81. Diastereoselective Radical Reactions Starting from Cyclic Iodohydrin Derivatives

by **Nadira Moufid** and **Philippe Renaud***

Université de Fribourg, Institut de Chimie Organique, Pérolles, CH-1700 Fribourg

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The stereoselectivity of radical reactions using cyclic iodohydrins and 2-alkoxy iodides was investigated on a simple model system obtained from indene (see **1a–d**). The low level of stereoselectivity inherent to this type of systems could neither be overcome by using large protective group on the O-atom of **1c** nor by complexation with *Lewis* acids. However, starting from the free alcohol **1c**, it was possible to obtain very high selectivities (*trans*/*cis* > 100:1) by forming an aluminium alkoxide derivative upon treatment with methylaluminium bis[2,6-di(*tert*-butyl)-4-methylphenoxide] (MAD) before running the radical reaction. Despite the high steric demand of these complexes, the reactions gave satisfactory yields even for the formation of C–C bonds.

Introduction. – Halohydrins and 2-alkoxy halides are easily prepared in enantiomerically pure form from cyclic alkenes and epoxides and are, therefore, very useful starting materials for EPC synthesis [1]. An interesting transformation involves the formation of C–C bonds *via* a radical pathway [2]. Preferential formation of a *trans*-compound was observed, but the low level of diastereoselectivity was discouraging [3]. We report here a study of a model system derived from indene using deuteration and allylation experiments. A simple procedure to achieve an extremely high level of stereocontrol is reported.

Results and Discussion. – The starting iodohydrins **1a–d** were prepared from 1*H*-indene in a straightforward manner (*Scheme 1*).

Scheme 1

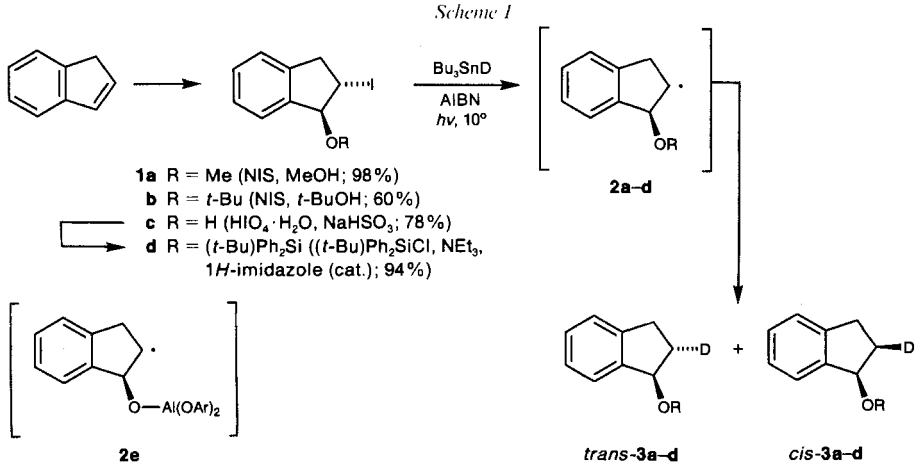


Table. *Stereoselectivity of the Radical-Mediated Reduction of Iodides* **1a–d** *with* Bu_3SnD

Entry	Iodide	Solvent	Product	*Lewis* acid (eqiv.)	*trans/cis*	Yield [%]
1	**1a**	C_6H_6	**3a**	–	3.0:1	93
2	**1a**	CH_2Cl_2	**3a**	–	5.6:1	93
3	**1a**	CF_3CH_2OH	**3a**	–	10:1	69
4	**1a**	CH_2Cl_2	**3a**	MAD[b]) (1.1)	5.6:1	75
5	**1a**	CH_2Cl_2	**3a**	$Ti(i\text{-}PrO)_3Cl$ (1.1)	10:1	87
6	**1b**	CH_2Cl_2	**3b**	–	7:1	84
7	**1d**	CH_2Cl_2	**3c**[a])	–	8.3:1	80
8	**1c**	CH_2Cl_2	**3c**	–	5.0:1	89
9	**1c**	CH_2Cl_2	**3c**	MAD[b]) (1.1)	100:1	86

[a]) After desilylation (Bu_4NF/THF).
[b]) MAD = Methylaluminium bis[2,6-di(*tert*-butyl)-4-methylphenoxide].

