Archive for Organic Chemistry

The Free Internet Journal for Organic Chemistry

Paper

Arkivoc **2018**, part vii, 20-27

Enantioselective synthesis of (-)-(5*R*,6*S*)-6-acetoxyhexadecan-5-olide *via* tandem α-aminooxylation-Henry reaction

Rachana Pandey,[a] Yuvraj Garg,[a] Ranjana Prakash,[a]* and Satyendra Kumar Pandey[a,b]*

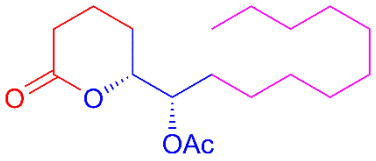
[a]*School of Chemistry and Biochemistry, Thapar Institute of Engineering and Technology, Patiala-147004, India*
[b]*Department of Chemistry, Institute of Science, Banaras Hindu University, Varanasi-221 005, India*
Email: rprakash@thapar.edu, skpandey.chem@bhu.ac.in

Dedicated to Prof. Gordon W. Gribble in recognition of his seminal contributions to so many aspects of organic chemistry

Received 05-23-2018 **Accepted** 07-30-2018 **Published on line** 08-25-2018

Abstract

A novel enantioselective synthetic approach of (-)-(5*R*,6*S*)-6-acetoxyhexadecan-5-olide, an oviposition attractant pheromone of the mosquito *Culex pipiens fatigans* is presented, starting from *n*-dodecanal. The synthesis features tandem α-aminooxylation-Henry and Yamaguchi-Hirao alkylation reactions as key steps.



(-)-(5*R*,6*S*)-6-acetoxyhexadecan-5-olide

Keywords: *δ*-lactone, (-)-(5*R*,6*S*)-6-acetoxyhexadecanolide, tandem α-aminooxylation-Henry reaction, regioselective epoxide opening, Yamaguchi-Hirao reaction

 ©**ARKAT USA, Inc**

Introduction

Functionalized γ- and δ-lactone motifs possess intriguing biological activities and are important building blocks to synthesize a variety of biologically active natural products.[1-9] In 1982, Laurence and Pickett isolated (-)-(5*R*,6*S*)-6-acetoxyhexadecanolide **1a**, a functionalized δ-lactone, as a major constituent that forms on the mosquito *Culex pipens fatigans* eggs.[10] This mosquito is a possible vector of malaria, West Nile virus and filarial infections.[11] The (-)-(5*R*,6*S*)-6-acetoxyhexadecan-5-olide **1a** attracts other gravid females of the identical and few allied mosquitos tempting them to oviposit in the same place where the original eggs are found. Owing to the potential of (-)-(5*R*,6*S*)-6-acetoxy-5-hexadecanolide **1a** in controlling mosquito populations, several enantioselective synthetic approaches for **1a** and its unnatural isomer (+)-6-acetoxy-5-hexadecanolide **1b** (Figure 1) have been disclosed in the literature.[12-29] As part of our research program aimed at developing the asymmetric synthesis of bioactive natural compounds,[30-37] we turned our attention to developing a flexible and simple approach for the asymmetric synthesis of functionalized δ-lactones and its application to asymmetric synthesis of (-)-(5*R*,6*S*)-6-acetoxyhexadecan-5-olide **1a**. Herein, we report a new enantioselective synthesis of (-)-(5*R*,6*S*)-6-acetoxyhexadecanolide **1a** employing tandem α-aminooxylation-Henry reaction as the source of chirality.

