Synthesis of Enantioenriched Tertiary Benzylic Alcohols via Stereospecific Lithiation of Secondary Benzyl Carbamates – Design of Dialkylcarbamates, Cleavable under Basic, Mild Conditions

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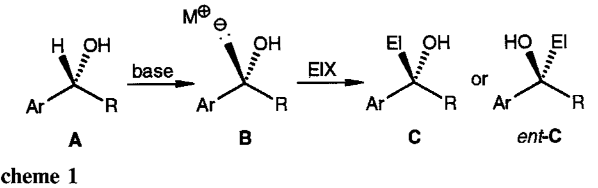
Dedicated to Professor H.J. Bestmann on the occasion of his 70th birthday

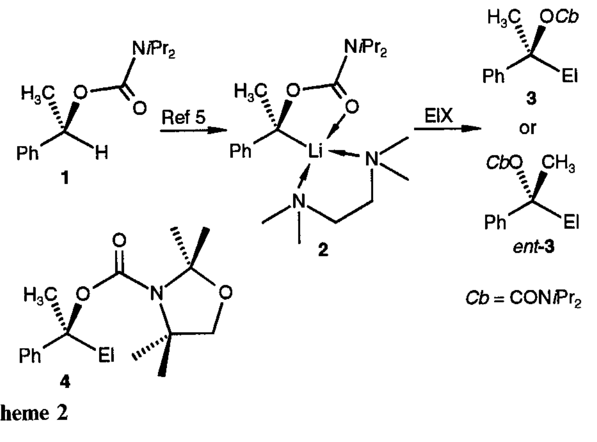
Enantiomerically enriched, secondary benzyl *N*-[2-(*tert*-butyldiphenylsilyloxy)ethyl]-*N*-isopropylcarbamates were prepared, lithiated, and stereospecifically substituted by several electrophiles. Deprotection under basic conditions furnished optically active tertiary benzylic alcohols and glycols or 2-hydroxy-2-arylalkanoic acid esters. In summary, the sequence achieves the stereospecific chain elongation of d^1-synthons, derived from secondary benzyl alcohols.

Enantioenriched secondary benzylic alcohols of type **A** are efficiently prepared by a number of methods, such as enzymatic kinetic resolution,[1,2] enantioselective reduction,[3] or asymmetric nucleophilic alkylation.[4] Optically active tertiary benzylic alcohols are less readily accessible. Under this aspect, a method, which converts **A** stereospecifically via a carbanionic intermediate **B** by electrophilic substitution to **C** (with overall retention of the configuration) or to its enantiomer *ent*-**C** (inversion), is desirable.



Scheme 1

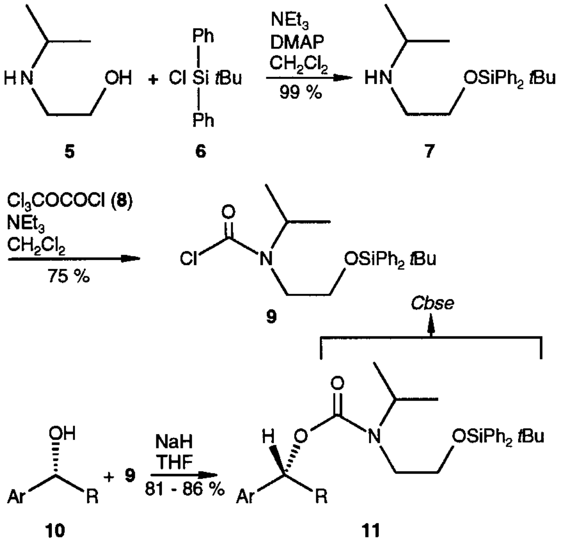
We recently reported[5,6] on the first and still only known strategy, which, in principle, achieves this transformation via the appropriate *N*,*N*-diisopropylcarbamate **1**. Deprotonation[7,8] leads to the chelate-stabilized lithium carbanion pair **2**, configurationally stable at −78 °C in ether or hydrocarbon solution.[9–12] The substitution of **2** proceeds either with retention or inversion to form the products **3** or *ent*-**3**, respectively, depending on the nature of the electrophile. However, the *N*,*N*-diisopropylcarbamoyl (*Cb*) group could not be removed without destruction of the tertiary alcohols. The same problem arises, when the acid-labile 2,2,4,4-tetramethyl-1,3-oxazolidine-3-carbonyl (*Cby*) derivatives **4** were applied in this situation.[13,14]

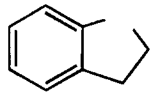


Cb = CONiPr$_2$

Scheme 2

For these reasons, we developed the *N*-[2-(*tert*-butyldiphenylsilyloxy)ethyl]-*N*-isopropylcarbamoyl (*Cbse*) group. It is perfectly stable under the strongly basic deprotonation conditions, but is removed smoothly by basic reagents attacking at the silyl group[15] (see below). 2-(Hydroxyethyl)isopropylamine (**5**) is converted to its TBDPS ether[16] **7**, followed by chlorocarbonylation[13] by means of diphosgene (**8**) to yield the carbamoyl chloride **9**. The carbamoylation of enantioenriched secondary benzyl alcohols **10a–c** (95–97% ee), prepared by enzymatic hydrolysis of the racemic acetates,[2] gives the appropriate carbamate esters with high yield.

