Chiral Benzyllithium Compounds: High Configurative Stability of (*R*)- and (*S*)-1-Lithioindan-1-yl *N*,*N*-Diisopropylcarbamate and Unexpected Stereochemical Course of the Substitution Reactions[1,2]

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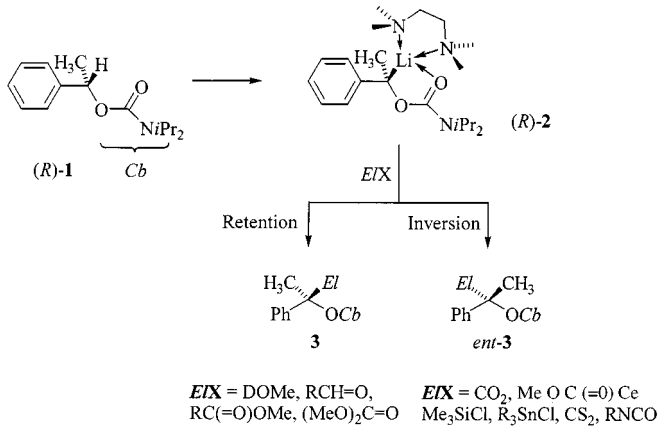
The title compound, **6**, was generated by stereospecific deprotonation of the optically active carbamate **5** with *sec*-butyllithium/TMEDA and proved to be configuratively completely stable in ethereal solution at –78 °C. Compared with open-chain analogs, the trend for stereoretentive substitution is enhanced. Even the reaction with trialkyltin chlorides leads to partial racemization due to competing front face attack. Semiempirical calculations point to an increased degree of pyramidalization and to a higher barrier for planarization in the cyclic benzyllithium compound, both of which disfavor the rear face attack.

Introduction

Enantioenriched organolithium compounds with a stereogenic center at the metal-bearing carbon atom have become important tools in stereoselective synthesis.[3] In 1990 we reported on the first enantioenriched and configuratively stable benzyllithium derivative, which was generated by deprotonation of the optically active carbamate ester **1**.[4] Further examples of configuratively stable α-oxy-,[1][5] α-amino-,[6] and α-thio-substituted[7] benzyllithium compounds have been discovered by Hammerschmidt, Beak, and our research group.

Whereas nonmesomerically stabilized, sp^3-hybridized organolithium compounds react with most electrophiles with strict stereoretention, the stereochemical course of the substitution at the benzylic position is largely dependent on the electrophile and, in some degree, also on the reaction conditions. It was found that the lithium compound (*R*)-**2** [as well as (*S*)-**2**] in ethereal solution does not racemize[4] (Scheme 1) when kept below −70 °C; it is trapped by many electrophiles with a high degree of inversion of configuration. A few types of electrophiles − proton acids, aliphatic aldehydes, ketones, methyl carboxylates, and also dimethyl carbonate − lead to retention of configuration.[4] We concluded from these results that an electrophile usually prefers attacking from the less shielded rear face. Only when a strong complexation of the lithium cation by the electrophilic reagent precedes does the attack occur at the front face of the carbanionic center.[4b]



Scheme 1. Reaction of lithiated carbamate (*R*)-**2** with electrophiles

Results

(*R*)- and (*S*)-1-indanol (**4**, 96 to 98% *ee*) were prepared by enzymatic kinetic resolution of the corresponding racemic acetate,[8] and converted into the carbamates (*R*)- and (*S*)-**5**, respectively (Scheme 2).[4b] Compound (*R*)-**5**, as a 0.5 M solution in diethyl ether in the presence of 1.0 equiv. of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) at −78 °C, was smoothly deprotonated by the addition of 1.1 equiv. of a 1.2−1.4 M *sec*-butyllithium solution in cyclohexane/isopentane. The electrophile (1.1 equiv.) was added after 5 min of stirring at −78 °C to the deeply yellow solution of (*R*)-**6**. The reaction mixture was kept for 30 min at this temperature before it was allowed to warm to room temperature and, subsequently, acidic aqueous workup was performed.[9] The results are collected in Table 1.

