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TOMO XLVIII

Celebratory Symposium
A – Catalysis and the Periodic Table

From a 175 year old Ruthenium to its Empire on Green Catalysis and Sustainable Chemistry

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ACADEMIA DAS CIÊNCIAS
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LISBOA • 2022

From a 175 year old Ruthenium to its Empire on Green Catalysis and Sustainable Chemistry

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Pierre H. Dixneuf after his doctorate es Sciences with Prof René Dabard on ferrocene chemistry did a post-doctorate research with Prof. Michael F. Lappert in Brighton UK on the initial steps of N-Heterocyclic Carbene--Metal complexes. Professor at the University of Rennes since 1978 his research interests included bimetallic systems and organometallic chemistry toward carbon rich complexes and in 1985 he initiated the Rennes center for Homogeneous Catalysis. He developed catalytic processes promoted with ruthenium catalysts for the transformations of alkynes and incorporation of CO_2, ruthenium-vinylidenes and -allenylidenes in catalysis, enantioselective catalysis to amines, alkene metathesis catalysts from Ru(II)allenylidenes and for transformation of plant oils. He is now contributing since 2007 to C–H bond activation/functionalization using Ru(II) catalysts especially operating in water and to the catalytic Cu(I) catalyzed sp^3C-H bond functionalization.

He has co-authored 470 publications and reviews, co-edited 7 books, received several international prizes: A. v Humboldt prize for Research 1990, Le Bel SFC award and Grignard-Wittig Prize (GDCh) in 2000, Institut universitaire de France membership in 2000, French Académie des Sciences IFP prize and Sacconi medal (Italy) in 2006, Spanish and Chinese Society of Chemistry awards in 2014, election as a member of the European Academy of Sciences in 2016 and of the Portugal Academy of Sciences in 2017. Former CNRS deputy Director of chemistry in Paris (1996-1999), he is currently a Research Professor at the University of Rennes, France, where he founded the CNRS-UR1 research Institut de chimie de Rennes in 2000 and was university vice-president for research (2001-2004).

Platinum metal complexes, derivatives of Ru, Os, Rh, Ir, Pd, Pt metals, have been revealed as efficient catalysts to perform combinations of simple molecules to produce useful compounds with low waste and via green processes for sustainable development [1]. The Ruthenium element was the last Platinum group metals to be discovered in 1844 by Karl Klaus from platinum ore residue [2]. The ruthenium salts were later easily transformed into a variety of simple ruthenium(II) and Ru(0) complexes which showed efficiency as catalysts for several simple reactions and it was preferably used as the less expensive of the platinum group metals [3].

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During the last 2 decades more sophisticated ruthenium complexes were designed in attempts to perform reactions of interest for industry. Now more efforts are made to contribute to clean processes and green catalysis and the transformations of renewables by molecular ruthenium catalysts attract innovations for the development of sustainable chemistry [3].

Several useful catalytic reactions discovered in Rennes with Ru(II) and Rh(I) catalysts have contributed to Green and Sustainable Chemistry such as the alkene metathesis applied to the natural products terpenes, the synthesis of linear aminoacids precursors of polyamides, the sp^2 C-H bond functionalisation of (hetero)arenes with Ru(II) and of biphenylphosphines with Rh(I) catalysts.

RUTHENIUM CATALYZED ALKENE METATHESIS AND TERPENES TRANSFORMATIONS

Almost three decades ago it was shown by R. H. Grubbs that alkylidene-ruthenium catalysts could perform efficiently the alkene metathesis reaction, the exchange of carbon groups on olefin double C=C bond, under mild conditions to lead to many useful transformations, even to produce ROMP polymers. This discovery contributed for one part for the Nobel Prize shared in 2005 by Chauvin, Grubbs and Schrock for their contributions to catalyzed alkene metathesis reactions. This discovery led chemists to design more efficient Ru=CR$_2$ catalysts to apply them for new transformations of olefins.

