82. Efficient Control of the Stereoselectivity in Reactions of 2-Oxy-Substituted Benzylic Radicals

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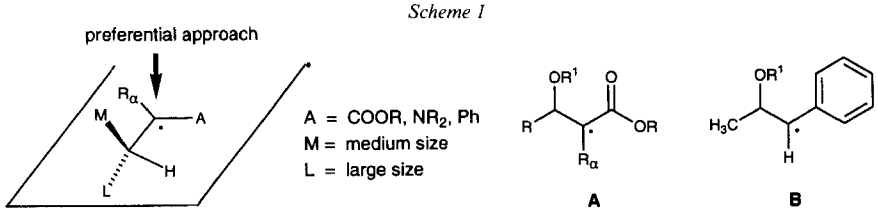
The stereoselectivity in reactions of 2-oxy-substituted radicals of type **B** was investigated. As expected, minimization of allylic 1,3-strain was the major controlling factor. Under standard conditions, only a modest level of stereoselectivity was observed. *E.g.*, deuteration of the benzylated radical (R^1 = benzyl) gave diastereoisomer ratios $\leq$ 2:1. Use of a bulky protective group on the O-atom (R^1 = (*t*-Bu)Ph_2Si) enhanced slightly the selectivity (ratio 4.1:1). However, a dramatic increase of the stereoselectivity (ratio 13:1) was obtained, when the reaction was performed with the free alcohol after treatment with bulky methylaluminium bis(phenoxide) derivatives (methylaluminium bis[2,6-di(*tert*-butyl)-4-methylphenoxide] (MAD) and methylaluminium bis(2,6-diphenylphenoxide) (MAPH)).

Introduction. – Recently, spectacular progresses were achieved in the control of the stereoselectivity of radical reactions in acyclic systems [1]. A model based on minimization of allylic 1,3-strain ($A^{1,3}$ strain) allowed to rationalize the results for alkoxycarbonyl- [2], dialkylamino- [3] and phenyl-substituted [2c] [3e, g] [4] radicals (*Scheme 1*). Preferred reaction from the less hindered face, *cis* to the medium-sized group M, leads to the major diastereoisomer. Good level of stereoselectivity may only be obtained when the large group L and the medium group M are well differentiated in size.

Scheme 1



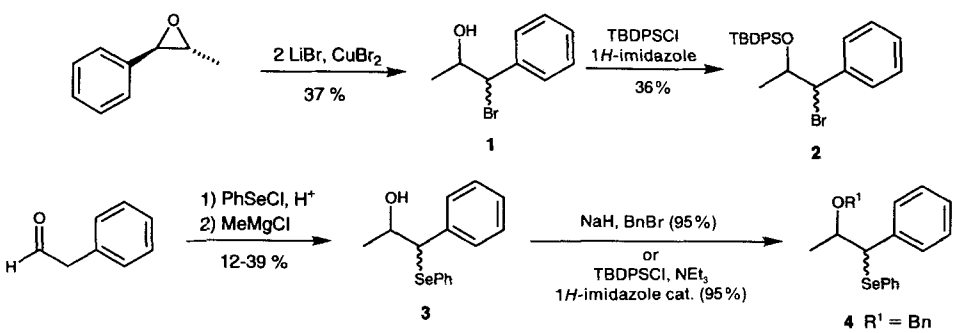
Ester-substituted radicals possessing an adjacent oxy group or medium-sized substituent at the chiral center (see **A**) were investigated extensively [2b, e, h] [5], and good diastereoselectivities were only observed with large substituents R at the chiral center (R = Ph, *t*-Bu, and C_6H_{11}). When R was a Me group and R_x an H-atom[1]), the stereoselectivity was low, despite favorable dipole-dipole interactions. Based on these results, a low

[1]) R_x plays an important role, since it generates allylic 1,2-strain which usually enhances noticeably the stereoselectivity of ester radical reactions, see [2b, h].

stereoselectivity was expected for radicals of type **B**. Therefore, we decided to investigate different possibilities to overcome this problem. In the preceding paper[2]), we reported an efficient method to control the stereoselectivity in cyclic 2-oxy-substituted radicals. Using a similar strategy, we show here that it is possible to obtain a high level of asymmetric 1,2-induction with acyclic benzylic radicals of type **B**.

Results and Discussion. – The radical precursor **2** was prepared from 1-methyl-2-phenyloxirane *via* **1**, and precursors **3**–**5** were obtained from phenylacetaldehyde according to *Scheme 2*.

