Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron Letters 45 (2004) 7599–7603
Tetrahedron Letters

trans-Stereoselective intramolecular crossed pinacol coupling of aromatic 1,4-, 1,5-, and 1,6-diketones by electroreduction

Naoki Kise,* Yousuke Shiozawa and Nasuo Ueda

Department of Biotechnology, Faculty of Engineering, Tottori University, Koyama, Tottori 680-8552, Japan

Received 14 July 2004; revised 13 August 2004; accepted 19 August 2004

Abstract—Electroreduction of aromatic 1,4-, 1,5-, and 1,6-diketones in the presence of chlorotrimethylsilane and triethylamine gave four-, five-, and six-membered 1,2-diols with *trans*-stereoselectivity.

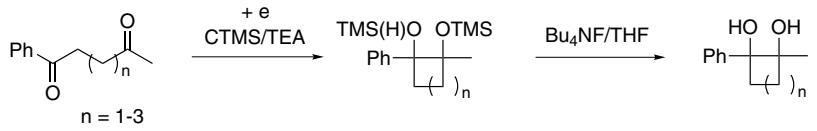
Crossed pinacol coupling is a useful method for the synthesis of unsymmetrical 1,2-diols. This type of reaction has been realized with SmI_2[1] or low-valent titanium[2] as a reducing agent. By this method, it has been known that the intramolecular pinacol coupling of 1,4-, 1,5-, and 1,6-diketones gave the corresponding *cis*-diols stereoselectively.[1–3] On the other hand, we have recently reported that electroreduction is a useful tool for the reductive intramolecular coupling of aromatic δ- and ε-keto esters.[4] We wish to report herein that the electroreduction of aromatic 1,4-, 1,5-, and 1,6-diketones in the presence of chlorotrimethylsilane (CTMS) effected intramolecular crossed pinacol coupling of an aromatic ketone with an aliphatic ketone (Scheme 1). In addition, the *trans*-isomers of four-, five-, and six-membered 1,2-diols were produced preferentially after desilylation of the resulted trimethylsiloxy ethers. This reaction provides a complementary method to the reduction with metal reducing agents.

Electroreduction of aromatic diketones was carried out according to the reported procedure for the reductive coupling of ketoesters.[4] A typical procedure is as follows. A 0.3 M solution of Bu_4NPF_6 in THF (15 mL) was placed in the cathodic chamber of a divided cell (40 mL beaker) equipped with a lead cathode ($5 \times 5\,cm^2$), a platinum anode ($2 \times 1\,cm^2$), and a ceramic cylindrical diaphragm. A 0.3 M solution of Bu_4NClO_4 in DMF (4 mL) was placed in the anodic chamber.[5] 1-Phenylpentane-1,4-dione (**1**) (176 mg, 1 mmol), CTMS (0.64 mL, 5 mmol), and triethylamine (0.70 mL, 5 mmol) were added to the cathodic chamber. After 300 C of electricity was passed at a constant current of 100 mA at room temperature, the catholyte was evaporated in vacuo. To the residue was added Et_2O (30 mL) and insoluble Bu_4NPF_6 was filtered off. After removal of the solvent, the crude mixture was purified by column chromatography on silica gel (hexane/ethyl acetate, 50:1) to give ditrimethylsiloxy ether **2** in a 60% yield. 1,2-Diol **3** was obtained from **2** by treatment with Bu_4NF (2.5 equiv) in THF at 25 °C for 24 h. Two stereoisomers of **3** were separated (81% yield, *trans*:*cis* = 67:33) by column chromatography on silica gel (hexane/ethyl acetate = 5:1).