Strong efforts have been done to transform natural products such as terpenes via alkene metathesis with alkylidene-ruthenium catalysts [4,5]. By cross metathesis C. Bruneau has succesfully transformed a variety of terpenes that are natural products often used as natural fragrances or in cosmetics. He has shown that by selecting alkylidene-ruthenium catalysts of type $RuCl_2(=CH(o-C_6H_4OiPr))(NHCarbene)$ the cross metathesis of terpenes such as citronellal or citronellol took place with acrylate and methacrylate with high stereoselectivity (Scheme 1) [6].
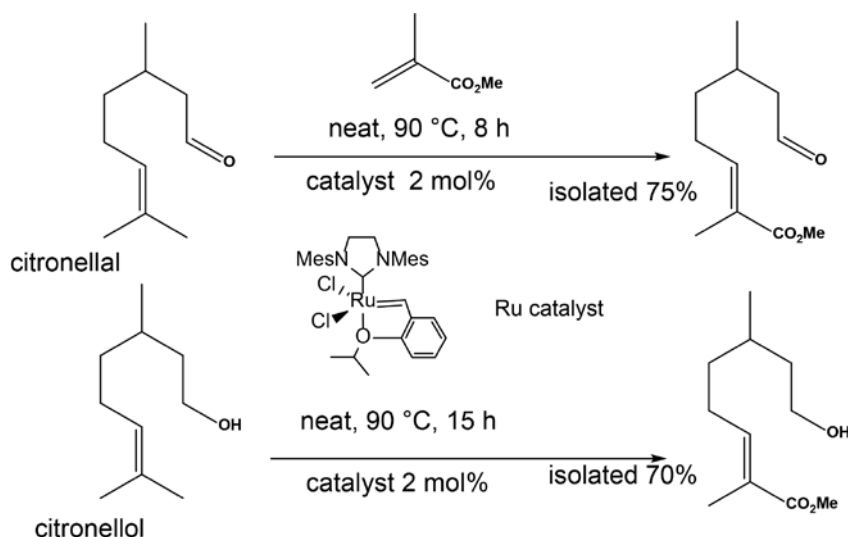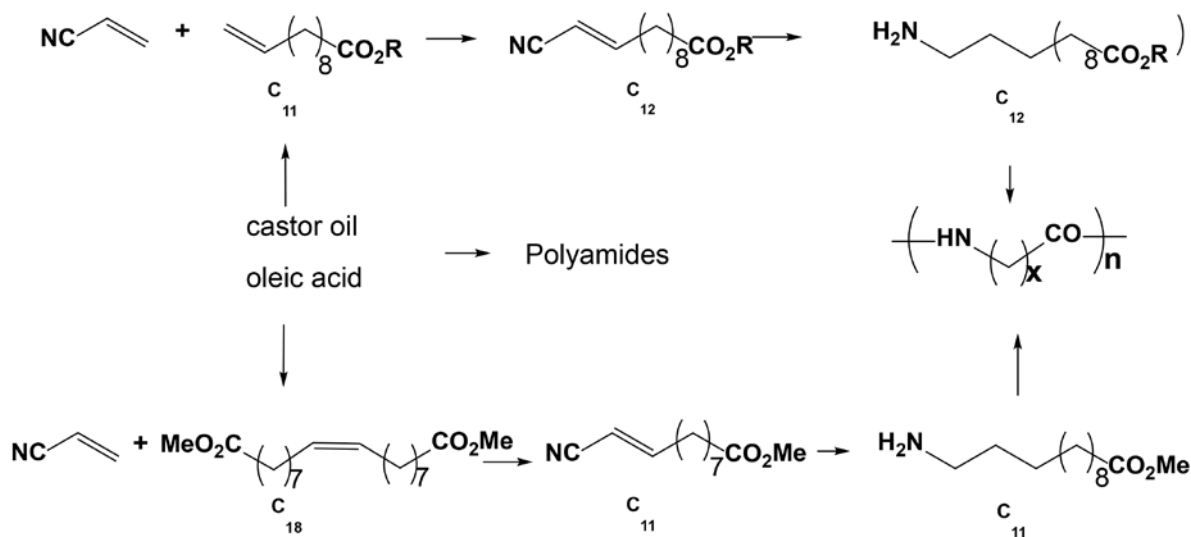

Scheme 1.
Ruthenium-alkylidene catalyzed stereoselective alkene metathesis of terpenes

This was a contribution to green chemistry as the reaction can be performed without solvent with methacrylate but also in non toxic dialkycarbonate and it involves only one step whereas to reach the same products before three steps for oxidation of one methyl and esterification were required. Functionalization of (-)-β-pinene and (-)-limonene *via* cross metathesis with symmetrical internal olefins can also be achieved using the same type of catalysts [7].