Scheme 2



TBDPS = (*t*-Bu)Ph_2Si

The reduction of these radical precursors with tributyltin deuteride (Bu_3SnD) gave compounds **6**–**9** which were analyzed for their diastereoisomer contents by ^{1}H- and ^{2}H-NMR. The results of the deuteration experiments are summarized in the *Table*. In a first series of experiments (*Entries 1–5*), we investigated the effect of the *Lewis* acids[3]) for the deuteration of the benzyl ether **4**. As already observed with cyclic ethers[2]), the results were disappointing. In the absence of *Lewis* acid, the reaction gave a 1:1 mixture of *u*- and *l*-**6** (*Entry 1*). A low selectivity was observed in the presence of methylaluminium bis(phenoxide) (MAP, *Entry 2*), methylaluminium bis[2,6-di(*tert*-butyl)-4-methylphenoxide] (MAD, *Entry 3*), and methylaluminium bis[4-bromo-2,6-di(*tert*-butyl)phenoxide] (MABR, *Entry 4*) [6]. Other *Lewis* acids such as Et_2AlCl (*Entry 5*), $BF_3 \cdot OEt_2$, and $(i\text{-}PrO)_{4-n}TiCl_n$ were either inefficient or lowered significantly the chemical yield. In a second series of experiments, we covalently bound a large (*tert*-butyl)diphenylsilyl protective group on the O-atom to enhance the shielding difference of the two faces of radical **B**. Starting from the bromide **2**, product **7** was obtained as a *u*/*l* 3.6:1 mixture of isomers in refluxing benzene (*Entry 6*). The reaction was repeated at 20° using triethylborane as initiator, but the stereoselectivity remained almost unchanged (*u*/*l* 4.1:1). Similarly, selenide **5** gave **8** after desilylation and benzoylation as a *u*/*l* 3.6:1 mixture of isomers (*Entry 7*)[4]). Finally, the deuteration of the non-protected alcohol **3** was examined. A low

[2]) See the preceding paper in this issue.

[3]) *Lewis* acids were applied with success to control the diastereoselectivity (1,2-induction) with sulfinylated benzyl radicals, see [4b]. Other examples with different types of cyclic and acyclic radicals were reported recently, see ref. in the preceding paper.

[4]) The analogous tertiary benzylic radical with a heptyl substituent at the radical center also reacted with a low selectivity of 5:1, see [1c].

Table. *Reaction of Radical Precursors* **2**–**5** *with* $Bu_3SnD/AIBN$ *at 10° (Scheme 3)*

Entry	Radical precursor	R^1	Product	R^2	Additive[a] (equiv.)	Yield [%]	*u/l*
1	**4**	Bn	**6**	Bn	–	79	1:1
2	**4**	Bn	**6**	Bn	MAP (1.1)	56	1.5:1
3	**4**	Bn	**6**	Bn	MAD (1.1)	87	2.0:1
4	**4**	Bn	**6**	Bn	MABR (1.1)	36	2.0:1
5	**4**	Bn	**6**	Bn	Et_2AlCl (1.1)	48	1.1:1
6	**2**	(*t*-Bu)Ph_2Si	**7**	(*t*-Bu)Ph_2Si	–	60	4.1:1[b]
7	**5**	(*t*-Bu)Ph_2Si	**8**[c]	Bz	–	78	3.6:1
8	**3**	H	**8**[d]	Bz	–	75	1.4:1
9	**3**	H	**8**[d]	Bz	MAD (1.1)	75	13:1
10	**3**	H	**8**[d]	Bz	MAPH (1.1)	60	13:1
11	**3**	H	**8**[d]	Bz	Me_3Al (0.33)	78	4.3:1

[a]) MAP = Methylaluminium bis(phenoxide); MAD = methylaluminium bis[2,6-di(*tert*-butyl)-4-methylphenoxide]; MABR = methylaluminium bis[4-bromo-2,6-di(*tert*-butyl)phenoxide]; MAPH = methylaluminium bis(2,6-diphenylphenoxide).

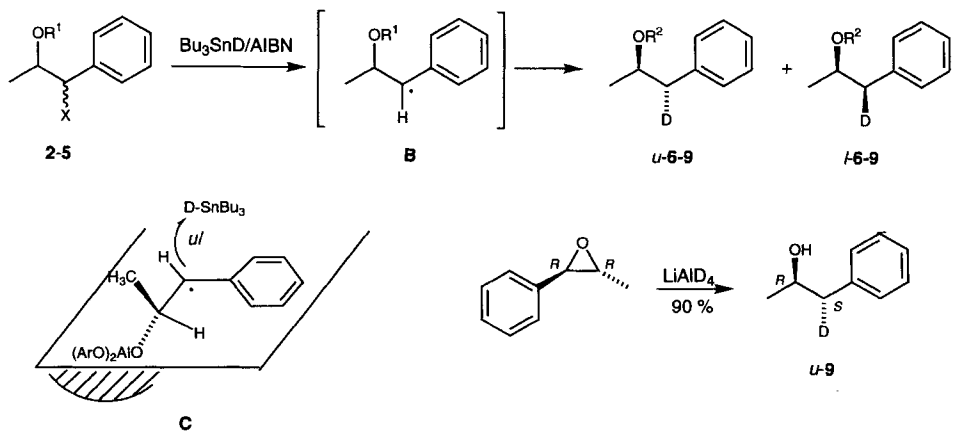
[b]) At 20°; a 3.6:1 ratio was obtained in refluxing benzene (80°).

[c]) After desilylation (Bu_4NF) and benzoylation (BzCl/pyridine/4-(dimethylamino)pyridine).