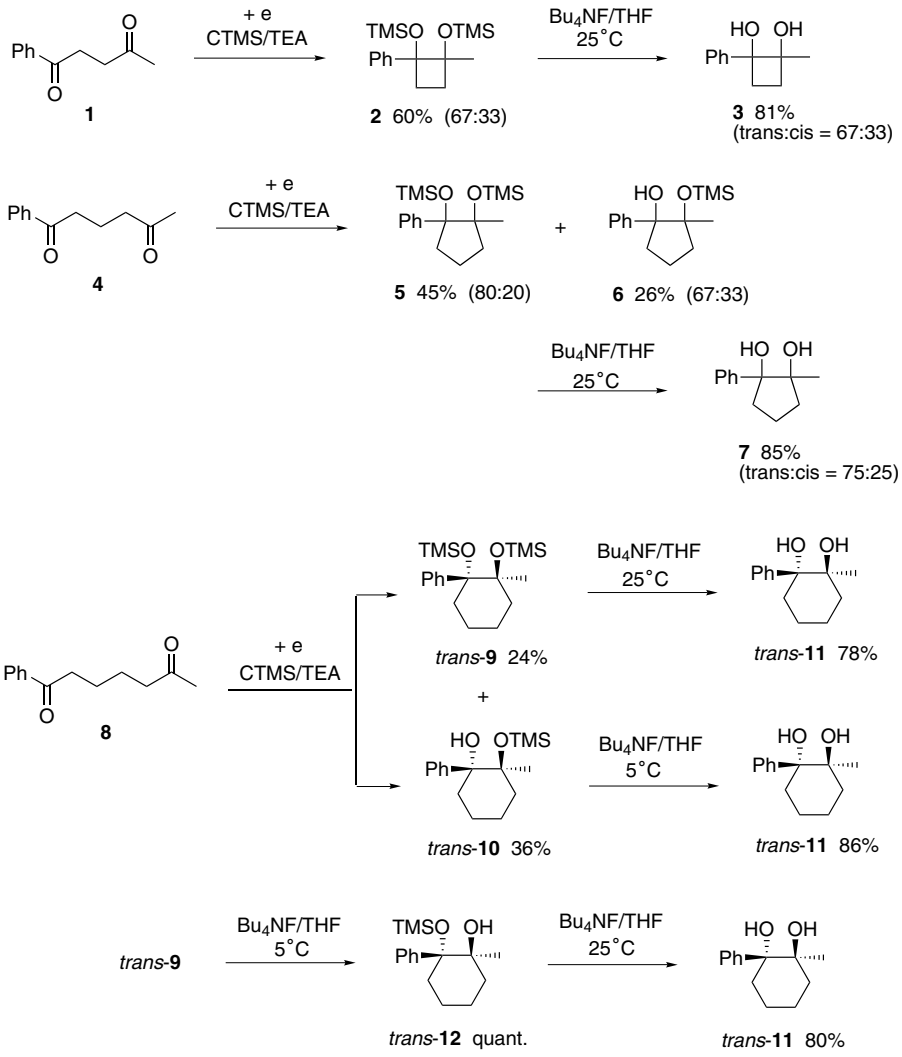
The results of the electroreduction of aromatic diketones **1**, **4**, and **8**, and subsequent desilylation of the resulted trimethylsiloxy ethers are shown in Scheme 2. The electroreduction of 1,4-diketone **1** afforded four-membered cyclized ditrimethylsiloxy ether **2**: the diastereomeric ratio (dr) of which was estimated to be 67:33 by its ^1H NMR analysis.[6] After desilylation of **2**, the minor isomer of 1,2-diol **3** was confirmed to be *cis* by the comparison of its ^1H and ^{13}C NMR spectra with the reported data of *cis*-**3**.[1a,7] In the electroreduction of 1,5-diketones **4**, ditrimethylsiloxy ether **5** and monotrimethylsiloxy ether **6** were obtained in 80:20 and 67:33 dr, respectively (by ^1H NMR analysis).[8] The five-membered cyclized products, **5** and **6**, were desilylated together by the treatment with Bu_4NF at 25 °C to give 1,2-diol **7** in a 75:25 dr (by isolation). The minor isomer of **7** was consistent

Keywords: Electroreduction; Crossed pinacol coupling; 1,4-Diketones; 1,5-Diketones; 1,6-Diketones; 1,2-Diols.
* Corresponding author. Fax: +81 857 31 5636; e-mail: kise@bio.tottori-u.ac.jp

0040-4039/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2004.08.120



Scheme 1.

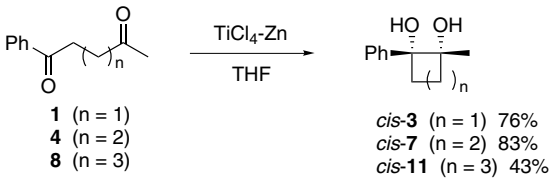


Scheme 2.