The enantiomeric excesses could be determined (with the exception of stannane *ent*-**7g**) by ^{1}H-NMR analysis in the

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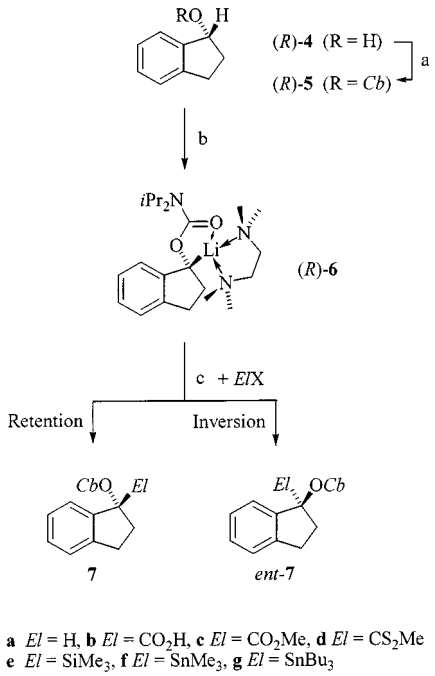


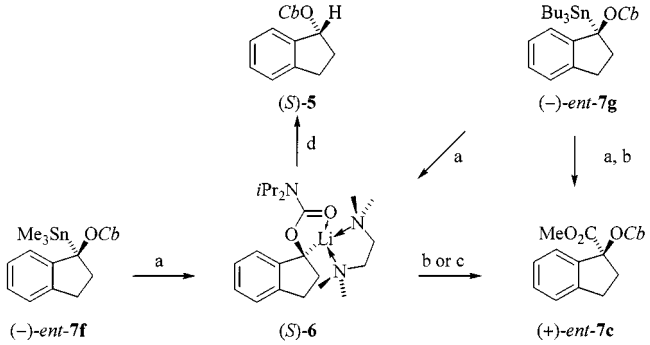
a *El* = H, **b** *El* = CO_2H, **c** *El* = CO_2Me, **d** *El* = CS_2Me
e *El* = $SiMe_3$, **f** *El* = $SnMe_3$, **g** *El* = $SnBu_3$

Scheme 2. a) $(iPr)_2NC(=O)Cl$, dry pyridine, 65°C, 20 h; b) *s*BuLi, TMEDA, −78°C, 5 min; c) *El*X, −78°C, 30 min, then → r.t.; for **7b**: CH_2N_2; for **7d**: MeI

presence of the optically active shift reagents $Pr(hfc)_3$ or $Eu(hfc)_3$.

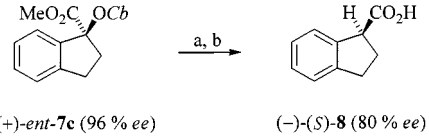
Quenching the reaction mixture with methanol (Entry 1) yields the starting material **7a** (= **5**) without loss of enantiomeric enrichment, providing good evidence that both reaction steps − deprotonation and protonation − proceed with strict stereoretention. Surprisingly, the intermediate (*R*)-**6** yielded the identical methyl ester (−)-**7c** with the three different carboxylation agents; dimethyl carbonate, methyl chloroformate, and carbon dioxide, (after *O*-methylation; for configurational assignment, see below). In another experiment (according to Entry 2) dimethyl carbonate was added after the solution of (*R*)-**6** had been kept for 13 h at −78°C. Although the yield decreased to 42%, the *e.r.* remained constant within the experimental error (approx. 1%). The reaction with trialkyltin chlorides[10] (Entries 7 and 8) to form the stannanes (−)-(*S*)-**7e** and (−)-(*S*)-**7f** proceeds with the usual stereoinversion,[4b] although with decreased stereospecificity.

