Cellulose recycling as a source of raw chirality*

Valeria Corne, María Celeste Botta, Enrique D. V. Giordano,
Germán F. Giri, David F. Llompart, Hernán D. Biava, Ariel M. Sarotti,
María I. Mangione, Ernesto G. Mata, Alejandra G. Suárez, and
Rolando A. Spanevello‡

*Instituto de Química Rosario, Facultad de Ciencias Bioquímicas y Farmacéuticas,
Universidad Nacional de Rosario – CONICET, Suipacha 531, S2002LRK, Rosario,
Argentina*

Abstract: Modern organic chemistry requires easily obtainable chiral building blocks that show high chemical versatility for their application in the synthesis of enantiopure compounds. Biomass has been demonstrated to be a widely available raw material that represents the only abundant source of renewable organic carbon. Through the pyrolitic conversion of cellulose or cellulose-containing materials it is possible to produce levoglucosenone, a highly functionalized chiral structure. This compound has been innovatively used as a template for the synthesis of key intermediates of biologically active products and for the preparation of chiral auxiliaries, catalysts, and organocatalysts for their application in asymmetric synthesis.

Keywords: asymmetric synthesis; biomass; catalysts; cellulose; chiral auxiliaries; D-allal; levoglucosenone; organocatalysts.

INTRODUCTION

It is generally recognized that the resources of the world are limited and sustainability has become a crucial point for the development of chemical products. These circumstances impose a great urgency to find renewable sources for their transformation in useful products including chemicals, fuels, and materials for replacing the enormous demand for petroleum.

Biomass has received particular attention because it represents the only abundant source of renewable organic carbon. More importantly, its oxygenated nature, chemical diversity, and chirality render biomass a highly suitable raw material to manufacture a multitude of high-added-value compounds [1]. Chirality at the molecular level has emerged as one of the major issues in the development of chemical technology, especially in the areas of drug synthesis and advanced materials. Among the plethora of natural molecules, carbohydrates are the most prominent members of the chiral pool since they are main constituents of all foremost structural molecules in living systems. By far, carbohydrates are the leading annually renewable biofeedstocks from which to develop viable organic chemicals that can compete or eventually replace those derived from fossil sources.

The main example is cellulose, the most widely spread biopolymer on Earth, based on cellobiose as monomer. This disaccharide, formed by two units of D-glucose linked by a β(1 → 4) bond, is a great source of chirality if appropriately treated.

Nowadays, paper manufacturing is a major industrial demand, and the annual paper production in weight is equivalent to three times the car industry production measured in the same way. Due to this production volume, it is easy to foresee the great amount of waste paper that is accumulated as a result of human activity. Paper can be recycled, but only for a limited number of turn-overs, and for this reason it is important to find other uses for any cellulosic material.

The pyrolitic treatment of microcrystalline cellulose or cellulose-containing materials, such as waste paper, degrade the cellulose polymeric chain into a useful building block named levoglucosenone (1,6-anhydro-3,4-dideoxy-β-D-glycero-hex-3-enopyranos-2-ulose) (**1**). The highly functionalized structure of **1** makes it an attractive chiral synthon for the synthesis of a wide variety of natural and unnatural compounds [2]. The 1,6-anhydro bridge locked the pyranose ring in the $^1C_4$ conformation and sterically hinders the β-face of the molecule. Since the first report on the preparation of levoglucosenone 40 years ago [3], different research was conducted to develop a wide variety of applications of this chiral template for the synthesis of enantiomerically pure compounds, some of them with interesting biological activity.

In the context of our ongoing interest in the development of new tools for the preparation of optically active compounds, we are devoted to the design and synthesis of original chiral synthons and inductors derived from levoglucosenone. The novel compounds can enable the generation of new functional materials, thus broadening the current portfolio of chiral chemicals. Furthermore, the present research attempts to incorporate the principles of sustainability and green chemistry in the preparation and application of the new chiral compounds.