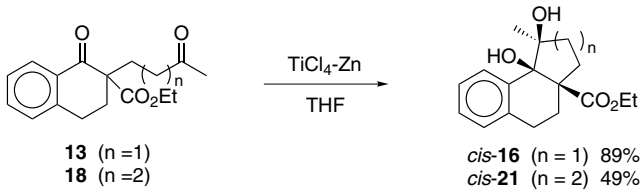
with authentic *cis*-**7** prepared by the reduction with $TiCl_4$–Zn (vide infra).[9] Similarly, ditrimethylsiloxy ether **9** and monotrimethylsiloxy ether **10** were produced by the electroreduction of 1,6-diketone **8**. In this case, the both six-membered cyclized products **9** and **10** were formed as single stereoisomers.[10] The isomer of 1,2-diol **11** derived from **9** and **10** was determined to be *trans* by the comparison of its ^1H and ^{13}C NMR spectra with the reported data of *trans*-**11**.[11] Therefore, the electroreductive coupling of **8** afforded only *trans*-isomers of **9** and **10**. Desilylation of *trans*-**9** with Bu_4NF (1 equiv) at 5 °C for 30 min afforded monotrimethylsiloxy ether *trans*-**12**,[12] which was different from *trans*-**10**. Further desilylation of *trans*-**12** with Bu_4NF (1.5 equiv) at 25 °C for 24 h gave the *trans*-**11**. Although the desilylation of *trans*-**12** at 5 °C was very slow, the desilylation of *trans*-**10** was completed within 1 h under the same conditions. These results imply that *trans*-**10** is a 2-trimethylsiloxy ether and *trans*-**12** is a sterically hindered 1-trimethylsiloxy ether.

It has been reported that the *cis*-isomer of **11** was prepared by the reduction of **8** with $TiCl_4$–Zn.[2] To confirm this result and to obtain authentic samples of the *cis*-isomers of **3**, **7**, and **11**, we also examined the reduction of **1**, **4**, and **8** with $TiCl_4$–Zn in THF. From all of the substrates employed, *cis*-diols **3**, **7**, and **11** were formed exclusively (Scheme 3).

Next, cyclic diketones **13** and **18** derived from 1-tetralone were used as the substrate for the crossed pinacol coupling and the results are exhibited in Scheme 4.



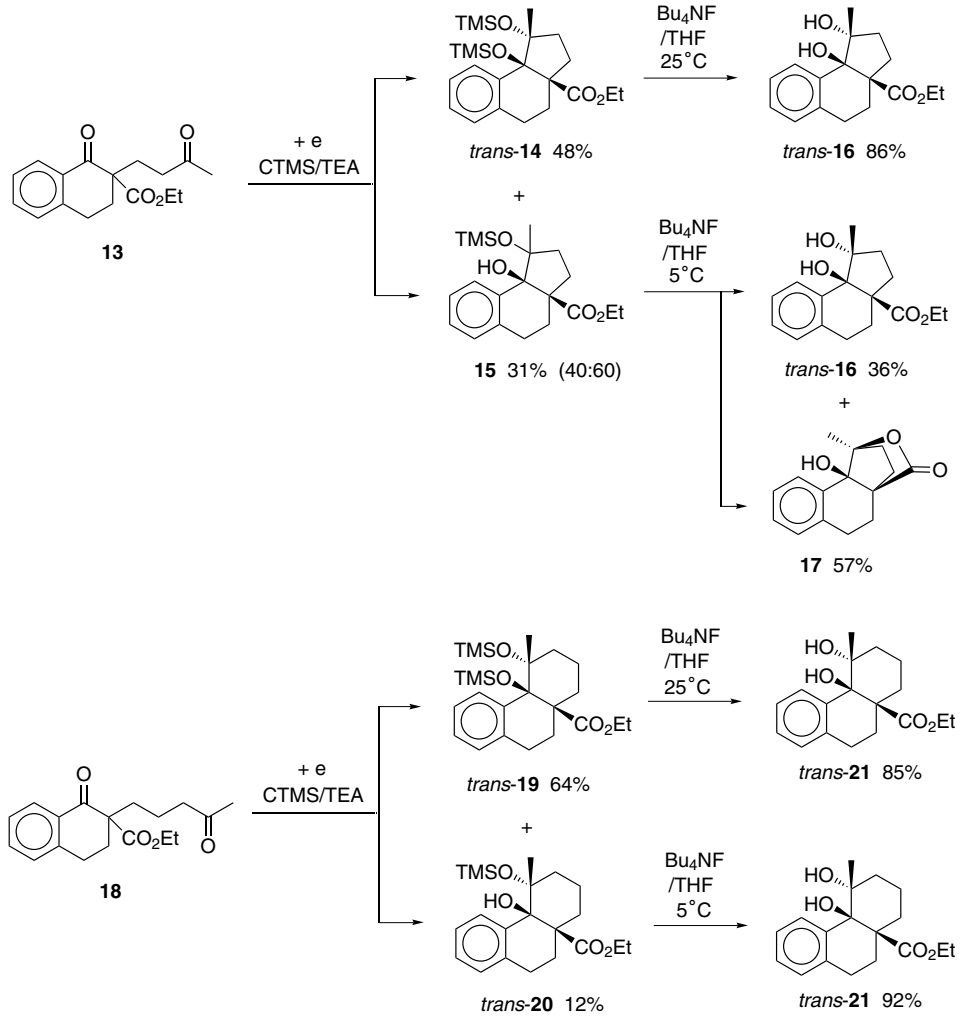
Scheme 3.