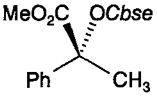
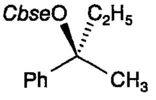
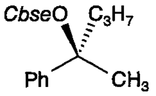
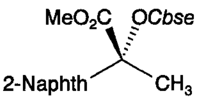
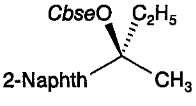
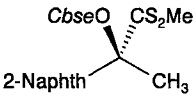
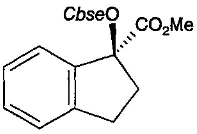
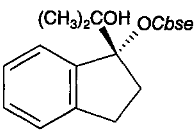


10, 11	Ar	R	Yield (%)	% *ee*
a	C_6H_5	CH_3	86	97
b	2-naphthyl	CH_3	82	96
c			81	95

Scheme 3

The deprotonation of **11a** and **11c** by *sec*-butyllithium/TMEDA in diethyl ether at −78 °C proceeds with the same ease as for the appropriate *N*,*N*-diisopropylcarbamates[5,6] and leads to carbanionic intermediates, which are configurationally stable under the reaction condi-

Table 1. Prepared Carbamates **12** and Some Physical Data

Product[a]	Educt (% ee)	ElX	Yield (%)	$[\alpha]_D^{20}$ (*c*, solvent)	Selected IR Data; ν (cm^{-1})	^1H NMR[c] ($CDCl_3$) [δ (ppm)]	^{13}C NMR[d] ($CDCl_3$) [δ (ppm)]
 **12aa**	**11a** (97)	$(MeO)_2CO$	74	− 6.5 (1.0, CH_2Cl_2)	1740, 1690, 1100, 815	1.90–1.96 (m, 3-H_3), 3.63 (s, $COOCH_3$), 7.29–7.65 (m, Ar-H)	25.11 (C-3), 52.37 ($COOCH_3$), 81.65 (C-2), 140.76 (Ar-C-1), 171.96 (C-1)
ent-**12aa**	**11a**	$CO_2(CH_2N_2)$[b]	90	+ 5.4 (2.0			
 *ent*-**12ab**	**11a** (97)	C_2H_5Br	81	− 9.4 (1.2, CH_2Cl_2)	1685, 1100, 815	0.72–0.91 (m, 3-H_3), 1.76–1.85 (m, 1-CH_3), 1.93–2.04 (m, 2-H_2), 7.17–7.73 (m, Ar-H)	8.26 (C-3), 25.07 (1-CH_3), 35.45 (C-2), 83.64 (C-1), 145.81 (Ar-C-1)
ent-**12ab**	**11a**	C_2H_5I	68	− 15.5 (1.1)			
 *ent*-**12ac**	**11a**	*n*-C_3H_7I	89	− 18.4 (1.2, CH_2Cl_2)	1680, 1100, 810	0.81–0.90 (m, 4-H_3), 1.14–1.26 (m, 3-H_2), 1.77–1.82 (m, 1-CH_3), 1.87–1.94 (m, 2-H_2), 7.16–7.72 (m, Ar-H)	14.25 (C-4), 17.15 (C-3), 25.48 (1-CH_3), 45.05 (C-2), 83.34 (C-1), 146.08 (Ar-C-1)
 **12ba**	**12a** (96)	$(MeO)_2CO$	66	+ 2.1 (1.2, MeOH)	1730, 1680, 1095, 810	1.99–2.06 (m, 3-H_3), 3.64 (s, $COOCH_3$), 7.28–7.93 (m, Ar-H)	25.00 (C-3), 52.43 ($COOCH_3$), 81.75 (C-2), 138.03 (Ar-C-2), 171.96 (C-1)
ent-**12ba**	**12a**	$CO_2(CH_2N_2)$[b]	65	− 0.3 (1.2)			
 *ent*-**12bb**	**12a**	C_2H_5I	67	− 19.6 (1.2, MeOH)	1675, 1100, 810	0.72 – 0.82 (m, 3-H_3), 1.85–1.92 (m, 1-CH_3), 2.04–2.15 (m, 2-H_2), 7.34–7.79 (m, Ar-H)	8.29 (C-3), 24.90 (1-CH_3), 35.25 (C-2), 83.71 (C-1), 143.18 (Ar-C-2)
 *ent*-**12bd**	**12a** (96)	CS_2 (CH_3I)	54	− 117.7 (1.1, MeOH)	1685, 1290, 810	2.40–2.45 (m, 3-H_3), 2.47–2.51 (m, $CSSCH_3$), 7.30–8.01 (m, Ar-H)	19.68 ($CSSCH_3$), 27.97 (C-3), 92.94 (C-2), 140.25 (Ar-C-2), 239.83 (C-1)
 *ent*-**12ca**	*ent*-**11c** (96)	$(MeO)_2CO$	82	+ 68.7 (1.3, ($CHCl_3$)	1735, 1695, 1150, 815	2.15–2.32 (m, 2-H), 2.91–3.38 (m, 2-H and 3-H_2), 3.64 (s, 1-$COOCH_3$), 7.12–7.64 (m, Ar-H)	30.73 (C-3), 37.27 (C-2), 52.33 (1-$COOCH_3$), 88.56 (C-1), 171.46 (1-COO)
 **12ce**	**11c** (95)	$(CH_3)_2C{=}O$	56	+ 5.8 (1.1, ($CHCl_3$)	3330, 1690, 1105, 815	0.97–1.32 (2′-H_3 and 1′-CH_3), 2.30–2.36 (m, 2-H), 2.89–2.94 (m, 2-H) and 3-H_2), 5.16 (s, OH), 7.10–7.63 (m, Ar-H)	25.37 and 25.78 (1′-CH_3 and C-2′), 31.00 (C-3), 33.77 (C-2), 75.21 (C-1′), 99.44 (C-1)

