Efficient Desymmetrization of *meso-cis*-1,2-Cyclohexanedimethanol with Differentiation between Diastereotopic and Enantiotopic C–H Bonds by (–)-Sparteine-Mediated Deprotonation

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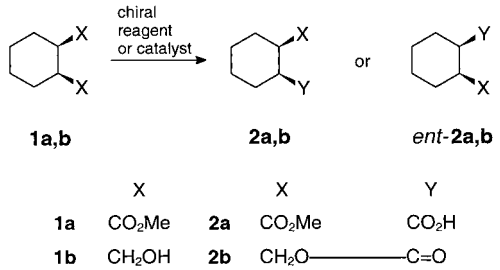
Dedicated to Professor Armin de Meijere on the occasion of his 60th birthday

Abstract: The deprotonation of a dicarbamate prepared from *cis*-1,2-cyclohexanedimethanol by *sec*-butyllithium/(–)-sparteine proceeds with efficient selection between the enantiotopic branches and their diastereotopic protons with high preference for the pro-*S* proton at the *R* branch to afford the intermediate, configurationally stable lithium compound as a single diastereomer. Trapping of this intermediate by electrophiles (DOMe, CO_2, CH_3I, Me_3SiCl, or R_3SnCl) takes place with retention of the configuration to yield highly enantiomerically and diastereomerically enriched substitution products, which are easily converted to diols, to anellated tetrahydrofurans, or to γ-lactones. The chiral base is also capable of efficient kinetic resolution of the racemic α-deuterated starting material, by the utilization of an extraordinarily high kinetic H/D isotope effect within the deprotonation step. The, presumably, first example of the kinetic resolution of a racemic stannane by lithiodestannylation, utilizing methyllithium/(–)-sparteine, is reported.

Keywords: desymmetrization · isotope effects · kinetic resolution · stereotopic differentiation

Introduction

The desymmetrization of *meso*-substrates[1] is particularly rewarding in *cis*-1,2-disubstituted cyclohexanes; it leads to products **2** or *ent*-**2**, in which one of the enantiotopic X groups has been selectively converted into a Y group. Frequently, *cis*-cyclohexane dicarboxylic acids and their derivatives[2] or *cis*-cyclohexanedimethanols[3] have been used as substrates (Scheme 1),[4] and desymmetrization is achieved by means of enzymes[5] or other chiral reagents.[1d, 6]



Scheme 1. Desymmetrization of *cis*-1,2-disubstituted cyclohexanes **1**.

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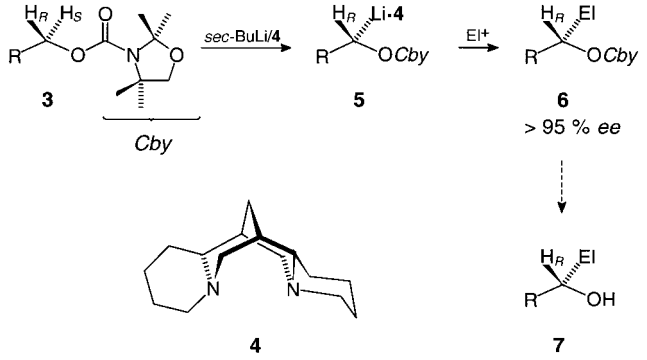
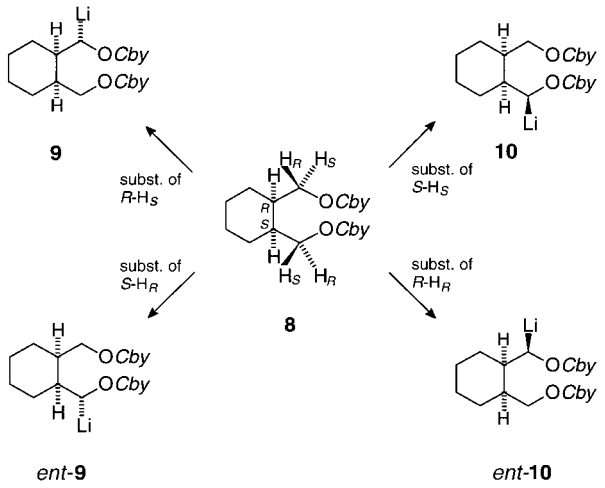
As we have already reported,[7, 8] the chiral base butyllithium/(–)-sparteine[9] has a pronounced tendency to discriminate in the rate of abstraction of enantiotopic protons in alkyl carbamates. The method has also been applied to *N*-Boc-pyrrolidines,[10, 11] several benzylic substrates,[12] ferrocenes,[13] *P*,*P*-dimethylarylphosphane derivatives,[14] as well as to the kinetic resolution of a racemic allyl carbamate[15] and of several β-stereogenic alkyl carbamates.[16] Moreover, a desymmetrization of *meso*-oxabicycles by alkyllithium/(–)-sparteine-induced ring-opening has been described by Lautens et al.[17] and Hodgson et al.[18]

