the carbon contained in bio-ethanol is fully or partly of biogenic origin, it has to be considered as carbon storage. This carbon is sequestered from the atmosphere during photosynthesis and it can be retained from several years. In order to calculate the biogenic carbon, it is firstly necessary to determine the mass of biogenic carbon, m(bio C), as shown in Eq. III-5:

$$\mathrm{m\ (bio\ C)} = \frac{\mathrm{n\ x\ M(C)}}{\mathrm{M(chemical)}} = \frac{2\ \mathrm{x}\ 12}{46.07} = 0.52\mathrm{kg\ C_{biogenic}\ /kg\ ethanol} \qquad \text{Eq. III-5}$$

where: m(bio C) is the mass of biogenic carbon (kg/kg of chemical), n is the number of carbon atom in the chemical, M(C) is the molar mass of carbon (12g/mol) and M(chemical) is the molar mass of the chemical (g/mol).

Then, it was necessary to calculate the mass of stored CO_2 per kg of bio-based chemical. The following equation was used:

$$\mathrm{m}\ (\mathrm{CO_2}) = \frac{\mathrm{m(bio\ C)} \cdot \mathrm{M(CO_2)}}{\mathrm{M(C)}} \qquad \text{Eq. III-6}$$

where: m (CO_2) is the mass of stored carbon dioxide (kg/kg of chemical), m(bio C) is the mass of biogenic carbon (kg/kg of chemical), M(CO_2) is the molar mass of carbon dioxide (44g/mol), and M(C) is the molar mass of carbon (12g/mol).

By substituting in the equation we obtained:

$$\mathrm{m}\ (\mathrm{CO_2}) = = \frac{0.52\ \mathrm{Kg}\ \mathrm{C_{biogenic}}\ /\mathrm{Kg\ ethanol} \cdot\ 44\mathrm{g/mol}}{12\mathrm{g/mol}} = 1.91kg\,\frac{CO_2}{kg\ ethanol} \qquad \text{Eq. III-7}$$

For the bio-ethanol, it was thus considered as biogenic 1.91 kg of CO_2/kg of ethanol.

3.4.1.3.a Impact assessment: bio-ethyl acetate

After collection data, the environmental impacts of the production of 1kg of ethyl acetate from bio-ethanol and acetic anhydride were evaluated. The contribution to the environmental impact of each stage of the process was analysed. The results are presented in the following figure 51.

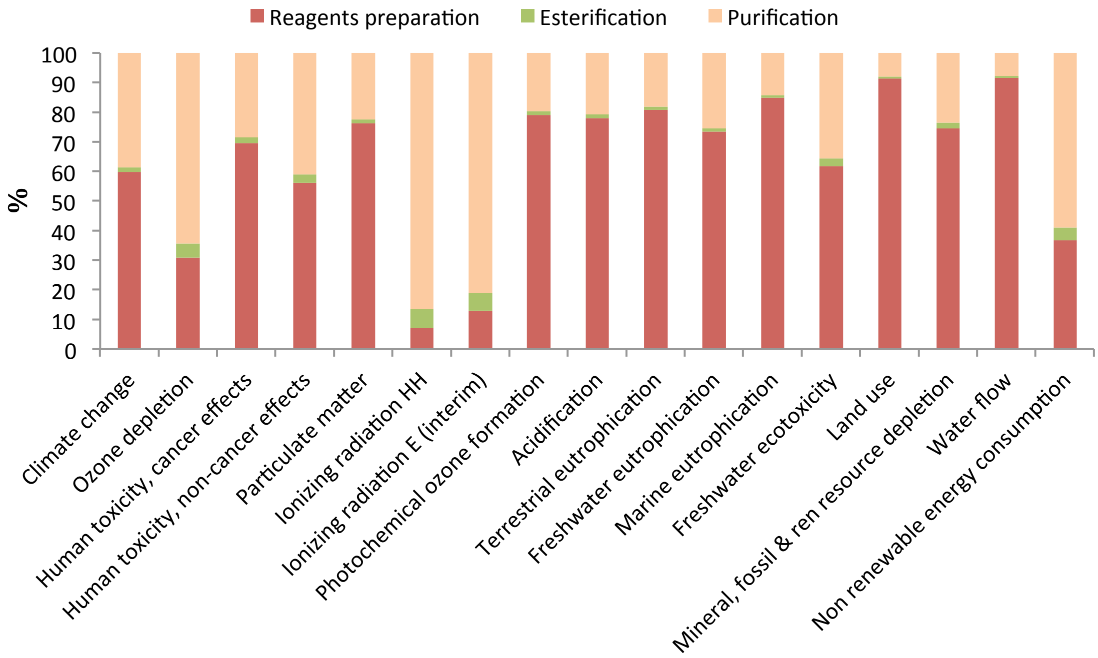


Figure 51. Hot spot identification of the bio-ethyl acetate production. Impact characterization by a derivative of the ILCD 2011 1.05 method

As can be seen in Figure 51, the preparation of reagents is the stage that contributes the most to the environmental impacts (between 53 and 90%), in 13 of the 17 categories. This is mainly due to the preparation of acetic anhydride. In the remaining four categories, the purification of ethyl acetate has the greatest impact, due to the energy consumption during the 8h of distillation necessary to obtain ethyl acetate with a purity of 92.1%.

3.4.1.3.b Sensitivity analysis: influence of the bioethanol sources

There are different sources for the production of bioethanol. A sensitivity analysis on the biomass source for the production of ethanol was performed. Four different feedstocks were analysed (Table 57).

Data	Source
Ethanol, without water, in 95 % solution state, from fermentation {RoW}/ ethanol from maize	Ecoinvent 3.1
Ethanol, without water, in 95 % solution state, from fermentation {Br}/ ethanol from sugarcane	Ecoinvent 3.1
Ethanol, without water, in 95 % solution state, from fermentation {RoW}/ ethanol from wood	Ecoinvent 3.1
Ethanol from Brazilian sugarcane, from ABE fermentation	Pereira et al (2015)[377]

Table 57. Different sources for the production of bio-ethanol

Figure 52 presents the impacts related to the different sources of ethanol.

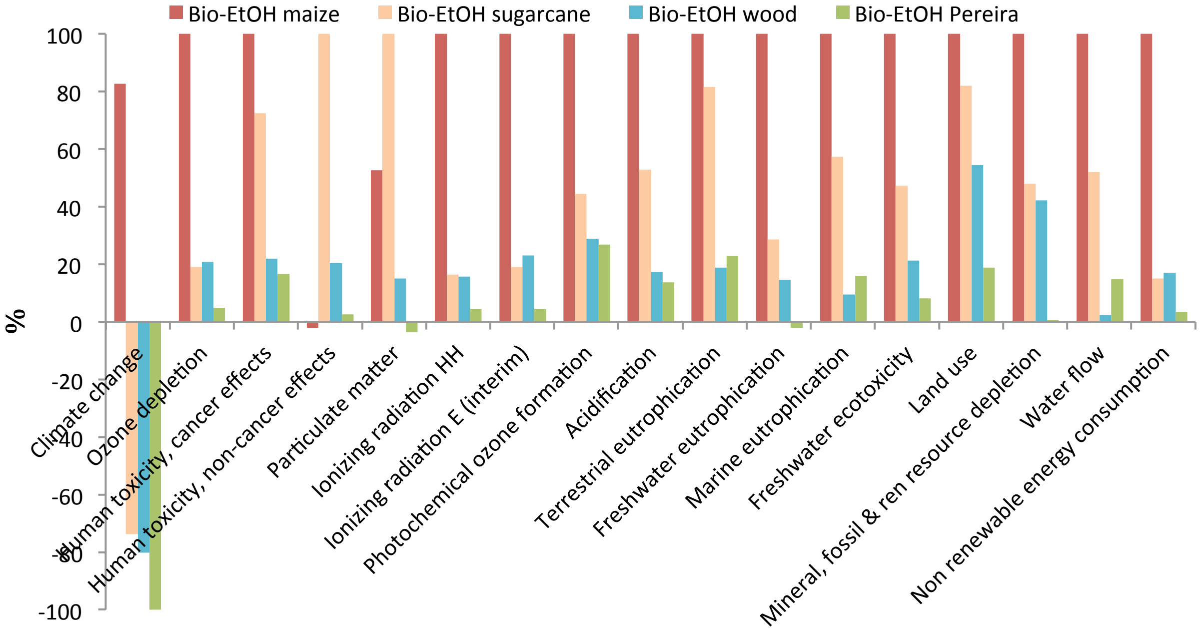


Figure 52. Sensitivity analysis on the choice of the source of bioethanol. Impact characterization by a derivative of the ILCD 2011 1.05 method

These results clearly show that the biomass source of bioethanol has an influence on the impact on the environment. It can be seen that the impacts are reduced almost 10 times, by replacing the ethanol produced from maize by that reported in Pereira's work.[377] It is important to highlight that the impact on climate change is negative when using ethanol produced from cane sugar, wood and cane sugar from Pereira's work. This can be explained by the fact that for each kg of bioethanol used, the release of 1.91 kg of CO_2 is avoided. In the case of corn bioethanol, although the emission of biogenic carbon is avoided, 1.4 kg of CO_2 are released during corn production, which involves the use of pesticides, lime, and nitrogen fertilizers.[398]

3.4.1.4 Life cycle assessment of the independent syntheses (scenario 1): bio-n-butyl acetate

The inventory data for the production of bio-*n*-butanol were collected according to the process flowchart of the figure 49b and with the experimental results obtained in the laboratory (Table 58).

Functional Unit = 1kg of bio-*n*-Butyl Acetate		Reagents preparation	Esterification	Purification	Separation
INPUTS					
Bio-based *n*-butanol (kg/FU)	Literature	0.840	-	-	-
Acetic acid (kg/FU)	Ecoinvent 3.1	0.640	-	-	-
Cationic resin (kg/FU)	Proxy	0.042	-	-	-
Cyclohexane (kg/FU)	Ecoinvent 3.1	-	0.050	-	-
Sodium chloride (kg/FU)	Ecoinvent 3.1	-	0.010	-	-
Water, deionised (kg/FU)	Ecoinvent 3.1	-	0.010	-	-
Transport, train (kgkm/FU)	Ecoinvent 3.1	937.1	36	-	-
Transport, lorry (kgkm/FU)	Ecoinvent 3.1	156.2	6	-	-
Chemical factory (p/FU)	Ecoinvent 3.1	4.10^{-10}	-	-	-
Electricity (kWh/FU)	Ecoinvent 3.1	-	18.8	9.4	-
OUTPUTS					
1-Butanol – into air (kg/FU)		$1.68.10^{-3}$	-	-	-
Acetic acid – into air (kg/FU)		$1.34.10^{-3}$	-	-	-
Cyclohexane – into air (kg/FU)		-	$0.1.10^{-3}$		-
Cyclohexane – avoided product (kg/FU)		-	-	0.050	-
Cationic resin – avoided product (kg/FU)		-	-	-	0.042
Spent solvent (kg/FU)		-	0.493	-	-

Table 58. Inventory data for the bio-n-butyl acetate production

Bio-based *n*-butanol was considered for the synthesis of bio-butyl acetate. As the lowest impacts to the environment were obtained with the data from Pereira's work in the synthesis of bio-ethyl acetate, we decided, to perform the analysis of bio-butyl acetate also with the data reported by Pereira et *al.* for bio-butanol production from sugarcane fermentation by *Clostridium saccharoperbutylacetonicum.*[377]

We considered that the carbon from the bio-*n*-butanol is biogenic carbon and we calculated the storage carbon with the equations reported in section 3.4.1.3. The mass of biogenic carbon was calculated as shown in Eq. III-8.

$$\mathrm{m\ (bio\ C)} = \frac{4 \times 12}{74.1} = 0.65\mathrm{kg\ C_{biogenic}\ /kg\ butanol} \qquad \text{Eq. III-8}$$

Then, the mass of stored CO_2 per kg of bio-butanol was calculated in Eq. III-9.

$$\mathrm{m(CO_2)} = \frac{0.65\ \mathrm{Kg\ C_{biogenic}\ /kg\ butanol} \cdot\ 44\mathrm{g/mol}}{12\mathrm{g/mol}} = 2.38\ \mathrm{kg}\frac{\mathrm{CO_2}}{\mathrm{kg\ butanol}} \qquad \text{Eq. III-9}$$

For the bio-butanol, 2.38 kg of CO_2/kg of butanol are considered as biogenic.

3.4.1.4.a Impact assessment: bio-n-butyl acetate

The environmental impacts of the production of 1kg of purified butyl acetate from bio-*n*-butanol were evaluated. The contribution to the environmental impact of each stage of the process was analysed. Results are presented in figure 53:

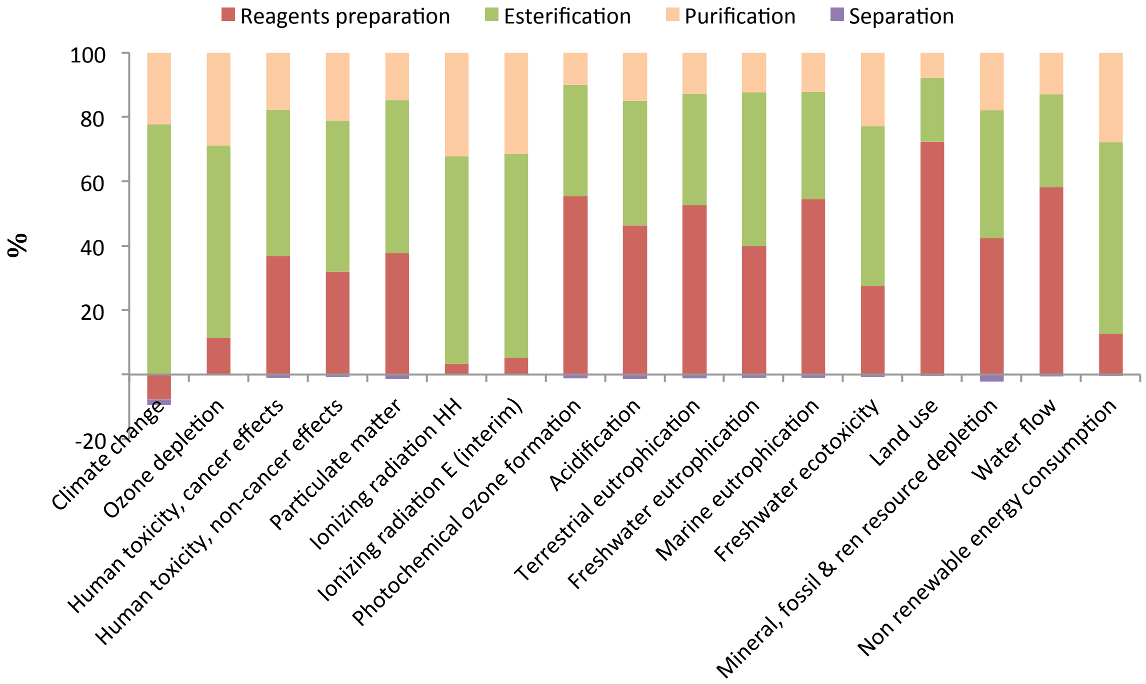


Figure 53. Hot spot identification of the bio-n-butyl acetate production. Impact characterization by a derivative of the ILCD 2011 1.05 method

The analysis showed that the esterification step produced the largest environmental impact (between 45 and 78%) in 10 of the 17 impacts categories (Figure 53). These results are related with the high energy consumed during the 8 hours necessaries for the esterification. Moreover, if we observe the category of climate change, negative values were obtained in the preparation of reagents. This is thanks to the 2.38 kg of CO_2/kg of butanol stored as biogenic carbon.

3.4.1.5 Life cycle assessment of the bio-acetates coproduction process (scenario 2)

The inventory data for the coproduction process were collected according to the flowchart of the figure 48. Data were directly collected at laboratory scale (Table 59).

	Reagents preparation	Esterification EtAc	Purification EtAc	Esterification *n*-BuAc	Purification *n*-BuAc	Separation
INPUTS						
Bio-ethanol (kg/FU)	0.686	-	-	-	-	-
Acetic anhydride (kg/FU)	1.520	-	-	-	-	-
Cationic resin (kg/FU)	0.034	-	-	0.012	-	-
Bio-*n*-butanol (kg/FU)	-	-	-	0.925	-	-
Cyclohexane (kg/FU)	-	-	-	0.050	-	-
Sodium chloride (kg/FU)	-	-	-	0.010	-	-
Water, deionised (kg/FU)	-	-	-	0.010	-	-
Transport, train (kgkm/FU)	1343.7	-	-	598.0	-	-
Transport, lorry (kgkm/FU)	224.0	-	-	99.7	-	-
Chemical factory (p/FU)	4.10^{-10}	-				-
Electricity (kWh/FU)	-	1.4	18.8	18.8	9.4	-
OUTPUTS						
Ethanol – *into air* (kg/FU)	$1.202.10^{-3}$	-				-
Acetic anhydride – *into air* (kg/FU)	$2.664.10^{-3}$	-				-
1-Butanol – *into air* (kg/FU)	-	-	-	$1.85.10^{-3}$	-	-
Cyclohexane – *into air* (kg/FU)	-	-	-	$0.1.10^{-3}$	-	-
Cyclohexane – *avoided product* (kg/FU)	-	-	-	-	0.050	-
Cationic resin – *avoided product* (kg/FU)	-	-	-	-	-	0.046
Spent solvent (kg/FU)	-	-	-	0.664	-	-

Table 59. Inventory data for the coproduction of bio-ethyl and bio-butyl acetates

As in the case of the individual syntheses of bio-ethanol and bio-butanol, the life cycle assessment were performed according with the data reported by Pereira et al. Biogenic carbon was the same as the calculated in the individual syntheses: 1.91 kg of CO_2/kg of ethanol and 2.38 kg of CO_2/kg of butanol.

3.4.1.5.a Impact assessment: coproduction of bio-ethyl and bio-n-butyl acetates

The impact on the environmental categories of each step of the coproduction was studied. Results are showed in figure 54.

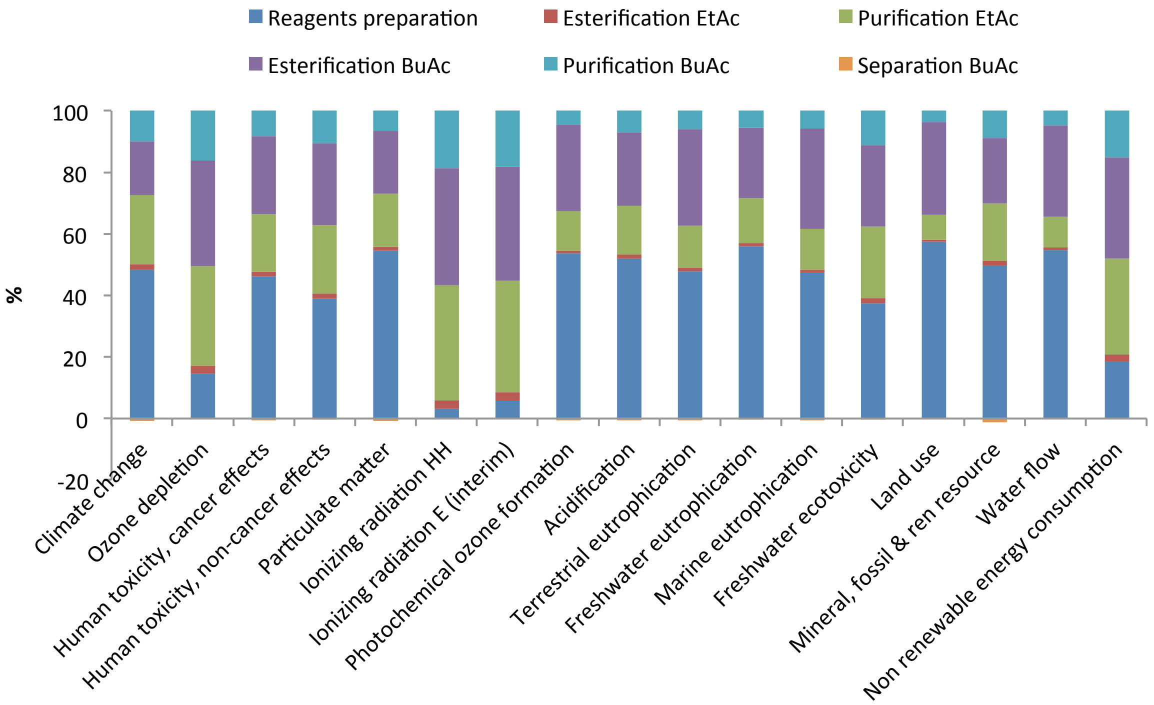


Figure 54. Hot spot identification of the coproduction of bio-ethyl and bio-butyl acetates-Impact characterization by a derivative of the ILCD 2011 1.05 method

Similar results to those of the individual syntheses were obtained with the coproduction process. The reagent preparation represents the higher impact on the environment in 13 of the 17 categories. These results are explained because of the strong impact generated by the production of acetic anhydride used in the ethyl acetate synthesis.

3.4.1.6 Comparison between the individual syntheses (scenario 1) and the coproduction of bio-ethyl and bio-butyl acetates (scenario 2)

In the acetates coproduction process, the production of wastes were reduced due to the recycling of the acetic acid produced from the esterification of ethanol and acetic anhydride that is used in the production of butyl acetate. In order to evaluate the environmental benefit of the coproduction process, the environmental impacts of both syntheses pathways were compared (Figure 55).

As in the section 3.3.3.2c, here the production of 1.141 kg of bio-ethyl acetate and 1kg of bio-butyl acetate were considered as functional unit.

The figure 55 shows that the coproduction process generated lowest impact to the environment than the individual syntheses in all the categories.

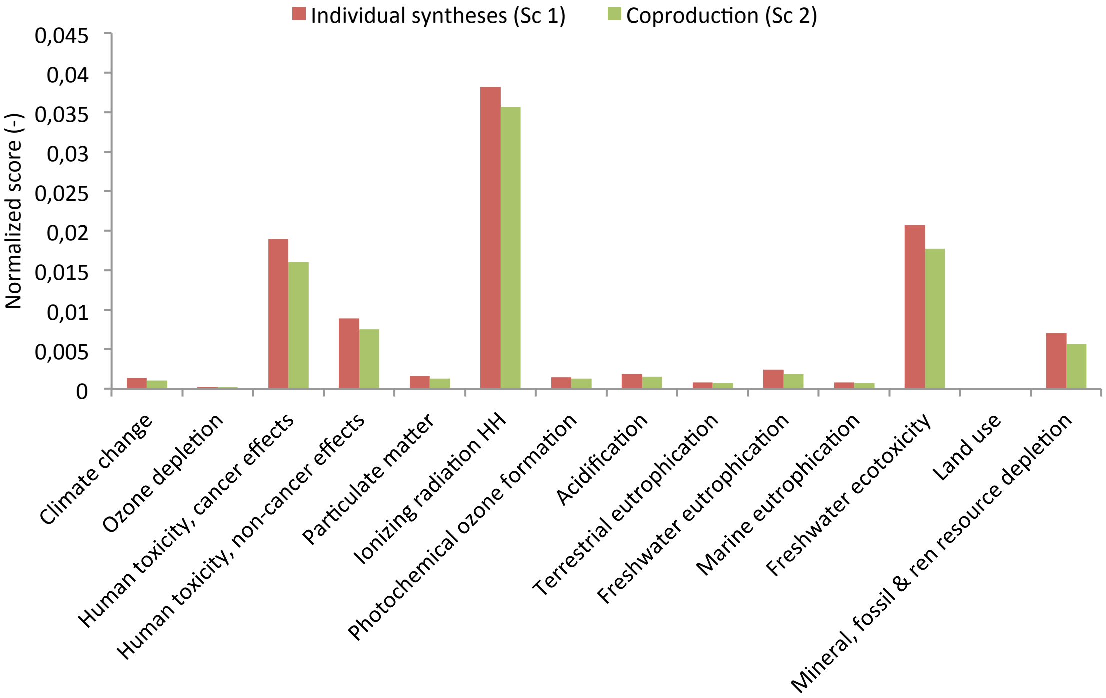


Figure 55. Comparison between the individual syntheses (Sc1) and the coproduction process (Sc2)-Normalization of the impacts by a derivative of the ILCD 2011 1.05 method

These results were confirmed by a Monte Carlo analysis, over 5000 interactions (Figure 56)

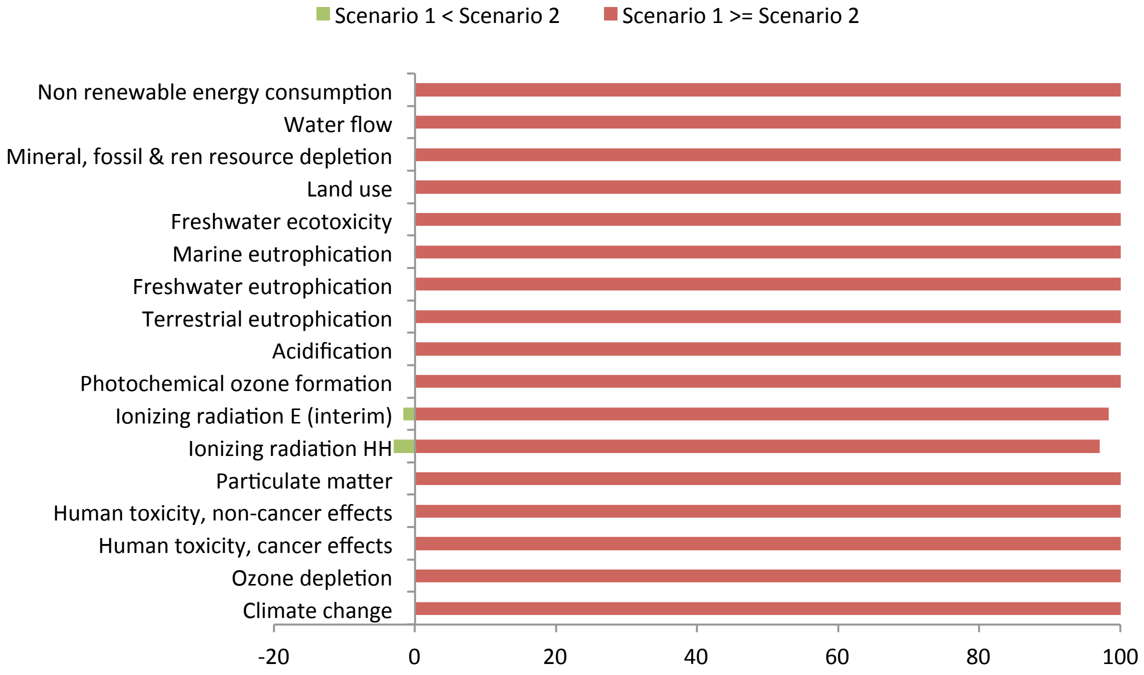


Figure 56. Comparison between the independent syntheses (Scenario1) and the coproduction process (Scenario2)-Normalization of the impacts by a derivative of the ILCD 2011 1.05 method

As we can observe in Figure 56, the environmental impact of the coproduction process is significantly favourable compared with the individual syntheses. These results are related to the recycling of the acetic acid, produced during the synthesis of ethyl acetate, in the production of butyl acetate. The recycling of acetic acid thus reduced the treatment of wastes.

3.4.2 Comparison between bio-based and petrochemical ethyl and butyl acetates produced through the developed syntheses

In this section, we presented the influence of the starting material origin, bio-based or petrochemical alcohols, on the environmental impacts generated from the developed syntheses. Herein, we compared the use of bio-ethanol or petrochemical ethanol for ethyl acetate production and bio-butanol or fossil-butanol for butyl acetate synthesis. As a reminder, herein we consider the following criteria:

- ethyl acetate produced from ethanol and acetic anhydride (1:1);
- butyl acetate produced from butanol and acetic acid (1:1);
- in both esterification, 5%w/v ion exchange resin respect to the alcohol are used.

For the analyses we have considered the same flowchart presented in Figure 47a and 47b for ethyl and butyl acetates, respectively.

3.4.2.1 Bio-ethyl acetate versus petrochemical ethyl acetate

As in the previously section, we have considered that ethyl acetate was produced from bio-ethanol. Herein, we considered that bio-ethanol is produced from sugarcane modelled in section 3.4.1.3b with the data reported by Pereira et al.,[377] as it presented the lowest environmental impact comparing with the bioethanol from maize, sugarcane and wood. In the other hand, petrochemical ethanol was taken from the Ecoinvent 3.0 database, *i.e.* ethanol, without water, in 99.7% solution state, from ethylene {GLO}/market for.

Figure 57 show the comparison of the environmental impacts generated from the developed synthesis when using bio-ethanol or its fossil equivalent.

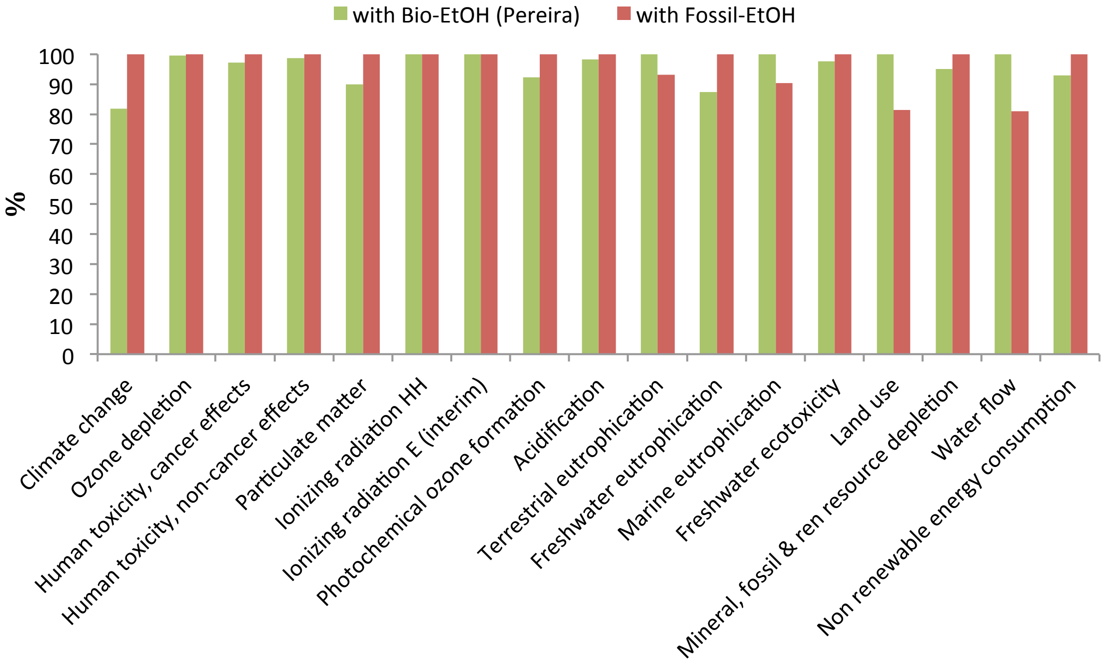


Figure 57. Comparison between the bio-based ethanol and the petrochemical equivalent for ethyl acetate production-Impact characterization by a derivative of the ILCD 2011 1.05 method

As we can observe in figure 57, in 12 of the 17 categories, there is not significant difference between the bio-based and the fossil-based ethanol (difference lower than 10 % are observed). However, a reduction of the impacts on climate change, particulate matter and freshwater eutrophication was observed when using bio-ethanol. These results can be related with the storage of CO_2 and with the sugarcane cultivation method, *i.e*. semi-mechanical planting and mechanical harvesting. The impacts reduction on freshwater eutrophication when using bio-ethanol comparing with the fossil one can be related with the high P emissions from fossil ethanol production.[399] Besides, reduction of particulate matter may be due to the reduction of fossil fuel used in bio-ethanol production. Indeed, wastes from sugarcane cultivation are used as fuel.

Otherwise, lower impacts are observed in land use and water flow when using fossil-ethanol, which can be related with the use of land for sugarcane cultivation and water for irrigation.

3.4.2.2 *Bio-n-butyl acetate versus petrochemical n-butyl acetate*

For the production of bio-*n*-butyl acetate, we have considered the use of bio-based butanol. Herein, we compared the environmental impacts generated from the synthesis of butyl acetate when using: i) the bio-butanol modelled with the data reported by Pereira et *al.*[377] presented in section 3.4.1.3b and ii) the petrochemical butanol available in the Ecoinvent 3.1 database, *i.e.* 1-butanol {GLO}/market for.

The contribution to the environmental impact when using bio-based and petrochemical butanol in the developed synthesis is presented in figure 58.

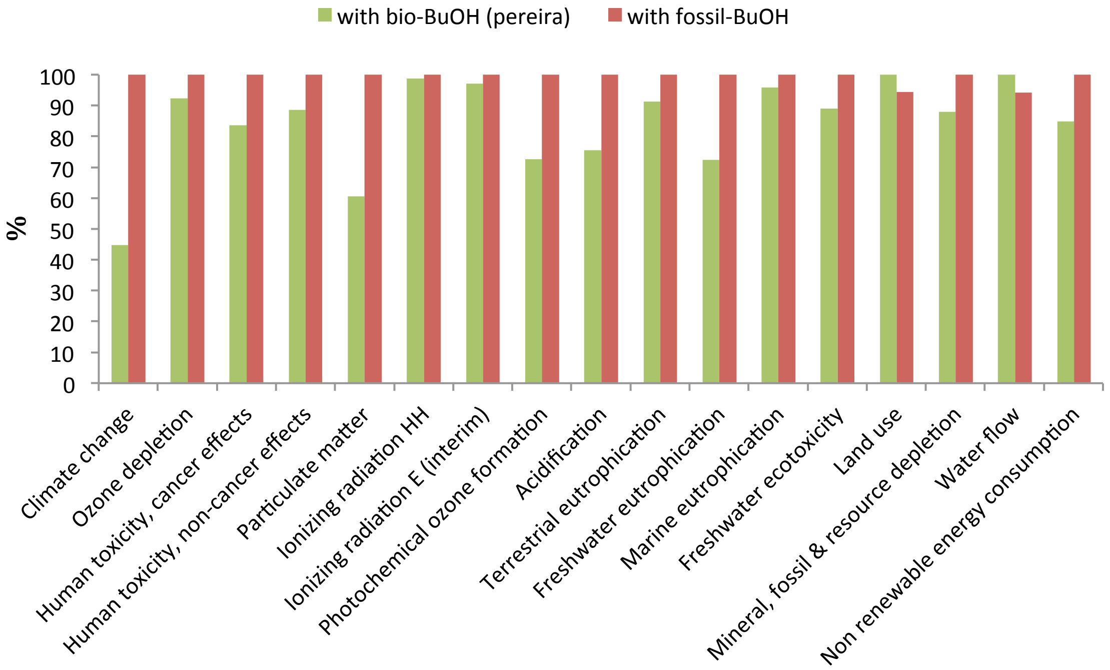


Figure 58. Comparison between the use of bio-based and petrochemical n-butanol for butyl acetate production - Impact characterization by a derivative of the ILCD 2011 1.05 method

By using bio-butanol instead of the fossil-butanol, the environmental impacts were reduced in 10 of the 17 categories. Remarkably, the impact on climate change was reduced in a 53 % when using bio-butanol. These results may be related with the storage of CO_2 when using bio-butanol, with its production, and with sugarcane cultivation method (*e.g.* mechanical harvesting). According to Pereira et *al.*,[377] no waste is generated during bio-butanol production. Furthermore, wastes from sugarcane cultivation are used as fuel. Besides, residues from sugar production are employed as natural nutrient in plantation areas, thus reducing the contribution on environment. Otherwise, no significant differences (less than 10%) were observed in the rest of the categories (7 of the 17 categories).

3.4.3 Comparison of the developed syntheses with the current industrial petrochemical one: contribution of LCA versus green metrics

In this work, bio-ethyl and bio-butyl acetates were synthesized with a greener approach, respecting as far as possible the principles of the green chemistry. It is important to highlight that in the proposed chemical routes we have replaced the sulphuric acid catalyst, used in the current industrial processes, by heterogeneous ion exchange resins. This strategy facilitated the purification of both acetates and reduced waste production related with the treatment of the homogeneous acid. Furthermore, the use of acetic anhydride instead of acetic acid facilitated the purification of ethyl acetate. The avoidance of water production permits to purify the molecule by simple distillation. In the classical process, several azeotropic distillations are needed to obtain ethyl acetate at a purity of 95%.

This study allowed us to determine that environmental impacts can be reduced by using bio-ethanol and bio-butanol for the syntheses of acetates through the developed processes. Therefore, we were interested in compare these greener syntheses with the petrochemical industrial ones. In this case, it is necessary to remark that the syntheses studied here were developed on a laboratory scale, for which the direct comparison of their life cycle with that of the industrial processes would not be pertinent. In this context, the calculation of green metrics is a useful tool that allows performing an easy and fast comparison of these syntheses.

The green metrics of ethyl and *n*-butyl acetate syntheses, through both the independent syntheses and the coproduction process, using bio-ethanol and bio-butanol, are compared with the classical process (that use acetic acid and ethanol or butanol for ethyl or butyl acetate syntheses) in table 60.

Process	% AE	E-factor	% PRS
Bio-ethyl and bio-butyl acetates through individual syntheses	72.4	0.68	57.9[a]
Bio-ethyl and bio-butyl acetates through coproduction process	91.9	0.31	57.9[a]
Petro-acetates: EAc and BAc through traditional process	85	14.7	0

Table 60. Green metrics: comparison between the developed syntheses (individual and coproduction) and the current industrial ones. [a]Percentage from renewable sources calculated considering that ethanol and butanol are from bio-based feedstock.

According to the green metrics shown in the table 60, the co-production process developed in this work leads to the best results, followed by the individual syntheses.

The percentage of renewable sources, is higher for bio-base acetates, 58 % was obtained when using bio-based ethanol and butanol for their syntheses.

Regarding the atom economy, higher value was obtained with the co-production process than with the traditional one, 91.9% *vs.* 85%.

The environmental factor (E-factor) of the co-production process and the individual syntheses were better than the obtained with the traditional ones. The lowest E-factor values were obtained for the coproduction process (0.31), thanks to the recycling of the acetic acid produced in the 1st esterification that serves as reactant in the 2nd one, avoiding thus the waste production.

3.5 Conclusions

In this work, two synthetic routes were proposed for the production of ethyl and butyl acetates: i) independent syntheses, from acetic anhydride and ethanol (1:1) for the production of ethyl acetate and from acetic acid and *n*-butanol (1:1) for butyl acetate, and ii) the coproduction process, ethyl acetate is produced from acetic anhydride and ethanol (1:1). The acetic acid produced in this reaction was used as a reagent for its esterification with *n*-butanol for the production of butyl acetate.

These syntheses were designed following the principles of green chemistry, for example, prevention, atom economy, use of less hazardous chemicals, lower toxicity, and avoidance of auxiliary solvents. It is important to note that in these syntheses, sulphuric acid, currently used in the industrial processes, was replaced by Dowex 50WX8 ion exchange resin, reducing the toxicity of the reaction and facilitating purification steps.

With the development of the acetates coproduction process, we achieved:

- the reduction of the amount of wastes and co-products
- the prevention of hazardous reagents, such as sulphuric acid
- the purification of ethyl acetate was facilitated, thanks to the avoidance of the production of water with which it forms a homogenous azeotrope.

The advantages of the coproduction process were clearly demonstrated through the calculation of green metrics:

- Atom economy was greater in the co-production process, thanks to the reuse of acetic acid produced in the first esterification, for the synthesis of butyl acetate.
- Likewise, the environmental factor was better in co-production than the individual acetates syntheses (0.31 *vs* 0.68, respectively), due to waste reduction.

Notwithstanding, green metrics showed the environmental benefits of the coproduction process against individual syntheses. Life cycle assessment was completed to get information of the whole life cycle of the acetates and to highlight the environmental advantages of the coproduction pathway.

- In the individual syntheses and in the co-production process, the reagents preparation stage showed the greatest impact on the environment, due to the production of acetic anhydride and *n*-butanol.
- By comparing the both synthetic pathways through a Monte Carlo analysis, it was attested that the coproduction process generated lower impacts to the environment in all the categories than the individual syntheses.

These results can be principally explained by waste reduction thanks to the use of the acetic acid (co-product for the first esterification) in the second esterification.

Green metrics and life cycle assessment were useful tools to assess the environmental benefit of the developed coproduction process. This synthesis strategy not only represents technical advantages, such as the easy purification by distillation, but also impacts reduction on the environment.

During life cycle evaluation of the acetates syntheses, two problems were identified: i) lack of chemical data in the available databases and ii) determination of the functional unit when comparing different syntheses processes. In order to solve these problems, the missing data were estimated through proxies and bibliographic analyses and the functional unit was adapted to the study.

The influence on the environmental impact generated by the origin of the starting material, bio-based or petrochemical, used in the developed processes was also evaluated.

- For ethyl acetate, no significant differences were obtained in the majority of the categories (15 of 17). However, lower impacts on climate change, particulate matter and freshwater eutrophication were obtained when using bio-ethanol.
- For butyl acetate, the use of bio-butanol reduced the environmental impacts in 10 of the 17 categories. Remarkably, impact on climate change was reduced in a 53 % when bio-butanol was used instead of fossil-butanol.

Finally, green metrics calculated with the syntheses developed in this work were compared with those obtained with the classical current ones.

- The bio-acetates syntheses through the coproduction process presented better results than the classical petrochemical syntheses: higher atom economy (91.9%), lower E-factor (0.31) and higher PMR (57.9%).

CHAPTER IV. Synthesis of bio-based methyl ethyl ketone

4.1 Introduction

The methyl ethyl ketone (MEK) is the second most important ketone, after acetone, and is a solvent widely used in the paint and coating industry: more than 60% of its production is destined to these sectors. MEK is currently produced from fossil sources, using high temperatures and homogeneous catalysts obtaining MEK in low yields and with quite poor selectivity.

In the context of green chemistry, we have been interested in developing a new protocol more efficient and that uses a bio-sourced molecule as starting material. The decarboxylation of levulinic acid (LA), in the presence of potassium persulfate and different silver species, has thus been envisaged as this acid is an attractive renewable source.

This chapter is divided into three parts: the first part is devoted to the presentation of the physicochemical characteristics of MEK and the industrial processes currently used for its production.

In the second section of this chapter, an extensive study of the decarboxylation of levulinic acid for the production of methyl ethyl ketone is presented. The role of the different reactants such as the silver species and the persulfate ions is explored in order to elucidate the decarboxylation mechanism for this reaction. The comprehension of this mechanism allowed us to remarkably improve the LA conversion and the MEK yield. As in the two previous chapters, this research work is presented in the form of publication.

During the reaction, changes in the colour of the solid phase were observed. These changes suggested the possible evolution of the silver species into different forms. In order to gain more insight about these modifications, we decided to analyse the solid phase of the reaction through different spectroscopic methods in the third section of this chapter. The characterization of the solid phase through scanning electron microscopy (SEM-EDX), solid-state nuclear magnetic resonance (SSNMR), X-ray diffraction (XRD), and X-ray photoelectron spectroscopy (XPS) showed the evolution of silver species along the reaction and lend support to the reaction mechanism previously proposed in second section of this chapter.

4.2 Generalities: from conventional to bio-based methyl ethyl ketone (MEK)

4.2.1 Methyl ethyl ketone (MEK): properties, applications and industrial production

4.2.1.1 Properties and applications

Methyl ethyl ketone (MEK), also known as 2-butanone (IUPAC: butan-2-one), is a flammable colourless liquid with low viscosity and a characteristic ketone odour similar to acetone.[400] This ketone is classified by the FDA in class 3 which means that it is less toxic and of lower risk to human health than solvents of class 1 and 2 such as benzene and toluene, respectively.[1] Its physicochemical properties are shown in the following table 61.

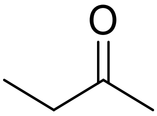
Structure	Properties	Value
 CAS: 78-93-3	Molecular formula	C_4H_8O
	Molecular weight	72.11 g/mol
	Flash point	-6.1°C
	Boiling point	79.6°C
	Melting point	-86.0 °C
	Evaporation rate (relative to butyl acetate)	4
	Density	0.850 Kg/L
	Solubility in water, 20°C	27.5 g/L
	Viscosity, 25°C	0.43 cP
	Specific gravity D_{20}^{20}	0.805
	Refractive Index n_D^{20}	1.3788
	DL$_{50}$ (oral in rat)	2737 mg/kg[72]
	Biodegradability	Readily biodegradable
	Partition coefficient (log Kow)	0.26 (low potential for bioaccumulation)[401]

Table 61. Physicochemical and toxicological properties of methyl ethyl ketone[72,400,402]

MEK is classified in the solvent paint category as an oxygenated solvent with a high dissolvent power. For this reason, it is widely used in the paint and coating sector, principally as a low-boiling solvent for nitrocellulose, acrylic and vinyl resin-based coatings. Furthermore, its high volatility (b.p. 79.6°C) and high evaporation rate (4 respect to butyl acetate) make it a good solvent for acrylics and lacquers.[403] MEK can also be employed in rubber-based industrial cements and printing inks. Furthermore, this ketone is required in the polymerization processes of polystyrene, acrylonitrile, and styrene-butadiene rubber.[404]

After acetone, which has a very similar structure with only one less carbon, MEK is the most important commercially produced ketone. Its production in 2014 was estimated at 1.4 million tons and an increase of 35% is predicted for 2022.[405] The global market of MEK was valued at USD 2.56 billion in 2015,[406] [406] with 60 % of the total MEK production used by the paint and coating sectors (Figure 59).[407]

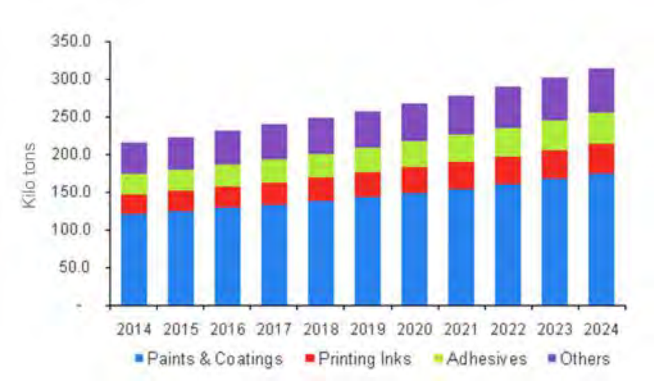


Figure 59. Consumption of MEK by sector of application[405]

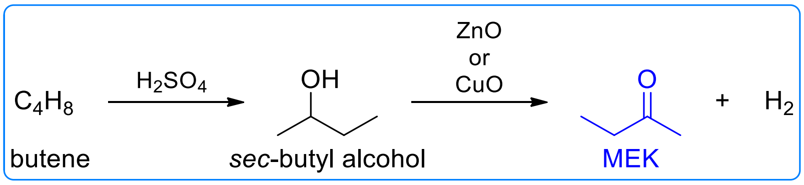
4.2.1.2 Current industrial production processes

Today, MEK is mainly produced by three processes:[400,408,409]

1. the dehydrogenation of 2-butanol that represents 92 % of all production capacities,
2. the Fisher-Tropsch process or
3. the liquid-phase oxidation of *n*-butane

4.2.1.2.a Dehydrogenation of 2-butanol

The principal process for the production of MEK is the dehydrogenation of 2-butanol (secondary-butyl alcohol, SBA) that is carried out in a two-step process: i) the hydration of butenes to produce 2-butanol using sulphuric acid as catalyst[404] and ii) the dehydrogenation of secondary-butyl alcohol using zinc or copper oxides as heterogeneous catalyst (Scheme 15).



Scheme 15. Synthesis of MEK by the dehydrogenation of 2-butanol

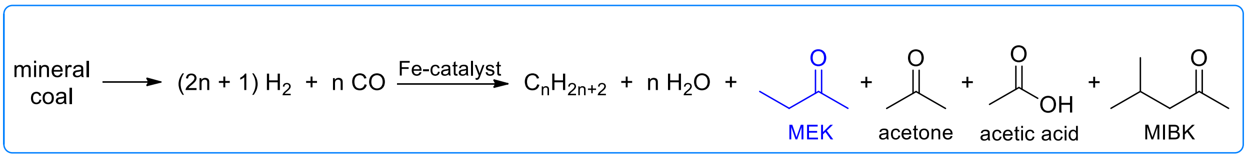
The dehydrogenation of 2-butanol is carried out at 400-500°C, under pressures of less than 4 bar.[410] The gas produced in the reaction is condensed and then separated into a liquid crude phase containing MEK and a gaseous hydrogen phase. This reaction allows obtaining a *sec*-butanol conversion between 80 and 95% with a selectivity of MEK around 95 %.[409,411]

Different versions of this reaction have been adopted. For example, a liquid-phase technology in which SBA is mixed with an inert high boiling solvent was developed in Europe. This process employs Raney nickel or copper chromite as catalyst. The reaction is run at 150°C under atmospheric pressure. Here, the formed hydrogen and MEK are driven off in a vapour form to be separated as soon as each is formed.[409] Furthermore, Deutsche Texaco (USA) developed a process that consists in the dehydrogenation of anhydrous *sec*-butyl alcohol using a copper-based catalyst at 240-260°C under atmospheric pressure. In this reaction, SBA is produced *via* direct hydration of *n*-butenes catalysed by an ion-exchange resin. Then, the dehydrogenation of the produced SBA is carried out on a copper catalyst. A gaseous mixture of hydrogen and crude MEK is obtained from this reaction. It also contains unconverted SBA, higher ketones and water, which after cooling allow their separation from the gaseous hydrogen phase. The purification of MEK consists in three consecutive distillations. In the first one, crude MEK (containing SBA and higher ketones) is separated from the azeotropic mixture MEK-water. In the second distillation, the unconverted SBA and the higher ketones are separated from MEK to obtain a purity of 99%. The last distillation is for separating the higher ketones from the SBA that are sent back to the process feed tank.[400] The Texaco process has the advantage of using an heterogeneous catalyst that can be recycled.[412] Nevertheless, several co-products are obtained (higher ketones).

To sum up, the principal process for the production of MEK still uses sulphuric acid as homogeneous catalyst for the hydration of butenes. Furthermore, all the developed versions have the disadvantage of using high temperatures for the SBA dehydrogenation (150°C, 240-260°C and 400-500°C).

4.2.1.2.b *Fisher Tropsch coal to liquid process*

The second process used for the production of MEK is the Fischer-Tropsch method developed by Franz Fisher and Hans Tropsch in 1940 and adopted by Sasol.[413] This technology consists in the conversion of H_2 and CO (synthesis gas produced from coal) into hydrocarbons of various molecular weights, generally molecules between C_1-C_{20} and oxygenated products such as alcohols, acetic acid, acetone, methyl isobutyl ketone (MIBK) and methyl ethyl ketone (MEK; scheme 16).[400,413–416]



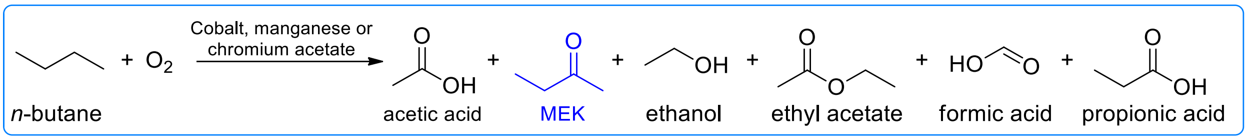
Scheme 16. Synthesis of MEK by the Fisher Tropsch method

The reaction is catalysed by an iron-based catalyst at temperatures between 180 and 200°C.[413] In the first step of the process, mineral coal is gasified to produce the synthesis gas. In the second step the synthesis gas is converted into the hydrocarbons and oxygenated products such as MEK (with low selectivities between 3-6 %w/w[417]). In the last step, each of the products are separated and purified.[400]

The drawbacks of this process are the use of high temperatures and the formation of several by-products.

4.2.1.2.c *Liquid-phase oxidation of n-butane*

MEK can also be obtained as a by-product of the oxidation of *n*-butane into acetic acid. The general process consists in the reaction between *n*-butane and compressed air or oxygen in the presence of a catalyst, typically cobalt, manganese or chromium acetates. The main product of the reaction is acetic acid. Several by-products are also obtained, such as MEK, ethanol, ethyl acetate, formic acid and propionic acid (Scheme 17).[409]



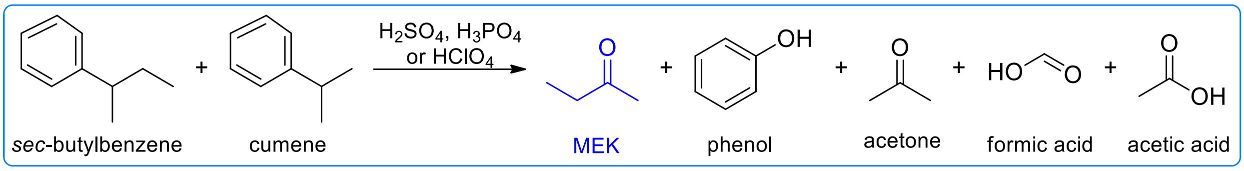
Scheme 17. Synthesis of MEK by the liquid-phase oxidation of *n*-butane

Celanese Corp. (USA) uses this technology at temperatures between 160 and 165°C, obtaining a mass *ratio* of MEK:acetic acid of 0.4:1.[227] Nevertheless, the process has the disadvantages of using high temperatures and obtaining low MEK yield.