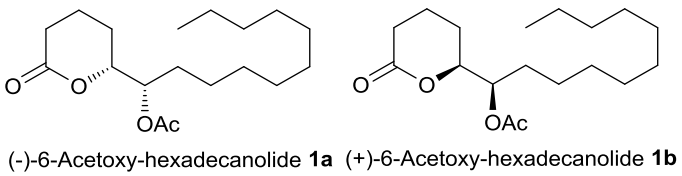
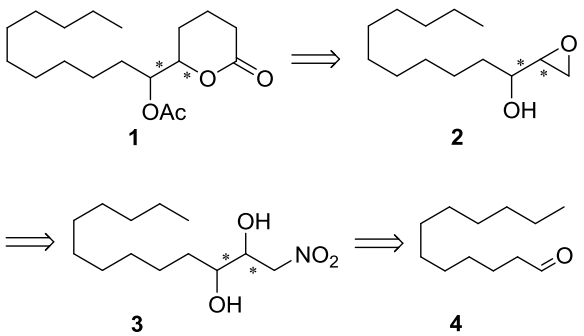


Figure 1. Structures of stereoisomers of 6-acetoxy-hexadecanolide.

Results and Discussion

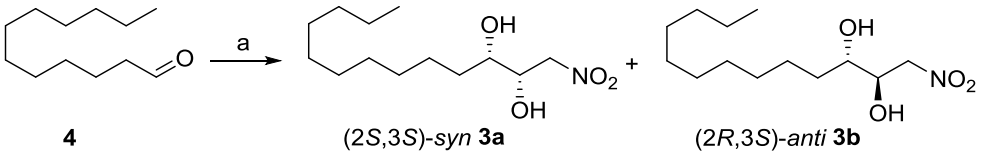
Our retrosynthetic route to the synthesis of (-)-(5*R*,6*S*)-6-acetoxyhexadecanolide is displayed in Scheme 1. The epoxy alcohol **2** was envisioned as a key intermediate from which δ-lactone **1** and 6-acetoxy-5-hexadecanolide **1a-1b** could be synthesized via a Yamaguchi-Hirao alkylation reaction followed by standard organic transformations. The key fragment **2** could in turn be prepared from the diol **3** in simple steps including oxidation, reduction and epoxide formation. Subsequently, compound **3** could be envisaged from commercially available *n*-dodecanal **4** *via* a tandem α-aminooxylation-Henry reaction.



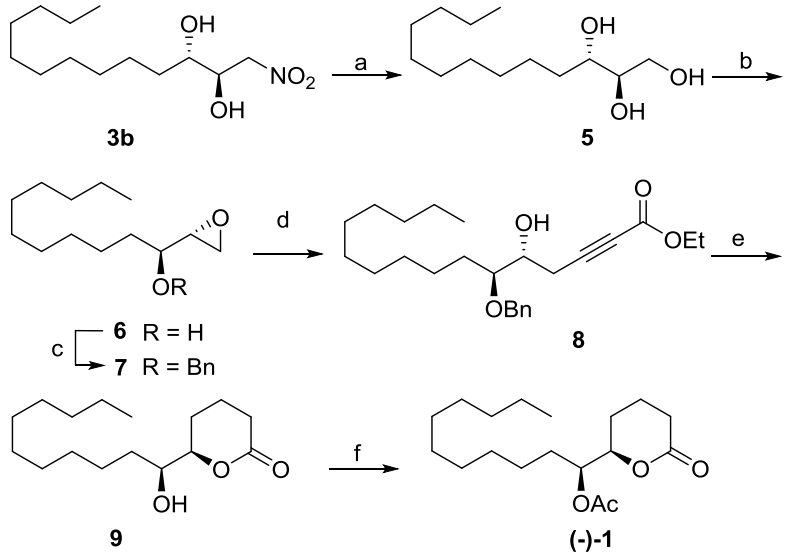
Scheme 1. Retrosynthetic strategy for 6-acetoxy-hexadecanolide **1**.

©**ARKAT USA, Inc**

As illustrated in Scheme 2, the synthetic endeavor towards (-)-(5*R*,6*S*)-6-acetoxyhexadecanolide **1a** commenced with commercially available *n*-dodecanal **4**. Compound **4**, on tandem α-aminooxylation-Henry reaction[38] in the presence of catalytic amount of D-proline and without ligand, furnished the *syn*-β,γ-dihydroxynitrotridecane **3a** along with its *anti*-diastereomer **3b** in 1:1 ratio with 62% overall yield and excellent enantioselectivities (>99% ees for both *syn*- and *anti*-diastereomers).[39] Both (2*S,*3*S*)-*syn* **3a** *and* (2*R,*3*S*)-*anti* **3b** diastereomers were carefully separated by silica gel column chromatography.