The (–)-sparteine-induced deprotonation of alkyl carbamates **3** generated from primary alcohols, which bear non-mesomerically stabilizing groups adjacent to the carbanionic center in **5**, is characterized by a pronounced pro-*S* selectivity in the deprotonation step. The intermediates **5** are configurationally stable and the reaction with most electrophiles occurs with retention of the configuration to produce the adducts **6** (Scheme 2).[19, 20]

This method has been applied to the desymmetrization of the *cis*-1,2-(cyclohexane)dimethyl dicarbamate **8**, which offers an interesting stereochemical situation:[21] The *R* and *S* branches are enantiotopic; each bears a pair of diastereotopic methylene protons (Scheme 3). The desymmetrization of this substrate is possible by the preferential abstraction of diastereotopic pro-*S* protons, *R*-H_S and *S*-H_S (which leads to the intermediates **9** and **10**), over the diastereotopic pro-*R* protons *R*-H_R and *S*-H_R in the (–)-sparteine-mediated, kinetically controlled deprotonation. Additionally, the ratio



Scheme 2. (−)-Sparteine-induced deprotonation of alkyl carbamates **3** to give enantiomerically enriched carbamates **6**.



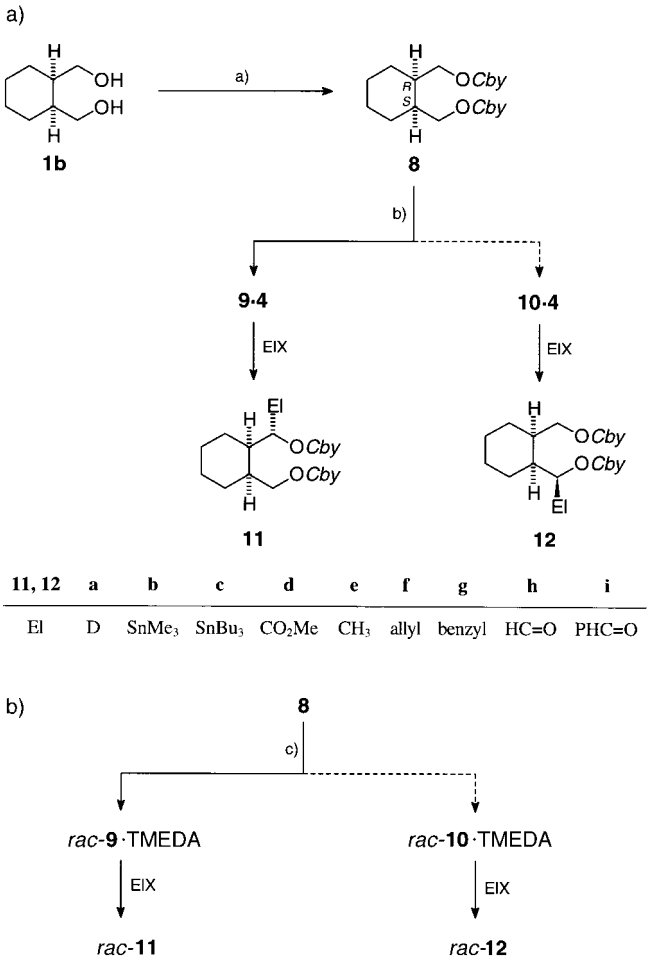
Scheme 3. The four possible stereoisomers formed by the deprotonation of **8**.

of proton abstraction between the diastereotopic pro-*S* protons *R*-H_S and *S*-H_S is determined by the sense and strength of the substrate-inherent chiral induction.[22]

Results and Discussion

The dicarbamate **8** was obtained by treatment of the disodium bisalkoxide of the diol **1b**[23] with 2.2 equivalents of 2,2,4,4-tetramethyl-1,3-oxazolidine-3-carbonyl chloride (*Cby*Cl) (Scheme 4).[24]

The deprotonation of **8** with 2.2 equivalents of *sec*-BuLi/TMEDA in toluene (−78 °C, 4–5 h), proceeded smoothly to give the major intermediate *rac*-**9**·TMEDA, which reacted with tributyltin chloride to afford the stannanes *rac*-**11c** and *rac*-**12c** in 77% yield and a diastereomeric ratio (*dr*) of 99:1 (Table 1, entry 5). Similarly, if the intermediate mixture was trapped with carbon dioxide followed by methylation of the crude acids with diazomethane, the esters *rac*-**11d** and *rac*-**12d** were formed (yield: 70%, *dr* = 98:2; entry 9). If the same procedure was used but only 3 h were allowed for the deprotonation, the yield increased to 85%, while the *dr* decreased to 91:9 (Table 1, entry 10). It can be concluded from these experiments that the kinetically controlled, substrate-induced deprotonation step favors the *unlike*-process[25] [*R*-pro-*S* and *S*-pro-*R*] by 9:1. Fortunately, the selective decomposition of the minor diastereomer, *rac*-**10**, leads to a diastereomeric enrichment of up to 99:1.