RUTHENIUM CATALYZED ALKENE METATHESIS
### AND LINEAR AMINOACIDS SYNTHESIS

Polyamides and copolyamides are well known industrial precursors for a variety of materials resistant to chemicals or heat and for cloth fibers or sport equipments. It was thus attractive to prepare such linear polyamides precursors from renewable materials. Thus efforts were made in Rennes in cooperation with Arkema company to prepare linear aminoacids by cross metathesis of plant oil unsaturated esters derivatives with acrylonitrile or of methyl acrylate with long chain unsaturated nitrile (Scheme 2) [8].
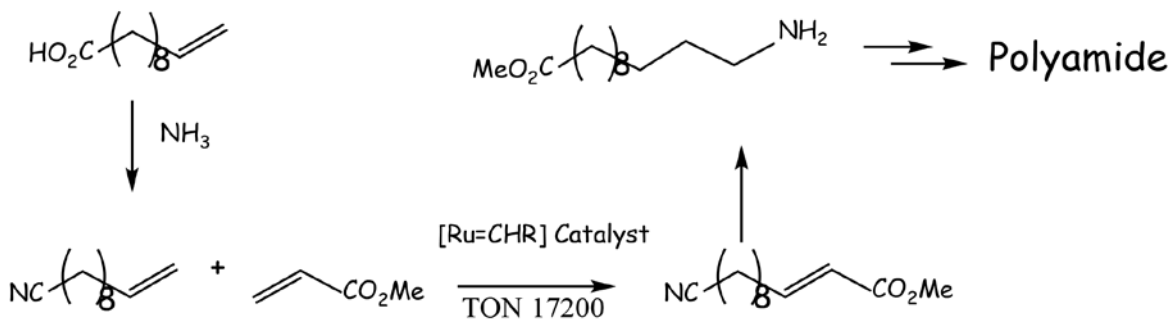

Scheme 2.
Principle of plant oils derivatives as precursors of polyamides via cross metathesis.

Cross metathesis of acrylonitrile and C11 unsaturated ester with the Hoveyda II catalyst $RuCl_2(=CH(o\text{-}C_6H_4OiPr))(NHCarbene)$ containing a saturated NHC carbene proceeds easily at 100°C with a TON of 3000. (Scheme 3). Just after cross metathesis the products of the reaction are transfered to an autoclave and under 20 bar of hydrogen in the presence of a base the ruthenium residue arising from the Hoveyda catalyst efficiently allows the hydrogenation of both the C=C and CN bonds to produce the linear aminoacid [9].
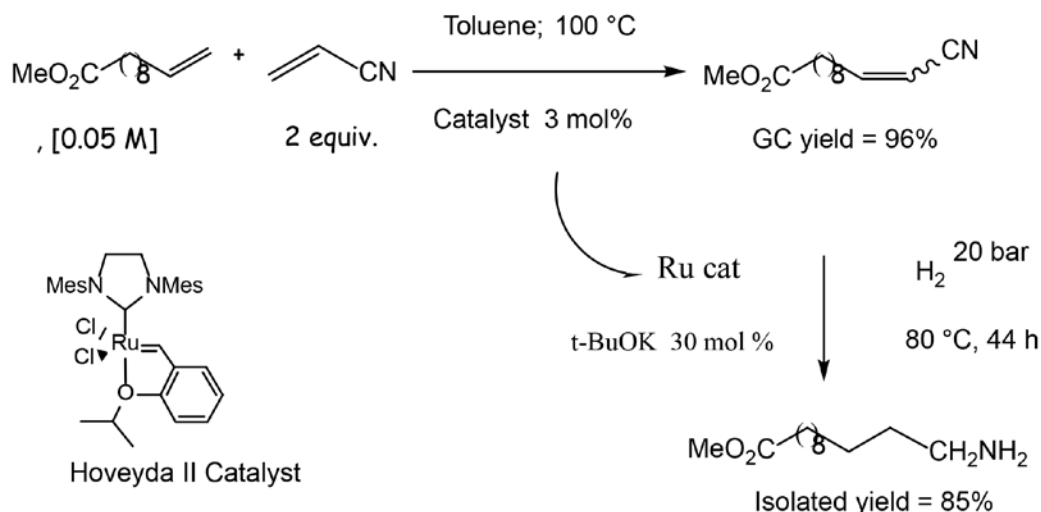
Scheme 3.
Synthesis of linear saturated amino-ester by tandem Cross Metathesis/Hydrogenation