Scheme 5.

The electroreduction of 1,5-diketone **13** gave five-membered cyclized products **14** and **15**. Ditrimethylsiloxy ether **14**[13] was formed as a single stereoisomer and the desilylation of **14** with Bu_4NF (2.5 equiv) at 25 °C afforded the *trans*-isomer of diol **16**. Monotrimethylsiloxy ether **15** was obtained as a 40:60 mixture of two diastereomers (by ^1H NMR analysis)[14] and treatment of **15** with Bu_4NF (1.2 equiv) at 5 °C gave *trans*-**16** and lactone **17** derived from *cis*-**16**. In the electroreduction of 1,6-diketone **18**, ditrimethylsiloxy ether **19** and monotrimethylsiloxy ether **20** were formed as single stereoisomers.[15] The both six-membered cyclized products, **19** and **20,** were transformed to the *trans*-isomer of diol **21** by the treatment with Bu_4NF, and *cis*-**21** could not be detected. The electroreductive six-membered cyclization of **18**, similarly to that of **8**, proceeds with complete *trans*-selectivity. In contrast with the electroreduction, the reduction of **13** and **18** with $TiCl_4$–Zn in THF produced *cis*-**16** and *cis*-**21** exclusively (Scheme 5). The stereostructures of *trans*-**16**, **17**, and *trans*-**21** were established by X-ray crystallographic analysis (Fig. 1).[16]

The reaction mechanism can be speculated to be as shown in Scheme 6. Anion **22** is formed from 1,5-diketone **4** by two-electron transfer and subsequent O-silylation. The carbanion in **22** attacks the keto carbonyl group intramolecularly through transition state **23**. Since *trans*-**23** is more stable than *cis*-**23** due to the electronic repulsion between the two oxygen atoms in **23**, *trans*-**24** is formed preferentially. In the next step,



Scheme 4.