Scheme 2. *Reagents and conditions*: (a) i) PhNO, D-proline (30 mol%), DMSO, rt, 30 min, ii) CH_3NO_2, aq. NaOH, MeOH, $Cu(OAc)_2 \cdot H_2O$, rt, 12 h, 62%.



Scheme 3. *Reagents and conditions:* (a) i) $NaNO_2$, AcOH, DMSO, 35 °C, 24 h, ii) $LiAlH_4$, THF, 0 °C to rt, 3 h, 62% (over two steps); (b) i) TsCl, Bu_2SnO, Et_3N, CH_2Cl_2, 0 °C to rt, 1 h; ii) K_2CO_3, MeOH, rt, 30 min, 76% (over two steps); (c) NaH, BnBr, DMF, 0 °C, 4 h, 92%; (d) *n*-BuLi, $BF_3 \cdot OEt_2$, $HCCCO_2Et$, dry THF, -78 °C, 2 h, 81%; (e) i) H_2, Pd/C (10%), MeOH, rt, 12 h; ii) *p*-TSA, benzene, reflux, 1 h, 91% (over two steps); (f) Ac_2O, DMAP, DCM, 30 min, 95%.

Having *anti*-diastereomer (*2R,3S*)-*anti* **3b** in hand, we then performed an oxidation using $NaNO_2$/acetic acid in DMSO to provide the acid[40-41] which on immediate reduction with $LiAlH_4$ afforded the triol derivative **5** in 62% yield (Scheme 3). Our next goal was to achieve the synthesis of the terminal epoxide moiety. Towards this end, triol **5** on regioselective monotosylation using $TsCl/NEt_3$ in the presence of a catalytic amount of dibutyltin oxide[42-43] followed by base treatment, successfully furnished the terminal epoxide **6** in 76% yield, $[\alpha]_D^{25}$ +16.4 (*c* 1.0, $CHCl_3$); {lit.[27] $[\alpha]_D^{20}$ +16.2 [*c* 1.01, $CHCl_3$]}. The free hydroxyl group of intermediate **6** was then alkylated with benzyl bromide in the presence of sodium hydride as base to produce the benzyl ether derivative **7** in 92% yield. Next, regioselective ring opening of epoxide **7** with lithium salt of ethyl propiolate under the Yamaguchi-Hirao conditions[44] afforded homopropargylic alcohol derivative **8** in 81% yield. Subsequently, the

 ©ARKAT USA, Inc

lactone **9** was obtained from compound **8** *via* a two-step procedure involving catalytic (Pd/C, 10%) hydrogenation and *p*-TSA catalyzed lactonization in 91% yield. Finally, treatment of alcohol **9** with acetic anhydride and catalytic DMAP in dichloromethane at room temperature furnished (-)-(5*R*,6*S*)-6-acetoxyhexadecanolide **1a** in 95% yield; $[\alpha]_D^{25}$ -36.89 (*c* 1.0, $CHCl_3$); {lit.[26] $[\alpha]_D^{32}$ -36.8 (*c* 1.0, $CHCl_3$)}. The physical and spectroscopic data of (-)-(5*R*,6*S*)-6-acetoxyhexa-decanolide **1a** were in full agreement with literature data.

Conclusions

In summary, we have demonstrated a general and flexible synthetic approach for functionalized δ-lactones and its application to the asymmetric synthesis of (-)-(5*R*,6*S*)-6-acetoxyhexadecan-5-olide employing asymmetric tandem α-aminooxylation-Henry reaction on the commercially available *n*-dodecanal. Further extension of the tandem α-aminooxylation-Henry reaction strategy to biologically active molecules of more structural complexity and diversity is in progress.