A better approach could be found with the cross metathesis of methyl acrylate with 10-undecenenitrile readily obtained by amination of the corresponding unsaturated carboxylic acid arising from plant oil. The same ruthenium catalyst offered a better efficiency of the cross metathesis with a TON of 17200, showing that the position of the nitrile close to the double bond disfavors the reaction when acrylonitrile is used (TON 3000 only) (Scheme 4) [10].
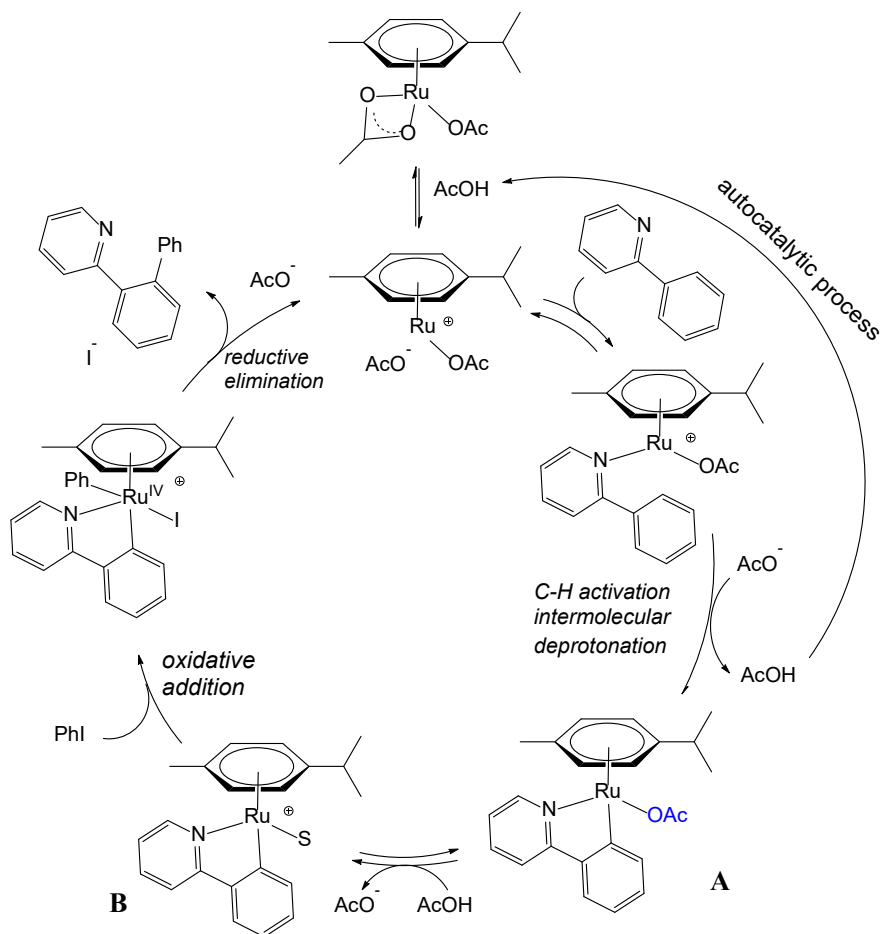

Scheme 4.
Synthesis of linear saturated amino-ester from 10-undecenenitrile and methyl acrylate

RUTHENIUM(II) CATALYZED (HETERO)ARENE SP² C-H BOND ACTIVATION

One of the most important reaction for the construction of useful molecules for pharmacy and even molecular materials is based on the catalytic C_1-C_2 cross-coupling reaction between a simple organo-metallic RMgX, RLi, RZnX, ArB(OH)$_2$, RSnX$_3$, RSiX$_3$, etc with an arylhalide mostly catalyzed with Ni(0) or Pd(0) catalysts and known as the Tamao-Kumada, Negishi, Miyaura-Suzuki, Stille and Hiyama reactions. Their usefulness has led the nobel prize of chemistry 2010 to be awarded to Negishi, Heck

and Suzuki. Since two decades there is a strong motivation among synthesis promoters to build the same C_1-C_2 bond directly form a C_1-H and (aryl)C_2-Br bonds. However the sp^2 C-H bond is very stable and new ways to functionalize it had to be found.

We have thus considered to use ruthenium(II) catalysts to favour the C-H bond deprotonation as a way to make an activated C-Ru(II) bond [11]. We have shown that ruthenium(II) catalysts associated to a carboxylate partner are able to promote the regioselective sp^2 C-H bond activation of functional arenes and heterocycles to selectively lead to cross-couplings with hetero(aryl) halides. F. Pozgan showed that phenyl pyridine with Ru(II) catalyst are ortho arylated in the presence of aryl chlorides but with 2 equiv. of KOAc per Ru(II) site, whereas the presence of a phosphine or a NHCarbene ligand has not a strong influence, which supported the initial deprotonation. He could prepared a variety of di(hetero)arylated compounds or tridentate heterocycles [12]. A. Jutand studied the kinetic of this reaction at 27°C and found that the first product to be formed is the cyclometalated intermediate **A** resulting from ortho C-H bond deprotonation by KOAc via an autocatalytic process (Scheme 5). This initial deprotonation is an easy process with respect to the following oxidative addition of arylhalide which requires more energy [13].

