153. 1,2-Stereoinduction in Radical Reactions: Stereoselective Synthesis of 2-Alkyl-3-hydroxybutanoates

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Radical addition to 2-cyclohexyl-5-methylidene-6-methyl-1,3-dioxan-4-one (**2**) affords stereoselectively 5,6-*trans*-products *trans*-**3**. The size of the radical has no influence on the selectivity. These *trans*-acetals are converted into *threo*-3-hydroxy-butanoates **4**. Methyl 2-methylidene-3-[(*tert*-butyl)diphenylsilyloxy]butanoate (**5**), treated under the same conditions, leads mainly to the *erythro*-isomer of **4** after deprotection. An influence of the steric bulkyness of the radical is observed. The stereochemical course of the reactions is discussed.

Introduction. – For many years, radical reactions had the reputation to be of low chemo-, regio-, and stereoselectivity. In the last decade, it had been shown that chemo- and regioselectivity [1] of radical processes as well as the stereochemical course of cyclic radicals [2] are highly predictable. Only recently, first examples of auxiliary and substrate control for the stereoselectivity of acyclic radical reactions have been observed [3].

In our continuing study concerning 1,2-stereoinduction in radical reactions, we were interested in comparing the stereoselectivity of cyclic and acyclic systems [4] in reactions with different radicals. The dioxanone ring was a suitable choice, because it could be compared to the corresponding acyclic β-hydroxy-ester, and also because such ring systems are known to give stereoinduction in anionic chemistry [5].

Preparation of Starting Materials. – Following the suggestion of *Perlmutter* and *Tabone*[1]), methyl 2-methylidene-3-hydroxybutanoate (**1**) was prepared by the known reaction of methyl acrylate and acetaldehyde in presence of DABCO [7]. The procedure described by *Seebach et al.* [8] was used to synthesize the 5-methylidene-1,3-dioxan-4-one ring[2]). As aldehyde for the cyclizations in this system, cyclohexanecarbaldehyde turned out to be more useful than pivalaldehyde or benzaldehyde, and we obtained the corresponding dioxanone with 95% d.e. Recrystallization in pentane at 4° afforded pure *cis*-**2** (*Scheme 1*). The *cis*-configuration was checked by NOE experiments.

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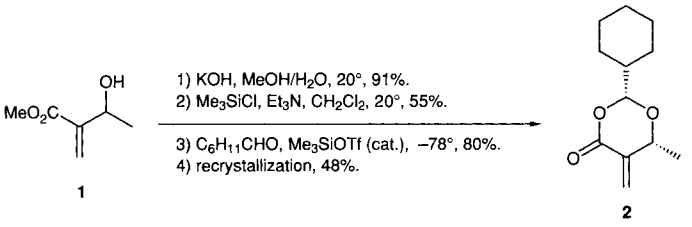
[1]) *Perlmutter* and *Tabone* used compound **1** and some of its derivatives for ionic reactions [6]. They suggested to use similar compounds also for radical reactions. Unfortunately, we failed to cite them in our former publication [4].

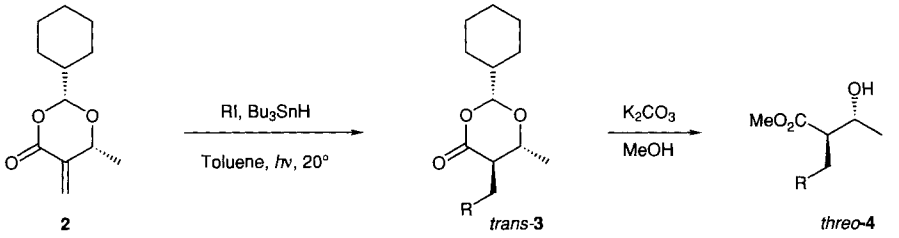
[2]) All experiments were carried out with racemic mixtures.

Scheme 1



Radical Reactions. – *tert*-Butyl-radical addition to dioxanone **2** using the tin method [1] gave the adduct **3a** in excellent yield as one isomer (*Scheme 2*). By comparison with ^{1}H-NMR data, given in the literature for similar products [9], we concluded that the 10-Hz coupling between H–C(5) and H–C(6) is characteristic for a *trans*-relationship of the Me and neopentyl groups. Furthermore, X-ray crystal analysis unambiguously established the structure of the product (*Fig.*).

Scheme 2



a R = *t*-Bu ; **b** R =cyclohexyl; **c** R = C_8H_{17}

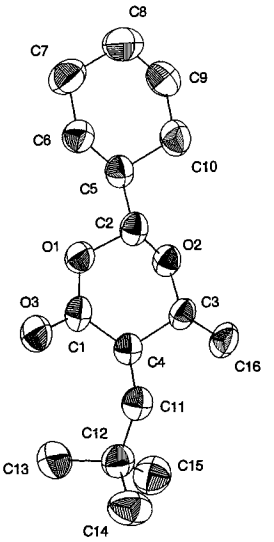


Figure. *Molecular structure of* **3a**. ORTEP plot, 50 % probability ellipsoids with atomic numbering; H-atoms omitted for clarity.