4.2.1.2.d *Other developed processes for the production of MEK*

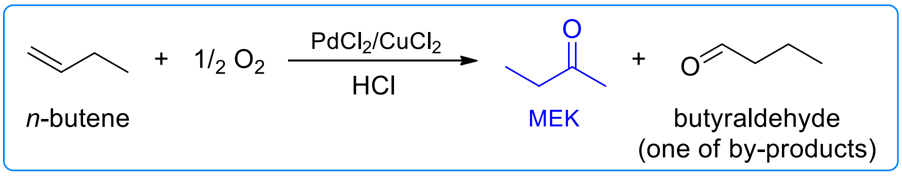
Other production processes such as the oxidation of *sec*-butylbenzene and the Hoechst-Wacker process were studied with no industrial success because of the disadvantages they present, such as long reaction times, low product yields, undesired by-products formation, and technical difficulties in the process.

The production of MEK starting from ***sec*-butylbenzene** was studied by the Shell Company. This process consists in the oxidation of *sec*-butylbenzene and cumene into butylbenzene hydroperoxide and cumene hydroperoxide, which are then decomposed by acid catalysis into a mixture containing MEK, phenol and acetone. The acid catalyst used in the process can be sulphuric acid, perchloric acid or phosphoric acid.[418,419] In this method, the oxidation rate of *sec*-butylbenzene is lower than the one of cumene provoking side reactions, leading in a mixture of by-products including formic acid and acetic acid and thus reducing MEK yield. This low selectivity and the use of a homogeneous acid explain why this process has never been industrialized (Scheme 18).[400]



Scheme 18. Synthesis of MEK by the oxidation of sec-butylbenzene

In the **Hoechst-Wacker process,** MEK is produced by the direct oxidation of *n*-butenes with oxygen. The reaction is carried out at 110°C, in the presence of $PdCl_2$ and $CuCl_2$ as catalysts. Through this process, 95% conversion of *n*-butenes can be obtained with a MEK yield around of 85 and 88 %. The disadvantages of this reaction are the formation of chlorinated butanones and butyraldehyde as by-products (Scheme 19).[420,421]

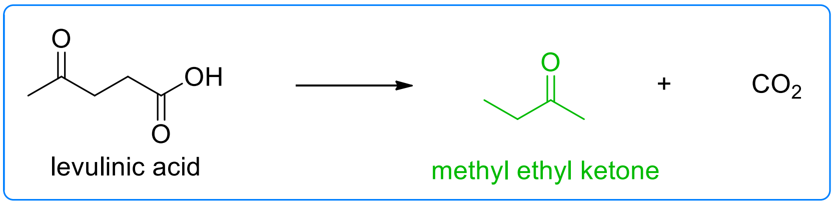


Scheme 19. Synthesis of MEK by the Hoechst-Wacker process.

4.2.2 Strategy for the synthesis of bio-based methyl ethyl ketone (MEK)

The previously described processes generally produce MEK in low yields with limited selectivities using high temperatures and homogeneous acid catalysts. Additionally, all the presented technologies use petrochemical-based starting materials, offering a negative impact on the environment. This is why the development of new processes for the production of MEK using bio-based building blocks is interesting and deserves to be explored.

As the world moves from fossil to renewable feedstocks, we propose herein the synthesis of methyl ethyl ketone through the decarboxylation of levulinic acid (LA), which is a versatile building block derived from the biomass (Scheme 20).

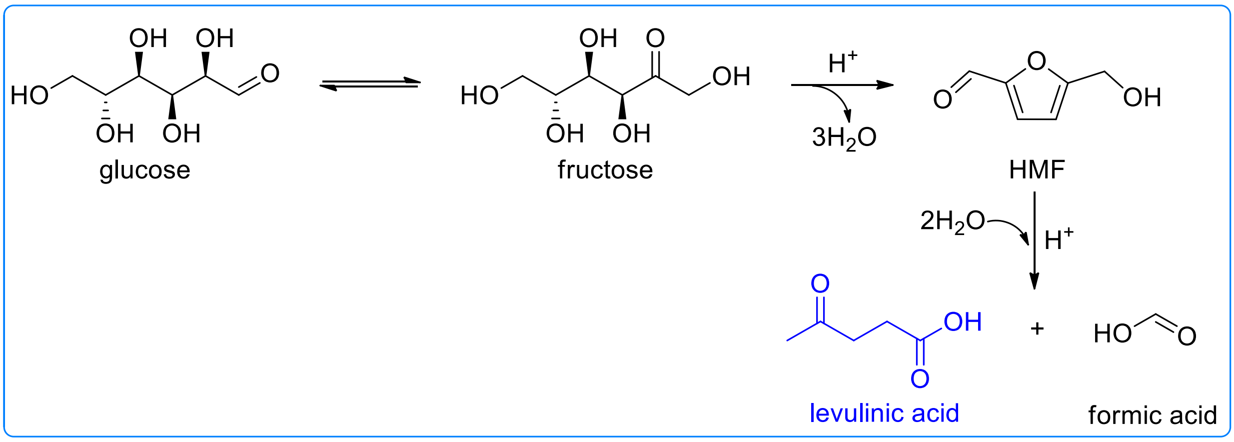


Scheme 20. Synthesis of MEK through LA decarboxylation

4.2.2.1 Levulinic acid: a bio-based synthon

Levulinic acid is the simplest and most important γ-oxocarboxylic acid. It contains two functional groups, a ketone and a carboxylic acid moiety, providing a great number of synthetic transformations, for example esterifications, alkylations, halogenations and condensations.[400,422,423]

LA has acquired a big interest in the chemical industry because it is one of the most available building blocks obtained from carbohydrates. Besides, it was recognized by the US Department of Energy as one of the main bio-based platform chemicals of the future.[215] LA is produced industrially from sugar polymers such as cellulose or starch, which are converted into monomeric hexoses. The hexoses are then dehydrated into hydroxymethylfurfural (HMF) that are finally hydrated to obtain levulinic acid (Schema 21).[424]



Scheme 21. Levulinic acid production[425,426]

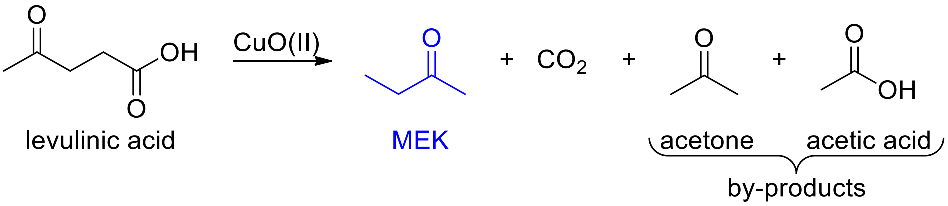
Recently, two important methods have been reported for the synthesis of LA from lignocellulosic biomass. The first one is the Biofine process developed by Biofine Technology LLC (USA).[427] This technology involves the rapid hydrolysis of lignocellulosic biomass using temperature between 190°C and 220°C and diluted sulphuric acid as catalyst. The process is carried out in a two-reactors system where levulinic acid is constantly removed avoiding side reactions and thus increasing the yield in LA.[428] Four mains products are obtained with this process: levulinic acid, formic acid, furfural and a carbonaceous powder. The LA yield of this process is between 70 and 80 wt%.[429–431] The Biofine process is still under development at the pilot plant. It is planned to move to a commercial scale and transform 100 tons of biomass per day.[427]

The second and the most important approach is the ATLAS technology developed by GFBiochemicals (Caserta, Italy). The plant that operates in Caserta since 2015 is the largest producer of levulinic acid from biomass with a production of 10,000 tonnes/year. The process consists in an acid pre-treatment of the biomass to liberate the sugars. Then, the hexoses are transformed into LA using a unique-reactor technology (GFB reactor technology). The GFB reactor maintains the concentration levels of HMF and thus increases the production of levulinic acid. The process can use various biomass feedstocks such as grass, wheat straw and wood.[225,432,433]

4.2.2.2 Decarboxylation of levulinic acid into methyl ethyl ketone: state-of-the-art

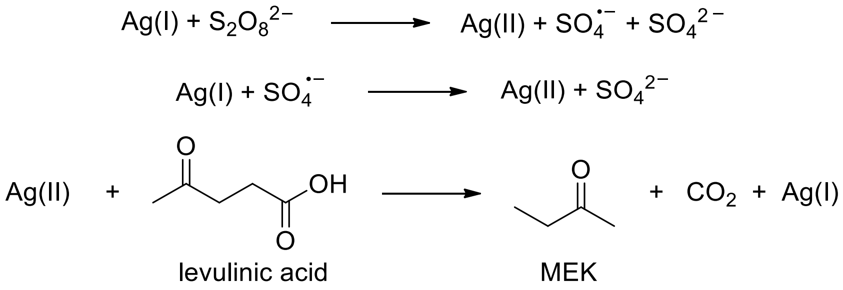
In the state-of-the-art, some methods have been reported for the synthesis of MEK from levulinic acid. For example, the decarboxylation of sodium levulinate in an electrolyte cell for the production of MEK and octanedione has been described in a patent.[434] The enzymatic decarboxylation of LA into MEK with an acetoacetate decarboxylase (AADC) from *Clostridium acetobutylicum* ATCC824 has also been reported. A yield in MEK of 90 % was obtained when 53 Units of AADC were used, at 30°C and pH 5.[435]

In 2010, Gong et co-workers have reported the decarboxylation of LA using CuO(I) and CuO(II) as catalyst. In their work, the reactions were carried out at 300 °C, during 2 h. A maximum MEK yield of 67.5 % was obtained using 69 wt% CuO(II) (respect to LA, Scheme 22).[436] Lower MEK yield was obtained when they used CuO(I). In both reactions, acetone and acetic acid were produced as by-products. The complete study involved the preparation of the CuO(I) and CuO(II) under high temperatures (between 500 to 800°C).[437]



Scheme 22. Decarboxylation of levulinic acid using CuO as co-reagent (Gong et al, 2010)[437]

One year later, this research group published its work on the oxidative decarboxylation of LA using 1 equivalent of silver nitrate and 0.5 equivalent of potassium persulfate ($K_2S_2O_8$; Scheme 23). Here, the reaction was carried out in a pressure reactor at 160°C, during 30 minutes. Under those conditions, a moderate MEK yield of 44.5 % was obtained. Other by-products such as acetone and acetic acid were also obtained.[438] In this paper, Gong *et al.* proposed a mechanism where the persulfate ion and the sulfate radical, obtained by its homolytic cleavage, oxidize Ag(I) into Ag(II) which then leads to the decarboxylation of LA:



Scheme 23. Decarboxylation of levulinic acid using silver nitrate and persulfate (Gong et al, 2011)[438]

4.2.2.3 *Persulfate and silver: an attractive approach for LA decarboxylation*

The use of persulfate ($S_2O_8^{2-}$) as an oxidizing agent is attractive due to the advantages it provides: it is economical to use and thermally stable. It is thus used in several industries processes, such as in the polymerization of plastics and rubber,[439–442] in cosmetics for hair bleaches and hair-colouring preparations,[443,444] in the preparation of adhesives,[445] in decolouration in the textile industry.[446,447] It has also been widely explored in the remediation of soils and wastewater.[448–451]

The persulfate ion ($S_2O_8^{2-}$) is considered as a powerful oxidizing agent, with a redox potential of 2.01 V. Under high temperature or ultraviolet (UV) irradiation, it can produce sulfate radicals by homolytic cleavage (Eq. IV-1). This free radical is itself a powerful oxidant with redox potential (2.6 V) higher than persulfate ions (2.01V).[452–457]

$$S_2O_8^{2-} \xrightarrow{\text{heat/UV}} 2SO_4^{\cdot -} \qquad \text{Eq. IV-1}$$

Persulfate ions can also be activated in alkaline conditions leading to the production of sulfate and superoxide radicals ($O_2^{\bullet}$) (Eq. IV-2). The sulfate radicals under alkaline conditions generate hydroxyl radicals ($OH^{\bullet}$) through a radical interconversion reaction (Eq. IV-3).[446,458–460] Noteworthy hydroxyl radicals also present higher redox potential (2.8 V) than persulfate anions.[446]

$$2S_2O_8^{2-} + 2H_2O \xrightarrow{\text{Base}} 3SO_4^{2-} + SO_4^{\cdot -} + O_2^{\cdot -} + 4H^+ \qquad \text{Eq. IV-2}$$

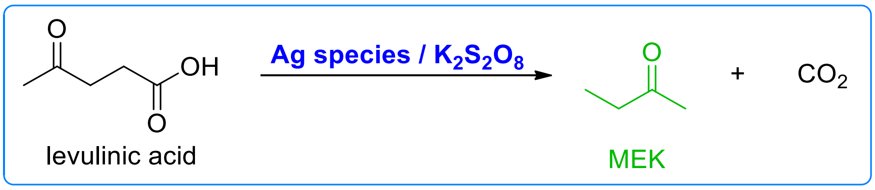
$$SO_4^{\cdot -} + OH^{-} \longrightarrow SO_4^{2-} + OH^{\cdot} \qquad \text{Eq. IV-3}$$

Transition metals can also be used for the persulfate activation, the metal transfers an electron to one of the sulfate radicals, produced from the persulfate, leading to the formation of a sulfate anion (Eq. IV-4).[453]

$$S_2O_8^{2-} + M^{(n)+} \longrightarrow SO_4^{\cdot -} + SO_4^{2-} + M^{(n+1)+} \qquad \text{Eq. IV-4}$$

Anderson and Kochi were the first to evaluate the influence of metals such as silver and copper on the activation of persulfate involved in the decarboxylation of *n*-butyric and isobutyric acids. They pointed out that both the persulfate activation and the decarboxylation increase in the presence of metals.[461] Since those observations, many investigations have been performed to analyse the influence of transition metals such as Fe(III), Fe(0), Ru(III), Co(II), Ce(III), V(III), Mn(II), Ni(II), Cu(II) and Ag(I) in the activation of persulfate.[453,462–470]

The use of transition metals is thus an interesting way to activate persulfate, as catalytic amounts of this reactant are generally needed. Inspired in the work of Gong et al.,[438] we therefore decided to study the decarboxylation of levulinic acid using different silver species and potassium persulfate (Scheme 24).



Scheme 24. Synthesis proposal for the production of bio-methyl ethyl ketone

To the best of our knowledge, only the report of Gong et al. is addressed to this subject using the silver salt-persulfate system. However, their method uses high temperatures (160°C) and yields only 44.4 % MEK. This is why a more in-depth study is necessary to gain a detailed comprehension of the reaction with the aim of improving the production of MEK using milder conditions.

In this chapter, we present an exploratory study to better understand the behaviour of silver-based species and persulfate in LA decarboxylation. This approach allowed us to determine the factors that affect the reaction and to identify the adequate operational conditions for improving the production of MEK.

4.3 Evolution of species during levulinic acid decarboxylation to produce methyl ethyl ketone in the $AgNO_3/K_2S_2O_8$ system

Nydia I. Guzmán B., Jérôme Peydecastaing, Jérôme Esvan, Philippe Behra, Emeline Vedrenne, Carlos Vaca-García, Sophie Thiébaud-Roux.

Laboratoire de Chimie Agro-industrielle (LCA), Université de Toulouse, INRA, INPT, Toulouse, France

ABSTRACT: An efficient method for the synthesis of methyl ethyl ketone (MEK) by levulinic acid (LA) decarboxylation with potassium persulfate and silver nitrate is presented. The role of $AgNO_3$ and $K_2S_2O_8$ in LA decarboxylation was studied. Other Ag salts, such as Ag_2O and AgO, were also evaluated in this reaction. XPS and XRD analyses confirmed the evolution of solid phases in the reaction. Based on the results obtained a radical decarboxylation mechanism is proposed, starting with the formation of sulfate radicals ($SO_4^{\bullet -}$) via the breakdown of $K_2S_2O_8$, catalysed by $AgNO_3$. Mechanistic insight and a parametric study of the reaction increase LA conversion to 97.9% and MEK yield to 86.6%.

4.3.1 Introduction

Methyl ethyl ketone (MEK) is used in the paint and coating industry, primarily as a low-boiling point solvent for nitrocellulose, acrylic and vinyl surface coatings. It is also often used in professional paint shops and by painters, to thin acrylics and lacquers.[403,404]

In recent years, interest has increased in the replacement of petroleum derivatives with products derived from biomass, due to environmental and legal concerns. The use of biomass feedstocks has become particularly attractive as a way of decreasing dependence on fossil resources and reducing negative impact on the environment. Studies of the synthesis of methyl ethyl ketone from renewable building blocks, such as levulinic acid, through environmental friendly processes, are therefore particularly pertinent.

Levulinic acid (LA) has been identified by the National Renewable Energy Laboratory (NREL) as one of the highest-value chemicals that can be produced from sugars or lignocellulosic materials by acid dehydration.[215] It is an abundant raw material, with a reported demand of 2606.2 tons in 2013.[471] LA is now considered to be an interesting platform molecule, due to the large number of compounds it can form: tetrahydrofuran (THF), 2-methyltetrahydrofuran (2-MeTHF), levulinate esters, γ-valerolactone (GVL), α-angelica lactone, 1,4-pentanediol (PDO), acrylic acid, β-acetyl acrylic acid and δ-aminolevulinic acid.[215,472]

The decarboxylation of aliphatic carboxylic acids, such as LA, has been much less studied than the decarboxylation reactions of heteroaromatic carboxylic acids.[473–476] The decarboxylation of heteroaromatic carboxylic acids involves the use of high temperatures and Brønsted-Lewis acid catalysts, such as SiO_2-Al_2O_3 and γ-Al_2O_3.[477] The use of hydroxyl radicals (•OH) has also been reported for the decarboxylation of organic acids, such as 2-methylalanine and amino acids.[478–482] Metal oxidants, such as Pb(IV), Co(III), Mn(III), Fe(II) and Cu(II), can also be used.[462,483]

Only a few studies describing the decarboxylation of LA have been published. Chum et al. described the photoelectrochemical decarboxylation of LA with n-TiO_2 as a semiconductor. However, MEK selectivity was low. Methanol, ethanol, propionic acid, acetic acid, acetone, acetaldehyde, ethyl acetate, methane and ethane were also produced during the reaction.[484] Gong et al. recently described the decarboxylation of LA with cupric oxides as the catalyst, under harsh conditions (300°C). The products of this reaction were MEK (67.5% yield), acetone and acetic acid.[437] Gong *et al.* also described LA decarboxylation with $AgNO_3/K_2S_2O_8$ as coreagents, at 160°C for 30 minutes in an aqueous solution of $NaOH/KH_2PO_4$ (pH 5). Under these milder conditions, a moderate yield (44.2%) of MEK was obtained.[438]

Decarboxylation reactions involving the Ag(I)/$K_2S_2O_8$ system have aroused the interest of many researchers.[463,465,467,485–487] It has been suggested that the decarboxylation mechanism of this system involves the oxidation of Ag(I) into Ag(II) by $S_2O_8^{2-}$. Then Ag(II) is then responsible for carboxyl radical formation, followed by decarboxylation and production of the corresponding alkyl radical.[461]

The main objective of this study was to determine the basis of the effect of different Ag salts and $K_2S_2O_8$ on the decarboxylation of levulinic acid (LA) for the synthesis of methyl ethyl ketone (MEK). The effects of different Ag species and $K_2S_2O_8$ were first investigated. The experimental conditions were then studied, to improve the reaction yield for MEK. Finally, solid phases were characterized by XPS and XRD, to support the proposed reaction mechanisms and for the development of a strategy to improve MEK production.

4.3.2 Material and methods

4.3.2.1 *Chemicals*

Levulinic acid, silver nitrate, silver oxide (I), silver oxide (II), silver chloride and potassium persulfate, all reagent grade, were purchased from Sigma-Aldrich (L'Isle d'Abeau Chesne, France). Methyl ethyl ketone was analytical grade also from Sigma-Aldrich.

4.3.2.2 *Decarboxylation of LA.*

The batch experiments were carried out in bushing-type ACE pressure tubes. In a typical run, the reaction was prepared by adding 0.035 g of levulinic acid (3 mmol) to 15 mL of K_2HPO_4/KH_2PO_4 (0.1:0.1 M in Milli-Q water, pH 6.86) followed by the Ag salt (3 mmol; silver salts should be weighed by avoiding contact with light in order to prevent oxidation. *e.g.* in a dark vial) and $K_2S_2O_8$ (3 mmol).
The reaction mixture was heated at 100°C for 30 or 60 minutes, with stirring. Liquid and solid phases were separated only by centrifugation.
Levulinic acid, acetic acid and methyl ethyl ketone were identified by GC-MS (Agilent 6980/5973, France) with an Agilent J&W DB-5MS column (30 m x 0.25 mm, 0.25 µm). The temperatures of the injector and detector were 250 and 230°C, respectively. The oven was initially at a temperature of 70°C, which was then increased to 160°C at a rate of 2°C/min and then to 280 °C at a rate of 4°C/min. The scan extended from 25-300 m/z, and the library used for compound identification was NIST98.1. Levulinic acid, acetic acid and methyl ethyl ketone were also identified and quantified by NMR ^1H. NMR spectra were recorded at 300 MHz in D_2O in a Bruker Fourier 300 machine (magnet system 300 MHz/54mm).

4.3.2.3 *XPS analyses*

Analyses were performed with a Thermo Scientific Kalpha device. Photoelectron emission spectra were recorded with Al–Kα radiation (hν = 1486.6 eV) from a monochromatized source. The X spot size was 400 µm. The pass energy was fixed at 40 eV for narrow scans (and 150 eV for the survey). We used Flood Gun for the charge effects. The spectrometer energy was calibrated with the Au $4f_{7/2}$ (83.9 ± 0.1 eV) and Cu $2p_{3/2}$ (932.8 ± 0.1 eV) photoelectron lines. XPS spectra were recorded in direct N(Ec) mode. The background signal was removed by the Shirley method. Atomic concentrations were determined with an accuracy of 10% from photoelectron peak areas, using the atomic sensitivity factors reported by Scofield, taking into account the transmission function of the analyzer. This function was calculated at different pass energies from Ag 3d and Ag MNN peaks collected for a reference silver sample, within the system. The binding energy scale was established by referencing the C 1s value of adventitious carbon (284.7 ± 0.1 eV). The photoelectron peaks were analyzed by Lorentzian/Gaussian (L/G = 30) peak fitting.

4.3.2.4 XRD analyses

The diffraction patterns were collected with a Bruker D8 Advance diffractometer with a LynXeye 1D detector. The X-ray tube was a ceramic tube with a copper anode. There was no monochromator. The main wavelengths used were Kα radiation, 0.154059 nm and Kα2 radiation, 0.15444 nm.

4.3.3 Results and discussion

LA decarboxylation was studied in the presence of an aqueous phosphate solution, as described in the previous papers from Gong et al.[437,438] The experimental media were multiphase systems including solids based on Ag salts, an aqueous solution containing LA and $K_2S_2O_8$, and a gaseous phase.

4.3.3.1 Influence of either $K_2S_2O_8$ or $AgNO_3$

For exploration of the role of $K_2S_2O_8$ and $AgNO_3$, reactions lacking one of these species were firstly run at 100°C. After a reaction time of 30 minutes, no LA decarboxylation was observed if only silver nitrate was added (Table 62, # 1), whereas, in the presence of 0.25 equivalents (eq) of persulfate, traces of MEK (2.6%) and acetic acid (1%, AcOH) were observed (Table 62, # 2). Increasing the amount of persulfate led to a rise in levulinic acid conversion, from 3.6 to 20% (Table 62, # 2-5). The thermal activation of persulfate to produce sulfate radicals ($SO_4^{\bullet -}$) in aqueous solutions has already been reported[452,454–457,485,488] and would explain the occurrence of LA decarboxylation even in the absence of $AgNO_3$. However, when 1 or 2 equivalents of persulfate were added, despite the increase in LA conversion, MEK yield fell to 4.3% and acetic acid production increased to 14.5% (Table 62, # 4 and 5).

	n_{eq} $AgNO_3$ / $K_2S_2O_8$	pH		LA conversion (%)	yield (%)	
		initial	final		AcOH	MEK
1	1/0	5	4	0.0	0.0	0.0
2	0/0.25	5	5	3.6	1.0	2.6
3	0/0.5	5	5	12.1	3.3	8.8
4	0/1	4	2	13.6	6.8	6.8
5	0/2	4	1	18.8	14.5	4.3

Table 62. Influence of $AgNO_3$ and $K_2S_2O_8$ in the decarboxylation of LA. n_{eq}= number of equivalents respect a LA. Conditions: K2HPO4/KH2PO4 (0.1:0.1 M), 100°C, 30 minutes

In these cases (in the absence of $AgNO_3$), the decarboxylation of LA can be explained by the mechanism described in scheme 24.

$$S_2O_8^{2-} \longrightarrow 2SO_4^{\cdot -}$$

$$CH_3COCH_2CH_2COOH + SO4^{\cdot -} \longrightarrow CH_3COCH_2CH_2COO^{\cdot} + HSO_4^{-}$$

$$CH_3COCH_2CH_2COO^{\cdot} + H_2O \longrightarrow CH_3COCH_2CH_3 + CO_2 + OH^{\cdot}$$

$$2OH^{\cdot} \longrightarrow H_2O + 1/_2\, O_2$$

Scheme 25. Decarboxylation of LA by thermal persulfate decomposition

The role of $K_2S_2O_8$ in the production of MEK was investigated further, to obtain greater insight into the production of acetic acid in these conditions, by studying reaction kinetics with 1 equivalent of persulfate (Table 62). MEK yield was highest during the first few minutes of the reaction. It then began to decrease slightly, while the concentration of acetic acid increased (Figure 60).

The behaviour of MEK in the presence of potassium persulfate was studied then by employing the same reaction conditions but with MEK as the starting material. A rate of 10% was obtained for the conversion of MEK into acetic acid at 30 and 60 min of reaction at 100°C. These results suggest that MEK can be oxidized into AcOH at 100°C, accounting for the decrease in MEK yield and the increase in acetic acid after 20 minutes of reaction. This reaction was also carried out at 25°C, but MEK was not converted into AcOH at that temperature suggesting that the temperature is determinant for this reaction.

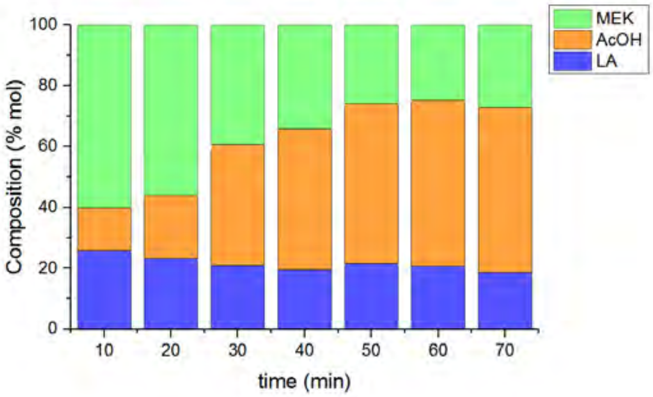


Figure 60. Decarboxylation of LA with 1 eq of $K_2S_2O_8$ in the absence of $AgNO_3$. Experimental conditions: K_2HPO_4/KH_2PO_4 (0.1:0.1M), 100 °C

4.3.3.2 Role of Ag salts

Decomposition of the $K_2S_2O_8$ moiety has been reported to be catalyzed by transition metal ions, such as silver species.[461,462,489] The influence of $AgNO_3$, AgCl, Ag_2O and AgO on decarboxylation was, therefore, evaluated. The reactions were carried out with a 1:1 *ratio* of Ag salt/$K_2S_2O_8$, at 100°C, in the same phosphate solution.

An improvement in LA conversion, from 14% to 46.8% was observed, with an outstanding increase in MEK yield, from 6.8 to 32% when 1 eq each of $AgNO_3$ and $K_2S_2O_8$ were used (Table 62, # 4 *vs.* Table 63, # 1). In the presence of AgCl, MEK yield was slightly lower (Table 63, # 2). By contrast, when Ag_2O or AgO and persulfate were used, the yield of MEK remained similar to that obtained with $AgNO_3$, but the yield of acetic acid increased markedly (Table 63, # 1, 3 and 4). Thus, the breakdown of $K_2S_2O_8$ is catalyzed by Ag species, increasing the LA decarboxylation.

Entry	Ag salt	n_{eq} Ag salt/ $K_2S_2O_8$	pH		LA conversion (%)	yield (%)	
			initial	final		AcOH	MEK
1	$AgNO_3$	1/1	5	2	46.9	14.4	32.5
2	AgCl	1/1	6	5	38.7	13.5	25.2
3	Ag_2O	1/1	4	3	54.3	17.8	36.5
4	AgO	1/1	5	3	57.6	22.9	34.8
5	AgO	1/0	4	1	0.0	0.0	0.0

Table 63. Study of different silver species in the decarboxylation of levulinic acid. Experimental conditions: K_2HPO_4/KH_2PO_4 (0.1:0.1 M), 100°C, 30 minutes. #1 is used for comparison in the following tables

The mechanism first proposed by Anderson and Kochi in 1970[461] and then by other authors[438,486,490–492] for decarboxylation in the presence of Ag(I) and $K_2S_2O_8$ involves a Ag(I)-Ag(II) catalytic cycle, in which Ag(II) is assumed to be responsible for acid decarboxylation. In the proposed mechanism, both persulfate and sulfate radicals resulting from $K_2S_2O_8$ decomposition oxidize Ag(I) to Ag(II), triggering decarboxylation of the acid. Ag(I) is then regenerated from Ag(II).

Assuming that the role of persulfate in the reaction is to oxidize Ag(I) to Ag(II), as previously suggested, and that Ag(II) is directly responsible for decarboxylation of the carboxylic acid, a reaction with 1 equivalent of AgO (Ag(II)) was performed in the absence of $K_2S_2O_8$. However, no LA conversion occurred with Ag(II) as the sole oxidant (Table 63, # 5). $K_2S_2O_8$ is, thus, essential for LA decarboxylation. This suggests that LA decarboxylation may be a radical reaction, beginning with the formation of sulfate radical anions ($SO_4^{\bullet -}$) from $K_2S_2O_8$ during the decomposition of this molecule. Our results are consistent with those reported by Seipled et *al.*, who found that no arylation of various heterocycles occurred with arylboronic acid in the presence of Ag(II) as the sole oxidant.[467]

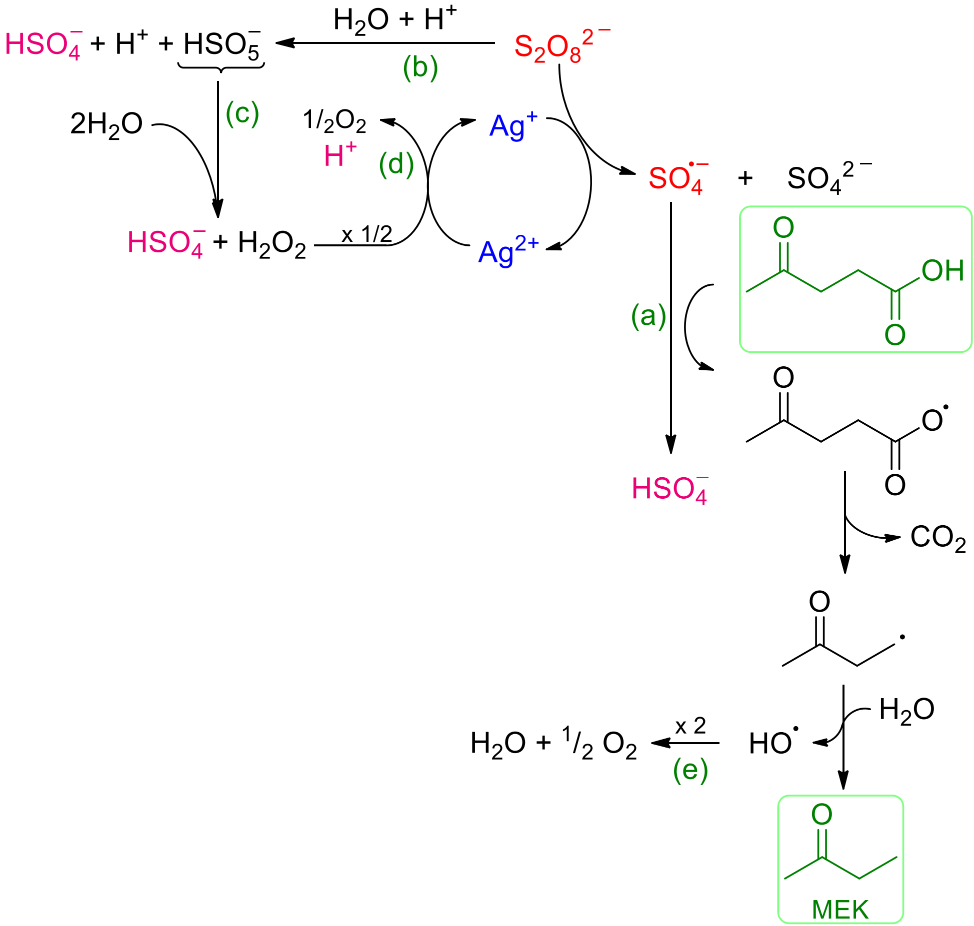
4.3.3.3 Role of $K_2S_2O_8$ in the presence of $AgNO_3$

A reaction was performed in the presence of a radical scavenger, TEMPO ((2,2,6,6-tetramethylpiperidin-1-yl)oxyl), to check that LA decarboxylation did, indeed, occur through a radical mechanism, initiated by the decomposition of $K_2S_2O_8$ into $SO_4^{\bullet -}$. The reaction was carried out in the same conditions, in the presence of $AgNO_3/K_2S_2O_8$ (1:1 equivalent) and 1 or 2 equivalents of TEMPO.

The addition of TEMPO completely prevented the reaction, and no LA conversion was observed. This confirms our hypothesis that the reaction between Ag(I) and $S_2O_8^{2-}$ ions produces Ag(II) and $SO_4^{\bullet -}$, which is the radical responsible for LA decarboxylation (Scheme 26). Moreover, a solution pH decrease was also observed during the reaction. This change in pH can be explained by formation of the bisulfate ion (HSO_4^-; Scheme 26, equation a), which is involve in the following reaction:

$$HSO_4^- + H_2O \rightleftharpoons H_3O^+ + SO_4^{2-} \qquad \text{Eq. IV-5}$$

Under such acidic conditions, potassium persulfate ($K_2S_2O_8$) may also break down into the conjugate bases of sulphuric acid and Caro's acid (HSO_4^- and HSO_5^- respectively, reaction b, Schema 26),[456] which would also contribute to the pH decrease. The oxidation of H_2O by HSO_5^- would then lead to formation of H_2O_2 (reaction c) and HSO_4^-. An oxidizing-reducing reaction between H_2O_2 and Ag(II) would finally regenerate Ag(I) and produce O_2 and H^+ (reaction d, Scheme 26). Noteworthy, in this mechanism, HSO_4^- and H^+ are accumulated explaining the pH drop profile of the reaction.



Scheme 26. Proposed mechanism

As $AgNO_3/K_2S_2O_8$ provided the best yields of MEK and the lowest levels of AcOH production (Table 63, # 1), this combination was selected for the parametric study to gain more insight into this system.

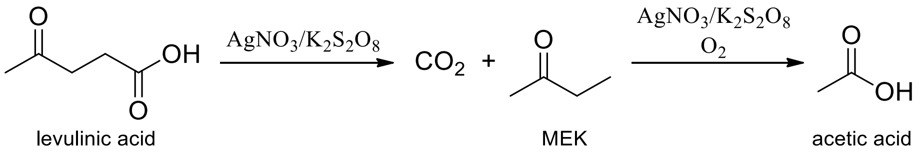
4.3.3.4 Influence of $AgNO_3/K_2S_2O_8$ ratio

Various reactions were performed, with different $AgNO_3/K_2S_2O_8$ ratios. Lower LA conversion and MEK yield were obtained when smaller amounts of $AgNO_3$ and $K_2S_2O_8$ were used (Table 64, # 1 and 2). As observed in the absence of $AgNO_3$ (Table 62, # 5), an increase in the amount of $K_2S_2O_8$ to 2 equivalents increased AcOH production, but not MEK yield (Table 64, # 4).

#	n_{eq} $AgNO_3$ / $K_2S_2O_8$	pH		LA conversion (%)	yield (%)	
		initial	final		AcOH	MEK
1	0.5/0.5	5	3	22.8	13.6	9.2
2	1/0.5	5	2	34.2	15.8	18.4
3	1/1	5	2	46.9	14.4	32.5
4	1/2	4	1	49.2	21.3	27.9

Table 64. Influence of $AgNO_3/K_2S_2O_8$ *ratio* on LA decarboxylation. Experimental conditions: K_2HPO_4/KH_2PO_4 (0.1:0.1M), 100°C, 30 minutes

For confirmation that acetic acid was produced subsequently to MEK formation, as suggested above, a reaction was performed with MEK as the starting material, in the presence of 1 equivalent each of $AgNO_3$ and $K_2S_2O_8$, at 100°C. After 30 and 60 minutes of reaction, rates of MEK conversion into AcOH of 10% and 17%, respectively, were obtained. We therefore assumed that, during LA decarboxylation under acidic conditions, the MEK produced could be oxidized to AcOH in a subsequent reaction (Scheme 27). These results are consistent with those reported by Hobbs and coworkers,[493] who found that MEK was oxidized to AcOH in the presence of O_2 and a metal catalyst. In our case, O_2 would be produced during the reduction of Ag(II) to Ag(I) (reaction d, Scheme 26) and during the termination reaction (reaction e, Scheme 26).



Scheme 27. Subsequent AcOH production by the subsequent oxidation of MEK

4.3.3.5 Influence of temperature and duration

A kinetic study of LA decarboxylation was performed at 100, 60 and 25°C, to shed further light on this phenomenon and to optimize MEK production (Figure 61). The reactions were carried out with 1 equivalent each of $AgNO_3$ and $K_2S_2O_8$. In Figure 61a, it can be seen that MEK is produced more rapidly than AcOH at 100°C. Maximum MEK yield was reached after 5 minutes of reaction. At 60°C, slightly more acetic acid was produced, reaching a maximum level of 20% after 20 minutes of reaction. Both LA conversion and MEK production were slower. The amounts of MEK and acetic acid remained stable after 10 minutes of reaction (Figure 61b). At room temperature, more AcOH than MEK was produced (Figure 61c). The conversion of MEK into AcOH therefore seems to outstrip its production at low temperatures. There are two possible phenomena that could explain these findings: (i) at low temperature, O_2 is more soluble in the aqueous medium, favoring MEK oxidation,[493] (ii) at higher temperatures, such as 100 °C, some of the MEK is in the gaseous phase. This second hypothesis was ruled out by PROSIM computations of the vapor-liquid equilibrium at 100°C and atmospheric pressure. These calculations showed that less than 1% of MEK was in the gas phase. Thus the oxidation of MEK into AcOH may be related with the increase of soluble oxygen at lower temperatures. Otherwise, the increase on MEK production as temperature increases suggests that LA decarboxylation may be an endothermic reaction, with an equilibrium shifted to the right (Figure 61a). Similar observations have already been reported for the decarboxylation of malonic acid, butylmalonic acid and 2-aminoisobutyric acid. In these cases, the reactions were described as endothermic, with a range of ΔH from 17.0 to 39.9 kcal/mol.[494–496]

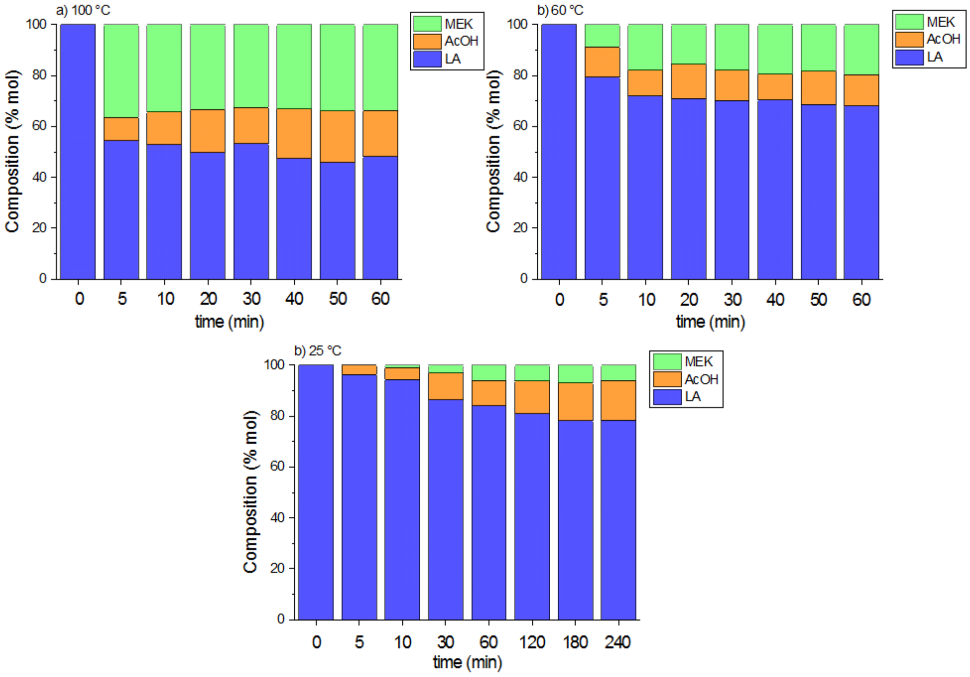


Figure 61. Decarboxylation of LA against time at different temperatures a) 100 °C, b) 60 °C and c) 25 °C. Experimental conditions: $AgNO_3/K_2S_2O_8$ (1:1), KH_2PO_4/K_2HPO_4 (0.1:0.1 M)

Given that low temperatures did not give the best results, reactions were carried out under the same conditions but at 125 and 150°C. However, no significant increase in MEK production was observed at temperatures above 100°C, with 25 and 28% MEK at 125 and 150°C, respectively.

4.3.3.6 Characterization of solid phases

X-ray diffraction (XRD) and X-ray photoelectron spectroscopy (XPS) were used to study the evolution of the solid phase during the reaction, to determine why MEK yields did not exceed 33%.

A sudden change in color, from colorless to yellow, was observed when $AgNO_3$ was added to the solution of phosphates (KH_2PO_4/K_2HPO_4), containing LA and $K_2S_2O_8$ at the start of the reaction, suggesting that Ag_3PO_4 was formed. This was confirmed by X-ray diffraction, which demonstrated that the solid phases consisted mostly of Ag_3PO_4 with distinct diffraction peaks at 20.9, 29.7, 33.3, 36.6, 42.5, 47.8, 52.7, 55.0, 57.3, 61.7, 65.9, 69.9, and 71.9° (JCPDS No. 06-0505).[497] Traces of $K_2S_2O_8$ (major peaks at 24.0, 25.9, 27.3, 27.6, 29.3, 32.7, 35.2, and 36.4°; ICSD No. 16972),[498] Ag_2SO_4 (major peaks at 22.2, 31.1, 33.8, 37.2, 47.0, and 53.5°),[499] KH_2PO_4 (major peaks at 23.8, 30.7, and 46.5°; ICSD 201371),[500] and $Ag_4P_2O_7$ (major peaks at 27.1, 32.3, and 32.5°) were also identified (Figure 62).

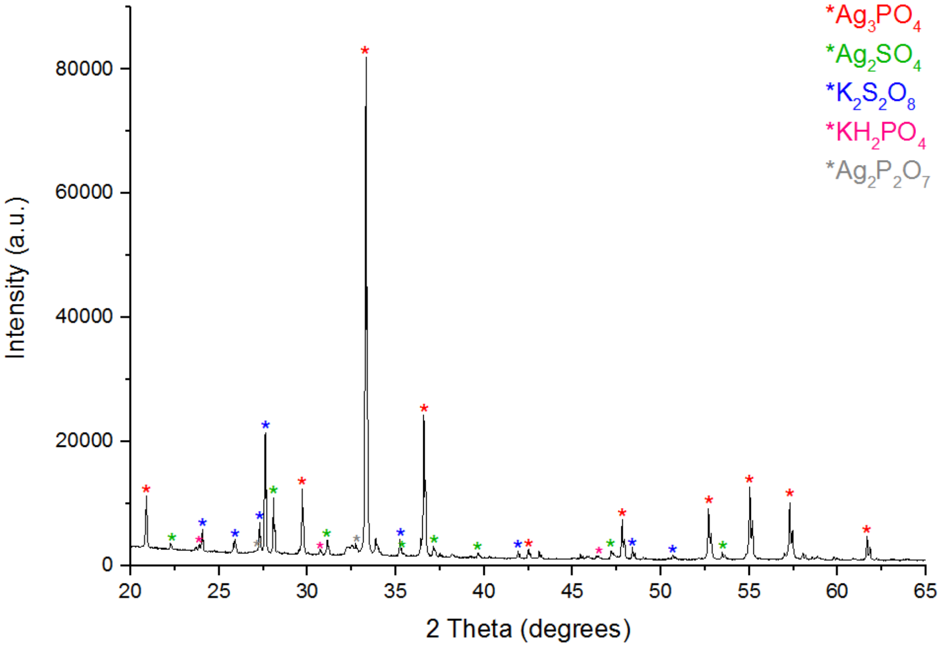


Figure 62. XRD patterns for the solid phase before the reaction. Experimental conditions: $AgNO_3$/$K_2S_2O_8$ (1/1), KH_2PO_4/K_2HPO_4 (0.1:0.1M)

Ag_3PO_4 may be formed in the reaction between $AgNO_3$ and $H_2PO_4^-/HPO_4^{2-}$, through the following reactions (Equations IV-6 and IV-7):

$$3AgNO_{3(s)} + HPO_4^{2-} \longrightarrow Ag_3PO_{4(s)} + 3NO_3^- + H^+ \qquad \text{Eq. IV-6}$$

$$3AgNO_3(s) + H_2PO_4^- \longrightarrow Ag_3PO_4(s) + 3NO_3^- + 2H^+ \qquad \text{Eq. IV-7}$$

$Ag_4P_2O_7$ may be formed according to the following equations (Eq. IV-8 and IV-9):

$$2K_2HPO_{4(s)} \longrightarrow K_4P_2O_{7(s)} + H_2O \qquad \text{Eq. IV-8}$$

$$4AgNO_{3(s)} + K_4P_2O_{7(s)} \longrightarrow Ag_4P_2O_{7(s)} + 4NO_3^- + 4K^+ \qquad \text{Eq. IV-9}$$

Finally, Ag_2SO_4 may be formed through the interaction of HSO_4^- with $AgNO_3$ (Eq. IV-11). HSO_4^- may be generated by the decomposition of $K_2S_2O_8$ in aqueous medium at low pH, *i.e.* < 3, potentially initiated by the presence of $AgNO_3$ or light (Eq. IV-10).[453,501–503]

$$2K_2S_2O_{8(s)} + 2H_2O \longrightarrow 4HSO_4^- + 4K^+ + O_{2(g)} \qquad \text{Eq. IV-10}$$

$$HSO_4^- + 2AgNO_{3(s)} \longrightarrow Ag_2SO_{4(s)} + 2NO_3^- + H^+ \qquad \text{Eq. IV-11}$$

The X-ray patterns for the solid phase measured at the end of the reaction (Figure 63) showed the presence of mostly Ag_2SO_4, with traces of Ag_3PO_4, $Ag_4P_2O_7$, Ag_3O_4 and elementary silver, Ag(0). This implies that Ag_3PO_4 was converted into Ag_2SO_4 during the reaction. Ag_2SO_4 may be formed by a reaction between the HSO_4^- generated and the silver phosphate formed at the beginning of the reaction (Equation IV-12):

$$2Ag_3PO_{4(s)} + 3HSO_4^- + 3H^+ \longrightarrow 3Ag_2SO_4(s) + 2H_3PO_4 \qquad \text{Eq. IV-12}$$

Diffraction peaks for Ag(0) were observed at 38.6° (111), 44.3° (200), 64.4° (220) and 77.3° (311).[504] These results suggest that Ag(0) may be produced during the reaction. Deb *et al.* also demonstrated, through XPS analyses, the formation of Ag(0) during the oxidative trifluoromethylation of alkenes with $AgNO_3/K_2S_2O_8$. Based on their results, they suggested a novel catalytic cycle involving Ag(I)-Ag(0).[505] A similar pattern of behaviour was reported by Hatamura *et al.*, who described the reduction of Ag(I) to Ag(0) during the decarboxylation of Ag(I) β-ketocarboxylates.[506]

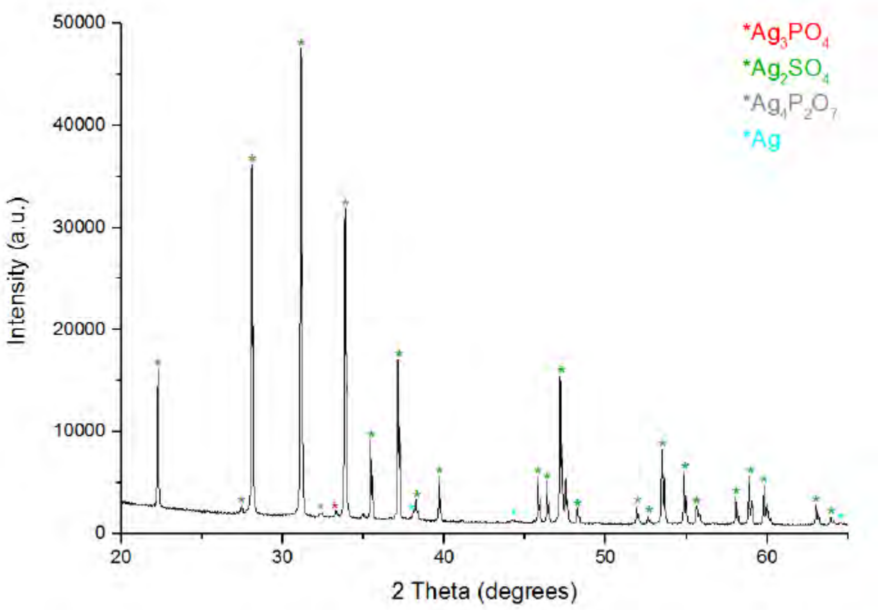


Figure 63. XRD patterns of solid phase after reaction. Experimental conditions: $AgNO_3/K_2S_2O_8$ (1:1), KH_2PO_4/K_2HPO_4 (0.1:0.1 M), 100°C, 30 minutes

Weak diffraction peaks at 27.7, 33.5, 35.8 and 39.7 degrees were also detected in the solid phase at the end of the LA decarboxylation reaction. They were attributed to Ag_3O_4 (ICSD No. 59225). Nevertheless, the presence of Ag_3O_4 was not considered likely, because this molecule breaks down when exposed to X-ray irradiation at room temperature.[507] It should be borne in mind that Ag_3O_4 is a binary oxide compound, $Ag^{2+}(Ag^{3+})_2O_4$,[508] and that its detection may be related to the presence of other oxide species.

XPS surface analyses of precipitates were performed to gain greater insight into LA decarboxylation. The XPS spectrum of Ag $3d_{5/2}$ at the beginning of the reaction showed binding energies (BE) of 367.9 eV with a FWHM (full width at half maximum) value of 1.17 eV (FWHM of Ag metal ref < 0.8 eV), potentially indicating a single silver oxidation state.[509] By contrast, after the reaction, a shift to higher binding energies (368.05 eV) was observed, with an increase in peak width FWHM of 1.46 eV. This increase in peak width after the reaction suggests the possible presence of a mixture of silver species. The small shift in BE for the Ag $3d_{5/2}$ spectrum made it difficult to determine which Ag species were involved in the reaction. However Auger electron analysis facilitated the identification of the Ag oxide species present. On the spectra (Figure 64) before and after the reaction, an Auger $AgM_5N_{45}N_{45}$ signal centered on 348.6 eV, and another at 354.5 eV can be seen, from the Auger $AgM_4N_{45}N_{45}$ peak assigned to Ag_3PO_4.[510] The peak centered on 354.5 eV can also be assigned to Ag_2SO_4.[511] Furthermore, both sulfates (S$2p_{3/2}$ at 169.24 eV) and phosphates (P$2p_{3/2}$ at 133.17 eV) were detected by XPS, so a mixture of these two compounds was present, confirming the XRD results. Otherwise, after the reaction, two Auger signals, $AgM_5N_{45}N_{45}$ at 350.7 eV and $AgM_4N_{45}N_{45}$ at 356.6 eV, were visible and could be attributed to a mixture of Ag_2O and AgO.[512–514]

Ag_3O_4 was identified in XRD patterns, but neither Ag_2O nor AgO were detected. The mixed valence of Ag_3O_4 ($Ag^{2+}(Ag^{3+})_2O_4$) may have interfered with the identification of Ag_2O and AgO in the XRD analysis.