Experimental Section

General. All reactions were carried out under argon or nitrogen in oven-dried glassware using standard glass syringes and septa. The solvents and chemicals were purchased from Merck and Sigma Aldrich chemical company. Solvents and reagents were purified and dried by standard methods prior to use. Progress of the reactions was monitored by TLC using precoated aluminium plates of Merck kieselgel 60 F254. Column chromatography was performed on silica gel (60-120 and 100-200 mesh) using a mixture of *n*-hexane and EtOAc. Optical rotations were measured on an automatic polarimeter, AA-65. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ (unless otherwise mentioned) on JEOL ECS operating at 400 and 100 MHz, respectively. Chemical shifts are reported in *δ* (ppm), referenced to TMS. HRMS were recorded on Agilent 6530 Accurate-Mass Q-TOF using electrospray ionization. IR spectra were recorded on an Agilent resolution Pro 600 FT-IR spectrometer, fitted with a beam-condensing ATR accessory.

***syn*-(2*S*,3*S*)-/*anti*-(2*R*,3*S*)-1-Nitrotridecane-2,3-diol (3a)/(3b).** To a DMSO (15 mL) solution of aldehyde **4** (2.0 g, 10.80 mmol) was added nitrosobenzene (1.16 g, 10.8 mmol), followed by D-proline (375 mg, 3.26 mmol, 30 mol%) and the reaction mixture stirred for about 20-30 min at rt. The completion of the reaction was monitored by its color change from green to orange or by TLC until all the nitrosobenzene was consumed and used as such for the next step without further purification. To the above crude solution was added MeOH (15 mL), nitromethane (6.58 g, 5.8 mL, 108 mmol), aq. NaOH (650 mg, 16.2 mmol, 8M), and above synthesized α-aminooxylated aldehyde were added. The reaction mixture was stirred for 30 min, then $Cu(OAc)_2 \cdot H_2O$ (3.24 g, 16.2 mmol) was added and the mixture further stirred for additional 12 h at rt. After completion of the reaction (monitored by TLC), the reaction mixture was evaporated, diluted with H_2O, extracted with EtOAc (3 x 50 mL), dried over Na_2SO_4, and concentrated. The *syn*/*anti* diastereomers were separated and purified by silica gel column chromatography (EtOAc/hexane, 1:9 v/v) as eluent, which furnished the *syn*-diastereomer **3a** (874 mg, 31%) as a white solid. $[\alpha]_D^{25}$ +55.2 (c 0.20, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 4.63-4.49 (m, 2H), 4.27-4.18 (m, 1H), 3.75-3.72 (m, 1H), 2.41 (br s, 2H), 1.56-1.20 (m, 18H), 0.86 (t, *J* 8.6 Hz, 3H); ^{13}C NMR (100

 ©**ARKAT USA, Inc**

MHz, $CDCl_3$) *δ*: 77.5, 73.1, 72.0, 33.0, 32.2, 29.9, 29.8, 29.7, 29.6, 25.9, 22.9, 14.4. HRMS (ESI) m/z calcd for $C_{13}H_{27}NO_4$ ([M-H]$^+$) 260.1867; found 260.1872.

After separating the *syn*-diastereomer, the quickly eluting *anti*-diastereomer **3b** was then isolated (EtOAc/hexane, 1:5 v/v) as a white solid (874 mg, 31%). $[\alpha]_D^{25}$ +72.5 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 4.62-4.48 (m, 2H), 4.25-4.21 (m, 1H), 3.59-3.51 (m, 1H), 1.61-1.20 (m, 18H), 0.86 (t, *J* 8.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 78.3, 71.4, 70.4, 33.2, 31.5, 29.3, 29.2, 29.1, 29.1, 29.0, 25.1, 22.3, 13.8.