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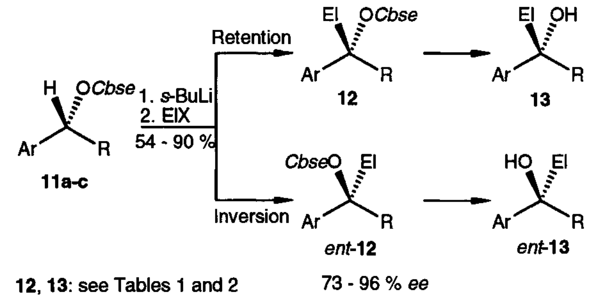
[a] All compounds gave satisfactory elemental analyses (C ± 0.40, H ± 0.29, N ± 0.28).

[b] Methyl ester was prepared from the crude carboxylic acid.

[c] ^1H NMR data of the *Cbse* group are omitted.

[d] ^{13}C NMR data of the *Cbse* group and the aromatic ring (except the substituted Ar-C) are omitted.

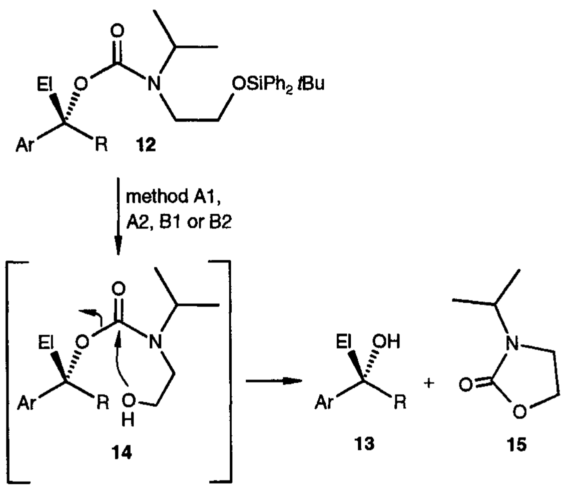
tions. Methoxycarbonylation by dimethyl carbonate (retention) and carboxylation of **11a** (inversion), followed by esterification, take opposite stereochemical courses, as was reported for **2**,[5,6] to yield methyl esters **12aa**, **12ca**, or *ent*-**12aa**, respectively (Table 1). The ethylation and propylation of **11a** both proceed with inversion of the configuration, since the products *ent*-**12ab**, **ac** lead to the known alcohols (*R*)-**13ab**[17] and (*R*)-**13ac**.[18] A reinvestigation[14] of the ethylation of **2** revealed that the *retention*, claimed by Carstens,[5,19] contains an experimental error in the stereochemical correlation and has to be revised to *inversion*.



Scheme 4

The deprotonation of the *β*-naphthyl derivative **11c** in the presence of TMEDA led to a rapidly racemizing intermediate. It is most likely that the origin of the increased configurational lability of **11c** · Li · TMEDA is due to the extended mesomeric system in the carbanion, giving rise to a facilitated ion pair separation.[20] However, in the absence of TMEDA, a synthetically useful degree of configurational stability is restored.

Two methods, A1 and B1, turned out to be superior for deprotection: By refluxing the carbamate with 25 equivalents of lithium hydroxide in methanol (method A1), the free alcohol **13** is produced in one synthetic step (Table 2). Lower yields are observed when applying potassium hydroxide (method A2). However, methyl carboxylates are hydrolyzed under these conditions and reesterification (CH_2N_2) is required. Here the utilization of two-step procedure B1 is advisable. Treatment of **12** with tetrabutylammonium fluoride in THF yields the *N*-(2-hydroxyethyl)urethanes **14**, which under the influence of lithium hexamethyldisilazide (method B1) undergo decarbamoylation, presumably assisted by the 2-hydroxy group. The methoxycarbonyl group is not attacked. If ester groups are not present, stirring the urethane **14** with sodium hydride in THF (method B2) does suffice.



Method A1 LiOH (25 eq.)/ MeOH, Δ, 4-24 h
A2 KOH (25 eq.)/ MeOH, Δ, 4-24 h
B1 i) Bu_4NF (2 eq.), THF, 1 h at r.t.
ii) $LiN(SiMe_3)_2$ (1.1 eq.), THF, 1 h at r.t.
B2 i) as B1 ii) NaH (2 eq.), THF, 1 h at r.t.