Secondary and primary radicals were also added under the same conditions to methylidene-dioxanone **2** leading to products with a lower yield but the same stereoselectivity (*Table 1*). Transformation of these acetals *trans*-**3** into the corresponding β-hydroxy-esters *threo*-**4** was carried out with K_2CO_3 in MeOH[3]). GC Analysis confirmed the high degree of stereoselectivity of the radical reaction.

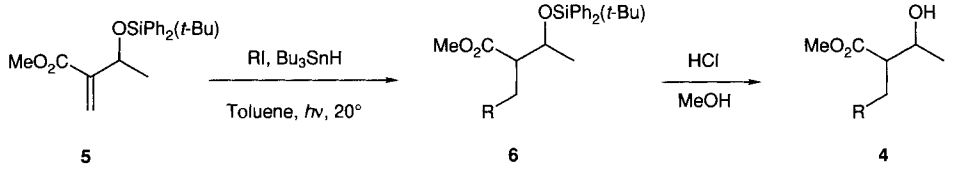
Table 1. *Radical Reactions* (20°) *of* **2** *and* **5**, *and Subsequent Deprotection*

		Radical reaction			Deprotection reaction		
Radical	Alkene	Product	Yield [%]	*threo/erythro*	Product	Yield [%]	*threo/erythro*
t-Bu	**2**	**3a**	97	> 50:1[a])	**4a**	78	> 50:1
Cyclohexyl	**2**	**3b**	71	> 50:1[a])	**4b**	55	> 50:1
Octyl	**2**	**3c**	49	> 50:1[a])	**4c**	98	> 50:1
t-Bu	**5**	**6a**	97	1:19	**4a**	68	1:42
Cyclohexyl	**5**	**6b**	87	1:7.0	**4b**	57	1:13
Octyl	**5**	**6c**	75	1:4.3	**4c**	56	1:6.7

[a]) *trans/cis*, see *Scheme 2*.

Analogous radical reaction with the corresponding acyclic alkene **5**, synthesized by silylation of the alcohol **1**, yielded *erythro*-isomers of **6** as main products (*Scheme 3*, *Table 1*). Deprotection of the silyl ethers **6** was carried out with concentrated HCl in MeOH [10]. Due to the faster reaction of *erythro*-isomers of **6**, diastereoisomeric ratios of deprotected products **4** were higher than those for **6**. A small amount of *threo*-**6** remained unreacted.

Scheme 3

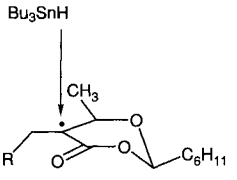


5 **6** **4**

a R = *t*-Bu; **b** R = cyclohexyl ; **c** R = C_8H_{17}

Discussion. – The data in *Table 1* show that radical addition to **2** yields *trans*-**3** and after deprotection *threo*-**4** stereoselectively. Thus, the intermediate radical is attacked by Bu_3SnH *cis* to the Me group at the ring. In analogy to ionic alkylation reaction [11], this stereoselectivity can be explained by a preferred conformation **7** in which substituent R is turned away from the Me group at the cyclic radical. In this conformation, one face of the radical is shielded by R, and the attack occurs from the opposite side. It is interesting to note that radicals **7** exhibit similar selectivities as analogous enolates **8** [11].

[3]) For convenience, we use *threo* and *erythro* to denote the configurations of the racemic products **4** and **6**.



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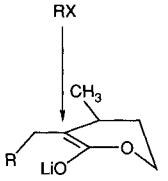

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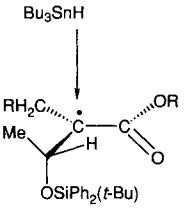

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The preferred formation of *erythro*-**6** *via* radical addition to acyclic alkene **5** (*Table1*) can be easily explained by allylic strain effects. Recently, we have suggested that radicals substituted by an ester and a chiral *tertiary* center adopt preferred conformations in which the H-atom at the chiral center points in the direction of the ester O-atom [12]. It is likely that the C–H bond and the ester group are twisted against each other, because of the steric repulsion between the bulky silyloxy group and the RCH_2 substituent at the radical center. With bulky substituents R, this twisting will be more pronounced in the preferred conformation **9**, shielding one face of the radical even more effectively. This could explain the increase of the *erythro*-selectivity in going from *primary* to *tertiary* alkyl groups R (*Table 1*). Again, analogous ionic reactions give similar 1,2-induction [6][13]. Thus, our experiments demonstrate that radicals can react with stereoselectivities that are comparable to ionic reactions, and that the selectivities can be reversed by going from cyclic to acyclic radicals.

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Experimental Part

General. All radical reactions were carried out under Ar. Silica gel used for chromatography: *C 560KV* 35–70 mm, *Chemische Fabrik Uetikon*. GC: *Carlo Erba 6000* with flame ionization detector coupled to a *Shimadzu C-R4A* integrator (conditions: 30 m *OV-1* or 30 m *SE-30*, 70° to 260° at 5°/min). M.p.: *Büchi* apparatus, uncorrected. IR: *Perkin Elmer 781* spectrophotometer. ^{1}H- (300 MHz) and ^{13}C-NMR (75 MHz): *Varian Gemini 300* (TMS as internal standard and $CDCl_3$ as solvent). MS: *VG 70-250* (CI, NH_3 for chemical ionization, FAB: fast atom bombardment). FC = flash chromatography.