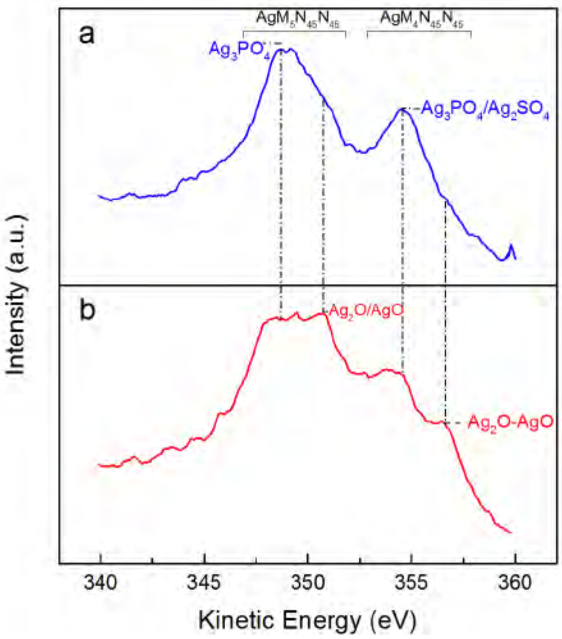


Figure 64. AgMNN Auger signals of the solid phase a) before and b) after levulinic acid decarboxylation

To sum up, the solid-phase analyses revealed the presence of trace amounts of Ag(II) and Ag(0). The main component of this phase during the reaction is Ag(I). Several forms were detected (*e.g.* Ag_3PO_4, Ag_2SO_4 and $Ag_4P_2O_7$), depending on its interaction with the solution. Thus, the evolution of the solid phase does not explain the limitation of LA decarboxylation if Ag(I) species remain present throughout the reaction. This situation may occur because acidification of the reaction medium limits the production of ($SO_4^{\bullet -}$), instead favoring the production of Caro's acid, which seems to be a competitive reaction (Schema 26, reaction b *vs.* reaction a).

4.3.3.7 Influence of pH variation

As previously described, the pH of the solution changed during the reaction. It decreased as the amount of $K_2S_2O_8$ increased from pH 5 to 2 or 1 when 1 or 2 equivalents of $K_2S_2O_8$, respectively, were used. Under these conditions, the K_2HPO_4/KH_2PO_4 solution cannot buffer the pH, due to the formation of strong-acid anions, such as the sulfate and nitrate ions produced during the reaction, together with phosphoric acid. Other acid-base pairs were tested, to evaluate their effect on the change in pH of the reaction solution and the production of MEK (Table 65). As expected, the pH of the reaction decreased in all cases, even when a KCl/NaOH solution at pH 12 was used. Lower LA conversion and MEK yields were obtained if NaOH was used alone (Table 65, # 1 and 8). Similar LA conversion and MEK yields were obtained with KCl/NaOH, K_2HPO_4/KH_2PO_4, and KH_2PO_4 solutions (Table 65, # 2-4, 6). MEK yield was increased only slightly by the use of K_2HPO_4 and Na_2HPO_4/NaH_2PO_4 solutions (Table 65, # 5 and 7).

#	Aqueous composition	Solution concentration [M]	*solution pH	pH		LA conversion (%)	Yield (%)	
				Initial	Final		AcOH	MEK
1	Water	-	6	3	1	29.6	14.8	14.8
2	KCl/NaOH	0.2	12	4	1	48.8	12.3	36.5
3	K_2HPO_4/KH_2PO_4	0.2	6.9	5	2	46.8	14.4	32.5
4	K_2HPO_4/KH_2PO_4	0.2	8.0	5	2	47.6	15.7	31.0
5	Na_2HPO_4/NaH_2PO_4	0.2	7.2	4	2	50.5	10.9	39.6
6	KH_2PO_4	0.2	4.5	3	1	48.9	21.3	27.9
7	K_2HPO_4	0.2	8	5	1	50.0	11	39.0
8	NaOH	$9\ 10^{-4}$	8	5	1	30.5	9.7	20.8

Table 65. Effect on LA decarboxylation of aqueous composition and initial pH. Experimental conditions: $AgNO_3/K_2S_2O_8$ (1:1), 100°C, 30 minutes. *Solution pH measured before addition of reactants

As none of the tested solutions allowed the maintenance of a constant reaction pH, the pH was adjusted to 5 with NaOH (0.2 M solution) after 30 minutes of reaction. The reaction was then run for 30 minutes more, but no further increase in LA conversion and MEK yield over the general reaction was observed (Table 66, # 1 *vs.* # 2). The pH was thus adjusted with NaOH after 30 minutes, but this time an additional equivalent of persulfate was added, and the reaction was run for 30 minutes more. This increased the LA conversion rate considerably, to 99%, and an excellent MEK yield (87%) was obtained, demonstrating the importance of these two parameters (Table 66, # 3). By contrast, the addition of persulfate after 30 minutes of reaction did not increase MEK yield if reaction pH was not adjusted, whereas the addition of both persulfate and silver nitrate slightly increased MEK yield, from 31 to 38 %. Nevertheless, in both cases, an increase in AcOH production was observed (Table 66, # 4-5). These results suggest that MEK production is limited by the decrease in pH during the reaction.

#	Description of reaction	n_{eq} $AgNO_3$ / $K_2S_2O_8$	LA conversion (%)	pH		Yield (%)	
				Initial	Final	AcOH	MEK
1	[a]Initial reaction: Medium 1 (M1)	1/1	46.8	5	2	14.4	32.5
After adjustment to pH=5							
2	[b]Addition of NaOH to M1	0/0	48.8	5	2	11.8	32
3	[b]Addition of NaOH & $K_2S_2O_8$ to M1	0/1	97.9	5	1	11.3	86.6
Without pH adjustment							
4	[b]Addition of $K_2S_2O_8$ to M1	0/1	54.3	3	1	22.8	31.5
5	[b]Addition of $AgNO_3$ / $K_2S_2O_8$ to M1	1/1	67	2	1	28.7	38.3

Table 66. Improvement of LA conversion and MEK yield following the adjustment of reaction pH. Experimental conditions: $AgNO_3/K_2S_2O_8$ (1:1), KH_2PO_4/K_2HPO_4 (0.1:0.1 M), 100°C. [a]1st cycle of 30 minutes, [b]after 2nd cycle of 30 min.

XRD and XPS analyses of the solid phase were performed after the addition of NaOH to the medium and the 2nd reaction cycle, to determine the reasons for the increase in LA conversion rate and, thus, in MEK production following pH adjustment.

XRD patterns showed the presence principally of Ag_3PO_4 after adjustment of the pH of the medium with NaOH. Traces of $Ag_4P_2O_7$ and Ag(0) were also detected (Figure 65a). The solid phase of the adjusted medium seemed to be similar to that previously observed in the XRD patterns obtained at the start of the 1st reaction cycle (Figure 62). These analyses suggest that the reaction medium can be regenerated by adding NaOH. This regeneration of the reaction medium explains the improvement in LA conversion rate in the 2nd cycle of the reaction.

The XRD patterns obtained after the 2nd cycle of the reaction are reported in Figure 65b. The conversion of Ag_3PO_4 into Ag_2SO_4 was detected, as observed after the 1st cycle of the reaction (Figure 63). Ag_2SO_4 was the principal species present, along with traces of Ag_3PO_4, KH_2PO_4 and $Ag_4P_2O_7$.

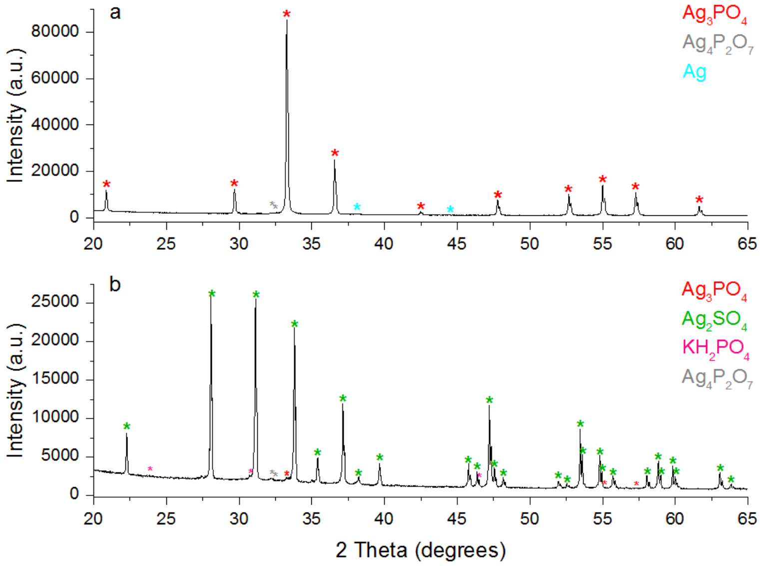


Figure 65. XRD patterns for the solid phase: a) after M1 neutralization, b) after the 2nd cycle of the reaction, with the addition of $K_2S_2O_8$.. Experimental conditions: $AgNO_3/K_2S_2O_8$ (1:1), KH_2PO_4/K_2HPO_4 (0.1:0.1 M), 100°C

The XPS analyses were, thus, consistent with the XRD results. On the Auger spectrum obtained after the addition of NaOH (Figure 66a), the peaks corresponding to the Ag_2O-AgO mixture at the kinetic energies of 350.7 eV (Ag $M_5N_{45}N_{45}$) and 356.6 eV (Ag $M_4N_{45}N_{45}$) disappeared, confirming that the medium could be regenerated by adding NaOH. This spectrum has a profile similar to that obtained at the start of the 1st cycle of reaction. The formation of the Ag_2O and AgO was confirmed after the 2nd cycle of the reaction, by the appearance of the characteristic Auger peaks at 350.6 eV and 356.5 eV (Figure 66b).

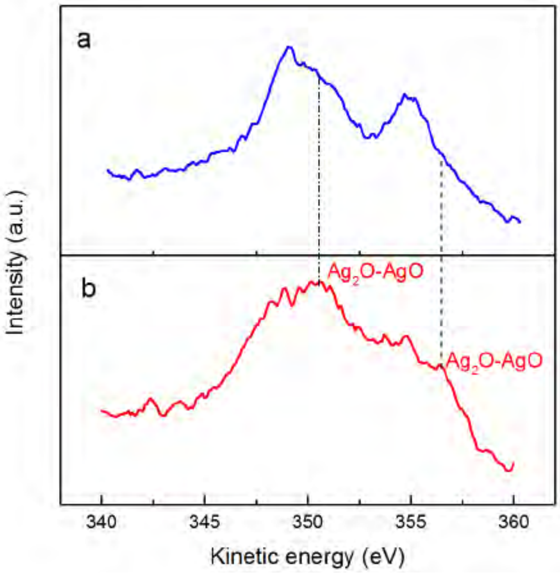


Figure 66. AgMNN Auger signals for the solid phase: a) after M1 neutralization, b) after the 2nd cycle of reaction Experimental conditions: $AgNO_3/K_2S_2O_8$ (1:1), KH_2PO_4/K_2HPO_4 (0.1:0.1 M), 100°C, 30 minutes

These results imply that $AgNO_3$ can be reused for further reactions and that only the addition of $K_2S_2O_8$ would be required to achieve high LA conversion and MEK yields. This study thus constitutes a very interesting step towards the development of greener processes of MEK production.

4.3.4 Conclusions

LA decarboxylation for the production of MEK with the $AgNO_3/K_2S_2O_8$ system was studied. MEK can be produced in the absence of $AgNO_3$, but $K_2S_2O_8$ is required for the reaction even in the presence of Ag(II). These results show that sulfate free radicals ($SO_4^{\bullet -}$) are directly responsible for LA decarboxylation, and a radical mechanism for MEK synthesis is proposed.

XRD and XPS analyses of the solid phases throughout the reaction demonstrated the presence principally of Ag(I) species. Traces of Ag(II), as AgO and elementary Ag(0), were also observed, with no reaction limitation. It was also possible to show that acidification of the reaction medium limited LA decarboxylation. Adjustment of the pH to 5 and the addition of 1 equivalent of $K_2S_2O_8$ after 30 minutes of reaction resulted in the highest LA conversion, at up to 99%, and a MEK yield of 87% in a 2nd cycle of reaction. $AgNO_3$ recycling is, therefore, possible. These results constitute an interesting step towards continuous MEK production requiring only the addition of $K_2S_2O_8$.

4.4 Decarboxylation of levulinic acid using $AgNO_3/K_2S_2O_8$: study of the evolution of the solid system during the reaction by SEM-EDX, SSNMR, XRD and XPS spectroscopy.

In the previous section, we have presented the study of the decarboxylation of levulinic acid using potassium persulfate ($K_2S_2O_8$) and silver nitrate ($AgNO_3$). During this preliminary study, we analysed the composition of the solid phase by XPS and XRD analyses, at the beginning and at the end of the reaction. This allowed us to propose a radical mechanism where Ag(I) catalyzes the formation of sulfate radicals ($SO_4^{\bullet-}$) from $K_2S_2O_8$, which lead to the decarboxylation of LA. The elucidation of this mechanism led us to develop a pH adjustment strategy that increased the LA conversion from 46.8% to 97.9% and the MEK yields from 36.5 to 86.6%.

In order to provide additional support for the proposed mechanism and to gain a deep understanding of the evolution of the species involved on the LA decarboxylation, we thus decided to study the changes that occur throughout the reaction at several reaction times (0, 4, 13 and 30 minutes), but also after the pH adjustment and at the end of the second cycle of reaction. In this section, we present a detailed characterization of the solid phase using solid-state nuclear magnetic resonance (SSNMR), X-ray diffraction (XRD), X-ray photoelectron spectroscopy (XPS) and scanning electron microscopy (SEM-EDX).

4.4.1 Materials and methods

4.4.1.1 Chemicals

All the reagents were used without further purification. Levulinic acid, $AgNO_3$, Ag_2O(I), AgO(II), Ag_3PO_4, $K_2S_2O_8$, KH_2PO_4 and K_2HPO_4 were purchased from Sigma-Aldrich (L'Isle d'Abeau Chesne, France). Methyl ethyl ketone was analytical grade from Sigma-Aldrich. Silver sulfate was prepared by adding sulfuric acid to a saturated solution of silver $AgNO_3$. The formed white precipitate, corresponding to Ag_2SO_4, was washed with hot water to eliminate any leftover of silver nitrate. Finally, Ag_2SO_4 was dried in a vacuum desiccator (Selecta vacuo-Temp) at 40 °C.

4.4.1.2 Solids preparation

In a typical run, the reactions were carried out in ACE pressure tubes (bushing type) by adding 0.35 g of levulinic acid (L.A.; 3 mmol) into 15 mL of K_2HPO_4/KH_2PO_4 solutions (0.1:0.1 M, pH 6.86). Then $AgNO_3$ (3 mmol; $AgNO_3$ should be weighed by avoiding contact with light in order to prevent its oxidation. *e.g* in a dark vial) and $K_2S_2O_8$ (3 mmol) were added to the reaction medium. The solid phase was recovered: at the very beginning of the reaction (0 minute), after 4 minutes, after 13 minutes and after 30 minutes of reaction (1st cycle of reaction), at 100 ºC. Additionally, solids were recovered after pH adjustment and after the 2nd cycle of reaction. Furthermore, a blank was prepared as the general reaction without adding levulinic acid. All the solids were collected by filtration with a membrane of 10 kDa in a MDM-millipore system, then washed with distillated water and dried in a vacuum desiccator (Selecta vacuo-Temp) at 40 °C. These steps were performed in dark conditions in order to avoid any modification of the compounds.

4.4.1.3 Solids characterization

4.4.1.3.a Scanning electron microscopy (SEM-EDS)

For the analyses, the powders were deposited on a double-sided carbon adhesive, then coated with 0.3 nm of platinum with a JEOL JFC 2300HR. The scanning electron microscopy (SEM) measurements were carried out using a JEOL JSM 7800F. The energy dispersive X-ray spectroscopy (EDX) was carried out with an Oxford Instrument attached to the JEOL JSM 7800F. The elemental identification was performed with the AZtecEnergy software.

4.4.1.3.b Solid-state Nuclear Magnetic Resonance (SSNMR)

The MAS ^{109}Ag NMR spectra were recorded on a BRUKER Avance 400 spectrometer (9.4 T). A solution of $AgNO_3$ (1 M) was used as external reference for the chemical shift. The samples were placed in 4 mm zirconia rotors. The rotation speed around the magic angle (MAS) was set to 8 kHz. The experiments were carried out at room temperature at 21 °C. The ^{109}Ag spectra were recorded with a recycling delay between 5s and 10s. The duration of the excitation RF pulses has been adjusted to correspond to magnetization rotations of 30°.

4.4.1.3.c X-ray powder diffraction (XRD).

The diffraction patterns were collected using a BRUKER D8 Advance diffractometer with a detector LynXeye 1D. The X-ray tube was a ceramic tube with a cooper anode. There was no monochromator. Therefore the main wavelengths used were $K\alpha$ radiation, 0.154059 nm and $K\alpha 2$ radiation, 0.15444 nm.

4.4.1.3.d *X-ray photoelectron spectroscopy (XPS)*

The analyses were performed on a Thermo scientific Kalpha XPS spectrometer. The photoelectron emission spectra were recorded using Al–Kα radiation (hv = 1486.6 eV) from a monochromatized source. The X spot size was 400 µm. The pass energy was fixed at 40 eV for narrow scan (and 150 eV for the survey). Flood Gun was used for the charge effects. The spectrometer energy was calibrated using the Au 4f7/2 (83.9 ± 0.1 eV) and Cu 2p3/2 (932.8 ± 0.1 eV) photoelectron lines. XPS spectra were recorded in direct N(Ec). The background signal was removed using the Shirley method. The atomic concentrations were determined with an accuracy of 10% from photoelectron peak areas using the atomic sensitivity factors reported by Scofield, taking into account the transmission function of the analyzer. This function was calculated at different pass energies from Ag 3d and Ag MNN peaks collected for a silver reference sample, inside the system. The binding energy scale was established by referencing the C1s value of adventitious carbon (284.7 ± 0.1 eV). The photoelectron peaks were analysed by Lorentzian/Gaussian (L/G = 30) peak fitting.

4.4.2 Results and Discussion

In the section 4.3, we have studied the decarboxylation of levulinic acid using $K_2S_2O_8$ and $AgNO_3$ in a solution of KH_2PO_4/K_2HPO_4 (0.1:0.1 M). During the reaction, changes in the color of the solid phase were observed.

When $AgNO_3$ was added to the phosphate solution, which also contains LA and $K_2S_2O_8$, the color of the solid phase changed from white to yellow (Figure 67a). A decrease in color intensity was then observed: the reaction medium started to whiten. After 4 minutes of reaction, the solid phase is almost white (Figure 67b). Then, the solid phase begins to slowly darken to become slightly brown after 13 minutes of reaction (Figure 67c). Finally, at the end of the reaction, a dark brown coloration of the solids was observed (Figure 67d).

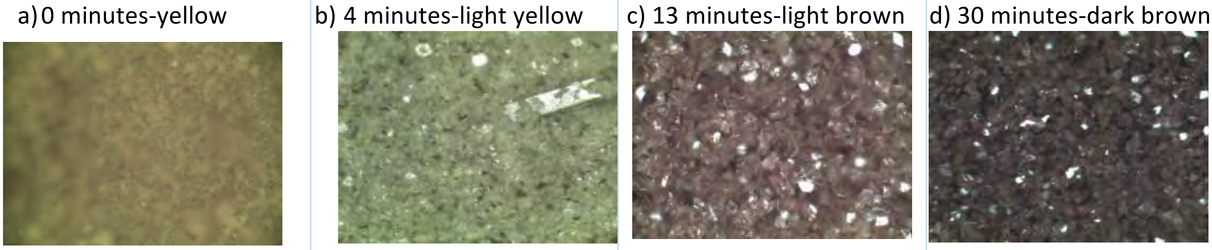


Figure 67. Optical microscopy (x10) of solid phase during the reaction. Experimental conditions: $AgNO_3/K_2S_2O_8$ (1:1), KH_2PO_4/K_2HPO_4 (0.1:0.1 M), 100°C.

Those color changes can be related to the formation of different silver-compounds. The formation of Ag_3PO_4, which is a yellow solid, was postulated when the reaction medium turned from white to yellow. After 4 minutes of reaction, the reaction medium started to whiten. Silver phosphate is thus highly likely converted into Ag_2SO_4, which is a white solid. Finally, the darkening of the solid phase, from white to a dark brown color, could be explained by the formation of silver oxide species, as we have stated above in the section 4.3.3.6.

The color changes that occur during the reaction have been schematically represented in the following figure (Figure 68):

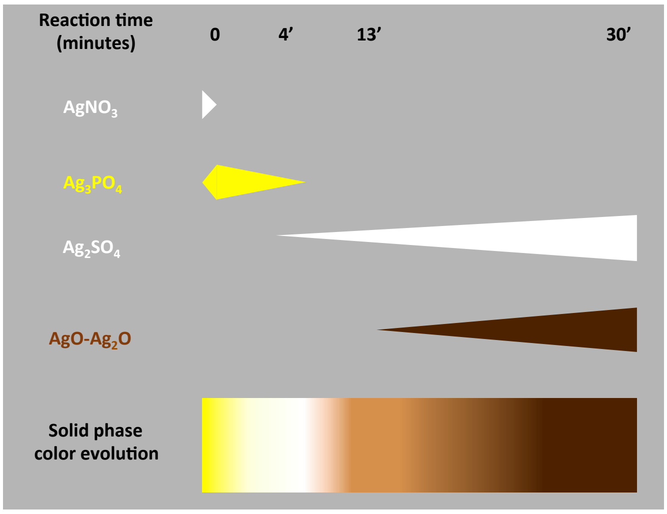


Figure 68. Graphic representation of the color evolution of the solid phase during the reaction

Moreover, as described in section 4.3.3.7, the LA decarboxylation is limited by the acidification of the reaction medium (pH from 5 to 2), which is due to the formation of nitric acid, bisulfate ion (HSO_4^-), sulphuric acid and Caro's acid (H_2SO_5). We demonstrated that this limitation (LA conversion 46.8%; MEK yield 32.5%) can be overcome by the pH adjustment of the medium M1 (pH from 2 to 5) and the addition of 1 equivalent of $K_2S_2O_8$. Interestingly, this pH adjustment led to a change of the color of the solid phase from dark brown to yellow, which is similar to the color observed after the addition of $AgNO_3$ at the beginning of the first cycle of reaction (Figure 69a *vs* figure 67a).

After the 2nd cycle of reaction, which led to a LA conversion of 97.9% and a MEK yield of 86.6% (section 4.3.3.7), the solid phase darkened again (Figure 69b vs 67d).

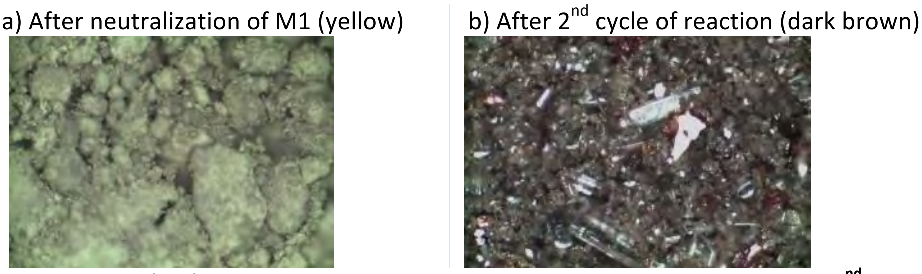


Figure 69. Optical microscopy (x10) of solid phase after adjustment to pH 5 with NaOH and after 2nd cycle of reactions. Experimental conditions: $AgNO_3/K_2S_2O_8$ (1:1), KH_2PO_4/K_2HPO_4 (0.1:0.1 M), 100°C, 30 minutes

In order to check if the change of the silver species were related to LA decarboxylation or to reaction conditions (for example the reaction temperature), we carried out the reaction without the addition of levulinic acid. After 30 minutes, the color of the solid phase changed from yellow to metallic-like white, but not to dark brown. From these results, we can suggest that the solid darkening, that has been observed during the LA decarboxylation, is not related to the reaction conditions but indeed to the reaction itself (Figure 70).

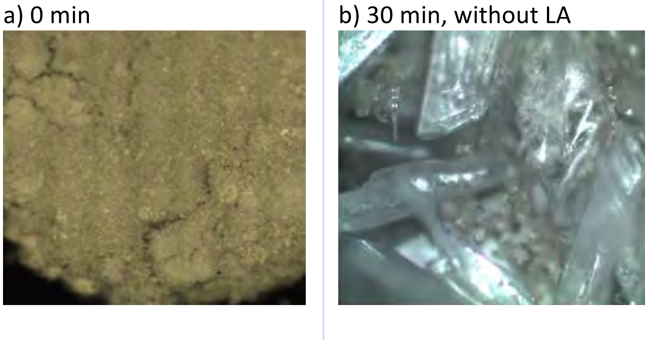

a) 0 min
b) 30 min, without LA

Figure 70. Optical microscopy of solid phase obtained after 30 min of reaction without LA (x50). Experimental conditions: $AgNO_3/K_2S_2O_8$ (1/1), 100 °C, 30 min. Experimental conditions: $AgNO_3/K_2S_2O_8$ (1:1), KH_2PO_4/K_2HPO_4 (0.1:0.1 M), 100°C, 30 minutes

These color changes of the solid phase are interesting and deserve a more thorough study. Different spectrometric techniques (SSNMR, XRD, XPS and SEM-EDX) were thus used to characterize the solid phase and to explain the evolution of the compounds involved in the LA decarboxylation.

4.4.2.1 Solid state Nuclear Magnetic Resonance (SSNMR)

In order to gain more insight about the color changes that occur during the reaction, solid-state NMR analyses of the solid phase were performed. This technique is based on the resonance frequencies that are emitted by nuclei that are irradiated with radio waves.[515] It provides specific chemical shifts that are characteristic of compounds and allow their identification in a sample. The SSNMR spectroscopy is thus a useful tool for the identification of crystalline and amorphous compounds at the solid surface.[516]

Herein, we decided to use the ^{109}Ag NMR spectroscopy to try to identify the oxidation state of silver and the different silver species tan can make up the solid phase. Indeed, the chemical shift values of silver species are characteristic and easily identifiable through ^{109}Ag NMR spectroscopy.[517]

The analyses of $AgNO_3$, Ag_3PO_4, Ag_2SO_4, Ag_2O, and AgO standards were carried out. The chemical shifts obtained for each compound are gathered in Table 67.

Compound	Chemical shift (ppm)
$AgNO_3$	-108.3
Ag_3PO_4	309.3
Ag_2SO_4	32.4
Ag_2O	1689.4
AgO	671.3

Table 67. ^{109}Ag NMR Chemical shift for several silver compounds

The SSNMR spectra of the solid phase obtained after 0, 4, 13 and 30 minutes of reaction were then compared with the standards (Figure 71).

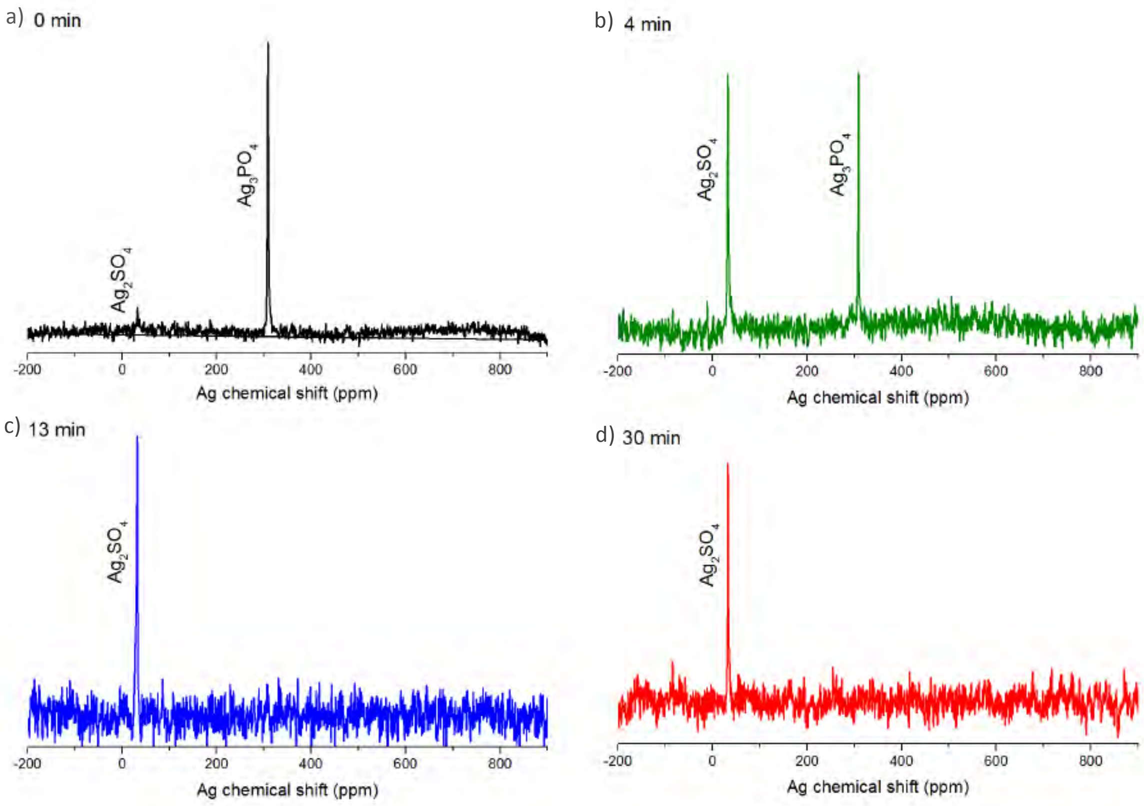


Figure 71. ^{109}Ag solid state NMR spectrum of the solid phase at a) 0, b) 4, c) 13 and d) 30 minutes. Experimental conditions: $AgNO_3/K_2S_2O_8$ (1:1), KH_2PO_4/K_2HPO_4 (0.1:0.1 M), 100°C, 30 minutes

At the very beginning of the reaction, a peak of high intensity at 308.8 ppm corresponding to Ag_3PO_4 and a small signal at 32.3 ppm attributed to Ag_2SO_4 were detected (Figure 71a).

After 4 minutes of reaction, two signals of same intensity were perceived at 308.8 ppm and 32.4 ppm corresponding to Ag_3PO_4 and Ag_2SO_4, respectively (Figure 71b).

After 13 minutes, the signal corresponding to Ag_3PO_4 disappeared and only the peak of Ag_2SO_4 at 31.8 ppm was observed (Figure 71c).

Similar results were obtained after 30 minutes of reaction: the SSNMR spectrum showed only the characteristic peak of Ag_2SO_4 at 32.5 ppm (Figure 71d).

These results are in accordance with the appearance followed by the disappearance of the yellow color that have been observed during the reaction. This behavior can be summarized in the following table (Table 68):

		Reaction time (min)			
		0	**4**	**13**	**30**
Silver species	Ag_3PO_4 (309,3 ppm) 🟨	+++	++	traces	traces
	Ag_2SO_4 (32,4 ppm) ⬜	traces	++	+++	+++
Solid phase color		yellow	light yellow	light brown	dark brown

Table 68. Identification of silver species along the reaction.

Additional experiments were conducted to highlight the presence of silver oxides between 600 and 2600 ppm at 30 minutes of reaction. No peak was detected in this region of the spectra (spectra not shown). However, it cannot be concluded from these experiments that silver oxides have not been formed during the reaction because the ^{109}Ag isotope has a very low sensitivity in SSNMR and their concentration might be too low to be detected. The identification of their presence would require to acquire data using longer relaxation times.[517–520] Several days would thus be needed to obtain such a spectrum. We could not perform those analyses because the spectrometer could not be booked for such a long time.

The SSRMN spectrum of the solid phase, obtained after adjustment of M1 (reaction medium obtained after 30 min of reaction) to pH 5 with NaOH was then realized. It showed the presence of a single resonance signal at 308.8 ppm attributed to Ag_3PO_4 (Figure 72a). These results are close to those obtained at the very beginning of the reaction (0 minute of reaction time; Figure 71a) and are in agreement with the reappearance of the yellow color.

After the 2nd cycle of reaction, only the characteristic peak of Ag_2SO_4 was observed (Figure 72a) which confirms the disappearance of Ag_3PO_4 and explains the whitening of the reaction medium (Figure 71a) before its darkening.

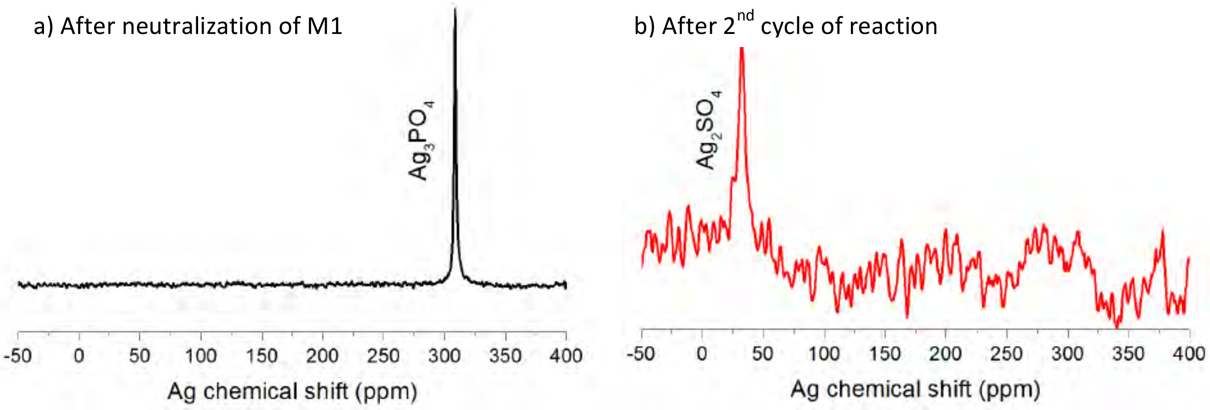


Figure 72. ^{109}Ag solid state NMR spectra of the solid phase a) after neutralization to pH 5 with NaOH and b) after 2nd cycle of reaction. Experimental conditions: $AgNO_3/K_2S_2O_8$ (1:1), KH_2PO_4/K_2HPO_4 (0.1:0.1 M), 100°C, 30 minutes

The evolution of the presence of the silver species and the reaction color are summarized in the following table:

		After pH adjustment	After 2nd reaction cycle
Silver species	Ag_3PO_4 (309,3 ppm) 🟨	+++	x
	Ag_2SO_4 (32,4 ppm) ⬜	x	+++
Solid phase color		yellow	dark brown

Table 69. Evolution of Ag_3PO_4 and Ag_2SO_4 after pH adjustment of M1 to pH5 and after 2nd cycle of reaction.

These findings corroborate that Ag_3PO_4 has been regenerated with the addition of NaOH and is then consumed during the second cycle leading to an improvement of the LA decarboxylation.

However, these SSNMR analyses did not permit to demonstrate the presence of the silver oxides species that are supposed to be responsible for the darkening of the reaction medium at the end of the reaction. Therefore, to highlight their formation, XRD and XPS analyzes were performed.

4.4.2.2 X-Ray Diffraction spectroscopy

The X-ray powder diffraction spectroscopy (XRD) is widely used to identify and characterize crystalline solids: X-rays are shot at a compound and XRD measures the diffraction of the beam.[521] Diffraction is characteristic of a compound: each crystalline compound present its own characteristic pattern ("fingerprint") that allows its identification.[522] The analysis of the XRD spectra to identify the different fingerprints can thus give information on the composition on an atomic level.

We thus decided to use this technique to study the evolution of silver species during the reaction. XRD analyses were thus carried out on the solid phases obtained at 0, 4, 13 and 30 minutes of reaction (Figure 73).

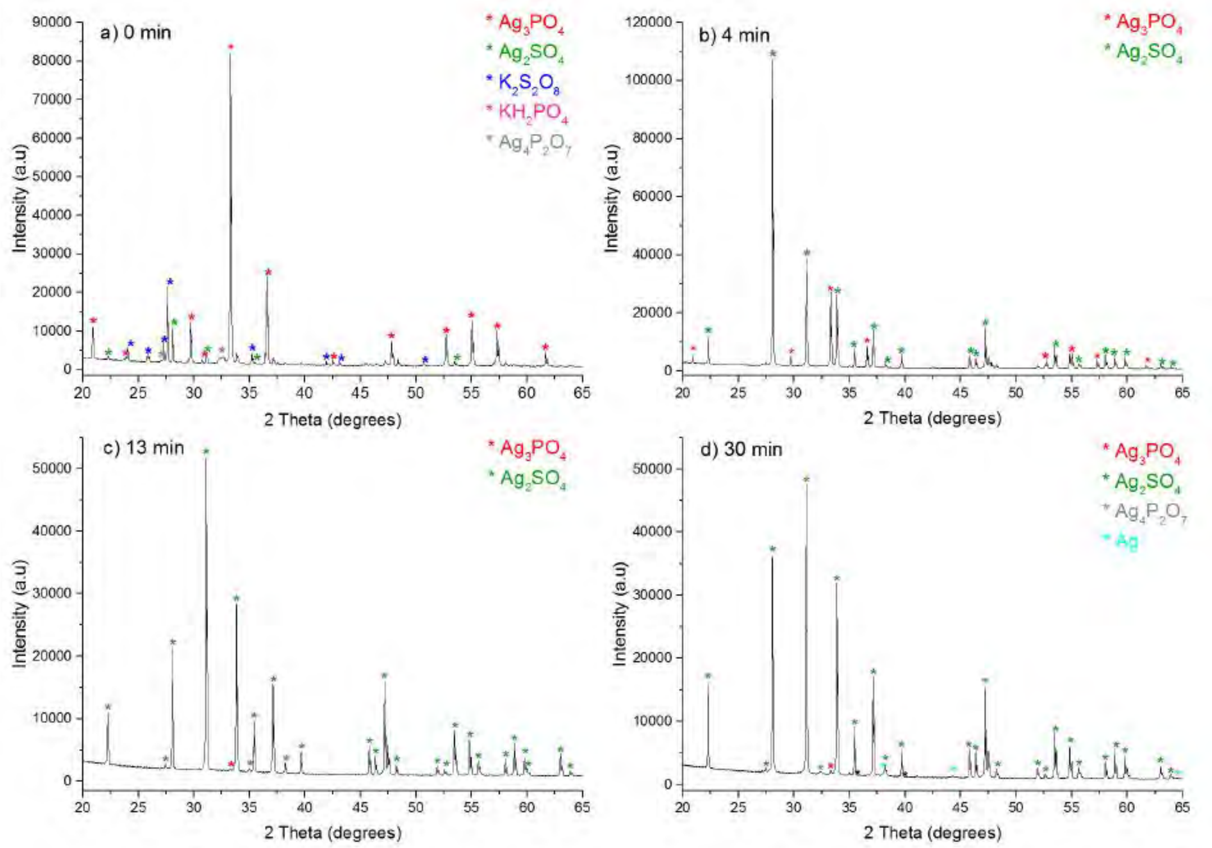


Figure 73. XRD patterns of the solid phase at 0, 4, 13 and 30 minutes. Experimental conditions: $AgNO_3/K_2S_2O_8$ (1:1), KH_2PO_4/K_2HPO_4 (0.1:0.1 M), 100°C, 30 minutes

As seen in figure 73a, the $AgNO_3$ was consumed almost instantly as soon as the reaction started (0 minute): it was not detected on the XRD patterns. The major compound was Ag_3PO_4 with diffractions peaks at 20.9, 29.7, 33.3, 36.6, 42.5, 47.8, 52.7, 55.0, 57.3, 61.7, 65.9, 69.9, 71.9° (JCPDS No. 06-0505).[497]

From these results, it can be suggested that $AgNO_3$ was totally converted into Ag_3PO_4. As exposed in section 4.3.3.6, this can be explained by the reaction between $AgNO_3$ and the $H_2PO_4^-/HPO_4^{2-}$ ions from the phosphate solution (KH_2PO_4/K_2HPO_4; equations IV-13 and IV-14).

$$3AgNO_{3(s)} + HPO_4^{2-} \longrightarrow Ag_3PO_{4(s)} + 3NO_3^- + H^+ \qquad \text{Eq. IV-13}$$

$$3AgNO_3(s) + H_2PO_4^- \longrightarrow Ag_3PO_4(s) + 3NO_3^- + 2H^+ \qquad \text{Eq. IV-14}$$

Traces of $K_2S_2O_8$ (major peaks at 24.0, 25.9, 27.3, 27.6, 29.3, 32.7, 35.2, 36.4°; ICSD No. 16972),[498] Ag_2SO_4 (major peaks at 22.2, 31.1, 33.8, 37.2, 47.0, 53.5°),[499] KH_2PO_4 from the phosphate solution (major peaks at 23.8, 30.7, 46.5°; ICSD 201371),[500] and $Ag_4P_2O_7$ (major peaks at 27.1, 32.3, 32.5°) were also detected.

Silver sulfate (Ag_2SO_4) can be formed by the reaction of silver nitrate ($AgNO_3$) with hydrogen sulfate (HSO_4^-) that is produced from the decomposition of potassium persulfate ($K_2S_2O_8$) in water, according to the following equations:

$$2K_2S_2O_{8(s)} + 2H_2O \longrightarrow 4HSO_4^- + 4K^+ + O_{2(g)} \qquad \text{Eq. IV-15}$$

$$HSO_4^- + 2AgNO_{3(s)} \longrightarrow Ag_2SO_{4(s)} + 2NO_3^- + H^+ \qquad \text{Eq. IV-16}$$

The presence of silver pyrophosphate ($Ag_4P_2O_7$) can be explained by the reaction between silver nitrate ($AgNO_3$) and potassium pyrophosphate ($K_4P_2O_7$) that is formed from K_2HPO_4 (buffer solution).

$$2K_2HPO_{4(s)} \longrightarrow K_4P_2O_{7(s)} + H_2O \qquad \text{Eq. IV-17}$$

$$4AgNO_{3(s)} + K_4P_2O_{7(s)} \longrightarrow Ag_4P_2O_{7(s)} + 4NO_3^- + 4K^+ \qquad \text{Eq. IV-18}$$

The XRD patterns of the solid phases obtained after 4 and 13 minutes of reaction showed important changes in their composition. The major component of the solid phase was Ag_2SO_4 and only traces of Ag_3PO_4 were detected. These results confirmed those obtained by SSNMR, and suggested that Ag_3PO_4 was converted into Ag_2SO_4 (Figure 73b and 73c). This conversion could be performed in the presence of hydrogen sulfate ions (HSO_4^-) (Equations IV-19).

$$2Ag_3PO_{4(s)} + 3HSO_4^- + 3H^+ \longrightarrow 3Ag_2SO_4(s) + 2H_3PO_4 \qquad \text{Eq. IV-19}$$

After 30 minutes of reaction, Ag_2SO_4 remained the major compound of the solid phase. Traces of Ag_3PO_4, $Ag_4P_2O_7$, Ag_3O_4 (major peaks at 27.7, 33.5, 35.8 and 39.7°) and Ag(0) (major peaks at 38.6, 44.3, 64.4, and 77.3°) were also identified.[504] Again, these results corroborate the SSNMR analyses and the color changes of the solid phase. Noteworthy, as exposed in the section 4.3.3.6, the presence of Ag_3O_4 in the solid is unlikely as this compound is unstable at room temperatures and under X-ray radiation.[507] Its detection can be related with an overlap of crystal reflexions of other silver oxide species, a recurrent problem in this type of analyses.[523]

The XRD patterns of the solid phase obtained after the adjustment of the pH medium M1 showed the disappearance of Ag_2SO_4 and the formation of Ag_3PO_4. Traces of Ag(0) and $Ag_4P_2O_7$ remained (Figure 74a).

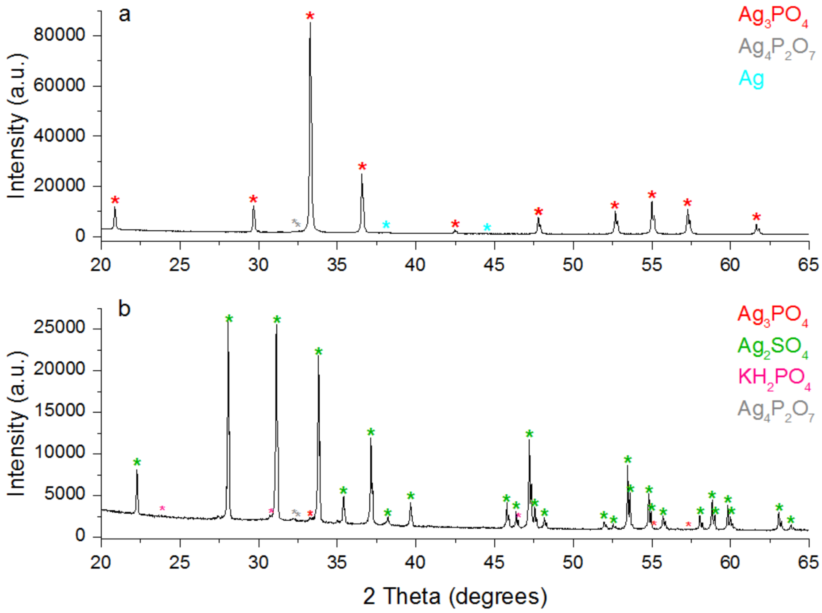


Figure 74. XRD spectra of the solid phase a) after adjustment of M1 to pH 5 with NaOH, and b) after 2nd cycle of reaction. Experimental conditions: $AgNO_3/K_2S_2O_8$ (1:1), KH_2PO_4/K_2HPO_4 (0.1:0.1 M), 100°C, 30 minutes

The transformation of Ag_2SO_4 into Ag_3PO_4 may be be explained by the reaction of Ag_2SO_4 with NaOH to form the intermediate AgOH (Equations IV-20). This intermediate can react with the H_3PO_4 from the reaction medium producing Ag_3PO_4 (Equations IV-21).

$$Ag_2SO_4(s) + 2Na^+ + 2OH^- \longrightarrow 2AgOH(s) + Na_2SO_4(s) \qquad \text{Eq. IV-20}$$

$$3AgOH + H_3PO_4 \longrightarrow Ag_3PO_4(s) + 3H_2O \qquad \text{Eq. IV-21}$$

These traces aside, the composition of the solid phase was thus close to the one obtained at the very beginning of the first cycle (minute 0, Figure 73a), which is in agreement with the results obtained by SSNMR: the reaction medium was thus regenerated.

After the 2nd cycle of reaction, the presence of Ag_2SO_4 was mainly identified with traces of Ag_3PO_4, KH_2PO_4 and $Ag_4P_2O_7$ (Figure 74b). A very similar XRD profile was obtained after the 1st cycle of reaction.

Again, these findings highlight that the regeneration of the medium is possible by the addition of NaOH, which explains the improvement of the LA conversion and the MEK yield after the 2nd cycle of reaction.

To recapitulate, the compositions of the different solid phases analysed by XRD spectroscopy that led to our conclusions can be summarized in the following table (Table 70):

		Reaction time (min)				After pH adjustment	After 2nd cycle
		0	4	13	30		
Species	$AgNO_3$ ⬜	x	x	x	x	X	x
	Ag_3PO_4 🟨	+++	traces	traces	traces	+++	traces
	Ag_2SO_4 ⬜	traces	+++	+++	+++	X	+++
	$Ag_4P_2O_7$ ⬜	traces	x	x	traces	traces	traces
	Ag(0)	x	x	x	traces	traces	x
	$K_2S_2O_8$	traces	x	x	x	X	x
	KH_2PO_4	traces	x	x	x	X	traces
Solid phase color		yellow	light yellow	light brown	dark brown	yellow	dark brown

Table 70. Summary of the identification of various silver species along the reaction.

To sum up, the XRD analyses are in accordance with the SSNRM analyses. However, the presence of stable silver oxides species such as AgO or Ag_2O, was not clearly observed on the XRD patterns obtained after the first and the second reaction cycles. As the formation of Ag_3O_4 is also very unlikely despite its detection, we thought that the XRD analyses might not relevant enough to identify the different silver oxide species. We decided thus to perform XPS spectroscopy analyses to clearly demonstrate their formation during the reaction.

4.4.2.3 Characterization by X-ray photoelectron spectroscopy

The X-ray photoelectron spectroscopy (XPS) is a surface-sensitive technique that allows to study the chemical composition and the electronic states of the elements present in solids in a thickness from 1-10 micrometers (extreme surface).[521,524] X-rays are shot at a compound and XPS measures the kinetic energy and number of core level electrons that are ejected from the material being analyzed. As it provides sets of binding energies (BE) that are characteristic of the electronic and chemical states of each element, it is thus a useful technique to elucidate the presence of silver oxides.

Variations in the binding energies for a given element depend of the chemical potential and polarization of the compounds.[525] In table 71 are presented the assignments of the binding energy of the Ag $3d_{5/2}$ peak for Ag(0), $AgNO_3$, Ag_2O, AgO, Ag_3PO_4 and Ag_2CO_3. The reported binding energy values of metallic silver and silver oxides are close and even coincident with each other, which could make their identification difficult in our samples.

	Binding Energy (eV) Ag $3d_{5/2}$	FWHM (eV)	Auger parameters $3d_{5/2}$, $M_4N_{45}N_{45}$	Auger parameters $3d_{5/2}$, $M_5N_{45}N_{45}$
Ag	368.3[b] 368.24[c] 368.2[d] 368.1[e]	1.12[b] 0.63[c] - 1.15[e]	726.5[b] - - -	720.5[b] - - -
$AgNO_3$	**368.3**[a] 368.8[b]	**1.1**[a] 1.39[b]	- 723.8[b]	- 718.3[b]
Ag_2O	368.6[b] 367.3[c] 367.8[d] 367.7[e]	1.25[b] 1.1[c] - 1.4[e]	723.9[b] - - -	717.8[b] - - -
AgO	367.8[b] 367.4[d] 367.4[e]	1.22[b] - 1.8[e]	724.4[b] - -	718.4[b] - -
Ag_3PO_4	**367.8**[a]	**1.1**[a]	-	-
Ag_2CO_3	**367.9**[a]	**1.06**[a]	-	-

Table 71. Assignments for several silver species. FWHM (full width at half maximum). [a] In this work; [b]Ferraria et al.;[526] [c]Kaspar et al.;[509] [d]Gao et al.;[527] [e]Schon et al.[528]

In the figure 75 are presented the XPS full spectra of the solid phases analyzed at 0, 4, 13, and 30 minutes of reaction.

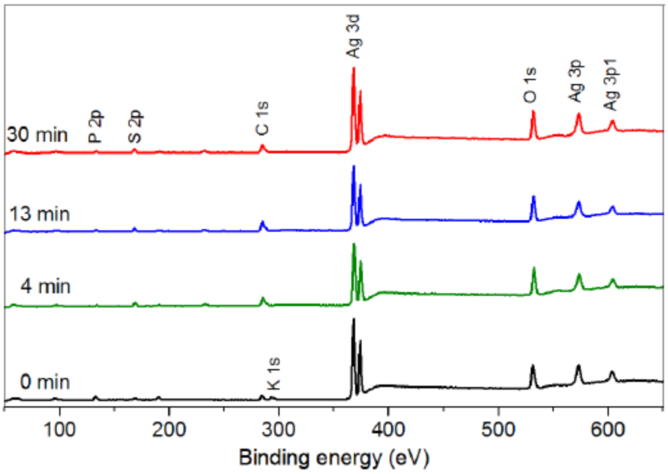


Figure 75. XPS full spectra and the core levels of the solid phase at different times of reaction.

The absence of the N1s signal, even at time 0 reveals that all the $AgNO_3$ was converted into other silver species. The presence of the P2p and S2p signals may suggest the formation of Ag_3PO_4 and Ag_2SO_4. These results corroborate the XRD and the SSNMR analyses, previously described. Noteworthy, the signal of C can be attributed to environmental pollution when the analyses were performed.

From this spectrum, it is possible to determine the atomic concentration of the chemical elements that composed the solid phase. Therefore, an easy way to assess the evolution of Ag_3PO_4 and Ag_2SO_4

is to calculate the Ag/P and Ag/S *ratios.* As shown in table 72, at the very beginning of the reaction (0 minute), the *ratio* Ag/P found was very low (1.8), suggesting the majority presence of Ag_3PO_4. Then, this *ratio* increased after 4 min and remained stable throughout the reaction, which could be associated with the reduction and the stabilization of the amount of Ag_3PO_4.

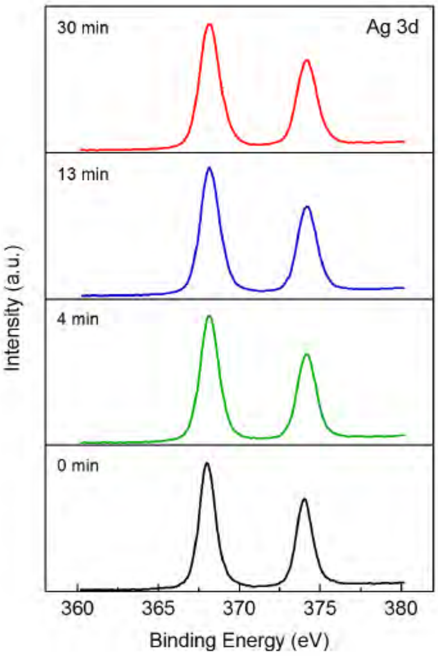
Atomic ratio	Reaction time (min)			
	0	4	13	30
Ag/P	1.8	4.6	4	4.5
Ag/S	7.2	2.5	3.1	3

Table 72. Atomic ratio of Ag/P and Ag/S at different reaction times

On the contrary, the highest Ag/S ratio was obtained at 0 minute showing that Ag_2SO_4 was present in a negligible amount. But after 4 min of reaction, the *ratio* Ag/S decreased and remained stable for the rest of the reaction, demonstrating the formation of Ag_2SO_4.