The correct stereochemical assignment is supported by the following experiments (Scheme 3) and by the results obtained by Hammerschmidt et al.[1] The enantiomeric intermediate (*S*)-**6** is produced by lithiodestannylation of (−)-*ent*-**7f** and (−)-*ent*-**7g** (Scheme 3), and is trapped by protonation to give (*S*)-**5** and also by methoxycarboxylation to form ester (+)-*ent*-**7c**.



Scheme 3. a) *s*BuLi, TMEDA, Et_2O, −78°C; b) dimethyl carbamate, −78°C; c) *i*. CO_2, *ii*. CH_2N_2; d) MeOH; for *ee* values see text

The Pd-catalyzed hydrogenolysis of chiral benzylic esters is known to proceed with (incomplete) inversion of configuration.[11] The carbamate ester (+)-*ent*-**7c** afforded the known[12] (*S*)-1-indanecarboxylic acid (−)-(*S*)-**8** after *O*-demethylation (Scheme 4), providing further evidence for the correct assignment.



Scheme 4. a) H_2, Pd/C (10%), 21 h, 87%, *e.r.* = 90:10 (80% *ee*); b) Me_3SiCl, NaI, MeCN, reflux, 25 h

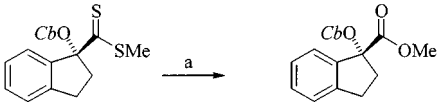
The reaction of (*S*)-**5**, via (*S*)-**6**, with carbon disulfide takes the opposite stereochemical course with complete stereospecificity: The methyl dithiocarboxylate (−)-(*R*)-**7d** (98% *ee*), isolated after *S*-methylation of the primarily formed intermediate lithium salt (Entry 5), was hydro-

Table 1. Synthesis of compounds **7** from (*R*)- or (*S*)-**5**

Entry	Starting materials **5** and *El*-X	Main product	El	Yield [%]	*e.r.* **7**/*ent*-**7** [% *ee*][a]	$[\alpha]_D^{20}$[b]	Stereochem. course and configuration
1	(*R*)-**5**[c], *H*-OMe	**7a** = (*R*)-**5**	H	92	≥ 97:3 [> 94]	−7.0	retention, (*R*)
2	(*R*)-**5**, *MeOC(=O)*OMe	**7c**	CO_2Me	85	≥ 97:3 [> 94]	−133	retention, (*R*)
3	(*R*)-**5**, *MeOC(=O)*Cl	**7c**	CO_2Me	72	97:3 [94]		retention, (*R*)
4	(*R*)-**5**, *O=C=*O	**7c**	CO_2Me[d]	82	≥ 97:3 [> 94]		retention, (*R*)
5	(*S*)-**5**[e], *S=C=*S	**7d**	CS_2Me[f]	80	99:1 [98]	−165	inversion, (*R*)
6	(*R*)-**5**, Me_3SiCl	**7e**	$SiMe_3$	46	96:4 [92]	−8.2	retention, (*S*)
7	(*R*)-**5**, Me_3SnCl	*ent*-**7f**	$SnMe_3$	74	25:75 [50]	−13.8	inversion, (*R*)
8	(*R*)-**5**, Bu_3SnCl	*ent*-**7g**	$SnBu_3$	81	< 10:> 90[g] [80]	−19.5	inversion, (*R*)

[a] Determined by ^{1}H-NMR spectroscopy in the presence of chiral lanthanide shift reagents, see Experimental Section. − [b] *c* = 1 − 1.2 ($CHCl_3$). − [c] *e.r.* ≥ 97:3 (94% *ee*). − [d] The crude acid **7b** was methylated by means of diazomethane. − [e] *e.r.* = 99:1 (98% *ee*). − [f] The crude lithium dithiocarboxylate was methylated by means of methyl iodide. − [g] The *e.r.* could not be determined directly. It was concluded by the sequence lithiodestannylation − methoxycarboxylation, see text.

lytically desulfurized and converted into *O*-methyl ester (−)-(*R*)-**7c** (Scheme 5).