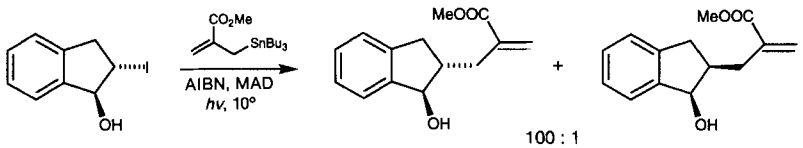
Deuteration experiments were run (*Scheme 1*) to study the diastereoselectivity of cyclic 2-alkoxy- or 2-hydroxy-substituted radicals. Results are summarized in the *Table*. In a first series of experiments, the effect of the solvent[1]) was examined for the MeO-substituted radical **2a** (*Table, Entries 1–3*). A low selectivity was observed in benzene (*trans/cis* 3.0:1). The use of CH_2Cl_2 allowed to raise slightly the selectivity to a *trans/cis* ratio of 5.6:1. The highest *trans/cis* ratio (10:1) was obtained in 3,3,3-trifluoroethanol (TFE). We attribute this result to H-bonding with the O-atom of the MeO group[2]). Encouraged by these results, we tried to use *Lewis* acids[3]) to achieve an efficient complexation of the ether moiety. This procedure which was successful with sulfoxides [6] gave disappointing results (*Table, Entries 4* and *5*). *E.g.*, methylaluminium bis[2,6-di(*tert*-butyl)-4-methylphenoxide] (MAD) [7] was found to be inefficient (*trans/cis* 5.6:1). The reaction presumably proceeds *via* an uncomplexed radical intermediate. A slightly better result (*trans/cis* 10:1) was observed in the presence of $Ti(i\text{-}PrO)_3Cl$.

An alternative to this approach, *i.e.*, the covalent binding of a bulky protective group on the O-atom, was investigated next (*Table, Entries 6* and *7*). The *tert*-butyl derivative **1b** gave a *trans/cis* 7:1 ratio. Even the presence of the very bulky (*tert*-butyl)diphenylsilyl group in **1d** did not allow to obtain a high selectivity (*trans/cis* 8.3:1).

Finally, we studied the non-protected halohydrin **1c**, and a *trans/cis* ratio of 5.0:1 was obtained in CH_2Cl_2 (*Table, Entry 8*). By treating the free alcohol **1c** with 1.1 equiv. of MAD before running the radical reaction, an almost complete control of the stereoselectivity was observed (*trans/cis* 100:1). Formation of the aluminium alkoxide **2e** was clearly demonstrated by methane evolution during the addition of the alcohol to MAD. The exceptional steric hindrance of the substituted bis(phenoxy)aluminium moiety explains the very high *trans*-selectivity. Interestingly, this complete stereocontrol can be extended to the C–C bond formation. Treatment of the non-protected halohydrin **1c** with methyl 2-[(tributylstannyl)methyl]propenoate led to a 1.2:1 mixture of *trans/cis*-**4**. When the same reaction was run after formation of the aluminium alkoxide by adding 1.1 equiv. of MAD, a 100:1 *trans/cis*-ratio was obtained in 69% yield (*Scheme 2*).

[1]) The role of the solvent was already briefly mentioned for 2-alkoxy-substituted cyclic radicals (see [3a]).
[2]) TFE was reported to be particularly efficient for the control of the stereoselectivity of cyclic sulfinylated radicals [4].
[3]) Recently, several reports using complexation with *Lewis* acids for the stereoselectivity control of radical reactions were published (for leading references in this field see [5] [6]).

Scheme 2



1c *trans*-**4** *cis*-**4**

In conclusion, we demonstrated that high *trans*-selectivity can be achieved with 2-hydroxy-substituted radicals by first formation of very bulky aluminium alkoxides. Despite the high steric demand of the complexes, the reactions gave satisfactory yields.