Scheme 5

The absolute configuration of the known alcohols **13aa**,[21] *ent*-**13ab**,[17] and *ent*-**13ac**[18] was established by comparison of the optical rotations with the reported ones. The configurations of **12ba**, *ent*-**12bb**, **12ca**, and **12ce** were concluded by analogies in the stereochemical course of the substitution reaction. Dithiocarbamate *ent*-**12bd** afforded the methyl carboxylate on hydrolysis and subsequent reesterification. *ee*-Values were determined by ^1H NMR spectroscopy in the presence of the chiral shift reagent $Eu(hfc)_3$, or at the stage of the alcohols **13** by GC-analyses of the corresponding (*S*)-1-(phenylethyl)-urethanes.[22]

Experiments were carried out under Ar atmosphere. All solvents were purified by distillation and dried, if necessary, prior to use. ^1H and ^{13}C NMR spectra were recorded on Bruker WM 300 spectrometer. IR spectra were recorded on Perkin-Elmer 298 spectrophotometer. Optical rotations were recorded on Perkin-Elmer polarimeter 241. Melting points were obtained on a Büchi melting point apparatus 510 and are uncorrected. Products were purified by flash column chromatography on silica gel (60–200 mesh). (*R*)-1-Phenylethanol[23] (**10a**), 97% *ee*, $[\alpha]_D^{20}$ +50.2 (*c* = 2.1, CH_2Cl_2); (*R*)-1-(2-naphthyl)ethanol[24] (**10b**), 96% *ee*, $[\alpha]_D^{20}$ +39.6 (*c* = 1.2, MeOH); (*R*)-1-indanol[25] (**10c**), 95% *ee*, $[\alpha]_D^{20}$ −28.5 (*c* = 1.1, $CHCl_3$), were prepared, according to Schneider et al.[2], by partial (47–49%) enzymatic hydrolysis of the corresponding acetates with the commercial lipase SAM-II. (*S*)-1-Indanol (*ent*-**10c**) was obtained by hydrolysis of the remaining acetate. Compounds **7**, **9**, **11b**, **11c**, ent-**14ca**, and ent-**14ab** gave satisfactory C,H,N analysis of ± 0.3%.

N-[2-(*tert*-Butyldiphenylsilyloxy)ethyl]-*N*-isopropylamine (7):

A solution of 2-(isopropylamino)ethanol (**5**; 1.03 g, 10.0 mmol), Et_3N (1.01 g, 10.0 mmol), 4-(dimethylamino)pyridine (0.62 g, 5.0 mmol), and *tert*-butyldiphenylsilyl chloride (3.02 g; 11.0 mmol) in anhydrous CH_2Cl_2 (30 mL) was heated under reflux for 12 h. Workup with Et_2O (50 mL) and water (20 mL), extraction of the aq. layer with Et_2O (3 × 10 mL, each), drying of the combined organic solutions ($MgSO_4$), evaporation of the solvent under vacuum, and chromatographic purification (silica gel, Et_2O/petroleum ether, 1:1) afforded **7** (3.39 g, 99%) as a colourless oil.

IR (film): ν = 1100 (C–O), 815 cm^{-1} (SiC).

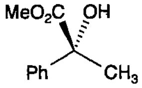
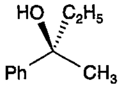
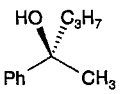
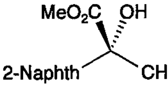
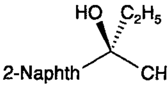
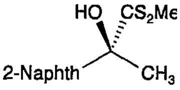
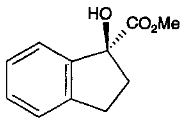
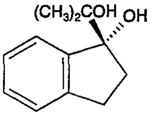
^1HNMR ($CDCl_3$, 300 MHz): δ = 1.04 [d, $NCH(CH_3)_2$, ^3J = 6.2 Hz], 1.05 [s, $SiC(CH_3)_3$], 1.51 (s, NH), 2.73 (t, 1-H_2, $^3J_{1,2}$ = 5.5 Hz), 2.79 (hep, NCH), 3.78 (t, 2-H_2), 7.33–7.69 (m, Ar-H).

^{13}CNMR ($CDCl_3$, 75 MHz): δ = 19.14 [$SiC(CH_3)_3$], 22.91 [$NCH(CH_3)_2$], 26.79 [$SiC(CH_3)_3$], 48.29 (NCH), 49.20 (C-1), 63.29 (C-2), 127.58 (Ar-C-2), 129.57 (Ar-C-3), 133.68 (Ar-C-1), 135.47 (Ar-C-4).