Scheme 4. Deprotonation of *cis*-1,2-cyclohexanedimethyl dicarbamate (**8**) with *sec*-BuLi in the presence of (−)-sparteine or TMEDA and the subsequent reaction with electrophiles. Reaction conditions: a) 1) NaH, THF, 30 min, room temperature, 2) *Cby*Cl, THF, reflux, 16 h. b) *sec*-BuLi/**4** (2.2 equiv), toluene, −78 °C, 4 h. c) *sec*-BuLi/TMEDA (2.2 equiv), toluene, −78 °C, 4 h.

Initially, we carried out the reactions with diethyl ether as the solvent, before we noticed that under these conditions a slow ether-mediated nonselective deprotonation takes place (entry 12).

When **8** was deprotonated by *sec*-BuLi/(−)-sparteine (2.2/2.3 equiv; toluene), the essentially pure stannane **11c** or ester **11d**, respectively, was formed (Table 1, entries 4 and 6). We assume that the minor diastereomer **12** results from the intermediate **10**·**4** (Scheme 4a), which is produced by the removal of H_S in the *S* branch.[26]

The reactions of *rac*-**9**·TMEDA/*rac*-**10**·TMEDA and **9**·**4**/**10**·**4** with further electrophiles are collected in Table 1. Formylation leads to 9:1 mixtures of the diastereomeric aldehydes *rac*-**11h** and *rac*-**12h** (entry 20), or to 7:3 mixtures of **11h** and *ent*-**12h** (entry 19). This is due to base-catalyzed epimerization of the major isomer **11h** which is formed initially. This hypothesis is supported by the fact that the ratio is influenced by the stirring time of **10** with the electrophile (≈50:50, for 2 h).

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Table 1. Deprotonation and electrophilic substitution of **8**.

Entry	Diamine	ElX	Products	**11** + **12** (recovered **8**) Yield [%]	Ratio **11**:**12**	*ee* [%]
1	**4**	H_3CCO_2D	**11a** + **12a**	64 (16)[a]	–	> 95[b]
2	**4**	Me_3SnCl	**11b** + **12b**	65 (19)	98:2	> 95
3	TMEDA	Me_3SnCl	*rac*-**11b** + *rac*-**12b**	75 (–)	99:1	–
4	**4**	Bu_3SnCl	**11c** + **12c**	43 (25)	99:1[c]	> 95[c]
5	TMEDA	Bu_3SnCl	*rac*-**11c** + *rac*-**12c**	77 (–)	99:1[c]	–
6	**4**	CO_2[d]	**11d** + **12d**	63 (16)	96:4	> 95
7	**4**	MeOC(O)Cl	**11d** + **12d**	46 (36)	96:4	> 95
8	**4**	MeOC(O)OMe	**11d** + **12d**	25 (62)	96:4	> 95
9	TMEDA	CO_2[d]	*rac*-**11d** + *rac*-**12d**	70 (–)	98:2	–
10[e]	TMEDA	CO_2[d]	*rac*-**11d** + *rac*-**12d**	85 (–)	91:9	–
11	TMEDA	MeOC(O)Cl	*rac*-**11d** + *rac*-**12d**	40 (28)	88:12	–
12	none[f]	CO_2[d]	*rac*-**11d** + *rac*-**12d**	18 (72)	40:60	–
13	**4**	MeI	**11e** + **12e**	70 (8)	95:5[g]	> 95
14	TMEDA	MeI	*rac*-**11e** + *rac*-**12e**	51 (–)	99:1[g]	–
15	**4**	CH_2=CH-CH_2Br	**11f** + *ent*-**12f**	59 (24)	68:32	> 95[h]
16	TMEDA	CH_2=CH-CH_2Br	*rac*-**11f** + *rac*-**12f**	68 (3)	70:30	–
17	**4**	$C_6H_5CH_2Br$	**11g** + *ent*-**12g**	44 (25)	74:26	> 95[h]
18	TMEDA	$C_6H_5CH_2Br$	*rac*-**11g** + *rac*-**12g**	58 (7)	85:15	–
19	**4**	HCO_2Et	**11h** + *ent*-**12h**	16 (56)[i]	70:30[i]	> 95[h]
20	TMEDA	HCO_2Et	*rac*-**11h** + *rac*-**12h**	45 (–)[i]	90:10[i]	–
21	**4**	$PhCO_2Et$	**11i** + *ent*-**12i**	42 (33)	85:15	> 95[h]
22	TMEDA	$PhCO_2Et$	*rac*-**11i** + *rac*-**12i**	58 (6)	90:10	–