PREPARATION OF LEVOGLUCOSENONE

The most common method to obtain levoglucosenone in preparative scale is the pyrolysis of cellulosic materials [2–4]. In an alternative approach, the group of Shibagaki reported the synthesis of **1** starting from D-galactose [5]. In a typical experiment, the acid pretreated sample is introduced in an electric furnace at 270–300 °C affording the desired enone in 3–5 % yield, with 2-furfuraldehyde as the major impurity [2–4]. The use of this conventional heating method suffers from several drawbacks, such as poor heat transfer, long reaction times, high energy consumption, and the need of specially designed equipment. For these reasons, we envisaged the use of microwave irradiation in the pyrolytic step, as this alternative heating method would provide a fast, simple, and environmentally friendly process to achieve our goals. Using domestic microwave ovens, along with simple and economic glass equipment, we could obtain levoglucosenone in 7–8 % yield, Scheme 1. Under these conditions, the major impurities detected were 2-hydroxymethylfurfural and levulinic acid, which could be easily separated upon standard work-up and vacuum distillation, to afford >97 % purity levoglucosenone [6]. The implementation of design of experiments approach allowed us to easily identify the most influent variables and to carry out the optimization with a reduced number of experiments [7].
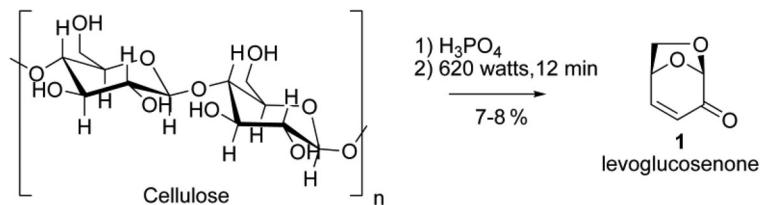

Scheme 1 Microwave-assisted preparation of levoglucosenone.

LEVOGLUCOSENONE IN ASYMMETRIC SYNTHESIS

The privileged structure of levoglucosenone makes this chiral synthon a useful building block for the development of new tools of asymmetric synthesis. Our research group has been a pioneer in this field, as discussed in this section.
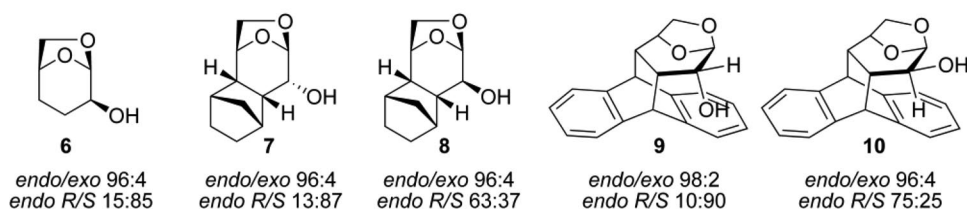
Chiral auxiliaries

Initially, we examined the usefulness of levoglucosenone in the development of chiral alcohols that could be used as efficient chiral auxiliaries in Diels–Alder cycloadditions between the corresponding acrylic esters **2** and different cyclic and acyclic dienes **3**, Scheme 2. The resultant adducts **4** can be further hydrolyzed to afford enantiomerically pure carboxylic acids **5** with concomitant recovery of the chiral auxiliary.
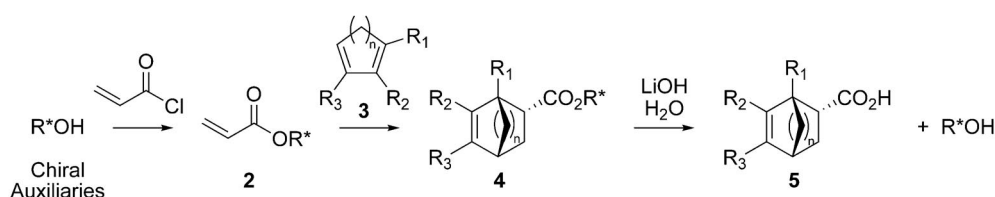

Scheme 2 Chiral auxiliaries derived from levoglucosenone in asymmetric Diels–Alder reactions.

The first generation of inductors was synthesized following a [4 + 2] cycloaddition reaction with a suitable diene followed by the reduction of the carbonyl group. The inductive capacity of the resulting alcohols was evaluated as depicted in Scheme 2 using cyclopentadiene as the dienic counterpart. Under thermal conditions, the cycloaddition step afforded high yields and modest diastereoselectivities; this was reasoned as a consequence of the conformational flexibility of the dienophile. On the other hand, the use of Lewis acids such as Et_2AlCl and $EtAlCl_2$ not only increased the *endo/exo* ratio but also the π-facial selectivity (*endo R/S*). As shown in Fig. 1, the best levels of asymmetric induction were achieved with alcohol **9**, while compounds **6** and **7** afforded slightly lower selectivities [8].

endo/exo 96:4   *endo/exo* 96:4   *endo/exo* 96:4   *endo/exo* 98:2   *endo/exo* 96:4
endo R/S 15:85   *endo R/S* 13:87   *endo R/S* 63:37   *endo R/S* 10:90   *endo R/S* 75:25

Fig. 1 Inductive capacity of the first generation of chiral auxiliaries.