2-Cyclohexyl-5-methylidene-6-methyl-1,3-dioxan-4-one (**2**). The method described by *Seebach et al.* [8] was applied. Methyl 3-hydroxy-2-methylidenebutanoate (**1**; 1.3 g, 10 mmol) [6a] in MeOH (10 ml) and aq. KOH soln. (4M, 5 ml) were stirred at 20° for 24 h. After dilution with Et_2O (75 ml), addition of dil. HCl (2N, 30 ml), the org. layer was dried ($MgSO_4$) and the solvent removed *in vacuo*: 1.06 g (91%) of crude hydroxy-acid was isolated and treated with Et_3N (2.8 ml, 20 mmol) and Me_3SiCl (2.6 ml, 20 mmol) in CH_2Cl_2 (20 ml) at 20° for 48 h. After addition of pentane (10 ml) and filtration, the solvent was evaporated. Distillation of the residue (90°/3 · 10^{-2} Torr) gave 1.3 g (55%) of the disilylated product, that was directly used in the following reaction. The disilylated product (700 mg, 2.7 mmol), cyclohexanecarbaldehyde (300 mg, 2.7 mmol), and trimethylsilyl triflate (0.02 ml) in CH_2Cl_2 (20 ml) reacted for 18 h at –75°. After addition of pyridine (0.2 ml) at –75°, the product was extracted with Et_2O (75 ml) and washed with H_2O (3 × 10 ml). The crude product was purified by FC (silica gel; pentane/AcOEt 16:1) to give **2** (450 mg, 80%) as a 97:3 *cis/trans*-mixture (NMR). After recrystallization in pentane (10 ml) at 4°, *cis*-isomer **2** (274 mg, 48%) was isolated as pure compound. M.p. 52–56°. IR (KBr): 1740, 1280, 1200. ^{1}H-NMR: 6.49 (*d*, *J* = 2.3, 1 H); 5.58 (*d*, *J* = 2.3, 1 H); 5.10 (*d*, *J* = 4.7, 1 H); 4.60 (*ddd*, *J* = 2.3, 4.7, 6.3, 1 H); 1.66–1.89 (*m*, 6 H); 1.47 (*d*, *J* = 6.3, 3 H); 1.12–1.27 (*m*, 5 H). ^{13}C-NMR: 163.5; 138.2; 125.1; 104.9; 74.1; 41.9; 26.4; 26.3; 26.2; 25.5; 20.2. CI-MS: 228 (51), 121 (14), 211 (100), 112 (45). Anal. calc. for $C_{12}H_{18}O_3$ (209.39): C 68.74, H 8.74; found: C 68.61, H 8.92.

2-Cyclohexyl-5-(2',2'-dimethylpropyl)-6-methyl-1,3-dioxan-4-one (**3a**). To a water-cooled (20°) soln. of **2** (52 mg, 0.25 mmol) and *t*-BuI (0.2 ml, 1.6 mmol) in toluene (2 ml) was added Bu_3SnH (0.15 ml, 0.5 mmol) in toluene (0.5 ml) under irradiation with a 100-W tungsten lamp over a period of 1.5 h. Irradiation was continued, until the reaction of **2** (2 h) was completed. The excess *t*-BuI and the solvent were evaporated, and the residue was stirred with Et_2O (5 ml) and a sat. aq. KF soln. (1 ml) at r.t. for 12 h. After filtration, the org. layer was dried and the solvent evaporated. The product was purified by FC (silica gel; pentane/AcOEt 16:1) affording **3a** (65 mg, 97%); 5,6-*trans*/5,6-*cis* > 50:1 (^{1}H-NMR). M.p. 71–72°. IR (KBr): 1740, 1230, 990. ^{1}H-NMR: 5.06 (*d*, *J* = 4.6, 1 H); 3.70 (*dq*, *J* = 6.1, 9.8, 1 H); 2.26 (*ddd*, *J* = 2.7, 6.1, 9.8, 1 H); 1.87 (*dd*, *J* = 6.1, 14.3, 1 H); 1.65–1.81 (*m*, 6 H); 1.33 (*d*, *J* = 6.1, 3 H); 1.11–1.26 (*m*, 6 H); 0.96 (*s*, 9 H). ^{13}C-NMR: 172.4; 105.2; 76.3; 45.0; 42.2; 41.2; 30.9; 29.8; 26.5; 26.3; 26.2; 25.6; 20.1. CI-MS: 270 (9), 269 (55), 174 (34), 158 (6), 157 (68), 156 (14), 140 (10), 139 (100), 112 (59). Anal. calc. for $C_{16}H_{28}O_3$ (268.40): C 71.60, H 10.51; found: C 71.56, H 10.55. This product was crystallized in hexane and the relative configuration established by X-ray crystal analysis.