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Experimental Part

1. *General.* THF was freshly distilled from K under N_2, CH_2Cl_2 and benzene from CaH_2 under N_2. All solvents for chromatography were distilled prior to use. Irradiations were conducted using a sun lamp *Osram Ultra-Vitalux* 300 W. Flash column chromatography (FC): *Baker* silica gel *60* (0.060–0.200 mm). TLC: *Merck* silica gel *60* F_{254} anal. plates; detection either with UV or by spraying with a soln. of 25 g of phosphomolybdic acid, 10 g of $Ce(SO_4)_2 \cdot 4\ H_2O$, 60 ml of conc. H_2SO_4, and 940 ml of H_2O with subsequent heating. M.p.: not corrected; *Büchi Tottoli* apparatus. IR: *Perkin-Elmer 16PC* and *Mattson Unicam 5000;* in cm^{-1}. NMR: *Varian Gemini 200* (^1H, 200 MHz; ^{13}C, 50.3 MHz), *Bruker AM 360* (^2H 55.28 MHz); δ in ppm rel. to Me_4Si (= 0 ppm) for ^1H, δ in ppm rel. to $CDCl_3$ (= 7.27 ppm) for ^2H, and δ in ppm rel. to $CDCl_3$ (= 77.0 ppm) for ^{13}C; unless otherwise stated, ^1H- and ^{13}C-NMR spectra were recorded in $CDCl_3$ and ^2H-NMR in $CHCl_3$; ^{13}C multiplicities were determined by the APT sequence; coupling constants *J* in Hz. MS: *Vacuum Generators Micromass VG 70/70E DS 11-250*; EI (70 eV), CI (NH_3 gas); *m/z* (%). Elemental analyses: *Ilse Beetz, Mikroanalytisches Laboratorium*, D-8640 Kronach, Germany, and *Ciba-Geigy AG*, Mikrolabor, Marly, Switzerland.

2. *Radical Precursors.* trans-*2-Iodo-1-methoxyindan* (**1a**) [8]. To a soln. of *N*-iodosuccinimide (NIS; 5.84 g, 26 mmol) in CH_2Cl_2 (50 ml) was added successively 1*H*-indene (2.6 ml, 20 mmol) and MeOH (1.6 ml, 40 mmol) at 0°. The mixture was stirred at 0° in the dark for 1.5 h and then at r.t. overnight and poured into H_2O. The soln. was extracted with CH_2Cl_2, washed with $Na_2S_2O_3$ and H_2O, dried ($MgSO_4$), and evaporated. The residue was purified by FC (Et_2O/petroleum ether 1:20): **1a** (5.35 g, 98%). White solid. M.p. 58°. IR (KBr): 2986, 2963, 2859, 1967, 1934, 1831, 1605. ^1H-NMR: 7.5–7.2 (*m*, 4 arom. H); 5.11 (*d*, *J* = 3.5, H–C(1)); 4.5 (*ddd*, *J* = 3.5, 4.5, 7, H–C(2)); 3.75 (*dd*, *J* = 7, 17, 1 H–C(3)); 3.59 (*s*, MeO); 3.30 (*dd*, *J* = 4.5, 17, 1 H–C(3)). ^{13}C-NMR: 141.27 (*s*); 140.14 (*s*); 128.96 (*d*); 127 (*d*); 125.03 (*d*); 124.56 (*d*); 93.29 (*d*); 57.44 (*q*); 43.47 (*t*); 25.49 (*d*). EI-MS: 274 (8, M^+), 148 (16), 147 (100), 131 (15), 127 (38), 117 (65), 116 (66), 115 (90), 63 (24), 51 (20). Anal. calc. for $C_{10}H_{11}IO$ (273.98): C 43.82, H 4.05; found: C 44.05, H 4.10.

trans-*1-(*tert-*Butoxy)-2-iodoindan* (**1b**) [8]. From NIS (2.92 g, 13 mmol), 1*H*-indene (1.3 ml, 10 mmol), and *tert*-butyl alcohol (1.9 ml, 20 mmol) as described for **1a**. FC (Et_2O/petroleum ether 1:20) gave **1b** (1.91 g, 60%). Colorless oil. IR (film): 3073, 2972, 1952, 1915, 1838, 1633. ^1H-NMR: 7.45–7.2 (*m*, 4 arom. H); 5.31 (*d*, *J* = 2.2, H–C(1)); 4.38 (*ddd*, *J* = 2.2, 3, 6.5, H–C(2)); 3.85 (*dd*, *J* = 6.5, 17.5, 1 H–C(3)); 3.32 (*dd*, *J* = 3, 17.5, 1 H–C(3)); 1.4 (*s*, *t*-Bu). ^{13}C-NMR: 141.28 (*s*); 138.95 (*s*); 128.65 (*d*); 127.27 (*d*); 125.38 (*d*); 124.61 (*d*); 85.45 (*d*); 74.60 (*s*); 43.70 (*t*); 31.00 (*d*); 29.07 (*q*). EI-MS: 316 (3.5, M^+), 134 (13), 133 (100), 116 (78), 115 (67), 103 (10), 77 (14). Anal. calc. for $C_{13}H_{17}IO$ (316.03): C 49.38, H 5.42; found: C 49.51, H 5.50.