In an attempt to improve the levels of π-facial selectivities, a second generation of chiral auxiliaries was next designed using the structures of **9** and **10** as templates. It was thought that the introduction of different substituents at the benzylic position, closer to the hydroxyl group, would provide a new element of steric control by imposing additional restrictions to the approach of the dienes through that face of the molecule. As depicted in Scheme 3, this structural modification could be easily achieved through a regioselective Diels–Alder reaction between levoglucosenone and a variety of 9-substituted anthracenes **11a–d**, easily obtained from commercially available 9-anthracene methanol. Since this key chemical transformation did not perform well using Lewis acids as catalysts, the desired products could
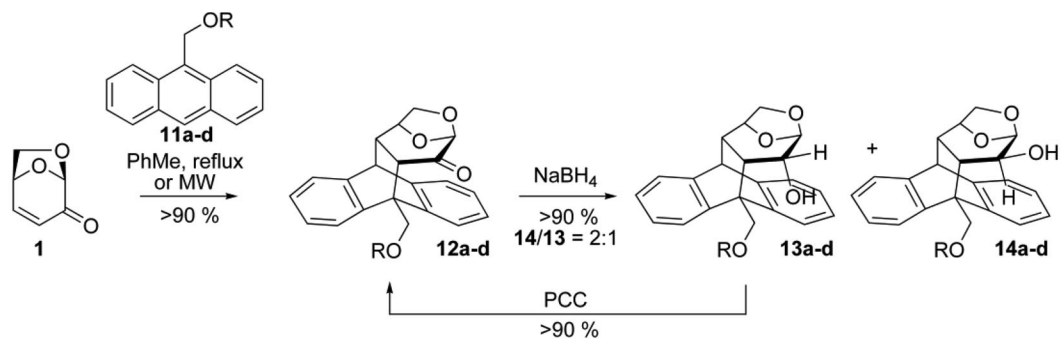
**Scheme 3** Synthesis of the second generation of chiral auxiliaries.

only be obtained after several days in refluxing toluene. In order to reduce the reaction time and therefore increase the energy saving, we found that these reactions could be efficiently carried out under microwave irradiation, affording the desired products **12a–d** in very good yields and selectivities after only 4–5 hours of irradiation [9]. Further reduction of the ketone function with $NaBH_4$ led to the formation of alcohols **13** and **14**, both having the appropriate functionality to be tested as chiral auxiliaries. However, the steric hindrance exerted by the substituents at the benzylic position made the esterification step of alcohols **13a–d** notably difficult. For this reason, experimental conditions were developed to obtain higher amounts of the other desired auxiliaries **14a–d** [10].

The inductive capacity of chiral auxiliaries **14a–d** was tested in asymmetric Diels–Alder reactions between the corresponding acrylates and five representative dienes (Scheme 2), under thermal, Lewis acid and microwave-promoted conditions [10]. In all cases, high stereo- (*endo/exo*>96:4), regio- (*ortho/meta* or *para/meta* >99:1), and π-facial selectivities (up to 98 % d.e.) were observed when using Et_2AlCl or $EtAlCl_2$ as Lewis acids, Fig. 2. The sense of asymmetric induction depended upon the diene and the nature of the benzylic substituent of the chiral auxiliary, the smallest ones (R = Me, R = Ph) being the most effective in terms of π-facial selectivity. Further hydrolysis of the Diels–Alder adducts (Scheme 2) afforded the corresponding free carboxylic acids in high enantiomeric purity along with the quantitative recovering of the chiral auxiliaries to be reused.

	MeO 14a	PhO 14b	TBSO 14c	TBDPSO 14d
cyclopentadiene	98 % d.e.	94 % d.e.	82 % d.e.	92 % d.e.
cyclohexadiene	92 % d.e.	88 % d.e.	68 % d.e.	86 % d.e.
trans-piperylene	90 % d.e.	92 % d.e.	78 % d.e.	66 % d.e.
isoprene	94 % d.e.	94 % d.e.	86 % d.e.	84 % d.e.
2,3-dimethyl-1,3-butadiene	72 % d.e.	66 % d.e.	52 % d.e.	38 % d.e.

Fig. 2 π-Facial selectivity of the second generation of chiral auxiliaries.