X-*Ray Structure Analysis of* trans-**3a**. Suitable crystals for X-ray analysis were obtained by slow evaporation of the solvent (hexane) at r. t. Data collection was carried out on an *Enraf-Nonius-CAD-4* diffractometer using $\omega/2\theta$ scan mode. The structure was solved by direct-method techniques using the program SHELXS-86 [14] leading to two independent molecules per asymmetric unit of the monoclinic centrosymmetric unit cell. No correction for absorbance was applied. Anisotropic full-matrix least-squares refinements were carried out for all non-H atoms. H-Atoms were calculated with C–H distance of 1.08 Å and refined isotropically using fixed thermal *U* values of 0.07. Crystal data and acquisition parameters are given in *Table 2*. Final parameters, and a list of bond lengths and angles are deposited at the *Cambridge Crystallographic Data Centre*, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, England.

Table 2. *Crystal Data and Parameters of Data Collection*

Formula	$C_{16}H_{28}O_3$
Crystal system and space group	monoclinic $P2_1/n$ (No. 14)
a [Å]	11.450(6)
b [Å]	27.379(15)
c [Å]	11.601(6)
α [deg]	90.0
β [deg]	115.70(6)
γ [deg]	90.0
V [Å^3]	3277.01(3.5)
Z	8 (2 independent molecules/asymm. unit)
Crystal size [mm]	0.2 × 0.2 × 0.2
Temp. [K]	293
Θ_{max} [deg]	28
Radiation	MoK_α (l = 0.71069)
μ [mm^{-1}]	4.1
F(000)	1184
Scan type	$\omega/2\Theta$
Collected intensities	$\pm h, +k, +l$
No. of independent reflections	5439
No. of refl. used in refinements	3011 ($F_0 > 4\sigma(F_0)$)
No. of variables	367
Observations per parameter	8.2
Largest shift error of refinement	0.01
Largest Peak on final ΔF-*Fourier*	0.47e/Å^3
Final R_w	0.069
Weighting system	$3.20/\sigma^2(F) + 5.55 \cdot 10^{-4}$ (F^2))

2-Cyclohexyl-5-(cyclohexylmethyl)-6-methyl-1,3-dioxan-4-one (**3b**). The same procedure as for the formation of **3a** was used. To **2** (52 mg, 0.25 mmol) and cyclohexyl iodide (0.22 ml, 1.7 mmol) in toluene (2 ml) was added

Bu_3SnH (0.15 ml, 0.5 mmol) in toluene (0.5 ml) under irradiation for 2 h. The reaction was completed within 12 h. Usual workup with sat. aq. KF soln. (1 ml) afforded the crude product which was purified by FC (silica gel; pentane/AcOEt 16:1) leading to **3b** (52 mg, 71%); 5,6-*trans* /5,6-*cis* > 50:1 (^{1}H-NMR). M.p. 59–61°. IR (KBr): 1740, 1230, 990. ^{1}H -NMR: 5.05 (*d*, *J* = 4.6, 1 H); 3.71 (*dq*, *J* = 6.1, 9.9, 1 H); 2.38 (*ddd*, *J* = 4.5, 7.1, 9.9, 1 H); 1.86–0.85 (*m*, 24 H); 1.32 (*d*, *J* = 6.1, 3 H). ^{13}C-NMR: 171.5; 105.3; 75.4; 45.5; 42.2; 36.2; 35.4; 33.7; 32.9; 26.4; 26.4; 26.3; 26.2; 26.1; 25.5; 20.1. CI-MS: 296 (7), 295 (36), 201 (7), 200 (58), 184 (13), 183 (100), 182 (15), 165 (58). Anal. calc. for $C_{18}H_{30}O_3$ (294.44): C 73.43, H 10.27; found: C 73.61, H 10.02.

2-Cyclohexyl-6-methyl-5-nonyl-1,3-dioxan-4-one (**3c**). The same procedure as for the formation of **3a** was used. To **2** (104 mg, 0.5 mmol) and octyl iodide (1.0 ml, 5.4 mmol) in toluene (2 ml) was added Bu_3SnH (0.4 ml, 1.5 mmol) in toluene (0.5 ml) under irradiation for 2 h. After completion of the reaction (48 h); usual workup with sat. aq. KF soln. (1 ml) and purification by FC (silica gel; pentane/AcOEt 16:1) led to **3c** (80 mg, 49%); 5,6-*trans* /5,6-*cis* > 50:1 (^{1}H-NMR). Oil. IR (KBr): 1740, 1230, 990. ^{1}H-NMR: 5.02 (*d*, *J* = 4.7, 1 H); 3.76 (*dq*, *J* = 6.0, 10.1, 1 H); 2.34 (*dt*, *J* = 4.9, 10.1, 1 H); 1.83–1.05 (*m*, 27 H); 1.30 (*d*, *J* = 6.0, 3 H); 0.85 (*t*, *J* = 6.9, 3 H). ^{13}C-NMR: 171.0; 105.5; 74.5; 48.2; 42.2; 31.8; 29.8; 29.5; 29.3; 29.2; 28.1; 26.6; 26.4; 26.3; 26.2; 25.6; 25.5; 22.6; 20.1; 14.1. CI-MS: 326 (9), 325 (48), 230 (40), 214 (13), 213 (85), 212 (23), 196 (13), 195 (94), 112 (100). Anal. calc. for $C_{20}H_{36}O_3$ (324.51): C 74.03, H 11.18; found: C 74.15, H 10.92.