trans-*2-Iodoindan-1-ol* (**1c**) [9]. To a soln. of 1*H*-indene (2.4 ml, 20 mmol) in MeCN (40 ml) was added $HIO_4 \cdot 2\ H_2O$ (5.47 g, 24 mmol) in H_2O (12 ml), followed by aq. $NaHSO_3$ (27 mmol) soln. in H_2O (40 ml) within 20 min at 0° under stirring. The soln. was allowed to stand for an additional 2.5 h at r.t. The mixture was extracted with Et_2O, and the extract washed with aq. $Na_2S_2O_3$ soln., dried ($MgSO_4$), and evaporated. FC (hexane/AcOEt 9:1) gave pure **1c** (4 g, 78%) which was stored at −15°. White solid. M.p. 114°. IR (KBr): 3325, 3258, 1991, 1925, 1838, 1628. ^1H-NMR: 7.5–7.15 (*m*, 4 arom. H); 5.39 (*dd*, *J* = 6.05, 6.06, H–C(1)); 4.19 (*ddd*, *J* = 6.05, 7.5, 8, H–C(2)); 3.58 (*dd*, *J* = 7.5, 16, 1 H–C(3)); 3.30 (*dd*, *J* = 8, 16, 1 H–C(3)); 2.75 (*d*, *J* = 6.06, OH). ^{13}C-NMR: 142.10 (*s*); 140.94 (*s*); 128.74 (*d*); 127.46 (*d*); 124.27 (*d*); 123.86 (*d*); 85.06 (*d*); 42.33 (*t*); 29.96 (*d*). EI-MS: 261 (2),

260 (20, M^+), 254 (4), 134 (18), 133 (100), 131 (21), 126 (49), 116 (32), 115 (58), 105 (27), 103 (33), 79 (21), 77 (45), 63 (14).

trans-*1-[(* tert-*Butyl)diphenylsilyloxy]-2-iodoindan* (**1d**). To a soln. of **1c** (780 mg, 3 mmol) in CH_2Cl_2 (9 ml) was added at r.t. successively. Et_3N (0.52 ml, 3.9 mmol), 1*H*-imidazole (cat.) and (*t*-Bu)Ph_2SiCl (0.98 ml, 4.5 mmol). The mixture was stirred for 20 h at r.t. and extracted with CH_2Cl_2. The org. layer was washed with H_2O, dried ($MgSO_4$), and evaporated. FC (hexane) gave **1d** (1.4 g, 94%). Colorless oil. IR (film): 3071, 2957, 2930, 2857, 1959, 1890, 1825, 1589, 1472, 1427. ^{1}H-NMR: 7.8–7.05 (*m*, 14 arom. H); 5.43 (*d*, *J* = 2.9, H–C(1)); 4.36 (*ddd*, *J* = 2.9, 3.7, 6.4, H–C(2)); 3.81 (*dd*, *J* = 6.4, 17, 1 H–C(3)); 3.20 (*dd*, *J* = 3.7, 17, 1 H–C(3)); 1.05 (*s*, *t*-Bu). ^{13}C-NMR: 142.02 (*s*); 141.47 (*s*); 136.01 (*d*); 133.57 (*s*); 129.97 (*d*); 129.82 (*d*); 128.66 (*d*); 127.82 (*d*); 127.64 (*d*); 126.98 (*d*); 125.46 (*d*); 124.65 (*d*); 86.12 (*d*); 43.27 (*t*); 30.90 (*d*); 27.08 (*q*); 19.36 (*s*). CI-MS (CH_4): 499 (16, $[M + 1]^+$), 498 (1), 497 (3), 441 (45), 421 (95), 371 (100), 229 (48), 187 (28). Anal. calc. for $C_{25}H_{27}IOSi$ (498.08): C 60.24, H 5.46; found: C 60.44, H 5.67.