It is important to note, that to evaluate in an easy way the evolution of Ag_3PO_4 and Ag_2SO_4 throughout the reaction, we have considered in this calculation that silver is only as Ag_3PO_4 or Ag_2SO_4 forms. However, we can found these two silver compounds at same reaction time, as we have previously observed by XRD analyses.

After determining the principal elements that make up the solid phases, the analyses of the Ag 3d region (360-380 eV) was performed to try to identified the presence of silvers oxides species. The XPS spectra of Ag 3d region of the solid phases obtained at 0, 4, 13 and 30 minutes are shown in the Figure 76.



Time (min)	BE (eV)	FWHM (eV)
0	367.9	1.17
4	368.05	1.34
13	368.05	1.39
30	368.05	1.43

Figure 76. High resolution XPS spectra of Ag3d region of the solid phase at 0, 4, 13 and 30 minutes. Experimental conditions: $AgNO_3/K_2S_2O_8$ (1:1), KH_2PO_4/K_2HPO_4 (0.1:0.1 M), 100°C, 30 minutes

At the very beginning of the reaction (0 minute), the signal corresponding at Ag $3d_{5/2}$ was observed at a binding energy (BE) of 367.9 eV with a FWHM (full width at half maximum) of 1.17 eV (FWHM of Ag metal ref <0,8 eV). This narrow peak indicates a single silver oxidation state, according to the results reported by Kaspar *et al.*[509] After 4, 13 and 30 minutes of reaction, shifts to higher binding energy were observed (368.05 eV). Moreover, an increase in the FWHM of the peaks was noticed: 1.34, 1.39 and 1.46 eV for 4, 13 and 30 min of reaction, respectively. The shift of the peaks and the increase in the width of these peaks suggest the formation of a mixture of silver species.[508,529] According to the literature, the Ag $3d_{5/2}$ binding energies for Ag(0) are generally ranged between 368.1 eV and 368.3 eV, for Ag_2O from 367.3 eV to 368.6 eV and for AgO from 367.4 to 367.8 eV.[526] Considering that these described binding energies are very close and that the shifts obtained during the LA decarboxylation are very small, the identification of specific silver species is very difficult.

The Auger electron spectroscopy (AES) could help to figure out what are the silver oxide species that are present in our solid phases. This technique allows the identification of the elemental composition of surfaces by measuring the energies of Auger electrons.

When an atom is excited, it can relax by ejecting a core level photoelectron in one step (XPS). It can also relax in a two-step emission process (AES): an electron from a higher energy level fills the orbital of the inner shell that is vacant after the first emission. This electron transfer released energy to an outer shell electron, the Auger electron, which is ejected from the atom.[521] Due to the nature of the emitted electrons, Auger spectra might be more sensitive to chemical state than XPS spectra.

The Auger electron spectroscopy (AES) was thus envisaged to obtain further information, as the identification of the different silver compounds can be possible thanks to changes in the shape and shift of the peaks of the AES spectra.[530]

Auger electron analyses were thus performed on the different solid phases. At 0 minute, a peak in the region of Ag $M_4N_{45}N_{45}$ centered at a kinetic energy (KE) of 354.5 eV and another in the region $M_5N_{45}N_{45}$ centered at 348.6 eV were observed (Figure 77). These peaks were attributed to the presence of Ag_3PO_4.[510]

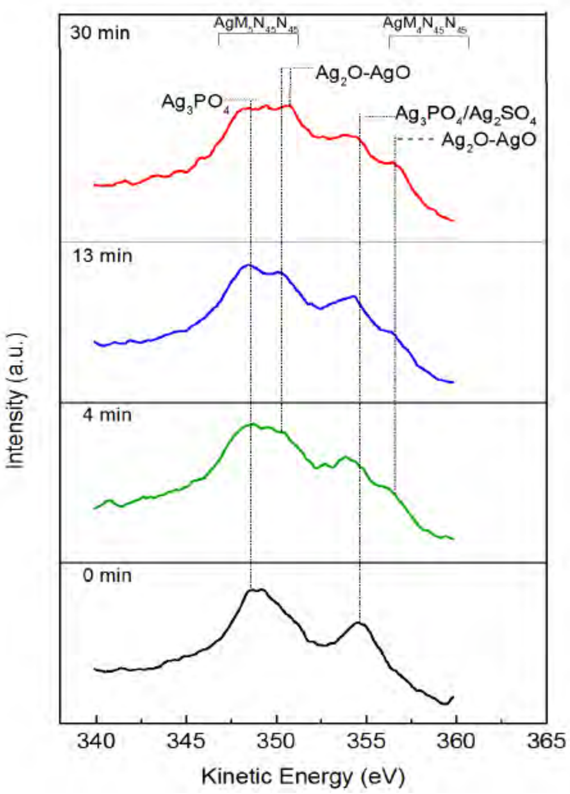


Figure 77. AgMMN Auger signals of the solid phase at 0, 4, 13 and 30 minutes. Experimental conditions: $AgNO_3/K_2S_2O_8$ (1:1), KH_2PO_4/K_2HPO_4 (0.1:0.1 M), 100°C, 30 minutes

The AES spectra of the solid phases after 4, 13, and 30 minutes showed a modification of the shape of the peak of Ag_3PO_4 at 354.5 eV, indicating the possible presence of other silver species (Figure 78). A mixture of Ag_3PO_4 and Ag_2SO_4 (which has similar BE, *i.e.* 355.2, 354.7, and 354.2 eV),[531] may explain the changes in the peak shape. Again, these results are in agreement with the change of color of the solid phase, the SSNMR and XRD analyses.

Furthermore, the appearance of two Auger signals $AgM_5N_{45}N_{45}$ at 350.7 eV and $AgM_4N_{45}N_{45}$ at 356.6 eV were detected (Figure 77). These peaks were assigned to a mixture of Ag_2O and AgO, as reported by Kumar *et al*. who have identified two peaks centered at 356.4 eV and 356.7 eV corresponding to

Ag_2O and AgO.[514] This analysis technique therefore ultimately allows the detection of silver oxide species that explain the darkening of the reaction medium at 30 minutes of reaction.

The AES analyses run after the pH adjustment of M1 showed that the Auger MMN peaks centered at 350.7 eV and at 356.6 eV attributed to the Ag_2O-AgO mixture disappeared (Figure 78a) explaining why the solid phase cleared. The obtained Auger spectrum profile was similar to that obtained before the 1st cycle of reaction. These results again demonstrated that the regeneration of the reaction medium by adjustment of pH with NaOH is possible.

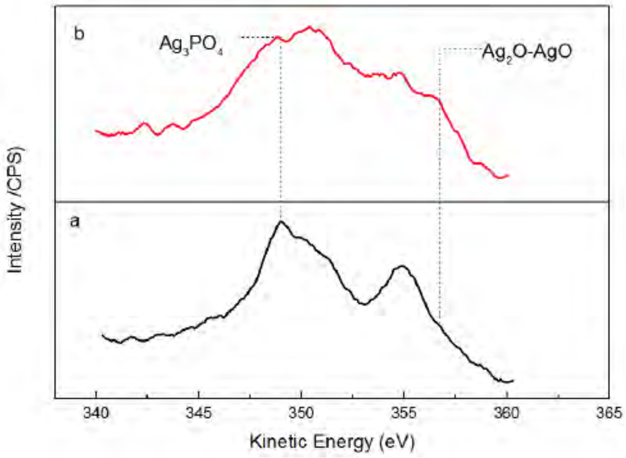


Figure 78. AgMMN Auger signals of the solid phase a) after adjustment of M1 to pH 5 with NaOH and b) after 2nd cycle of reaction. Experimental conditions: $AgNO_3/K_2S_2O_8$ (1:1), KH_2PO_4/K_2HPO_4 (0.1:0.1 M), 100°C, 30 minutes

The AES spectra obtained after the 2nd cycle of reaction showed the appearance of the two characteristics peaks of silver oxides species at a KE of 350.6 eV and 356.5 eV (Figure 78b). These oxides are thus formed during the first reaction, transformed into other silver species after the pH adjustment and formed again during the 2nd cycle of the reaction. For example, Ag_2O in aqueous medium can form AgOH (Eq. IV-22)[532,533] that, as we have previously mentioned, can react with the H_3PO_4[534] present in the medium (Eq. IV-23).

$$Ag_2O + H_2O \longrightarrow 2AgOH \qquad \text{Eq. IV-22}$$

$$3AgOH + H_3PO_4 \longrightarrow Ag_3PO_4(s) + 3H_2O \qquad \text{Eq. IV-23}$$

Otherwise, we deduced that the improvement in LA conversion and MEK yield after pH adjustment of the reaction medium M1 with NaOH is related to the elimination of HSO_4^- ions that acidified the medium, as indicated in equation IV-24.

$$HSO_4^- + OH^- \longrightarrow SO_4^{2-} + H_2O \qquad \text{Eq. IV-24}$$

As we have mentioned before, under acidic conditions the decomposition of $K_2S_2O_8$ into sulfuric acid and Caro's acid (H_2SO_5) is favored and thus limiting the formation of $SO_4^{\bullet-}$ radicals for the LA decarboxylation.

Thus, the SSNMR, XPS, XRD and AES analyses led us to a better understanding of the evolution of the silver species during the reaction. To complete these analyses, SEM-EDX studies were realized, particularly to study the evolution of the morphology of solid phase.

4.4.2.4 *Characterization of the solid phase by Scanning electron microscopy-Energy dispersive X-ray spectroscopy (SEM-EDX).*

The scanning electron microscopy with electric dispersive X-ray spectroscopy is one of the most used techniques for surface topography and composition analyses. The analysed sample is scanned by a focused electron beam. This generates a variety of signals that will allow creating nanoscale images. The detection of backscattered electrons can for example produce images with contrast that carries information on the differences in atomic number; secondary electrons can give information on the topography of the solid.

The following scheme illustrates the different kinds of emissions that can be observed when a sample is scanned by electron beam (Figure 79):[535]

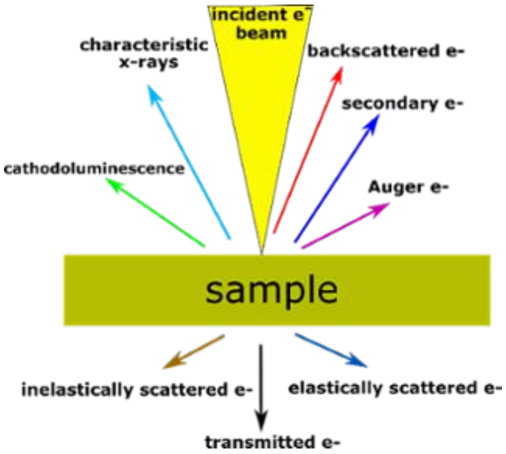


Figure 79. Signals produced from the Interaction between electron beam-sample[535]

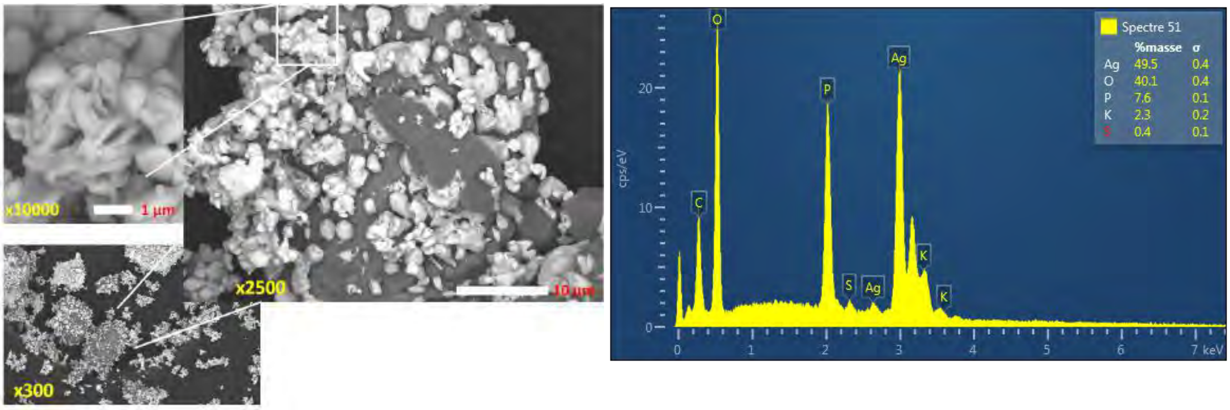
X-rays are also generated during this process, when an electron from an outer shell fills the core created by the departure of a core level electron. The analysis of the emitted X-ray (EDX) allow to identify the type of elements that exist in the analysed sample.[536]

The morphology of the solid phase recovered at different reaction time (0, 4, 13 and 30 minutes) was examined by scanning electron microscopy (SEM; Figure 80).

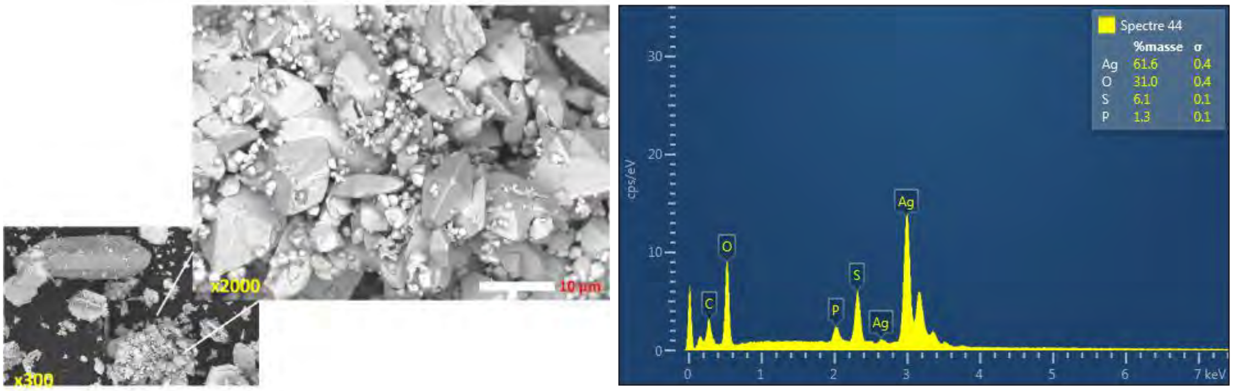
SEM micrograph

EDX elemental identification

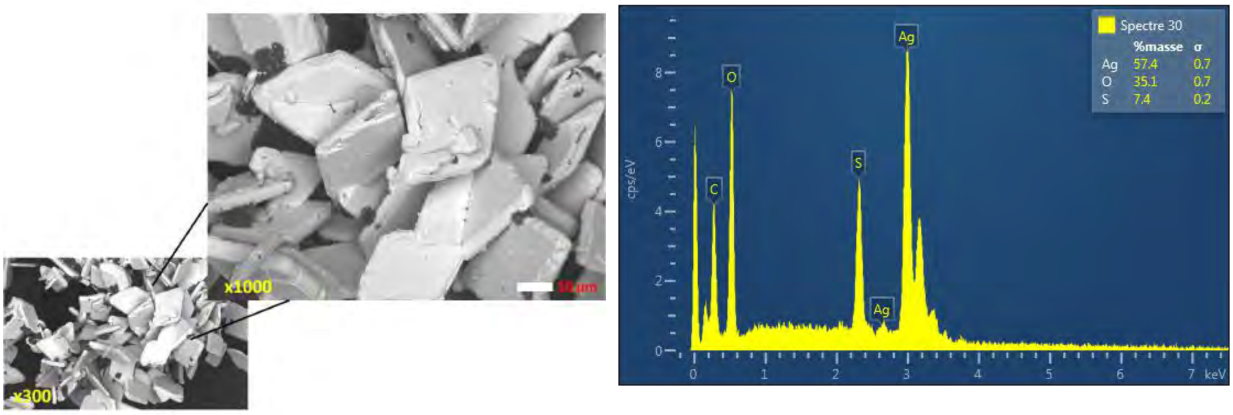
a) 0 minutes



b) 4 minutes



c) 13 minutes



d) 30 minutes

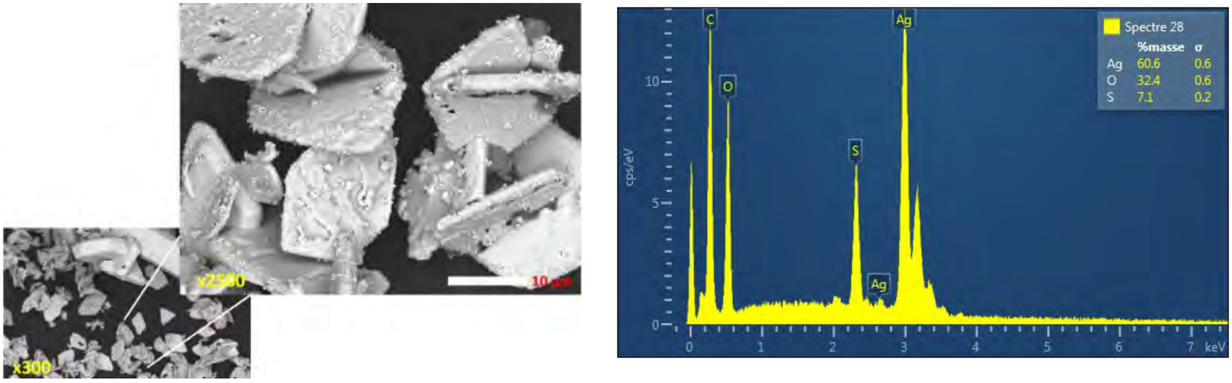


Figure 80. SEM images of the solid phase at different reaction times. Experimental conditions: $AgNO_3/K_2S_2O_8$ (1:1), KH_2PO_4/K_2HPO_4 (0.1:0.1 M), 100°C, 30 minutes

In the electron micrograph of the solids obtained at the very beginning of the reaction (0 minute), a bulk of small polycrystalline aggregates with a diameter between 1-2 µm was observed. They principally presented a spherical form, but dendrites-like particles were also observed (Figure 80a). The components identified by EDX analyses were Ag, O, P, K and S, which are in agreement with the presence of Ag_3PO_4, Ag_2SO_4, $K_2S_2O_8$, KH_2PO_4 and $Ag_4P_2O_7$ (see XRD and SSNMR analyses).

After 4 min of reaction, a reduction of particles size was observed. Two principally types of particles were distinguished: i) spherical crystallites with a size smaller than 2 µm, and ii) polyhedral crystallites with an average size of 10 µm (Figure 80b). EDX analyses showed the presence of Ag, O, P, and S, which underlined the disappearance in the solid phase of $K_2S_2O_8$ and KH_2PO_4.

Then, after 13 min of reaction, the size of the particles increased to a range between 10 µm and 30 µm. Additionally, their shape changed from polyhedral to platelets-like particles (Figure 80c). The elemental composition also changed, EDX analyses showed only the presence of Ag, O and S. The absence of P is thus in accordance with the consumption of Ag_3PO_4.

Finally, at the end of the reaction, the particles remained platelet-shaped but a slight reduction of their size was observed (around 15 µm). EDX analyses showed an elemental composition of Ag, O and S (Figure 80d).

The shape that silver crystallites acquire depends of different parameters, such as the medium pH or the presence of nitrates and oxygen. In the literature, the pH has shown to particularly influence the growth and shape of silver crystals.[537–541]
For example, small dendrites and spherical particles are characteristic forms of silver crystals from pH 5 to 6.[540,542] These are indeed the shape of the particles we observed at the very beginning of the reaction with an experimental pH of 5 (Figure 80a).
Moreover, the formation of crystals of different geometrical forms (triangular, octahedral, triangular prism, Figure 80b), that we noticed during the reaction, along with the decrease of reaction pH (from 5 to 3) is in agreement with the results reported by George *et al.* in 1981.[542]
Besides, the formation of silver crystals platelets at 13 and 30 minutes of reaction can be explained by a slow pH decrease (final reaction pH=2; Figure 80c and 80d), according to the observations made by the groups of George (1982)[540] and Lu.[539]

The pH adjustment of the medium (M1) with NaOH after the first cycle of reaction provoked the reduction of crystal sizes and a change in crystals shape, *i.e.* from platelets to spherical form (Figure 81). This crystal shapes can be due to a rapid nucleation as described in the work of Lu *et al.*, where they suggested that the atoms that are added to the pre-crystal do not have time to grow along in direction to a specific crystal facet, resulting thus in this isometric-spherical particles.[539] The elemental identification by EDX showed the presence of Ag, O and P, which in agreement of the conversion of Ag_2SO_4 into Ag_3PO_4 (Figure 81).

SEM micrograph EDX elemental identification

After neutralization of M1

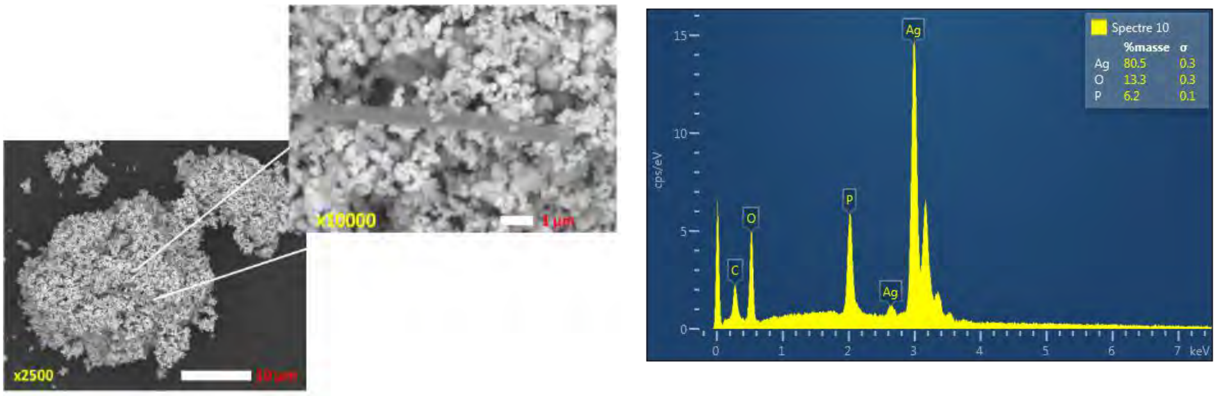


Figure 81. SEM images of the solid phase a) after neutralization to pH 5 with NaOH. Experimental conditions: $AgNO_3/K_2S_2O_8$ (1:1), KH_2PO_4/K_2HPO_4 (0.1:0.1 M), 100°C, 30 minutes

After the 2nd cycle of reaction, the spherical crystals changed to platelet shapes (Figure 82). The presence of Ag, O, S and Na (from the NaOH used in pH adjustment) was identified by EDX. These results were similar to those obtained after the 1st cycle of reaction (Figure 82 *vs* 80d) and underlined the formation of Ag_2SO_4 during this second cycle.

SEM micrograph EDX elemental identification

After neutralization of M1and 2nd cycle of reaction

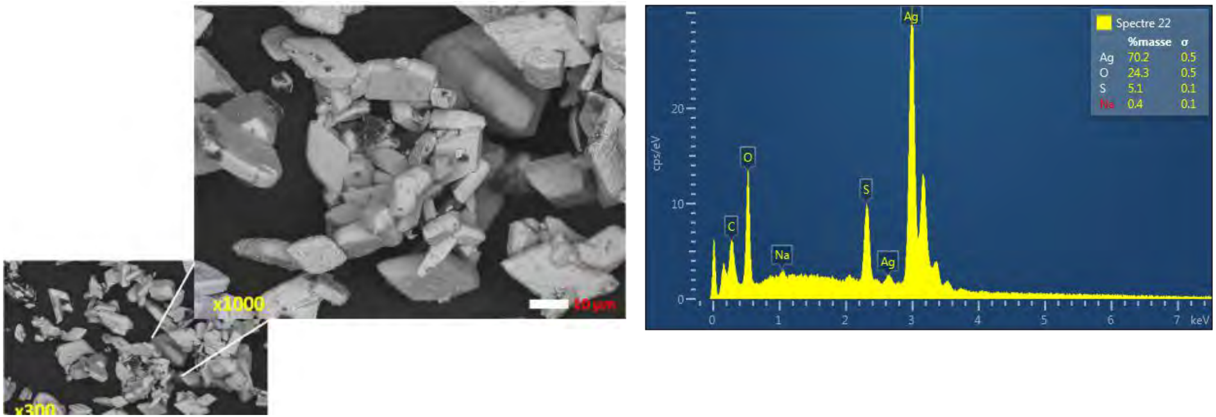


Figure 82. SEM images of the solid phase b) after 2nd cycle of reaction. Experimental conditions: $AgNO_3/K_2S_2O_8$ (1:1), KH_2PO_4/K_2HPO_4 (0.1:0.1 M), 100°C, 30 minutes

To sum up, the scanning electron microscopy (SEM) allowed us to observe the changes in the shape of crystals along the reaction. i.e. 0, 4, 13, and 30 minutes. The EDX analyses were in complete agreement with the results obtained by SSNMR, XRD, XPS and AES spectroscopies.

4.4.3 Conclusions of solid analyses by SSNMR, XRD, XPS and SEM spectroscopy

The study of the solid phase by the different spectroscopy techniques (SSNMR, XRD, XPS, SEM) were thus useful to expand our knowledge and to better understand the LA decarboxylation.
The color changes of the solid phase were a first insight of the evolution of the compounds involved in the reaction. These changes were successfully identified thought spectroscopic analyses:

- The disappearance of $AgNO_3$ as soon as the reaction starts was demonstrated by the XRD patterns obtained at 0 minute,
- The concomitant formation of Ag_3PO_4 was highlighted by the SSNMR, XRD, XPS, AES, EDX analyses and the evolution of the Ag/P *ratio*: the solid phase became yellow,
- The conversion of Ag_3PO_4 into Ag_2SO_4 was demonstrated by the SSNMR, XRD, XPS, AES, EDX analyses and the evolution of the Ag/P and Ag/S *ratio*: the solid phase whitened,
- The formation of Ag_2O-AgO in small amounts at the end of the reaction was finally proven by AES analyses: the solid phase darkened.

After 30 minutes of reaction, the adjustment of reaction pH to 5, the addition of 1 equivalent of $K_2S_2O_8$ allowed to obtain excellent LA conversion (99%) and MEK yield (87%). The spectroscopy analyses of the solid phase obtained after the adjustment of pH and after the second cycle allowed to better understand the evolution of the silver species:

- After the pH adjustment, the presence of Ag_3PO_4 and the disappearance of Ag_2SO_4 were highlighted by the SSNMR, XRD, AES, EDX analyses. The disappearance of Ag_2O and AgO was proven by AES: the solid phase cleared and became yellow again,
- The conversion of Ag_3PO_4 into Ag_2SO_4 was demonstrated by the SSNMR, XRD, AES, EDX analyses: the solid phase whitened,
- The formation of Ag_2O-AgO at the end of the second cycle was proven by AES analyses: the solid phase darkened again.

The evolution of the silver species thorough the reaction can be summarized by the following figure (Figure 83):

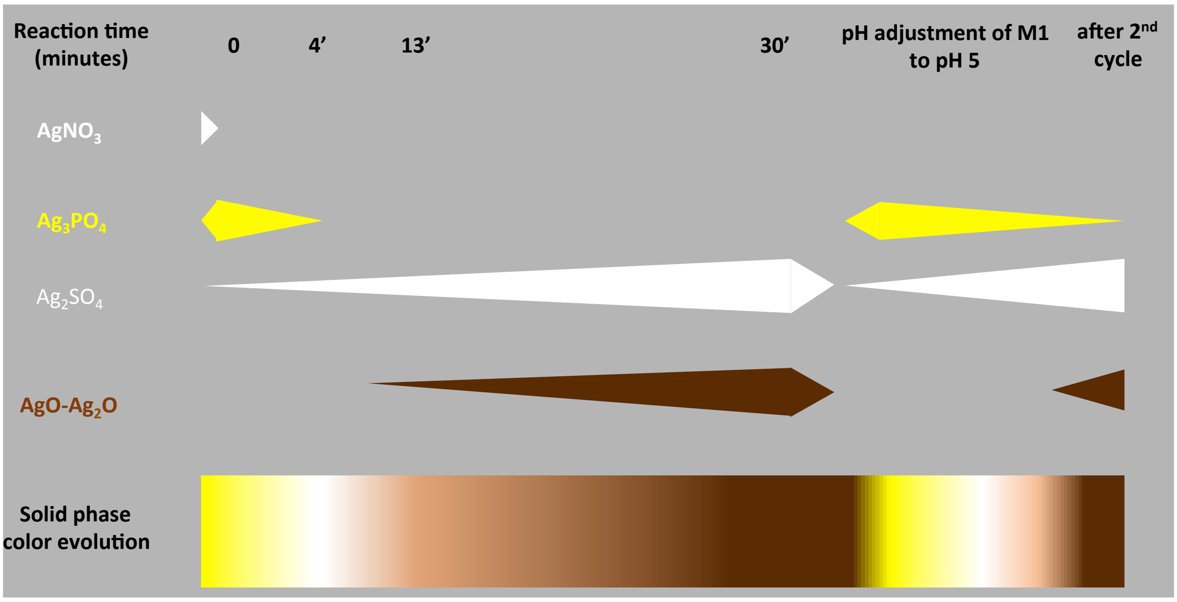


Figure 83. Graphical representation of the evolution of the species of the solid phase during the reaction, after pH adjustment of M1 and after the 2nd cycle of reaction.

4.5 Conclusions

Methyl ethyl ketone (MEK) is a solvent that is widely used in the paint and coating industry. It is nowadays produced from petrochemical feedstock, through methods that use homogeneous catalyst under harsh conditions. In order to offer a greener alternative, we proposed the synthesis of MEK *via* decarboxylation of bio-based levulinic acid using potassium persulfate ($K_2S_2O_8$) and silver nitrate ($AgNO_3$) as reactants.

Through a parametric study, we identified that the best conditions for the LA decarboxylation are 1 equivalent of both $K_2S_2O_8$ and $AgNO_3$, at 100°C, during 30 minutes in a phosphate solution (KH_2PO_4/K_2HPO_4; 0.1:0.1 M). A moderate LA conversion of 46.5% and a MEK yield of 32.5% were obtained using these conditions. Moreover, acetic acid was obtained as co-product in 14.4% yield. We have shown that it is produced through the subsequent oxidation of MEK,.

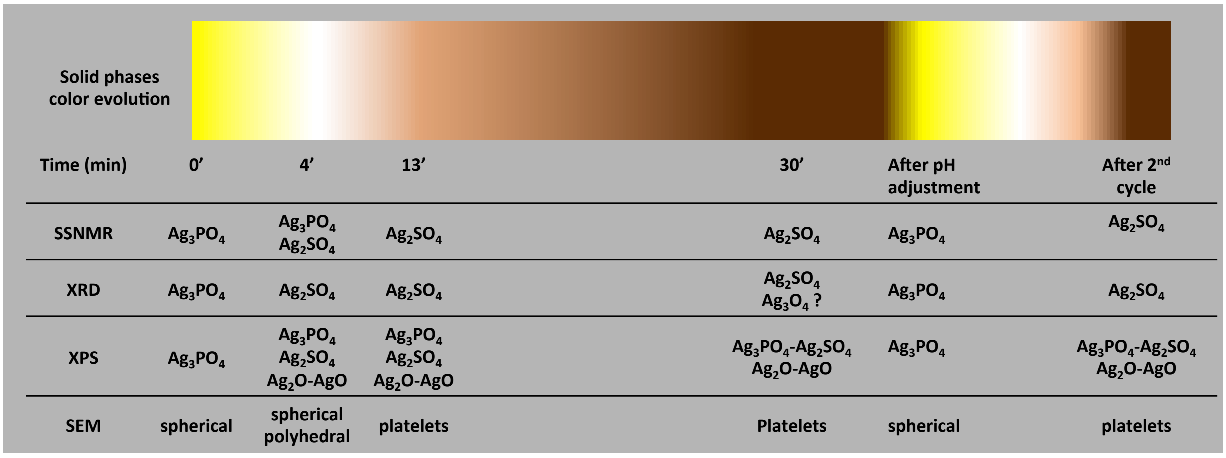
Similar yields in MEK can be obtained when other silver salts, such as Ag_2O and AgO, were tested. However, the yield in acetic acid was higher when these silver oxides were used, 17.8% and 22.9%, respectively.

The use of a radical trap (TEMPO) completely prevented the reaction: we thus proposed a radical decarboxylation mechanism. It relies on the decomposition of potassium persulfate ($K_2S_2O_8$) into sulfate radicals ($SO_4^{\bullet -}$) in the presence of $AgNO_3$. Sulfate radicals are then the directly responsible for decarboxylation of levulinic acid.

With the elucidation of this mechanism, we put forward a strategy to improve the conversion and the yield of the reaction. The addition of 1 more equivalent of $K_2S_2O_8$ and NaOH to adjust the reaction pH to 5 allowed to increase the LA conversion from 46.5% to 99% and the MEK yield from 32.4% to 88.6% after a 2nd cycle of reaction.

The implementation of this strategy allowed us to highlight the regeneration of the reaction medium, which implies that $AgNO_3$ can be reused in several cycles of reaction.

To better understand the reaction and explain the improvement in LA conversion and MEK yield, the solid phases obtained at different reaction time (0, 4, 13 and 30 min, after the pH adjustment and after the 2nd cycle of reaction) were characterized using different spectroscopy techniques (SSNMR, XRD, XPS, AES and SEM-EDX). It allowed us to elucidate the evolution of the silver species throughout the reaction: the assumptions that we made based on the color changes of the solids were validated for the reaction, the regeneration of the system and the second reaction cycle.
In the following figure, we summarized the silver species that were identified by the spectroscopic analyses at different reaction time: silver phosphate is formed right at the beginning of the reaction and then disappears as silver sulfate is formed. Auger electron spectroscopy (AES-XPS) also showed the formation of a mixture of silver oxide species (Ag_2O and AgO) after 4 minutes of reaction. The same behavior was observed for the second reaction cycle. The SEM images highlighted the changes in the morphology of the silver particles that are linked to the variation of the reaction pH.



Time (min)	0'	4'	13'	30'	After pH adjustment	After 2nd cycle
SSNMR	Ag_3PO_4	Ag_3PO_4 Ag_2SO_4	Ag_2SO_4	Ag_2SO_4	Ag_3PO_4	Ag_2SO_4
XRD	Ag_3PO_4	Ag_2SO_4	Ag_2SO_4	Ag_2SO_4 Ag_3O_4 ?	Ag_3PO_4	Ag_2SO_4
XPS	Ag_3PO_4	Ag_3PO_4 Ag_2SO_4 Ag_2O-AgO	Ag_3PO_4 Ag_2SO_4 Ag_2O-AgO	Ag_3PO_4-Ag_2SO_4 Ag_2O-AgO	Ag_3PO_4	Ag_3PO_4-Ag_2SO_4 Ag_2O-AgO
SEM	spherical	spherical polyhedral	platelets	Platelets	spherical	platelets

To our knowledge, this is the first report on the evolution of the species involved in the $AgNO_3/K_2S_2O_8$ system. The comprehension of the reaction mechanism allowed us to obtain high LA conversion (99 %) and an excellent yield in MEK of 88.6%.

This approach offers a greener alternative process to produce bio-based methyl ethyl ketone under milder conditions.

General conclusion

Nowadays, the interest in replacing petrochemical solvents with greener ones that are friendlier to the environment and human health has increased. In this context, researches have been focused on alternative solvents, including those derived from biomass. The European Union has launched several research projects to encourage the development of this type of solvent. Accordingly, the European project ECOBIOFOR was founded to synthesize some of the most used solvents in the paint and coating industry from bio-based synthons. In this project, the role of the *Laboratoire de Chimie Agro-industrielle* was to develop new green syntheses of ethyl acetate, butyl acetate and methyl ethyl ketone starting from bio-based building blocks.

FOR THE PRODUCTION OF ETHYL ACETATE AND BUTYL ACETATE:

We decided to study two different synthesis pathways: the first one started from acetic acid and the corresponding alcohol (ethanol for ethyl acetate and butanol for butyl acetate); the second one using acetic anhydride instead of acetic acid. In this work, we replaced the currently used homogeneous acid catalysts by ion exchange resins that are easy to remove from the reaction medium and can be recycled. Kinetic and thermodynamic studies were performed on the two reactions pathways (acetic acid/acetic anhydride) with four resins: Amberlyst 15, Amberlyst 16, Amberlyst 36 and Dowex 50WX8. The lowest activation energy (Ea) value was obtained with Dowex 50WX8, which was identified as the best-performing resin that could be reused at least in four runs without regeneration. For both acetates, the syntheses starting from acetic anhydride and the corresponding alcohol (in a 1:2 *ratio*) were faster than the syntheses starting from acetic acid (in a 1:1 *ratio*). Thus, higher conversions of alcohols (*ca*. 80%) and acetate yields (*ca*. 80%) were obtained using acetic anhydride.

However, the purification of the obtained acetates was difficult due to the presence of water-azeotropes. A new strategy was thus adopted here: in order to minimize the production of water, a 1:1 acetic anhydride:ethanol ratio was used to produce ethyl acetate and acetic acid. Ethyl acetate was easily separated from a mixture acetic acid/resin by distillation. This mixture was then involved in a second esterification reaction with butanol. This novel two-step process for the coproduction of ethyl and butyl acetates yielded both acetates at high purity (Figure 84):

- Ethyl acetate was synthesized in the first step of the coproduction process, starting from acetic anhydride and ethanol in a *ratio* 1:1. From this reaction, a mixture composed of 59 wt% ethyl acetate, 40.1 wt% acetic acid, 0.2 wt% ethanol and 0.7wt% water was produced. Water was remarkably reduced, allowing the purification of ethyl acetate by simple distillation. A final ethyl acetate purity of 92.1% was obtained with a yield of 87%.

- Butyl acetate was produced adding butanol to the remaining mixture acetic acid/resin from the first step. At the end of the reaction, a butyl acetate yield of 98% was obtained and the reaction mixture was composed of 97.1 wt% butyl acetate, 0.1 wt% acetic acid, 1.9 wt% butanol, 0.2 wt% ethyl acetate and 0.6 wt% water.

This coproduction process is very efficient since both acetates are obtained with high yield and purity. Besides, it avoids the use of several purification steps and reduces waste production.

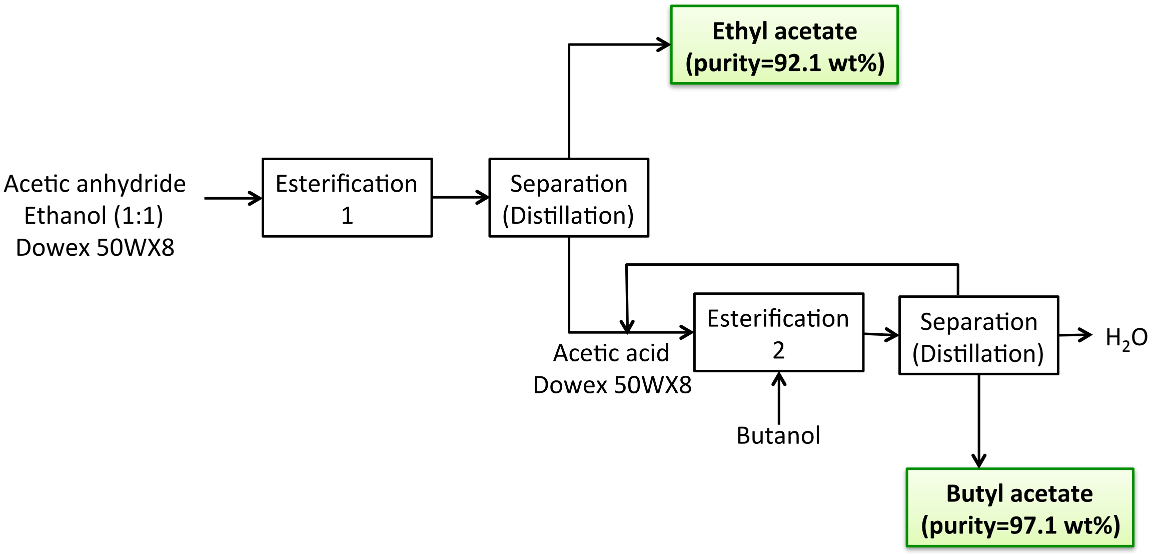


Figure 84. Coproduction process developed in this thesis work

The environmental benefits of the coproduction process were highlighted with green metrics calculation and life cycle assessment:

- Higher atom economy was obtained with the coproduction process (91.9 %) compared with the individual syntheses (72.4%).
- The environmental factor was better with the coproduction process (0.31 versus 0.68 for the individual syntheses) confirming the reduction of waste.
- Life cycle assessment evidenced that the coproduction process generates lower impacts on the environment, in all the categories, than the individual syntheses.

Furthermore, the influence of the environmental impact generated by the origin of the alcohols, bio-based or petrochemical was evaluated. Lower impacts on climate change were observed starting from bio-based ethanol or butanol, due to the storage of biogenic carbon.

The syntheses of ethyl and butyl acetates were studied at laboratory scale using a 2 liters reactor. To complete the study, ethyl acetate was prepared at a 20 liters scale.

The synthesized acetates were characterized and evaluated in formulations of nitrocellulose lacquers and polyurethane varnishes (after having easily removed the traces of water and acetic acid). The results showed that the synthesized solvents can perfectly replace their fossil equivalents in these coatings formulations.

FOR THE SYNTHESIS OF METHYL ETHYL KETONE (MEK):

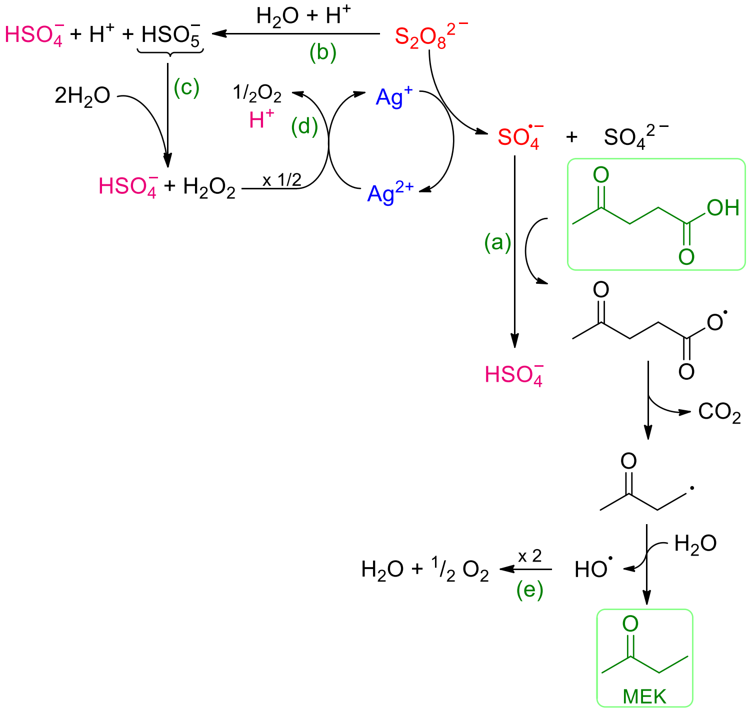
We decided to study the decarboxylation of levulinic acid (LA) using a system of silver species and potassium persulfate. Indeed, levulinic acid is an interesting bio-based synthon, considered among the 12 renewable platform molecules with the greatest potential for chemicals production, due to its versatile reactivity.

This work was focused on the understanding of the role of silver species and potassium persulfate ($K_2S_2O_8$) on LA decarboxylation and in the elucidation of the reaction mechanism in order to obtain high MEK yields. A phosphate solution KH_2PO_4/K_2HPO_4 (0.1:0.1 M) was selected as reaction medium.

Preliminary reactions were carried out using $AgNO_3$ and $K_2S_2O_8$ in equimolar *ratio*. We observed that the levulinic acid decarboxylation did not occur using only silver nitrate ($AgNO_3$), whereas MEK was produced in the sole presence of persulfate. This was possible, since persulfate can be activated with temperature, generating sulfate radicals ($SO_4^{\bullet-}$) that lead to the decarboxylation. However, low MEK yields were obtained.

The use of both potassium persulfate and silver nitrate (which catalyzed the formation of sulfate radicals) increased levulinic acid decarboxylation, yielding not only MEK (in 32.5% yield) but also acetic acid (in 14.4 % yield). Complementary studies showed that this by-product is produced through a subsequent oxidation of MEK. The same behaviour was observed when silver nitrate was replaced by other silver species such as AgCl, Ag_2O and AgO. In these cases, a slight increase of the acetic acid amount was found. These results led us to select $AgNO_3$ and $K_2S_2O_8$ for LA decarboxylation as higher MEK yields and lower acetic acid yields were obtained with these two reactants. Evaluation of the influence of reaction time and temperature and $AgNO_3/K_2S_2O_8$ *ratio* on MEK yield allowed us to establish the best results were obtained using a 1:1 $AgNO_3/K_2S_2O_8$ *ratio* at 100°C during 30 minutes.

Reactions carried out with radical scavengers showed that the reaction mechanism is a radical mechanism where free radical sulfates, $SO_4^{\bullet -}$, are directly responsible for LA decarboxylation (Scheme 28).



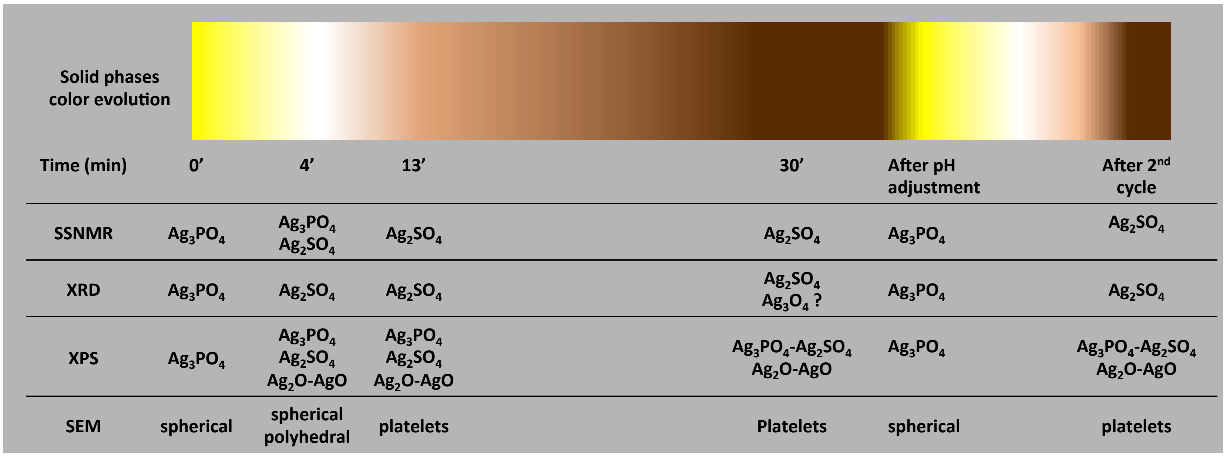
Scheme 28. Proposed mechanism

A pH decrease was observed during the reaction even in the presence of the KH_2PO_4/K_2HPO_4 solution. This decrease can be explained by the formation of HSO_4^- and H^+, *via* competitive reactions, preventing the formation of MEK in a good yield. We then showed that the addition of 1 more equivalent of $K_2S_2O_8$ and NaOH to adjust the reaction pH to 5 allowed to increase the LA conversion from 46.5% to 99% and the MEK yield from 32.4% to 88.6% after a 2nd cycle of reaction.

In order to gain more insight into reaction mechanism and to explain the observed color changes of reaction medium, the solid phases were analysed throughout the reaction, after the pH adjustment and after the 2nd cycle of reaction. Different spectroscopy techniques were used: solid-state nuclear magnetic resonance (SSNMR), X-ray diffraction (XRD), X-ray photoelectron spectroscopy (XPS) and scanning electron microscopy (SEM-EDX).

These analyses showed that the yellow coloration of the solid phase was due to the formation of Ag_3PO_4 from $AgNO_3$. Afterwards, a whitening of these solids was observed, which is due to the disappearance of Ag_3PO_4 and the formation of Ag_2SO_4. At the end of the reaction, the darkening of the solid phase until a dark-brown color was related to the formation of silver oxides Ag_2O-AgO.

The pH adjustment led to the formation of Ag_3PO_4, with the reappearance of the yellow color, which then reacts with $K_2S_2O_8$ leading to the production of MEK. The solution whitens again, as Ag_2SO_4 is formed and Ag_3PO_4 is consumed (Figure 85).



Solid phases color evolution						
Time (min)	0’	4’	13’	30’	After pH adjustment	After 2nd cycle
SSNMR	Ag_3PO_4	Ag_3PO_4 Ag_2SO_4	Ag_2SO_4	Ag_2SO_4	Ag_3PO_4	Ag_2SO_4
XRD	Ag_3PO_4	Ag_2SO_4	Ag_2SO_4	Ag_2SO_4 Ag_3O_4 ?	Ag_3PO_4	Ag_2SO_4
XPS	Ag_3PO_4	Ag_3PO_4 Ag_2SO_4 Ag_2O-AgO	Ag_3PO_4 Ag_2SO_4 Ag_2O-AgO	Ag_3PO_4-Ag_2SO_4 Ag_2O-AgO	Ag_3PO_4	Ag_3PO_4-Ag_2SO_4 Ag_2O-AgO
SEM	spherical	spherical polyhedral	platelets	Platelets	spherical	platelets

Figure 85. Color changes of solid phase at different reaction times and the compounds identified through different spectroscopy techniques

These results are of great importance, since they show that the reaction medium can be easily regenerated *via* pH adjustment and suggest that silver nitrate can be reused. To our knowledge, this is the first time that such excellent levulinic acid conversion and MEK yield are obtained. In addition, it is the first report that describes the evolution of the silver species during the reaction carried out with the $AgNO_3/K_2S_2O_8$ system in the presence of phosphates (KH_2PO_4/K_2HPO_4).

PERSPECTIVES:

As described, interesting results have emerged from this thesis work. However, some perspectives can be envisaged.

Regarding the syntheses of acetates:

- The optimization of the coproduction process on an industrial scale would allow comparing this innovative process with the industrial process currently used, through life cycle assessment (LCA).
- A technical-economic study of the optimized process would be useful to highlight the advantages of the coproduction process of the bio-based acetates compared to current industrial processes.

Regarding the synthesis of bio-based methyl ethyl ketone:

The reuse of silver nitrate in several reaction cycles must be verified. Thus, a continuous process for the production of MEK could be investigated. For this, there are some parameters that must be studied and defined:

- the time interval at which it is necessary to adjust the pH of the reaction medium, allowing the regeneration of silver species once the methyl ethyl ketone has been formed,
- the continuous separation of MEK from the reaction medium to avoid its oxidation in acetic acid.

References

(1) Guidance for Drugs in USA Food and Drugs Administration. Q3C: Tables and List Guidance for Industry https://www.fda.gov/downloads/drugs/guidances/ucm073395.pdf. (accessed Feb 13, 2018).

(2) Ethyl acetate - Registration Dossier - ECHA https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/15437/5/3/1 (accessed Apr 4, 2018).

(3) N-butyl acetate - Registration Dossier - ECHA https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/15948/5/3/1 (accessed Apr 4, 2018).

(4) Butanone - Registration Dossier - ECHA https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/15065/5/3/2 (accessed Apr 4, 2018).

(5) *Paint and surface coatings : Theory and Practice.*, Second Edition.; Lambourne, R., Strivens, T. A., Eds.; Woodhead Publishing Limited, 1999.

(6) Gooch, J. W. In *Lead-Based Paint Handbook*; Kluwer Academic Publishers: Boston, 2002; pp 13–35.

(7) Ball, P. *Bright earth : art and the invention of color*; The University of Chicago Press: Chicago, USA, 2003.

(8) Mannari, V.; Patel, C. J. *Understanding coatings raw materials*; Vincentz Network: Hanover, Germany, 2015.

(9) *El hilo continuo: La conservación de las tradiciones textiles de Oaxaca*; Klein, K., Ed.; Getty Trust Publications: Singapur, 1997.

(10) *La pintura mural prehispánica en México II. Area Maya*; Staines Cicero, L., Ed.; Universidad Nacional Autónoma de México, Instituto de Investigaciones Estéticas: Mexico, 2001.

(11) In *Actas del Seminario Internacional sobre Consolidación de Pinturas Murales* ; Fundación Sta María La Real, Centro de Estudios del Románico: Aguilar del Campoo, Palencia, 1998.

(12) Merrifield, M. P. *Medieval and Renaissance treatises on the arts of painting : original texts with English translations*; Dover Publications, 1999.