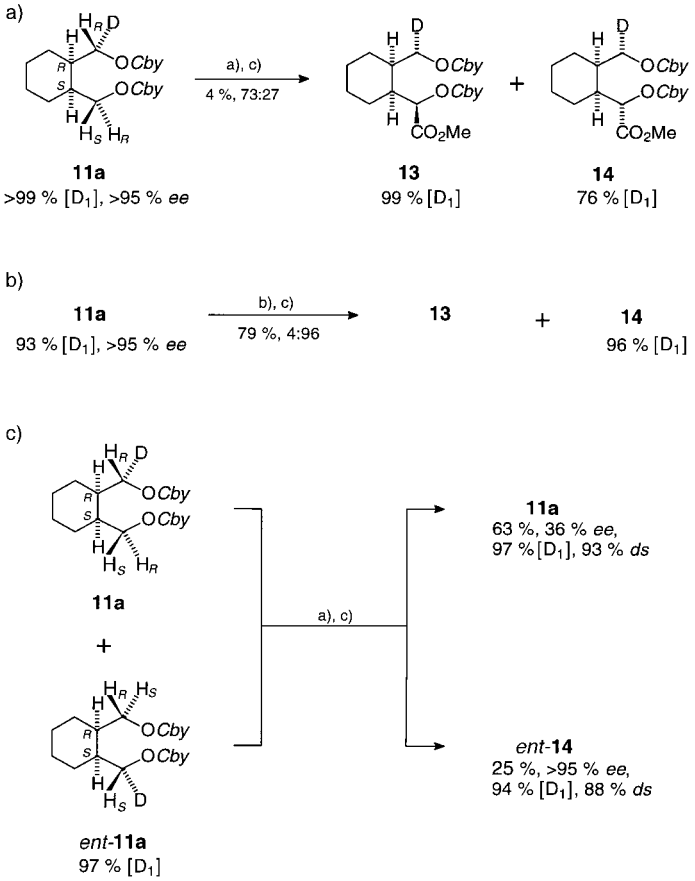
[a] Recovered in 80% yield as a mixture of **8** and **11a** with $[D_1] = 81\%$. [b] Determined after deprotonation and carboxylation to **14**. [c] Determined after lithiodestannylation and conversion into **11d**. [d] The crude acid was esterified with diazomethane. [e] Deprotonation time of 3 h. [f] Et_2O was used as the solvent. [g] Determined after conversion into the diol **15e**. [h] The *ee* > 95% was determined in the deprotonation step, as proved by the entries 2, 4, 6–8, and 13. [i] Reaction of **10** with the electrophile with a reduced reaction time.

Except for methyl iodide, ordinary alkyl halides do not react with the ion pairs **9** or **10**. Surprisingly, low diastereoselectivities are observed for the reaction with allyl and benzyl bromides (entries 15–18) to give **11f**/*ent*-**12f** and **11g**/*ent*-**12g**, respectively. It is quite likely that a single electron-transfer (SET) process,[27] which proceeds through a configurationally labile radical pair, is operating. This reaction path is supported by mesomeric stabilization in the alkyl residue (here allyl and benzyl). It should be pointed out that the enantioselectivity is not influenced, since it is determined in the deprotonation step by the selection between the enantiotopic methylene groups. Overall, a partial inversion at the *R* branch takes place, which is equivalent to the formal substitution of H_R in **8** via the lithium intermediate *ent*-**10** (see Scheme 3).

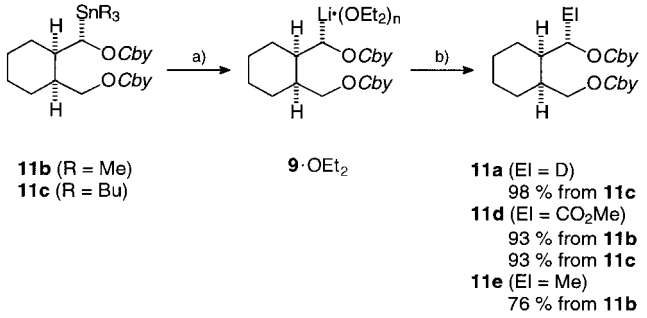
Studies with the deuterated substrates: Kinetic resolution: The deprotonation of alkyl carbamates[28] and thiocarbamates[29] exhibits an extraordinarily high kinetic H/D isotope effect with a magnitude of 100. We have already used this feature for the protection of acidic C–H bonds.[30, 31] In **11a**, the former *R*-H_S is blocked by D ($[D_1] > 99\%$[32]). Deprotonation of **11a** with *sec*-butyllithium/**4** under the usual conditions resulted in a very low conversion: only 4% of the carboxylic esters **13** and **14** (ratio 73:27) were obtained. In **13**, which arises from the removal of *S*-H_S, there is still 99% $[D_1]$ present, whereas **14** contains only 76% $[D_1]$. The decreased $[D_1]$-ratio of **14** is caused by the product **11d**, which is formed from traces of **8** present in **11a**. This result clearly shows that in competition of two possible mismatched situations—**4**/*S*-pro-*S*-H and **4**/*S*-pro-*R*-H—the preference of the reagent overrides the preference of the substrate by a factor of at least 3 (Scheme 5a). The latter is expressed by the result of the following experiment (Scheme 5b): When **11a** ($[D_1] = 93\%$) was deprotonated in the presence of the achiral ligand TMEDA, the esters **13** and **14** were isolated with 79% yield in a 4:96 ratio, with $[D_1] = 96\%$ in **14**; the major product was formed from the *S*-pro-*R*-H. From these results, the order of preferences of the (–)-sparteine base for the attack of the four nonequivalent protons can be concluded to be: *R*-H_S > *S*-H_S > *S*-$H_R \gg$ *R*-H_R. Blocking *R*-H_S by deuteration permits the access to (deuterated) diastereomers (with **4**) or enantiomers (with TMEDA) of the regularly produced products **11**. Furthermore, the high kinetic isotope effect enables the kinetic resolution of *rac*-**11a** by deprotonation (Scheme 5c).