3. *Radical Reactions. General Procedure 1.* A soln. of the radical precursor (1 mmol), Bu_3SnD (438 mg, 1.5 mmol), and AIBN (= 2,2′-azobis[isobutyronitrile]; 10 mg) in the solvent (2.5 ml) was irradiated (sun lamp, 300 W) at 10° until completion (TLC monitoring). After evaporation, the crude product was dissolved in MeOH (40 ml), KF (436 mg, 7.5 mmol) was added, and the mixture was stirred at r.t. overnight. After evaporation, dissolution in CH_2Cl_2 and filtration through silica gel, the diastereoselectivity was determined from ^{1}H-NMR.

cis- *and* trans-*1-Methoxy-(2-*$^2H_1$*)indan* (**3a**). a) *Solvent Effects.* From **1a** (274 mg, 1 mmol) in benzene, CH_2Cl_2, or CF_3CH_2OH (2.5 ml) according to the *General Procedure* (3 h of irradiation). FC (Et_2O/hexane 1:40) of the crude product gave **3a** (benzene: 139 mg (93%), *trans*/*cis* 3:1; CH_2Cl_2: 139 mg (93%), *trans*/*cis* 5.6:1; CF_3CH_2OH: 102 mg (69%), *trans*/*cis* 10:1).

b) *(i-PrO)$_3$TiCl Effect.* A soln. of **1a** (274 mg, 1 mmol), (i-PrO)$_3$TiCl (286 mg, 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 3 h at 10°. After dilution with CH_2Cl_2, solid $Na_2CO_3 \cdot 10\ H_2O$ (excess) was added and the mixture stirred 15 min at r.t. Filtration through *Celite*, evaporation and treatment with KF according to the *General Procedure* followed by FC (Et_2O/hexane 1:40) gave **3a** (130 mg (87%); *trans*/*cis* 10:1).

c) *MAD Effect:* To a soln. of 2,6-di(*tert*-butyl)-4-methylphenol (485 mg, 2.2 mmol) in dry CH_2Cl_2 (1.1 ml) was added at r.t. 2M Me_3Al (0.55 ml, 1.1 mmol) in heptane. CH_4 Gas evolved immediately. After stirring at r.t. for 1 h, a soln. of **1a** (274 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, the mixture stirred for 15 min and extracted with CH_2Cl_2, and the extraxt dried ($MgSO_4$) and evaporated. Treatment with KF according to the *General Procedure* and FC (Et_2O/hexane 1:40) gave **3a** (111 mg (75%); *trans*/*cis* 5.6:1). IR (film): 3040, 2928, 2820, 1915, 1732, 1589. ^{1}H-NMR: 7.5–7.2 (*m*, 5 arom. H); 4.86 (*d*, *J* = 4, H–C(1)); 3.46 (*s*, MeO); 3.13 (*dd*, *J* = 8, 16, 1 H–C(3)); 2.84 (*dd*, *J* = 6, 16, 1 H–C(3)); 2.3 (*m*, *J* = 2.1, 4, 6, 8, H–C(2), *cis*); 2.12 (*m*, *J* = 2, 4, 6, 8, H–C(2), *trans*). ^{13}C-NMR: 143.90 (*s*); 142.59 (*s*); 128.25 (*d*); 126.14 (*d*); 124.97 (*d*); 124.80 (*d*); 84.46 (*d*); 55.85 (*q*); 31.5 (*t*, *J*(C,D) = 20); 29.97 (*t*). EI-MS: 150 (4), 149 (37, M^+), 148 (37), 134 (7), 119 (19), 118 (100), 117 (26), 116 (57), 92 (15), 78 (16), 77 (15), 63 (18). Anal. calc. for $C_{10}H_{11}DO$ (149.09): C 80.50, H 8.76; found: C 80.48, H 8.58.