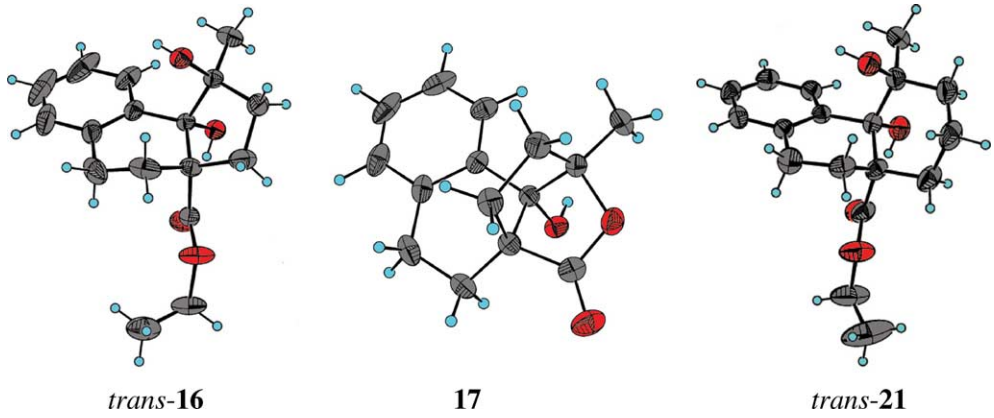
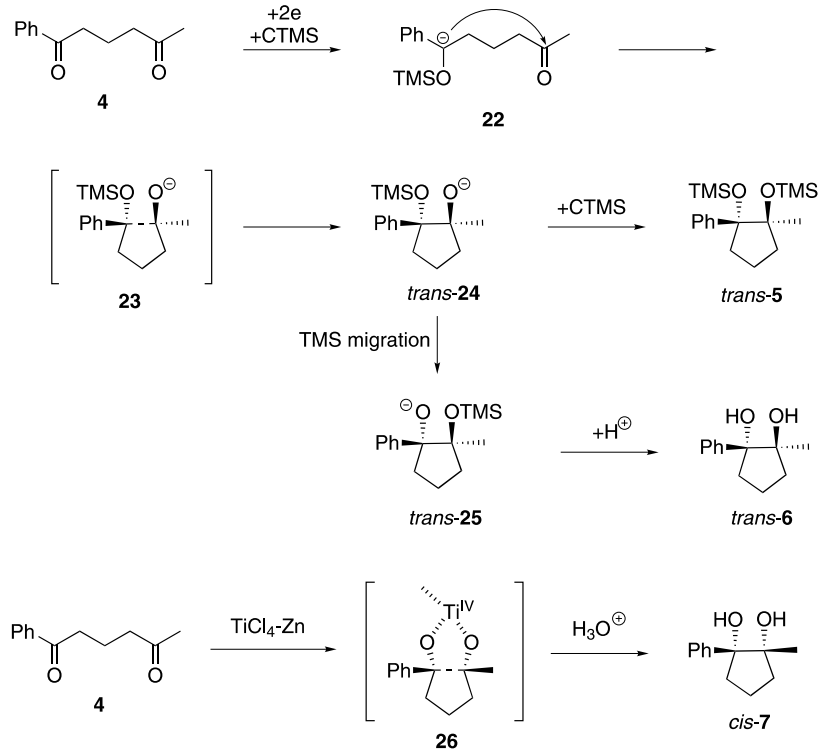


Figure 1. X-ray crystal structures of *trans*-**16**, **17**, and *trans*-**21**.



Scheme 6.

O-silylation of *trans*-**24** yields ditrimethylsiloxy ether *trans*-**5**, while migration of the trimethylsiloxy group leads to *trans*-**25**, which is then protonated to monotrimethylsiloxy ether *trans*-**6**. In the reduction of **4** with a low-valent titanium, on the contrary, *cis* transition state **26** is much favored because of the chelation of the two oxygen atoms to the titanium atom. Consequently, *cis*-**7** is produced exclusively.

In summary, the intramolecular crossed pinacol coupling of aromatic 1,4-, 1,5-, and 1,6-diketone was effectively achieved by electroreduction in the presence of chlorotrimethylsilane and triethylamine. The electroreductive coupling afforded *trans*-isomers of the four-, five-, and six-membered 1,2-diols preferentially, whereas the reduction of these diketones with a metal reducing agent produced *cis*-isomers of the cyclized 1,2-diols predominantly.

References and notes

1. (a) Hoffmann, H. M. R.; Münnich, I.; Nowitzki, O.; Stucke, H.; Williams, D. J. *Tetrahedron* **1996**, *52*, 11783; (b) Nowitzki, O.; Münnich, I.; Stucke, H.; Hoffmann, H. M. R. *Tetrahedron* **1996**, *52*, 11799.
2. Fujiwara, T.; Tsuruta, Y.; Arizono, K.; Takeda, T. *Synlett* **1997**, 962.

