



Cite this: *RSC Adv.*, 2020, 10, 16882

Received 2nd April 2020

Accepted 21st April 2020

DOI: 10.1039/d0ra02994g

rsc.li/rsc-advances

Concise asymmetric synthesis of two natural oxacyclododecindione-type macrolactones from industrial waste†

Xian Liu, Huifang Nie, Lin Yao, Ru Jiang * and Weiping Chen *

(*S*)-5-Methyl-tetrahydropyran-2-one **1** is a by-product in the production of key intermediates of steroidal hormones. Asymmetric synthesis of natural oxacyclododecindione-type macrolactones **2** and **3** has been realized for the first time from (*S*)-**1** in seven and eight steps with 37% and 27% overall yield, respectively.

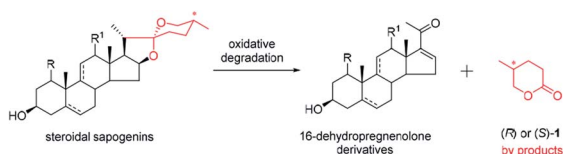
Introduction

Green chemistry, which was established about two decades ago, has attracted considerable attention due to its reduction or elimination of the use and generation of hazardous substances from a chemical process.¹ Most efforts have focused on waste minimization and avoiding the use of toxic or hazardous reagents and solvents, particularly in the pharmaceutical field. However, little attention has been paid on the rational reuse of industrial wastes.² Both (*R*)- and (*S*)-5-methyl-tetrahydropyran-2-one **1** are by-products in the production of key intermediates (16-dehydropregnenolone derivatives) of steroidal hormones from steroidal sapogenins by oxidative degradation (Scheme 1).³ To produce 100 kg of 16-dehydropregnenolone derivatives may generate more than 30 kg of (*R*)- or (*S*)-**1** as wastes,^{3b} and almost all of them are destroyed by burning or other methods.⁴ At present, the throughput of 16-dehydropregnenolone derivatives is kiloton each year only in China. There have been only very few examples to utilize (*R*)- and (*S*)-**1** as starting materials in the synthesis of bioactive compounds.⁵ Therefore, exploiting the synthesis application of (*R*)- or (*S*)-**1** is highly welcomed.

In 2008, three new 12-membered macrolactones 4-dechloro-14-deoxy-oxacyclododecindione **2**, 14-deoxy-oxacyclododecin-

dione **3** and oxacyclododecindione **4** were isolated as fungal secondary metabolites from imperfect fungus *Exserohilum rostratum* by Opatz and Erkel (Fig. 1).^{6a} They exhibit potent anti-inflammatory and anti-fibrotic activities in cell culture experiments and in an *in vivo* mouse model of systemic lupus erythematosus (SLE) and may serve as lead structures for therapeutics against chronic inflammatory and/or fibrotic diseases like asthma, rheumatoid arthritis, SLE or cancer.⁶ In 2005, Opatz attempted to finish the total synthesis of racemic **2** and **3**.⁷ Starting from commercially available *cis*-2,3-epoxybutane and allyl cuprate, the total synthesis of racemic **2** (24% yield over 10 steps) and **3** (18% yield over 11 steps) was accomplished by important steps such as ring-opening reaction, Wittig reaction, and a late-stage intramolecular Friedel-Crafts cyclization.^{7a} Protection and deprotection reactions are frequently used in the total synthesis of racemic **2** and **3** which made the synthesis route more complicated and led to a lower overall yield. Soon after, the absolute configuration of natural **2** and **3** was determined as (14*S*,15*R*) by X-ray crystallography.⁸ To date, the asymmetric synthesis of natural macrolactones **2** and **3** is still an untouched work.

Our retrosynthetic strategy for the synthesis of (14*S*,15*R*)-**2** commences with the disconnection of the C8–C9 bond, exposing *tert*-butyl ester (6*S*,7*R*,*E*)-**5** (Scheme 2). We envisioned that the intramolecular Friedel-Crafts cyclization of **5** in the presence of Lewis acid could form (14*S*,15*R*)-**2**, meanwhile the cleavage of *tert*-butyl ester bond could be simultaneously achieved. *Tert*-butyl ester **5** could be easily generated by esterification of arylacetic acid **6** and alcohol (6*S*,7*R*,*E*)-**7**. We envisioned



Scheme 1 Production of industrial wastes (*R*)- and (*S*)-**1**.