(2*R*,3*S*)-Tridecane-1,2,3-triol (5). To a stirred solution of *anti*-diastereomer **3b** (500 mg, 1.91 mmol) in DMSO (5 mL) at 35 °C were added $NaNO_2$ (396 mg, 5.75 mmol) and AcOH (1.1 mL, 19.0 mmol). After stirring for 24 h at the same temperature, the reaction mixture was quenched with H_2O and acidified with 10% aq solution HCl (25 mL). The aqueous layer was extracted with Et_2O (3 x 30 mL), dried over anhydrous Na_2SO_4, concentrated in vacuo, and used as such for the next step without further purification. $LiAlH_4$ (145 mg, 3.82 mmol) was added to a solution of above crude material in THF (5 mL) at 0 ^{o}C under N_2 atmosphere. After 5 min, the reaction was allowed to reach rt and stirred for a further 3 h. Then the reaction mixture was quenched with 10% aq NaOH. The aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organic phases were dried with Na_2SO_4 and the solvent was removed under reduced pressure. The residue was subjected to silica gel column chromatography (EtOAc/hexanes, 4:1 v/v) to give triol **5** (274 mg, 62%) as a white solid. [R_f = 0.4, EtOAc]; $[\alpha]_D^{25}$ +40.4 (*c* 0.8, $CHCl_3$); IR (CH_2Cl_2) v: 3415, 2945, 2910, 2863, 1701, 1651 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 3.90-3.48 (m, 3H), 2.64 (br, 1H), 2.74 (br, 1H), 2.26 (br, 2H) 1.70-1.10 (m, 18H), 0.93 (t, *J* 6.88 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 73.0, 67.5, 62.8, 33.8, 31.9, 29.6, 29.5, 29.3, 25.3, 22.6, 14.1; HRMS (ESI)+ *m/z* calcd for $C_{13}H_{28}O_3Na^+$ [M+Na$^+$] 255.1930; found 255.1929.

(*S*)-1-((*R*)-Oxiran-2-yl)undecan-1-ol (6). To a stirred solution of **5** (200 mg, 0.86 mmol) in CH_2Cl_2 (6 mL) under N_2 atmosphere at 0 ^{o}C were added Et_3N (0.15 ml, 1.03 mmol), catalytic amount of Bu_2SnO (21 mg, 0.09 mmol) and TsCl (181 mg, 0.94 mmol). The resulting mixture was stirred at rt for 1 h. Then the reaction mixture was quenched with H_2O, extracted with CH_2Cl_2 and the extract dried over Na_2SO_4. The combined organic layers were concentrated under reduced pressure to afford crude tosylate which was used for next step.

K_2CO_3 (237 mg, 1.72 mmol) was added to a solution of above crude product in MeOH (5 mL) at rt and stirred for 30 min. The resulting mixture was diluted with H_2O (10 mL) and EtOAc (20 mL). The organic layer was separated, and aqueous layer was extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography (EtOAc/hexane, 1:4) to give epoxide **6** (140 mg, 76%) as a colourless liquid. [R_f = 0.3, EtOAc/hexane 1:4 v/v]; $[\alpha]_D^{25}$ +16.4 (*c* 1.0, $CHCl_3$); {lit.[27] $[\alpha]_D^{20}$ +16.2 [*c* 1.01, $CHCl_3$]}; IR (CH_2Cl_2) *v*: 3453, 2935, 2856, 1256, 1426 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 3.71-3.68 (m, 1H), 3.01-2.99 (m, 1H), 2.84-2.83 (m, 1H), 2.79-2.77 (m, 1H), 1.69-1.66 (m, 2H), 1.50-1.21 (m, 16H), 0.93 (t, *J* 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 68.4, 54.5, 43.4, 33.4, 31.9, 29.7, 29.6, 29.5, 29.3, 25.3, 22.7, 14.1; HRMS (ESI)+ *m/z* calcd for $C_{13}H_{27}O_2$+[M+H$^+$] 215.2011; found 215.2012.