Scheme 5.
Kinetic study of Ru(II) catalyzed ortho functionalization of arene C-H bond

This mechanism via C-H bond deprotonation can also be operative in water as most ruthenium(II) catalysts are stable in water. It is possible now to perform such processes in a greener way: in water as renewable solvent without surfactant and with higher catalyst activity. Many C-H bond functionalizations take place in water but in the presence of pivalate and K_2CO_3 with arylchorides which are more soluble in water [14]. C-H bond functionalization in water can take place even directed by imines to produce tridentate ligands [15].

The trispyridine benzene only could be easily prepared in NMP solvent at 150°C from phenyl pyridine by F. Pozgan using a LnRu(OAc)$_2$ catalyst (Scheme 6) [12] but only recently he succeeded to reach the synthesis of hexapyridylbenzene with Ru(II)/KOPiv/PPh$_3$ catalyst in water but under microwave irradiation (Scheme 6) [16]. Catalytic sp^2 C-H bond activation/functionalization in water can be directed to produce a variety of Hexaheteroarylbenzenes, as potential ligands for photocatalysis.
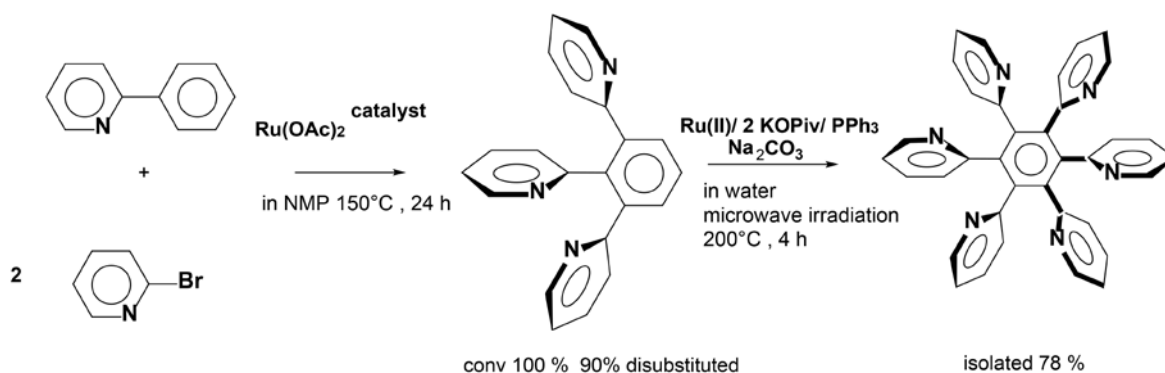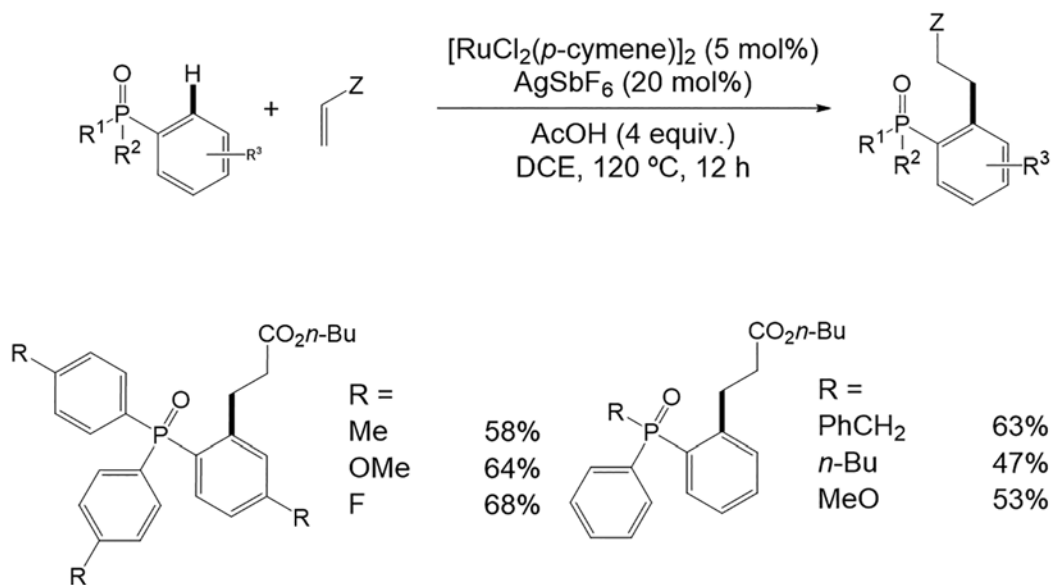