Lithiodestannylations and kinetic resolution of racemic stannanes: The reaction of enantiomerically enriched (1-alkoxyalkyl)trialkylstannanes provided the first route to nonracemic (1-alkoxyalkyl)lithium derivatives, since it proceeds with rigid stereoretention.[11, 20a, 20b, 33, 34] The application of this method to stannylated alkyl carbamates, such as **11b**, **c**, provides a route to the lithio derivatives in amine-free solutions.[35] The treatment of the trimethyl- or tributylstannane **11b** or **11c**, respectively, with *n*-butyllithium in diethyl ether at $-78\,^{\circ}C$, generates the intermediates **9**·OEt_2 with high yields and purities, as estimated from the trapping experiments (Scheme 6); the products reached diastereomeric ratios of 99:1 and *ee* values of > 95%.

In principle, chiral alkyllithium complexes should be able to differentiate between enantiomeric, *C*-stereogenic stannanes, although we are not aware of an efficient example.[36] When



Scheme 5. Deprotonation and carboxylation of the deuterated carbamate **11a**. Reaction conditions: a) *sec*-BuLi/**4** (2.2 equiv), toluene, −78 °C, 4 h. b) *sec*-BuLi/TMEDA (2.2 equiv), toluene, −78 °C, 4 h. c) i) CO_2, −78 °C, ii) CH_2N_2, room temperature.



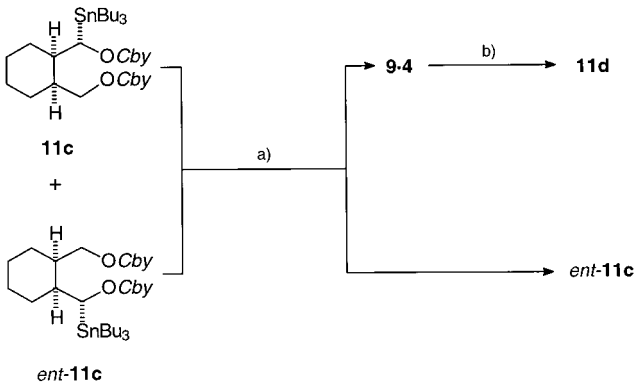
Scheme 6. Lithiodestannylation of the stannanes **11b** and **11c** and electrophilic substitution of the intermediate **9**·OEt_2. Reaction conditions: a) *n*BuLi (2.2 equiv), Et_2O, −78 °C, 1 h. b) ElX.

rac-**11c** in diethyl ether was allowed to react with about two equivalents[37] of methyllithium/(−)-sparteine (**4**) at −78 °C for 30–140 min with subsequent trapping of the reaction mixture by carbon dioxide (followed by esterification of the crude acid), both enantiomerically enriched **11d** and stannane *ent*-**11c** were isolated with medium *ee* values (Scheme 7, Table 2).