(13) Gettens, R. J.; Stout, G. L. *Painting Materials: A Short Encyclopedia*; Dover Publications, Inc.: New York, 2012.

(14) Outland, R. B. *Tapping the pines: The Naval Stores Industry in the American South*; Louisiana State University Press, 2004.

(15) 6 Advantages of Using Turpentine | DoItYourself.com https://www.doityourself.com/stry/6-advantages-of-using-turpentine (accessed Apr 9, 2018).

(16) *Performance of bio-based building materials*; Jones, D., Brischke, C., Eds.; Woodhead Publishing: Kidlington, UK, 2017.

(17) *Paints, coatings, and solvents*, 2 Edition.; Stoye, D., Freitag, W., Eds.; Wiley-VCH: Germany, 1998.

(18) Schweitzer, P. A. *Paint and coatings : applications and corrosion resistance*; CRC-Taylor & Francis group, 2006.

(19) Composition of paints http://www.substech.com/dokuwiki/doku.php?id=composition_of_paints (accessed Oct 18, 2017).

(20) Talbert, R. *Paint Technology Handbook*; Taylor & Francis Group, LLC: USA, 2008.

(21) Bentley, J.; Turner, G. P. A. *Introduction to paint chemistry and principles of paint technology*; Chapman and Hall: London, UK, 1998.

(22) *Paint and Coating Testing Manual: Fourthenth Edition of the Gardner-Sward Handbook*, 14 Sub edi.; Joseph V, K., Ed.; ASTM Intl.: Philadelphia, 1995.

(23) *Corrosion mechanisms in theory and practice.*, Third Edit.; Marcus, P., Ed.; CRC Press: Boca Raton, USA., 2012.

(24) Schweitzer, P. A. *Paint and coatings: Applications and Corrosion Resistance*; CRC Press Taylor & Francis: Boca Raton, USA, 2005.

(25) Weldon, D. G. *Failure analysis of paints and coatings*; Wiley: UK, 2009.

(26) *The chemistry and physics of coatings*, Second.; Marrion, A., Ed.; Royal Society of Chemistry: UK, 2004.

(27) Global Solvents: Opportunities for Greener Solvents. IHS Chemical https://www.ihs.com/products/chemical-special-reports-global-solvents.html (accessed Oct 16, 2017).

(28) Solvents Market worth 28.25 Billion USD by 2021 http://www.marketsandmarkets.com/PressReleases/solvent.asp (accessed Oct 13, 2017).

(29) ESIG Facts and figures. The European solvents industry in brief http://www.esig.org/category/publications/ (accessed Oct 16, 2017).

(30) Global Solvents Market. Industry Analysis, Size, Share, Growth, Trends and Forecast https://www.transparencymarketresearch.com/solvents-market.html (accessed Oct 17, 2017).

(31) European Coatings: Global demand for solvents to increase http://www.european-coatings.com/Markets-companies/Raw-materials-market/Global-demand-for-solvents-to-increase (accessed Oct 17, 2017).

(32) Bulian, F.; Graystone, J. *Wood coatings : theory and practice*; Elsevier Science, 2009.

(33) Pereira, C. S. M.; Silva, V. M. T. M.; Rodrigues, A. E. *Green Chem.* 2011, *13* (10), 2658.

(34) Brock, T.; Groteklaes, M.; Mischke, P. *European Coatings Handbook*; Zorll, U., Ed.; Vincentz Verlag: Germany, 2000.

(35) Solvents Tech note 2.2: Safe use of solvents http://www.duluxprotectivecoatings.com.au/technotespdf/2.2 Solvents.pdf (accessed Oct 17, 2017).

(36) Parsons, P. *Surface Coatings: Raw Materials and Their Usage*, Third Edit.; Springer Science+Bussiness Media, B.V, 1993.

(37) NPCS Board. *Manufacture of Paint, Varnish & Allied Products*; NIIR Project Consultancy Services: Delhi, India, 2013.

(38) Paints & Coatings Solvents Air Monitoring Applications. Sigma-Aldrich http://www.sigmaaldrich.com/technical-documents/articles/analytical/applications/paints-and-coatings-solvents-air-monitoring.html (accessed Oct 17, 2017).

(39) Goldschmidt, A.; Streitberger, H.-J. *BASF handbook on basics of coating technology*; Vincentz Network: Germany, 2003.

(40) Wicks Jr, Z. W.; Jones, F. N.; Pappas, S. P.; Wichs, D. A. *Organic coatings : Science and Technology*, Third Edit.; John Wiley & Sons, Inc.: USA, 2007.

(41) Kerton, F.; Marriott, R. *Alternative Solvents for Green Chemistry*; Green Chemistry Series; Royal Society of Chemistry: Cambridge, 2013.

(42) *Manual on Hydrocarbon Analysis*, Sixth edition.; Drews, A. W., Ed.; ASTM: Baltimore, USA, 1998.

(43) *Paint Testing Manual: Physical and Chemical Examination of Paints, Varnishes, Lacquers, and Colors*, Thirteenth edition.; Sward, G., Ed.; American Society for Testing and Materials: Philadelphia, USA, 1972.

(44) ISO 758:1976(en), Liquid chemical products for industrial use — Determination of density at 20 degrees C https://www.iso.org/obp/ui/#iso:std:iso:758:ed-1:v1:en (accessed Mar 5, 2018).

(45) European Chemicals Agency (ECHA). *Guidance on the application of the CLP criteria*; 2017.

(46) EUR-Lex: Acces to European Union Law http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex:32004L0042 (accessed Oct 19, 2017).

(47) Triolet, J.; Sallé, B. *Évaluation de la vitesse d'évaporation et de la concentration d'un composé organique volaltil dans l'atmosphère d'un local de travail*; 2009.

(48) Durkee, J. B. *Cleaning with solvents: Science and technology*; Elsevier Science: Oxford, UK, 2014.

(49) *Principles and methods of toxicology*, Fifth edition.; Hayes, A. W., Ed.; Informa Healthcare USA, Inc: New York, USA, 2008.

(50) Hansen, C. M. *Hansen Solubility Parameters: A User's Handbook.*, Second.; CRC Press, 2007.

(51) Hansen, C. M. The tree dimensional solubility parameter and solvent diffusion coefficient. Their importance in surfance coating formulations https://hansen-solubility.com/contents/HSP1967-OCR.pdf (accessed Oct 19, 2017).

(52) Burrell, H. *Interchem. Rev.* 1955, *14*, 3–19.

(53) Burrell, H. *Interchem. Rev.* 1955, *14*, 31–46.

(54) *Handbook for critical cleaning. Cleaning agents and systems*, Second.; Kanegsberg, B., Kanegsberg, E., Eds.; CRC Press: USA, 2011.

(55) The officiel site of Hansen Solubility Parameters and HSPiP software. Hansen Solubility Parameters. HSP for Beginners https://www.hansen-solubility.com/HSP-science/for-beginners.php (accessed Jan 16, 2018).

(56) *Blood compatible materials and devices : perspectives towards the 21st century*; Sharma, C. P., Szycher, M., Eds.; Technomic Publishing Company, Inc: United States, 1991.

(57) HSPiP: Hansen Solubility Parameters https://www.hansen-solubility.com/HSPiP/ (accessed Feb 5, 2018).

(58) Gharagheizi, F.; Torabi Angaji, M. *J. Macromol. Sci. Part B Phys.* 2006, *45* (2), 285–290.

(59) *Computational pharmaceutical solid state chemistry*; Abramov, Y. A., Ed.; John Wiley and Sons, Inc: New Jersey, USA, 2016.

(60) *Development and applications in solubility*; Letcher, T. M., Ed.; RSC Publishing: Cambridge, UK, 2007.

(61) *Handbook of Green Chemistry. Volumen 10: Tools for Green Chemistry*; Anastas, P. T., Ed.; Wiley-VCH: Weinheim, Germany, 2017.

(62) Moity, L.; Durand, M.; Benazzouz, A.; Pierlot, C.; Molinier, V.; Aubry, J.-M. *Green Chem.* 2012, *14* (4), 1132.

(63) Durand, M.; Molinier, V.; Kunz, W.; Aubry, J.-M. *Chem. - A Eur. J.* 2011, *17* (18), 5155–5164.

(64) Breil, C.; Meullemiestre, A.; Vian, M.; Chemat, F. *Molecules.* 2016, *21* (12), 196.

(65) Environmental Protection Agency (EPA). Code of Federal Regulations, 40: Chapter 1, subchapter C, Part 51, Subpart F, 51100 https://www.ecfr.gov/cgi-bin/text-idx?SID=053139573ff22a328e23bb0ed81b1b6c&mc=true&node=se40.2.51_1100&rgn=div8 (accessed Mar 21, 2018).

(66) GPO- U.S Government Publishing Oficce. Code of federal regulations, 40: Chapter 1, subchapter C, Part 51, Subpart F, section 51.100 https://www.gpo.gov/fdsys/granule/CFR-2012-title40-vol2/CFR-2012-title40-vol2-sec51-100 (accessed Apr 11, 2018).

(67) Environmental Protection Agency (EPA). Volatile Organic Compounds' Impact on Indoor Air Quality https://www.epa.gov/indoor-air-quality-iaq/volatile-organic-compounds-impact-indoor-air-quality (accessed Oct 18, 2017).

(68) Koppmann, R. *Volatile organic compounds in the atmosphere*; Blackwell Pub, 2007.

(69) Sanchez, M.; Karnae, S.; John, K. *Int. J. Environ. Res. Public Health.* 2008, *5* (3), 130–138.

(70) Wang, W. *Volatile organic compounds in the environment*; ASTM: Fredericksburg, VA., 1996.

(71) Bonnard, N.; Brondeau, M. T.; Jargot, D.; Nikolova-Pavageau, N.; Pilliere, F.; Scheneider, O. Base de données FICHES TOXICOLOGIQUES : Acétate d'éthyle http://webcache.googleusercontent.com/search?q=cache:KL44AW2oPqoJ:www.inrs.fr/dms/ficheTox/FicheFicheTox/FICHETOX_18-4/FicheTox_18.pdf+&cd=10&hl=es&ct=clnk&gl=fr&client=firefox-b-ab (accessed Apr 20, 2018).

(72) METHYL ETHYL KETONE-ANACHEMIA MSDS https://crn2.3it.usherbrooke.ca/guide_sb/produits/solvants/methylethylcetone.pdf. (accessed Apr 10, 2018).

(73) Lethal Dose Table http://whs.rocklinusd.org/documents/Science/Lethal_Dose_Table.pdf. (accessed Apr 10, 2018).

(74) Canadian Centre for Occupational Health and Safety. What is a LD50 and LC50? https://www.ccohs.ca/oshanswers/chemicals/ld50.html (accessed Apr 10, 2018).

(75) *Pesticide profiles: toxicity, environmental impact, and fate*; Kamrin, M. A., Ed.; CRC/Lewis Publishers: Boca Raton, USA, 1997.

(76) Reduction of VOC Emissions in the Paint and Coatings Industry http://www2.diw.go.th/PIC/download/Guidelines/APM10-VOC-reduction-paint-industry.pdf. (accessed Oct 19, 2017).

(77) Guidance on VOC Substitution and Reduction for Activities Covered by the VOC Solvents Emissions Directive (Directive 1999/13/EC) http://www.subsport.eu/images/stories/pdf_archive/legislation/21_guide_paint_production.pdf. (accessed Nov 6, 2017).

(78) Ramsden, E. N. *Chemistry of the environment*; Stanley Thornes Ltd.: Cheltenham, UK., 1996.

(79) Capello, C.; Fischer, U.; Hungerbühler, K. *Green Chem.* 2007, *9* (9), 927.

(80) *Biodegradability Prediction*; Peijnenburg, W. J. G. M., Damborský, J., Eds.; Springer Science-Business Media Dordrecht, 1996.

(81) European Centre for ecotoxicology and toxicology of chemicals (ECETOC). Definition(s) according to OECD-Ecetoc http://www.ecetoc.org/report/measured-partitioning-property-data/biodegradation/definitions-according-to-oecd/ (accessed Apr 11, 2018).

(82) Arnot, J. A.; Gobas, F. A. *Environ. Rev.* 2006, *14* (4), 257–297.

(83) Connell, D. W.; Miller, G. J. *Chemistry and ecotoxicology of pollution*; Wiley-Interscience Publication: New York, USA, 1984.

(84) *Ecotoxicology modeling*; Devillers, J., Ed.; Springer: New York, USA, 2009.

(85) Novotny, V. *Water quality: Diffuse pollution and watershed management*, Second Edi.; John Wiley & Sons, Inc: New Jersey, USA, 2003.

(86) European Chemicals Agency (ECHA). Information sur les produits chimiques https://echa.europa.eu/fr/information-on-chemicals (accessed Apr 11, 2018).

(87) ABB List of Prohibited and Restricted Substances, ver. 1.3 http://new.abb.com/docs/librariesprovider27/lieferantenportal/abb-list-of-prohibited-and-restricted-substances-v1-3.pdf. (accessed Apr 11, 2018).

(88) PCI: A Review of Compulsory Coatings Standards in China https://www.pcimag.com/articles/96652-a-review-of-compulsory-coatings-standards-in-china (accessed Nov 28, 2017).

(89) PaintSquare News: China Slaps VOC Tax on Coatings http://www.paintsquare.com/news/?fuseaction=view&id=12741 (accessed Nov 28, 2017).

(90) Technology for Environmentally Friendly Paints. Chemical Engineering http://www.chemengonline.com/painting-it-green/?printmode=1 (accessed Oct 20, 2017).

(91) Facts about the Paint and coatings industry http://www.paint.org/documents/2015/09/env_footprint.pdf. (accessed Oct 19, 2017).

(92) European Chemicals Agency (ECHA). Comprendre REACH https://echa.europa.eu/fr/regulations/reach/understanding-reach (accessed Mar 16, 2018).

(93) EUR-Lex. Thematic Strategy on Air Pollution http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=LEGISSUM:l28159 (accessed Nov 17, 2017).

(94) EUR-Lex Acces to European Union law. Directive 2010/75/UE https://eur-lex.europa.eu/legal-content/FR/ALL/?uri=CELEX%3A32010L0075 (accessed Apr 11, 2018).

(95) Sparks, T.; Chase, G.; Institution of Chemical Engineers (Great Britain). *Filters and filtration handbook.*, Sixth.; Elsevier: UK.

(96) M/491 Mandate Addressed to CEN, CENELEC and ETSI for the Development of European Standards and Technical Specifications and/or Technical Reports for Bio-Surfactants and Bio-Solvents in Relation to Bio-Based Product Aspects http://ec.europa.eu/growth/tools-

databases/mandates/index.cfm?fuseaction=search.detail&id=476# (accessed Oct 13, 2017).

(97) European Commission. CORDIS. Projects and Results: REnewable SOLVEnts with high performance in application and improved toxicity profile http://cordis.europa.eu/project/rcn/210285_en.html (accessed Oct 25, 2017).

(98) European Commission. CORDIS. Ecopaint BIO-based FORmulations http://cordis.europa.eu/project/rcn/188526_en.html (accessed Oct 25, 2017).

(99) Comisión Europea. CORDIS. Demonstration of solvent and resin production from lignocellulosic biomass via the platform chemical levulinic acid http://cordis.europa.eu/project/rcn/205450_es.html (accessed Oct 25, 2017).

(100) Byrne, F.; Jin, S.; Paggiola, G.; Petchey, T.; Clark, J. H.; Farmer, T. J.; Hunt, A. J.; McElroy, R. C.; Sherwood, J. *Sustain. Chem. Process.* 2016, *4* (7), 1–24.

(101) *Alternative solvents for natural products extraction*; Chémat, F., Vian, M. A., Eds.; Springer-Verlag Berlin Heidelberg, 2014.

(102) 12 Principles of Green Chemistry https://www.acs.org/content/acs/en/greenchemistry/what-is-green-chemistry/principles/12-principles-of-green-chemistry.html (accessed Oct 25, 2017).

(103) Gu, Y.; Jérôme, F. *Chem. Soc. Rev.* 2013, *42* (24), 9550.

(104) Welton, T. *Proceedings. Math. Phys. Eng. Sci.* 2015, *471* (2183), 20150502.

(105) Roy Choudhury, A. K. *Text. Prog.* 2013, *45* (1), 3–143.

(106) Sheldon, R. A. *Green Chem.* 2005, *7* (5), 267.

(107) Wai, C. M.; Hunt, F.; Ji, M.; Chen, X. *J. Chem. Educ.* 1998, *75* (12).

(108) Chemical Engineering. Supercritical CO2: A Green Solvent http://www.chemengonline.com/supercritical-co2-a-green-solvent/?printmode=1 (accessed Oct 27, 2017).

(109) Kerton, F.; Marriott, R. In *Alternative Solvents for Green Chemistry*; Royal Society of Chemistry, 2013; pp 115–148.

(110) Oakes, R. S.; Clifford, A. A.; Rayner, C. M. *J. Chem. Soc. Perkin Trans. 1* . 2001, *0* (9), 917–941.

(111) *Green solvents II. Properties and Applications of Ionic Liquids*; Mohammad, A., Inamuddin, Eds.; Springer, 2012.

(112) Kerton, F.; Marriott, R. In *Alternative Solvents for Green Chemistry*; Royal Society of Chemistry, 2013; pp 175–209.

(113) Mallakpour, S.; Dinari, M. In *Green Solvents II*; Springer Netherlands: Dordrecht, 2012; pp 1–32.

(114) Gathergood, N.; Garcia, M. T.; Scammells, P. J. *Green Chem.* 2004, *6* (3), 166.

(115) Shamsuri, A. A.; Abdullah, D. K. *Makara J. Sci.* 2010, *14* (2), 101–106.

(116) Kerton, F.; Marriott, R. In *Alternative Solvents for Green Chemistry*; Royal Society of Chemistry, 2013; pp 242–261.

(117) Heldebrant, D. J.; Witt, H. N.; Walsh, S. M.; Ellis, T.; Rauscher, J.; Jessop, P. G. *Green Chem.* 2006, *8* (9), 807.

(118) Chen, J.; Spear, S. K.; Huddleston, J. G.; Rogers, R. D. *Green Chem.* 2005, *7* (2), 64.

(119) Zhang, W.; Cai, C. *Chem. Commun.* 2008, *129* (44), 5686.

(120) Horváth, I. T.; Rábai, J. *Science.* 1994, *266* (5182).

(121) Zhang, W. *Green Chem.* 2009, *11* (7), 911.

(122) Kerton, F.; Marriott, R. In *Alternative Solvents for Green Chemistry*; Royal Society of Chemistry, 2013; pp 210–241.

(123) Bio-based products - European Commission http://ec.europa.eu/growth/sectors/biotechnology/bio-based-products_es (accessed Oct 16, 2017).

(124) Mandate M/429 Mandate Addressed to CEN, CENELEC and ETSI for the Elaboration of a Standardisation Programme for Bio-Based Products http://ec.europa.eu/growth/tools-databases/mandates/index.cfm?fuseaction=search.detail&id=407# (accessed Oct 16, 2017).

(125) Global Bio-based Chemical Market, Forecast 2017-2025 https://www.inkwoodresearch.com/reports/global-bio-based-chemicals-market-2017-2025/ (accessed Oct 16, 2017).

(126) Bright Future for the Bio-Based Chemical Industry - Acme-Hardesty http://www.acme-hardesty.com/sustainability/bio-based-chemical-industry/ (accessed Oct 16, 2017).

(127) Green & Bio-based Solvents Market - Global Industry Analysis, Size, Share, Growth, Trends, Forecast 2015 – 2023 https://www.transparencymarketresearch.com/green-biobased-solvents-market.html (accessed Oct 13, 2017).

(128) Global Bio-Solvents Market worth USD 9.43 Billion in 2022 https://www.zionmarketresearch.com/news/bio-solvents-market (accessed Oct 13, 2017).

(129) D2.3 - Report on the "Assessment of the Bio-based Products Market Potential for Innovation" https://www.google.fr/url?sa=t&rct=j&q=&esrc=s&source=web&cd=6&ved=0ahUKEwiwuqb6kfXWAhVkGsAKHYYKCoUQFghUMAU&url=http%3A%2F%2Fwww.biochem-project.eu%2Fdownload%2Ftoolbox%2Finnovation%2F06%2FBio-based%2520product%2520market%2520potential.pdf&usg=AOvVaw2Nfy0 (accessed Oct 16, 2017).

(130) Jessop, P. G.; Brown, H.; Peterson, T.; White, J.; Hodgson, A.; Jessop, P. G.; Jessop, P. G.; Pollet, P.; Eckert, C. A.; Liotta, C. L.; Jessop, P. G.; Zaksh, A.; Zhang, T. Y. *Green Chem.* 2011, *13* (6), 1391.

(131) Bandres, M.; De Caro, P.; Thiebaud-Roux, S.; Borredon, M. E. *Comptes Rendus Chim.* 2011, *14*, 636–646.

(132) Ibanez, J. G.; Hernandez-Esparza, M.; Doria-Serrano, C.; Fregoso-Infante, A.; Singh, M. M. *Environmental Chemistry: Fundamentals*; Springer Science & Business Media, 2010.

(133) Clark, J. H.; Farmer, T. J.; Hunt, A. J.; Sherwood, J. *Int. J. Mol. Sci.* 2015, *16* (8), 17101–17159.

(134) Corma, A.; Iborra, S.; Velty, A. *Chem. Rev.* 2007, *107* (6), 2411–2502.

(135) Prat, D.; Pardigon, O.; Flemming, H.-W.; Letestu, S.; Ducandas, V.; Isnard, P.; Guntrum, E.; Senac, T.; Ruisseau, S.; Cruciani, P.; Hosek, P. *Org. Process Res. Dev.* 2013, *17* (12), 1517–1525.

(136) Prat, D.; Hayler, J.; Wells, A. *Green Chem.* 2014, *16*, 4546–4550.

(137) European Chemicals Agency. Tetrahydrofuran - Substance Information - ECHA https://echa.europa.eu/substance-information/-/substanceinfo/100.003.389 (accessed Jul 3, 2018).

(138) Standard EN 16766:2017 Bio-based solvents-Requirements and test methods

(139) Vennestrøm, P. N. R.; Osmundsen, C. M.; Christensen, C. H.; Taarning, E. *Angew. Chemie Int. Ed.* 2011, *50* (45), 10502–10509.

(140) Huber, G. W.; Corma, A. *Angew. Chemie Int. Ed.* 2007, *46* (38), 7184–7201.

(141) Soh, L.; Eckelman, M. J. *ACS Sustain. Chem. Eng.* 2016, *4* (11), 5821–5837.

(142) Farrán, A.; Cai, C.; Sandoval, M.; Xu, Y.; Liu, J.; Hernáiz, M. J.; Linhardt, R. J. *Chem. Rev.* 2015, *115* (14), 6811–6853.

(143) Scott, E.; Peter, F.; Sanders, J. *Appl. Microbiol. Biotechnol.* 2007, *75* (4), 751–762.

(144) Lammens, T. M.; Franssen, M. C. R.; Scott, E. L.; Sanders, J. P. M. *Green Chem.* 2010, *12* (8), 1430.

(145) De Schouwer, F.; Claes, L.; Claes, N.; Bals, S.; Degrève, J.; De Vos, D. E. *Green Chem.* 2015, *17* (4), 2263–2270.

(146) Anwar, Z.; Gulfraz, M.; Irshad, M. *J. Radiat. Res. Appl. Sci.* 2014, *7* (2), 163–173.

(147) Ali Kamel H., A. J. Effect of Intermediate Washing on Ozonolysis Delignification and Enzymatic Hydrolysis of Wheat Straw, Ryerson University, 2012.

(148) Kumar, P.; Kumar, P.; Barrett, D. M.; Barrett, D. M.; Delwiche, M. J.; Delwiche, M. J.; Stroeve, P.; Stroeve, P. *Ind. Eng. Chem. Analytical Ed.* 2009, 3713–3729.

(149) Chukwuemeka Ezeji, T.; Qureshi, N.; Blascher, H. P. *Curr. Opin. Biotechnol.* 2007, *18* (3), 220–227.

(150) Pace, V.; Hoyos, P.; Castoldi, L.; Domínguez de María, P.; Alcántara, A. R. *ChemSusChem* 2012, *5* (8), 1369–1379.

(151) *Bio-based solvents*; Jerome, F., Luque, R., Eds.; John Wiley & Sons Ltd.: Oxford, UK, 2017.

(152) Maschio, G.; Lucchesi, A.; Stoppato, G. *Bioresour. Technol.* 1994, *48* (2), 119–126.

(153) Abad, A.; Concepción, P.; Corma, A.; García, H. *Angew. Chemie Int. Ed.* 2005, *44* (26), 4066–4069.

(154) Kerton, F.; Marriott, R. In *Alternative Solvents for Green Chemistry*; 2013; pp 149–174.

(155) Benninga, H. (Harm). *A history of lactic acid making : a chapter in the history of biotechnology*; Kluwer Academic Publishers, 1990.

(156) Gao, C.; Ma, C.; Xu, P. *Biotechnol. Adv.* 2011, *29* (6), 930–939.

(157) Yang, J.; Tan, J.-N.; Gu, Y. *Green Chem.* 2012, *14* (12), 3304.

(158) *The application of green solvents in separation processes*, First Edit.; Pena-Pereira, F., Tobiszewski, M., Eds.; Elsevier Inc., 2017.

(159) Yilmaztekin, M.; Erten, H.; Cabaroglu, T. *Food Chem.* 2009, *112* (2), 290–294.

(160) Patil, A.; Koolwal, S. M.; Butala, H. D. *Int. Sugar J.* 2002, *104* (1238), 51–58.

(161) Mayer, F. D.; Feris, L. A.; Marcilio, N. R.; Staudt, P. B.; Hoffmann, R.; Baldo, V.; Mayer, F. D.; Feris, L. A.; Marcilio, N. R.; Staudt, P. B.; Hoffmann, R.; Baldo, V. *Brazilian J. Chem. Eng.* 2015, *32* (2), 585–593.

(162) Alonso, D. M.; Wettstein, S. G.; Dumesic, J. A. *Green Chem.* 2013, *15* (3), 584.

(163) Horváth, I. T. *Green Chem.* 2008, *10* (10), 1024.

(164) Gürbüz, E. I.; Gallo, J. M. R.; Alonso, D. M.; Wettstein, S. G.; Lim, W. Y.; Dumesic, J. A. *Angew. Chemie Int. Ed.* 2013, *52* (4), 1270–1274.

(165) Duan, Z.-Q.; Hu, F. *Green Chem.* 2012, *14* (6), 1581.

(166) Tundo, P.; Aricò, F.; Gauthier, G.; Rossi, L.; Rosamilia, A. E.; Bevinakatti, H. S.; Sievert, R. L.; Newman, C. P. *ChemSusChem* 2010, *3* (5), 566–570.

(167) Chaloupka, J. C.; Huddle, D. C.; Alderman, J.; Fink, S.; Hammond, R.; Vinters, H. V; Rüfenacht, D. A.; Doelker, E.; Felix, R. *AJNR. Am. J. Neuroradiol.* 1999, *20* (3), 401–410.

(168) Chang, J.; Fu, Y.; Luo, Z. *Biomass and Bioenergy.* 2012, *39*, 67–72.

(169) Wang, T.; Li, Y.; Ma, L.; Wu, C. *Front. Energy Power Eng. China.* 2010, *5* (3), 330–339.

(170) Li, P.; Makino, H. In *Alternative Solvents for Natural Products Extraction*; Springer, Berlin, Heidelberg, 2014; pp 91–106.

(171) The European Food Safety Autority. The *EFSA Journal.* 2009, *984*, 1–13.

(172) Kanda, H.; Li, P.; Yoshimura, T.; Okada, S. *Fuel* 2013, *105*, 535–539.

(173) Catchpole, O. J.; Grey, J. B.; Perry, N. B.; Burgess, E. J.; Redmond, W. A.; Porter, N. G. *J. Agric. Food Chem.* 2003, *51*, 4853–4860.

(174) Kanda, H.; Li, P.; Makino, H. *Food Bioprod. Process.* 2013, *91* (4), 376–380.

(175) Goto, M.; Kanda, H.; Wahyudiono; Machmudah, S. *J. Supercrit. Fluids.* 2015, *96*, 245–251.

(176) Karak, N. *Vegetable oil-based polymers: properties, processing and applications*; Woodhead Publishing Limited: Cambridge, UK, 2012.

(177) *Food composition and analysis: methods and strategies*; Haghi, A. K., Carvajal-Millan, E., Eds.; Apple Academic Press, Inc: Ontario, Canada, 2014.

(178) Vaskova, H.; Buckova, M. *Procedia Eng.* 2015, *100*, 630–635.

(179) Medina Gonzalez, Y.; de Caro, P.; Thiebaud-Roux, S.; Lacaze-Dufaure, C. *J. Solution Chem.* 2007, *36* (4), 437–446.

(180) *Sustainable polymers from biomass*; Tang, C., Ryu, C. Y., Eds.; Wiley-VCH Verlag GmbH & Co.: Germany, 2017.

(181) De Caro, P.; Thiebaud-Roux, S. *Tech. l'ingénieur* 2015, *CHV 4020*, 1–14.

(182) Liu, C.; Si, C.; Wang, G.; Jia, H.; Ma, L. *Ind. Crops Prod.* 2018, *111*, 201–211.

(183) Wolfson, A.; Dlugy, C.; Shotland, Y. *Environ. Chem. Lett.* 2007, *5* (2), 67–71.

(184) Gu, Y.; Jérôme, F. *Green Chem.* 2010, *12* (7), 1127.

(185) Clark, J. H.; Hunt, A. J.; Topi, C.; Paggiola, G.; Sherwood, J. *Sustainable Solvents: Perspectives from Research, Business and International Policy*, Green Chem.; The Royal Society of Chemistry: United Kingdom, 2017.

(186) García, J. I.; García-Marín, H.; Pires, E. *Green Chem.* 2014, *16* (3), 1007–1033.

(187) Ou, G.; He, B.; Li, X.; Lei, J. *Sci. World J.* 2012, *2012*, 1–6.

(188) *Introduction to chemicals from biomass*, Second edition.; Clark, J., Deswarte, F., Eds.; John Wiley & Sons, Ltd: United Kingdom, 2015.

(189) Yara-Varón, E.; Selka, A.; Fabiano-Tixier, A. S.; Balcells, M.; Canela-Garayoa, R.; Bily, A.; Touaibia, M.; Chemat, F. *Green Chem.* 2016, *18* (24), 6596–6608.

(190) Chemat, S.; Tomao, V.; Chemat, F. In *Green Solvents I*; Springer Netherlands: Dordrecht, 2012; pp 175–186.

(191) Sell, C. S. *A fragrant introduction to terpenoid chemistry*; Royal Society of Chemistry: Cambridge, UK, 2003.

(192) Kim, B.; Lee, Y.-H.; Ryu, J.-H.; Suh, K.-D. *Colloids Surfaces A Physicochem. Eng. Asp.* 2006, *273* (1–3), 161–164.

(193) Negishi, N.; Takeuchi, K. *Res. Chem. Intermed.* 2003, *29* (7–9), 861–879.

(194) GmbH. Import-Export: Terpineol/Pine Oil http://www.weissmeer.de/en/products/terpineol-pine-oil.php?lang=EN (accessed Apr 16, 2018).

(195) *Monomers, polymers and composites from renewable resources*, First.; Belgacem, M. N., Gandini, A., Eds.; Elsevier, 2008.

(196) Calvo-Flores, F. G.; Dobado Jiménez, J. A.; Garcia, J. I.; Martín-Martínez, F. J. *Lignin and lignans as renewable raw materials: chemistry, technology and applications*, First.; John Wiley & Sons Ltd.: United Kingdom, 2015.

(197) Wool, R. P.; Sun, X. S. *Bio-based polymers and composites*, First.; Elsevier Academic Press, 2005.

(198) Wikimedia Commons: Lignin https://commons.wikimedia.org/wiki/File:Lignin.png (accessed Nov 3, 2017).

(199) Azadi, P.; Carrasquillo-Flores, R.; Pagán-Torres, Y. J.; Gürbüz, E. I.; Farnood, R.; Dumesic, J. A. *Green Chem.* 2012, *14* (6), 1573–1576.

(200) Alfonsi, K.; Colberg, J.; Dunn, P. J.; Fevig, T.; Jennings, S.; Johnson, T. A.; Kleine, H. P.; Knight, C.; Nagy, M. A.; Perry, D. A.; Stefaniak, M. *Green Chem.* 2008, *10* (1), 31–36.

(201) Henderson, R. K.; Jiménez-González, C.; Constable, D. J. C.; Alston, S. R.; Inglis, G. G. A.; Fisher, G.; Sherwood, J.; Binks, S. P.; Curzons, A. D. *Green Chem.* 2011, *13* (4), 854.

(202) Jiménez-González, C.; Curzons, A. D.; Constable, D. J. C.; Cunningham, V. L. *Clean Technol. Environ. Policy*. 2004, *7* (1), 42–50.

(203) Hargreaves, C. R.; American Institute of Chemical Engineers. In *Collaboratin to deliver a solvent selection guide for the pharmaceutical industry*; AlChE: Philadelphia, Pa, 2008; p 12.

(204) Goldschmidt, G. *Am. Ind. Hyg. Assoc. J.* 1993, *54* (1), 36–43.

(205) Bégin, D.; Gérin, M. *Substitution des solvants: études des cas d'implantation*; 2001.

(206) Bergez-Lacoste, M.; Thiebaud-Roux, S.; De Caro, P.; Fabre, J.-F.; Gerbaud, V.; Mouloungui, Z. *Biofuels, Bioprod. Biorefining.* 2014, *8* (3), 438–451.

(207) Bergez-Lacoste, M. Conception de biosolvants à partir de la molécule plateforme furfural, en laboratoires virtuel et réel, Université de Toulouse, 2013.

(208) Heintz, J.; Belaud, J.-P.; Pandya, N.; Teles Dos Santos, M.; Gerbaud, V. *Comput. Chem. Eng.* 2014, *71*, 362–376.

(209) Heintz, J.; Touche, I.; Teles dos Santos, M.; Gerbaud, V. *Comput. Aided Chem. Eng.* 2012, *30*, 702–706.

(210) SEKAB http://www.sekab.com/chemistry/ (accessed Oct 26, 2017).

(211) GreenBiologics. GreenBiologics. Renewable Derivatives http://www.greenbiologics.com/derivatives.php (accessed Oct 26, 2017).

(212) Ouellette, R. J.; Rawn, J. D. *Organic chemistry study guide: Key Concepts, Problems, and Solutions*; Elsevier Inc., 2015.

(213) Fuhrhop, J.-H.; Li, G. *Organic synthesis: Concepts and Methods*; Wiley-VCH Gmb<h & Co.: Germany, 2003.

(214) Šunjić, V.; Petrović Peroković, V. In *Organic Chemistry from Retrosynthesis to Asymmetric Synthesis*; Springer International Publishing: Switzerland, 2016; pp 1–20.

(215) Werpy, T.; Petersen, G.; Aden, A.; Bozell, J.; Holladay, J.; White, J.; Manheim, A.; Elliot, D.; Lasure, L.; Jones, S.; Gerber, M.; Ibsen, K.; Lumber, L.; Kelley, S. In *Top value added chemicals from biomass*; 2004; p 76.

(216) ZeaChem. Technology — ZeaChem http://www.zeachem.com/technology/.

(217) LanzaTech. Chemicals http://www.lanzatech.com/innovation/markets/chemicals/ (accessed Nov 6, 2017).

(218) Abengoa. Abengoa Bioenergía http://www.abengoabioenergy.com/web/es/index.html.

(219) Betarenewables. Second generation biofuel http://www.betarenewables.com/en/sustainability/second-generation-biofuel (accessed Nov 6, 2017).

(220) Green Plains Inc. Ethanol, Ethanol Marketing, Distillers Grains and Agribusiness | Green Plains Inc. http://www.gpreinc.com/ (accessed Nov 6, 2017).

(221) Shell Global. Shell Global. Biofuels http://www.shell.com/energy-and-innovation/the-energy-future/future-transport/biofuels.html (accessed Nov 6, 2017).

(222) Pacific ethanol Inc. Pacific Ethanol Inc. http://www.pacificethanol.net/products-and-services/ethanol (accessed Nov 6, 2017).

(223) Petrobras. Petrobras. BioEthanol http://controverses.sciences-po.fr/climateblogs/bioethanol/actors/companies/petrobras/ (accessed Nov 6, 2017).

(224) Group, T. A. E. The Andersons Ethanol Group http://www.andersonsethanol.com/ (accessed Nov 6, 2017).

(225) GFBiochemicals http://www.gfbiochemicals.com/products/#existing-products (accessed Nov 6, 2017).

(226) Anastas, P. T.; Warner, J. C. *Green chemistry: Theory and Practice*; Oxford University Press: New York, 1998.

(227) Cheung, H.; Tanke, R. S.; Torrence, G. P.; Cheung, H.; Tanke, R. S.; Torrence, G. P. In *Ullmann's Encyclopedia of Industrial Chemistry*; Wiley-VCH: Weinheim, Germany, 2011; pp 209–237.

(228) Celanase. Product Description and Handling Guide: Ethyl Acetate https://www.celanese.com/-/media/Intermediate Chemistry/Files/Product Descriptions/Product_Description_and_Handling_Guide-Ethyl_Acetate.pdf. (accessed Jan 26, 2018).

(229) *Encyclopaedia of occupational health and safety.*, Fourth Edition.; Stellman, J. M., Ed.; International Labor Office: Geneva, 1998.

(230) Celanase. Ethyl Acetate https://www.celanese.com/intermediate-chemistry/products/ethyl-acetate.aspx (accessed Feb 13, 2018).

(231) Johanson Fund, P. H.; Wolf, K. *Safer Alternative Nail Polish Removers for Salons and Consumers*; 2016.

(232) Taylor, S. In *Encyclopedia of Food Sciences and Nutrition*; Elsevier, 2003; pp 5737–5743.

(233) New World Encyclopedia. Ethyl acetate http://www.newworldencyclopedia.org/entry/Ethyl_acetate (accessed Feb 13, 2018).

(234) Yara-Varón, E.; Fabiano-Tixier, A. S.; Balcells, M.; Canela-Garayoa, R.; Bily, A.; Chemat, F. *RSC Adv.* 2016, *6*, 27750–27758.

(235) Cue, B. W.; Zhang, J. *Green Chem. Lett. Rev.* 2009, *24*, 193–211.

(236) Joana Gil-Chávez, G.; Villa, J. A.; Fernando Ayala-Zavala, J.; Basilio Heredia, J.; Sepulveda, D.; Yahia, E. M.; González-Aguilar, G. A. *Compr. Rev. Food Sci. Food Saf.* 2013, *12* (1), 5–23.

(237) Global ETAC Production http://www.prweb.com/releases/2014/02/prweb11619424.htm (accessed Jan 26, 2018).

(238) Fischer, E.; Speier, A. *Berichte der Dtsch. Chem. Gesellschaft.* 1895, *28* (3), 3252–3258.

(239) Chemindustry.RU. Ethyl acetate http://chemindustry.ru/Ethyl_Acetate.php (accessed Jan 26, 2018).

(240) Pattanaik, B. N.; Mandalia, H. C. *Int. J. Curr. Res. Rev.* 2011, *3* (12), 23–40.

(241) Chan, J.-R.; Chuang, K.; Lin, T.-B.; Tsai, K.-Y. Process for ethyl acetate production. EP0937029 A1, 1997.

(242) ICIS. Ethyl Acetate Production and Manufacturing Process https://www.icis.com/resources/news/2007/11/02/9075322/ethyl-acetate-production-and-manufacturing-process/ (accessed Feb 14, 2018).

(243) Nemerow, N. L.; Agardy, F. J. *Strategies of industrial and hazardous waste management*; International Thomson Publishing Company: New York, USA, 1998.

(244) Ogata, H.; Tanaka, N. Reduction of Waste in Semiconductor Manufacturing Plant (Sulfuric Acid Recycling Technology) http://www.oki.com/en/otr/downloads/otr-160-10.pdf. (accessed Mar 21, 2018).

(245) Muralidhar, J. In *Proceedings of the national seminar on Management of Industrial Effluents and wastes*; Swamy, Y. V., Das, S. N., Parida, K. M., Vinhuti, N., Eds.; Allied Publishers PVT. Limited, 2001.

(246) Weissermel, K.; Arpe, H. J. *Industrial Organic Chemistry*, 4th ed.; Wiley-VCH Verlag GmbH & Co. KGaA, 2003.

(247) Seitz, H. K.; Stickel, F. *Genes Nutr.* 2010, *5* (2), 121–128.

(248) Glossary: Standard IARC classification http://ec.europa.eu/health/scientific_committees/opinions_layman/en/electromagnetic-fields/glossary/ghi/iarc-classification.htm (accessed Feb 1, 2018).

(249) University of Liverpool. REF2014. Economical and beneficial environmental impact on industrial production of ethyl acetate http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=5577 (accessed Nov 22, 2017).

(250) Rothenberg, G. *Catalysis: Concepts and Green Applications*; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, Germany, 2008.

(251) University of liverpool, C. D. Environmentally friendly industrial production of a widely/used solvent https://www.liverpool.ac.uk/chemistry/research/research-impact/etac/ (accessed Jun 28, 2015).

(252) Yamamoto, Y.; Hatanaka, S.; Uchida, H.; Tsuji, K. In . *Silica-supported heteropoly acid catalyst for newly developed ethyl acetate roduction process*; Elsevier Science Ltd: Tokyo, 2007; p 631.

(253) BASF. Technical information n-Butyl Acetate http://www.solvents.basf.com/portal/streamer?fid=278913 (accessed Nov 22, 2017).

(254) Lederer, J.; Levering, W. W.; Bailer, O.; Morävek, P.; Smejkal, Q.; Macek, V. Process and apparatus for the production of butylacetate and isobutylacetate. US 6,458,992 B1, October 2002.

(255) Berg, L.; Ratanapupech, P. Separation of ethyl acetate from ethanol and water by extractive distillation. US4379028 A, 1982.

(256) Tian, H.; Zheng, H.; Huang, Z.; Qiu, T.; Wu, Y. *Ind. Eng. Chem. Res.* 2012, *51* (15), 5535–5541.

(257) Tian, H.; Zhao, S.; Zheng, H.; Huang, Z. *Chinese J. Chem. Eng.* 2015, *23* (4), 667–674.

(258) Tang, Y.-T.; Chen, Y.-W.; Huang, H.-P.; Yu, C.-C.; Hung, S.-B.; Lee, M.-J. *AIChE J.* 2005, *51* (6), 1683–1699.

(259) Arporniwichanop, A.; Koomsup, K.; Assabumrungrat, S. *J. Ind. Eng. Chem.* 2008, *14* (6), 796–803.

(260) Giwa, A.; Giwa, S. O. *Int. J. Eng. Res. Africa.* 2017, *30*, 154–166.

(261) Steinigeweg, S.; Gmehling, J. *Ind. Eng. Chem. Res.* 2002, *41* (22), 5483–5490.

(262) Singh, A.; Hiwale, R.; Mahajani, S. M.; Gudi, R. D.; Gangadwala, J.; Kienle, A. *Ind. Eng. Chem. Res.* 2005, *44*, 3042.

(263) Sert, E.; Atalay, F. S. *Chem. Biochem. Eng. Q.* 2011, *25* (2), 221–227.

(264) Kantam, M. L.; Bhaskar, V.; Choudary, B. M. *Catal. Letters.* 2002, *78* (1–4), 185–188.

(265) Cheremisinoff, N. *Industrial Solvents Handbook*, 2nd ed.; Marcel Dekker, Inc: New York, USA, 2003.

(266) Chakrabarti, A.; Sharma, M. M. *React. Polym.* 1993, *20* (1–2), 1–45.

(267) Wachinski, A. M. *Environmental ion exchange : principles and design*; Taylor & Francis Group, LLC: Boca Raton, USA, 2017.

(268) Lee, M.-J.; Wu, H.-T.; Lin, H. *Ind. Eng. Chem. Res.* 2000, *39* (11), 4094–4099.

(269) Ali, S. H.; Al-Rashed, O.; Azeez, F. A.; Merchant, S. *Bioresour. Technol.* 2011, *102* (21), 10094–10103.

(270) Van de Steene, E.; De Clerq, J.; Thybaut, J. W. *Chem. Eng. J.* 2014, *242*, 170–179.

(271) Harland, C. E. *Ion exchange: Theory and Practice*, Second Edition.; Royal Society of Chemistry: Cambridge, UK., 1994.

(272) Inamuddin; Luqman, M. *Ion-exchange technology I: Theory and materials*; Springer, 2012.

(273) Altiokka, M. R.; Çitak, A. *Appl. Catal. A Gen.* 2003, *239* (1–2), 141–148.

(274) Barbaro, P.; Liguori, F. *Chem. Rev.* 2009, *109* (2), 515–529.

(275) Alexandratos, S. D. *Ind. Eng. Chem. Res.* 2009, *48* (1), 388–398.

(276) JagadeeshBabu, P. E.; Sandesh, K.; Saidutta, M. B. *Ind. Eng. Chem. Res.* 2011, *50*, 7155–7160.

(277) Peters, T. A.; Benes, N. E.; Holmen, A.; Keurentjes, J. T. F. *Appl. Catal. A Gen.* 2006, *297* (2), 182–188.

(278) Wang, N.; Wang, R.; Shi, X.; Zou, G. *Beilstein J. Org. Chem.* 2012, *8* (1), 227–233.

(279) Harmer, M. a.; Sun, Q. *Appl. Catal. A Gen.* 2001, *221* (1–2), 45–62.

(280) *Ion exchange technology*; Nachod, F. C., Schubert, J., Eds.; Academic Press INC.: New York, USA, 1956.

(281) Gates, B. C.; Wisnouskas, J. S.; Heath, H. W. *J. Catal.* 1972, *24* (2), 320–327.

(282) Ancillotti, F.; Mauri, M. M.; Pescarollo, E. *J. Catal.* 1977, *46* (1), 49–57.

(283) Jayadeokar, S. S.; Sharma, M. M. *React. Polym.* 1993, *20* (1–2), 57–67.

(284) Rönnback, R.; Salmi, T.; Vuori, A.; Haario, H.; Lehtonen, J.; Sundqvist, A.; Tirronen, E. *Chem. Eng. Sci.* 1997, *52* (19), 3369–3381.

(285) Liu, Y.; Lotero, E.; Goodwin, J. *J. Catal.* 2006, *242* (2), 278–286.

(286) Izci, A.; Bodur, F. *React. Funct. Polym.* 2007, *67* (12), 1458–1464.

(287) Gangadwala, J.; Mankar, S.; Mahajani, S.; Kienle, A.; Stein, E. *Ind. Eng. Chem. Res.* 2003, *42* (10), 2146–2155.

(288) Teo, H.; Saha, B. *J. Catal.* 2004, *228* (1), 174–182.

(289) Karakus, S.; Sert, E.; Buluklu, D.; Atalay, F. S. *Ind. Eng. Chem. Res.* 2014, *53*, 4192–4198.

(290) Ali, S. H.; Merchant, S. Q. *Int. J. Chem. Kinet.* 2006, *38* (10), 593–612.

(291) Anasthas, H. M.; Gaikar, V. G. *React. Funct. Polym.* 2001, *47* (1), 23–35.

(292) Jagadeesh, R.; Junge, H.; Pohl, M.; Radnik, J.; Bru, A.; Beller, M. *J. Am. Chem. Soc.* 2013, *135*, 10776–10782.

(293) Berg, L.; Ratanapupech, P. Process for the separation of ethyl acetate from ethanol and water by extractive distillation. US4569726A, July 19, 1984.

(294) Zhu, Z.; Ri, Y.; Jia, H.; Li, X.; Wang, Y.; Wang, Y. *Sep. Purif. Technol.* 2017, *181*, 44–52.

(295) Andreatta, A. E.; Charnley, M. P.; Brennecke, J. F. *ACS Sustain. Chem. Eng.* 2015, *3* (12), 3435–3444.

(296) Colley Stephen William; Fawcett, C. R.; Sharif, M.; Marshall Tuck, M. W.; Watson, D. J.; Wood, M. A. Purification of ethyl acetate from mixtures comprising ethanol and water by pressure swing distillation. EP1117629B1, September 29, 1999.

(297) Zhang, Q.; Liu, M.; Li, C.; Zeng, A. *Sep. Purif. Technol.* 2017, *189*, 310–334.

(298) Yang, J.; Zhou, M.; Wang, Y.; Zhang, X.; Wu, G. *IOP Conf. Ser. Mater. Sci. Eng.* 2017, *274* (12026).

(299) Lee, H.-Y.; Huang, H.-P.; Chien, I.-L. *J. Process Control.* 2007, *17* (4), 363–377.

(300) Fernandez, M. F.; Barroso, B.; Meyer, X.-M.; Meyer, M.; Le Lann, M.-V.; Le Roux, G. C.; Brehelin, M. *Chem. Eng. Res. Des.* 2013, *91* (12), 2309–2322.

(301) Lv, B.; Liu, G.; Dong, X.; Wei, W.; Jin, W. *Ind. Eng. Chem. Res.* 2012, *51*, 8079–8086.

(302) Lai, I.-K.; Liu, Y.-C.; Yu, C.-C.; Lee, M.-J.; Huang, H.-P. *Chem. Eng. Process. Process Intensif.* 2008, *47* (9–10), 1831–1843.

(303) Santaella, M. A.; Orjuela, A.; Narváez, P. C. *Chem. Eng. Process. Process Intensif.* 2015, *96*, 1–13.

(304) Gadewar, S. B. Ethyl acetate production. US 8,562,921 B2, 2013.

(305) Toteja, R. S. D.; Jangida, B. L.; Sundaresan, M.; Venkataramani, B. *Langmuir* 1997, *13* (11), 2980–2982.

(306) Beula, C.; Sai, P. S. T. *Indian Chem. Eng.* 2015, *57* (2), 177–196.

(307) Atalay, F. S. *Dev. Chem. Eng. Miner. Process.* 2008, *2* (2–3), 181–184.

(308) Xu, Z. P.; Chuang, K. T. *Can. J. Chem. Eng.* 1996, *74* (4), 493–500.

(309) Kolena, J.; Lederer, J.; Morávek, P.; Hanika, J.; Smejkal, Q.; Skála, D. Method of producing ethyl acetate and an equipment for carrying out this method. US6693213 B1, 2004.

(310) Casson, V.; Lister, D. G.; Milazzo, M. F.; Maschio, G. *J. Loss Prev. Process Ind.* 2012, *25* (1), 209–217.

(311) Duh, Y.-S.; Hsu, C.-C.; Kao, C.-S.; Yu, S. W. *Thermochim. Acta.* 1996, *285* (1), 67–79.

(312) Horsley, L. H. *Azeotropic Data—III*; Horsley, L. H., Ed.; Advances in Chemistry; AMERICAN CHEMICAL SOCIETY: Washington, DC, 1973; Vol. 116.

(313) Gmehling, J.; Menke, J.; Krafczyk, J.; Fischer, K.; Fontaine, J.-C.; Kehiaian, H. V. In *Handbook of Chemistry and Physics*; CRC Press: Boca Raton, FL., 2005; pp 6–210.

(314) Singh, D.; Gupta, R. K.; Kumar, V. *Ind. Eng. Chem. Res.* 2014, *53*, 10448–10456.

(315) Brandt, S.; Horstmann, S.; Steinigeweg, S.; Gmehling, J. *Fluid Phase Equilib.* 2014, *376*, 48–54.

(316) Van Baelen, D.; Van der Bruggen, B.; Van den Dungen, K.; Degreve, J.; Vandecasteele, C. *Chem. Eng. Sci.* 2005, *60* (6), 1583–1590.

(317) Dutta, B. K.; Sikdar, S. K. *AIChE J.* 1991, *37* (4), 581–588.

(318) Lipnizki, F.; Field, R. W.; Ten, P.-K. *J. Memb. Sci.* 1999, *153* (2), 183–210.

(319) Buchaly, C.; Kreis, P. *Chem. Eng. Process. Process Intensif.* 2007, *46* (9), 790–799.

(320) Berg, L.; Yeh, A.-I. Separation of n-butyl acetate from n-butanol by extractive distillation. US4507176A, 1984.

(321) Sert, E.; Atalay, F. S. *Chem. Biochem. Eng. Q.* 2011, *25* (2), 221–227.

(322) Goldschmidt, A.; Streitberger Hans-Joachim. *BASF Handbook Basics of Coating Technology: 3rd Revised Edition - Hans-Joachim Streitberger, Artur Goldschmidt - Google Libros*, Third Edit.; Vincentz Network: Hangover, Germany, 2018.

(323) Efstathiou Kypros. *Synthesis and characterization of a Polyurethane Prepolymer for the development of a novel acrylate-based polymer foam*; 2011.

(324) V., J.; H., L.; Hernandez-Sanchez, F.; M., J. In *Advances in Biomaterials Science and Biomedical Applications*; InTech, 2013.

(325) In *ASM Handbook, volume 5B, Protective Organic Coatings*; Tator, K. B., Ed.; ASM International, 2015.