Detailed NMR studies and quantum mechanical calculations were made to rationalize the stereochemical outcome of these highly selective reactions [10a,b]. In particular, we found a π-stacking interaction between the phenyl ring and the alkene moiety present in the acrylate **15** as the key element of stereocontrol when using **14b** as chiral auxiliary, which was initially proposed based on the NMR data,
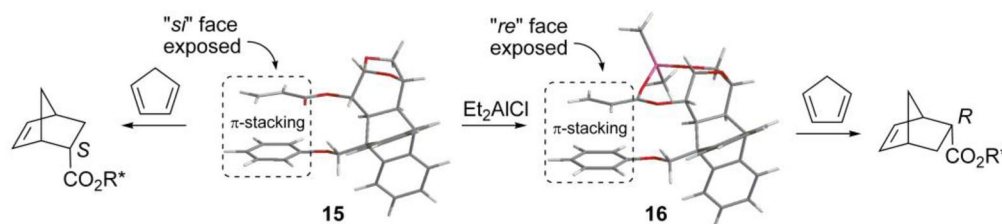
Scheme 4 Effect of π-stacking interactions and Lewis acids in the inversion of the π-facial selectivity in Diels–Alder reactions.

Scheme 4. Further detailed quantum chemical calculations allowed us to rationalize the participation of π–π interactions in the sense of asymmetric induction, including the appealing effect of inversion of the diastereoselectivity observed under Lewis-acid-promoted conditions, via the formation of chelate **16** [10b]. More recently, we aimed at exploring the effect of electron density of the arene moiety with the relative strength of the π-stacking interaction exerted with the acrylate counterpart. Preliminary results showed that the introduction of electron-releasing and -withdrawing groups at the *para* position of the phenoxy group of **14b** had a slightly effect on both the π–π interaction and the facial selectivity in the corresponding Diels–Alder reaction with cyclopentadiene.

In order to explore the scope of the chiral auxiliaries in other chemical transformations, we next envisaged the construction of polysubstituted pyrrolidines by mean of using acrylates **17** as chiral dipolarophiles in asymmetric 1,3-dipolar cycloadditions, Scheme 5.
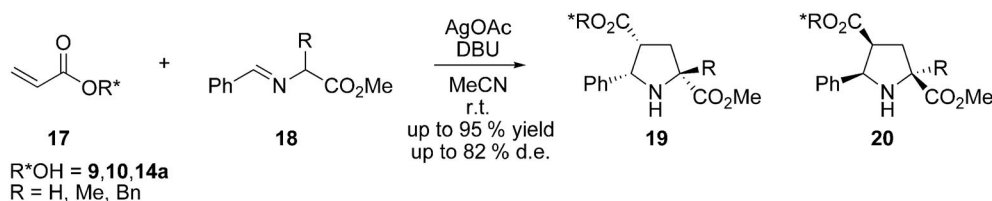
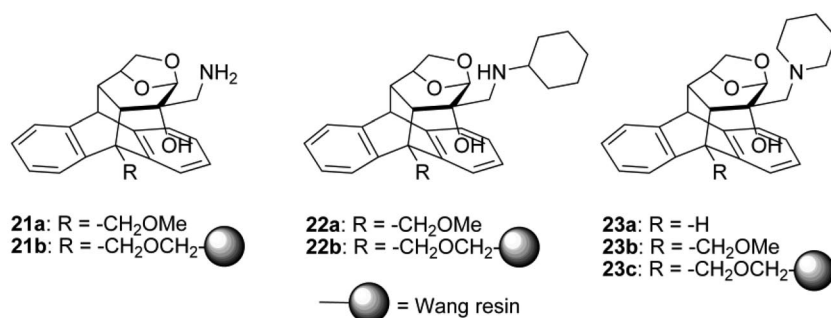**Scheme 5** Asymmetric synthesis of chiral pyrrolidines.

Pyrrolidines are five-membered ring heterocycles containing a nitrogen atom, which are profoundly distributed in naturally occurring secondary metabolites and also in synthetic pharmaceutical and agrochemical agents. The best-known examples are the L-proline and the 4-hydroxy-L-proline, but there is a lengthy list of biologically active compounds that share this key structural feature in their molecular framework [11]. Not surprisingly, this heterocyclic ring system has attracted the attention for new synthetic developments [12].

Our experimental results indicated that using the corresponding silver metallo-azomethine ylides derived from **18**, *endo*-substituted pyrrolidines **19–20** were obtained in very good yields (up to 95 %) and diastereomeric excess (up to 82 %). The isolation of only two adducts of all possible 16 isomers constitutes a remarkable feature of this system, which is currently being studied in detail and will be published in due course.