Deprotection and stereochemical correlation: Three methods have been developed for the removal of the *Cby* group:

1. Stepwise deprotection by acid-catalyzed deketalization and cleavage of the 1,3-oxazolidine ring, followed by base-mediated cleavage of the (2-hydroxy)alkyl urethanes in methanol (method A).[7, 24]
2. One-step hydrolysis with aqueous 5 N HCl (method B).[38]
3. Reductive cleavage with metal hydrides (methods C1 and C2).[38b, 39, 40]

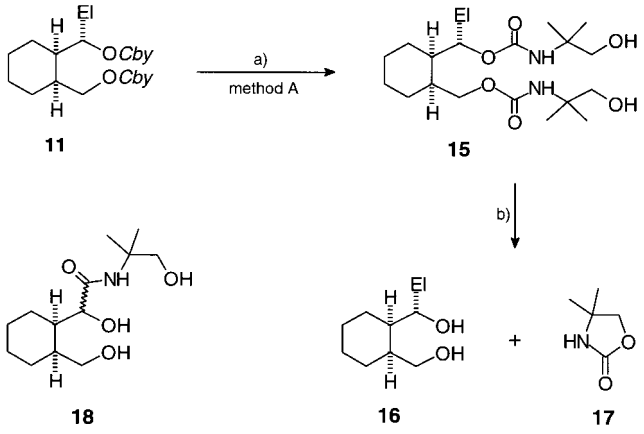
If the dicarbamates **11** are heated together with one equivalent of methanesulfonic acid in methanol, the amino-acetal moiety of the oxazolidine group is split off and the bisurethanes **15** are formed (Scheme 8). Treatment of the crude products with NaOH or K_2CO_3 in methanol yields the



Scheme 7. Kinetic resolution of the tributylstannane **11c** to give the enantiomerically enriched products **11d** and *ent*-**11c**. Reaction conditions: a) MeLi/**4** (1.7–2.0 equiv), Et_2O, −78 °C, 0.5–2.3 h. b) 1) CO_2, −78 °C, 2) CH_2N_2, room temperature.

Table 2. Cleavage of *rac*-**11c** with kinetic resolution by methyllithium/(−)-sparteine.

Run	equiv MeLi/**4**	Time [min]	Yield **11d** [%] (*ee* [%])	Yield *ent*-**11c** [%] (*ee* [%])
1	1.9	30	16 (52)	63 (13)
2	2.0	60	32 (48)	54 (27)
3	1.7	140	53 (44)	33 (60)



15	**a**	**d**	**e**	**g**[a]	**16**	**1a**	**d**	**e**	**g**[a]
R	H	CO_2Me	CH_3	$PhCH_2$	R	H	CO_2Me	CH_3	$PhCH_2$
yield [%]	89	96	80	61	yield [%]	98	[b]	100	96

[a] 81:19 mixture of diastereomers. [b] Formation of amide **18**.

Scheme 8. Cleavage of the carbamates **11** by method A. Reaction conditions: a) $MeSO_3H$ (1.0 equiv), MeOH, reflux, 3 h. b) K_2CO_3 (0.5 equiv), MeOH, reflux, 3 h.

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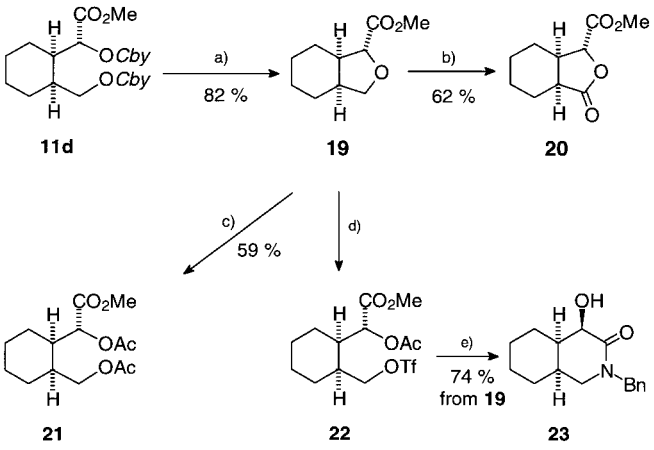
diols **16**. The formation of 1,3-oxazolidine **17**[41] as a by-product illustrates the anchimeric assistance of the β-hydroxy group in the final deblocking step. Unfortunately, methyl ester **15d** undergoes an intramolecular aminolysis to form the amide **18**, which epimerizes at C2 of the acetic acid moiety.

Refluxing the ester **11d** in aqueous 5 N HCl[38] converted it to the tetrahydrofuran-carboxylic acid **19** (H for Me in **19**, Scheme 9), which was reesterified by diazomethane. Ruthenium-catalyzed metaperiodate oxidation furnished the crystalline lactonic acid ester **20**.[42] The quality of the crystal was



Scheme 9. Cleavage by method B and stereochemical correlation of **11d**; products derived from **11d**. Reaction conditions: a) (i) Aqueous HCl (5 N), reflux, 3 h, (ii) CH_2N_2, room temperature. b) $NaIO_4/RuCl_3$. c) $FeCl_3/Ac_2O$. d) AgO_3SCF_3/CH_3COCl. e) $BnNH_2$, room temperature, 13 h.

outstanding, so that by application of anomalous X-ray dispersion the absolute configuration depicted in Figure 1, which is that expected,[43], is almost certain (Flack Parameter, calcd: 0 for the *R* and +1 for the *S* enantiomer; found: −0.5). Selective opening of the tetrahydrofuran ring following the