(326) Jones, F. N.; Nichols, M. E.; Pappas, S. P. *Organic coatings: science and technology*, Fourth edi.; Wiley, 2017.

(327) BASF. n-Butyl Acetate http://www.basf.com/group/corporate/en_GB/brand/N_BUTYL_ACETATE (accessed Nov 22, 2017).

(328) *Modern technology of paints, varnishes and lacquers*, Second Edition.; Asia Pacific Business Press: Delhi, 2007.

(329) Iberica, Pce. Copa de viscosidad http://www.pce-iberica.es/ (accessed Nov 30, 2017).

(330) Paint Quality Institute. Acrylic Coatings & Oil-Based Alkyds http://www.industrialpaintquality.com/education/inthecan/vs03.html (accessed Nov 30, 2017).

(331) Eastlack, H. E. In *Symposium on Paint and Paint Materials*; American Society for Testing Materials: Baltimore, USA., 1935; pp 57–65.

(332) Standeven, H. A. L. In *House paints, 1900-1960: History and Use*; Getty Conservation Institute, 2011; pp 53–60.

(333) ISO 2813:2014, Peintures et vernis — Détermination de l’indice de brillance à 20 degrés, 60 degrés et 85 degrés https://www.iso.org/obp/ui/#iso:std:56807:fr (accessed Mar 23, 2018).

(334) Duncan, B.; Mera, R.; Leatherdale, D.; Taylor, M.; Musgrove, R. *Techniques for characterising the wetting, coating and spreading of adhesives on surfaces*; 2005.

(335) ISO 2409:2013.Paints and varnishes: Cross-cut test https://www.iso.org/standard/51923.html (accessed Dec 5, 2017).

(336) Davies, N.; Jokiniemi, E. *Dictionary of architecture and building construction*; Elsevier/Architectural Press, 2008.

(337) Oosten, T. van; Lorne, A.; Béringuer, O. *PUR Facts: Conservation of Polyurethane Foam in Art and Design*; Amsterdam University Press, 2011.

(338) Wang, L. *Chemical and Engineering news*. The American Chemical Society; 2006, p 48.

(339) Tobiszewski, M.; Marć, M.; Gałuszka, A.; Namieśnik, J. *Molecules* 2015, *20* (6), 10928–10946.

(340) Anastas, P. T.; Zimmerman, J. B. *Innovations in green chemistry and green engineering: Selected entries from the Encyclopedia of sustainability science and technology*; Springer, 2013.

(341) Constable, D. J. C.; Curzons, A. D.; Cunningham, V. L. *Green Chem.* 2002, *4* (6), 521–527.

(342) Trost, B. M. *Science.* 1991, *254* (5037), 1471–1477.

(343) Dicks, A. P.; Hent, A. *Green chemistry metrics: A Guide to Determining and Evaluating Process Greenness*.

(344) Sheldon, R. A. *Green Chem.* 2017, *19* (1), 18–43.

(345) Organic Chemistry Portal http://www.organic-chemistry.org/topics/green-chemistry.shtm (accessed Jan 18, 2018).

(346) Tabone, M. D.; Cregg, J. J.; Beckman, E. J.; Landis, A. E. *Environ. Sci. Technol.* 2010, *44* (21), 8264–8269.

(347) Julio, R.; Albet, J.; Vialle, C.; Vaca-Garcia, C.; Sablayrolles, C. *Biofuels, Bioprod. Biorefining* 2017, *11* (2), 373–395.

(348) Ghatak, H. R. *Renew. Sustain. Energy Rev.* 2011, *15* (8), 4042–4052.

(349) Jacquemin, L.; Pontalier, P.-Y.; Sablayrolles, C. *Int. J. Life Cycle Assess.* 2012, *17* (8), 1028–1041.

(350) ISO 14040 : 2006 https://www.iso.org/standard/37456.html (accessed Nov 8, 2017).

(351) INTERNATIONAL STANDARD 14040 https://web.stanford.edu/class/cee214/Readings/ISOLCA.pdf. (accessed Nov 8, 2017).

(352) Klöpffer, W.; Grahl, B. *Life cycle assessment (LCA): a guide to best practice*; Wiley-VCH: Germany, 2014.

(353) *Environmental engineering. Environmental health and safety for municipal infrastructure, land use and planning, and industry*, Sixth Edit.; Nemerow, N., Agardy, F. J., Sullivan, P., Salvato, J. A., Eds.; John Wiley & Sons, Inc.: NJ, 2009.

(354) *Goal and scope definition in life cycle assessment*; Curran, M. A., Ed.; Springer Nature, 2017.

(355) Curran, M. A. *Curr. Opin. Chem. Eng.* 2013, *2* (3), 273–277.

(356) Consequential LCA. The functional unit https://consequential-lca.org/clca/the-functional-unit/ (accessed Jan 19, 2018).

(357) Tillman, A.-M.; Ekvall, T.; Baumann, H.; Rydberg, T. *J. Clean. Prod.* 1994, *2* (1), 21–29.

(358) Ciambrone, D. F. *Environmental life cycle analysis*; Lewis Publishers, 1997.

(359) Babu, B. V. In *Life Cycle Inventory Analysis*; Malasya, 2006.

(360) Hauschild, M. Z.; Rosenbaum, R. K.; Olsen, S. I. *Life Cycle Assessment: Theory and Practice*.

(361) Life Cycle Impact Assessment – EPLCA http://eplca.jrc.ec.europa.eu/?page_id=1159 (accessed Nov 27, 2017).

(362) Skone, T. J. *Environ. Prog.* 2000, *19* (2), 92–100.

(363) Linak, E.; Bizzari, S. *Global Solvents: Opportunities for Greener Solvents*; IHS Chemical, 2013.

(364) Ceresana. *Market Study: Solvents*, Ceresana.; 2014.

(365) Khire, S.; Bhagwat, P. V.; Femandes, M.; Gangundi, P. B.; Vadalia, H. *New Math. Nat. Comput.* 2012, *19* (5), 342–350.

(366) Bamunusingha, B.; De Silva, E.; Gunasekera, M. *J. Natl. Sci. Found. Sri Lanka.* 2016, *44* (1), 83.

(367) Chen, X.; Xu, Z.; Okuhara, T. *Appl. Catal. A Gen.* 1999, *180* (1–2), 261–269.

(368) Gurav, H.; Bokade, V. V. *J. Nat. Gas Chem.* 2010, *19* (2), 161–164.

(369) El-Sharkawy, E. A.; Al-Shihry, S. S. *Mater. Lett.* 2004, *58* (15), 2122–2127.

(370) Cho, M.; Jo, S.; Kim, G.; Han, M. *Ind. Eng. Chem. Res.* 2014, *53* (19), 8095–8105.

(371) Hanika, J.; Kolena, J.; Smejkal, Q. *Chem. Eng. Sci.* 1999, *54* (21), 5205–5209.

(372) Gould, R. F., Ed. *Advance in Chemistry*; American Chemical Society, 1973; pp i–vi.

(373) Lutze, P.; Górak, A. *Reactive and Membrane-Assisted Separations*; Walter de Gruyter GmbH & Co KG, 2016.

(374) ISO 14040. *Management environnemental - Analyse du cycle de vie - Principes et cadre*; 2006.

(375) ISO 14044. *Management environnemental - Analyse de Cycle de Vie - Exigences et lignes directrices*; 2006.

(376) Dias, M. O. S.; Pereira, L. G.; Junqueira, T. L.; Pavanello, L. G.; Chagas, M. F.; Cavalett, O.; Maciel Filho, R.; Bonomi, A. *Chem. Eng. Res. Des.* 2014, *92* (8), 1441–1451.

(377) Pereira, L. G.; Chagas, M. F.; Dias, M. O. S.; Cavalett, O.; Bonomi, A. *J. Clean. Prod.* 2015, *96*, 557–568.

(378) Wang, Q.; Vural Gürsel, I.; Shang, M.; Hessel, V. *Chem. Eng. J.* 2013, *234*, 300–311.

(379) EVEA. *Modélisation de la synthèse de substances chimiques en ACV*; 2015.

(380) Weidema, B. P.; Wesnaes, M. S. *2.-0 LCA Consult.* 1996, *4*, 167–174.

(381) Tavan, Y.; Hosseini, S. H. *J. Taiwan Inst. Chem. Eng.* 2013, *44* (4), 577–585.

(382) Hasanoğlu, A.; Salt, Y.; Keleşer, S.; Dinçer, S. *Desalination.* 2009, *245* (1–3), 662–669.

(383) Hu, W. W.; Zhang, X. H.; Zhang, Q. G.; Liu, Q. L.; Zhu, A. M. *J. Appl. Polym. Sci.* 2012, *126* (2), 778–787.

(384) Ong, Y. T.; Tan, S. H. *Chem. Eng. Res. Des.* 2016, *109*, 116–126.

(385) Domènech, X.; Ayllón, J. A.; Peral, J.; Rieradevall, J. *Environ. Sci. Technol.* 2002, *36* (24), 5517–5520.

(386) Groslambert, S.; Léonard, A. In *SETAC Europe 25th Annual Meeting*; Barcelona (Spain), 2014.

(387) Jödicke, G.; Zenklusen, O.; Weidenhaupt, A.; Hungerbühler, K. *J. Clean. Prod.* 1999, *7* (2), 159–166.

(388) Aresta, M.; Galatola, M. *J. Clean. Prod.* 1999, *7* (3), 181–193.

(389) Kalkeren, H. A. van; Blom, A. L.; Rutjes, F. P. J. T.; Huijbregts, M. A. J. *Green Chem.* 2013, *15* (5), 1255–1263.

(390) Subramanian, V.; Golden, J. S. *J. Clean. Prod.* 2016, *115*, 354–361.

(391) Saling, P.; Kicherer, A.; Dittrich-Krämer, B.; Wittlinger, R.; Zombik, W.; Schmidt, I.; Schrott, W.; Schmidt, S. *Int. J. Life Cycle Assess.* 2002, *7* (4), 203–218.

(392) Jiménez-González, C.; Curzons, A. D.; Constable, D. J. C.; Cunningham, V. L. *Int. J. Life Cycle Assess.* 2004, *9* (2), 114–121.

(393) Geisler, G.; Hofstetter, T. B.; Hungerbühler, K. *Int. J. Life Cycle Assess.* 2004, *9* (2), 101–113.

(394) Hischier, R.; Hellweg, S.; Capello, C.; Primas, A. *Int. J. Life Cycle Assess.* 2004, *10* (1), 59–67.

(395) Burgess, A. A.; Brennan, D. J. *Chem. Eng. Sci.* 2001, *56* (8), 2589–2604.

(396) U.S. Energy Information Administration (EIA) - Data https://www.eia.gov/totalenergy/data/browser/index.php?tbl=T10.03#/?f=A&start=2013&end=2017&charted=8 (accessed Mar 28, 2018).

(397) USDA ERS - U.S. Bioenergy Statistics https://www.ers.usda.gov/data-products/us-bioenergy-statistics/ (accessed Mar 28, 2018).

(398) Greenhouse Gas Emissions of Corn Ethanol Production | Agricultural Marketing Resource Center https://www.agmrc.org/renewable-energy/climate-change/greenhouse-gas-emissions-of-corn-ethanol-production/ (accessed Mar 28, 2018).

(399) Muñoz, I.; Flury, K.; Jungbluth, N.; Rigarlsford, G.; i Canals, L. M.; King, H. *Int. J. Life Cycle Assess.* 2014, *19* (1), 109–119.

(400) Hoell, D.; Mensing, T.; Roggenbuck, R.; Sakuth, M.; Sperlich, E.; Urban, T.; Neier, W.; Strehlke, G. In *Ullmann's Encyclopedia of Industrial Chemistry*; Wiley-VCH: Weinheim, Germany, 2009; pp 431–444.

(401) Methyl Ethyl Ketone (2-Butanone) https://www.epa.gov/sites/production/files/2016-09/documents/methyl-ethyl-ketone.pdf (accessed Apr 27, 2018).

(402) Arora, D.; Sharma, M. *Chem. Wkly.* 2010, 189–194.

(403) Rocochem Inc. http://www.recochem.com/products/paint_thinners_solvents/mek (accessed Oct 9, 2015).

(404) ICIS. US chemical profile: Methyl ethyl ketone http://www.icis.com/resources/news/2010/06/07/9365325/us-chemical-profile-methyl-ethyl-ketone/ (accessed Oct 9, 2015).

(405) Global Market Insights. MEK Market Size: Global Industry Share Report 2022 https://www.gminsights.com/industry-analysis/methyl-ethyl-ketone-MEK-market (accessed Dec 6, 2017).

(406) Grand View Research. Methyl ethyl ketone (MEK) Market Analysis by Application (Paints & Coatings, Printing Inks, Adhesives) and Segment Forecasts to 2024 http://www.grandviewresearch.com/industry-analysis/methyl-ethyl-ketone-mek-market (accessed Oct 3, 2017).

(407) Methyl Ethyl Ketone (MEK): 2017 World Market Outlook and Forecast up to 2027 https://mcgroup.co.uk/researches/methyl-ethyl-ketone-mek (accessed Dec 6, 2017).

(408) Cox, N. R. Oxidation of hydrocarbons. Patent US 3196182 A, July 20, 1965.

(409) Office of Air Quality Planning and Standards; U.S. Environental Protection Agency. *Locating and Estimating Air Emissions From Sources of Methyl Ethyl Ketone*; 1994.

(410) *Riegel's handbook of industrial chemistry*, Ninth edit.; Kent, J. A., Ed.; Springer Science & Business Media: New York, 1992.

(411) Weissermel, K.; Arpe, H.-J. *Industrial organic chemistry*; Wiley-VCH, 2003.

(412) Webers, W. Sandhack L, Neier, W. Process for the production of lower alcohols by direct catalytic hydration lower olefins. US3994983, November 30, 1976.

(413) *Fischer-Tropsch Technology*; Steynberg, A., Dry, M., Eds.; Elsevier, 2004.

(414) Kreutz, T. G.; Larson, E. D.; Liu, G.; Williams, R. In *25th Annual International Pittsburgh Coal Conference*; Pittsburgh, USA, 2008; pp 1–81.

(415) Tolman, W. B. *Activation of small molecules: Organometallic and Bioinorganic Perspectives*; Wiley-VCH, 2006.

(416) Nierop, P. van; Erasmus, H.; Zyl, J. van. In *SASOL's achievements in the 20th century as a building block for the 21st*; San Francisco, California, USA, 2000; pp 1–13.

(417) Hester, R. E.; Harrison, R. M. *Coal in the 21st century: energy needs, chemicals and environmental controls*; Royal Society of Chemistry, London, UK, 2018.

(418) Iwanaga, K.; Tamura, M.; Nakayama, T.; Usui, M.; Umida, H.; Nagaoka, H. Process for producing phenol and methyl ethyl ketone. EP0548986 A1, June 30, 1993.

(419) Iwanaga, K.; Tamura, M.; Nakayama, T.; Usui, M.; Umida, H.; Nagaoka, Hi. Process for producing phenol and methyl ethyl ketone. US5298667 A, March 29, 1994.

(420) DSRI. *Technology in Indian Methyl Ethyl Ketone Industry*. www.dsri.gov.in/reports/techreps/tsr140.pdf (accessed Feb 15, 2018)

(421) Chauvel, A.; Levebvre, G. *Petrochemical Processes: Mayor oxigenated, chlorinated and nitrated derivatives*, Second edition.; Éditions Technip, Paris: France, 1989.

(422) Timokhin, B. V; Baransky, V. A.; Eliseeva, G. D. *Russ. Chem. Rev.* 1999, *68* (1), 73–84.

(423) Karwa, S.; Gajiwala, V. M.; Heltzel, J.; Patil, S. K. R.; Lund, C. R. F. *Catal. Today.* 2016, *263*, 16–21.

(424) Di Mondo, D.; Ashok, D.; Waldie, F.; Schrier, N.; Morrison, M.; Schlaf, M. *ACS Catal.* 2011, *1* (4), 355–364.

(425) Weingarten, R.; Conner, W. C.; Huber, G. W. *Energy Environ. Sci.* 2012, *5* (6), 7559.

(426) Morone, A.; Apte, M.; Pandey, R. A. *Renew. Sustain. Energy Rev.* 2015, *51*, 548–565.

(427) Biofine Technology http://biofinetechnology.com/ (accessed Feb 15, 2018).

(428) Fitzpatrick, S. W. Production of levulinic acid from carbohydrate-containing materials. US5608105 A, 1997.

(429) Hayes, D. J.; Ross, J.; Hayes, M. H. B.; Fitzpatrick, S. In *Biorefineries-Industrial Processes and Products*; Kamm, B., Gruber, P. R., Kamm, M., Eds.; Wiley-VCH Verlag GmbH: Weinheim, Germany, 2005.

(430) Fitzpatrick, S. W. In *ACS Symposium Series*; 2006; pp 271–287.

(431) Frankiewicz, A. *CHEMIK.* 2016, *70* (4), 203–208.

(432) Mullen, B. D.; Leibig, C. M. Process to prepare levulilnic acid. 20160251296, 2014.

(433) Mullen, B.; Yontz, D. J.; Leibig, C. M. Process to prepare levulinic acid. 9598341, 2017.

(434) Bhavaraju, S.; Karanjikar, M. Decarboxylation of levulinic acid to ketone solvents. WO2013096225 A1, December 17, 2013.

(435) Min, K.; Kim, S.; Yum, T.; Kim, Y.; Sang, B.-I.; Um, Y. *Appl. Microbiol. Biotechnol.* 2013, *97* (12), 5627–5634.

(436) Gong, Y.; Lin, L.; Yan, Z. *BioResources*. 2011, 6 (1), 686–699.

(437) Gong, Y.; Lin, L.; Shi, J.; Liu, S. *Molecules.* 2010, *15* (11), 7946–7960.

(438) Gong, Y.; Lin, L. *Molecules.* 2011, *16* (3), 2714–2725.

(439) *Surface Phenomena in Enhanced Oil Recovery*; Shah, D. O., Ed.; Springer Science+Business Media New York: New York, USA, 1981.

(440) Lin, H.-R. *Eur. Polym. J.* 2001, *37* (7), 1507–1510.

(441) Hunkeler, D. *Macromolecules.* 1991, *24* (9), 2160–2171.

(442) Okaya, T.; Kikuchi, K.; Morii, Y. *Polym. J.* 1997, *29* (6), 545–549.

(443) Pang, S.; Fiume, M. Z. *Int. J. Toxicol.* 2001, *20* (3), 7–21.

(444) Johnson, W. *Amended Safety Assessment of Persulfates as Used in Cosmetics*; 2017.

(445) *Bio-based wood adhesives: Preparation, Characterization, and Testing*; He, Z., Ed.; CRC Press: USA, 2017.

(446) Frontistis, Z.; Hapeshi, E.; Fatta-Kassinos, D.; Mantzavinos, D. *Photochem. Photobiol. Sci.* 2015, *14* (3), 528–535.

(447) Ghanbari, F.; Moradi, M.; Manshouri, M. *J. Environ. Chem. Eng.* 2014, *2* (3), 1846–1851.

(448) FMC. Persulfate technical information http://www.peroxychem.com/media/90826/AOD_Brochure_Persulfate.pdf. (accessed Feb 8, 2018).

(449) Wacławek, S.; Lutze, H. V.; Grübel, K.; Padil, V. V. T.; Černík, M.; Dionysiou, D. D. *Chem. Eng. J.* 2017, *330*, 44–62.

(450) Chen, F.; Luo, Z.; Liu, G.; Yang, Y.; Zhang, S.; Ma, J. *J. Environ. Manage.* 2017, *204*, 170–178.

(451) Medina, R.; David Gara, P. M.; Fernández-González, A. J.; Rosso, J. A.; Del Panno, M. T. *Sci. Total Environ.* 2018, *618*, 518–530.

(452) Bartlett, P. D.; Cotman, J. D. *J. Am. Chem. Soc.* 1949, *71* (4), 1419–1422.

(453) House, D. A. *Chem. Rev.* 1962, *62* (3), 185–203.

(454) Berlin, A. A.; Kislenko, V. N.; Medvedevskikh, Y. G. *Theor. Exp. Chem.* 1990, *26* (3), 337–341.

(455) Berlin; A.A. *Kinet. Catal.* 1986, *27*, 34–39.

(456) Kolthoff, I. M.; Miller, I. K. *J. Am. Chem. Soc.* 1951, *73* (7), 3055–3059.

(457) Hussain, I.; Zhang, Y.; Huang, S.; Du, X. *Chem. Eng. J.* 2012, *203*, 269–276.

(458) Liang, C. J.; Bruell, C. J.; Marley, M. C.; Sperry, K. L. *Soil Sediment Contam.* 2003, *12* (2), 207–228.

(459) Zhao, D.; Liao, X.; Yan, X.; Huling, S. G.; Chai, T.; Tao, H. *J. Hazard. Mater.* 2013, *254–255*, 228–235.

(460) Furman, O. S.; Teel, A. L.; Watts, R. J. *Environ. Sci. Technol.* 2010, *44* (16), 6423–6428.

(461) Anderson, J. M.; Kochi, J. K. *J. Am. Chem. Soc.* 1970, *92* (6), 1651–1659.

(462) Fristad, W. E.; Fry, M. A.; Klang, J. A. *J. Org. Chem.* 1983, *48* (20), 3575–3577.

(463) Fristad, W. E.; Klang, J. A. *Tetrahedron Lett.* 1983, *24* (22), 2219–2222.

(464) Anipsitakis, G. P.; Dionysiou, D. D. *Environ. Sci. Technol.* 2004, *38* (13), 3705–3712.

(465) Walling, C.; Camaioni, D. M. *J. Org. Chem.* 1978, *43* (17), 3266–3271.

(466) Liang, C.; Lai, M.-C. *Environ. Eng. Sci.* 2008, *25* (7), 1071–1078.

(467) Seiple, I. B.; Su, S.; Rodriguez, R. A.; Gianatassio, R.; Fujiwara, Y.; Sobel, A. L.; Baran, P. S. *J. Am. Chem. Soc.* 2010, *132* (38), 13194–13196.

(468) Oh, S.-Y.; Kang, S.-G.; Chiu, P. C. *Sci. Total Environ.* 2010, *408* (16), 3464–3468.

(469) Zhang, Y.; Xie, X.; Huang, W.; Huang, S. *J. Cent. South Univ.* 2013, *20* (4), 1010–1014.

(470) Wei, X.; Gao, N.; Li, C.; Deng, Y.; Zhou, S.; Li, L. *Chem. Eng. J.* 2016, *285*, 660–670.

(471) Grand View Research https://www.grandviewresearch.com/press-release/global-levulinic-acid-market (accessed Oct 3, 2017).

(472) Bozell, J. J.; Moens, L.; Elliott, D. C.; Wang, Y.; Neuenscwander, G. G.; Fitzpatrick, S. W.; Bilski, R. J.; Jarnefeld, J. L. *Resour. Conserv. Recycl.* 2000, *28* (3–4), 227–239.

(473) Stapley, J. A.; Bemiller, J. N. *Carbohydr. Res.* 2007, *342* (3–4), 610–613.

(474) Mundle, S. O. C.; Kluger, R. *J. Am. Chem. Soc.* 2009, *131* (33), 11674–11675.

(475) Rodríguez, N.; Goossen, L. J. *Chem. Soc. Rev.* 2011, *40* (10), 5030–5048.

(476) Mirkhani, V.; Tangestaninejad, S.; Moghadam, M.; Moghbel, M. *Bioorg. Med. Chem.* 2004, *12* (5), 903–906.

(477) Wang, D.; Hakim, S. H.; Alonso, D. M.; Dumesic, J. A. *Chem. Commun. (Camb).* 2013, *49* (63), 7040–7042.

(478) Monig, J.; Chapman, R.; Asmus, K.-D. *J. Phys. Chem.* 1985, *89*, 3139–3144.

(479) Steffen, L. K.; Glass, R. S.; Sabahi, M.; Wilson, G. S.; Schoeneich, C.; Mahling, S.; Asmus, K. D. *J. Am.*

Chem. Soc. 1991, *113* (6), 2141–2145.

(480) Goldstein, S.; Czapski, G.; Cohen, H.; Meyerstein, D. *Inorg. Chem.* 1992, *31* (12), 2439–2444.

(481) Bobrowski, K.; Pogocki, D.; Schoneich, C. *J. Phys. Chem.* 1993, *97* (51), 13677–13684.

(482) Guitton, J.; Tinardon, F.; Lamrini, R.; Lacan, P.; Desage, M.; Francina, A. *Free Radic. Biol. Med.* 1998, *25* (3), 340–345.

(483) Zhu, Y.; Li, X.; Wang, X.; Huang, X.; Shen, T.; Zhang, Y.; Sun, X.; Zou, M.; Song, S.; Jiao, N. *Org. Lett.* 2015, *17* (19), 4702–4705.

(484) Chum, H. L.; Ratcliff, M.; Posey, F. L.; Turner, J. A.; Nozik, A. J. *J. Phys. Chem.* 1983, *87* (16), 3089–3093.

(485) Tanner, D. D.; Osman, S. A. A. *J. Org. Chem.* 1987, *52* (21), 4689–4693.

(486) Patel, N. R.; Flowers, R. A. *J. Am. Chem. Soc.* 2013, *135* (12), 4672–4675.

(487) Kan, J.; Huang, S.; Lin, J.; Zhang, M.; Su, W. *Angew. Chem. Int. Ed. Engl.* 2015, *54* (7), 2199–2203.

(488) Couttenye, R. A.; Huang, K. C.; Hoag, G. E.; Suib, S. L. In *En Proceedings of the 19th Petroleum Hydrocarbons and Organic Chemicals in Ground Water: Prevention, Assessment, and Remediation, Conference and Exposition*; Atlanta, GA, 2002; pp 345–350.

(489) Kimura, M.; Kawajiri, T.; Tanida, M. *J. Chem. Soc. Dalt. Trans.* 1980, No. 5, 726.

(490) Liu, K.; Han, J. *J. Agric. Food Chem.* 2012, *60*, 4212–4221.

(491) Xia, X.-F.; Zhu, S.-L.; Chen, C.; Wang, H.; Liang, Y.-M. *J. Org. Chem.* 2016, *81* (3), 1277–1284.

(492) Liu, J.; Fan, C.; Yin, H.; Qin, C.; Zhang, G.; Zhang, X.; Yi, H.; Lei, A. *Chem. Commun. (Camb).* 2014, *50* (17), 2145–2147.

(493) Hobbs, C. C.; Van't Hof, H. Liquid phase oxidation of methyl ethyl ketone to form acetic acid therefrom. US3947497A, 1974.

(494) Clark, L. W. *Int. J. Chem. Kinet.* 1976, *8* (4), 609–624.

(495) Stockbridge, R. B.; Lewis, C. A.; Yuan, Y.; Wolfenden, R.; Wolfenden, R. *Proc. Natl. Acad. Sci. U. S. A.* 2010, *107* (51), 22102–22105.

(496) Wolfenden, R.; Lewis, C. A.; Yuan, Y.; Yuan, Y. *J. Am. Chem. Soc.* 2011, *133* (15), 5683–5685.

(497) Ng, H. N.; Calvo, C.; Faggiani, R.; IUCr. *Acta Crystallogr. Sect. B Struct. Crystallogr. Cryst. Chem.* 1978, *34* (3), 898–899.

(498) Keen, R. C. *Zeitschrift für Krist. - Cryst. Mater.* 1935, *91* (1–6), 129–135.

(499) Morris, M.; McMurdie, H.; Evans, E.; Paretzkin, B.; Groot, J.; Hubbard, C.; Carmel, S. In *Standard X-ray Diffraction Powder Patterns*; 1976; p 37.

(500) Tibballs, J. E.; Nelmes, R. J.; McIntyre, G. J. *J. Phys. C Solid State Phys.* 1982, *15* (1), 37–58.

(501) Morgan, J. L. R.; Crist, R. H. *J. Am. Chem. Soc.* 1927, *49* (1), 16–25.

(502) Morgan, J. L. R.; Crist, R. H. *J. Am. Chem. Soc.* 1927, *49* (2), 338–346.

(503) Heidt, L. J. *J. Chem. Phys.* 1942, *10* (5), 297–302.

(504) Jette, E. R.; Foote, F. *J. Chem. Phys.* 1935, *3* (10), 605–616.

(505) Deb, A.; Manna, S.; Modak, A.; Patra, T.; Maity, S.; Maiti, D. *Angew. Chemie Int. Ed.* 2013, *52* (37), 9747–9750.

(506) Hatamura, M.; Yamaguchi, S.; Takane, S.; Chen, Y.; Suganuma, K. *Dalton Trans.* 2015, *44* (19), 8993–9003.

(507) Standke, B.; Jansen, M. *Angew. Chemie Int. Ed. English.* 1986, *25* (1), 77–78.

(508) Waterhouse, G. I. N.; Metson, J. B.; Bowmaker, G. A. *Polyhedron* 2007, *26* (13), 3310–3322.

(509) Kaspar, T. C.; Droubay, T.; Chambers, S. A.; Bagus, P. S. *J. Phys. Chem. C.* 2010, *114* (49), 21562–21571.

(510) Wang, W.; Cheng, B.; Yu, J.; Liu, G.; Fan, W. *Chem. - An Asian J.* 2012, *7* (8), 1902–1908.

(511) Turner, N. H.; Murday, J. S.; Ramaker, D. E. *Anal. Chem.* 1980, *52* (1), 84–92.

(512) Gaarenstroom, S. W.; Winograd, N. *J. Chem. Phys.* 1977, *67* (8), 3500–3506.

(513) Tjeng, L. H.; Meinders, B. J.; Van Elp, J.; Ghinjsen, J.; Sawatzky, G. A.; Johnson, R. L. *Phys. Rev. B* 1990, *41* (5), 3190–3199.

(514) Kaushik, V. K. *J. Electron Spectros. Relat. Phenomena.* 1991, *56* (3), 273–277.

(515) *Encyclopedia of chemical physics and physical chemistry*; Moore, J. H., Spencer, N. D., Eds.; Institute of Physics Publishing: Bristol, UK, 2001.

(516) Applications of solid-state NMR spectroscopy to pharmaceuticals - European Pharmaceutical Review https://www.europeanpharmaceuticalreview.com/article/17182/applications-of-solid-state-nmr-spectroscopy-to-pharmaceuticals/ (accessed Mar 27, 2018).

(517) Van Wüllen, L.; Vensky, S.; Hoffbauer, W.; Jansen, M. *Solid State Sci.* 2005, *7* (8), 920–924.

(518) Penner, G. H.; Li, W. *Inorg. Chem.* 2004, *43*, 5588–5597.

(519) Pavlovskaya, G. E.; Horton-Garcia, C. F.; Dybowski, C.; Corbin, D. R.; Meersmann, T. *J. Phys. Chem.* 2004, *108*, 1584–1589.

(520) Plischke, J. K.; Benesi, A. J.; Vannice, M. A. *J. Phys. Chem.* 1992, *96* (9), 3799–3806.

(521) EAG Laboratories-Techniques http://www.eaglabs.fr/cm/xrd.html (accessed Mar 27, 2018).

(522) Pecharsky, V. K.; Zavalij, P. Y. *Fundamentals of powder diffraction and structural characterization of materials*, Second Edition.; Springer: New York, USA, 2009.

(523) Langford, J. I.; Louër, D. *Reports Prog. Phys.* 1996, *59* (2), 131–234.

(524) Beccat, P.; Da Silva, P.; Huiban, Y.; Kasztelan, S. *Oil Gas Sci. Technol.* 1999, *54* (4), 487–496.

(525) Benz, L. B. Deposition and investigation of Mass Selected Gold and Silver Clusters on a Titaknium Dioxide (110) Surface: Preparation of a Model Catalyst, University of California, 2007.

(526) Ferraria, A. M.; Carapeto, A. P.; Botelho do Rego, A. M. *Vacuum.* 2012, *86* (12), 1988–1991.

(527) Gao, X.-Y.; Wang, S.-Y.; Li, J.; Zheng, Y.-X.; Zhang, R.-J.; Zhou, P.; Yang, Y.-M.; Chen, L.-Y. *Thin Solid Films* 2004, *455–456*, 438–442.

(528) Schön, G.; Tummavuori, J.; Lindström, B.; Enzell, C. R.; Swahn, C.-G. *Acta Chem. Scand.* 1973, *27*, 2623–2633.

(529) Schön, G. *Acta Chem. Scand.* 1973, *27*, 2623–2633.

(530) Marie, E.; Torbjörn, W. In *Handbook for Cleaning/Decontamination of Surfaces*; Elsevier, 2007; pp 747–789.

(531) Naumkin, A. V; Kraut-Vass, A.; Gaarenstroom, S. W.; Powell, C. J. NIST X-ray Photoelectron Spectroscopy (XPS) Database, Version 4.1 https://srdata.nist.gov/xps/ (accessed Jun 14, 2017).

(532) Iwasaki, N.; Sasaki, Y.; Nishina, Y. *Surf. Sci.* 1988, *198* (3), 524–540.

(533) Wei, J.; Lei, Y.; Jia, H.; Cheng, J.; Hou, H.; Zheng, Z. *Dalt. Trans.* 2014, *43* (29), 11333–11338.

(534) Preuksarattanawut, T.; Asavavisithchai, S.; Nisaratanaporn, E. *Mater. Chem. Phys.* 2011, *130* (1–2), 481–486.

(535) How EDX analysis with a scanning electron microscope (SEM) works http://blog.phenom-world.com/edx-analysis-scanning-electron-micrscope-sem (accessed Apr 6, 2018).

(536) Surface Science Western at the University of Western Ontario SEM/EDX Analysis, SEM/EDS Analysis Services at Surface Science Western http://www.surfacesciencewestern.com/analytical-services/scanning-electron-microscopy-coupled-with-energy-dispersive-x-ray-semedx-spectroscopy/ (accessed Mar 27, 2018).

(537) Dong, X.; Ji, X.; Wu, H.; Zhao, L.; Li, J.; Yang, W. *J. Phys. Chem. C* 2009, *113* (16), 6573–6576.

(538) Dong, X.; Ji, X.; Jing, J.; Li, M.; Li, J.; Yang, W. *J. Phys. Chem. C* 2010, *114* (5), 2070–2074.

(539) Lu, L.; Sevonkaev, I.; Kumar, A.; Goia, D. V. *Powder Technol.* 2014, *261*, 87–97.

(540) George, M. T.; Vaidyan, V. K. *J. Appl. Electrochem.* 1982, *12* (3), 359–367.

(541) González, P.; Recio, F. J.; Ribera, D.; González, O.; DaSilva, P.; Herrasti, P.; Avila-Rodriguez, M. In *Mass Transfers-Advanced Aspects*; InTech, 2011; pp 439–460.

(542) George, M. T.; Vaidyan, V. K. *J. Cryst. Growth.* 1981, *53* (2), 300–304.

Synthèses éco-compatibles des solvants biosourcés pour l'industrie des peintures et revêtements

(Résumé de thèse)

Tableau de contenu

INTRODUCTION

Les solvants sont des liquides capables de dissoudre, de suspendre ou d'extraire d'autres composés. Ils sont principalement utilisés dans les procédés d'extraction, les synthèses chimiques, les procédés de nettoyage et la formulation de produits commerciaux, tels que les adhésifs, les produits ménagers, les peintures et les revêtements.

Dans l'industrie des peintures et revêtements, les solvants sont essentiels car ils permettent la dissolution et la dispersion des pigments, des liants et des additifs. Ainsi, l'utilisation des solvants permet d'obtenir une formulation de peinture avec une viscosité adéquate, facile à appliquer sur le support. Une fois que la peinture ou le revêtement est appliqué, le solvant s'évapore pour laisser un film continu sur la surface.

Les solvants traditionnels sont actuellement produits à partir de ressources pétrochimiques. Actuellement, l'Union européenne encourage le remplacement de ces solvants par des alternatives plus écologiques issues de la biomasse. En effet, la biomasse permet de synthétiser des produits présentant une empreinte carbone plus faible ce qui pourrait avoir un impact positif sur l'économie à long terme.

Ce travail de thèse a été développé dans le cadre du projet européen ECOBIOFOR (ECOpaint BIO-FORmulations, FP7 / 2007-2013) [Grant Agreement no 605215]). L'objectif de ce projet est de développer et de produire des solvants biosourcés par des voies de production chimique et biotechnologique simples. Ces solvants pourront posséder soit une structure identique aux solvants existants (avec une empreinte carbone plus faible en raison d'une nouvelle voie de production éco-compatible), soit une structure différente mais n'émettant pas de composés organiques volatiles car ils pourront réagir dans la formulation pour aboutir à un film sec de peinture (http://ecobiofor.eu/Home).

Afin d'atteindre les objectifs du projet européen, un consortium multidisciplinaire a été mis en place. Il est composé de :

- 5 associations de PME: Asociación Española de Bioempresas (ASEBIO, Espagne), Associação Portuguesa de Bioindústrias (APBIO, Portugal), Swiss Biotech Association (SBA, Suisse), Consorzio per la Promozione dei Prodotti Vernicianti e Ricopenti (PROCOAT, Italie), Conseil Européen de l'Industrie des Peintures, Encres d'Imprimerie et des Couleurs d'Art (CEPE, Belgique),
- 3 entreprises : Stéarinerie Dubois Fils (France), Castellano Peintures (France), Industrias Químicas Irurena (Espagne),
- 3 partenaires scientifiques (R&D) : Fundación Tecnalia Research & Innovation (Espagne, coordinateur), Institut Universitari De Cienca i Tecnologia (IUCT, Espagne), Institut National Polytechnique de Toulouse (Laboratoire de Chimie Agro-industrielle, LCA, France).

Résumé de thèse

Dans le cadre de ce projet européen, une partie des recherches a été développée au Laboratoire de Chimie Agro-industrielle (INP-LCA de Toulouse), dont le rôle était de mettre au point de nouvelles voies de synthèse vertes de l'acétate d'éthyle, de l'acétate de butyle et de la méthyl éthyl cétone à partir de la biomasse. Les solvants synthétisés répondront aux critères requis pour remplacer les solvants pétrochimiques traditionnels dans les formulations de peintures et de revêtements car ils auront les mêmes propriétés physico-chimiques.

Ces solvants ont été choisis car ils sont considérés comme faisant partie des solvants les moins toxiques présentant un risque faible pour la santé, selon la *Food and Drug Administration* (FDA).[1] De plus, ces solvants sont facilement biodégradables selon l'Agence européenne des produits chimiques (ECHA).[2–4]

Dans ce travail de thèse, nous nous sommes donc fixés comme objectifs principaux de :

- synthétiser l'acétate d'éthyle, l'acétate de butyle et la méthyl éthyl cétone à partir de synthons bio-sourcées,
- produire ces solvants selon un procédé éco-compatible, en utilisant des conditions réactionnelles douces et respectant autant que possible les principes de la chimie verte. Dans ce contexte, nous viserons notamment une économie d'atome maximum, un nombre d'étapes de réaction réduit, l'utilisation de catalyseurs faciles à séparer et/ou recycler et une production de déchets minimum.

Ce manuscrit est composé de 4 chapitres :

Le premier chapitre présente un aperçu de l'utilisation de solvants dans l'industrie des peintures et des revêtements et décrit les propriétés que ces solvants doivent posséder pour être incorporés dans des formulations. Comme la plupart des solvants utilisés ont des effets négatifs sur l'environnement et la santé, des mesures ont été prises pour réglementer leur utilisation. Des solvants alternatifs, tels que des solvants biosourcés, ont été développés pour les remplacer. Dans ce contexte, à la fin de ce chapitre, nous proposons les synthons biosourcés à partir desquels l'acétate d'éthyle, l'acétate de butyle et la méthyl éthyl cétone, pourraient être synthétisés.

Le deuxième chapitre s'intéresse au développement des synthèses des acétates d'éthyle et de butyle selon les principes de la chimie verte. Ce travail a été publié dans le journal *Green and Sustainable Chemistry*. Dans cet article, le développement d'un procédé de coproduction innovant des esters ciblés est décrit. De plus, les acétates synthétisés ont été caractérisés et testés dans deux formulations de revêtement de laques de nitrocellulose et de vernis de polyuréthane.

Dans le troisième chapitre, les synthèses des acétates développées précédemment sont évaluées d'un point de vue environnemental selon deux approches : le calcul des indicateurs de la chimie verte (*green metrics*) et l'analyse du cycle de vie (ACV). Ces travaux ont été publiés dans la revue scientifique *International Journal of Life Cycle Assessment*. Le bénéfice de l'utilisation d'alcools biosourcés en tant que réactif (remplaçant les molécules pétrochimiques correspondantes) est étudié.

Le dernier chapitre aborde l'étude de la synthèse de la méthyl éthyl cétone par décarboxylation de l'acide lévulinique issu de la biomasse. Un système sel d'argent/persulfate de potassium est utilisé pour cette réaction. Nous avons alors étudié l'évolution des espèces chimiques à base d'argent impliquées dans la réaction grâce à plusieurs techniques spectroscopiques (résonnance magnétique nucléaire du solide, diffraction des rayons X, spectrométrie photoélectronique X, spectroscopie Auger et microscope électronique à balayage couplé à la microanalyse X) afin de mieux comprendre le mécanisme de cette réaction et d'améliorer le rendement de conversion et de réaction. Ce travail a été soumis au *Journal of American Chemical Society*.

CHAPITRE I. L'industrie des peintures et des revêtements : de la pétrochimie aux solvants biosourcés

Depuis la préhistoire jusqu'au Moyen-Age, les peintures ne contenaient aucun solvant. Peu à peu, leur incorporation est apparue nécessaire pour faciliter l'application de la peinture. Le premier solvant utilisé était l'essence de térébenthine issue de conifères. Bien que ce solvant fournisse des formulations de peinture adéquates, il fut rapidement remplacé par des solvants pétrochimiques plus compétitifs d'un point de vue économique.

Aujourd'hui, le secteur des peintures et des revêtements est le principal consommateur de solvants (Figure 1). Ils sont notamment utilisés dans les formulations à base de solvants organiques. Ils peuvent être aussi incorporés dans des formulations aqueuses (jusqu'à 20% de la composition).

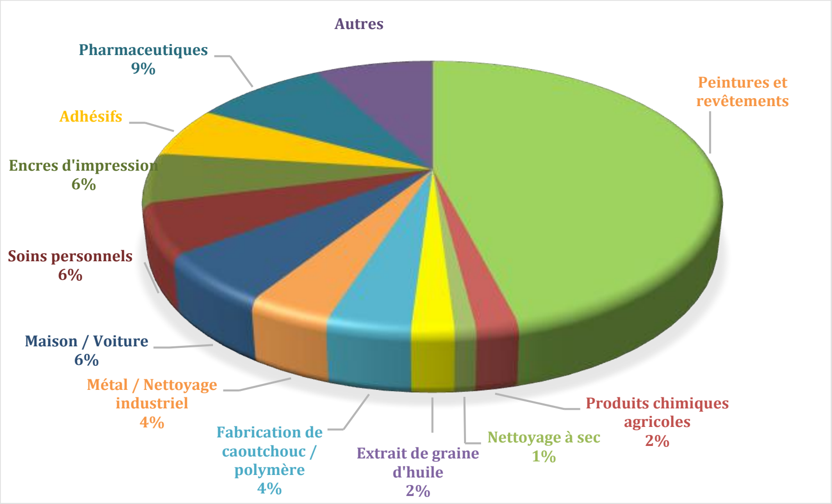


Figure 1. Industrie des solvants en Europe[5]

L'utilisation de solvants dans les peintures et les revêtements permet d'obtenir des formulations homogènes ayant des temps de séchage et des viscosités adaptés à leur procédé d'application. Il est également nécessaire d'évaluer d'autres propriétés pour les solvants :

- des propriétés physico-chimiques (indice de réfraction, couleur, densité, point d'ébullition, pression de vapeur, taux d'évaporation et pouvoir solvant) afin de garantir les bonnes performances de la peinture,

- des propriétés liées à l'Hygiène, la Sécurité et l'Environnement afin de s'assurer de l'innocuité du solvant et de son faible impact sur l'environnement.

Néanmoins, les solvants sont généralement une source importante d'émissions de Composé Organiques Volatiles (COV), qui ont un impact négatif sur la santé et l'environnement puisqu'ils contribuent à la formation de gaz à effet de serre dont l'ozone. En conséquence, de nouvelles réglementations sont apparues pour réguler leur utilisation (REACH, directive 2010/75/ UE et directive 2004/42 / CE en Europe) et ont conduit les entreprises à rechercher des solvants alternatifs plus respectueux de l'environnement et de la santé. Parmi les alternatives plus vertes, les fluides supercritiques, les liquides ioniques, les solvants eutectiques profonds, les polymères liquides, les solvants fluorés et les solvants dérivés de la biomasse sont apparus sur le marché des solvants.

Les acétates d'éthyle et de butyle ainsi que la méthyl éthyl cétone, sont parmi les solvants les plus couramment utilisés dans l'industrie des peintures et des revêtements, car ce sont des solvants faiblement toxiques et facilement biodégradables. Ces solvants sont produits industriellement à partir de ressources fossiles en utilisant des catalyseurs homogènes, sources de déchets, et les conditions de réaction et de purification énergivores. Afin de remplacer ces molécules d'origine pétrochimique sans développer des molécules innovantes non enregistrées dans REACH, nous avons envisagé de produire les mêmes structures chimiques à partir des synthons biosourcés selon de nouveaux procédés verts. Nous pourrons par exemple utiliser des catalyseurs hétérogènes au lieu de catalyseurs homogènes généralement utilisés dans les procédés classiques. Ceux-ci seront en effet faciles à séparer du milieu réactionnel et pourront être recyclés.

Afin de sélectionner les molécules plateformes d'origine naturelle à partir desquels nous pourrons synthétiser l'acétate d'éthyle, l'acétate de butyle et la méthyl éthyl cétone, nous avons entrepris des analyses rétrosynthétiques. Celles-ci nous ont permis d'identifier de nouvelles voies de synthèses des molécules cibles.

L'acétate d'éthyle peut par exemple être obtenu à partir d'éthanol et d'acide acétique ou d'anhydride acétique par réaction d'estérification (Schéma 1).

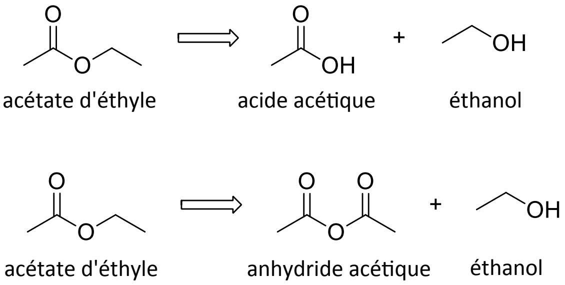


Schéma 1. Voies de synthèse proposées pour la production d'acétate d'éthyle

L'acétate de butyle peut être synthétisé à partir de *n*-butanol et d'acide acétique ou d'anhydride acétique (Schéma 2).

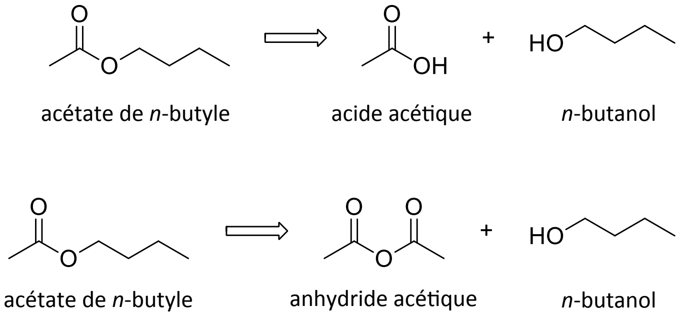


Schéma 2. Voies de synthèse proposées identifiées pour la production d'acétate de butyle

La méthyl éthyl cétone peut être produite à partir de l'acide lévulinique issu de la biomasse par une réaction de décarboxylation (Schéma 3).

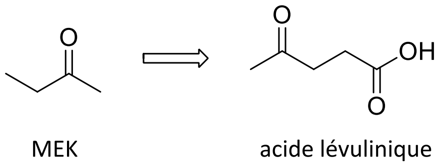


Schéma 3. Voie de synthèse proposée pour la production de la méthyl éthyl cétone

Parmi les synthons sélectionnés, certains tels que l'éthanol, le butanol, l'acide acétique et l'acide lévulinique, sont disponibles sur le marché actuel en version biosourcée. Ils pourront être utilisés pour le développement des synthèses décrites dans les chapitres suivants.

CHAPITRE II. Développement des synthèses éco-compatibles d'acétates d'éthyle et de butyle

2.1 Introduction

Les acétates d'éthyle et de butyle sont des solvants largement utilisés dans l'industrie alimentaire, la parfumerie, l'imprimerie, l'industrie pharmaceutique mais également dans l'industrie des peintures et des revêtements. Ces solvants ont des qualités qui les rendent intéressants pour ces deux dernières applications. On peut citer en particulier leur capacité à sécher rapidement, leur odeur de faible intensité et leur faible toxicité.
Ils sont produits principalement à partir de sources pétrochimiques. Les procédés de production actuellement utilisés impliquent l'utilisation d'acide sulfurique et d'acide *p*-toluènesulfonique (APTS) en tant que catalyseurs homogènes. Or, ces acides peuvent entrainer la corrosion des équipements, des problèmes de purification du produit et génèrent des déchets liés à leur traitement. Par conséquent, le premier objectif de notre travail a été de développer des procédés de synthèse des acétates à partir d’alcools biosourcés en respectant les principes de la chimie verte.
Ainsi, le chapitre II présente la mise de ces procédés de synthèse, dans lesquels le catalyseur homogène est remplacé par un catalyseur hétérogène. Deux voies de synthèse ont été étudiées pour chacun des acétates : la première utilise l'acide acétique et la seconde l'anhydride acétique.

Ces deux études nous ensuite permis de proposer un procédé innovant de coproduction d'acétates cibles. Ce procédé facilite la purification des molécules visées et évite la production de déchets et de coproduits. Ce travail a abouti à une première publication scientifique publiée dans le journal *Green and Sustainable Chemistry*.

Les solvants synthétisés ont finalement été évalués dans deux formulations de revêtement : une laque à base de nitrocellulose et un vernis à base de polyuréthane. Ces travaux ont été réalisés conjointement avec nos partenaires TECNALIA (Espagne) et Industrias Químicas IRURENA (PME, ESPAGNE, experts en revêtements de bois).

2.2 Etat de l’art sur les procédés de production actuels

2.2.1 Les procédés de production de l’acétate d'éthyle (EAc)

La production mondiale d'acétate d'éthyle a dépassé 3 millions de tonnes en 2012.[6] De nos jours, l'acétate d'éthyle est synthétisé en utilisant des ressources pétrochimiques à partir de trois procédés de production différents :

1. La réaction d'estérification de Fischer qui consiste en l'estérification de l'acide acétique avec un excès d'éthanol en présence d'un catalyseur homogène, généralement de l'acide sulfurique ou de l'acide *p*-toluènesulfonique.[7]
2. La réaction de Tishchenko qui fait intervenir deux molécules d'acétaldéhyde en présence d'une base alcoxyde comme catalyseur.[8]
3. L'addition d'acide acétique sur l'éthylène (procédé AVADA) en présence d'un hétéropolyacide phosphotungstique en tant que catalyseur (supporté sur de la silice).[9]

2.2.2 Les procédés de production de l'acétate de butyle (BAc)

LE seul procédé industriel de production de l'acétate de butyle implique la réaction d'estérification de Fisher entre l'acide acétique glacial et le *n*-butanol, en présence d'acide sulfurique concentré comme catalyseur homogène.[10 11]

Le produit obtenu est cependant difficile à purifier en raison de la présence d'azéotropes multiples avec l'eau et le butanol non transformé. Afin de surmonter ces difficultés, la distillation réactive est devenue une alternative intéressante faisant l'objet de nombreuses simulations[12–16] et de quelques rares cas d'études expérimentales en raison de la complexité du procédé.[17–19]

Les procédés industriels actuels de production d'acétates d'éthyle et de butyle présentent divers inconvénients, principalement liés à la toxicité des réactifs, à l'utilisation de catalyseurs homogènes et à la nécessité de mettre en œuvre plusieurs étapes de distillation pour une séparation efficace des esters.

Dans ces travaux de thèse, nous proposons le remplacement de catalyseurs homogènes par des catalyseurs hétérogènes tels que des résines échangeuses d'ions acides qui aboutissent à un procédé plus vert (Tableau 1) :

Tableau 1. Avantages des résines échangeuses d'ions par rapport aux catalyseurs homogènes

Procédé de production actuel	Proposition alternative
• Catalyseur: H_2SO_4 or *p*-TSA. • Séparation difficile du catalyseur et du produit : au cours de la réaction, les produits et les réactifs sont dans la même phase homogène et la séparation des produits nécessite d'une ou plusieurs distillations.	• Catalyseur hétérogène : résines échangeuses d'ions. • Les produits sans catalyseur peuvent être obtenus par simple filtration.
• Post-traitements lourds : l'élimination des déchets comprenant la neutralisation de l'effluent acide-aqueux.	• Le catalyseur peut être récupéré facilement par simple filtration.
• Récupération de catalyseur : la récupération de l'acide implique une grande dépense énergétique, une distillation à haute température est nécessaire.	• Recyclage: la résine échangeuse d'ions peut être réutilisée dans plusieurs cycles de réaction sans régénération.
• Corrosion de l'équipement.	• Un équipement spécial résistant à la corrosion n'est pas nécessaire.