N-[2-(*tert*-Butyldiphenylsilyloxy)ethyl]-*N*-isopropylcarbamoyl Chloride (9):

To a solution of trichloromethyl chloroformate (0.99 g, 5.0 mmol)

Table 2. Deprotection of Carbamates **12** to Alcohols **13**

Product[a]	Educt	Method	Intermediate [Yield (%)]	Yield (%)	ee (%)	$[\alpha]_D^{20}$ (*c*, solvent)	Selected IR Data; ν (cm^{-1})	^{1}H NMR[c] (CDCl$_3$) [δ (ppm)]	^{13}C NMR[d] (CDCl$_3$) [δ (ppm)]
 **13aa**	**12aa**	A1	–	89	94	−4.5 (1.0, EtOH)[c]	Ref.[21]		
13aa	**12aa**	B1	**14aa** (95)	79	92	−4.0 (1.3)			
ent-**13aa**	*ent*-**12aa**	B1	*ent*-**14aa** (95)	76	84	+4.4 (1.6)			
 *ent*-**13ab**	*ent*-**12ab** (EtBr)	A2	–	72	58	+9.1 (0.8, CH$_2$Cl$_2$)[d]	Ref.[17]		
ent-**13ab**	*ent*-**12ab** (EtBr)	B2	*ent*-**14ab**	94	58	+8.8 (1.0)			
ent-**13ab**	*ent*-**12ab** (EtI)	A1	–	81	86	+13.3 (1.0)			
 *ent*-**13ac**	*ent*-**12ac**	A1	–	76	92	+5.1 (1.2, MeOH)[e]	Ref.[18]		
 **13ba**	**12ba**	A1	–	96	76	−12.6 (1,1 MeOH)	3450, 1720, 1130	1.89 (s, 3-H$_3$), 3.77 (s, COOCH$_3$), 3.89 (s, OH), 7.43–8.03 (m, Ar-H)	26.66 (C-3), 53.21 (COO*C*H$_3$), 75.96 (C-2), 140.05 (Ar-C-2), 176.04 (C-1)
ent-**13ba**	*ent*-**12ba**	A1	–	89	73	+11.3 (1.4)			
 *ent*-**13bb**	*ent*-**12bb**	A1	–	75	91	+16.3 (1.0, MeOH)	3380, 1120	0.82 (t, 4-H$_3$, $^3J_{3,4}$ = 7.4 Hz), 1.63 (s, 1-H$_3$), 1.80 (s, OH), 1.93 (m, 3-H$_2$), 7.39–7.91 (m, Ar-H)	8.32 (C-4), 29.72 (C-1), 36.50 (C-3), 75.08 (C-2), 145.14 (Ar-C-2)
 *ent*-**13bd**	*ent*-**12bd**	B1	*ent*-**14bd** (75)	21	≥95	−210.7 (0.9, MeOH)	3360, 1240	2.11 (s, 3-H$_3$), 2.57 (s, CSSCH$_3$), 5.11 (s, OH), 7.43–8.07 (m, Ar-H)	21.03 (CSSCH$_3$), 30.23 (C-3), 84.55 (C-2), 141.60 (Ar-C-2), 247.04 (C-1)
 *ent*-**13ca**	*ent*-**12ca**	A1	–	87	96	+113.5 (1.1, CHCl$_3$)	3380, 1720, 1240	2.22–2.31 and 2.62–2.71 (each m, 2-H), 2.99–3.16 (m, 3-H$_2$), 3.72 (s, 1-COOCH$_3$), 3.80 (s, OH), 7.18–7.31 (m, Ar-H)	30.36 (C-3), 38.69 (C-2), 53.04 (1-COO*C*H$_3$), 83.74 (C-1), 176.24 (1-COO)
ent-**13ca**	*ent*-**12ca**	B1	*ent*-**14ca** (95)	89	93	+96.9 (0.9)			
 **13ce**	**12ce**	A2 (r.t.)	–	78[f]	≥95	+15.6 (1.0, CHCl$_3$)	3360, 3280, 1160	1.15 and 1.31 (each s, 1′-CH$_3$ and 2′-H$_3$), 2.00–2.10 (m, 2-H), 2.40–2.49 (m, 2-H and 1-OH and 1′-OH), 2.80–2.90 and 2.96–3.06 (each m, 3-H), 7.18–7.59 (m, Ar-H)	24.73 and 24.87 (1′-CH$_3$ and C-2′), 30.13 (C-3), 36.93 (C-2), 75.75 (C-1′), 88.29 (C-1)

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[a] All compounds gave satisfactory elemental analyses (C ± 0.49, H ± 0.25).

[b] ^{13}C NMR data of the *Cbse* group and the aromatic ring (except the substituted Ar-C) are omitted.

[c] Ref.[21]: $[\alpha]_D^{20}$ − 5.0 (*c* = 4.9, EtOH).

[d] Ref.[17]: $[\alpha]_D^{27}$ −17.7 (neat) for **12ab.**

[e] Ref.[18]: $[\alpha]_D^{25}$ + 5.8 (*c* = 4.5, MeOH).

[f] solid, mp 80 °C (Et$_2$O/petroleum ether).

in anhydrous CH_2Cl_2 (20 mL) at 0 °C were successively added amine **7** (3.42 g, 10.0 mmol) and triethylamine (1.52 g, 15.0 mmol). After stirring for 16 h at r.t., the reaction mixture was poured onto ice-water (30 mL), the aq. layer extracted with CH_2Cl_2 (3 × 20 mL, each), the CH_2Cl_2 solutions dried ($MgSO_4$), and the solvent evaporated under vacuum. The dark, crude product (4.4 g) was used without further purification.