Scheme 6.
Ru(II) catalyzed polyheteroarylation of phenyl pyridine

RUTHENIUM(II) CATALYZED PHOSPHINE OXIDE SP^2 C-H
BOND FUNCTIONALIZATION

The nature of the ligands linked to a metal center is crucial to reach efficiency of the related catalyst. Thus it is a challenge to quickly modify the ligands to reach better catalyst activity. Phosphine ligands have been shown to be very useful in metal complexes however the functionalization of aryl phosphine is inhibited by the difficulty to produce a 4-membered cyclometalate by deprotonation of ortho C-H bonds with formation of M-C bond. By contrast their phosphorous oxides should allow the formation of 5-membered cyclometalate more easily. Indeed we have shown that ruthenium(II) catalysts are able to assist the deprotonation of the ortho C-H bond of phosphine oxides and in the presence of a functional alkene its C=C bond can insert into the metallacycle Ru-C(ortho) bond and an alkyl group is generated on protonation (Scheme 7) [17]. Thus we have produced alkylation of a variety of phosphine oxides at ortho position of the phosphorous. We were able to show that the ruthenium(II) is maintained and that the use of an oxidant such as Cu(II) is not required. This approach allows the synthesis of phosphines with a pendant functional group attached at the ortho carbon atom. It has the potential to easily modify chiral diphosphines currently used for enantioselective catalysis.
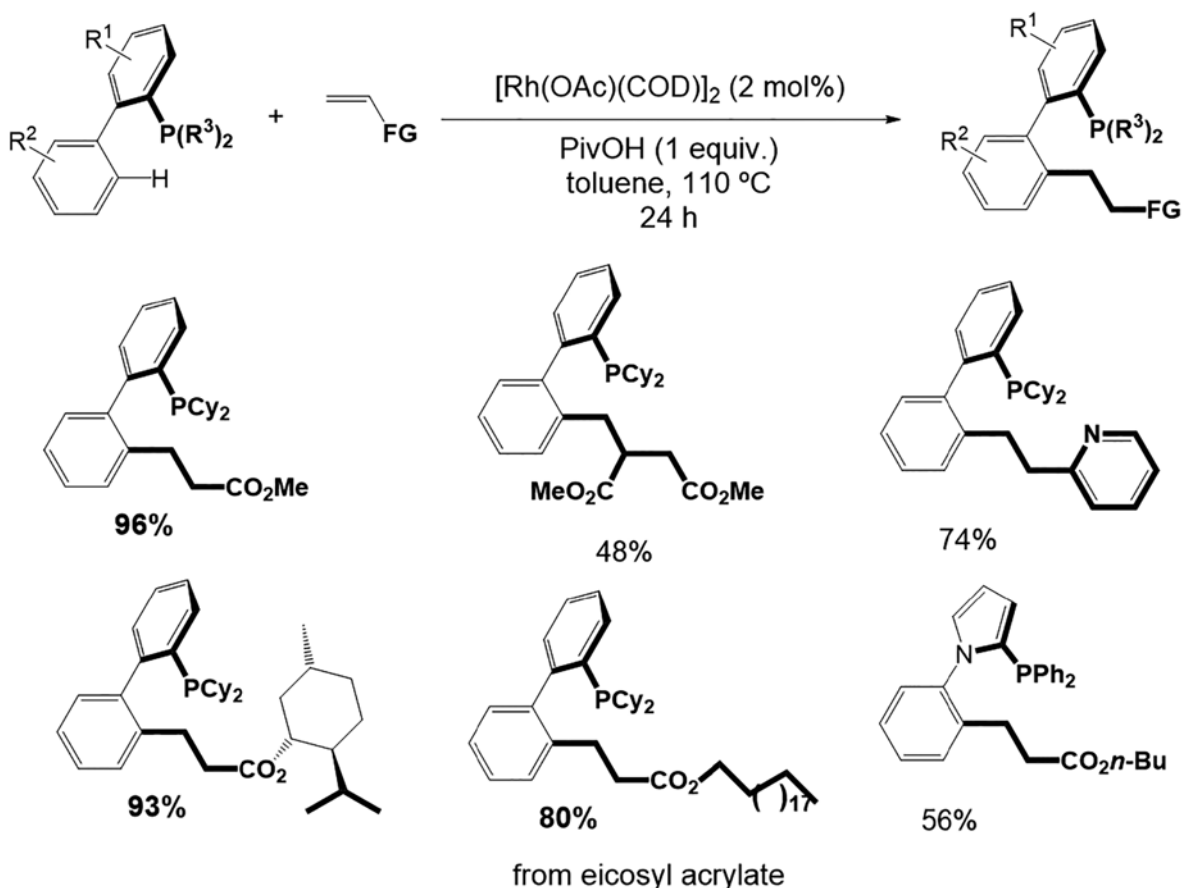

Scheme 7.
Ru(II) catalyzed alkylation of ortho C-H bonds of phosphine oxide aryl groups