(−)-**7d** (98 % *ee*) (−)-**7c** (98 % *ee*)

Scheme 5. a) *i*. KOH, MeOH, reflux; *ii*. CH_2N_2/Et_2O, 74%

No direct evidence for the configuration of the silane (−)-**7e** (Entry 6) could be obtained experimentally. The assigned (*S*) configuration is based on the trend for stereoretention observed in ion-pairs **6**. Since stannylation takes place with reduced antarafacial stereospecificity (50−80% *ee*), it is very unlikely that an even higher preference for inversion (92% *ee*) will occur in trimethylsilylation.

Removal of the *N*,*N*-diisopropylcarbamoyl group in tertiary benzylic esters is difficult to achieve.[13][14] We recently introduced the *N*-[2-(*tert*-butyldiphenylsiloxy)ethyl]-*N*-isopropylcarbamoyl (*Cbse*) group, which is cleavable under mild conditions and was also successfully applied to the synthesis of enantioenriched indanols.[4c]

Theoretical Investigations and Discussion

The preceding experiments demonstrate that the indanyllithium **6** has a lower tendency to undergo attack by an electrophile from the rear face than the 1-phenylethyl derivative **1**. X-ray crystal structure analyses of a 1-carbamoyloxy-substituted allyllithium derivative[15] and benzyllithium complexes[16] reveal a pyramidalized lithium-bearing carbon atom. The deviation from planarity is a compromise between maximal delocalization of the electron pair with the attached π-system and charge neutralization by the cation. The larger orbital lobe is directed towards the lithium cation. Two pathways are possible for an approaching electrophile. In the first, the electrophile enters from the front face and shares the orbital lobe with lithium before replacing it; this pathway is greatly facilitated by the ability to form a complex with lithium and will result in stereoretention. The second possibility involves attack from the rear face in which the electrophile joins with the less shielded lobe of smaller electron density, but in order to finally achieve stereoinversion, the pyramidalized carbon moiety needs to fold back via a planar transition state. The difference in Free Energy of Activation for both pathways is expected to be influenced by structural features in the carbanion, the ligands at lithium, the solvent, and the electrophilic reagent.

The question remains as to why the reaction of the indanyllithium **6** with methyl chloroformate (Table 1, Entry 3) proceeds with essentially complete retention whereas inversion (corrected *e.r.* 94:6) occurs in the open-chain system **2**. Aside from the structural features, the remaining parameters are kept identical in both experiments. We suspect that, with a given electrophilic reagent, the ease with which the planar arrangement can be achieved within the carb-