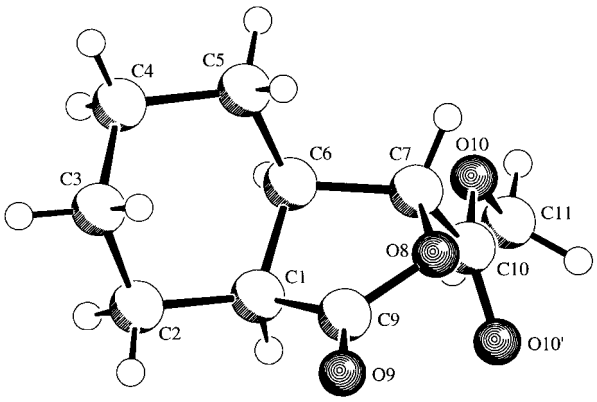
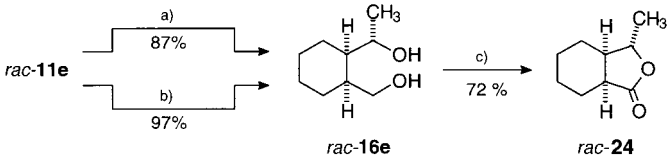


Figure 1. X-ray crystal structure of the lactone **20**.[43]

method employed by Ganem et al.[44] with iron(III) chloride and acetic anhydride gave the diacetate **21**. Regiodifferentiation was achieved by treatment of **19** with acetyl chloride/silver triflate, according the method used by Effenberger et al.,[45] to give the triflate **22**. Treatment of **22** with benzylamine—evidently by the substitution of the triflate moiety, intramolecular aminolysis, and deacetylation—led to the *cis*-fused 4-hydroxy-decahydroisoquinolin-3-one **23**.

Reductive cleavage[39] of the methylated dicarbamate **11e** with excess lithium alanate in refluxing THF (method C1) furnished the diol **16e** in high yield. Alternatively, a large excess of diisobutylaluminum hydride (DIBAH) can be used in THF at room temperature.[40] Ruthenium-mediated oxidation according to Ley et al.[46a, 46c] and Bloch et al.[46b] gave the stereohomogeneous γ-lactone *rac*-**24**, which correlates well with the published data (Scheme 10).[47, 48]



Scheme 10. Methods C1 and C2 and transformations of **11e**. a) $LiAlH_4$ (4 equiv), THF, reflux, 5 h. b) DIBAH (16 equiv), THF, room temperature, 17 h. c) NMO/TPAP.

Conclusions

The desymmetrization of the dicarbamate **8** by means of (−)-sparteine-mediated deprotonation is a powerful route to enantiomer-enriched *cis*-1,2-dicarbon-substituted cyclohexanes. In contrast to all of the known methods for desymmetrization of *cis*-1,2-disubstituted cyclohexanes,[5] a third stereo center is introduced incidentally with a high diastereoselectivity as a result of the outstanding preference of the (−)-sparteine reagent for pro-*S* protons.

Experimental Section

General methods: ^1H and ^{13}C NMR spectra were recorded on Bruker AW200 or WM300 instruments with 200 MHz or 300 MHz and 50 or 75.5 MHz, respectively. Chemical shifts in $CDCl_3$ are reported in ppm relative to tetramethylsilane (TMS). The doubling of some signals occurs as a result of the *E*/*Z* isomerism of the carbamate group; the minor signal is given in parentheses. IR spectra were registered on a Perkin–Elmer 298 spectrometer. Optical rotations were measured with a Perkin–Elmer 241 polarimeter. Melting points were obtained on a Gallenkamp melting point apparatus and are uncorrected. Elementary analyses were performed by the Mikroanalytische Abteilung des Organisch-Chemischen Institutes der Universität Münster on a Perkin–Elmer CHN analyser 240. All products were purified by flash column chromatography on silica gel (Merck, 60–200 mesh). The solvents for extraction and chromatography were distilled before use. The solvents for the reactions were purified by distillation and dried, if necessary, prior to use. (−)-Sparteine is commercially available (Sigma) and was stored under argon. *N*,*N*,*N*′,*N*′-Tetramethylethylenediamine (TMEDA) was dried over CaH_2 and distilled before use. *sec*-Butyllithium was received as a 1.4 M solution in cyclohexane/hexane (92:8), *n*-butyllithium as 3.0 M or 1.6 M solutions in hexane, and methyllithium as a 1.6 M solution in hexane. All organolithium compounds were titrated before use.[49] The determination of the diastereomeric ratios was carried out by ^1H NMR spectroscopy (by integration of the methine signal of the newly generated stereocenter) or with analytical gas chromatography (Hewlett Packard HP 5890 II chromatograph with a 25 m HP1 column (for the dicarbamates) or on a HP 6890 chromatograph with a 25 m HP 1701 column (for the diols)). The *ee* values of the carbamates **11** were determined by ^1H NMR spectroscopy in the presence of the chiral shift reagent (+)-Eu(hfc)$_3$ or as their alcohols, **16**, by GC analyses of the corresponding (*S*)-1-phenylethylurethanes.[50]