School of Pharmacy, Fourth Military Medical University, 169 Changle West Road, Xian, 710032, P. R. China. E-mail: jiangru@fmmu.edu.cn

† Electronic supplementary information (ESI) available. See DOI: 10.1039/d0ra02994g

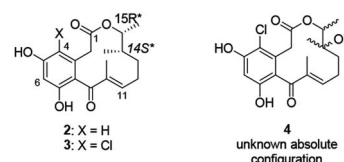
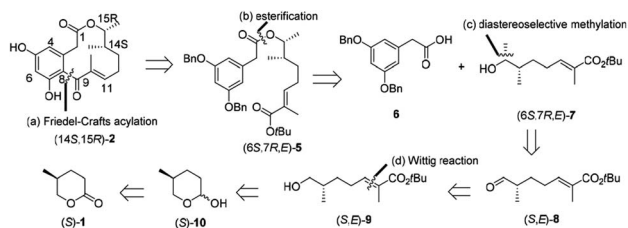


Fig. 1 Structures of the oxacyclododecindiones **2**, **3** and **4**.



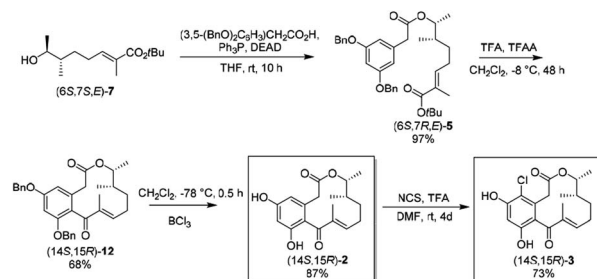


Scheme 2 Retrosynthetic analysis of (14S,15R)-2 by (a) an intra-molecular Friedel–Crafts acylation, (b) an esterification, (c) a diastereoselective methylation, and (d) a Wittig reaction.

that the key alcohol intermediate (6S,7R,E)-7 could be obtained from aldehyde (S,E)-8 by diastereoselective methylation, while the stereogenic center at C7 could be constructed according to Kovalenko and Matiushenkov's procedure.⁹ (S,E)-8 could be readily prepared by a sequential reduction, Wittig reaction and oxidation from (S)-1. Based on the retrosynthetic analysis, herein, we reported the first asymmetric total synthesis of natural (14S,15R)-2 and (14S,15R)-3 starting from abundant and renewable industrial waste (S)-1.

Results and discussion

With the synthetic blueprint in mind, our initial attention was focused on preparation of the key intermediate (6S,7R,E)-7 (Scheme 3). As depicted in Scheme 3, reduction of (S)-1 with DIBAL-H furnished the corresponding lactol (S)-10, which was subjected to a Wittig reaction with ylide **11** (ref. 10) without further purification to give (S,E)-9 in 82% yield with E : Z > 95 : 5 selectivity. TEMPO-mediated-oxidation of (S,E)-9 employing $\text{PhI}(\text{OAc})_2$ as a secondary oxidant, which is compatible with the presence of olefins,¹¹ afforded the corresponding aldehyde (S,E)-8 in 84% yield. Next, according to Kovalenko and Matiushenkov's procedure, (S,E)-8 was diastereoselectively methylated with $\text{MeTi}(\text{OiPr})_3$ (ref. 12) in the presence of 20 mol% of TADDOL- $\text{Ti}(\text{OiPr})_2$. Unfortunately, when [(S,S)-TADDOL] $\text{Ti}(\text{OiPr})_2$ was used as catalyst, the methylation of (S,E)-8 gave an inseparable mixture of two diastereomers (6S,7R,E)-7 and (6S,7S,E)-7 with d.r. 76 : 24 (the ratio of a peak of protons on C8 for (6S,7S,E)-7 at 1.17 ppm and (6S,7R,E)-7 at 1.14 ppm). To our delight, in the presence of [(R,R)-TADDOL] $\text{Ti}(\text{OiPr})_2$, (6S,7S,E)-7 was obtained in 94% yield with d.r. > 95 : 5 (the signal of



Scheme 4 Synthesis of (14S,15R)-2 and (14S,15R)-3 from (6S,7S,E)-7.