IR (film): $\nu = 1725$ (COCl), 1100 (C–O), 810 cm^{-1} (SiC).

^1H NMR ($CDCl_3$, 300 MHz): $\delta = 0.97$ [s, $SiC(CH_3)_3$], 1.06 [m, $NCH(CH_3)_2$], 3.38 [m, $NCH(CH_3)_2$], 3.48 (t, 1-H_2, $^3J_{1,2} = 6.9$ Hz), 3.77 (t, 2-H_2), 7.30–7.71 (m, Ar-H).

^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 19.11$ [$SiC(CH_3)_3$], 19.98 [$NCH(CH_3)_2$], 26.82 [$SiC(CH_3)_3$], 49.27 (C-1), 52.47 [$NCH(CH_3)_2$], 62.27 (C-2), 127.78 (Ar-C-2), 129.87 (Ar-C-3), 133.11 (Ar-C-1), 135.53 (Ar-C-4), 148.78 (NCOCl).

Carbamates 11; General Procedure:

To a suspension of NaH (0.48 g, 60 % in paraffin, 12.0 mmol) in anhydrous THF, the secondary benzyl alcohol **10** or *ent*-**10** (10.0 mmol) in THF (5 mL) was continuously added and the reaction mixture stirred at r.t. After the evolution of H_2 had ceased (0.5 h), crude carbamoyl chloride **9** (4.8 g, approx. 10 mmol) was added and stirring was continued for 16 h under reflux. The cool reaction mixture was poured onto water/Et_2O (30 mL + 30 mL), the layers separated, and the aq. layer was extracted with Et_2O (3 × 30 mL, each). After drying ($MgSO_4$), the combined ether solutions were subjected to chromatographic purification (silica gel, Et_2O/petroleum ether, 1:2 to 1:10) to yield the carbamates **11** or *ent*-**11**, respectively.

11a: 4.20 g (86 %), $[\alpha]_D^{20}$ +4.2 ($c = 1.3$, MeOH), 97 % *ee*.

IR (film): $\nu = 1685$ (OCON), 1100 (C–O), 810 cm^{-1} (SiC).

^1H NMR ($CDCl_3$, 300 MHz): $\delta = 1.01–1.07$ [m, $SiC(CH_3)_3$ and $NCH(CH_3)_2$], 1.41 (m, 2-H_3), 3.31 (t, NCH_2CH_2O, $^3J = 7.0$ Hz), 3.73 (t, NCH_2CH_2O), 4.19 [m, $NCH(CH_3)_2$], 5.78 (m, 1-H), 7.24–7.74 (m, Ar-H).

^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 19.17$ [$SiC(CH_3)_3$], 20.42 [$NCH(CH_3)_2$], 22.75 (C-2), 26.86 [$SiC(CH_3)_3$], 44.11 (NCH_2CH_2O), 47.62 [$NCH(CH_3)_2$], 62.71 (NCH_2CH_2O), 72.89 (C-1), 125.86 (Ar-C-2 and Ar-C-6), 127.45 (Ar-C-4), 127.68 (Ar-C-2′), 128.36 (Ar-C-3 and Ar-C-5), 129.67 (Ar-C-3′), 133.68 (Ar-C-1′), 135.53 (Ar-C-4′), 142.58 (Ar-C-1), 155.35 (OCON).

11b: 4.42 g (82 %), $[\alpha]_D^{20}$ +5.5° ($c = 2.3$, MeOH), 96 % *ee*.

IR (film): $\nu = 1680$ (OCON), 1100 (C–O), 810 cm^{-1} (SiC).

^1H NMR ($CDCl_3$, 300 MHz): $\delta = 1.01–1.08$ [m, $SiC(CH_3)_3$ and $NCH(CH_3)_2$], 1.50 (m, 2-H_3), 3.33 (m, NCH_2CH_2O), 3.74 (m, NCH_2CH_2O), 4.21 [m, $NCH(CH_3)_2$], 5.96 (m, 1-H), 7.31–7.82 (m, Ar-H).

^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 19.17$ [$SiC(CH_3)_3$], 20.42 [$NCH(CH_3)_2$], 22.58 (C-2), 26.86 [$SiC(CH_3)_3$], 44.04 (NCH_2CH_2O), 47.75 [$NCH(CH_3)_2$], 63.05 (NCH_2CH_2O), 73.02 (C-1), 124.11 (Ar-C-3), 124.78 (Ar-C-1), 125.83 (Ar-C-6), 126.03 (Ar-C-7), 127.68 (Ar-C-2′ and Ar-C-5), 128.05 (Ar-C-8), 128.22 (Ar-C-4), 129.64 (Ar-C-3′), 132.4 (Ar-C-9), 133.24 (Ar-C-10), 133.65 (Ar-C-1′), 135.53 (Ar-C-4′), 139.88 (Ar-C-2), 155.35 (OCON).

11c: 4.05 g (81 %), $[\alpha]_D^{20}$: +4.5 ($c = 1.0$, $CHCl_3$), 95 % *ee*.

IR (film): $\nu =$ (OCON), 1100 (C–O), 815 cm^{-1} (SiC).