Pour cette étude, quatre résines ont été sélectionnées comme catalyseurs dans les synthèses des acétates : l'Amberlyst 15 (A15), l'Amberlyst 16 (A16), l'Amberlyst 36 (A36) en tant que résines macroporeuses et la Dowex 50WX8 (D50) en tant que résine gel.

Pour la production d'acétate d'éthyle, deux voies de synthèse ont été étudiées. Le premier utilise l'acide acétique et l'éthanol (qui peuvent être bio-sourcés) en présence d'une résine acide (Schéma 4).

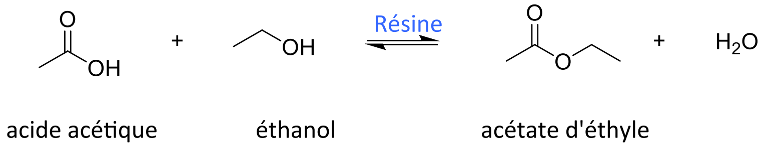


Schéma 4. Synthèse d'acétate d'éthyle à partir d'éthanol et d'acide acétique.

La deuxième méthode utilise de l'anhydride acétique à la place de l'acide acétique (Schéma 5).

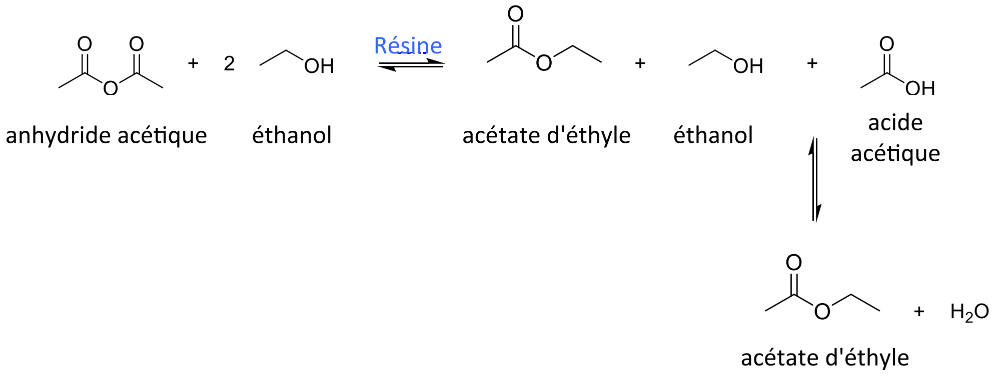


Schéma 5. Synthèse d'acétate d'éthyle à partir d'éthanol et d'anhydride acétique

Pour la production d'acétate de *n*-butyle, la même méthodologie a été appliquée en remplaçant l'éthanol par du butanol (schémas 6 et 7).

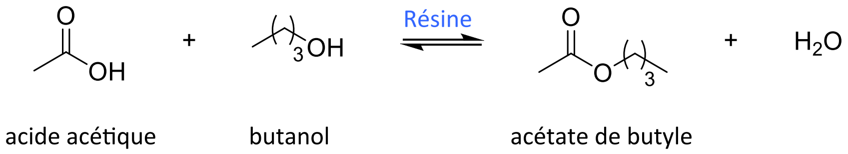


Schéma 6. Synthèse de l'acétate de butyle à partir du n-butanol et de l'acide acétique.

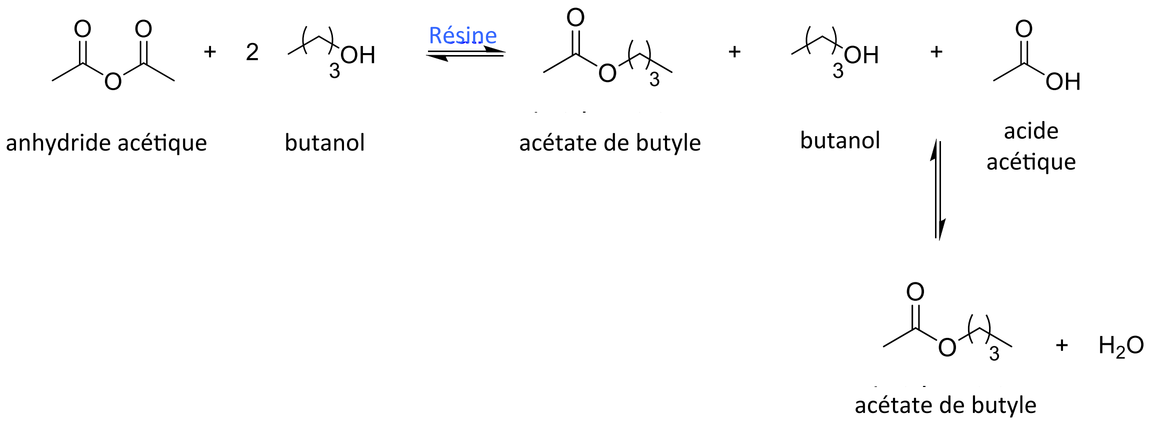


Schéma 7. Synthèse de l'acétate de butyle à partir du n-butanol et de l'anhydride acétique.

2.3 Un nouveau procédé utilisant des résines échangeuses d'ions pour la coproduction d'acétates d'éthyle et de butyle

2.3.1 Etude de la synthèse de l'acétate d'éthyle avec différentes résines échangeuses d'ions

Pour réaliser la réaction entre l'éthanol et l'acide acétique, un rapport molaire de 1:1 a été utilisé. Dans le cas de la réaction de l'éthanol avec l'anhydride acétique, le rapport molaire éthanol:anhydride acétique a été fixé à 2:1 pour respecter la stœchiométrie de la réaction (Schéma 4). Les deux réactions ont été effectuées à 80 °C avec une charge de catalyseur de 5 % massique par rapport à l'éthanol.

Une étude cinétique a été réalisée pour les deux voies de synthèse en présence des quatre résines. L'équilibre de la réaction a été atteint plus rapidement avec l'anhydride acétique. Pour les résines macroporeuses A15, A16 et A36, l'équilibre a été atteint après 90 min avec de l'anhydride acétique et après 180 min avec de l'acide acétique. Dans le cas de la résine Dowex 50WX8, la réaction s'est révélée plus rapide : 60 min avec l'anhydride acétique contre 90 min avec l'acide acétique.
La conversion de l'éthanol et le rendement en acétate d'éthyle ont été déterminés par chromatographie en phase gazeuse. Des conversions et des rendements plus élevés (environ 80 %) ont été obtenus pour les réactions à partir de l'anhydride acétique comparativement aux réactions avec l'acide acétique (environ 69 %).

- **Effet de la température de réaction sur la conversion de l'éthanol**

L'effet de la température sur la vitesse de réaction a été étudié à 40, 50, 65 et 80 °C. La vitesse de réaction augmente avec la température (Figure 2a), quelle que soit la résine utilisée.

L'énergie d'activation apparente de la réaction (Ea) a été déterminée pour toutes les résines, grâce à l'équation d'Arrhenius appliquée sur les données initiales obtenues (Figure 2b), la réaction d'estérification étant une réaction de second ordre.

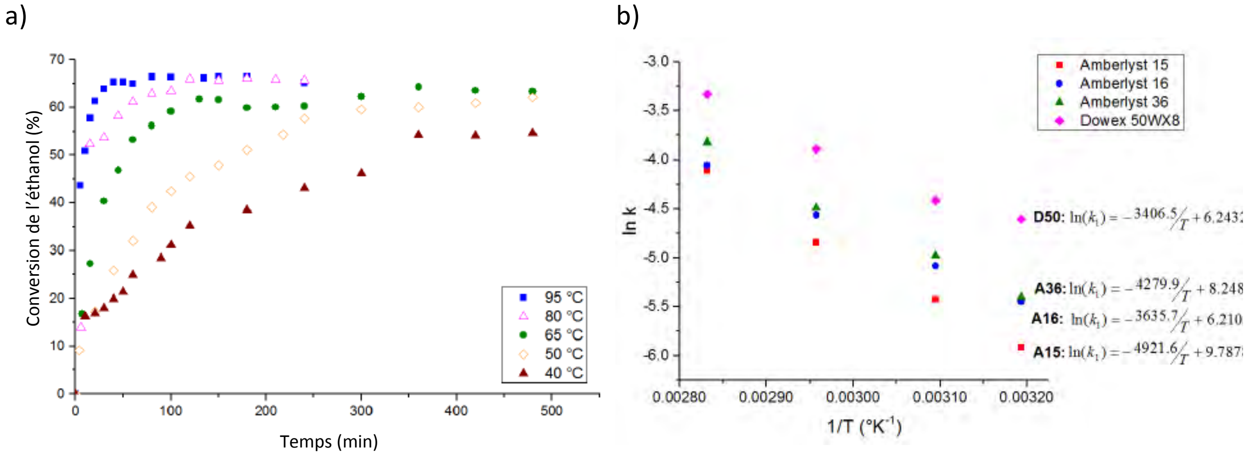


Figure 2. a) Effet de la température sur la conversion de l'éthanol avec la résine Dowex 50WX8, b) Détermination de l'énergie d'activation de la réaction (second ordre).

L'énergie d'activation (Ea) la plus élevée a été obtenue avec l'Amberlyst 15 (40,9 kJ · mol^{-1}), suivie par l'Amberlyst 36 (35,5 kJ · mol^{-1}) et l'Amberlyst 16 (30,1 kJ · mol^{-1}). La plus faible valeur a été obtenue avec la résine Dowex 50WX8 : 28,3 kJ · mol^{-1}.

Sur la base de ces résultats, la résine Dowex 50WX8 a été considérée comme la plus efficace pour la production de l'acétate d'éthyle.

- **Effet de la quantité de catalyseur (Dowex 50WX8) et de son recyclage**

L'influence de la quantité de catalyseur (2,5%, 5% et 10 % massique par rapport à l'éthanol), sur le rendement en acétate d'éthyle à l'équilibre a été évaluée en utilisant un rapport molaire éthanol:anhydride acétique de 2:1.

L'analyse statistique (ANOVA et test de Tukey) a montré que l'utilisation de 5% de catalyseur est suffisante pour obtenir des rendements maximum en acétate.

La réutilisation de la résine Dowex 50WX8, sans régénération intermédiaire, a également été évaluée pendant quatre cycles de réactions consécutives. L'analyse de variance (ANOVA) a montré qu'il n'y avait pas de différence significative sur les résultats (α = 0,05, p = 0,073), démontrant ainsi que le recyclage de la résine est envisageable.

2.3.2 Etude de la synthèse de l'acétate de *n*-butyle avec diverses résines échangeuses d'ions

Après avoir étudié la synthèse de l'acétate d'éthyle, nous avons décidé d'évaluer les résines échangeuses d'ions comme catalyseur lors de la production de l'acétate de butyle (BAc).

Les réactions ont été réalisées à 100 °C et l'évolution de la composition du milieu réactionnel a été suivie pendant 4 h. Comme pour la production d'acétate d'éthyle, les meilleurs résultats ont été obtenus avec le *n*-butanol et l'anhydride acétique en tant que réactifs et la résine Dowex 50WX8 en tant que catalyseur. La conversion du butanol et le rendement en acétate de butyle sont plus élevés lorsque l'acide anhydride est utilisé à la place de l'acide acétique (80% *vs* 70%).

- **Effet de la température de réaction sur la conversion du *n*-butanol**

L'effet de la température sur la conversion du *n*-butanol a également été étudié entre 50 °C et 100 °C. La vitesse de réaction augmente avec la température, la conversion la plus rapide étant observée à 100 °C (Figure 3).

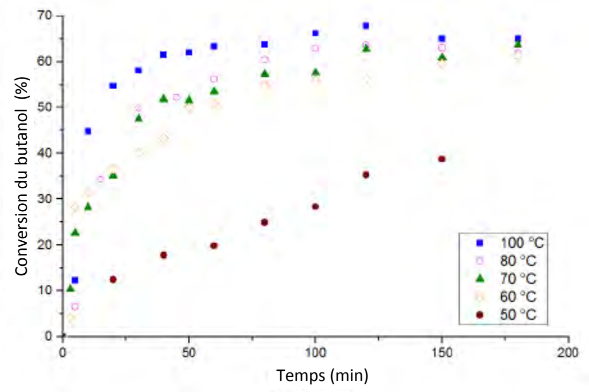


Figure 3. Effet de la température sur la conversion du *n*-butanol déterminée par CPG

2.3.3 Coproduction d'acétate d'éthyle et de *n*-butyle

Etant donné que l’acétate d’éthyle est difficile à purifier en raison de la formation d'azéotropes avec l'eau et l’alcool, une stratégie de coproduction d'acétates a été adoptée (Figure 4).

- **1ère étape** : la réaction de l'anhydride acétique avec l’éthanol (1:1), en présence de la résine échangeuse d'ions Dowex 50WX8, génère de l'acétate d'éthyle et de l'acide acétique en quantité stœchiométrique. En raison de l’absence d’eau, l'acétate d'éthyle est facilement séparé du mélange réactionnel par simple distillation.

- **2nd étape** : cette étape met en jeu l’addition du *n*-butanol sur le milieu réactionnel de la première étape obtenu après la distillation (contenant de l’acide acétique et la résine échangeuse d’ions). L’acétate de *n*-butyle est ainsi produit.

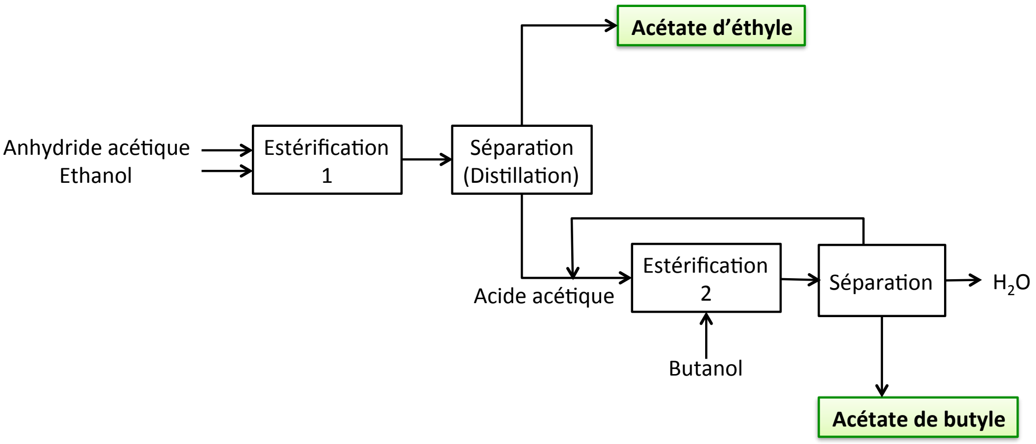


Figure 4. Procédé de coproduction d'acétates d'éthyle et de butyle

2.3.3.1 Résultats de la première étape de la coproduction

La synthèse de l'acétate d'éthyle à partir de l'éthanol et de l'anhydride acétique (rapport molaire de 1:1), aboutit à un rendement et une conversion très élevés (Tableau 2). La production d'eau étant très faible, la purification de l'acétate d'éthyle est réalisée par simple distillation.

Tableau 2. Composition du mélange réactionnel brut et de l'acétate d'éthyle purifié (conditions de réaction : éthanol/anhydride acétique 1:1, température ambiante, 4 h).

	Conversion EtOH (%)	Rendement en EAc (%)	Composition du milieu réactionnel (% m/m)			
			AcOH	EtOH	EAc	H_2O
À la fin de la réaction	99,4	98	40,1	0,2	59,0	0,7
Après la distillation	100	87	6,7	0,0	92,1	1,2

2.3.3.2 Résultats de la deuxième étape

Suite à la distillation du milieu réactionnel de la première estérification, un mélange d'acide acétique (AcOH) et d'acétate d'éthyle (77,5% et 22,5 % m/m) reste dans le réacteur avec la résine. L'ajout de *n*-butanol dans le réacteur permet d'obtenir de l'acétate de *n*-butyle. L'équilibre de la réaction est déplacé par élimination de l'eau en continu : du cyclohexane est ajouté en faible quantité dans le milieu réactionnel formant ainsi un azéotrope avec l'eau, que l'on distille au fur et à mesure de la réaction. L'acétate de *n*-butanol est finalement purifié par distillation (Tableau 3).

Tableau 3. Composition de l'acétate de butyle purifié obtenu avec le procédé de coproduction.

Conversion de BuOH (%)	Rendement en BAc (%)	Composition du milieu réactionnel						
		%	AcOH	BuOH	EtOH	BAc	EAc	H_2O
94	69	m/m	0,1	1,9	0,0	97,1	0,2	0,6

Le nouveau procédé de coproduction proposé permet de produire de l'acétate d'éthyle et de l'acétate de butyle avec d'excellents rendements, sans générer de déchets. Le recyclage de la résine est également possible.

Ce nouveau procédé a été mise en œuvre en utilisant du bioéthanol fourni par la société espagnole ABENGOA. Par contre, nous n'avons pas pu utiliser du biobutanol car aucune société n'était alors en mesure d'en fournir.

L'acétate d'éthyle a été produit à une échelle pilote (20L) pour des tests en formulation de peinture et revêtement. Une quantité de 5L d'acétate de butyle a également été synthétisée pour ces tests.

2.4 Caractérisation des acétates d'éthyle et de butyle synthétisés selon le procédé de coproduction

Les esters obtenus lors du procédé de coproduction ont ensuite été purifiés afin de répondre aux exigences des formulateurs de peintures et de revêtements : les quantités d'acide acétique et d'eau doivent être inférieures à 0.1%.

L'acide acétique a été neutralisé à l'aide d'hydroxyde de potassium, en quantité équimolaire par rapport à celui-ci. L'eau a été éliminée grâce à du tamis moléculaire 3A (20% m/v du solvant, 48h).

La composition des acétates après neutralisation et séchage est indiquée dans les tableaux suivants :

Tableau 4 Composition de l'acétate d'éthyle (% massique) après neutralisation (KOH) et séchage sur tamis moléculaire 3A.

Composition de l'acétate d'éthyle	AcOH (% w/w)	EtOH (% w/w)	EAc (% w/w)	H_2O (% w/w)
Après distillation	6,7	0,0	92,1	1,2
Après neutralisation et séchage	0,0	0,0	99,93	0,07

Tableau 5. Composition d'acétate de butyle (% massique) après neutralisation (KOH) et séchage sur des tamis moléculaire 3A.

Composition de l'acétate de butyle (BAc)	AcOH (% w/w)	BuOH (% w/w)	BAc (% w/w)	H_2O (% w/w)
Après distillation	0,4	1,1	97,4	1,1
Après neutralisation et séchage	0,0	1,5	98,1	0,4

Tableau 6. Composition de l'acétate de butyle issue du procédé de coproduction (% massique) après neutralisation (KOH) et séchage sur tamis moléculaire 3A.

Composition de l'acétate de butyle de la coproduction	AcOH (% w/w)	BuOH (% w/w)	EtOH (% w/w)	BAc (% w/w)	EAc (% w/w)	H_2O (% w/w)
Après distillation	0,1	1,9	0,0	97,1	0,2	0,6
Après neutralisation et séchage	0,0	5,5	0,0	94,2	0,2	0.03

La neutralisation par KOH et le séchage sur tamis moléculaire ont permis de satisfaire aux exigences des formulateurs pour l'utilisation des acétates d'éthyle et de butyle dans les formulations de peinture et de revêtement.

Des analyses structurales de RMN et de FTIR ont ainsi été effectuées. Ces analyses sont conformes aux données de la littérature.
Les paramètres de solubilité de Hansen ont également été déterminés. Les paramètres expérimentaux se sont révélés identiques à ceux des acétates pétrochimiques.

2.5 Validation des performances des acétates d'éthyle et de butyle synthétisés dans des formulations de revêtement à base de solvant

Les acétates produits dans la coproduction ont ainsi été utilisés et évalués dans des laques de nitrocellulose et des vernis polyuréthanes préparés par TECNALIA (Espagne). Ces formulations ont été comparées avec leurs formulations commerciales respectives fournies par Industrias Quimicas Irurena, SA (Espagne). Différentes propriétés ont été déterminées, telles que la viscosité, le comportement de formation du film et les performances incluant la dureté, le gloss et l'adhérence au substrat.

2.5.1 Dans des laques de nitrocellulose (NC)

Les résultats obtenus à partir de l'évaluation des acétates synthétisés dans la formulation de laque de nitrocellulose NC-Formulation ECOBIOFOR sont résumés dans le tableau suivant (Tableau 7) :

Tableau 7. Évaluation des acétates synthétisés dans une formulation de laque de nitrocellulose

Propriétés évaluées		NC- Formulation ECOBIOFOR	NC- Formulation commerciale
Viscosité en secondes (Ford No4. Efflux Cup)		70 s	63 s
Formation de film (Bois Sapelly)			
1ère couche et 2ème couche		Temps de séchage : ✓ 45 minutes ✓ 24 h	Temps de séchage : ✓ 45 minutes ✓ 24 h
Brillance à l'angle du réflectomètre (UB)	60° (verre)	70	65
	85° (verre)	90	82
	60° (bois)	37-39	39-40
	85 ° (bois)	48-50	47-48
Mouillage et adhérence selon l’évaluation « coupe transversale »	Bois (Sapelly)	 **Class 0-1**	 **Class 0-1**
	Métal (acier/carbone)	 **Class 0**	 **Class 0**
	Plastique (PVC)	 **Class 0**	 **Class 0**

Des résultats similaires ont été obtenus entre la formulation ECOBIOFOR et la formulation commerciale, ce qui confirme l’efficacité des solvants synthétisés en tant que substituants de leur équivalents pétrochimiques. Les traces d'eau présentes dans les acétates d'éthyle et de butyle synthétisés n'ont pas eu de conséquences sur les propriétés du film.

2.5.2 Dans des formulations de vernis polyuréthane (PU)

Comme dans le cas des formulations de laques de nitrocellulose, nous avons obtenu ici des résultats équivalents entre les formulations PU-ECOBIOFOR et commerciales (Tableau 8).

Tableau 8. Évaluation des acétates synthétisés dans une formulation de vernis polyuréthane

Propriétés évaluées		NC- Formulation ECOBIOFOR	NC- Formulation commerciale
Viscosité en secondes (Ford No4. Efflux Cup)		23 s	25 s
Formation de film	Bois (Sapelly)		
	Bois (Chêne)		
Temps de séchage :	1ère couche 2ème couche	✓ 10 min ✓ 2-3 h	✓ 10 min ✓ 2-3 h
Douceur en bois et bonne formation du film		✓ Bonne finition	✓ Bonne finition
Mouillage et adhérence selon l’évaluation « coupe transversale »	Bois (Sapelly)	 **Class 0-1**	 **Class 0-1**
	Métal (acier/carbone)	 **Class 0-1**	 **Class 0-1**

Les propriétés obtenues avec les deux formulations sont donc conformes aux spécifications fournies par IRURENA (Espagne).

Grâce à cette étude, nous avons pu vérifier que les solvants synthétisés avaient les mêmes propriétés dans les systèmes de revêtements que les solvants conventionnels, ce qui nous permet d'assurer la faisabilité du remplacement des solvants pétrochimiques classiques par les acétates synthétisés dans ces travaux.

2.6 Conclusion

Dans ce travail, deux voies de synthèse des acétate ont été étudiées: une utilisant l'acide acétique, l'autre l'anhydride acétique. Quatre résines échangeuses d'ions ont été testées dans le cadre de la substitution du catalyseur acide homogène (A15, A16, A36, D50WX8). La détermination de l'énergie d'activation pour chaque réaction a permis de sélectionner la résine Dowex 50WX8. De plus, l'étude paramétrique nous a permis de choisir les meilleures conditions opératoires et les réactifs les plus adaptés à la synthèse des solvants cibles.

Afin de pallier les problèmes liés à la purification des acétates, nous avons proposé un procédé innovant de coproduction qui évite l'utilisation de procédés intensifs de distillation et réduit la production de déchets. Avec ce procédé, nous avons pu produire, après distillation, de l'acétate d'éthyle et de l'acétate de butyle d'une pureté élevée, respectivement de 92,1 et 97,1 % massique.

Un procédé de coproduction d'acétates plus verts a été développé afin de répondre aux besoins des partenaires du projet ECOBIOFOR dédiés à la production de peintures et de revêtements. L'évaluation du comportement des solvants synthétisés dans les formulations de laque de nitrocellulose et de vernis polyuréthane a permis de valider les critères requis (séchage, viscosité, formation de film, brillance, mouillabilité et adhérence) dans l'objectif de remplacer les solvants pétrochimiques conventionnels dans les peintures et les revêtements.

CHAPITRE III. Évaluation environnementale de la production et de la coproduction des acétates d'éthyle et de *n*-butyle : indicateurs de la chimie verte et analyse du cycle de vie (ACV)

3.1 Introduction

L'un des aspects les plus importants de la chimie verte est l'évaluation de l'impact environnemental d'un procédé chimique, car il est ainsi plus facile de choisir l'option la plus avantageuse d'un point de vue environnemental, parmi les différentes voies de synthèse proposées.[20]

Le calcul des indicateurs de la chimie verte a été la première approche que nous avons envisagée afin d'évaluer et comparer facilement les synthèses individuelles et le procédé de coproduction développés (présentés au chapitre II). Cependant, ces indicateurs ne donnent que des informations sur le procédé lui-même sans tenir compte de l'impact du cycle de vie complet, c'est à dire les contributions d'origine et de préparation des réactifs, l'énergie utilisée pendant le procédé, et l'élimination finale du produit.

Dans le chapitre III, des généralités sur le calcul des indicateurs de la chimie verte et sur la méthodologie d'évaluation du cycle de vie sont tout d'abord présentées. Afin de déterminer quelle synthèse présente un intérêt majeur en terme d'environnement, l'évaluation du cycle de vie et le calcul des indicateurs des synthèses individuelles et du procédé de coproduction ont été réalisés. Ce travail a été publié dans International Journal of Life Cycle Assessment (DOI 10.1007/s11367-017-1317-8).

Enfin, nous avons comparé l'évaluation du cycle de vie des synthèses individuelles et du procédé de coproduction des acétates en utilisant des matières premières biosourcées (bioéthanol pour les synthèses de l'acétate d'éthyle et bio-butanol pour la production de l'acétate de butyle). Par ailleurs, les impacts environnementaux des synthèses développées ont été comparés à ceux de la production industrielle des acétates d'origine fossile.

3.2 Généralités : Évaluation de la durabilité des solvants alternatifs éco-compatibles

3.2.1 Indicateurs de la chimie verte

Les indicateurs de la chimie verte sont un moyen simple d'obtenir des informations concrètes et quantitatives sur le caractère vert d'un procédé en tenant compte des matières premières, des co-produits, des déchets et de l'énergie utilisée, de la réaction jusqu'à la purification du produit visé.[21] Les indicateurs de la chimie verte les plus étudiés sont l'économie d'atome (EA), le facteur d'impact environnemental (E-facteur) et le pourcentage de ressources renouvelables dans le cas de la synthèse de bioproduits. Leurs méthodes d'évaluation sont indiquées dans le tableau 9.

- **Economie d’atome**

Le deuxième principe de la chimie verte est lié à l'économie d’atome qui est considérée comme un des indicateurs fondamentaux.[22] L’économie d'atome est le calcul de le pourcentage massique de réactif dans le produit final.[23]

- **Facteur d'impact environnemental (E-facteur)**

D'autres moyens simples d'évaluer un procédé consistent à déterminer la production de déchets.[23] L'objectif du E-facteur est de mesurer la masse de déchets générés par rapport à la masse de produit final obtenue.

- **Pourcentage de sources renouvelables**

Le développement de voies chimiques impliquant des matières premières dérivées de ressources renouvelables est préconisée dans le cadre de la politique européenne environnementale. La teneur biosourcée des produits (PB – Norme NF EN 16785-2) exprime, comme son nom l'indique, le pourcentage de matière provenant de ressources renouvelables (utilisées dans la synthèse chimique) présente dans le produit final.[24]

Les indicateurs de la chimie verte sont liés à certains des principes proposés par Anastas et Warner,[25] comme cela est mentionné dans le tableau 9.

Tableau 9. Principaux indicateurs de la chimie verte considérés pour l'évaluation d'une nouvelle synthèse

Indicateurs de la chimie verte	Calcul	Principes
L’économie d'atome	$EA = \frac{M\ produit}{\Sigma M\ réactifs} \times 100$	2nd
Facteur environnemental (E-Facteur)	$E - facteur = \frac{\sum déchets\ (g)}{produit\ (g)}$	1st, 5th, 8th
Teneur biosourcée (TB)	$TB = \frac{masse\ de\ matière\ renouvelable\ (g)}{masse\ de\ produit\ (g)}\ x100$	7th

3.2.2 Méthode d'analyse du cycle de vie (ACV)

L'analyse du cycle de vie (ACV) a été définie dans la norme internationale ISO 14040 comme une méthode permettant de déterminer les aspects environnementaux et les impacts sur la santé humaine et l'environnement causés par la vie du produit, de l’origine de sa matière première à son élimination.[26,27] Pour mener à bien ce type d'analyse, il est nécessaire de suivre les étapes suivantes :

- La définition du système;
- La compilation d'un inventaire avec les intrants et extrants d'un système de produits;
- L'évaluation des impacts environnementaux potentiels associés à l'ensemble du cycle de vie;
- L'interprétation des résultats obtenus à partir de l'analyse de l'inventaire et des phases d’evaluation liées aux objectifs de l'étude.

Dans l'analyse du cycle de vie, l'objectif est d'évaluer l'impact potentiel dans les différentes catégories causées par les émissions et les extractions déterminées au cours de l'inventaire du cycle de vie.

Pour les procédés chimiques étudiés, l'évaluation de plusieurs indicateurs liés à leur environnement et la mise en œuvre de principes de chimie verte sont un moyen de guider le choix du procédé le plus vert entre différentes alternatives.

3.3 Étude de cas d'ACV : comparaison de différentes voies chimiques pour la production d'acétates d'éthyle et de n-butyle

3.3.1 Introduction

Afin d'évaluer d'un point de vue environnemental la voie chimique développée et présentée dans la section 2 de ce manuscrit, l'analyse du cycle de vie (ACV) a été utilisée comme outil de décision. En effet, cette méthode standardisée et précise consiste à mesurer et comparer les impacts environnementaux potentiels de ces procédé de production sur l'ensemble de leur cycle de vie, *i.e.* « du berceau à la porte du laboratoire » (dans notre cas). L'analyse du cycle de vie a été réalisée en utilisant les normes ISO 14040[28] et 1044.[29]

Dans cette étude, les synthèses indépendantes des esters (scénario 1) et de la coproduction (scénario 2) ont été modélisées, après un inventaire complet à l'échelle du laboratoire. Les résultats ont été comparés pour mettre en évidence l'intérêt de cette nouvelle voie de coproduction d'un point de vue environnemental. La production de 1 kg d'éthyle acétate ou n- butyle acétate a été choisie comme unité fonctionnelle.

Toutes les données de l'inventaire du cycle de vie ont été recueillies à partir des résultats expérimentaux à l'échelle du laboratoire. Les données d'émissions et d'extractions ont été obtenues à partir de la base de données Ecoinvent 3.1. Les impacts environnementaux ont été analysés à travers un dérivé de la méthode ILCD 2011 1.05. L'inventaire et les calculs d'impact ont été effectués sur SimaPro 8.1.1.

3.3.2 Résultats et discussion

3.3.2.1 Évaluation du cycle de vie des synthèses individuelles des acétates d'éthyle et de n-butyle

Les impacts environnementaux des réactions chimiques ont été évalués en fonction de l'unité fonctionnelle (UF) définie précédemment (1 kg de solvant purifié). Seuls les esters purifiés (acétate d'éthyle et acétate de *n*-butyle) ont été considérés dans cette étude.
Les résultats de l'évaluation de la production d'acétate d'éthyle et du butyle sont présentés dans la Figure 5.

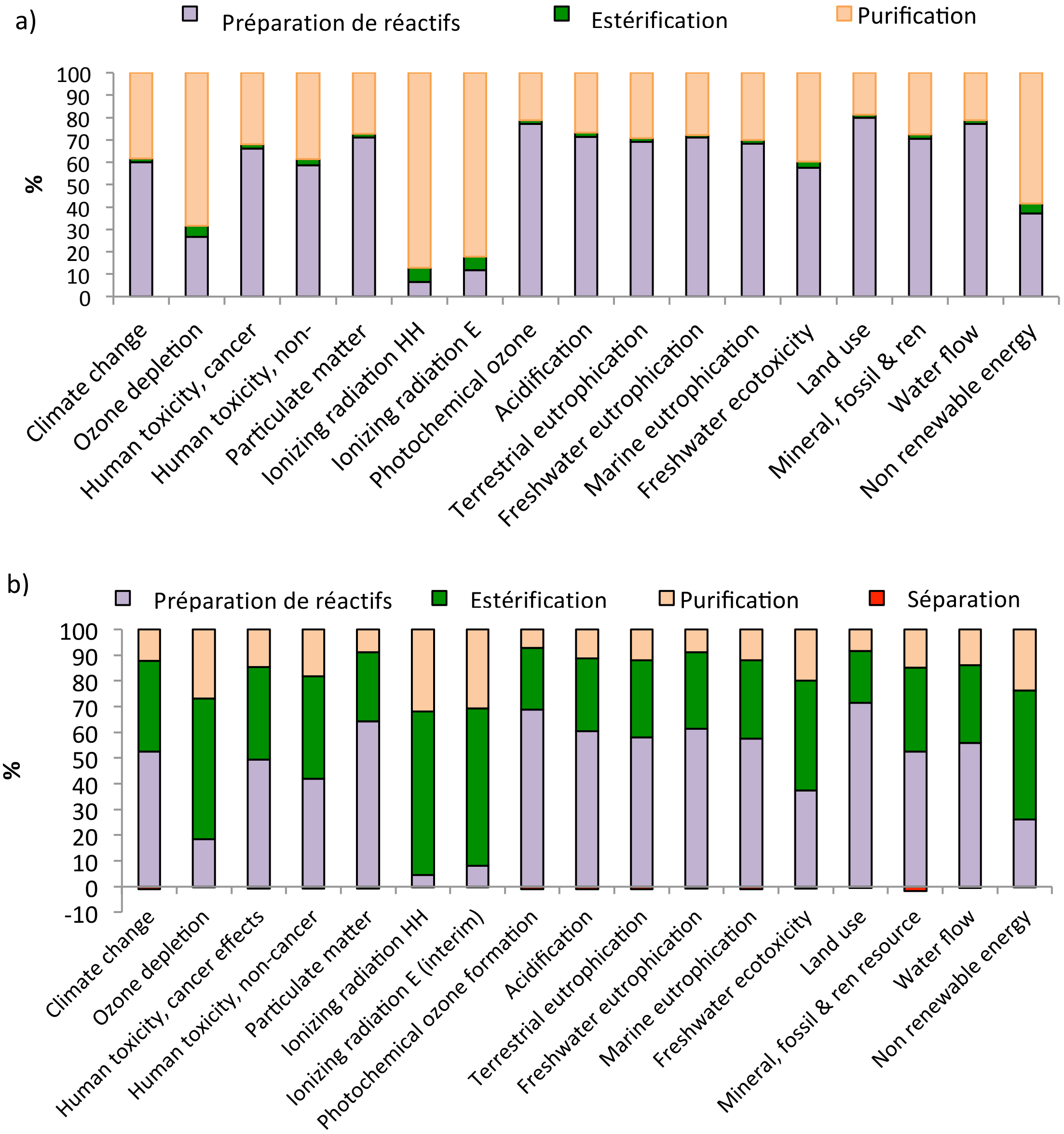


Figure 5. Evaluation des impacts de la production de a) l'acétate d'éthyle b) l'acétate de *n*-butyle - Caractérisation de l'impact par un dérivé de la méthode ILCD 2011 1.05

Dans les deux synthèses, d'acétate d'éthyle et de butyle, l'étape de préparation des réactifs est responsable de la majorité des impacts environnementaux (12 catégories d'impact sur 17), due à l'utilisation d'anhydride acétique et de *n*-butanol comme réactif.

3.3.2.2 Evaluation du cycle de vie de la coproduction d'acétates (scénario 2)

Après avoir étudié les deux estérifications séparément (scénario 1), elles ont été étudiées selon un procédé de coproduction (scénario 2) où les coproduits de la première synthèse ont été recyclés dans le second. Les dommages environnementaux produits pendant le procédé de coproduction sont indiqués dans le Figure 6.

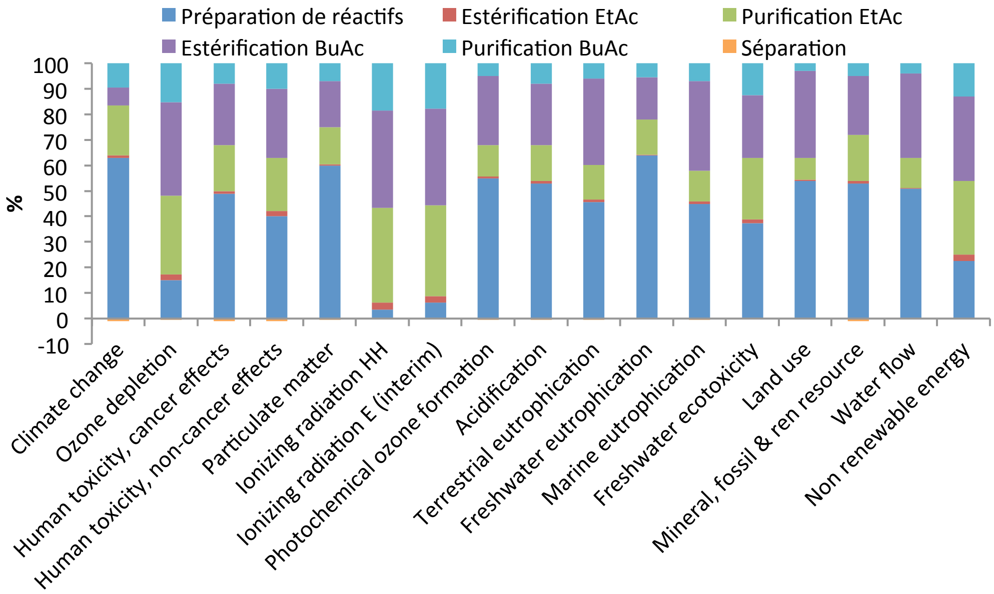


Figure 6. Evaluation des impacts du procédé de coproduction (scénario 2). Caractérisation de l'impact par un dérivé de la méthode ILCD 2011 1.05.

Les résultats obtenus pour la coproduction (scénario 2) semblent assez proches de ceux obtenus pour les estérifications indépendantes (scénario 1) : l'étape de préparation des réactifs est toujours responsable de la majorité des impacts environnementaux pour 13 catégories d'impacts.

3.3.2.3 Comparaison des synthèses individuelles (Sc 1) et du procédé de coproduction (Sc 2) des acétates d'éthyle et de n-butyle

Une comparaison entre les deux scénarios a été faite. Il convient de noter que le scénario 2 génère 1,141 kg d'acétate d'éthyle et 1 kg d'acétate de *n*-butyle; les mêmes facteurs ont été utilisés pour le scénario 1.

En fait, une comparaison plus détaillée de ces deux procédés montre que la coproduction présente les impacts environnementaux les plus faibles (Figure 7).

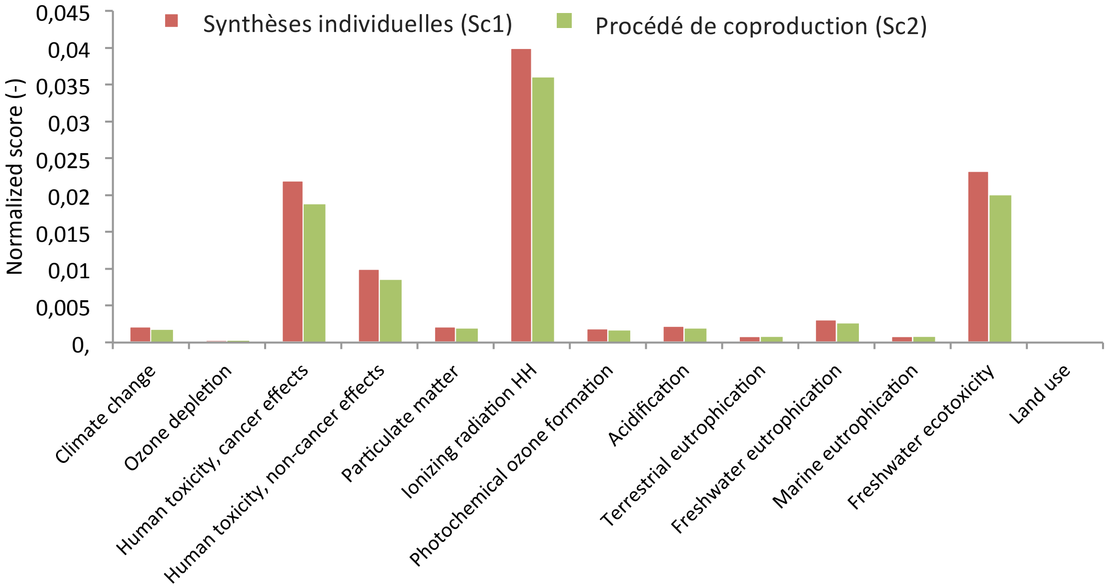


Figure 7. Comparaison entre la synthèse indépendante des acétates (Sc1) et le procédé de coproduction (Sc2). Normalisation des impacts par dérivé de la méthode ILCD 2011 1.05.

Ces résultats peuvent s'expliquer principalement par la réduction des déchets grâce à l'utilisation de l'acide acétique (coproduit pour la première estérification) dans la seconde estérification et par le recyclage de la résine échangeuse d’ions

3.3.3 Contribution de l'ACV et des indicateurs de la chimie verte

L'économie de l'atome (EA), le facteur environnemental (E-facteur) et la teneur biosourcée (TB) ont été calculés pour les synthèses individuelles et le procédé de coproduction (Tableau 10).

Tableau 10. Les indicateurs de la chimie verte pour les synthèses individuelles et le procédé de coproduction développé dans ce travail. [a]Pourcentage de sources renouvelables calculé en considérant que l'éthanol et le butanol proviennent de matières premières bio-sourcées.

Procédé	% EA	E-facteur	% TB
Acétates d'éthyle et de butyle par des synthèses individuelles	72,4	0,68	57,9[a]
Acétates d'éthyle et de butyle par le procédé de coproduction	**91,9**	**0,31**	57,9[a]

D'après les indicateurs de la chimie verte rassemblés dans le tableau 11, la voie de coproduction développée conduit à un procédé plus intéressant en terme de chimie verte par rapport aux synthèses individuelles (économie d'atome plus élevée, E-facteur plus faible).

3.4 Analyse du cycle de vie des synthèses des bio-acétates d'éthyle et de butyle a porté sur les synthèses individuelles et le procédé de coproduction.

Dans la section précédente, nous avons étudié l'impact environnemental des synthèses d'acétates en utilisant l'éthanol et le butanol commercial (d'origine pétrochimique), que l'on trouve dans la base de données Ecoivent 3.1. Dans cette section, nous nous sommes intéressés à analyser l'impact environnemental de ces synthèses, mais cette fois en considérant leur production à partir de bioéthanol et de bio-butanol, respectivement pour l'acétate d'éthyle et l'acétate de butyle.

3.4.1 Evaluation de l'utilisation des bio-alcools dans la synthèse de l'acétate d'éthyle et du butyle

Dans ce résumé, nous nous concentrons sur la présentation des résultats de la comparaison entre les synthèses individuelles et le procédé de coproduction. Dans les deux cas, l'analyse a été réalisée avec du bio-éthanol et du bio-butanol modélisées à partir du travail de Pereira parce qu'il a généré moins d'impacts sur l'environnement que d'autres sources de bioéthanol : maïs, canne à sucre, bois et canne à sucre brésilien transformé par une fermentation avec *Clostridium saccharoperbutylacetonicum* rapporté dans le travail de Pereira et *al.*[30] (Figure 8).

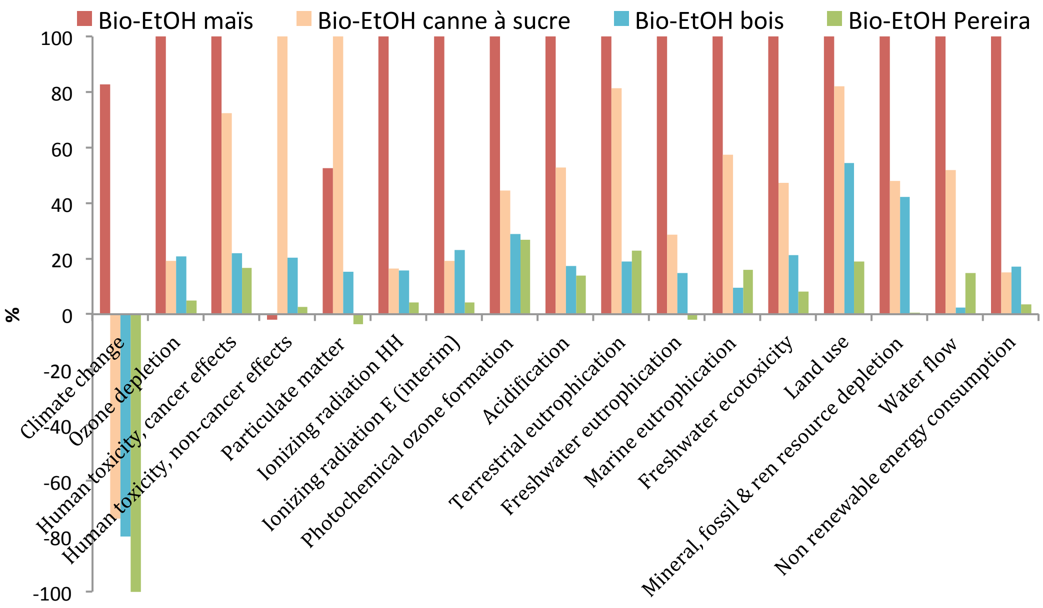


Figure 8. Analyse de sensibilité sur le choix de la source de bioéthanol. Caractérisation de l'impact par un dérivé de la méthode ILCD 2011 1.05

3.4.2 Comparaison entre les synthèses individuelles (scénario 1) et la coproduction d'acétates de bio-éthyle et de bio-butyle (scénario 2)

Il a été montré que le procédé de coproduction génère le plus faible impact sur l'environnement comparé aux synthèses individuelles, et ce, pour toutes les catégories (Figure 9).

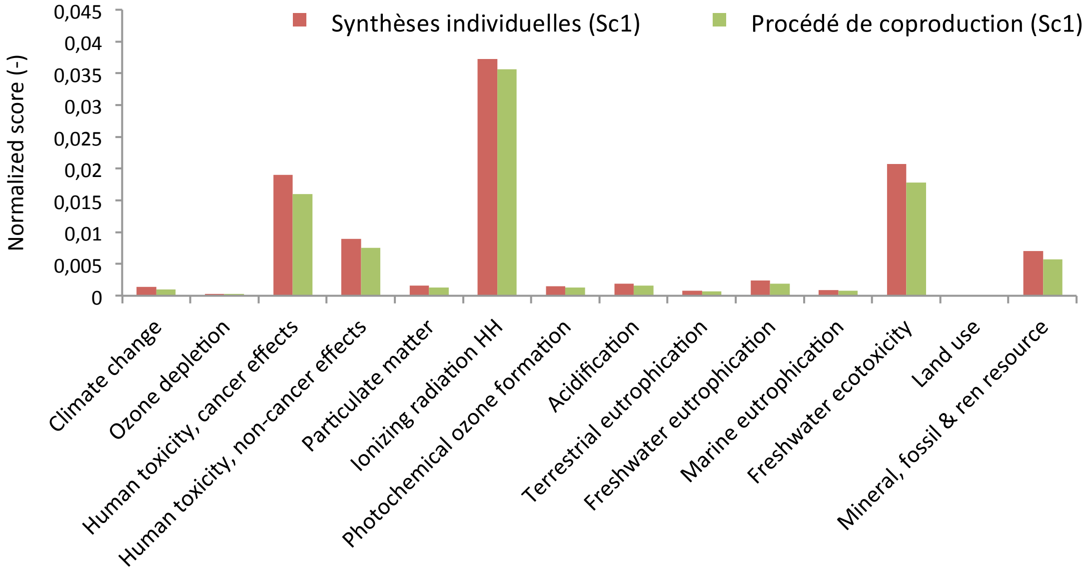


Figure 9. Comparaison entre les synthèses individuelles (Sc1) et le procédé de coproduction (Sc2)-Normalisation des impacts par une dérivé de la méthode ILCD 2011 1.05

Ces résultats sont liés au recyclage de l'acide acétique, produit lors de la synthèse de l'acétate d'éthyle, dans la production d'acétate de butyle. Le recyclage de l'acide acétique a ainsi réduit le traitement des déchets.

3.4.3 Comparaison entre les acétates d'éthyle et de butyle bio-sourcés et pétrochimiques issus des synthèses développées

Dans cette section, nous présentons la comparaison des impacts environnementaux produits avec les synthèses développées concernant l'origine du matériau de départ, c'est à dire, en utilisant les bio-alcools ou ces équivalentes pétrochimiques correspondantes pour la production d'acétate d'éthyle et du butyle. Les bio-alcools ont été modélisés à partir du travail de Pereira[30] et ont été comparés aux alcools pétrochimiques obtenus à partir de la base de données Ecoinvent 3.1.

Pour le cas de l'acétate d'éthyle, aucune différence significative entre l'éthanol biosourcé et l'éthanol fossile (différence inférieure à 10%) n'a été observée dans 12 des 17 catégories. Cependant, une réduction des impacts sur le changement climatique a été observée lors de l'utilisation du bioéthanol, en raison du stockage du $CO_{2.}$

D'autre part, en ce qui concerne l'acétate de butyle, en utilisant du bio-butanol à la place du butanol- fossile, les impacts environnementaux ont été réduits dans 10 des 17 catégories.
L'impact sur le changement climatique a été réduit dans 53% en utilisant le bio-butanol. Ces résultats peuvent être liés au stockage de CO_2 lors de l'utilisation de bio-butanol.

3.4.4 Comparaison des procédés de synthèse développés à partir d’alcools biosourcés avec le procédé industriel actuel utilisant des ressources fossiles : contribution de l'ACV et des indicateurs de la chimie verte

Cette étude en ACV a permis de déterminer que les impacts environnementaux peuvent être réduits en utilisant du bioéthanol et du bio-butanol pour les synthèses d'acétates à travers les procédés de synthèse développés. Nous nous sommes ensuite intéressés à comparer ces synthèses plus vertes avec les synthèses industrielles utilisant des matières premières pétrochimiques. Il faut remarquer que les synthèses étudiées ici ont été développées à l'échelle du laboratoire, pour lesquelles la comparaison directe de leur cycle de vie avec celui des procédés industriels n’est pas vraiment pertinente. Dans ce contexte, le calcul des indicateurs de la chimie verte a été réalisé afin d'effectuer une comparaison simple et rapide de ces procédés de synthèse.

Les indicateurs verts des synthèses individuelles et de la coproduction d'acétates d'éthyle et de *n*-butyle, utilisant le bioéthanol et le bio-butanol, ont été calculés au même titre que ceux du procédé industriel classique (mettant en œuvre l’acide acétique et l’éthanol ou le butanol en présence d’acide sulfurique comme catalyseur). Ils sont indiqués dans le Tableau 11.

Tableau 11. Indicateurs verts: comparaison entre les procédés de synthèse développés (individuels et coproduction) et les synthèses industrielles actuelles. [a]Teneur biosourcée calculée en considérant que l'éthanol et le butanol proviennent de matières premières biosourcées.

Procédé	% AE	Facteur-E	% TB
Bio-acétates d’éthyle et de butyle par des synthèses individuelles	72,4	0,68	57,9[a]
Bio-acétates d’éthyle et de butyle par le procédé de coproduction	91,9	0,31	57,9[a]
Pétro-acétates : EAc et BAc par un procédé traditionnel	85,01	14,71	0

Selon les trois indicateurs étudiés, le procédé de coproduction des acétates présente de meilleurs résultats que le procédé traditionnel. Avec la coproduction, l’économie d'atomes est plus importante et la production de déchets réduite (E- Facteur inférieur).

3.5 Conclusions

Dans ce travail, les impacts environnementaux ont été étudiés pour deux voies de production de des acétates d'éthyle et de butyle:

- des synthèses indépendantes à partir d'anhydride acétique et d'éthanol (1:1) pour la production d'acétate d'éthyle et d'acide acétique et de *n*-butanol (1:1) pour l'acétate de butyle
- un procédé de coproduction dans lequel l'acétate d'éthyle est produit à partir d'anhydride acétique et d'éthanol (1:1), l'acide acétique produit dans cette réaction étant alors utilisé comme réactif pour l’estérification avec du *n*-butanol pour la production d'acétate de butyle.