(6S,7R,E)-7 was undetectable in ^1H NMR). Although the configuration at C7 was opposite to that of key intermediates (6S,7R,E)-7, it could be converted by Mitsunobu reaction. Therefore, the next synthesis route was adjusted as Scheme 4.

Reaction of (6S,7S,E)-7 with 3,5-bis(benzyloxy)phenylacetic acid under Mitsunobu reaction conditions gave ester (6S,7R,E)-5 in 97% yield. As we expected, when the diluted solution of (6S,7R,E)-5 in CH_2Cl_2 was treated with a mixture of trifluoroacetic anhydride and trifluoroacetic acid, the cleavage of the *tert*-butyl ester bond and intramolecular Friedel–Crafts acylation took place simultaneously to give the desired lactone (14S,15R)-12 in 68% yield. Finally, deprotection of the benzyl ethers with boron trichloride afforded (14S,15R)-2 in 87% yield, which was further converted to (14S,15R)-3 (in 73% yield) by chlorination with *N*-chlorosuccinimide. ^1H and ^{13}C NMR spectra of both synthetic (14S,15R)-2 and (14S,15R)-3 were in good agreement with the data of the natural products.⁸

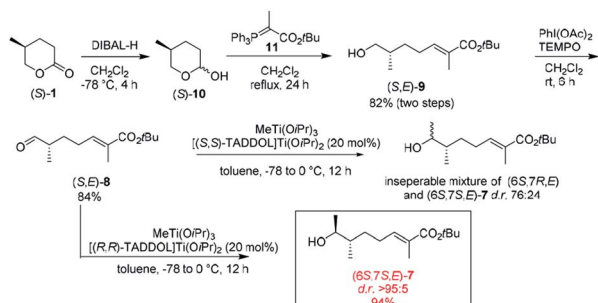
Conclusions

In summary, concise and efficient asymmetric total synthesis of natural 4-dechloro-14-deoxy-oxacyclododecindione **2** and 14-deoxy-oxacyclododecindione **3** has been accomplished for the first time. Using industrial waste (S)-5-methyl-tetrahydropyran-2-one **1** as starting material, (14S,15R)-2 and **3** were obtained in seven and eight steps with 37% and 27% overall yield, respectively. The chirality of C14 originates from the starting material, and the stereogenic center at C15 is stereospecifically constructed by highly diastereoselective methylation and Mitsunobu reaction.

Experimental section

General methods

Unless otherwise noted, all reactions sensitive to air or moisture were performed under nitrogen atmosphere. All commercially available chemicals including solvents were used without further purification. (S)-5-Methyl-tetrahydropyran-2-one (S)-1 was prepared from sarsasapogenin according to Tian's procedure.^{3b} NMR spectra were recorded on Bruker 400 spectrometer. ^1H NMR and ^{13}C NMR spectra were measured at 400 MHz and 101 MHz. High resolution mass measurements (HRMS) were obtained on Bruker smart apex II. Optical rotations were measured on the PerkinElmer 343 polarimeter.



Scheme 3 Synthesis of key intermediate (6S,7S,E)-7.



(*S,E*)-tert-Butyl 7-hydroxy-2,6-dimethylhept-2-enoate (*S,E*)-9.