^1H NMR ($CDCl_3$, 300 MHz): $\delta = 1.02–1.07$ [m, $SiC(CH_3)_3$ and $NCH(CH_3)_2$, 1.86–2.13 and 2.37–2.59 (each m, 2-H), 2.73–3.12 (m, 3-H_2), 3.16–3.42 (m, NCH_2CH_2O), 3.62–3.84 (m, NCH_2CH_2O), 3.93–4.35 [m, $NCH(CH_3)_2$], 6.12 (m, 1-H), 7.16–7.74 (m, Ar-H).

^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 19.11$ [$SiC(CH_3)_3$], 20.56 [$NCH(CH_3)_2$], 26.82 [$SiC(CH_3)_3$], 30.03 (C-3), 32.65 (C-2), 44.17 (NCH_2CH_2O), 47.78 [$NCH(CH_3)_2$], 62.85 (NCH_2CH_2O), 78.75 (C-1), 124.62 (C-4), 125.29 (C-7), 126.50 (C-6), 127.61 (Ar-C-2′), 128.46 (C-5), 129.57 (Ar-C-3′), 133.65 (Ar-C-1′), 135.50 (Ar-C-4′), 141.77 (C-8), 143.89 (C-9), 156.06 (OCON).

ent-**11c**: 3.76 g (75 %), $[\alpha]_D^{20}$ −3.1 ($c = 1.275$, $CHCl_3$), 96 % *ee*.

Deprotonation of Carbamates 11 and Preparation of Substituted Products 12; General Procedure:

To a solution of carbamate **11** (1.0 mmol) and *N,N,N′,N′*-tetramethylethylendiamine (TMEDA; 117 mg, 1.0 mmol; except for the deprotonation of **11b**) in Et_2O (2 mL), stirred under Ar in a dry ice/acetone bath, 1.2–1.4 M *sec*-butyllithium solution in cyclohexane/isopentane (1.1 mmol) was introduced with a syringe within approx. 2 min. Stirring was continued for 5 min before the electrophile (1.1 mmol) was added. The reaction mixture was stirred for further 30 min (in case of alkylation 90 min) at −78 °C and allowed to warm up to r.t. After adding Et_2O (10 mL) and water (2 mL), the layers were separated and the aq. layer was extracted with Et_2O (3 × 20 mL, each). The organic layer was dried ($MgSO_4$), evaporated under vacuum, and the residue purified by flash chromatography (silica gel, Et_2O/petroleum ether, 1:2 to 1:10) to yield substituted carbamates **12** (see Table 1).

For carboxylation a stream of excess gaseous CO_2 was introduced 5 min after the addition of *sec*-BuLi. The reaction mixture was allowed to warm up to r.t. and stirred for 1 h before 2 N hydrochloric acid (20 mL) and Et_2O (10 mL) were added. The aq. layer was extracted with Et_2O (3 × 20 mL, each). The organic layers were treated with an etheral CH_2N_2 solution until remaining yellow and stirred for 30 min. Before stirring for further 15 min silica gel (0.5 g) was added to destroy excess CH_2N_2.

For dithiocarboxylation, CS_2 (1.1 mmol) was introduced as electrophile and immediately thereafter, methyl iodide (1.1 mmol) was added. After stirring for 30 min at −78 °C, the reaction mixture was worked up as usual.

Deprotection of Carbamates 12, Alcohols 13; Representative Procedures:

Method A1; (R)-2-Phenylbutan-2-ol (ent-**13ab**):

A solution of *ent*-**12b** (519 mg, 1.0 mmol) and LiOH (600 mg, 25 mmol) in MeOH (10 mL) was stirred under reflux for 24 h. The cool reaction mixture was poured onto 1 N HCL (20 mL) and Et_2O (20 mL). The layers were separated, the aq. layer extracted with Et_2O (3 × 20 mL, each) and the combined ether solutions dried ($MgSO_4$). After evaporation under vacuum the residue was purified by flash chromatography (silica gel, Et_2O/petroleum ether, 1:4) to yield 126 mg (81 %) *ent*-**13ab** (see Table 2).

Method A2; (R)-2-Phenylbutan-2-ol (ent-**13ab**):

A solution of *ent*-**12ab** (167 mg, 0.32 mmol) and KOH (452 mg, 8.1 mmol) in MeOH (7 mL) was stirred under reflux for 17 h. The cool reaction mixture was poured onto 1 N hydrochloric acid (10 mL) and Et_2O (10 mL). The layers were separated, the aq. layer extracted with Et_2O (3 × 10 mL, each) and the combined ether solutions dried ($MgSO_4$). After evaporation under vacuum the residue was purified by flash chromatography (silica gel, Et_2O/petroleum ether, 1:4) to yield 36 mg (72 %) *ent*-**13ab** (see Table 2).