cis- *and* trans-*1-(* tert-*Butoxyl)(2-*$^2H_1$*)indan* (**3b**). From **1b** (316 mg, 1 mmol) in CH_2Cl_2 (2.5 ml) according to the *General Procedure*. FC (Et_2O/hexane 1:40) gave **3b** (160 mg (84%); *trans*/*cis* 7:1). IR (film): 3026, 2972, 2931, 1944, 1832, 1606. ^{1}H-NMR: 7.35–7.15 (*m*, 4 arom. H); 5.07 (*d*, *J* = 6.5, H–C(1)); 2.98 (*dd*, *J* = 9, 16, 1 H–C(3)); 2.75 (*dd*, *J* = 8.5, 16, 1 H–C(3)); 1.91 (*m*, *J* = 2, 6.5, 8.5, 9, H–C(2)); 1.35 (*s*, *t*-Bu). ^{13}C-NMR: 144.98 (*s*); 142.58 (*s*); 127.59 (*d*); 126.46 (*d*); 124.60 (*d*); 75.94 (*d*); 73.54 (*s*); 35.91 (*t*, *J*(C,D) = 20); 29.90 (*t*); 28.88 (*q*). EI-MS: 192 (3), 191 (21, M^+), 176 (10), 135 (43), 134 (100), 119 (19), 18 (99), 117 (30), 116 (58), 106 (21), 92 (20), 91 (17), 78 (12). Anal. calc. for $C_{13}H_{17}DO$ (191.13): C 81.65, H 9.97; found: C 81.73, H 9.85.

cis- *and* trans-*(2-*$^2H_1$*)Indan-1-ol* (**3c**). *a*) From **1d** (498 mg, 1 mmol) in CH_2Cl_2 (2.5 ml) according to the *General Procedure* (3 h of irradiation), without KF treatment. The residue obtained after evaporation was dissolved in THF (4 ml), treated with 1M Bu_4NF in THF (5.3 ml, 5.3 mmol), and heated 4 d under reflux. The mixture was extracted with CH_2Cl_2, washed with H_2O, dried ($MgSO_4$), and evaporated. FC (AcOEt/hexane 1:9) gave **3c** (108 mg (80%); *trans*/*cis* 8.3:1). White solid.

b) From **1c** (260 mg, 1 mmol) in $CHCl_2$ (3 ml) according to the *General Procedure* (4 h of irradiation). FC (AcOEt/hexane 1:9) gave **3c** (120 mg (89%); *trans*/*cis* 5:1). White solid.

c) To a soln. of MAD (1.1 mmol) in CH_2Cl (1.1 ml), prepared according to the procedure for **3a**, was added a soln. of **1c** (260 mg, 1 mmol) in CH_2Cl_2 (1.5 ml). CH_4 Gas evolved immediately. After stirring for 1 h at r.t., Bu_3SnD (438 mg, 1.5 mmol) and AIBN were added. The mixture was irradiated at 10° overnight and then diluted with

$CHCl_2$ (15 ml). After addition of 1N HCl (3 ml) and stirring for 15 min, the mixture was extracted (CH_2Cl_2), the extract dried ($MgSO_4$) and evaporated, and the residue treated with KF according to *General Procedure*. FC (AcOEt/hexane 1:9) gave **3c** (116 mg (86%); *trans/cis* 100:1). IR (KBr): 3327, 3246, 2953, 2912, 2851, 1966, 1927, 1813, 1630. ^{1}H-NMR: 7.5–7.2 (*m*, 4 arom. H); 5.21 (*dd*, J = 5, 6, H–C(1)); 3.05 (*dd*, J = 8, 16, 1 H–C(3)); 2.8 (*dd*, J = 7, 16, 1 H–C(3)); 2.35 (*d*, J = 6, OH); 1.93 (*m*, J = 2, 5, 7, 8, H–C(2)). ^{2}H-NMR: 2.5 (br. *s*, *trans*); 1.9 (br. *s*, *cis*). ^{13}C-NMR: 145.01 (*s*); 143.15 (*s*); 128.08 (*d*); 126.51 (*d*); 124.69 (*d*); 124.11 (*d*); 76.10 (*d*); 35.38 (*t*, J(C,D) = 20); 29.58 (*t*). EI-MS: 136 (9), 135 (85, M^+), 134 (100), 118 (29), 117 (20), 116 (40), 106 (33), 105 (20), 92 (20), 91 (26), 89 (11), 80 (14), 79 (14), 78 (24), 77 (28). Anal. calc. for C_9H_9DO (135.07): C 80.01, H 8.14; found C 80.14, H 8.16.