To a stirred solution of (*S*)-**1** (3.00 g, 26.32 mmol) in dry CH₂Cl₂ (20 mL) was added DIBAL-H (1.0 M in hexane, 26.3 mL, 26.3 mmol) at −78 °C. After 4 h stirring at the same temperature, saturated Rochelle salt (15 mL) was added and further stirred for 6 h at room temperature. The mixture was extracted with CH₂Cl₂, dried over anhydrous Na₂SO₄, and evaporated to give the corresponding lactol (*S*)-**10** as a yellow oil (2.51 g), which was used directly without purification. The crude product was added to the solution of *tert*-butyl 2-(triphenylphosphoranylidene) propanoate (12.52 g, 32.07 mol) in CH₂Cl₂ (20 mL). After being refluxed for 24 h, the solvent was removed *in vacuo*. Purification by flash chromatography on silica gel (petroleum ether : EtOAc = 5 : 1) yielded (*S,E*)-**9** (4.91 g, 82%). [α]_D²⁰ = −11.1 (*c* 0.31, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 6.65 (t, *J* = 1.2 Hz, 1H), 3.54–3.44 (m, 2H), 2.33–2.05 (m, 2H), 1.79 (s, 3H), 1.68–1.54 (m, 2H), 1.48 (s, 9H), 1.32–1.26 (m, 1H), 0.95 (d, *J* = 6.7 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃): δ 167.6, 140.9, 129.2, 80.0, 68.1, 35.4, 32.0, 28.1, 26.1, 16.4, 12.4. HRMS (ESI): calcd for [C₁₃H₂₄O₃ + Na]⁺: 251.1618, found: 251.1620.

(6*S*,7*S,E*)-tert-Butyl-7-hydroxy-2,6-dimethyloct-2-enoate (6*S*,7*S,E*)-7**.** Step 1: a solution of alcohol (*S,E*)-**9** (3.00 g, 13.16 mmol), iodobenzene diacetate (4.6 g, 14.28 mmol) and 2,2,6,6-tetramethylpiperidinoxy (205 mg, 1.31 mmol) in CH₂Cl₂ (26 mL, 0.5 M) was stirred at room temperature. After stirring for 3 h, the reaction mixture is washed successively with an aqueous sodium thiosulfate solution and brine. The organic solution is dried over anhydrous Na₂SO₄, and concentrated. Purification by flash chromatography on silica gel (petroleum ether : EtOAc = 10 : 1) yielded the (*S,E*)-**8** (2.50 g, 84%) as a light red oil which was used immediately. Step 2: a solution of ((4*R*,5*R*)-2,2-dimethyl-1,3-dioxolane-4,5-diyl)bis(di-phenyl-methanol) [(*R,R*)-TADDOL] (488 mg, 1.05 mmol) and Ti(O^{*i*}Pr)₄ (446 mg, 1.57 mmol) in toluene (8 mL) was heated at 110 °C for 3 h under an argon atmosphere. The solvent was removed *in vacuo*, after which the residue was diluted with dry toluene (28 mL) in −78 °C mixed with MeTi(O^{*i*}Pr)₃ (1.88 g, 7.84 mmol) and stirred at the same temperature for 0.5 h. The aldehyde (*S,E*)-**8** (1.18 g, 5.23 mmol) in toluene (3 mL) was added dropwise to the resulting stirred solution at −78 °C. The mixture was stirred for 12 h at −78 °C and then gradually warmed to 0 °C for 12 h, diluted with saturated aqueous NH₄Cl (5 mL), and filtered. The filter cake was washed with CH₂Cl₂. The organic phase was separated and washed with saturated aqueous NaHCO₃, dried over anhydrous Na₂SO₄. The solvent was removed *in vacuo*. Purification by flash chromatography on silica gel (petroleum ether : EtOAc = 10 : 1) yielded (6*S*,7*S,E*)-**7** (1.20 g, 94%) with d.r. > 95 : 5. [α]_D²⁰ = −18.5 (*c* 1.27, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 6.65 (td, *J* = 7.4, 1.4 Hz, 1H), 3.77–3.71 (m, 1H), 2.22–2.11 (m, 2H), 1.79 (s, 3H), 1.62–1.56 (m, 1H), 1.49 (s, 9H), 1.32–1.25 (m, 2H), 1.17 (d, *J* = 6.4 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃): δ 167.6, 141.0, 129.2, 80.0, 71.2, 39.4, 31.5, 28.2, 26.5, 20.3, 14.0, 12.4. HRMS (ESI): calcd for [C₃₆H₄₄O₆ + Na]⁺: 265.1774, found: 265.1775.