Method B1; Methyl (S)-1-[N-(2-Hydroxyethyl)-N-isopropylcarbamoyloxy]indane-1-carboxylate (ent-**14ca**) *and Methyl (S)-1-Hydroxyindane-1-carboxylate* (ent-**13ca**):

A solution of *ent*-**12ca** (428 mg, 0.77 mmol) in THF (3 mL) and 1 M Bu_4NF in THF (1.5 mL, 1.54 mmol) was stirred for 45 min at r.t. The reaction mixture was diluted with Et_2O (10 mL) and water (10 mL), the aq. layer extracted with Et_2O (3 × 10 mL, each). The combined ether solutions were dried ($MgSO_4$), concentrated under vacuum and purified by flash chromatography (silica gel, Et_2O/petroleum ether, 1:1) to afford 233 mg (95 %) of *ent*-**14ca**, mp 106 °C (Et_2O/petroleum ether), $R_f = 0.05$ (Et_2O/petroleum ether, 1:1), $[\alpha]_D^{20}$ +136.0 ($c = 1.1$, $CHCl_3$).

IR (KBr): $\nu = 3430$ (OH), 1730 (COO), 1675 (OCON), 1110 cm^{-1} (C–O).

^1H NMR ($CDCl_3$, 300 MHz): $\delta = 1.17$ [m, $NCH(CH_3)_2$], 1.59 (s, OH), 2.33 (m, 2-H), 2.99–3.38 [m, 2-H and 3-H_2 and NCH_2CH_2O], 3.69 (s, 1-$COOCH_3$), 3.74 (m, NCH_2CH_2O), 4.22 [m, $NCH(CH_3)_2$], 7.20–7.50 (m, Ar-H).

^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 20.69$ [$NCH(CH_3)_2$], 30.73 (C-3), 37.17 (C-2), 45.19 (NCH_2CH_2O), 48.23 [$NCH(CH_3)_2$], 52.50 (1-

$COOCH_3$), 62.76 (NCH_2CH_2O), 88.96 (C-1), 124.88 (C-4), 124.99 (C-7), 126.81 (C-6), 129.70 (C-5), 139.68 (C-8), 144.23 (C-9), 157.27 (OCON), 171.29 (1-COO).

A solution of *ent*-**14ca** (107 mg, 0.33 mmol) in THF (2 mL) was stirred with a 1.1 M solution of $LiN(SiMe_3)_2$ in THF/cyclohexane (0.40 mL, 0.44 mmol) for 1 h at r.t. Then, sat. aq. NH_4Cl (10 mL) and Et_2O (10 mL) were added. Usual workup, followed by flash chromatography (silica gel, Et_2O/petroleum ether, 1 : 2) afforded 57 mg (89 %) *ent*-**13ca** (see Table 2).

*Method B2; (R)-[1-Methyl-1-phenylpropyl] N-(2-Hydroxy)ethyl-N-isopropylcarbamate (ent-***14ab***) and (R)-2-Phenylbutan-2-ol (ent-***13ab***)*

A solution of *ent*-**12ab** (207 mg, 0.40 mmol) in THF (2 mL) and 1 M Bu_4NF in THF (0.8 mL, 0.8 mmol) was stirred for 1 h at r.t. The reaction mixture was diluted with Et_2O (10 mL) and water (10 mL), the aq. layer extracted with Et_2O (3 × 10 mL, each). The combined ether solutions were dried ($MgSO_4$), concentrated under vacuum, and purified by flash chromatography (silica gel, Et_2O/petroleum ether, 1 : 1) to afford 99 mg (89 %) of *ent*-**14ab**, $R_f = 0.11$ (Et_2O/petroleum ether, 1 : 1), $[\alpha]_D^{20}$ − 11.9 ($c = 1.0$, CH_2Cl_2).

IR (film): $\nu = 3500$ (OH), 1670 (OCON), 1110 cm^{-1} (C−O).

^1H NMR ($CDCl_3$, 300 MHz): $\delta = 0.82$ (t, 3-H_3, $^3J_{2,3} = 7.4$ Hz), 1.18–1.26 [m, $NCH(CH_3)_2$], 1.84 (s, 1-CH_3), 2.05 (q, 2-H_2), 3.31–3.32 (m, NCH_2CH_2O), 3.69 (m, NCH_2CH_2O), 4.33 [m, $NCH(CH_3)_2$], 7.19–7.35 (m, Ar-H).

^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 8.26$ (C-3), 20.96 [$NCH(CH_3)_2$], 24.90 (1-CH_3), 35.62 (C-2), 44.75 (NCH_2CH_2O), 47.95 [$NCH(CH_3)_2$], 64.13 (NCH_2CH_2O), 84.31 (C-1), 124.51 (Ar-C-2 and Ar-C-6), 126.64 (Ar-C-4), 128.09 (Ar-C-3 and Ar-C-5), 145.44 (Ar-C-1), 156.54 (OCON).

To a suspension of NaH (20 mg, 60 % in paraffin, 0.50 mmol) in anhydr. THF (1 mL) *ent*-**14ab** (69 mg, 0.25 mmol) in THF (1 mL) was added and the reaction mixture stirred at r.t. for 75 min. Then, sat. aq. NH_4Cl (10 mL) and Et_2O (10 mL) were added. Further workup, as described above, followed by flash chromatography (silica gel, Et_2O/petroleum ether, 1 : 4) afforded 36 mg (94 %) *ent*-**13ab** (see Table 2).

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