3. Nakayama, J.; Yamaoka, S.; Hoshino, M. *Tetrahedron Lett.* **1987**, *28*, 1799.
4. Kise, N.; Arimoto, K.; Ueda, N. *Tetrahedron Lett.* **2003**, *44*, 6281.
5. THF was oxidized at anode to polymeric compounds and these obstructed current supply. Therefore, DMF was employed as the solvent of the anolyte.
6. ^{1}H NMR of **2** ($CDCl_3$): δ −0.26 (s, 6H), −0.10 (s, 3H), −0.08 (s, 6H), 0.19 (s, 3H), 0.87 (s, 1H), 1.45 (s, 2H), 1.73–1.94 (m, 2.33H), 2.01–2.07 (m, 0.33H), 2.27–2.34 (m, 0.33H), 2.39–2.47 (m, 0.33H), 2.53–2.61 (m, 0.67H), 7.19–7.24 (m, 1H), 7.26–7.31 (m, 2H), 7.41–7.45 (m, 2H).
7. *trans*-**3**: ^{1}H NMR ($CDCl_3$): δ 1.50 (s, 3H), 1.62–1.70 (m, 1H), 1.85–1.93 (m, 1H), 2.00–2.07 (m, 1H), 2.60–2.68 (m, 1H), 7.32–7.36 (m, 1H), 7.40–7.45 (m, 2H), 7.51–7.56 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 21.8 (q), 28.5 (t), 31.6 (t), 77.9 (s), 82.1 (s), 126.6 (d), 127.9 (d), 128.6 (d), 140.1 (s).
8. The stereoisomers of **5** and **6** could be separated by further column chromatography on silica gel. ^{1}H NMR spectra ($CDCl_3$, δ) of these isomers are as follows. *trans*-**5**: −0.17 (s, 9H), 0.00 (s, 9H), 1.13 (s, 3H), 1.69–1.91 (m, 4H), 1.97–2.05 (m, 1H), 2.75–2.83 (m, 1H), 7.18–7.22 (m, 1H), 7.23–7.28 (m, 2H), 7.40–7.45 (m, 1H). *cis*-**5**: −0.10 (s, 9H), 0.15 (s, 9H), 0.84 (s, 3H), 1.60–1.72 (m, 2H), 1.89–1.98 (m, 1H), 1.99–2.06 (m, 1H), 2.13–2.21 (m, 1H), 2.32–2.39 (m, 1H), 7.20–7.28 (m, 3H), 7.49–7.53 (m, 2H). *trans*-**6**: 0.15 (s, 9H), 0.95 (s, 3H), 1.70–1.76 (m, 1H), 1.79–1.85 (m, 1H), 1.97–2.14 (m, 3H), 2.33–2.40 (m, 1H), 3.89 (s, 1H), 7.22–7.33 (m, 3H), 7.43–7.47 (m, 2H). *cis*-**6**: −0.03 (S, 9H), 0.81 (S, 3H), 1.70–1.78 (m, 2 H), 1.91–2.02 (m, 2H), 2.14–2.21 (m, 1H), 2.43–2.51 (m, 1H), 3.21 (s, 1H), 7.23–7.32 (m, 3H), 7.42–7.46 (m, 2H).
9. *trans*-**7**: ^{1}H NMR ($CDCl_3$): δ 0.97 (br s, 1H), 1.17 (s, 3H), 1.57 (br s, 1H), 1.71–1.78 (m, 1H), 1.87–2.00 (m, 3H), 2.06–2.15 (m, 1H), 2.81–2.88 (m, 1H), 7.29–7.33 (m, 1H), 7.36–7.41 (m, 2H), 7.59–7.62 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 19.4 (t), 20.9 (q), 37.6 (t), 37.8 (t), 82.4 (s), 85.6 (s), 127.0 (d), 127.4 (d), 128.0 (d), 141.2 (s).
10. ^{1}H NMR of *trans*-**9** ($CDCl_3$): δ −0.19 (s, 9H), 0.05 (s, 9H), 1.00 (s, 3H), 1.37–1.46 (m, 2H), 1.49–1.59 (m, 2H), 1.61–1.74 (m, 2H), 1.82–1.89 (m, 1H), 2.56–2.63 (m, 1H), 7.16–7.20 (m, 1H), 7.21–7.26 (m, 2H), 7.39–7.43 (m, 1H). ^{1}H NMR of *trans*-**10** ($CDCl_3$): δ 0.05 (s, 9H), 0.91 (br s, 1H), 1.01 (s, 3H), 1.47–1.77 (m, 6H), 1.88–1.97 (m, 1H), 2.58–2.66 (m, 1H), 7.20–7.35 (m, 3H), 7.47–7.51 (m, 2H).