(-)-(5*R*,6*S*)-6-Acetoxyhexadecan-5-olide (1a). To a stirred solution of the alcohol **9** (20 mg, 0.07 mmol) in anhydrous CH_2Cl_2 (3.0 mL) under N_2 atmosphere at rt were added DMAP (51 mg, 0.42 mmol) and Ac_2O (43 mg, 0.42 mmol). The resulting mixture was stirred for 30 min. at rt. Next, the reaction mixture was quenched by addition of cold H_2O and extracted with EtOAc (3 x 5 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and solvent was removed in *vacuo*. Silica gel column chromatography of the resultant residue furnished the target compound **1** (20 mg, 95%) as a colorless oil. [R_f = 0.4, EtOAc/hexane, 1:4 v/v]; $[\alpha]_D^{25}$ -36.89 (*c* 1.0, $CHCl_3$); {lit.[26] $[\alpha]_D^{32}$ -36.80 (*c* 1.0, $CHCl_3$)}; IR (CH_2Cl_2) *v*: 2935, 2844, 1740, 1361, 1236 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 4.99-4.95 (m, 1H), 4.38-4.31 (m, 1H), 2.65-2.57 (m, 1H), 2.50-2.41 (m, 1H), 2.08 (s, 3H), 2.00-1.79 (m, 2H), 1.72-1.56 (m, 4H), 1.38-1.20 (m, 16H), 0.88 (t, *J* 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$)

 ©ARKAT USA, Inc

δ: 170.9, 170.5, 80.5, 74.3, 31.9, 29.8, 29.7, 29.6, 29.5, 25.2, 23.5, 22.7, 21.0, 18.2, 14.1; HRMS $(ESI)^+$ *m/z* calcd for $C_{18}H_{33}O_4$+[M+H] 313.2379; found 313.2395.

Acknowledgements

The authors (R.P. and S.K.P.) acknowledge the research grant No. 02(0309)/17/EMR-II facilitated by the Council for Scientific and Industrial Research (CSIR), New Delhi, India for the carrying out the study. R. Pandey thanks Thapar Institute of Engineering and Technology for the research associateship and Y.G. thanks UGC, New Delhi for research fellowship.

Supplementary Material

Electronic supplementary information (ESI) available; copies of ^{1}H and ^{13}C NMR spectra of compounds **1a**, Rac-**3**, **3a**, **3b** and **5-9**; HPLC of Rac-**3**, **3a**, **3b**, and HRMS of final compound **1a**. This material can be found *via* the "Supplementary Content" section of this article's webpage.

References

1. Choi, J. H.; Horikawa, M.; Okumura, H.; Kodani, S.; Nagai, K.; Hashizume, D.; Koshino, H.; Kawagishi, H. *Tetrahedron* **2009**, *65*, 221. https://doi.org/10.1016/j.tet.2008.10.068
2. Reddy, P. P.; Yen, K. F.; Uang, B. J. *J. Org. Chem.* **2002**, *67*, 1034. https://doi.org/10.1021/jo016216g
3. Alali, F. Q.; Rogers, L.; Zhang, Y.; McLaughlin, J. L. *Tetrahedron* **1998**, *54*, 5833. https://doi.org/10.1016/S0040-4020(98)00286-5
4. Koch, S. S. C.; Chamberlin, A. R. In *Enantiomerically Pure c-Butyrolactones in Natural Products Synthesis*; Atta-ur-Rahman, Ed.; Elsevier Science: Amsterdam, 1995; pp 687.
5. Warmerdam, E.; Tranoy, I.; Renoux, B.; Gesson, J. P. *Tetrahedron Lett.* **1998**, *39*, 8077. https://doi.org/10.1016/S0040-4039(98)01786-9
6. Hanessian, S.; Grillo, T. A. *J. Org. Chem.* **1998**, *63*, 1049. https://doi.org/10.1021/jo9713621
7. Buisson, D.; Azerad, R. *Tetrahedron: Asymmetry* **1996**, *7*, 9. https://doi.org/10.1016/0957-4166(95)00408-4
8. Friesen, R. W.; Vanderwal, C. *J. Org. Chem.* **1996**, *61*, 9103. https://doi.org/10.1021/jo961653u
9. Ye, Q.; Zeng, Lu.; Zhang, Y.; Zhao, G. X.; McLaughlin, J. L. *J. Nat. Prod.* **1995**, *58*, 1398. https://doi.org/10.1021/np50123a010
10. Laurence, B. R.; Pickett, J. A. J. *Chem. Soc., Chem. Commun.* **1982**, 59. https://doi.org/10.1039/c39820000059