*Methyl 3-[(*tert*-Butyl)diphenylsilyloxy]-2-methylidenebutanoate* (**5**). Compound **1** (130 mg, 1.0 mmol) [7a], (*t*-Bu)Ph_3SiCl (275 mg, 1.0 mmol), and imidazole (140 mg, 2.0 mmol) in DMF (0.5 ml) were stirred for 24 h. After dilution with Et_2O (75 ml), the org. layer was washed with H_2O (3 × 10 ml), dried ($MgSO_4$), and concentrated *in vacuo*. The crude silyl ether was purified by FC (silica gel; pentane/AcOEt 32:1) and gave the known [13] compound **5** (326 mg, 88%). ^{1}H-NMR: 7.80 (*d*, *J* = 6.6, 2 H); 7.65 (*d*, *J* = 6.6, 2 H); 7.40 (*m*, 6 H); 6.28 (*s*, 1 H); 6.15 (*s*, 1 H); 4.78 (*q*, *J* = 6.2, 1 H); 3.70 (*s*, 3 H); 1.23 (*d*, *J* = 6.2, 3 H); 1.12 (*s*, 9 H). ^{13}C-NMR: 166.5; 145.1; 135.9; 135.8; 134.1; 133.9; 129.9; 129.6; 127.8; 127.6; 124.0; 66.8; 51.6; 25.8; 25.7; 24.6; 18.2.

Methyl erythro-*2-{1-[(*tert*-Butyl)diphenylsilyloxy]ethyl}-4,4-dimethylpentanoate* (*erythro*-**6a**). A similar procedure as described above was used. To **5** (92 mg, 0.25 mmol) and *t*-BuI (0.4 ml, 3.3 mmol) in toluene (2 ml) was added Bu_3SnH (0.2 ml, 0.7 mmol) in toluene (0.5 ml) under irradiation for 2 h. The reaction was completed within 4 h. Usual workup with sat. aq. KF soln. (1 ml) afforded, after FC (silica gel; pentane/AcOEt 32:1), **6a** (93 mg, 97%); *threo*-**6a**/*erythro*-**6a** 1:19 (^{1}H-NMR). Oil. The spectral data of *erythro*-**6a** were elucidated from this mixture. ^{1}H-NMR: 7.70 (*m*, 4 H); 7.40 (*m*, 6 H); 3.89 (*dd*, *J* = 6.0, 6.2, 1 H); 3.65 (*s*, 3 H); 2.58 (*dd*, *J* = 6.0, 10.7, 1 H); 1.68 (*dd*, *J* = 10.7, 13.9, 1 H); 1.23 (*d*, *J* = 13.9, 1 H); 1.09 (*d*, *J* = 6.2, 3 H); 1.07 (*s*, 9 H); 0.78 (*s*, 9 H). ^{13}C-NMR: 175.6; 135.9; 135.9; 134.3; 133.8; 129.6; 129.5; 127.5; 127.4; 71.9; 51.2; 48.9; 42.2; 30.4; 29.2; 26.9; 19.7; 19.3. FAB-MS: 427 (10), 370 (29), 329 (100), 349 (58), 213 (77). Anal. calc. for $C_{26}H_{38}O_3Si$ (426.67): C 73.19, H 8.98; found: C 73.31, H 8.83.

Compound threo-**6a**. The synthesis of *threo*-**6a** follows the same procedure as the formation of **5** from **1**. Compound *threo*-**4a** (81 mg, 0,43 mmol) reacted with (*t*-Bu)Ph_3SiCl (120 mg, 0.44 mmol) and imidazole (70 mg, 1.0 mmol) in DMF (0.5 ml) for 24 h. After dilution with Et_2O (50 ml), the org. layer was washed with H_2O (3 × 10 ml), dried ($MgSO_4$), and concentrated *in vacuo*. The crude product was purified by FC (silica gel; pentane/AcOEt 32:1) to give *threo*-**6a** (75 mg, 41%). Oil. ^{1}H-NMR: 7.64 (*m*, 4 H); 7.38 (*m*, 6 H); 3.98 (*dq*, *J* = 6.2, 6.4, 1 H); 3.58 (*s*, 3 H); 2.54 (*dd*, *J* = 6.4, 10.7, 1 H); 1.71 (*dd*, *J* = 10.7, 13.9, 1 H); 1.28 (*d*, *J* = 13.9, 1 H); 0.99 (*s*, 9 H); 0.93 (*d*, *J* = 6.2, 3 H); 0.80 (*s*, 9 H)