## Solution- and solid-phase chiral catalysts

Amino alcohols are versatile chiral building blocks for organic synthesis and have also been used extensively as chiral auxiliaries or catalysts in asymmetric synthesis. The enantioselective nucleophilic addition of organometallic reagents to carbonyl compounds in the presence of chiral β-amino alcohol as cat-

alysts is recognized as one of the most effective methods for generating optically active secondary alcohols [13]. Taking advantage of the keto functionality of the precursors of the chiral auxiliaries **12** (Scheme 3), we envisioned the development of amino alcohols through an epoxidation reaction [14] followed by the oxirane ring opening with different nucleophiles. Preliminary results demonstrate that this strategy efficiently affords the chiral amino alcohols **21–23** derived from levoglucosenone (Fig. 3). Additionally, amino alcohols were immobilized on Wang resin with the purpose to be used as supported catalysts.

21a: R = -CH$_2$OMe
21b: R = -CH$_2$OCH$_2$-⬤

22a: R = -CH$_2$OMe
22b: R = -CH$_2$OCH$_2$-⬤

23a: R = -H
23b: R = -CH$_2$OMe
23c: R = -CH$_2$OCH$_2$-⬤

—⬤ = Wang resin

Fig. 3 Chiral amino alcohols derived from levoglucosenone.

The inductive capacities of chiral catalysts **21–23** were evaluated in the asymmetric addition of Et$_2$Zn to benzaldehyde (**24**) (Scheme 6). In all cases, 1-phenylpropanol (**25**) was obtained in excellent yields with good enantiomeric excesses (up to 70 %). It is important to mention that the amino alcohols can be recycled and were reused without loose in the catalytic activity.


24   **25-(R)**   **25-(S)**
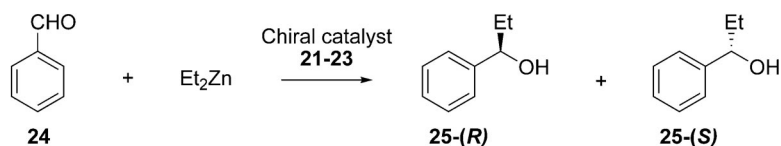
**Scheme 6** Asymmetric addition of Et$_2$Zn to benzaldehyde catalyzed by chiral amino alcohols.

Chiral organocatalysts

Chiral pyrrolidines are molecular scaffolds that are found in many efficient chiral organocatalysts. Taking advantage of the unique dipolarophilic reactivity present in **1**, we foresaw the 1,3-dipolar cycloaddition using azomethine ylide as a direct route for the development of novel organocatalysts. Using this methodology, new families of pyrrolidines **26** were synthesized in excellent yields, regioselectivities, and stereoselectivities. Furthermore, an unprecedented isomerization event led to a new family of pyrrolidines **27** with an unusual relative stereochemistry (Scheme 7) [15].