[d]) After benzoylation (BzCl/pyridine/4-(dimethylamino)pyridine).

selectivity was observed in the absence of additive (*Entry 8*). However, the diastereoselectivity was dramatically enhanced by adding 1.1 equiv. of MAD or methylaluminium bis(2,6-diphenylphenoxide) (MAPH) [7]. In these two cases, product **8** was obtained as a *u/l* 13:1 mixture of diastereoisomers. Methane evolution during the addition of the additive proved that an aluminium alkoxide of type **C** (*Scheme 3*) is involved in the reaction. As expected, the radical adopts a conformation which minimizes $A^{1,3}$ strain, and attack from the less hindered face (*ul* approach) leads to the *unlike* (*u*) diastereoisomer. The exceptional shielding effect of the aluminium diphenoxide group is responsible for the high diastereoselectivity observed. The large ligands on aluminium are necessary as shown by

Scheme 3[a])



[a]) For R^1 and R^2, see *Table*.

the reaction using 0.33 equiv. of $AlMe_3$ (*Entry 11*). In that case, an aluminium tris(alkoxide) is formed, but the diastereoselectivity remains moderate (*u/l* 4.3:1).

The relative configuration of the products was established by independent synthesis of *u*-**9** *via* $LiAlD_4$ reduction of (2*R*,3*R*)-2-methyl-3-phenyloxirane (*Scheme 3*). The relative configuration of compounds **6** and **8** was deduced after benzylation and benzoylation, respectively, of a pure sample of *u*-**9**. The relative configuration of **7** was established by deprotection of a *u/l* 4:1 mixture of diastereoisomers which gave **9** in a similar diastereoisomers ratio.

In conclusion, we demonstrated that bulky aluminium alkoxides are particularly efficient for the control of the 1,2-asymmetric induction in acyclic benzylic radicals of type **B**. The use of bulky alcohol-protective groups is far less efficient. Moreover, the direct use of the free alcohol as starting material allows to avoid tedious protection and deprotection steps. Synthetic applications of this strategy with different types of substrates are currently being investigated in our laboratories and will be reported in due course.

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Experimental Part

1. *General*[2]). Unless otherwise stated, commercially available reagents were used without purification. Solvents were dried by distillation over drying agents as follows: Et_2O (Na-benzophenone), THF (Na-benzophenone or K-metal), CH_2Cl_2 (CaH_2), and DMF (CaH_2). TLC: detection either by UV or by immersion in a soln. of $CeSO_4 \cdot 4\ H_2O$ (10 g), phosphomolybdic acid (25 g), and conc. H_2SO_4 (100 ml) in H_2O (900 ml), followed by heating. FC: *Chemische Fabrik Uetikon* silica gel 35–70 μm (230–400 mesh) and *Baker* silica gel 0.060–0.200 mm. M.p.: *Kofler* hot stage and *Büchi* (*Tottoli*) apparatus; uncorrected. FT-IR: *Perkin-Elmer 1600-FTIR*, *Perkin-Elmer 16PC*, and *Mattson Unicam 5000*. NMR: *Varian Gemini 300* (^1H, 300 MHz; ^{13}C, 75.5 MHz), *Varian Gemini 200* (^1H, 200 MHz; ^{13}C, 50.3 MHz), *Varian VXR-400* (^2H, 61 MHz) and *Bruker AM 360* (^2H, 55.28 MHz); multiplicities in ^{13}C were determined by APT and DEPT sequences. MS: double-focusing mass spectrometer *VG 70–250* and *Vacuum Generators Micromass VG 70/70E DS 11-250*; FAB (positive mode; 2-nitrobenzyl alcohol matrix NBA). Elemental analyses: Mikroanalytisches Laboratorium der Universität Basel, *Ilse Beetz*, *Mikroanalytisches Laboratorium*, D–96317 Kronach, Germany, and *Ciba-Geigy AG*, Mikrolabor, Marly, Switzerland.

2. *Radical Precursors. 1-Bromo-1-phenylpropan-2-ol* (**1**) [8]. (+)-(1*R*,2*R*)-1-Methyl-2-phenyloxirane (260 mg, 1.94 mmol) was added dropwise to a deep green soln. of dry LiBr (1.03 g, 11.9 mmol) and $CuBr_2$ (1.32 g, 5.9 mmol) in THF (10 ml) at 0°. The mixture was stirred at r.t. for 2 d and then evaporated. The residue was dissolved in Et_2O (20 ml) and aq. buffer soln. (pH 7, 30 ml) added. The aq. layer was extracted with Et_2O (4 × 50 ml) and the combined org. phase washed with brine (50 ml), dried ($MgSO_4$), and evaporated. FC (50 g, Et_2O/pentane) gave **1** (156 mg, 37%) as a colorless oil (*u/l* 19:1 after FC) and epoxide (103 mg, 40%). Isomerization was observed after storage for 2 years at −8°, yielding a 1:1.2 mixture of 2 diastereoisomers. R_f 0.30 (*l*-**1**), 0.20 (*u*-**1**; Et_2O/pentane 1:2). IR (film): 3550–3300*s* (br.), 3030*m* (sh), 2975*m*, 1805, 1700*w*, 1490*m*, 1452*s*, 1370, 1250, 1200*m*, 1120, 1080, 940*s*. ^1H-NMR (300 MHz): *u*-**1**: 7.47–7.25 (*m*, 5 arom. H); 4.87 (*d*, *J* = 6.3, H–C(1)); 4.21 (*ddq*, *J* = 4.5, 6.3, 6.1, H–C(2)); 2.04 (*d*, *J* = 4.5, OH); 1.34 (*d*, *J* = 6.1, Me); *l*-**1**: 7.46–7.18 (*m*, 5 arom. H); 4.85 (*d*, *J* = 8.0, H–C(1)); 4.16 (*ddq*, *J* = 4.0, 8.0, 6.3, H–C(2)); 2.71 (*d*, *J* = 4.0, OH); 1.19 (*d*, *J* = 6.3, Me). ^{13}C-NMR (75.5 MHz): *u*-**1**: 138.2 (*s*); 128.8 (*d*); 128.7 (*d*); 128.6 (*d*); 71.6 (*d*); 60.8 (*d*); 20.0 (*q*); *l*-**1**: 139.1 (*s*); 128.8 (*d*); 128.7 (*d*); 128.6 (*d*); 71.6 (*d*); 65.1 (*d*); 19.7 (*q*). CI-MS (NH_3): 234 (7), 232 (7, $[M + NH_4]^+$), 216 (1), 214 (1, M^+, $C_9H_{11}BrO^+$), 152 (100, $[M - Br + NH_3]^+$).