Methyl erythro-*3-[(tert-Butyl)diphenylsilyloxy]-2-(cyclohexylmethyl)butanoate* (**6b**). A similar procedure as for the formation of **3a** *via* radical reaction of **2** with *t*-BuI was used. To **5** (92 mg, 0.25 mmol) and cyclohexyl iodide (0.45 ml, 2.5 mmol) in toluene (2 ml) was added Bu_3SnH (0.3 ml, 1.1 mmol) in toluene (0.5 ml) under irradiation for 2 h. The reaction was completed within 24 h. Usual workup with sat. aq. KF soln. (1 ml) afforded, after purification by FC (silica gel; pentane/AcOEt 32:1), **6b** (98 mg, 87%); *threo*-**6b**/ *erythro*-**6b** 1:7.0 (^{1}H-NMR). Oil. The spectral data of *erythro*-**6b** were elucidated from this mixture. ^{1}H-NMR: 7.67 (*m*, 4 H); 7.39 (*m*, 6 H); 3.93 (*dq*, *J* = 6.0, 6.2, 1 H); 3.64 (*s*, 3 H); 2.59 (*ddd*, *J* = 1.8, 6.0, 10.5, 1 H); 1.64–1.00 (*m*, 11 H); 0.99–0.73 (*m*, 2 H); 1.07 (*d*, *J* = 6.2, 3 H); 1.04 (*s*, 9 H). ^{13}C-NMR: 174.9; 135.9; 134.4; 133.8; 129.6; 129.5; 127.5; 127.4; 71.0; 51.2; 50.4; 36.3; 35.9; 35.9; 33.7; 32.6; 26.9; 26.8; 26.5; 26.2; 26.1; 20.1; 19.3. CI-MS: 454 (1), 453 (4), 395 (5), 376 (29), 275 (100). Anal. calc. for $C_{28}H_{40}O_3Si$ (452.71): C 74.29, H 8.91; found: C 74.46, H 8.86.

Compound threo-**6b.** The ^{1}H-NMR spectrum of *threo*-**6b** was elucidated from the spectrum of the mixture. ^{1}H-NMR: 7.67 (*m*, 4 H); 7.39 (*m*, 6 H); 4.06 (*dq*, *J* = 5.6, 6.6, 1 H); 3.62 (*s*, 3 H); 2.59 (*ddd*, *J* = 1.8, 6.6, 10.5, 1 H); 1.64–1.00 (*m*, 11 H); 0.99–0.73 (*m*, 2 H); 1.07 (*d*, *J* = 5.6, 3 H); 1.04 (*s*, 9 H).

Methyl erythro-*2-{1-[(*tert*-Butyl)diphenylsilyloxy]ethyl}undecanoate* (**6c**). A similar procedure as described above was used. To **5** (92 mg, 0.25 mmol) and octyl iodide (0.5 ml, 2.7 mmol) in toluene (2 ml) was added Bu_3SnH (0.4 ml, 1.5 mmol) in toluene (0.5 ml) under irradiation for 2 h. The reaction was completed within 24 h. Usual

workup with sat. aq. KF soln. (1 ml) and FC (silica gel; pentane/AcOEt 32:1) gave **6c** (90 mg, 75%); *threo*-**6c**/*erythro*-**6c** 1:4.3 (^{1}H-NMR). Oil. The spectral data of *erythro*-**6c** were elucidated from this mixture. ^{1}H-NMR: 7.77–7.36 (*m*, 10 H); 4.02 (*m*, 1 H); 3.67 (*s*, 3 H); 2.52 (*m*, 1 H); 1.65–0.79 (*m*, 22 H); 1.07 (*s*, 9 H). ^{13}C-NMR: 174.8; 135.9; 134.5; 133.9; 129.6; 129.5; 127.5; 127.4; 70.7; 53.4; 51.1; 31.9; 29.5; 29.4; 29.4; 29.3; 28.7; 27.7; 26.9; 26.8; 22.7; 20.5; 19.3; 14.1. Anal. calc. for $C_{26}H_{38}O_3Si$ (482.78): C 74.34, H 9.60; found: C 74.37, H 9.82.

Compound threo-**6c.** The ^{1}H-NMR spectrum of *threo*-**6c** was elucidated from the spectrum of the mixture. ^{1}H-NMR: 7.77–7.36 (*m*, 10 H); 4.09 (*m*, 1 H); 3.65 (*s*, 3 H); 2.52 (*m*, 1 H); 1.65–0.79 (*m*, 22 H); 1.07 (*s*, 9 H).

Methyl 2-(1-Hydroxyethyl)-4,4-dimethylpentanoate (**4a**). To **1** (130 mg, 1.0 mmol) and *t*-BuI (0.8 ml, 6.7 mmol) in toluene (3 ml) was added Bu_3SnH (0.35 ml, 1.3 mmol) in toluene (2 ml) under irradiation for 2 h. The reaction was completed within 3 h. The excess *t*-BuI and solvent were evaporated, and the residue was stirred with Et_2O (5 ml) and a sat. aq. KF soln. (1 ml) at r.t. for 12 h. After filtration, the org. layer was dried and the solvent evaporated. The crude product was purified by FC (silica gel; pentane/AcOEt 2: 1) and gave **4a** (181 mg, 96%); *threo*-**4a**/*erythro*-**4a** 2.2:1 (^{1}H-NMR and GC). Anal. calc. for $C_{10}H_{20}O_3$ (189.27): C.63.78, H 10.71; found: C 63.61, H 10.82.

The two isomers were separated by chromatography (silica gel; pentane/AcOEt 2:1): *threo*-**4a** (50 mg, 26%) and *erythro*-**4a** (33 mg, 17%) were obtained.