To evaluate the usefulness of levoglucosenone-derived chiral pyrrolidines in asymmetric synthesis, the compounds synthesized in this work were tested as novel organocatalysts in iminium-ion-based Diels–Alder reactions between (*E*)-cinnamaldehyde (**28**) and cyclopentadiene (**29**) (Scheme 8). All compounds demonstrated to be very active catalysts, typically achieving completeness of the reaction in 5–48 h using 15 mol % of catalysts load. The yields (up to 97 %), *exo/endo* selectivity (up to 85:15) and enantiomeric ratios (up to 90 % ee) were also high, making this system an excellent candidate for further optimization. It is important to point out that few organocatalytic systems have been reported to have a marked preference towards the *exo* adducts.
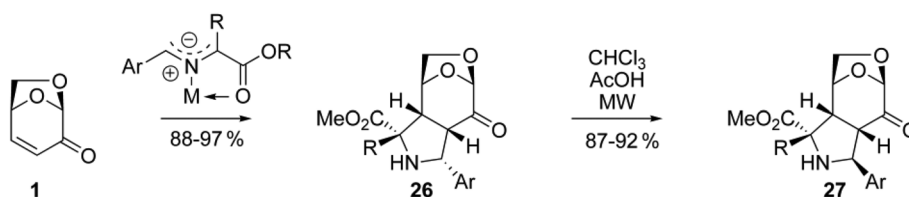
Scheme 7 Synthesis of chiral pyrrolidine organocatalysts derived from levoglucosenone.
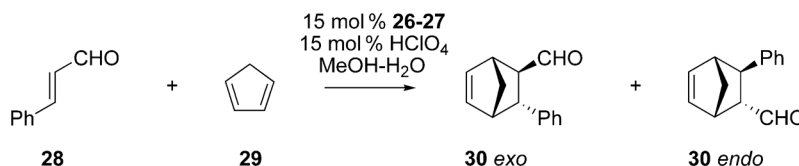
Scheme 8 Asymmetric Diels–Alder reaction catalyzed by chiral pyrrolidines.
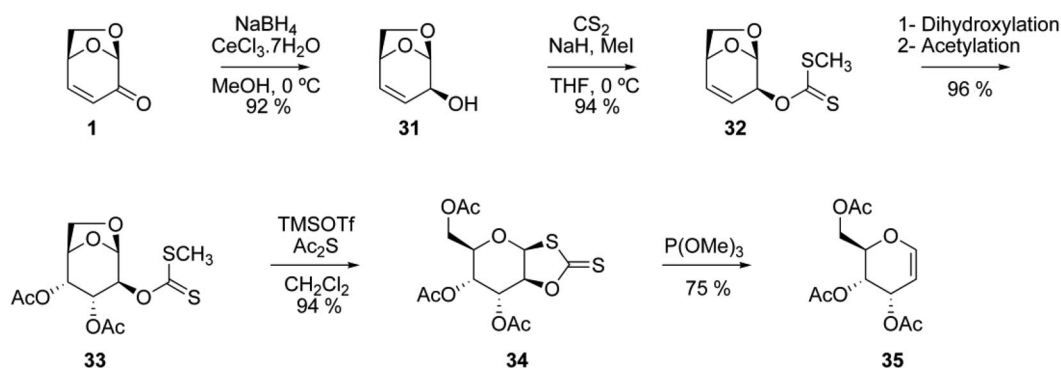
ENANTIOSPECIFIC SYNTHESIS

The term "glycal" is used to define pentose and hexose derivatives having a double bond between the anomeric carbon and the adjacent one [16]. These compounds are versatile synthetic intermediates, owing to the variety of transformations associated with their enol ether functionality.

Access to glycals is important in the glycosylation field for the synthesis of oligosaccharide motifs [17], *C*-glycosides [18], *C*-nucleosides [19], nucleosides [20], and other biologically important molecules. Much effort was committed to obtain glycoconjugated compounds using the glycal method [21] in order to prepare synthetic vaccines. If new structural scaffolds are to be built up, it will be necessary to provide a variety of glycals of different configurations. In this respect, the only pyranoid glycals that are readily accessible currently are either D-glucal and D-galactal or L-rhamnal. Other D-glycals, such as D-gulal and D-allal (which are derived from rare sugars) are not readily available [22]. Rare sugars are defined as monosaccharides that exist in nature but are present only in limited quantities. For example, D-allose, a rare sugar and a parent compound of D-allal, has exhibited several interesting biological activities [23]. However, due to its low natural abundance the studies of its biological effects are limited.

Several methods have been reported for the synthesis of D-allal [24], but to the best of our knowledge none of them have allowed this building block to become commercially available. Hence, the development of a straightforward synthetic route toward this glycal is still a challenging goal in carbohydrate synthesis. Based on the premises of simplicity and effectiveness, an innovative synthesis of tri-*O*-acetyl-D-allal was achieved from levoglucosenone, Scheme 9.

Reduction of levoglucosenone (**1**) under Luche conditions [25] afforded the allylic alcohol **31** in a chemo- and stereoselective way with very good yield. Although the configuration of C-2 is not crucial because it will be converted into a sp^2 carbon, our studies showed that selectivity in the dihydroxylation step is strongly dependent on the stereochemistry of this center. Allylic xanthate was envisioned as a good precursor for the generation of enol-ether functionality. *cis*-dihydroxylation of **32** under catalytic conditions, and further acetylation of the newly generated hydroxyl groups afforded a sole product **33** in excellent overall yield.

Treatment of xantate **33** with trimethylsilyl triflate and acetyl sulfide provoked the ring opening of the 1,6-anhydro bridge with concomitant formation of a five-membered ring 1,3-oxathiolane-2-thione, and acetylation of the primary alcohol cleanly furnished the bicyclic system **34** in 94 % yield. The lately formed 1,3-oxathiolane-2-thione functionality was considered an adequate precursor for the

Scheme 9 Enantiospecific synthesis of tri-*O*-acetyl-D-allal from levoglucosenone.

generation of the 1,2-double bond. When substrate **34** was submitted to Corey–Winter reaction conditions [26] tri-*O*-acetyl-D-allal (**35**) was obtained in 75 % yield.