Methyl cis- *and* trans-*2-[(3-Hydroxyindan-2-yl)methyl]propenoate* (**4**). *a*) A soln. of **1c** (200 mg, 0.76 mmol), methyl 2-[(tributylstannyl)methyl]propenoate (600 mg, 1.54 mmol), and AIBN (10 mg) in CH_2Cl_2 (2.3 ml) was irradiated for 5 h at 10°. After evaporation, the residue was dissolved in MeOH (30 ml) and KF (excess) added. The mixture was stirred overnight, and then evaporated, the residue dissolved in CH_2Cl_2, the soln. filtered and evaporated. FC (AcOEt/hexane 1:9) gave **4** (120 mg (67%); *trans/cis* 1.2:1). Separation of the diastereoisomers by FC (AcOEt/hexane 1:9) gave *cis*-**4** (54 mg, 30%) and *trans*-**4** (65 mg, 36%).

b) To a soln. of MAD (1.1 mmol) in CH_2Cl_2 (1.1 ml), prepared according to the procedure for **3a**, was added a soln. of **1c** (260 mg, 1 mmol) in CH_2Cl_2 (1.5 ml). CH_4 Gas evolved immediately. After stirring for 1 h at r.t., methyl 2-[(tributylstannyl)methyl]propenoate (1.56 g, 4 mmol) and AIBN (10 mg) were added. The mixture was irradiated at 10° overnight and then diluted with CH_2Cl_2 (15 ml). After addition of 1N HCl (3 ml) and stirring for 15 min, the mixture was poured into H_2O and extracted (CH_2Cl_2), the extract dried ($MgSO_4$) and evaporated, and the residue submitted to KF treatment according to the *General Procedure*. FC (AcOEt/hexane 1:9) gave **4** (160 mg (69%); *trans/cis* 100:1).

trans-**4**: M.p. 75°. ^{1}H-NMR: 7.41–7.19 (*m*, 4 arom. H); 6.25 (*d*, J = 1, 1 H, C=CH_2); 5.69 (*d*, J = 1, 1 H, C=CH_2); 4.85 (*d*, J = 6, H–C(1′)); 3.77 (*s*, MeO); 3.09 (*dd*, J = 6, 15, 1 H–C(3′)); 2.79 (*dd*, J = 5, 15, 1 H–C(3′)); 2.71 (br. *s*, OH); 2.57–2.44 (*m*, H–C(2′), CH_2C=CH_2). ^{13}C-NMR: 167.70 (*s*); 144.56 (*s*); 141.32 (*s*); 139.31 (*s*); 128.03 (*d*); 126.74 (*t*); 126.69 (*d*); 124.61 (*d*); 123.92 (*d*); 80.79 (*q*); 51.82 (*d*); 49.31 (*d*); 35.66 (*t*); 35.48 (*t*).

cis-**4**: M.p. 52°. ^{1}H-NMR: 7.41–7.19 (*m*, 4 arom. H); 6.25 (*d*, J = 1, 1 H, C=CH_2); 5.73 (*d*, J = 1, 1 H, C=CH_2); 4.99 (*d*, J = 5, H–C(1′)); 3.77 (*s*, MeO); 2.91–2.73 (*m*, 2 H–C(3′), OH); 2.62–2.4 (*m*, H–C(2′), CH_2C=CH_2). ^{13}C-NMR: 168.33 (*s*); 144.72 (*s*); 143.22 (*s*); 139.65 (*s*); 128.59 (*d*); 126.73 (*d*); 126.57 (*t*);124.84 (*d*); 75.85 (*q*); 51.97 (*d*); 45.16 (*d*); 35.96 (*t*); 31.16 (*t*).

cis- and *trans*-**4**: IR (KBr): 3339, 3027, 2949, 2851, 1998, 1906, 1726, 1630, 1441. CI-MS (CH_4): 231 (1), 215 (11), 214 (100), 201 (12), 183 (54), 155 (6). Anal. calc. for $C_{14}H_{16}O_3$ (232.10): C 72.39, H 6.94; found: C 72.32, H 7.06.

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