(6*S*,7*R,E*)-tert-Butyl-7-(2-(3,5-bis(benzyloxy)phenyl)acetoxy)-2,6-dimethyloct-2-enoate (6*S*,7*R,E*)-5**.** To a solution of (6*R*,7*R,E*)-

7 (100 mg, 0.41 mmol), 3,5-bis(benzyloxy)phenylacetic acid (216 mg, 0.62 mmol), and triphenylphosphine (163 mg, 0.62 mmol) in THF (1.2 mL) was added dropwise a THF (1 mL) solution of diisopropyl azodicarboxylate (125 mg, 0.62 mmol). After stirring for 10 h at room temperature, the solvent was removed *in vacuo*. Purification by column chromatography on silica gel (petroleum ether : EtOAc = 20 : 1) yielded (6*R*,7*S,E*)-**5** (230 mg, 97%) as a colorless oil. [α]_D²⁰ = −5.6 (*c* 0.60, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 7.49–7.29 (m, 10H), 6.65–6.49 (m, 4H), 5.02 (s, 4H), 4.89–4.76 (m, 1H), 3.53 (s, 2H), 2.26–1.98 (m, 2H), 1.77 (s, 3H), 1.73–1.60 (m, 1H), 1.47 (s, 9H), 1.27–1.15 (m, 2H), 1.13 (d, *J* = 6.4 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃): δ 170.9, 167.5, 160.0, 140.6, 136.9, 136.4, 129.4, 128.6, 128.0, 127.5, 108.5, 100.84, 80.0, 74.5, 70.0, 42.0, 37.1, 31.3, 28.1, 26.2, 16.0, 14.6, 12.4. HRMS (ESI): calcd for [C₃₆H₄₄O₆ + Na]⁺: 595.3030, found: 595.3014.

(14*S*,15*R*)-5,7-Di-*O*-benzyl-4-dechloro-14-deoxyoxacyclododecindione (14*S*,15*R*)-12**.** (6*S*,7*R,E*)-**5** (928 mg, 1.62 mmol), trifluoroacetic acid (167 mL) and trifluoroacetic anhydride (83.5 mL) were dissolved in CH₂Cl₂ (2100 mL) and cooled to −8 °C. The reaction mixture stood at −8 °C for 48 h. The solvent was removed *in vacuo*. Purification by flash chromatography on silica gel (petroleum ether : EtOAc = 15 : 1) yielded (14*S*,15*R*)-**12** (545 mg, 68%) as a colorless oil. [α]_D²⁰ = +36.6 (*c* 0.20, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 7.65–7.07 (m, 10H), 6.51 (d, *J* = 1.3 Hz, 3H), 5.17–4.90 (m, 4H), 4.59 (dq, *J* = 12.7, 6.2 Hz, 1H), 3.31 (t, *J* = 13.5 Hz, 2H), 2.42 (s, 1H), 2.11 (d, *J* = 20.3 Hz, 1H), 1.93 (s, 3H), 1.69–1.60 (m, 1H), 1.53–1.31 (m, 2H), 1.09 (d, *J* = 4.6 Hz, 3H), 0.92 (d, *J* = 7.0 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃): δ 199.3, 170.4, 159.9, 156.6, 152.9, 136.9, 136.7, 133.3, 128.8, 128.6, 128.2, 127.8, 127.8, 127.7, 126.9, 124.3, 107.7, 100.4, 77.3, 70.4, 70.3, 53.6, 39.7, 19.2, 10.5. HRMS (ESI): calcd for [C₃₂H₃₄O₅ + Na]⁺: 521.2298, found: 521.2294.