In this way, the synthesis of **35** was achieved in six steps and 56 % overall yield from a biomass-derived starting material [27]. Recently, in order to improve the *greenness* of the synthetic sequence a radical initiated fragmentation process was used to substitute the Corey–Winter protocol. Preliminary experiments showed promising results when using lauryl peroxide as radical initiator.

CONCLUSION

The pyrolytic degradation of the polymeric chain in cellulose-containing materials is a valuable route to produce chiral compounds and provides an opportunity to broaden the current portfolio of chemical products. Moreover, it has been demonstrated that the conversion of biomass in useful chemicals is an alternative that can compete or even replace the ones derived from fossil sources. Levoglucosenone has proven to be an important synthon for the development of chiral key intermediates, chiral auxiliaries, catalysts, and organocatalysts. These results, in addition to the fact that the starting material is inexpensive, renewable, and highly accessible, make these systems excellent models to be further employed in the preparation of other enantiopure products.

ACKNOWLEDGMENTS

REFERENCES

1. F. W. Lichtenthaler. *Acc. Chem. Res.* **35**, 728 (2002).
2. (a) Z. J. Witczak (Ed.). *Levoglucosenone and Levoglucosans: Chemistry and Applications*, ATL Press, Mount Prospect, USA (1994); (b) Z. J. Witczak, K. Tatsuta (Eds.). *Carbohydrate Synthons in Natural Products Chemistry. Synthesis, Functionalization, and Applications*, ACS Symposium Series No. 841, American Chemical Society, Washington, DC (2003); (c) A. M. Sarotti, M. M. Zanardi, R. A. Spanevello, A. G. Suárez. *Curr. Org. Synth.* **9**, 439 (2012) and refs. cited therein.
3. (a) Y. Tsuchiya, K. Sumi. *J. Appl. Polym. Sci.* **14**, 2003 (1970); (b) Y. Halpern, R. Riffer, A. Broido. *J. Org. Chem.* **38**, 204 (1973).

4. (a) F. Shafizadeh, R. H. Furneaux, T. T. Stevenson. *Carbohydr. Res.* **71**, 169 (1979); (b) J. S. Swenton, J. N. Freskos, P. Dalidowicz, M. L. Kerns. *J. Org. Chem.* **61**, 459 (1996).

5. M. Shibagaki, K. Takahashi, H. Kuno, I. Honda, H. Matsushita. *Chem. Lett.* 307 (1990).

6. A. M. Sarotti, R. A. Spanevello, A. G. Suárez. *Green Chem.* **9**, 1137 (2007).

7. E. Morgan. *Chemometrics: Experimental Design*, John Wiley, New York (1995).

8. (a) A. M. Sarotti, R. A. Spanevello, A. G. Suárez. *Tetrahedron Lett.* **45**, 8203 (2004); (b) A. M. Sarotti, R. A. Spanevello, A. G. Suárez. *Tetrahedron Lett.* **46**, 6987 (2005); (c) A. M. Sarotti, R. A. Spanevello, C. Duhayon, J.-P. Tuchagues, A. G. Suárez. *Tetrahedron* **63**, 241 (2007); (d) M. M. Zanardi, A. G. Suárez. *Tetrahedron Lett.* **50**, 999 (2009).

9. A. M. Sarotti, M. M. Joullie, R. A. Spanevello, A. G. Suárez. *Org. Lett.* **8**, 5561 (2006).

10. (a) A. M. Sarotti, R. A. Spanevello, A. G. Suárez. *Org. Lett.* **8**, 1487 (2006); (b) A. M. Sarotti, I. Fernandez, R. A. Spanevello, M. A. Sierra, A. G. Suárez. *Org. Lett.* **10**, 3389 (2008); (c) A. M. Sarotti, R. A. Spanevello, A. G. Suárez. *Tetrahedron* **65**, 3502 (2009); (d) A. M. Sarotti, R. A. Spanevello, A. G. Suárez. *Arkivoc* **vii**, 31 (2011).

11. (a) W. H. Pearson. *Pure Appl. Chem.* **74**, 1339 (2002); (b) C. V. Galliford, K. A. Scheidt. *Angew. Chem., Int. Ed.* **46**, 8748 (2007).