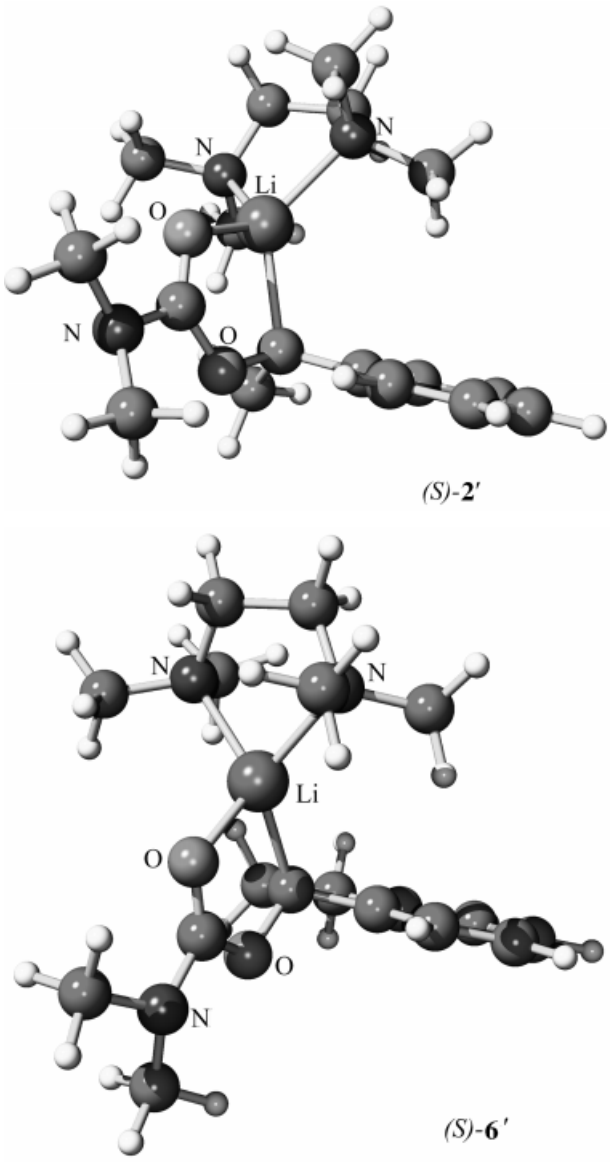


Figure 1. Optimized structures of the lithiated compounds; top: (*S*)-**2′**, bottom: (*S*)-**6′**

anionic part mainly contributes to the readiness to undergo invertive substitution.

Therefore, we performed semiempirical calculations, using MOPAC93[17] with the PM3 parameters, on the slightly simplified lithium compounds **2′** and **6′**, replacing $N(iPr)_2$ by $N(Me)_2$.[18] We started with geometry optimizations to obtain the ground-state conformations of **2′** and **6′** (lowest enthalpy of formation), beginning the optimizations from different starting geometries. For these favored conformations of **2′** and **6′** (Figure 1), the sum of the three dihedral angles at the lithium-bearing carbon atom was found to be 333.1° for **2′** and 323.8° for **6′**![19] It is clear that the angles at the lithium-bearing carbon atom in the open-chain compound **2′** are enlarged compared to a purely tetrahedral structure, while the sum of angles in the fixed and much more rigid indan compound **6′** is even smaller than 327°. Finally, structures **2′** and **6′** were forced to oc-

Table 2. Selected physical data of the new compounds

Compound	mp [°C]	R_f[a]	IR (KBr/film); ν [cm^{-1}]	^{1}H NMR (300 MHz, $CDCl_3$)[b] δ	^{13}C NMR (75 MHz, $CDCl_3$)[c] δ				
					C-1	C-2	C-3	OCON	*El* in Scheme 2
7c	101	0.43	1740 (C=O), 1695 (OCON), 1045 (C−O)	2.20−2.30 (m, 2-H), 2.92−3.12 (m, 2-H′, 3-H), 3.17−3.26 (m, 3-H′), 3.62 (s, 1-CO_2CH_3)	88.33	37.24	30.75	154.77	52.24 (CO_2CH_3), 171.60 (1-CO_2)
7d	98	0.5	1675 (OCON), 1305 (C=S)	2.50−2.60 (m, 2-H), 2.56 (s, 1-CS_2CH_3), 3.02−3.12 (m, 2-H′), 3.23−3.67 (m, 3-H), 3.59−3.67 (m, 3-H′)	99.31	42.33	31.95	153.84	19.34 (1-CS_2CH_3), 239.02 (1-CS_2CH_3)
7e	Yellow oil	0.62	1670 (OCON), 1045 (C−O), 835 (Si−C)	0.00 [s, $Si(CH_3)_3$], 2.28−2.38 (m, 2-H), 2.67−2.86 (m, 2-H′, 3-H), 2.99−3.07 (m, 3-H′)	87.59	38.59	32.55	157.37	0.00 [$Si(CH_3)_3$]
ent-**7f**	65	0.67	1660 (OCON), 1310 (C−O), 755 (Sn−C)	−0.09 [s, $Sn(CH_3)_3$], 2.04−2.15 (m, 2-H), 2.54−2.65 (m, 2-H′), 2.79−2.86 (m, 3-H), 2.94−3.02 (m, 3-H′)	87.43	39.45	30.15	157.02	−7.46 [$Sn(CH_3)_3$]
ent-**7g**	Colorless oil	0.68	1660 (OCON), 1325 (C−O), 750 (Sn−C)	0.55−0.91 and 1.11−1.36 (m, SnC_4H_9), 1.94−2.05 (m, 2-H), 2.57−2.66 (m, 2-H′), 2.79−2.98 (m, 3-H, 3-H′)	88.52	39.79	19.92	156.48	11.52 (Sn-C-4′), 13.01 (Sn-C-3′), 27.59 (Sn-C-2′), 28.97 (Sn-C-1′)