(14*S*,15*R*)-4-Dechloro-14-deoxyoxacyclododecindione (14*S*,15*R*)-2**.** A solution of (14*S*,15*R*)-**12** (460 mg, 0.923 mmol) in CH₂Cl₂ (138 mL) was cooled to −78 °C. Boron trichloride (1.0 M in hexane, 9.3 mL, 9.3 mmol) was added and the mixture was stirred at that temperature. After 30 min the reaction mixture was quenched with saturated aqueous NaHCO₃ (50 mL) and warmed up to room temperature. The organic layer was separated and the aqueous layer was extracted with CH₂Cl₂. The combined organic layers were dried over anhydrous Na₂SO₄ and filtered. The solvent was removed *in vacuo*. Purification by flash chromatography on silica gel (petroleum ether : EtOAc = 2 : 1) yielded (14*S*,15*R*)-**2** (256 mg, 87%) as a white solid. [α]_D²⁰ = +41.5 (*c* 0.3, MeOH) lit. [α]_D²⁰ = +29.1 (*c* 0.40, MeOH). ¹H NMR (400 MHz, MeOD): δ 6.52 (s, 1H), 6.30 (s, 1H), 6.26 (s, 1H), 4.67–4.50 (m, 1H), 3.23 (t, *J* = 16.3 Hz, 2H), 2.48–2.42 (m, 1H), 2.25–2.21 (m, 1H), 1.88 (s, 3H), 1.70 (dd, *J* = 14.1, 7.8 Hz, 1H), 1.56 (dd, *J* = 13.7, 6.9 Hz, 1H), 1.49–1.37 (m, 1H), 1.13 (d, *J* = 6.1 Hz, 3H), 0.93 (d, *J* = 7.0 Hz, 3H). ¹³C NMR (101 MHz, MeOD): δ 203.1, 172.1, 160.2, 157.5, 154.1, 138.1, 134.8, 120.9, 109.6, 102.5, 78.2, 40.8, 40.4, 34.3, 29.7, 19.5, 19.4, 10.6. HRMS (ESI): calcd for [C₁₈H₂₂O₅ + Na]⁺: 341.1359, found: 341.0360.

(14*S*,15*R*)-4-Deoxyoxacyclododecindione (14*S*,15*R*)-3**.** Lactone (14*S*,15*R*)-**2** (120 mg, 0.38 mmol) and *N*-chlorosuccinimide (51 mg, 0.38 mmol) were dissolved in dry DMF (15 mL) and



trifluoroacetic acid (41 μ L, 0.57 mmol) was added. The reaction mixture was stirred at room temperature for 4 days. The solvent was removed in *vacuo*. Purification by flash chromatography on silica gel (petroleum ether : EtOAc = 2 : 1) yielded (14*R*,15*R*)-2 (98 mg, 73%) as a white solid. (14*S*,15*R*)-3: $[\alpha]_{\text{D}}^{20} = +18.6$ (*c* 0.30, MeOH) lit. $[\alpha]_{\text{D}}^{20} = +9.6$ (*c* 0.34, CD₃OD). ¹H NMR (400 MHz, CD₃CN): δ 7.44 (s, 2H), 6.65 (d, *J* = 7.8 Hz, 1H), 6.50 (s, 1H), 4.64–4.57 (m, 1H), 3.54 (d, *J* = 17.1 Hz, 1H), 3.23 (d, *J* = 17.2 Hz, 1H), 2.53 (dd, *J* = 18.1, 11.9 Hz, 1H), 2.05–1.97 (m, 1H), 1.83 (s, 3H), 1.69–1.57 (m, 1H), 1.55–1.50 (m, 1H), 1.31–1.21 (m, 1H), 1.07 (d, *J* = 6.2 Hz, 3H), 0.90 (d, *J* = 7.1 Hz, 3H). ¹³C NMR (101 MHz, CD₃CN): δ 200.0, 169.6, 154.9, 154.8, 153.0, 137.8, 133.4, 123.3, 114.2, 103.9, 77.6, 40.0, 39.4, 34.8, 29.7, 19.7, 19.6, 10.8. HRMS (ESI): calcd for [C₁₈H₂₁ClO₅ + Na⁺]: 375.0970, found: 375.0953.

Conflicts of interest

There are no conflicts of interest to declare.

Acknowledgements

We thank the National Natural Science Foundation of China (21272271) for financial support and Chengdu Zhenhua Bio-Tech Co., Ltd for supplying the waste liquids of producing 16-dehydropregnenolone acetate from diosgenin.