12. (a) N. T. Jui, J. A. O. Garber, F. Gadini Finelli, D. W. C. MacMillan. *J. Am. Chem. Soc.* **134**, 11400 (2012); (b) L. R. Whitby, Y. Ando, V. Setola, P. K. Vogt, B. L. Roth, D. L. Boger. *J. Am. Chem. Soc.* **133**, 10184 (2011).

13. (a) E. Juaristi, C. Anaya de Parrodi. *Synlett* **17**, 2699 (2006); (b) R. Noyori. *Asymmetric Catalysis in Organic Synthesis*, Chap. 4, John Wiley, New York (1993).

14. E. J. Corey, M. Tchaikovsky. *J. Am. Chem. Soc.* **87**, 1353 (1965).

15. A. M. Sarotti, R. A. Spanevello, A. G. Suárez, G. Echeverría, O. Piro. *Org. Lett.* **14**, 2556 (2012).

16. (a) W. Priebe, G. Grynkiewicz. In *Glycoscience: Chemistry and Chemical Biology*, B. Fraser-Reid, K. Tatsuta, J. Thiem (Eds.), p. 749, Springer, Heidelberg (2008); (b) H. H. Franz, P. H. Gross, V. V. Samoshin. *Arkivoc* **i**, 271 (2008).

17. (a) S. J. Danishefsky, M. T. Bilodeau. *Angew. Chem., Int. Ed. Engl.* **35**, 1380 (1996); (b) J. Y. Roberge, X. Beebe, S. J. Danishefsky. *J. Am. Chem. Soc.* **120**, 3915 (1998); (c) F. E. McDonald, H. Y. H. Zhu. *J. Am. Chem. Soc.* **120**, 4246 (1998).

18. S. Hosokawa, B. Kirschbaum, M. Isobe. *Tetrahedron Lett.* **39**, 1917 (1998).

19. J. A. Walker II, J. J. Chen, J. M. Hinkley, D. S. Wise, L. B. Townsend. *Nucleosides Nucleotides* **16**, 1999 (1997).

20. (a) Y. Díaz, A. El-Laghdach, S. Castillón. *Tetrahedron* **53**, 10921 (1997); (b) F. Bravo, M. Kassou, Y. Díaz, S. Castillón. *Carbohydr. Res.* **336**, 83 (2001).

21. P. H. Seeberger, M. T. Bilodeau, S. J. Danishefsky. *Aldrichim. Acta* **30**, 75 (1997).

22. (a) M. D. Wittman, R. L. Halcomb, S. J. Danishefsky. *J. Org. Chem.* **55**, 1979 (1990); (b) R. D. Guthrie, R. W. Irvine. *Carbohydr. Res.* **72**, 285 (1979).

23. (a) F. Yamaguchi, M. Takata, K. Kamitori, M. Nonaka, Y. Dong, L. Sui, M. Tokuda. *Int. J. Oncol.* **32**, 377 (2008); (b) S. Tanaka, H. Sakamoto. *Cell Immunol.* **271**, 141 (2011); (c) T. Nakamura, S. Tanaka, K. Hirooka, T. Toyoshima, N. Kawai, T. Tamiya, F. Shiraga, M. Tokuda, R. Keep, T. Itano, O. Miyamoto. *Neurosci Lett.* **487**, 103 (2011).

24. (a) M. Kugelman, A. K. Mallams, H. F. Vernay. *J. Chem. Soc., Perkin Trans. 1* 1113 (1976); (b) R. D. Guthrie, R. W. Irvine. *Carbohydr. Res.* **72**, 285 (1979); (c) M. D. Wittman, R. L. Halcomb, S. J. Danishefsky, J. Golik, D. Vyas. *J. Org. Chem.* **55**, 1979 (1990); (d) R. L. Halcomb, S. J. Danishefsky, M. D. Wittman. U.S. Patent 5,104,982 (1992); (e) O. Boutureira, M. A. Rodríguez, M. I. Matheu. *Org. Lett.* **8**, 673 (2006); (f) T. Fujiwara, M. Hayashi. *J. Org. Chem.* **73**, 9161 (2008) and refs. cited therein.

25. L. Kurti, B. Czabo. *Strategic Applications of Named Reactions in Organic Synthesis*, Elsevier Academic, San Diego (2005).
26. E. J. Corey, R. A. E. Winter. *J. Am. Chem. Soc.* **85**, 2677 (1963).
27. E. D. V. Giordano, A. Frinchaboy, A. G. Suárez, R. A. Spanevello. *Org. Lett.* **14**, 4602 (2012).