Les avantages du procédé de coproduction ont été clairement démontrés par le calcul des indicateurs de la chimie verte :

- L'économie d’atomes est plus élevée dans le procédé de coproduction (91,9%), en raison de la réutilisation de l'acide acétique produit lors de la première estérification, dans la synthèse de l'acétate de butyle.

- De même, le facteur environnemental s'est avéré plus faible pour le procédé de coproduction que pour les synthèses individuelles d'acétates (0,31 contre 0,68, respectivement). Ce résultat montre bien la réduction des déchets générés en coproduction.

L'analyse du cycle de vie a été achevée pour obtenir des informations sur l'ensemble du cycle de vie des acétates et pour mettre en évidence les avantages environnementaux du procédé de coproduction :

- Dans les synthèses individuelles et dans le procédé de coproduction, l'étape de préparation des réactifs a montré le plus grand impact sur l'environnement.
- En comparant les deux voies de synthèse, il a été attesté que le procédé de coproduction générait des impacts plus faibles sur l'environnement dans toutes les catégories comparé aux synthèses individuelles.

L'influence sur l'impact environnemental généré par l'origine des matériaux de départ utilisés dans le procédé développés, bio-sourcé ou pétrochimique, a également été évaluée :

- Pour l'acétate d'éthyle : aucune différence significative n'a été obtenue dans la majorité des catégories quand le bioéthanol est utilisé à la place et de l'éthanol pétrochimique. Cependant, des impacts plus faibles sur le changement climatique ont été obtenus en utilisant du bioéthanol.
- Pour l'acétate de butyle, l'utilisation de bio-butanol à la place de butanol a réduit l'impact sur l'environnement dans 10 des 17 catégories. Les impacts sur le changement climatique ont été significativement réduits de 53%.

Enfin, les indicateurs de la chimie verte calculés á partir des synthèses développées ont été comparés à celles obtenues avec les synthèses classiques pétrochimiques.

Les synthèses de bio-acétates à travers le procédé de coproduction ont présenté de meilleurs résultats que les synthèses pétrochimiques classiques : Facteur-E plus faible (0,31), économie d'atome (91,9%) et PMR plus élevé (57,9%).

CHAPITRE IV. Synthèse de la méthyl éthyl cétone biosourcée

4.1 Introduction

La méthyl éthyl cétone (MEK) est un solvant largement utilisé dans l'industrie des peintures et des revêtements. Plus de 60% de sa production est destinée à ces secteurs. La MEK est actuellement produite à partir de ressources fossiles en utilisant des températures élevées et des catalyseurs homogènes (acide sulfurique). Ces réactions ont de faibles rendements et une faible sélectivité.

Dans le contexte de la chimie verte, l'objectif de ce travail a été de développer un nouveau protocole de synthèse de la MEK par décarboxylation d'une molécule biosourcée, l'acide lévulinique (AL), répertorié parmi les dix molécules plateformes les plus prometteuses identifiées par le *Department of Energy* (USA).

Dans le chapitre IV, cette réaction a été étudiée en présence de persulfate de potassium et de différentes espèces d'argent. Le rôle des différents réactifs tels que les sels d'argent et les ions persulfates a été exploré, nous conduisant à proposer un mécanisme de décarboxylation pour cette réaction. La compréhension de ce mécanisme nous a permis d'améliorer remarquablement la conversion de l'AL et le rendement en MEK.

4.2 Etat de l'art sur la production industrielle de la méthyl éthyl cétone

La méthyl éthyl cétone est actuellement produite selon trois procédés principaux :

1. La déshydrogénation du 2-butanol : 92% de la production mondiale est obtenue par cette méthode. Ce procédé de production est réalisé en deux étapes: i) l'hydrolyse de butènes pour produire du 2-butanol en utilisant l'acide sulfurique comme catalyseur et ii) la déshydrogénation du 2-butanol en présence d'oxydes de zinc ou de cuivre comme catalyseurs hétérogènes.

2. Le procédé Fisher-Tropsch : cette technologie consiste en la conversion de H_2 et de CO (gaz de synthèse) en hydrocarbures de poids moléculaires variés et des produits oxygénés tels que des alcools, de l'acide acétique, de l'acétone, de la méthyl isobutyl cétone (MIBK) et de la MEK. La réaction utilise un catalyseur à base de fer à des températures comprises entre 180 et 200 °C.[31] Cependant la sélectivité de la réaction en MEK reste très faible (entre 3-6% m/m[32]).[31,33–36]

3. L'oxydation en phase liquide du *n*-butane : dans cette réaction, la MEK est obtenue comme sous-produit de l'oxydation du *n*-butane en acide acétique. Le procédé général met en jeu la réaction du *n*-butane avec de l'air comprimé ou de l'oxygène en présence d'un catalyseur, typiquement des acétates de cobalt, de manganèse ou de chrome, à des températures de l'ordre de 160 °C. Le produit principal de la réaction est l'acide acétique. Plusieurs sous-produits sont également obtenus, tels que la MEK, l'éthanol, l'acétate d'éthyle, l'acide formique et l'acide propanoïque.[37]

4.2.1 Stratégie pour la synthèse de la MEK bio-sourcée

Les procédés décrits précédemment produisent généralement de la MEK avec de faibles rendements avec des sélectivités limitées en utilisant des températures élevées et des catalyseurs acides homogènes. De plus, toutes les technologies présentées utilisent des matériaux de départ pétrochimiques, ce qui a un impact négatif sur l'environnement. Dans ces travaux, nous avons proposé de synthèser la MEK par décarboxylation de l'acide lévulinique (AL) issu de la biomasse (Schéma 8). Nous nous sommes inspirés des travaux de Gong *et al.*[38] pour déterminer les conditions préliminaires de décarboxylation à mettre en œuvre. En effet, à notre connaissance, seuls ces travaux décrivent l'utilisation d'un système argent-persulfate pour la décarboxylation de l'AL. Cependant, leur méthode utilise des températures élevées (160 °C) et ne conduit qu'à un rendement de 44,4% en MEK.

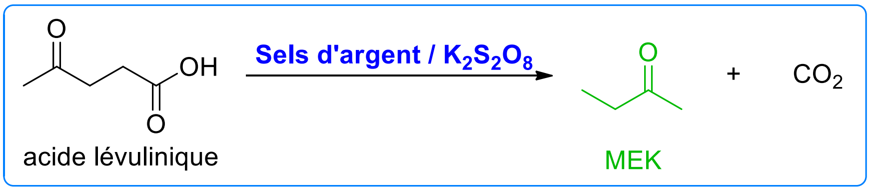


Schéma 8. Proposition de synthèse pour la production de bio-méthyl éthyl cétone

Afin d'améliorer la production de MEK, nous avons réalisé une étude exploratoire du mécanisme réactionnel. Celle-ci nous a permis de déterminer les facteurs qui affectent la réaction et d'identifier les conditions opérationnelles optimales.

4.3 Etude de l'évolution des espèces au cours de la décarboxylation de l'acide lévulinique pour la production de MEK à l'aide du système $AgNO_3/K_2S_2O_8$

4.3.1 Résultats préliminaires

La réaction de décarboxylation de l'acide lévulinique a été étudiée à 100°C dans une solution de phosphates K_2HPO_4/KH_2PO_4 (0,1:0,1 M), tel que l'avait décrit Gong, en présence de $K_2S_2O_8$ seul ou de $AgNO_3$ seul. Aucune décarboxylation de l'AL n'est observée avec $AgNO_3$ seul. Cependant, en présence de $K_2S_2O_8$, de faibles quantités de MEK et d'acide acétique sont obtenues (Tableau 12).

Tableau 12. Influence de $AgNO_3$ et $K_2S_2O_8$ dans la décarboxylation de LA. neq = nombre d'équivalents par rapport a LA. Conditions: K2HPO4/KH2PO4 (0.1:0.1 M), 100°C, 30 minutes

	n_{eq} $AgNO_3$ / $K_2S_2O_8$	pH		Conversion de AL (%)	Rendement (%)	
		initiale	Final		AcOH	MEK
1	1/0	5	4	0,0	0,0	0,0
2	0/0,25	5	5	3,6	1,0	2,6
3	0/0,5	5	5	12,1	3,3	8,8
4	0/1	4	2	13,6	6,8	6,8
5	0/2	4	1	18,8	14,5	4,3

4.3.2 Etude paramétrique de la réaction de décarboxylation en présence du système sels d'argent/ persulfate de potassium

- **Influence de la nature du sel d'argent**

Différents sels d'argent ont été testés pour la décarboxylation de l'AL : $AgNO_3$, AgCl, Ag_2O et AgO. Les réactions ont été réalisées avec un rapport 1:1 de sel d'Ag:$K_2S_2O_8$, à 100 ° C, dans la même solution de phosphates (K_2HPO_4/KH_2PO_4, Tableau 13).

Tableau 13. Effet des différentes espèces d'argent dans la décarboxylation de l'acide lévulinique. Conditions expérimentales: KH_2PO_4 :K_2HPO_4 (0.1:0.1M), 100°C, 30 minutes.

Entrée	Ag sel	n_{eq} Ag sel/ $K_2S_2O_8$	pH		Conversion AL (%)	Rendement (%)	
			initial	Final		AcOH	MEK
1	$AgNO_3$	1/1	5	2	46,9	14,4	32,5
2	AgCl	1/1	6	5	38,7	13,5	25,2
3	Ag_2O	1/1	4	3	54,3	17,8	36,5
4	AgO	1/1	5	3	57,6	22,9	34,8
5	AgO	1/0	4	1	0,0	0,0	0,0

L'utilisation de $AgNO_3$ a permis d'obtenir la MEK avec un rendement supérieur à 30% et une production d'acide acétique limitée (Tableau 13, # 1). Le couple $AgNO_3$/$K_2S_2O_8$ a donc été retenu une l'étude paramétrique de la réaction.

- **Influence du ratio molaire $AgNO_3$/$K_2S_2O_8$**

Différents ratio molaires entre $AgNO_3$/$K_2S_2O_8$ de 1:2 à 2 :1 ont été testés. Un excès de $K_2S_2O_8$ ne permet d'améliorer le rendement en MEK mais accroit la production d'acide acétique. Nous avons mis en évidence que la production d'acide acétique était due à une réaction de dégradation de la MEK en présence d'oxygène qui serait produit suite aux réactions suivantes :

$$S_2O_8^{2-} \longrightarrow 2SO_4^{\bullet -}$$

$$CH_3COCH_2CH_2COOH + SO4^{\bullet -} \longrightarrow CH_3COCH_2CH_2COO^{\bullet} + HSO_4^{-}$$

$$CH_3COCH_2CH_2COO^{\bullet} + H_2O \longrightarrow CH_3COCH_2CH_3 + CO_2 + OH^{\bullet}$$

$$2OH^{\bullet} \longrightarrow H_2O + 1/_2\ O_2$$

Schéma 9. Décarboxylation de l'AL en présence de persulfate de potassium

Notons que l'ajout de TEMPO (piège à radicaux) dans le milieu réactionnel a totalement inhibé la réaction prouvant que le mécanisme est bien radicalaire comme proposé ci-dessus.

- **Influence de la température et du temps de réaction**

Des études cinétiques ont été réalisées à différentes températures (100, 60 et 25°C). La réaction la plus rapide s'effectue à 100°C et le rendement maximum est atteint après 5 minutes de réaction. En revanche, la production d'acide acétique est plus élevée que celle de la MEK à température ambiante. Ce phénomène s'explique par le fait que l'oxygène à cette température est plus soluble dans le milieu réactionnel aqueux.

- **Influence des variations du pH du milieu réactionnel**

Quelles que soient les solutions aqueuses de sels de phosphates ou de soude utilisées, le pH diminue au cours de la réaction (Tableau 14). Le rendement de MEK le plus élevé est obtenu lors de l'utilisation de solutions de KH_2PO_4 et Na_2HPO_4/NaH_2PO_4.

Tableau 14. Effet de la composition de la phase aqueuse et du pH initial sur la décarboxylation de l'AL. Conditions expérimentales: 100°C, 30 minutes.

#	Composition de la phase aqueuse	Concentration de solution [M]	*pH de solution	pH		Conversion AL (%)	Rendement (%)	
				Initiale	Final		AcOH	MEK
1	Eau	-	6	3	1	29,6	14,8	14,8
2	KCl/NaOH	0,2	12	4	1	48,8	12,3	36,5
3	K_2HPO_4/KH_2PO_4	0,2	6,9	5	2	46,8	14,4	32,5
4	K_2HPO_4/KH_2PO_4	0,2	8,0	5	2	47,6	15,7	31,0
5	Na_2HPO_4/NaH_2PO_4	0,2	7,2	4	2	50,5	10,9	39,6
6	KH_2PO_4	0,2	4,5	3	1	48,9	21,3	27,9
7	K_2HPO_4	0,2	8	5	1	50,0	11	39,0
8	NaOH	$9\ 10^{-4}$	8	5	1	30,5	9,7	20,8

On peut penser qu'un pH acide de 1 empêche la réaction d'évoluer. Afin de le vérifier, des essais supplémentaires ont été réalisés (Tableau 15). Le fait d'ajuster le pH à 5 (avec une solution de soude) et de relancer la réaction avec un équivalent de $K_2S_2O_8$ a permis l'obtention d'un excellent rendement en MEK, de l'ordre de 87% avec une conversion d'AL pratiquement totale.

Tableau 15. Amélioration de la conversion de LA et du rendement en MEK suite à l'ajustement du pH de la réaction. Conditions expérimentales: KH_2PO_4 :K_2HPO_4 (0.1:0.1M), 100°C, 30 minutes. [a]1^{ere} cycle de 30 min, [b]après 2nd cycle de 30 min.

#	Description de la réaction	n_{eq} $AgNO_3$ / $K_2S_2O_8$	AL conversion (%)	pH		Rendement (%)	
				Initial	Final	AcOH	MEK
1	[a]Réaction initiale: Milieux 1 (M1)	1/1	46,8	5	2	14,4	32,5
Après ajustement à pH=5							
2	[b] Ajout de NaOH à M1	0/0	48,8	5	2	11,8	32
3	[b] Ajout de NaOH & $K_2S_2O_8$ to M1	0/1	97,9	5	1	11,3	86,6
Sans ajustement du pH							
4	[b] Ajout de $K_2S_2O_8$ to M1	0/1	54,3	3	1	22,8	31,5
5	[b] Ajout de $AgNO_3$ / $K_2S_2O_8$ to M1	1/1	67	2	1	28,7	38,3

Ces résultats nous ont amenés à supposer qu'une réaction compétitive est en jeu en milieu acide (réaction b, Schéma 10).

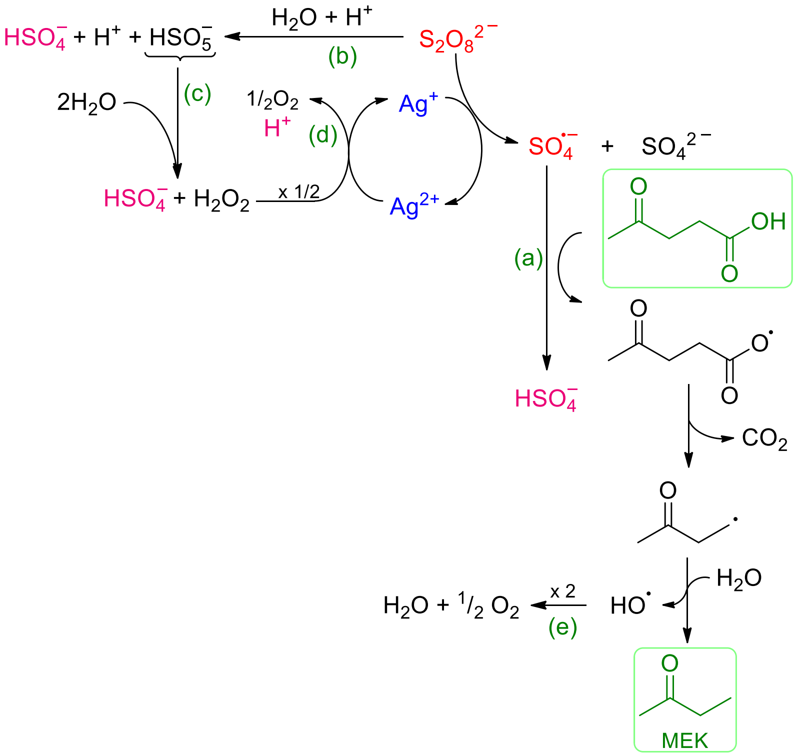


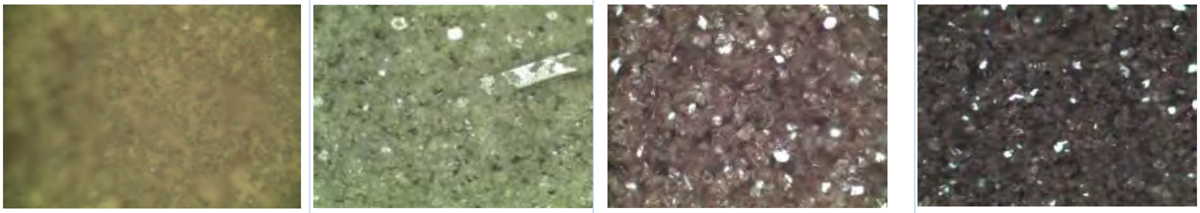
Schéma 10. Mécanisme proposé

4.3.3 Etude de l'évolution du système solide au cours de la réaction en présence de persulfate de potassium et de nitrate d’argent par spectroscopie RMN du solide, DRX et XPS et MEB-EDX.

Afin d’élucider le mécanisme réactionnel expliquant l’évolution des sels d’argent au cours de la réaction, nous avons étudié la composition des phases solides à différents temps de réaction (0, 4, 13 et 30 minutes), grâce aux techniques spectroscopiques suivantes : la résonance magnétique nucléaire du solide, la diffraction des rayons X (DRX), la spectroscopie de photoélectrons X (XPS) et la microscopie électronique à balayage (MEB-EDX).

- **Evolution de la couleur du milieu réactionnel**

Des changements de couleur de la phase solide ont été observés au cours de la réaction (Figure 10). Ils peuvent être liés à la formation de différents sels d'argent, tels que Ag_3PO_4 (solide jaune), Ag_2SO_4 (solide blanc) et des oxydes d'argent (marron foncé).



a) 0 minutes- jaune

b) 4 minutes- jaune clair

c) 13 minutes- marron clair

d) 30 minutes- marron foncé

Figure 10. Changements de couleur de la phase solide au cours de la réaction. Conditions expérimentales: $AgNO_3/K_2S_2O_8$ (1: 1), KH_2PO_4/K_2HPO_4 (0,1: 0,1 M), 100 ° C, 30 minutes

Après 30 minutes de réaction et ajustement du pH, le milieu redevient jaune, couleur similaire à celle observée au début du premier cycle. Après le deuxième de réaction, le milieu brunit à nouveau (Figure 11).

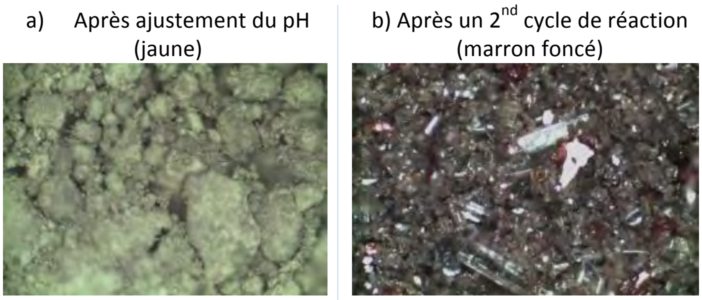


Figure 11. Changements de couleur de la phase solide après ajustement du pH à 5 avec NaOH et après un 2nd cycle de réaction. Conditions expérimentales: $AgNO_3/K_2S_2O_8$ (1: 1), KH_2PO_4/K_2HPO_4 (0,1: 0,1 M), 100 ° C, 30 minutes

Nous pouvons supposés que les changements de couleur sont dus à l'évolution du nitrate d'argent en phosphate, sulfate et oxydes d'argent au cours de la réaction. Cette évolution peut être schématisée dans la figure suivante (Figure 12) :

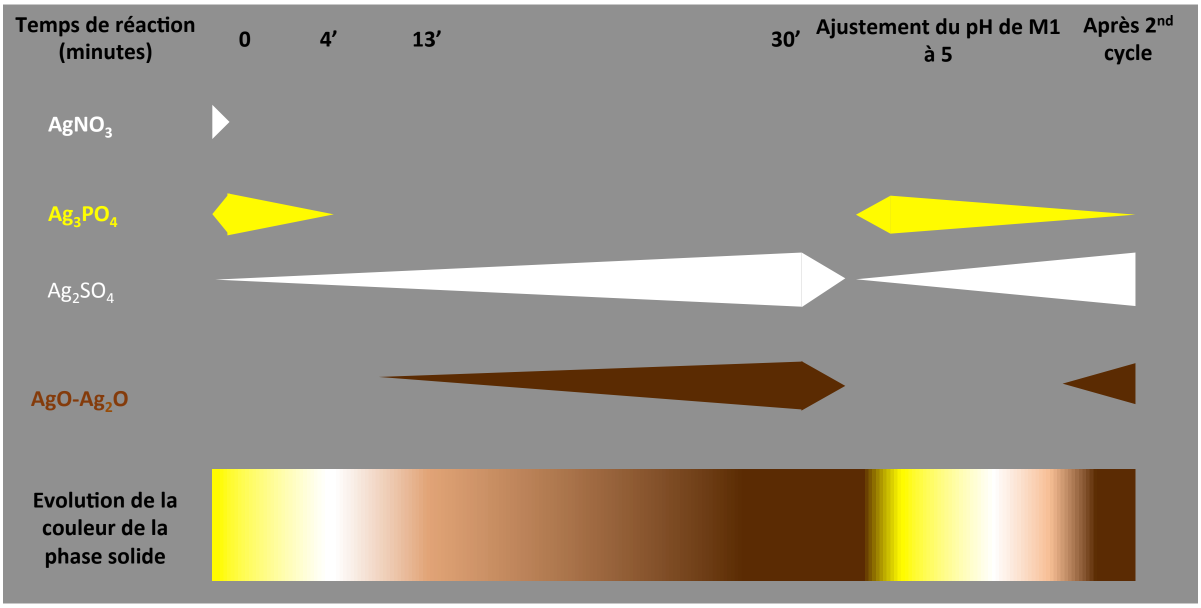


Figure 12. Représentation graphique de l'évolution au cours de la réaction des espèces d'argent dans la phase solide, après ajustement du pH du milieu après le 1er cycle de réaction (M1) et après le 2nd cycle de réaction.

Afin de valider cette évolution, les phases solides ont été caractérisées à différents temps de réaction (0, 4, 13 et 30 min, après ajustement du pH et après le 2ème cycle de réaction) à l'aide de diverses techniques spectroscopique (RMN du solide, DRX, XPS, AES et MEB-EDX) :

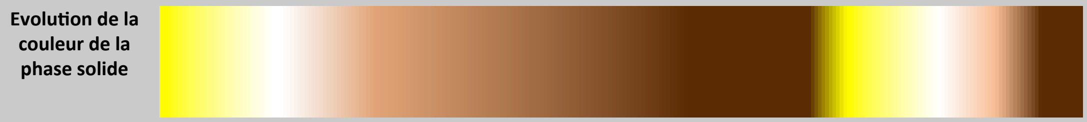
- La disparition d'$AgNO_3$ dès le début de la réaction a été démontrée par les diagrammes DRX obtenus dès le début de la réaction,
- La formation concomitante de Ag_3PO_4 a été mise en évidence par les analyses RMN du solide, DRX, XPS, spectroscopie des électrons Auger (AES) et EDX, expliquant la coloration jaune du solide,

- La conversion d'Ag_3PO_4 en Ag_2SO_4 a été démontrée par les analyses RMN du solide, DRX, XPS, AES, EDX, justifiant le blanchiment de la phase solide,
- La formation d'Ag_2O-AgO en petites quantités à la fin de la réaction a finalement été prouvée par des analyses AES : la phase solide s'assombrit.

Les analyses spectroscopiques de la phase solide obtenues après ajustement du pH et après le second cycle de réaction ont permis de mettre en évidence l'évolution des sels d'argent :

- Après l'ajustement du pH, la présence de Ag_3PO_4 et la disparition d'Ag_2SO_4 ont été observées par les analyses RMN du solide, XRD, AES, EDX. La disparition d'Ag_2O et d'AgO a été prouvée par AES : la phase solide s'est éclaircie et est redevenue jaune.
- La conversion de Ag_3PO_4 en Ag_2SO_4 au cours du second cycle de réaction a été démontrée par les analyses RMN du solide, XRD, AES, EDX: la phase solide redevient blanche.
- La formation d'Ag_2O-AgO à la fin du second cycle a été prouvée par des analyses AES: la phase solide s'est de nouveau assombrie.

Dans la figure suivante, nous avons résumé les espèces d'argent qui ont été identifiées par les analyses spectroscopiques à différents temps de réaction : le phosphate d'argent est formé dès le début de la réaction, puis disparaît à mesure que le sulfate d'argent se forme. La spectroscopie des électrons Auger (AES-XPS) a également montré la formation d'oxydes d'argent (Ag_2O-AgO) après 4 minutes de réaction. Le même comportement a été observé pour le second cycle de réaction. Les images MEB ont mis en évidence les modifications de la morphologie des particules d'argent liées à la variation du pH de la réaction (Figure 13).



Temps de réaction (minutes)	0'	4'	13'	30'	Après ajustement du pH de M1 à 5	Après 2nd cycle
SSNMR	Ag_3PO_4	Ag_3PO_4 Ag_2SO_4	Ag_2SO_4	Ag_2SO_4	Ag_3PO_4	Ag_2SO_4
XRD	Ag_3PO_4	Ag_2SO_4	Ag_2SO_4	Ag_2SO_4 Ag_3O_4 ?	Ag_3PO_4	Ag_2SO_4
XPS	Ag_3PO_4	Ag_3PO_4 Ag_2SO_4 Ag_2O-AgO	Ag_3PO_4 Ag_2SO_4 Ag_2O-AgO	Ag_3PO_4-Ag_2SO_4 Ag_2O-AgO	Ag_3PO_4	Ag_3PO_4-Ag_2SO_4 Ag_2O-AgO
MEB	sphérique	sphérique polyédrique	plaquettes	plaquettes	sphérique	plaquettes

Figure 13. Changements de couleur de la phase solide à différents temps de réaction et les composés identifiés par différentes techniques de spectroscopie.

À notre connaissance, il s'agit de la première étude sur l'évolution des sels d'argent impliqués dans le mécanisme de décarboxylation en présence du système $AgNO_3/K_2S_2O_8$.

4.4 Conclusions

La décarboxylation de l'acide lévulinique pour la production de la méthyl éthyl cétone (MEK) avec le système $AgNO_3$ / $K_2S_2O_8$ a été étudiée. La MEK peut être produite en l'absence de $AgNO_3$, mais $K_2S_2O_8$ est nécessaire pour la réaction même en présence de Ag(II). Ces résultats montrent que les radicaux sulfates ($SO4^{\bullet-}$) sont directement responsables de la décarboxylation de l'acide lévulinique, et un mécanisme radicalaire pour la synthèse de la MEK été proposé.

Les analyses DRX et XPS des phases solides tout au long de la réaction ont démontré la présence principalement d'espèces Ag (I). Des traces de Ag(II), AgO et Ag(0) élémentaire, ont également été observées, sans limitation de réaction. Il a également été possible de montrer que l'acidification du milieu réactionnel limitait la décarboxylation de l'acide lévulinique. L'ajustement du pH à 5 et l'addition de 1 équivalent de $K_2S_2O_8$ après 30 minutes de réaction ont conduit à une excellente conversion de l'AL (jusqu'à 99%), associée à un rendement en MEK de 87%. La régénération des sels d'argent est donc possible grâce à l'ajustement du pH. Ces résultats permettent d'envisager un procédé continu de production de la MEK via une alimentation en continu d'AL, de NaOH et de $K_2S_2O_8$ dans un réacteur contenant la solution de sels d'argent.

Conclusion générale

De nos jours, l'intérêt pour le remplacement des solvants pétrochimiques par des solvants plus verts et plus respectueux de l'environnement et de la santé humaine s'est accru. Dans ce contexte, les recherches se sont concentrées sur les solvants alternatifs, y compris ceux dérivés de la biomasse. L'Union européenne a lancé plusieurs projets de recherche pour encourager le développement de ce type de solvant. En conséquence, le projet européen ECOBIOFOR a été fondé pour synthétiser certains des solvants les plus utilisés dans l'industrie de la peinture et du revêtement : les acétates d'éthyle et de butyle et la MEK à partir de synthons issus de la biomasse. Dans ce projet, l'objectif de la thèse a été de développer de nouveaux procédés de synthèse de ces molécules respectant les principes de la chimie verte.

PRODUCTION D'ACÉTATE D'ÉTHYLE ET D'ACÉTATE DE BUTYLE :

Deux voies de synthèse différentes ont été étudiées : la première à partir de l'acide acétique et de l'alcool correspondant (éthanol pour l'acétate d'éthyle et butanol pour l'acétate de butyle) ; la seconde en utilisant l'anhydride acétique à la place de l'acide acétique. Dans ce travail, nous avons remplacé les catalyseurs acides homogènes actuellement utilisés dans l'industrie par des résines échangeuses d'ions, faciles à séparer du milieu réactionnel et recyclables. Des études cinétiques et thermodynamiques ont été effectuées sur les deux voies de réaction (acide acétique/anhydride acétique) en présence de quatre résines : Amberlyst 15, Amberlyst 16, Amberlyst 36 et Dowex 50WX8. La plus faible valeur d'énergie d'activation (Ea) a été obtenue avec la résine Dowex 50WX8, qui a été identifiée comme la résine la plus performante pouvant être réutilisée au moins en quatre fois sans régénération. Pour les deux acétates, les synthèses à partir de l'anhydride acétique et de l'alcool correspondant (dans un rapport de 1:2) étaient plus rapides que les synthèses à partir de l'acide acétique (dans un rapport de 1:1). Ainsi, des conversions plus élevées d'alcools (environ 80 %) et des rendements en acétate (environ 80 %) ont été obtenues avec l'anhydride acétique.

Cependant, en raison de la difficulté de purification des acétates obtenus à cause de la présence des azéotropes avec l'eau et afin d'améliorer les rendements, une nouvelle stratégie de coproduction des acétates a donc été adoptée : afin de minimiser la production d'eau, un rapport anhydride acétique:éthanol de 1:1 a été utilisé pour produire de l'acétate d'éthyle et de l'acide acétique. L'acétate d'éthyle a été facilement séparé d'un mélange d'acide acétique/résine par distillation. Ce mélange a ensuite été utilisé dans une seconde réaction d'estérification avec le butanol. Ce nouveau procédé de coproduction a permis d'obtenir des acétates avec d'excellents rendements et des puretés élevées (Figure 14). De plus, il évite l'utilisation de plusieurs étapes de purification et réduit la génération de déchets.

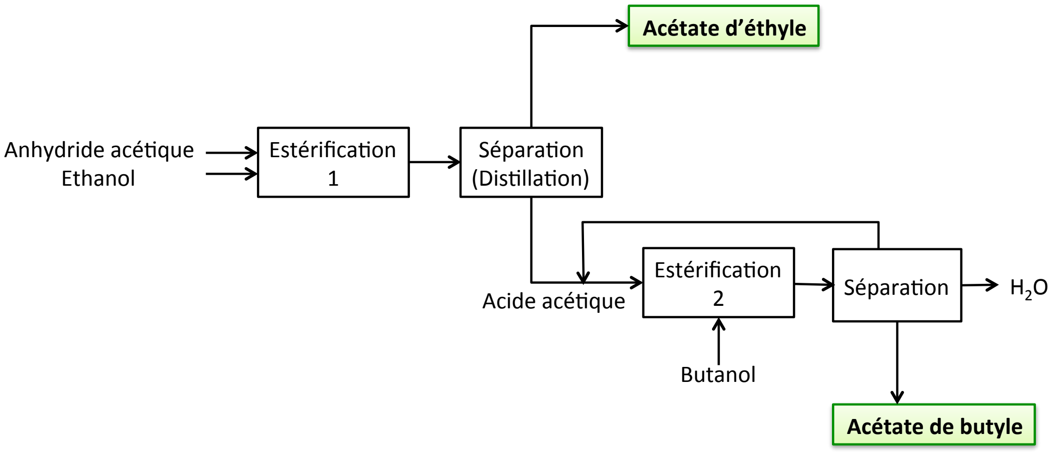


Figure 14. Procédé de coproduction d'acétates d'éthyle et de butyle

Les avantages environnementaux du procédé de coproduction ont été mis en évidence par le calcul des indicateurs de la chimie verte et de l'analyse du cycle de vie :

- Une économie d'atome plus élevée a été obtenue avec le procédé de coproduction (91,9 %) par rapport aux synthèses individuelles de chacun des acétates (72,4 %).
- Le facteur environnemental a diminué avec le procédé de coproduction (0,31 contre 0,68 pour les synthèses individuelles) confirmant la réduction de la production de déchets.
- L'évaluation du cycle de vie a montré que le procédé de coproduction génère moins d'impacts sur l'environnement que les synthèses individuelles et ce, dans toutes les catégories.

De plus, l'influence de l'impact environnemental généré par l'origine des alcools, bio-sourcés ou pétrochimiques a été évaluée. Des impacts plus faibles sur le changement climatique ont été observés à partir du bioéthanol ou du bio-butanol, en raison du stockage du carbone biogène.

Les synthèses d'acétate d'éthyle et d'acétate de butyle ont été étudiées dans le laboratoire à l'aide d'un réacteur de 2 litres. Pour compléter l'étude, l'acétate d'éthyle a été préparé à une échelle de 20 litres.
Les acétates synthétisés ont été caractérisés et évalués dans des formulations de laque nitrocellulosique et de vernis polyuréthane. Les résultats ont montré que les solvants synthétisés peuvent parfaitement remplacer leurs équivalents fossiles dans ces formulations de revêtements.

POUR LA SYNTHESE DE LA METHYL ETHYL CETONE (MEK) :

La production de MEK *via* la décarboxylation de l'acide lévulinique (AL) a ensuite été étudiée en présence d'un système de sels d'argent et de persulfate de potassium. En effet, l'acide lévulinique est identifié parmi les 10 molécules renouvelables les plus prometteuses pour la production de molécules d'intérêt.

Ce travail de thèse a porté sur la compréhension du mécanisme réactionnel de décarboxylation de l'AL et plus particulièrement sur l'évolution des sels d'argent.

Des réactions préliminaires ont été effectuées en utilisant $AgNO_3$ ou $K_2S_2O_8$. La décarboxylation de l'acide lévulinique n'a pas eu lieu en utilisant uniquement du nitrate d'argent ($AgNO_3$), alors que la MEK a été produite en présence de persulfate seul. Ceci peut s'expliquer par le fait que le persulfate peut être activé avec la température, générant des radicaux sulfate ($SO_4^{\bullet-}$) qui conduisent à la décarboxylation de l'AL. Cependant, de faibles rendements en MEK sont alors obtenus.

L'utilisation du système $AgNO_3/K_2S_2O_8$ a permis de produire la MEK (rendement de 32,5 %) mais aussi de l'acide acétique (rendement de 14,4 %). Des études complémentaires ont montré que ce sous-produit est généré par une oxydation de la MEK une fois formée. Le même comportement a été observé lorsque le nitrate d'argent a été remplacé par d'autres sels d'argent tels que AgCl, Ag_2O et AgO. Dans ces cas, une légère augmentation de la quantité d'acide acétique a constaté. Ces résultats nous ont conduit à sélectionner $AgNO_3$ and $K_2S_2O_8$ pour la décarboxylation de LA, car des rendements en MEK plus élevés et des rendements en acide acétique plus faibles ont été obtenus avec ces deux réactifs. L'évaluation de l'influence de la température, de la durée de réaction et du *ratio* molaire $AgNO_3/K_2S_2O_8$ sur le rendement en MEK nous a permis d'obtenir de meilleurs résultats en utilisant un *ratio* $AgNO_3/K_2S_2O_8$ de 1:1 à 100°C pendant 30 minutes.

Les réactions effectuées avec des pièges à radicaux ont montré que le mécanisme de réaction est un mécanisme radicalaire où les radicaux sulfates libres, $SO_4^{\bullet-}$, sont directement responsables de la décarboxylation de l'AL (Schéma 11).

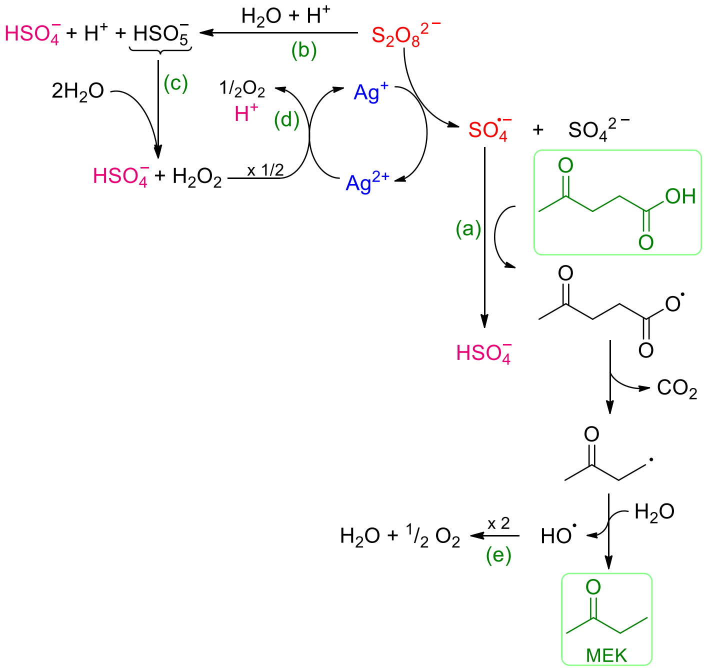


Schéma 11. Mécanisme proposé

Une diminution du pH a été observée pendant la réaction, même en présence de la solution de KH_2PO_4/K_2HPO_4. Cette diminution s'explique par la formation de HSO_4^- et de H^+, par des réactions compétitives, empêchant la formation de MEK avec un bon rendement. Nous avons ensuite montré que l'addition de NaOH pour ajuster le pH de réaction à 5 et d'un autre équivalent de $K_2S_2O_8$ permet d'augmenter la conversion d'AL de 46,5% à 99% et le rendement en MEK de 32,4% à 88,6% après un 2nd cycle de réaction.

Afin de mieux comprendre le mécanisme de réaction et d'expliquer les changements de couleur du milieu réactionnel observés, les phases solides ont été analysées tout au long de la réaction, après l'ajustement du pH et après le 2nd cycle de réaction. Différentes techniques de spectroscopie ont été utilisées : la résonance magnétique nucléaire du solide, la diffraction des rayons X (DRX), la spectrométrie photoélectronique à rayons X (XPS) et la microscopie électronique à balayage (MEB-EDX).

Ces analyses ont montré que la coloration jaune de la phase solide est due à la formation d'Ag_3PO_4 à partir d'$AgNO_3$. Par la suite, un blanchiment de ces solides a été observé, ce qui s'explique par la disparition de Ag_3PO_4 et par la formation de Ag_2SO_4. A la fin de la réaction, le brunissement de la phase solide est lié à la formation d'oxydes d'argent Ag_2O-AgO.

L'ajustement du pH a conduit à la formation de Ag_3PO_4, avec la réapparition de la couleur jaune, qui réagit ensuite avec $K_2S_2O_8$ conduisant à la production de MEK. La solution blanchit à nouveau, puisque Ag_2SO_4 est formé et Ag_3PO_4 est consommé (Figure 15).

Temps de réaction (minutes)	0’	4’	13’	30’	Après ajustement du pH de M1 à 5	Après 2^nd^ cycle
SSNMR	Ag_3PO_4	Ag_3PO_4 Ag_2SO_4	Ag_2SO_4	Ag_2SO_4	Ag_3PO_4	Ag_2SO_4
XRD	Ag_3PO_4	Ag_2SO_4	Ag_2SO_4	Ag_2SO_4 Ag_3O_4 ?	Ag_3PO_4	Ag_2SO_4
XPS	Ag_3PO_4	Ag_3PO_4 Ag_2SO_4 Ag_2O-AgO	Ag_3PO_4 Ag_2SO_4 Ag_2O-AgO	Ag_3PO_4-Ag_2SO_4 Ag_2O-AgO	Ag_3PO_4	Ag_3PO_4-Ag_2SO_4 Ag_2O-AgO
MEB	sphérique	sphérique polyédrique	plaquettes	plaquettes	sphérique	plaquettes

Figure 15. Changements de couleur de la phase solide à différents temps de réaction et les composés identifiés par différentes techniques de spectroscopie.

Ces résultats sont d'une grande importance, car ils montrent que le milieu réactionnel peut être facilement régénéré par ajustement du pH. A notre connaissance, c'est la première fois qu'une telle conversion de l'acide lévulinique associé un rendement élevé en MEK est obtenue.

PERSPECTIVES :

Certaines perspectives peuvent être envisagées à l’issu de ce travail de thèse.

En ce qui concerne les synthèses d'acétates :

- La transposition du procédé de coproduction à l'échelle industrielle devrait être étudiée.
- Une étude technico-économique du procédé optimisé permettrait de mettre en évidence les avantages du procédé de coproduction des acétates biosourcés par rapport aux procédés industriels actuels.

- Le bénéfice environnemental du procédé optimisé devrait être évalué à l'aide d'une analyse du cycle de vie (ACV).

En ce qui concerne la synthèse de la méthyl éthyl cétone biosourcée :

- Il conviendrait de mettre au point un procédé continu s'appuyant sur la régénération des sels d'argent et d'optimiser les paramètres de réaction
- La séparation en continue de la MEK du milieu réactionnel devrait être étudiée afin d'éviter son oxydation en acide acétique.

Références

(1) Guidance for Drugs in USA Food and Drugs Administration. Q3C: Tables and List Guidance for Industry https://www.fda.gov/downloads/drugs/guidances/ucm073395.pdf. (accessed Feb 13, 2018).

(2) Ethyl acetate - Registration Dossier - ECHA https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/15437/5/3/1 (accessed Apr 4, 2018).

(3) N-butyl acetate - Registration Dossier - ECHA https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/15948/5/3/1 (accessed Apr 4, 2018).

(4) Butanone - Registration Dossier - ECHA https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/15065/5/3/2 (accessed Apr 4, 2018).

(5) Pereira, C. S. M.; Silva, V. M. T. M.; Rodrigues, A. E. *Green Chem.* **2011**, *13* (10), 2658.

(6) Global ETAC Production http://www.prweb.com/releases/2014/02/prweb11619424.htm (accessed Jan 26, 2018).

(7) Fischer, E.; Speier, A. *Berichte der Dtsch. Chem. Gesellschaft* **1895**, *28* (3), 3252–3258.

(8) Weissermel, K.; Arpe, H. J. *Industrial Organic Chemistry*, 4th ed.; Wiley-VCH Verlag GmbH & Co. KGaA, 2003.

(9) University of Liverpool. REF2014. Economical and beneficial environmental impact on industrial production of ethyl acetate http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=5577 (accessed Nov 22, 2017).

(10) Lederer, J.; Levering, W. W.; Bailer, O.; Morävek, P.; Smejkal, Q.; Macek, V. Process and apparatus for the production of butylacetate and isobutylacetate. US 6,458,992 B1, October 2002.

(11) Berg, L.; Ratanapupech, P. Separation of ethyl acetate from ethanol and water by extractive distillation. US4379028 A, 1982.

(12) Tian, H.; Zheng, H.; Huang, Z.; Qiu, T.; Wu, Y. *Ind. Eng. Chem. Res.* **2012**, *51* (15), 5535–5541.

(13) Tian, H.; Zhao, S.; Zheng, H.; Huang, Z. *Chinese J. Chem. Eng.* **2015**, *23* (4), 667–674.

(14) Tang, Y.-T.; Chen, Y.-W.; Huang, H.-P.; Yu, C.-C.; Hung, S.-B.; Lee, M.-J. *AIChE J.* **2005**, *51* (6), 1683–1699.

(15) Arporniwichanop, A.; Koomsup, K.; Assabumrungrat, S. *J. Ind. Eng. Chem.* **2008**, *14* (6), 796–803.

(16) Giwa, A.; Giwa, S. O. *Int. J. Eng. Res. Africa* **2017**, *30*, 154–166.

(17) Steinigeweg, S.; Gmehling, J. *Ind. Eng. Chem. Res.* **2002**, *41* (22), 5483–5490.

(18) Ajay Singh; R. Hiwale; S. M. Mahajani, * and; Gudi, R. D.; and, J. G.; Kienle, A. **2005**.

(19) Sert, E.; Atalay, F. S. *Chem. Biochem. Eng. Q.* **2011**, *25* (2), 221–227.

(20) Tobiszewski, M.; Marć, M.; Gałuszka, A.; Namieśnik, J. *Molecules* **2015**, *20* (6), 10928–10946.

(21) Anastas, P. T.; Zimmerman, J. B. *Innovations in green chemistry and green engineering: Selected entries from the Encyclopedia of sustainability science and technology*; Springer, 2013.

(22) Trost, B. M. *Science (80-.).* **1991**, *254* (5037), 1471–1477.

(23) Dicks, A. P.; Hent, A. *Green chemistry metrics: A Guide to Determining and Evaluating Process Greenness*.

(24) Tabone, M. D.; Cregg, J. J.; Beckman, E. J.; Landis, A. E. *Environ. Sci. Technol.* **2010**, *44* (21), 8264–8269.

(25) 12 Principles of Green Chemistry https://www.acs.org/content/acs/en/greenchemistry/what-is-green-chemistry/principles/12-principles-of-green-chemistry.html (accessed Oct 25, 2017).

(26) ISO 14040 : 2006 https://www.iso.org/standard/37456.html (accessed Nov 8, 2017).

(27) INTERNATIONAL STANDARD 14040 https://web.stanford.edu/class/cee214/Readings/ISOLCA.pdf. (accessed Nov 8, 2017).

(28) ISO 14040. *Management environnemental - Analyse du cycle de vie - Principes et cadre*; 2006.

(29) ISO 14044. *Management environnemental - Analyse de Cycle de Vie - Exigences et lignes directrices*; 2006.

(30) Pereira, L. G.; Chagas, M. F.; Dias, M. O. S.; Cavalett, O.; Bonomi, A. *J. Clean. Prod.* **2015**, *96*, 557–568.

(31) *Fischer-Tropsch Technology*; Steynberg, A., Dry, M., Eds.; Elsevier, 2004.

(32) Hester, R. E. (; Harrison, R. M. *Coal in the 21st century: energy needs, chemicals and environmental controls*; Royal Society of Chemistry 2018: London, UK, 2018.

(33) Hoell, D.; Mensing, T.; Roggenbuck, R.; Sakuth, M.; Sperlich, E.; Urban, T.; Neier, W.; Strehlke, G. In *Ullmann's Encyclopedia of Industrial Chemistry*; Wiley-VCH: Weinheim, Germany, 2009; pp 431–444.

(34) Kreutz, T. G.; Larson, E. D.; Liu, G.; Williams, R. *25th Annu. Int. Pittsburgh Coal Conf.* **2008**, No. August, 1–81.

(35) Tolman, W. B. *Activation of small molecules: Organometallic and Bioinorganic Perspectives*; Wiley-VCH, 2006.

(36) Nierop, P. van; Erasmus, H.; Zyl, J. van. In *SASOL's achievements in the 20th century as a building block*

for the 21st; San Francisco, California, USA, 2000; pp 1–13.

(37) Office of Air Quality Planning and Standards; U.S. Environental Protection Agency. *Locating and Estimating Air Emissions From Sources of Methyl Ethyl Ketone*; 1994.

(38) Gong, Y.; Lin, L. *Molecules* **2011**, *16* (3), 2714–2725.

Production Scientifique

Publications

Publications acceptés dans des revues Internationales

[1] LCA case study: comparison between independent and co-production pathways for the production of ethyl and *n*-butyl acetates. C. Bories, N. Guzmán-Barrera, J. Peydecastaing, I. Etxeberria, E. Vedrenne, C. Vaca-García, S. Thiebaud-Roux, C. Sablayrolles. *The International Journal of Life Cycle Assessment*. 2018, 23, 151-266. DOI : 10.1007/s11367-017-1317-8

[2] A novel process using ion exchanges resins for the coproduction of ethyl and butyl acetates. N. Guzmán-Barrera, C. Bories, J. Peydecastaing, C. Sablayrolles. E. Vedrenne, C. Vaca-García, S. Thiebaud-Roux. Accepté 14 Avril 2018: Green and Sustainable Chemistry

Publications à soumettre dans des revues internationales

[1] Evolution of species during levulinic acid decarboxylation to produce methyl ethyl ketone in the $AgNO_3/K_2S_2O_8$ system. N. Guzmán-Barrera, J. Peydecastaing, J. Esvan, P. Behra, E. Vedrenne, C. Vaca-García, S. Thiebaud-Roux. A soumettre a fin Juin 2018 : Journal of the American Chemical Society

Autres publications

Rapport d'avancement de recherche du projet Européen ECOBIOFOR pour la commission Européen

[1] Characterisation of synthesised bio-based products. Idoia Etxeberria, N. Guzmán-Barrera, S. Thiebaud-Roux. *Rapport Européen du Projet ECOBIOFOR,* 2016.

[2] Synthesis of bio-based ethers. N. Guzmán-Barrera, C. Bories, J. Peydecastaing, E. Vedrenne, C. Vaca-García, S. Thiebaud-Roux. *Rapport Européen du Projet ECOBIOFOR*, 2016.

[3] 20 Litres of each solvent : Production of WP3 bio-based solvents. C. Bories, N. Guzmán-Barrera, J. Peydecastaing, E. Vedrenne, C. Vaca-García, S. Thiebaud-Roux. *Rapport Européen du Projet ECOBIOFOR,* 2016.

[4] Synthesis of ketone : Methyl ethyl ketone (MEK). N. Guzmán-Barrera, C. Bories, J. Peydecastaing, E. Vedrenne, C. Vaca-García, S. Thiebaud-Roux. *Rapport Européen du Projet ECOBIOFOR*, 2016.

[5] Synthesis of bio-based esters. N. Guzmán-Barrera, C. Bories, J. Peydecastaing, E. Vedrenne, C. Vaca-García, S. Thiebaud-Roux. *Rapport Européen du Projet ECOBIOFOR*, 2015.

[6] Starting materials and targeted biosolvents. Nati Bayarri, N. Guzmán, J. Peydecastaing, E. Vedrenne, S. Thiebaud-Roux, Izaskun Garmendia, Idoia Etxeberria. *Rapport Européen du Projet ECOBIOFOR*, 2014.

Communications

Communications orales dans de conférences internationales :

[1] Novel Co-production process for the synthesis of ethyl acetate and butyl acetate using ion exchange resins. Guzmán-Barrera, C. Bories, J. Peydecastaing, I. Etxeberria, C. Sablayrolles, E. Vedrenne, C. Vaca-García, S. Thiebaud-Roux. *13th International Conference on Renewable Resources and Biorefineries,* 7-9 June, 2017, Wroclaw (Pologne).

[2] LCA case study: Comparison of different chemical pathways for the production of ethyl and n-butyl acetates. C. Bories, N. Guzmán-Barrera, J. Peydecastaing, I. Etxeberria, E. Vedrenne, C. Vaca-García, S. Thiebaud-Roux, C. Sablayrolles. SETAC, 20-22 Sept, 2016, Montpellier (France).

Présentation de posters dans des congres internationaux :

[1] Synthesis of bio-based methyl ethyl ketone from the decarboxylation of levulinic acid. N. Guzmán-Barrera, C. Bories, J. Peydecastaing, P. Behra, C. Sablayrolles, E. Vedrenne, C. Vaca-García, S. Thiebaud-Roux. *2nd Green and Suistainable Chemistry Conference.* 14-17 mai, 2017, Berlin (GR).

[2] ECOBIOFOR : a European project on ECOpaint BIO-based FORmulations. N. Guzmán-Barrera, I. Etxeberria, C. Bories, J. Peydecastaing, C. Sablayrolles, E. Vedrenne, C. Vaca-García, S. Thiebaud-Roux, I. Garmendia, N. Bayarri, C. Estevez. *Biomeet*. 8 avril, 2016, Portugal.

[3] Life Cycle Assessment of bio-solvents for paint and coating industries. C. Bories, N. Guzmán-Barrera, J. Peydecastaing, I. Etxeberria, E. Vedrenne, C. Vaca-García, S. Thiebaud-Roux, C. Sablayrolles. *SETAC Europe.* 22-26 mai, 2016, Nantes (France).

[4] ECOBIOFOR : a European project on ECOpaint BIO-based FORmulations. N. Guzmán-Barrera, C. Bories, J. Peydecastaing, I. Etxeberria, C. Sablayrolles, E. Vedrenne, C. Vaca-García, S. Thiebaud-Roux. *11th International Conference on Renewable Resources and Biorefineries*. 3-5 June, 2015, York (UK).