Data of threo-**4a**: Oil. IR (KBr): 3500, 1740. ^{1}H-NMR: 3.88 (*ddq*, *J* = 4.7, 4.9, 6.2, 1 H); 3.70 (*s*, 3 H); 2.48 (*ddd*, *J* = 1.8, 4.9, 10.3, 1 H); 2.23 (*d*, *J* = 4.7, 1 H); 1.77 (*dd*, *J* = 10.3, 14.2, 1 H); 1.43 (*dd*, *J* = 1.8, 14.1, 1 H); 1.18 (*d*, *J* = 6.2, 3 H); 0.88 (*s*, 9 H). ^{13}C-NMR: 176.5; 70.4; 69.5; 51.8; 49.2; 48.8; 43.4; 40.9; 30.4; 29.3; 29.2; 26.6; 21.9; 20.2; 16.5; 13.6. CI-MS: 207 (9), 206 (82), 190 (9), 189 (83), 174 (18), 171 (100).

Data of erythro-**4a:** Oil. IR (KBr): 3500, 1740. ^{1}H-NMR: 3.80 (*ddq*, *J* = 5.8, 6.3, 8.0, 1 H); 3.71 (*s*, 3 H); 2.48 (*ddd*, *J* = 2.2, 5.8, 10.3, 1 H); 2.30 (*d*, *J* = 8.0, 1 H); 1.84 (*dd*, *J* = 10.3, 14.2, 1 H); 1.38 (*dd*, *J* = 2.2, 14.2, 1 H); 1.21 (*d*, *J* = 6.3, 3 H); 0.89 (*s*, 9 H). ^{13}C-NMR: 176.6; 70.3; 69.4; 51.6; 49.1; 43.3; 40.8; 30.5; 29.2; 21.8; 20.1. CI-MS: 207 (5), 206 (51), 190 (11), 189 (100), 174 (31), 171 (52).

threo-**4a** via *Deprotection of* **3a**. A soln. of **3a** (20 mg, 0.075 mmol) in MeOH (0.5 ml) was stirred with K_2CO_3 (10 mg, 0.075 mmol) for 4 h at 20°. This mixture was filtrated, and MeOH and cyclohexanecarbaldehyde were removed *in vacuo*: *threo*-**4a** (11 mg, 78%); *threo*-**4a**/*erythro*-**4a**> 50:1 (GC and NMR).

erythro-**4a** via *Deprotection of* **6a**. To **6a** (93 mg, 0.22 mmol; *threo*/*erythro* 1: 19) in MeOH (1 ml) was added 0.1 ml of conc. HCl. After 3 d reaction, the products were extracted with Et_2O. The org. layer was dried and concentrated *in vacuo*. The residue was chromatographed (silica gel; pentane/AcOEt 2:1) and gave **4a** (28 mg, 68%) as a mixture *threo*-**4a**/*erythro*-**4a** 1:42 (GC).

Methyl 2-(Cyclohexylmethyl)-3-hydroxybutanoate (**4b**). To **1** (130 mg, 1.0 mmol) and cyclohexyl iodide (0.9 ml, 7.0 mmol) in toluene (3 ml) was added Bu_3SnH (0.6 ml, 2.2 mmol) in toluene (2 ml) under irradiation for 2 h. The reaction was completed within 12 h. The excess iodide and the solvent were evaporated, and the residue was stirred with Et_2O (5 ml) and a sat. aq. KF soln. of (1 ml) at r.t. for 12 h. After filtration, the org. layer was dried and the solvent evaporated. After FC (silica gel; pentane/AcOEt 4:1), **4b** (176 mg, 82%) was obtained as a mixture *threo*-**4b**/*erythro*-**4b** 2.0: 1 (^{1}H-NMR and GC). Anal. calc. for $C_{12}H_{22}O_3$ (214.31): C 67.26, H 10.35; found: C 67.48, H 10.16.

The two isomers were separated by chromatography (silica gel; pentane/AcOEt 4:1) to give *threo*-**4b**: 30 mg (14%) and *erythro*-**4b**: 34 mg (16%).

Data of threo-**4b:** Oil. IR (KBr): 3500, 1740. ^{1}H-NMR: 3.94 (*ddq*, *J* = 4.5, 5.0, 6.3, 1 H); 3.71 (*s*, 3 H); 2.55 (*dt*, *J* = 4.5, 10.4, 1 H); 2.37 (*d*, *J* = 5.0, 1 H); 1.81–0.88 (*m*, 13 H); 1.18 (*d*, *J* = 6.3, 3 H). ^{13}C-NMR: 175.9; 68.6; 51.6; 49.5; 35.9; 34.9; 33.9; 32.5; 26.5; 26.2; 26.1; 20.2. CI-MS: 233 (12), 232 (100), 216 (6), 215 (53), 200 (12), 197 (16), 173 (12), 156 (22), 139 (24).