1-Bromo-2-[(tert-butyl)diphenylsilyloxy]-1-phenylpropane (**2**). A mixture of **1** (100 mg, 0.464 mmol), 1*H*-imidazole (190 mg, 2.68 mmol), (*t*-Bu)Ph_2SiCl (383 mg, 1.39 mmol), and dry DMF (2 ml) was prepared at 0° and stirred at r.t. for 2 d. The mixture was diluted with Et_2O (20 ml) and the org. phase washed with sat. aq. $NaHCO_3$

soln. (2 × 25 ml) and H_2O (2 × 10 ml), dried (MgSO), and evaporated. FC (20 g, Et_2O/pentane 1:20) gave **2** (2:1 ratio of diastereoisomers). Colorless oil. Higher reaction temperatures (70°) led to formation of an unidentified by-product, which could not be separated by FC. **2**: R_f 0.45 (Et_2O/pentane 1:20). IR (KBr): 3070, 2930, 2855*m*, 1640*s* (br.), 1470*w*, 1430*m*, 1375*m*, 1140*m* (sh), 1110*s*. ^{1}H-NMR (300 MHz): main isomer: 7.70–7.20 (*m*, 15 arom. H); 4.11 (*dq*, *J* = 6, 6, H–C(2)); 1.19 (*d*, *J* = 6, Me); 0.95 (*s*, *t*-Bu); minor isomer: 7.70–7.20 (*m*, 15 arom. H); 4.88 (*d*, *J* = 6, H–C(1)); 4.29 (*dq*, *J* = 6, 6, H–C(2)); 1.06 (*s*, *t*-Bu); 0.94 (*d*, *J* = 6, Me). ^{13}C-NMR (75 MHz): 139.3 (*s*); 138.9; 136.0 (*d*); 135.9; 134.3 (*s*); 134.2; 133.4; 133.3; 129.8 (*d*); 129.7; 129.6; 128.8; 128.2; 128.2; 128.0; 127.7; 127.6; 127.5; 73.5 (*d*); 61.4 (*d*); 60.9; 27.0 (*q*); 26.8; 20.7 (*q*); 20.6; 19.5 (*s*); 19.3. FAB-MS (NBA + KCl): 493 (7), 491 (6, $[M + K]^+$), 455 (3), 453 (4), 397 (51), 395 (50, $[M–C_4H_9]^+$), 373 (28), 263 (57), 261 (56), 199 (65), 197 (61), 135 (100). Anal. calc. for $C_{25}H_{29}BrOSi$ (453.50): C 66.21, H 6.45; found: C 66.20, H 6.62.

1-(Phenylseleno)-1-phenylpropan-2-ol (**3**) [9]. PhSeCl chloride (5.74 g, 30 mmol) in AcOEt (30 ml) was added with stirring to a soln. of freshly distilled phenylacetaldehyde (3.48 ml, 30 mmol) in AcOEt (90 ml). Conc. HCl soln. (1 drop) was added and the brown mixture stirred in the dark overnight. The yellow mixture was diluted with hexane (450 ml) and washed with H_2O (6 × 45 ml), dried ($MgSO_4$), and evaporated. After filtration through a short pad of silica gel (hexane/AcOEt 9:1), the residue was dissolved in THF (19 ml) and added dropwise to 22% MeMgCl (19 ml, 30 mmol) in THF at 0° under N_2. The mixture was stirred for 30 min at 0° and then at r.t. and finally treated with 10% aq. NH_4Cl soln. The aq. layer was extracted with Et_2O, and the combined org. layers were washed with brine, dried ($MgSO_4$), and evaporated. FC (AcOEt/hexane 1:9) gave **3** (3.43 g, 39%) as a 1:1 mixture of diastereoisomers. Colorless oil. IR (film): 3426, 3058, 2973, 1950, 1878, 1807, 1718, 1690. ^{1}H-NMR (200 MHz): 7.5–7.05 (*m*, 10 arom. H); 4.23 (*d*, *J* = 6, H–C(1) (1 isomer)); 4.22–4.09 (*m*, H–C(1) (1 isomer), H–C(2)); 2.85, 2.33 (2 br. *d*, *J* = 3, OH); 1.24 (*d*, *J* = 6, Me (1 isomer)); 1.15 (*d*, *J* = 5.5, Me (1 isomer)). ^{13}C-NMR (50.3 MHz): 20.59 (*q*); 20.77 (*q*); 57.31 (*d*); 60 (*d*); 69.33 (*d*); 69.65 (*d*); 127.05 (*d*); 127.31 (*d*); 127.82 (*d*); 128.03 (*d*); 128.28 (*d*); 128.36 (*d*); 128.54 (*s*); 128.83 (*d*); 128.91 (*d*); 129.17 (*s*); 129.38 (*d*); 134.89 (*d*); 134.99 (*d*); 135.32 (*d*); 135.42 (*d*); 138.88 (*s*); 140.55 (*s*). EI-MS: 292 (6, M^+), 290 (2), 167 (11), 158 (14), 135 (54), 117 (22), 91 (40), 77 (27), 57 (30). Anal. calc. for $C_{15}H_{16}OSe$ (292.03): C 61.86, H 5.54; found: C 61.97, H 5.59.