RHODIUM(I) CATALYZED SP²C-H BOND FUNCTIONALIZATION
AT *ORTHO'* POSITION OF BIPHENYLPHOSPHINES

Rhodium(I) catalysts by contrast can alkylate the *ortho'* biaryl C-H bonds of biaryl phosphines by formal insertion of alkene C=C bond into biaryl ortho' C-H bonds to produce functional alkylated and dialkylated phosphines, whereas the Ru(II) catalysts are mostly inert for this regioselective functionalization (Scheme 8) [18]. Thus the diphenyl phosphines Johnphos containing PCy_2 or PPh_2 groups, with acrylate and 2 mol% of $Rh(OAc)(COD)_2$ catalyst in acidic media (PivOH) in toluene can give regioselectively the ortho' alkylated phosphines in good yields. It is noteworthy that alkylation can take place with acrylate containing the chiral *L*-Menthol or with eicosyl acrylate leading respectively to optically active phosphine and to phosphine containing the long alkyl chain $CH_2CH_2CO_2(CH_2)_{19}CH_3$.
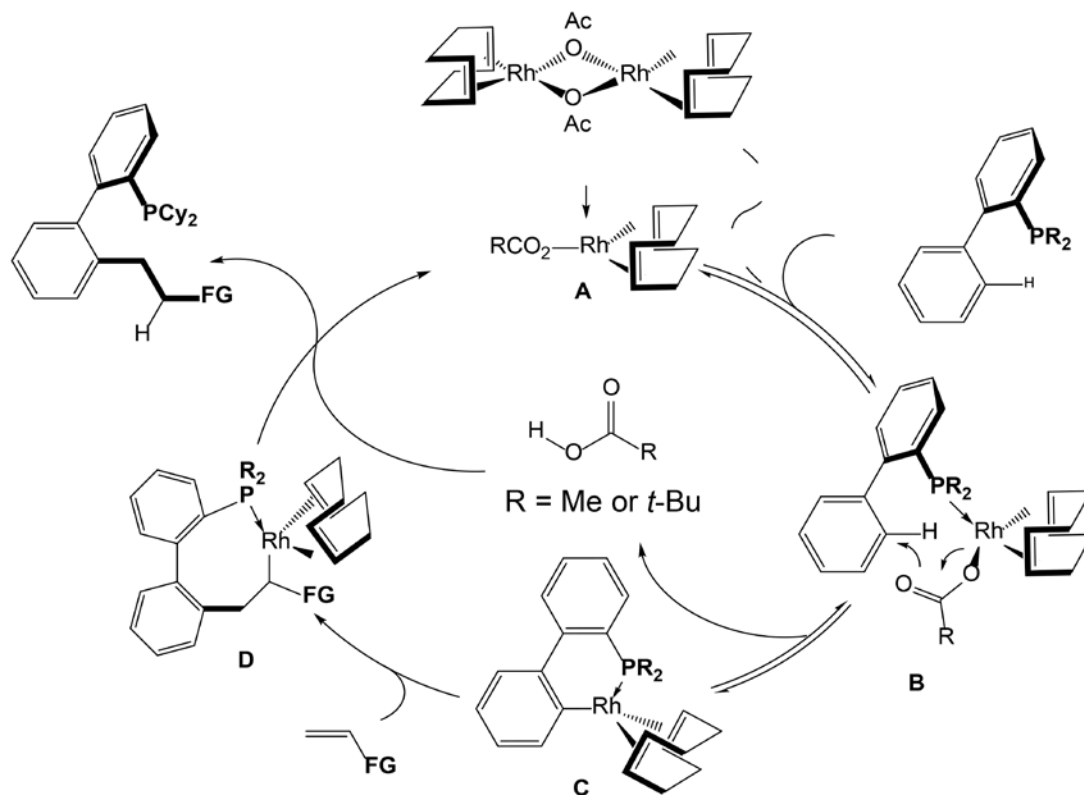

Scheme 8.
Rh(I) catalyzed alkylation of ortho' C-H bonds of biaryl phosphines

These JohnPhos type phosphines can thus be dialkylated at both ortho' C-H diaryl group either with identical or with two different functional alkyl groups.

The mechanism for this *ortho'* C-H bond alkylation was proposed to occur as shown on Scheme 9 [18]. As the reaction takes place under deprotonation conditions a first cyclometalate **C** is formed with

the help of the pivalate. Then the insertion of the acrylate into the *ortho*′C-Rh bond leads to intermediate **D** which on protonation with PivOH leads to the alkylated phosphine and the Rh(I) catalyst.