[a] All R_f values are measured in Et_2O/pentane (1:1, v:v). − [b] NMR data of the *Cb* group and the aromatic rings are omitted.

cupy a planar arrangement bearing the lithium cation above the plane in order to simulate one decisive feature in the reaction pathway for an S_E substitution with inversion.[20][21] An energy of 10.0 kcal/mol is required to planarize **2′** and 14.1 kcal/mol for the indan skeleton **6′**.[22] It is surprising that this very rough assessment for $\Delta\Delta H^{\neq}$ of 4.1 kcal/mol is in close agreement with the experimentally observed difference of 3.1 kcal/mol[23] (at −78 °C).[24]

Conclusion

The lithioindanyl carbamate **6** is configurationally completely stable in ethereal solution below −70 °C. Usually, electrophilic reagents attack the front site of the ion pair to result in stereoretention. Only very soft electrophiles such as carbon disulfide or trialkyltin chlorides cause stereoinversion. Quantum-chemical semiempirical calculations predict the pronounced pyramidalization, coupled with a higher energy barrier for planarization, to be the origin for these anomalous properties of (*R*)- and (*S*)-**6**

Experimental Section

General: All organometallic reactions were performed under Ar with exclusion of air and moisture. Toluene was dried with Na before use. LC separations were carried out at 0.5−1.5 bar on silica gel 40−63 μm (Merck, Darmstadt). − IR: Perkin−Elmer 298. − Optical rotations: Perkin−Elmer polarimeter 241. − NMR: Bruker WM 300 (300 MHz and 75.5 MHz for ^{1}H and ^{13}C NMR, respectively). For ^{1}H NMR, $CDCl_3$ was used as solvent, TMS as internal standard; for ^{13}C NMR, $CDCl_3$ δ_C = 77.0. The ^{1}H-NMR shift experiments were performed by addition of (+)-Eu(hfc)$_3$ or (+)-Pr(hfc)$_3$ to a solution of the enantioenriched products in $CDCl_3$ (0.8 mL). − Combustion analyses: Perkin−Elmer 240, Institute of Organic Chemistry, University of Münster.

(−)-(*R*)-1-Indanol [(*R*)-4]: $[\alpha]_D^{20}$ = −28.5 (*c* = 1.09, $CHCl_3$),[25] 98% *ee*, was prepared by kinetic enzymatic resolution of the racemic acetate, according to Laumen and Schneider.[8][26]

(−)-(*S*)-1-Indanol [(*S*)-4]: $[\alpha]_D^{20}$ = +31.5 (*c* = 1.03, $CHCl_3$),[24] 98% *ee*, was obtained by alkaline hydrolysis of the remaining (*S*)-acetate.

(*R*)-1-Indanyl *N*,*N*-Diisopropylcarbamate [(*R*)-5]: (*R*)-1-Indanol (98% *ee*, 3.03 g, 22.5 mmol), *N*,*N*-diisopropylcarbamoyl chloride (3.67 g, 22.4 mmol) and dry pyridine (2.16 mL, 32.4 mmol) were kept for 20 h at 65 °C with exclusion of moisture. The reaction mixture was cooled to room temperature and poured into a mixture of ice (15 g), 11 M aq. HCl (6 mL), and Et_2O (30 mL). The aqueous phase was extracted with Et_2O (3 times, 50 mL each), and the combined ethereal solutions were washed with saturated aqueous $NaHCO_3$ and NaCl. After drying ($MgSO_4$) and evaporation of the solvent in vacuum, the residue was purified by chromatography with Et_2O/pentane (1:4 → 1:2) to yield (*R*)-**5** (4.93 g, 84%) as a pale yellow oil.