2-(Benzyloxy)-1-phenyl-1-(phenylseleno)propane (**4**). A soln. of **3** (2.5 g, 8.5 mmol) in dry THF (4.5 ml) was added dropwise at 0° to a suspension of 50% NaH (616 mg, 12.8 mmol) in dry THF (34 ml) and stirred at 0° for 30 min. Benzyl bromide (1.5 ml, 12.8 mmol) was added. The mixture was stirred at 0° for 30 min and at r.t. overnight before treatment with pyridine and MeOH. After evaporation, CH_2Cl_2 was added and the org. phase washed with H_2O, dried ($MgSO_4$), and evaporated. FC (Et_2O/hexane 1:40) gave **4** (3.09 g, 95%) as a 1:1 mixture of diastereoisomers. White solid. IR (KBr): 3058, 3023, 2925, 2870, 1951, 1878, 1811, 1476, 1452. ^{1}H-NMR (200 MHz): 7.45–7.05 (*m*, 15 arom. H); 4.72 (*d*, *A* of *AB*, *J* = 11.5, 1 H, PhC*H*$_2$O (1 isomer)); 4.62 (*d*, *A* of *AB*, *J* = 11.5, 1 H, PhC*H*$_2$O (1 isomer)); 4.61 (*d*, *B* of *AB*, *J* = 11.5, 1 H, PhC*H*$_2$O (1 isomer)); 4.46 (*d*, *A* of *AB*, *J* = 11.5, 1 H, PhC*H*$_2$O (1 isomer)); 4.43 (*d*, *J* = 7.5, H–C(1) (1 isomer)); 4.3 (*d*, *J* = 6, H–C(1) (1 isomer)); 4.19–3.99 (*m*, H–C(2)); 1.27 (*d*, *J* = 6.2, Me (1 isomer)); 1.25 (*d*, *J* = 6.1, Me (1 isomer)). ^{13}C-NMR (50.3 MHz): 140.44 (*s*); 138.50 (*s*); 138.36 (*s*); 135.16 (*d*); 134.70 (*d*); 134.65 (*d*); 130.17 (*s*); 129.84 (*s*); 129.32 (*d*); 128.79 (*d*); 128.68 (*d*); 128.44 (*d*); 128.24 (*d*); 128.15 (*d*); 128.02 (*d*); 127.88 (*d*); 127.69 (*d*); 127.51 (*d*); 127.44 (*d*); 127.34 (*d*); 127.23 (*d*); 126.79 (*d*); 78.49 (*d*); 77.94 (*d*); 71.42 (*t*); 71.10 (*t*); 55.70 (*d*); 55.62 (*d*); 18.47 (*q*); 18.23 (*q*). EI-MS: 383 (1, $[M + 1]^+$), 382 (5, M^+), 247 (22), 245 (12), 167 (18), 157 (16), 117 (18), 92 (19), 91 (100), 77 (20), 65 (19). Anal. calc. for $C_{22}H_{22}OSe$ (382.08): C 69.29, H 5.81; found: C 69.38, H 5.84.

2-[(tert-Butyl)diphenylsilyloxy]-1-phenyl-1-(phenylseleno)propane (**5**). A mixture of **3** (233 mg, 0.8 mmol), NEt_3 (0.28 ml, 2.08 mmol), 1*H*-imidazole (cat.), and (*t*-Bu)Ph_2SiCl (0.52 ml, 2.08 mmol) in dry CH_2Cl_2 (2 ml) was stirred at r.t. for 3 d. The mixture was extracted with CH_2Cl_2, washed with H_2O, dried ($MgSO_4$), and evaporated. FC (Et_2O/hexane 1:20) gave **5** (400 mg, 95%). Colorless oil. IR (film): 3070, 2962, 2931, 2857, 1960, 1893, 1823, 1600, 1474. ^{1}H-NMR (200 MHz): 7.74–7.02 (*m*, 20 arom. H); 4.35–4.32 (*m*, H–C(2)); 4.16 (*d*, *J* = 5, H–C(1)); 1.05 (*s*, *t*-Bu (1 isomer)); 1.03 (*d*, *J* = 7, Me (1 isomer)); 1.01 (*s*, *t*-Bu (1 isomer)); 1 (*d*, *J* = 7, Me (1 isomer)). ^{13}C-NMR (50.3 MHz): 140.51 (*s*); 140.18 (*s*); 136.10 (*d*); 135.96 (*d*); 134.57 (*s*); 134.50 (*d*); 134.28 (*d*); 134.23 (*s*); 133.47 (*s*); 130.57 (*s*); 130.21 (*s*); 129.57 (*d*); 129.48 (*d*); 129.41 (*d*); 128.61 (*d*); 127.88 (*d*); 127.80 (*d*); 127.55 (*d*); 127.33 (*d*); 127.10 (*d*); 126.83 (*d*); 73.36 (*d*); 73.03 (*d*); 57.94 (*d*); 57.67 (*d*); 27.1 (*q*); 27 (*q*); 22.18 (*q*); 21.65 (*q*); 19.5 (*s*); 19.4 (*s*). CI-MS (CH_4): 530 (1, M^+), 528 (4), 527 (8), 474 (17), 473 (52), 472 (97), 470 (55), 452 (100), 450 (69), 372 (91), 274 (73). Anal. calc. for $C_{31}H_{34}OSeSi$ (530.15): C 70.30, H 6.47; found: C 70.48, H 6.72.