 ©**ARKAT USA, Inc**

11. Anderson, J. F.; Andeadis, T. G.; Vossbrinck, C. R.; Tirrell, S.; Waken, E. M.; French, R. A.; Garmendia, A. E.; Van Kruiningen, H. J. *Science* **1999**, *286*, 2331. https://doi.org/10.1126/science.286.5448.2331
12. Dong, H-B.; Yang, M-Y.; Zhang, X-T.; Wang, M-A. *Tetrahedron: Asymmetry* **2014**, *25*, 610. https://doi.org/10.1016/j.tetasy.2014.03.006
13. Das, S.; Mishra, A. K.; Kumar, A.; Ghamdi, A. A. K. A.; Yadav, J. S. *Carbohydrate Research* **2012**, *358*, 7. https://doi.org/10.1016/j.carres.2012.05.009
14. Park, Y.; Tae, J. *Synthesis* **2010**, *21*, 3627.
15. Singh, S.; Guiry, P. J. *Eur. J. Org. Chem.* **2009**, 1896.
16. Quinn, K. J.; Curto, J. M.; McGrath, K. P.; Biddick, N. A. *Tetrahedron Lett.* **2009**, *50*, 7121. https://doi.org/10.1016/j.tetlet.2009.09.179
17. Prasad, K. R.; Anbarasan, P. *Tetrahedron: Asymmetry* **2007**, *18*, 2479. https://doi.org/10.1016/j.tetasy.2007.10.006
18. Ikishima, H.; Sekiguchi, Y.; Ichikawa, Y.; Kotsuki, H. *Tetrahedron* **2006**, *62*, 311. https://doi.org/10.1016/j.tet.2005.08.111
19. Dhotare, B.; Goswami, D.; Chattopadhyay, A. *Tetrahedron Lett.* **2005**, *46*, 6219. https://doi.org/10.1016/j.tetlet.2005.07.063
20. Sun, B.; Peng, L.; Chen, X.; Li, Y. *Tetrahedron: Asymmetry* **2005**, *16*, 1305. https://doi.org/10.1016/j.tetasy.2005.02.017
21. Gao, X.; Hall, D. G. *J. Am. Chem. Soc.* **2003**, *125*, 9308. https://doi.org/10.1021/ja036368o
22. Gallos, J. K.; Mihelakis, D. S.; Dellios, C. C.; Pozarentzi, M. E. *Heterocycles* **2000**, *53*, 703. https://doi.org/10.3987/COM-99-8793
23. Couladouros, E. A.; Mihou, A. P. *Tetrahedron Lett.* **1999**, *40*, 4861. https://doi.org/10.1016/S0040-4039(99)00895-3
24. Lohray, B. B.; Venkateswarlu, S. *Tetrahedron: Asymmetry* **1997**, *8*, 633. https://doi.org/10.1016/S0957-4166(97)00011-6
25. Gravier-Pelletier, C.; Le Merrer, Y.; Depezay, J.-C. *Tetrahedron* **1995**, *51*, 1663. https://doi.org/10.1016/0040-4020(94)01033-V
26. Kotsuki, H.; Kadota, I.; Ochi, M. *J. Org. Chem.* **1990**, *55*, 4417. https://doi.org/10.1021/jo00301a038
27. Mori, K.; Otsuka, T. *Tetrahedron* **1983**, *39*, 3267. https://doi.org/10.1016/S0040-4020(01)91574-1
28. Hurema, D.; Dudding, T. *RSC Adv.*, **2015**, *5*, 101732. https://doi.org/10.1039/C5RA19306K
29. Schmidt, B.; Petersen, M. H.; Braun, D. *J. Org. Chem.* **2018**, *83*, 1627. https://doi.org/10.1021/acs.joc.7b02944
30. Kaur, A.; Prakash, R.; Pandey, S. K. *ChemistrySelect* **2018**, *3*, 105. https://doi.org/10.1002/slct.201702732
31. Garg, Y.; Tiwari, A. K.; Pandey, S. K. *Tetrahedron Lett.* **2017**, *58*, 3344. https://doi.org/10.1016/j.tetlet.2017.07.024
32. Garg, Y.; Sharma, P.; Pandey, S. K. *Tetrahedron Lett.* **2017**, *57*, 3493. https://doi.org/10.1016/j.tetlet.2017.07.069