Data of erythro-**4b**: Oil. IR (KBr): 3500, 1740. ^{1}H-NMR: 3.85 (*ddq*, *J* = 5.2, 6.4, 7.5, 1 H); 3.72 (*s*, 3 H); 2.51 (*ddd*, *J* = 5.0, 5.2, 10.1, 1 H); 2.46 (*d*, *J* = 7.5, 1 H); 1.83–0.81 (*m*, 13 H); 1.21 (*d*, *J* = 6.4, 3 H). ^{13}C-NMR: 176.1; 68.9; 51.5; 50.1; 37.1; 35.6; 33.7; 32.7; 26.5; 26.2; 26.1; 21.8. CI-MS: 233 (13), 232 (100), 216 (8), 215 (63), 200 (14), 197 (15), 173 (8), 156 (14), 139 (12)

threo-**4b** via *Deprotection of* **3b**. A soln. of **3b** (20 mg, 0.07 mmol) in MeOH (0.5 ml) was stirred with K_2CO_3 (10 mg, 0.075 mmol) for 4 h at 20°. This mixture was filtrated and MeOH and cyclohexanecarbaldehyde were removed *in vacuo*: *threo*-**4b** (8 mg, 55%) was obtained: *threo*-**4b**/*erythro*-**4b**> 50:1 (GC and NMR).

erythro-**4b** via *Deprotection of* **6b**. To **6b** (80 mg, 0.18 mmol; *threo* / *erythro* 1: 7.0) in MeOH (1 ml) was added 0.1 ml of conc. HCl. After 3 d reaction, the products were extracted with Et_2O. The org. layer was dried and concentrated *in vacuo*. The residue was chromatographed (silica gel; pentane/AcOEt 4:1) and gave a mixture of **4b** (22 mg, 57%) *threo*/*erythro* 1:13 (GC).

Methyl 2-(1-Hydroxyethyl)undecanoate (**4c**). To **1** (70 mg, 0.5 mmol) and octyl iodide (0.6 ml, 3.3 mmol) in

toluene (2 ml) was added Bu_3SnH (0.3 ml, 1.1 mmol) in toluene (1 ml) under irradiation for 2 h. The reaction was completed within 48 h. The solvent was evaporated, and the residue was stirred with Et_2O (5 ml) and a sat. aq. KF soln. (1 ml) at r.t. for 12 h. After filtration, the org. layer was dried and the solvent evaporated. The crude product was purified by FC (silica gel; pentane/AcOEt 4:1) and gave **4c** (110 mg, 90%); *threo*-**4c**/*erythro*-**4c** 2.0:1 (^{1}H-NMR and GC). *threo*- and *erythro*-Isomers were not separable by FC. Oil. IR (KBr): 3500, 1740. Anal. calc. for $C_{14}H_{28}O_3$ (244.38): C 68.81, H 11.55; found: C 69.09, H 11.45.

threo-**4c** via *Deprotection of* **3c**. A soln. of **3c** (70 mg, 0.22 mmol) in MeOH (0.5 ml) was stirred with K_2CO_3 (20 mg, 0.15 mmol) for 4 h at 20°. This mixture was filtrated and MeOH and cyclohexanecarbaldehyde were removed *in vacuo*: *threo*-**4c** (53 mg, 98%) was obtained: *threo*-**4c**/*erythro*-**4c** > 50:1 (GC and NMR). Oil. IR (KBr): 3500, 1740. ^{1}H-NMR: 3.89 (*dq*, *J* = 5.9, 6.3, 1 H); 3.71 (*s*, 3 H); 2.50 (*m*, 1 H); 2.38 (*dt*, *J* = 5.9, 9.1, 1 H); 1.67–1.53 (*m*, 2 H); 1.25 (*m*, 14 H); 1.21 (*d*, *J* = 6.3, 3 H); 0.87 (*m*, 3 H). ^{13}C-NMR: 175.9; 68.4; 52.8; 51.5; 31.8; 29.5; 29.4; 29.4; 29.2; 27.3; 22.6; 21.5; 14.0. CI-MS: 263 (15), 262 (100), 246 (7), 245 (47).

erythro-**4c** via *Deprotection of* **6c**.To the mixture of **6c** (56 mg, 0.12 mmol, *threo*/*erythro* 1:4.3) in MeOH (1 ml) was added conc. HCl (0.1 ml). After 3 d reaction, the products were extracted with Et_2O. The org. layer was dried and concentrated in *vacuo*. The residue was chromatographed (silica gel; pentane/AcOEt 4:1) and gave a mixture of **4c** (16 mg, 56%); *threo*-**4c**/*erythro*-**4c** 1:6.7 (GC). Oil. IR (KBr): 3500, 1740. The spectral data of *erythro*-**4c** were elucidated from this mixture. ^{1}H-NMR: 3.98 (*dq*, *J* = 5.2, 6.3, 1 H); 3.71 (*s*, 3 H); 2.43 (*dt*, *J* = 5.2, 9.9, 1 H); 2.04 (*m*, 1 H); 1.67–1.58 (*m*, 2 H); 1.26 (*m*, 14 H); 1.19 (*d*, *J* = 6.3, 3 H); 0.88 (*m*, 3 H). ^{13}C-NMR: 175.7; 68.3; 52.3; 51.6; 31.9; 29.6; 29.5; 29.4; 29.3; 27.7; 27.3; 22.7; 20.3; 14.1. CI-MS: 263 (12), 262 (100), 246 (6), 245 (51).

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