3. *Radical Deuteration. General Procedure 1.* A soln. of the radical precursor (1 mmol), Bu_3SnD (1.5 mmol), and AIBN (= 2,2′-azobis[isobutyronitrile]; 10 mg) in CH_2Cl_2 (2.5 ml) was irradiated (sun lamp, 300 W) at 10° until completion (TLC monitoring). After evaporation and filtration through a short column of silica gel, the diastereoselectivity was determined from ^{1}H- and ^{2}H-NMR spectra.

General Procedure 2. To a soln. of ArOH (MAP: ArOH = phenol; MAD: ArOH = 2,6-di(*tert*-butyl)-4-methylphenol; MABr: ArOH = 4-bromo-2,6-di(*tert*-butyl)phenol; MAPH: 2,6-diphenylphenol; 2.2 mmol) in CH_2Cl_2 (1.1 ml) was added at r.t. 2M Me_3Al in heptane (1.1 mmol; CH_4 evolution). After stirring at r.t. for 1 h, a soln. of **4** (382 mg, 1 mmol) in CH_2Cl_2 (0.85 ml) was added followed by Bu_3SnD (438 mg, 1.5 mmol) and AIBN (10 mg). The mixture was irradiated for 7 h at 10° and diluted with CH_2Cl_2 (20 ml). Then 1N NaOH (5 ml) was added and the mixture stirred for 15 min, extracted with CH_2Cl_2, and dried ($MgSO_4$). After evaporation and filtration through a short column of silica gel (hexane→Et_2O/hexane 1:20), the diastereoselectivity was determined from ^{1}H- and ^{2}H-NMR spectra.

General Procedure 3. To a soln. of $MeAl(OAr)_2$ (0.77 mmol, prepared as in *General Procedure 2*) in CH_2Cl_2 (1 ml) was added a soln. of **2** (204 mg, 0.7 mmol) in CH_2Cl_2 (0.5 ml; CH_4 evolution). After stirring for 1 h at r.t., Bu_3SnD (409 mg, 1.4 mmol) and AIBN were added. The mixture was irradiated at 10° for 12 h and diluted with CH_2Cl_2 (15 ml). Then 1N HCl (3 ml) was added and the mixture stirred for 15 min, extracted (CH_2Cl_2), and dried ($MgSO_4$). After evaporation and filtration through a short column of silica gel (AcOEt/hexane 1:9), the residue obtained was dissolved in dry CH_2Cl_2/pyridine 1:1 (2.5 ml). Benzoyl chloride (0.24 ml, 2.1 mmol) was added followed by 4-(dimethylamino)pyridine (cat.). The mixture was stirred for 2 d and extracted with CH_2Cl_2, the combined org. layer washed with 1N HCl, 1N NaOH, and H_2O, dried ($MgSO_4$), and evaporated, and the residue purified by filtration through silica gel (Et_2O/hexane 1:40): crude **8**. The diastereoselectivity was determined from ^{2}H-NMR.

u- *and* l-*2-(Benzyloxy)-1-phenyl(1-*$^2H_1$*)propane* (**6**; R^2 = $PhCH_2$). a) *According to* General Procedure 1. From **4** (382 mg, 1 mmol), 7 h of irradiation. FC (Et_2O/hexane 1:40) gave **6** (178 mg, 79%, *u*/*l* 1:1).

b) *According to* General Procedure 2. From **4** (382 mg, 1 mmol), 7 h of irradiation. FC (Et_2O/hexane 1:4) gave **6** (MAP: 127 mg (56%), *u*/*l* 1.5:1; MAD: 196 mg (87%), *u*/*l* 2:1; MABr: 80 mg (36%), *u*/*l* 2:1).