Deprotonation and Substitution of (*R*)-5 or (*S*)-5; Compounds 7 and *ent*-7: To a solution of (*R*)-**5** or (*S*)-**5** (261 mg, 1.00 mmol) and TMEDA (117 mg, 1.00 mmol) in dry Et_2O (2.0 mL), stirred at −78 °C, was added a 1.2−1.4 M solution of *sec*-butyllithium (1.10 mmol) in cyclohexane/isopentane with a syringe within 5 min. Stirring was continued for 5 min and a solution of the electrophile (1.10 mmol) in Et_2O (1 mL) was added to the deep yellow solution. After 30 min of stirring below −70 °C, the reaction mixture was allowed to warm to room temperature. Et_2O (10 mL) and 2 N aqueous HCl (2.0 mL) were added, the aqueous phase extracted with Et_2O (3 times, 20 mL each) and the combined extracts washed with saturated aqueous $NaHCO_3$ solution and dried ($MgSO_4$). After evaporation of the solvents in vacuum, the residue was purified by flash chromatography with Et_2O/pentane (1:10 → 1:2). − In the case of the crude carboxylic acid **7b** (obtained by introducing excess dry gaseous CO_2 by syringe), $NaHCO_3$ extraction was omitted and crude **7b** was treated with an excess of diazomethane. − For the synthesis of the methyl dithiocarboxylate **7d**, CS_2 was used as the electrophile and methyl iodide (213 mg, 1.5 mmol) was added to

Table 3: Elemental analyses − from all new compounds satisfactory C,H,N analyses were obtained

	Molecular mass	Calculated			Found		
		C	H	N	C	H	N
7c	$C_{18}H_{25}NO_4$ (319.40)	67.69	7.89	4.38	67.90	7.84	4.42
7d	$C_{18}H_{25}NO_2S_2$(351.53)	61.50	7.17	3.98	61.69	6.96	3.96
7e	$C_{19}H_{31}NO_2Si$ (333.54)	68.42	9.37	4.20	68.26	9.10	4.68
ent-**7f**	$C_{19}H_{31}NO_2Sn$ (424.17)	53.80	7.37	3.30	53.78	7.59	3.23
ent-**7g**	$C_{28}H_{49}NO_2Sn$ (550.41)	61.10	8.97	2.54	61.13	8.99	2.45

the reaction mixture before warming was allowed. − ^{1}H-NMR shift experiments were performed with 10−30% of tris[(3-heptafluoropropylhydroxymethylene)-(+)-camphorato]praeseodymium(III) [Pr(hfc)$_3$] or tris[(3-heptafluoropropylhydroxymethylene)-(+)-camphorato]europium(III) [Eu(hfc)$_3$] and a 0.25 M $CDCl_3$ solution of **7** at 300 MHz. The recorded signals and the corresponding enantiomers, which caused a shift to the lower field, were: (*S*)-**7c**, Pr(hfc)$_3$, OCH_3; (*R*)-**7d**, Eu(hfc)$_3$, SCH_3; (*R*)-**7c**, Eu(hfc)$_3$, $Si(CH_3)_3$; (*R*)-**7f**, Pr(hfc)$_3$, $Sn(CH_3)_3$.