11. Balskus, E. P.; Méndez-Andino, J.; Arbit, R. M.; Paquette, L. A. *J. Org. Chem.* **2001**, *66*, 6695.
12. ^{1}H NMR of *trans*-**12** ($CDCl_3$): δ −0.05 (s, 9H), 0.98 (s, 3H), 1.35–1.41 (m, 1H), 1.45 (s, 1H), 1.47–1.80 (m, 5H), 1.83–1.91 (m, 1H), 2.56–2.64 (m, 1H), 7.20–7.25 (m, 1H), 7.26–7.31 (m, 1H), 7.53–7.58 (m, 2H).
13. ^{1}H NMR of *trans*-**14** ($CDCl_3$): δ −0.29 (s, 9H), −0.03 (s, 9H), 1.18 (t, 3H, J = 7.1 Hz), 1.38 (s, 3H), 1.72–1.81 (m, 2H), 1.85–1.91 (m, 1H), 2.05–2.13 (m, 1H), 2.53–2.71 (m, 3H), 2.93–3.02 (m, 1H), 3.95–4.02 (m, 1H), 4.14–4.21 (m, 1H), 7.02–7.07 (m, 1H), 7.09–7.14 (m, 2H), 7.36–7.40 (m, 1H).
14. ^{1}H NMR of **15** ($CDCl_3$): δ −0.02 (s, 3.6H), 0.18 (s, 5.4H), 0.83 (s, 1.8H), 1.18 (t, 1.8H, J = 7.1 Hz), 1.20 (t, 1.2H, J = 7.1 Hz), 1.36 (s, 1.2H), 1.52–1.60 (m, 0.6H), 1.74–1.96 (m, 2.4H), 2.04–2.26 (m, 1.6H), 2.49–2.76 (m, 2.4H), 2.89–3.04 (m, 1H), 4.00–4.24 (m, 2H), 7.05–7.09 (m, 0.6H), 7.11–7.22 (m, 2.4H), 7.44–7.49 (m, 1H).
15. ^{1}H NMR of *trans*-**19** ($CDCl_3$): δ −0.25 (s, 9H), 0.10 (s, 9H), 1.03 (t, 3H, J = 7.3 Hz), 1.17 (s, 3H), 1.38–1.60 (m, 3H), 1.71–1.79 (m, 1H), 1.83–1.96 (m, 2H), 2.08–2.18 (m, 1H), 2.77–2.85 (m, 2H), 3.14–3.24 (m, 1H), 6.98–7.02 (m, 1H), 7.05–7.13 (m, 2H), 7.28–7.32 (m, 2H). ^{1}H NMR of *trans*-**20** ($CDCl_3$): δ 0.11 (s, 9H), 0.78 (s, 1H), 1.04 (t, 3H, J = 7.3 Hz), 1.10 (s, 3H), 1.48–1.68 (m, 3H), 1.76–1.99 (m, 3H), 2.10–2.18 (m, 1H), 2.78–2.91 (m, 2H), 3.23–3.32 (m, 1H), 0.01 (m, 2H), 7.03–7.07 (m, 1H), 7.12–7.17 (m, 2H), 7.38–7.42 (m, 2H).
16. Crystal data. *trans*-**16**: $C_{17}H_{22}O_4$, FW = 290.36, mp 100–101 °C, monoclinic, $P2_{1/n}$ (no 14), colorless block, a = 18.086(3) Å, b = 9.200(2) Å, c = 19.199(3) Å, β = 108.300(8)°, V = 3032.9(1) Å^3, T = 298 K, Z = 8, D_{calcd} = 1.272 g/cm^3, μ = 0.89 cm^{-1}, GOF = 1.00. Compound **17**: $C_{15}H_{16}O_3$, FW = 244.29, mp 164–165 °C, monoclinic, $P2_{1/n}$ (no 14), colorless block, a = 7.523(2) Å, b = 16.129(3) Å, c = 9.899(3) Å, β = 94.879(9)°, V = 1196.7(5) Å^3, T = 298 K, Z = 4, D_{calcd} = 1.356 g/cm^3, μ = 0.93 cm^{-1}, GOF = 1.000. *trans*-**21**: $C_{18}H_{24}O_4$, FW = 304.39, mp 89–90 °C, triclinic, P-1 (no 2), colorless block, a = 7.9339(5) Å, b = 9.2597(5) Å, c = 23.960(2) Å, α = 100.035(3)°, β = 92.198(5)°, γ = 105.216(3)°, V = 1666.0(2) Å^3, T = 298 K, Z = 4, D_{calcd} = 1.213 g/cm^3, μ = 0.84 cm^{-1}, GOF = 1.002.