References

- (a) P. T. Anastas and J. C. Warner, *Green Chemistry: Theory and Practice*, Oxford University Press, 1998; (b) P. J. Dunn, A. S. Wells and M. T. Williams, *Green Chemistry in the Pharmaceutical Industry*, Wiley-VCH, Weinheim, 2010; (c) P. J. Dunn, *Chem. Soc. Rev.*, 2012, **41**, 1452; (d) J. Clark, R. Sheldon, C. Raston, M. Poliakoff and W. Leitner, *Green Chem.*, 2014, **16**, 18–23; (e) D. Kralisch, D. Ott and D. Gericke, *Green Chem.*, 2015, **17**, 123–145.
- (a) *Catalytic Process Development for Renewable Materials*, ed. P. Imhof and J. C. van der Wal, Wiley-VCH, Weinheim, 2013; (b) P. Gallezot, *Green Chem.*, 2007, **9**, 295–302; (c) R. A. Sheldon, *Green Chem.*, 2014, **16**, 950–963.
- Oxidative degradation of diosgenin, tigogenin and rockogenin, *etc.* generates (*R*)-1, while sarsasapogenin and yamogenin give (*S*)-1(a) A. Goswami, R. Kotoky, R. C. Rastogi and A. C. Ghosh, *Org. Process Res. Dev.*, 2003, **7**, 306–308; (b) W. Tian, X. Xu, S. Liu, J. Shen and X. Wu, *US Pat.* 2006/0166955, 2006.
- ChengguZhenhua Bio-Tech Co., Ltd who produce more than 400 tons of 16-dehydropregnenolone acetate each year from diosgenin by oxidative degradation, but never recover any (*R*)-1.
- A few examples to utilize (*R*)- and (*S*)-1 as starting materials in the synthesis of bioactive compounds have been reported.(a) T. Suzuki, K. Usui, Y. Miyake, M. Namikoshi and M. Nakada, *Org. Lett.*, 2004, **6**, 553–556; (b) S. Yu, X. Pan, X. Lin and D. Ma, *Angew. Chem., Int. Ed.*, 2005, **44**, 135–138; (c) Z. Wang, Q. Xu, W. Tian and X. Pan, *Tetrahedron Lett.*, 2007, **48**, 7549–7551; (d) K. Takahashi, K. Komine, Y. Yokoi, J. Ishihara and S. Hatakeyama, *J. Org. Chem.*, 2012, **77**, 7364–7370; (e) S. Zhang, H. Dong, J. Gui and W. Tian, *Tetrahedron Lett.*, 2012, **53**, 1882–1884; (f) J. Cao and P. Perlmutter, *Org. Lett.*, 2013, **15**, 4327–4329; (g) J. Shen, Y. Shi and W. Tian, *Chin. J. Chem.*, 2015, **33**, 683–685.
- (a) G. Erkel, H. Belahmer, A. Serwe, T. Anke, H. Kunz, H. Kolshorn, J. C. Liermann and T. Opatz, *J. Antibiot.*, 2008, **61**, 285–290; (b) J. Richter, L. P. Sandjo, J. C. Liermann, T. Opatz and G. Erkel, *Bioorg. Med. Chem.*, 2015, **23**, 556–563.
- (a) J. Tauber, M. Rohr, T. Walter, G. Erkel and T. Opatz, *Org. Biomol. Chem.*, 2015, **13**, 7813–7821; (b) J. Tauber, K. Rudolph, M. Rohr, G. Erkel and T. Opatz, *Eur. J. Org. Chem.*, 2015, 3587–3608.
- J. Tauber, M. Rohr, T. Walter, D. Schollmeyer, K. Rahn-Hotze, G. Erkel and T. Opatz, *Org. Biomol. Chem.*, 2016, **14**, 3695–3698.
- V. Kovalenko and E. Matiushenkov, *Tetrahedron: Asymmetry*, 2012, **23**, 1393–1399.
- J.-L. Giner, *Tetrahedron Lett.*, 2002, **43**, 5457–5459.
- A. De Mico, R. Margarita, L. Parlanti, A. Vescovi and G. Piancatelli, *J. Org. Chem.*, 1997, **62**, 6974–6977.
- A. deMeijere, H. Winsel and B. Stecker, *Org. Synth.*, 2005, **81**, 14–25.