 ©ARKAT USA, Inc

33. Gahalawat, S.; Pandey, S. K. *Org. Biomol. Chem.* **2016**, *14*, 9287. https://doi.org/10.1039/C6OB01775D
34. Garg, Y.; Pandey, S. K. *RSC Adv.* **2016**, *6*, 25913. https://doi.org/10.1039/C6RA03915D
35. Gahalawat, S.; Garg, Y.; Pandey, S. K. *Asian J. Org. Chem.* **2015**, *4*, 1025. https://doi.org/10.1002/ajoc.201500301
36. Garg, Y.; Gahalawat , S.; Pandey, S. K. *RSC Adv.* **2015**, *5*, 38846. https://doi.org/10.1039/C5RA05987A
37. Garg, Y.; Pandey, S. K. *J. Org. Chem.* **2015**, *80*, 4201. https://doi.org/10.1021/acs.joc.5b00480
38. Garg, Y.; Kaur, R.; Pandey, S. K. *Eur. J. Org. Chem.* **2017**, *45*, 6700. https://doi.org/10.1002/ejoc.201701289
39. HPLC data of (*2S,3S*)-*syn* **3a**: >99% ee, The enantiomeric purity (ee) was determined by HPLC analysis using a Chirapak IA (4.6 x 250 mm) using mobile phase of (5:95 *i*-propanol:*n*-hexane, flow rate of 1 mL/min at 25 ^{o}C, UV detection at 210 nm): (*R*,*R*)-enantiomer: t_r = 25.847 min, (*S*,*S*)-enantiomer: t_r = 33.045 min. (*2R,3S*)-*anti* **3b**: >99% ee, The enantiomeric purity (ee) was determined by HPLC analysis using a Chirapak IA (4.6 × 250 mm) using mobile phase of *i*-propanol:*n*-hexane (5:95), flow rate of 1 mL/min at 25 ^{o}C, UV detection at 210 nm): (*S*,*R*)-enantiomer: tr = 20.995 min, (*R*,*S*)-enantiomer: tr = 23.045 min.
40. Lin, H.; Sun, X. W.; Lin, G. Q. *Org. Lett.* **2014**, *16*, 752. https://doi.org/10.1021/ol403463h
41. Zhu, D.; Lu, M.; Chua, P. J.; Tan, B.; Wang, F.; Yang, X.; Zhong, G. *Org. Lett.* **2008**, *10*, 4585. https://doi.org/10.1021/ol801864c
42. Yadav, J. S.; Sengupta, S. ; Yadav, N. N.; Chary, D. N.; Ghamdi, A. A. A. *Tetrahedron Lett.*, **2012**, *53*, 5952. https://doi.org/10.1016/j.tetlet.2012.08.112
43. Sabitha, G.; Reddy, K. P.; Reddy, S. P.; Yadav, J. S. *Tetrahedron Lett.*, **2014**, *55*, 3227. https://doi.org/10.1016/j.tetlet.2014.04.026
44. Yamaguchi, M.; Hirao, I. *Tetrahedron Lett.* **1983**, *24*, 391. https://doi.org/10.1016/S0040-4039(00)81416-1

 ©ARKAT USA, Inc