Scheme 9.
Mechanism of Rh(I) catalyzed alkylation of ortho′ C-H bonds of biaryl phosphines

The advantage of fast modification of JohnPhos phosphine ligand was demonstrated by the use of the just prepared bifunctional dialkylated Phosphine L_1 which offers the efficient carboxylation of arylbromides with CO_2 with the help of a Pd catalyst and a photoredox system as previously shown by R. Martin and N. Iwasawa [19]. The use of long chain containing phosphine L_1 with Pd(OAc)$_2$ allows the direct access to a variety of (hetero)aryl carboxylic acids in better yields without the use of carbonate according to Scheme 10 [18].
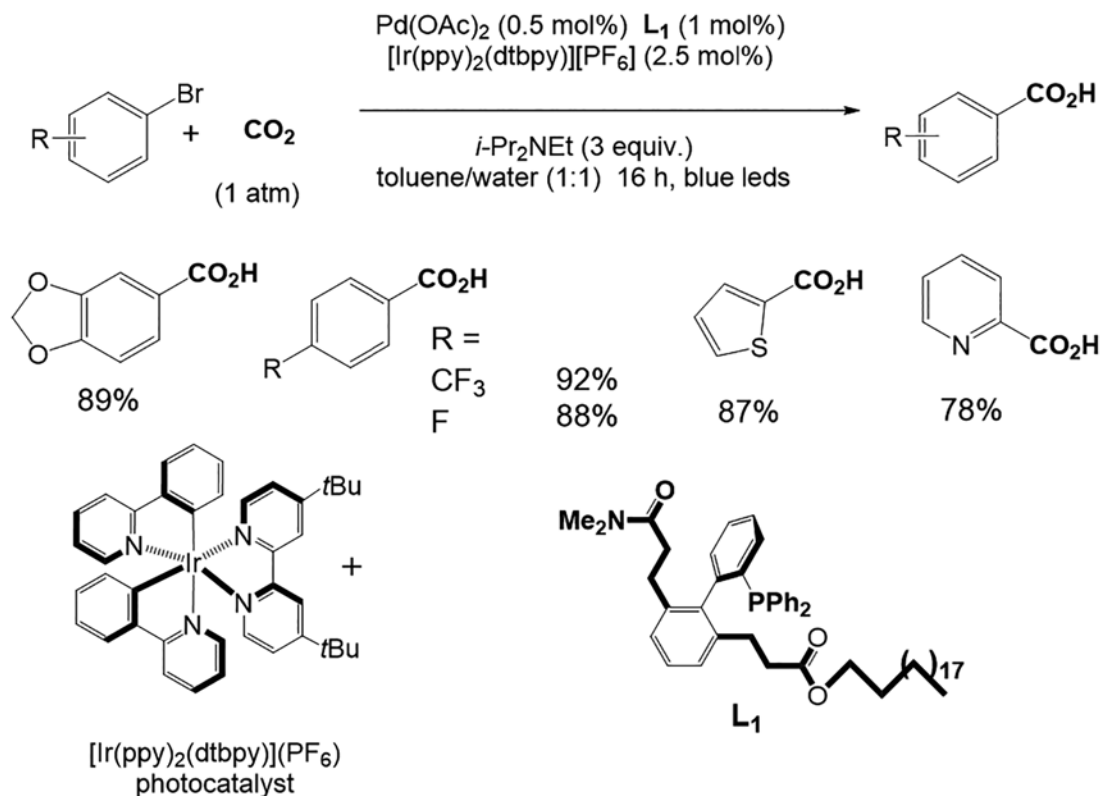
Scheme 10.
Carboxylation of arylbromides with CO_2 and $Pd(OAc)_2$ catalyst with long chain phosphine.

The reaction involves first the insertion of CO_2 into the formed XPd-Ar bond to give the carboxylate XPd-OCOAr and then 2 electrons are brought successively by the reduced photocatalyst. Under blue light irradiation the excited Ir(III) photocatalyst is reduced by the NR_3 amine and twice the resulting Ir(II) species allows an electron transfer to the XPd-OCOAr moiety to generate the carboxylate and the Pd(0) catalyst [20]..

CONCLUSION

Besides its contribution to alkene metathesis applied to renewable materials,ruthenium(II) catalysts have demonstrated a high efficiency to promote the C-H bond functionalizations of previously inert C-H bonds. The cleavage of C-H bond via deprotonation process requires very mild conditions, and takes place even in water without surfactants. However Ruthenium(II) systems are not able to regioselectively activate some C-H bonds and then especially the rhodium(I) catalyst can contribute to directly functionalize phosphines providing unexpected activity on association to the suitable metal complexes. All the catalytic reactions presented here from renewables transformations or by direct cross coupling C-C bond formation from C-H bonds contribute to the development of green and sustainable chemistry,

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