c) *Radical Deuteration with Et$_2$AlCl.* A soln. of **4** (382 mg, 1.0 mmol), 1M Et_2AlCl in hexane (1.1 ml, 1.1 mmol), Bu_3SnD (438 mg, 1.5 mmol), and AIBN (10 mg) in CH_2Cl_2 (2.5 ml) was irradiated (sun lamp, 300 W) for 7 h at 10°. After dilution with CH_2Cl_2, solid $Na_2CO_3 \cdot 10\ H_2O$ (excess) was added and the mixture stirred for 15 min at r.t., filtered through *Celite* and evaporated. FC (Et_2O/hexane 1:40) gave **6** (109 mg, 48%; *u*/*l* 1.1:1). Colorless oil. IR (film): 3062, 3027, 2970, 1948, 1874, 1807, 1604, 1496, 1453. ^{1}H-NMR (200 MHz): 7.5–7.15 (*m*, 10 arom. H); 4.66–4.46 (*m*, $PhCH_2O$); 3.78 (*quint.*, *J* = 6.3, H–C(2)); 3 (*dd*, *J*(H,D) = 1.5, 6.3, H–C(1), *u*-**6**); 2.74 (*dd*, *J*(H,D) = 1.5, 6.3, H–C(1), *l*-**6**); 1.24 (*d*, *J* = 6.3, Me). ^{13}C-NMR (50.3 MHz): 139.06 (*s*); 138.97 (*s*); 129.49 (*d*); 128.17 (*d*); 127.49 (*d*); 127.30 (*d*); 126.04 (*d*); 76.13 (*d*); 70.59 (*t*); 42.89 (*t*, *J*(C,D) = 20); 19.52 (*q*). EI-MS: 227 (8, M^+), 226 (2, $[M-1]^+$), 183 (16), 135 (43), 118 (2), 92 (68), 91 (100), 77 (13). Anal. calc. for $C_{16}H_{17}DO$ (227.13): C 84.56, H 8.39; found: C 84.57, H 8.33.

u- *and* l-*2-[(*tert*-Butyl)diphenylsilyloxy]-1-phenyl(1-*$^2H_1$*)propane* (R^2 = (*t*-Bu)Ph_2Si; **7**). a) *At 20°.* To a mixture of **2** (50 mg, 0.11 mmol), Bu_3SnD (64 mg, 0.22 mmol), and benzene (5 ml) at 20° was added 15% BEt_3 in hexane (110 µl, 0.11 mmol). Stirring at 20° for 2 h and evaporation afforded **7** (*u*/*l* 4.1:1, ^{1}H-NMR). The residue was dissolved in Et_2O (2 ml) and the soln. stirred overnight with KF (170 mg, 2.93 mmol) and H_2O (0.2 ml), filtered through a short pad of *Celite*/$MgSO_4$, and evaporated. FC (2×; Et_2O/pentane 1:40) of the residue gave **7** (25 mg, 60%) in the same isomer ratio as above. Colorless oil. R_f 0.40 (Et_2O/hexane 1:40).

b) *At 80°.* A mixture of **2** (43 mg, 0.10 mmol), Bu_3SnD (55 mg, 0.19 mmol), AIBN (3 mg, 0.02 mmol), and benzene (4 ml) was heated at reflux for 2 h. Evaporation and FC gave **7** (*u*/*l* 3.6:1). This crude product was used without purification for the preparation of **9** (see below). IR (film): 3070, 2960, 2930, 2860, 1960, 1890, 1820*w*, 1470*m*, 1430*s*, 1375*m*, 1135*m* (sh), 1110*s* (br.), 995*s*. ^{1}H-NMR (300 MHz): *u*-**7**: 7.69–6.98 (*m*, 15 arom. H); 4.02 (*dq*, *J* = 6, 7, H–C(2)); 2.78 (br. *d*, *J* = 6, H–C(1)); 1.00 (*s*, *t*-Bu); 1.00 (*d*, *J* = 7, Me); *l*-**7**: 7.69–6.98 (*m*, 15 arom. H); 4.02 (*quint.*, *J* = 7, H–C(2)); 2.62 (br. *d*, *J* = 7, H–C(1)); 1.00 (*d*, *J* = 7, Me); 1.00 (*s*, *t*-Bu). ^{2}H-NMR (61 MHz): *u*-**7**: 2.65 (br. *m*); *l*-**7**: 2.79 (br. *m*). ^{13}C-NMR (75.5 MHz): 138.7 (*s*); 135.8 (*d*); 134.7 (*s*); 134.2; 129.6 (*d*); 129.4; 128.0; 127.4; 125.9; 70.8 (*d*); 45.9 (*dt*, ^1J(C,D) = 19); 27.0 (*q*); 22.8 (*q*); 9.2 (*s*). CI-MS: (NH_3): 393 (4, $[M + NH_4]^+$), 376 (5, $[M+1]^+$), 335 (15), 196 (100), 137 (73, $[M - (t\text{-Bu})Ph_2Si]^+$), 136 (1); degree of deuteration ≥ 98.4% (MS). Anal. calc. for $C_{25}H_{29}DoSi$ (375.59): C 79.95; found: C 79.80.

u- *and* l-*2-(Benzoyloxy)-1-phenyl(1-*$^2H_1$*)propane* (R^2 = PhCO, **8**). a) *According to* General Procedure 1. From **5** (396 mg, 0.75 mmol). Filtration through a short column of silica gel (Et_2O/hexane 1:20) gave a residue which was dissolved in THF (3 ml) and stirred with 1M Bu_4NF (1.6 ml, 1.6 mmol) at r.t. for 3 d. The mixture was extracted with CH_2Cl_2, washed with H_2O, dried ($MgSO_4$), and evaporated. Without further purification, the residue obtained was dissolved in dry CH_2Cl_2/pyridine 1:1 (2.5 ml). Benzoyl chloride (0.24 ml, 2.1 mmol) was added followed by 4-(dimethylamino)pyridine (cat.). The mixture was stirred for 2 d and extracted with CH_2Cl_2. The combined org. phase was washed with 1N HCl, 1N NaOH, and H_2O, dried ($MgSO_4$), and evaporated and the residue purified by filtration through silica gel (Et_2O/hexane 1:40): **8** (141 mg, 78%; *u*/*l* 3.6:1).