Lithiodestannylation and Methoxycarboxylation of *ent*-7f and *ent*-7g; Synthesis of *ent*-7c: Stannane *ent*-**7f** (50% *ee*, 213 mg, 0.50 mmol) was subjected to the conditions of the deprotonation reaction (see above). After addition of dimethyl carbonate (50 mg, 0.55 mmol) and the usual workup, *ent*-**7c** {111 mg, 70%, $[\alpha]_D^{20}$ = +53.4 (*c* = 1.37, $CHCl_3$), 44% *ee*} was isolated. In a similar experiment, involving carboxylation with CO_2 and methylation by diazomethane, 111 mg of *ent*-**7c** (70%) with $[\alpha]_D^{20}$ = +55.2 (*c* = 1.21, $CHCl_3$), 49% *ee*, was obtained. − Similarly, *ent*-**7g** (275 mg, 0.50 mmol), $[\alpha]_D^{20}$ = −19.5 (*c* = 1.02, CH_2Cl_2), and dimethyl carbonate afforded *ent*-**7c** {10 mg, 6%, $[\alpha]_D^{20}$ = +98.6 (*c* = 0.91, $CHCl_3$), 80% *ee*}.

Conversion of Dithioester *ent*-7d to *ent*-7c: A mixture of compound **7d** (98% *ee*, 176 mg, 0.50 mmol) and KOH (85 mg, 1.50 mmol) was heated under reflux in MeOH (3 mL) under exclusion of air for 5 h. After cooling the mixture to room temperature, 2 N HCl (10 mL) was added. To the Et_2O extract (3 times, 10 mL each) was added an ethereal solution of diazomethane until the reaction mixture remained yellow. SiO_2 (100 mg) was added to destroy excess diazomethane, the solution dried ($MgSO_4$), and the solvent evaporated. Flash chromatography (Et_2O/pentane, 1:4) afforded the methyl carboxylate **7c** (119 mg, 74%) with $[\alpha]_D^{20}$ = −136.9 (*c* = 1.08, $CDCl_3$), (98% *ee*).

(*S*)-1-Indanecarboxylic Acid (*S*)-8 from *ent*-7c: A mixture of compound *ent*-**7c** (> 95% *ee*, 712 mg, 2.23 mmol) in MeOH (6 mL) and Pd on charcoal (10%, 94 mg) was stirred under H_2 for 21 h. The catalyst was carefully filtered off, washed with MeOH, and the combined MeOH solutions concentrated in vacuum. Flash chromatography (Et_2O/pentane, 1:4) afforded (+)-(*S*)-methyl 1-indancarboxylate (341 mg, 87%), $[\alpha]_D^{20}$ = +6.3 (*c* = 1.17, CH_2Cl_2). In a ^{1}H-NMR shift experiment (300 MHz, 12% Pr(hfc)$_3$, the OCH_3 signal of the major enantiomer shifted to lower field and 80% *ee* was determined. − To a stirred solution of a sample of the ester (240 mg, 1.65 mmol) was added NaI (742 mg, 4.95 mmol) in dry MeCN (4 mL) and Me_3SiCl (539 mg, 4.95 mmol) and the reaction mixture was heated under reflux for 25 h. Water (5 mL) was added at room temperature, followed by extraction with Et_2O (two times, 20 mL each). The combined organic fractions were washed with water (5 mL) and 10% aqueous $Na_2S_2O_3$ solution, and the carboxylic acid extracted with saturated aqueous $NaHCO_3$ (2 times, 10 mL each). The aqueous solution of the carboxylate was adjusted to pH = 1 by addition of 2 N HCl. The crystallized acid (*S*)-**8** (145 mg, 54%) was collected by filtration, $[\alpha]_D^{20}$ = −26.2 (*c* = 1.50, benzene); ref.[12] for (*R*)-**8**: $[\alpha]_D^{20}$ = +43.3 (*c* = 2.59, benzene).

Acknowledgments

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[23] The relative rate of stereoretentive substitution in **2** and **6** is taken as the internal standard. With a corrected ratio $S_{E,ret}/S_{E,inv}$ for the reaction with dimethyl chloroformate of 94:6[4b] for **2** and 0.5:99.5 for **6**, k_{rel} of approximately 3200 reflects the rate, the rear face attack is disfavored in **6** (compared to **2**) according to a $\Delta\Delta G^{\neq}$ of 3.1 kcal/mol calculated for −78°C.
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