b) *According to* General Procedure 3. From **3** (204 mg, 0.70 mmol) and MAD (0.77 mmol): **8** (126 mg, 76%; *u/l* 13:1).

c) *According to* General Procedure 3. From **3** (204 mg, 0.70 mmol) and MAPH (0.77 mmol): **8** (102 mg, 60%; *u/l* 13:1). From **3** (204 mg, 0.70 mmol) and Me_3Al (0.25 mmol): (131 mg, 78%; *u/l* 4.3:1). Colorless oil. IR (film): 3029, 2979, 1930, 1715. ^{1}H-NMR (200 MHz): *u*-**8**: 8.15–7.15 (*m*, 10 arom. H); 5.4 (*quint.*, *J* = 6.3, H–C(2)); 3.04 (*d*, *J* = 6.3, H–C(1)); 1.36 (*d*, *J* = 6.3, Me). ^{2}H-NMR (55.28 MHz): *u*-**8**: 2.99 (br. *s*); *l*-**8**: 3.18 (br. *s*). ^{13}C-NMR (50.3 MHz): 165.92 (*s*); 137.45 (*d*); 132.53 (*d*); 130.79 (*s*); 129.44 (*d*); 128.21 (*d*); 126.96 (*d*); 126.43 (*d*); 124.25 (*d*); 72.0 (*d*); 41.94 (*t*, *J*(C,D) = 19); 19.37 (*q*). EI-MS: 243 (9, $[M + 2]^+$), 242 (38, $[M + 1]^+$), 241 (5, M^+), 160 (5), 151 (18), 148 (28), 123 (44), 121 (45), 120 (100), 119 (75), 118 (21). Anal. calc. for $C_{16}H_{15}DO_2$ (241.11): C 79.64, H 7.09; found: C 79.59, H 7.09.

u-*and* l-*1-Phenyl(1-*$^2H_1$*)propan-2-ol* (**9**). Crude **7** (35 mg; *u/l* 3.6:1) obtained by the deuteration of **2** at 80° (see above) was dissolved in THF (2 ml) and stirred with 1M Bu_4NF in THF (0.6 ml, 0.6 mmol) at r.t. for 20 h. After evaporation, CH_2Cl_2 (10 ml) was added and the soln. washed with 1M aq. $NaHCO_3$. The org. layer was dried ($MgSO_4$) and evaporated. FC (5 g, Et_2O/hexane 1:40→CH_2Cl_2) of the residue gave **9** (8 mg, 61% from **2**; *u/l* 3.6:1). For characterized of *u*-**9** see below.

l-**9**: ^{1}H-NMR (300 MHz): 7.19–7.34 (*m*, 5 arom. H); 4.01 (*dq*, *J* = 6, 8, H–C(2)); 2.75–2.79 (*m*, H–C(1)); 1.52 (br. *s*, OH); 1.24 (*d*, *J* = 6.2, Me). ^{2}H-NMR (55.28 MHz): 2.67 (br. *s*).

(1S,2R)-1-Phenyl(1-$^2H_1$*)propan-2-ol* (*u*-**9**) [10]. (+)-(1*R*,2*R*)-2-Methyl-1-phenyloxirane (138 mg, 1 mmol) was added dropwise at −20° to a suspension of $LiAlD_4$ (84 mg, 2 mmol) in dry Et_2O (10 ml) and stirred at −20° for 1 h, 8 h at 0°, and then at r.t. overnight. The mixture was treated with H_2O (144 µl, 8 mmol) and then with 10% aq. NaOH soln. (200 µl) and extracted with CH_2Cl_2 (4 × 1.5 ml). The org. phase was dried ($MgSO_4$) and evaporated to give *u*-**9** (123 mg, 90%). Colorless oil. R_f 0.10 (CH_2Cl_2). IR (film): 3380*s* (br.), 2970*m*, 1640*m* (br.), 1495, 1450, 1090*m*. ^{1}H-NMR (300 MHz): 7.19–7.34 (*m*, 5 arom. H); 4.01 (*dq*, *J* = 8, 6, H–C(2)); 2.67 (*dt*, ^2J(D,H) = 2, ^3J(H,H) = 8, H–C(1)); 1.59 (br. *s*, OH); 1.24 (*d*, *J* = 6.2, Me). ^{2}H-NMR (61 MHz): 2.77 (br. *s*). ^{13}C-NMR (75.5 MHz): 138.5 (*s*); 129.2 (*d*); 128.3; 126.2; 68.6 (*d*); 45.2 (*dt*, ^1J(C,D) = 19.4); 22.5 (*q*). CI-MS (NH_3): 155 (64, $[M + NH_4]^+$), 137 (9, M^+), 93 (100, $[M - C_2H_4O]^+$). Degree of deuteration ≥ 99% (MS). Anal. calc. for $C_9H_{11}DO$ (137.19): C 78.80; found: C 78.70.

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