***cis*-1,2-Cyclohexanedimethyl bis(2,2,4,4-tetramethyl-1,3-oxazolidine-3-carboxylate) (8)**: A solution of *cis*-1,2-cyclohexanedimethanol[23] (5.67 g, 39.4 mmol) in anhydrous THF (25 mL) was added dropwise to an ice-cooled suspension of sodium hydride (3.37 g, 112 mmol, 80% in mineral oil) in THF (40 mL). The reaction mixture was stirred for 30 min at room temperature. 2,2,4,4-Tetramethyl-1,3-oxazolidine-3-carbonyl chloride[24] (*Cby*Cl, 14.7 g, 76.9 mmol) in THF (25 mL) was added and the mixture was refluxed for 16 h. After the mixture was allowed to cool to room temperature, HCl (2N, 50 mL) and Et_2O (50 mL) were carefully added. The organic layer was separated and the aqueous solution extracted with Et_2O (3×50 mL). The collected extracts were kept over $NaHCO_3/Na_2SO_4$. The solvents were evaporated in vacuo and the crude product was purified by flash chromatography on silica gel (Et_2O/hexanes 1:2) to yield **8** (15.4 g, 88%) as a colorless solid. M.p. 119–121°C (hexanes); IR (KBr): $\tilde{\nu} =$ 1685 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$): $\delta = 1.30-1.70$ (m, 8H; CH_2), 1.42 (1.35), 1.42 (1.36) (s, 12H; $NC(CH_3)_2CH_2$), 1.56 (1.51) and 1.56 (1.52) (s, 12H; $NC(CH_3)_2O$), 2.00–2.30 (m, 2H; CH), 3.73 (s, 4H, $CH_2OC(CH_3)_2$), 3.99–4.21 (m, 4H, CH_2OCby); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 23.18$ (2C; CH_2), 25.32 (24.16) (4C; $NC(CH_3)_2CH_2$), 26.42 (2C; CH_2), 26.57 (4C; $NC(CH_3)_2O$), 36.88 (2C; CH), 59.60 (60.67) (2C; $NC(CH_3)_2CH_2$), 64.54 (2C; CH_2OCby), 76.16 (2C; $CH_2OC(CH_3)_2$), 95.92 (94.73) (2C; $NC(CH_3)_2O$), 152.81 (152.11) (2C; NC=O); $C_{24}H_{42}N_2O_6$ (454.61): calcd C 63.41, H 9.31; found C 63.42, H 9.32.

Deprotonation of carbamate 8 and preparation of substituted products 11: **General procedure:** Carbamate **8** (454 mg, 1.00 mmol) was dissolved in toluene (10 mL) under argon and (−)-sparteine (501 mg, 2.20 mmol) was added. The stirred solution was cooled to −78°C and *sec*-BuLi (2.1 mmol, 1.2–1.4M) was introduced by a syringe. The mixture was stirred for 4 h at −78°C and the electrophile (2.5 mmol) was then added at this temperature. The reaction mixture was stirred for a further 2 h before HCl (2N, 1 mL) was added at −78°C. The mixture was allowed to warm to room temperature, HCl (2N, 10 mL) and Et_2O (10 mL) were added, the layers were separated, and the aqueous phase was extracted with Et_2O ($3 \times$ 10 mL). The combined organic layers were stirred over $NaHCO_3/Na_2SO_4$, concentrated in vacuo, and the residue was purified by column chromatography on silica gel (Et_2O/hexanes 1:4 to 1:1) to give the substituted carbamates **11**.

[1*R*,2*S*,1(1*S*)]-1[D_1]-*cis*-1,2-Cyclohexanedimethyl bis(2,2,4,4-tetramethyl-1,3-oxazolidine-3-carboxylate) (11a): To a solution of **8** (227 mg, 0.50 mmol) and (−)-sparteine (**4**) (290 mg, 1.24 mmol) in toluene (8 mL) was added *sec*-BuLi (1.30M, 0.88 mL, 1.14 mmol). After treatment with CH_3CO_2D (0.09 mL, 1.55 mmol), the reaction mixture was allowed to warm to room temperautre for 16 h. Workup and purification on silica gel (Et_2O/hexanes 1:2 then 1:1) afforded **11a** (184 mg (81%), $[D_1] = 80\%$) as a colorless solid. M.p. 117°C (hexanes); IR (KBr): $\tilde{\nu} = 2140-2130$ (C–D), 1675 cm^{-1} (C=O); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.31-1.72$ (m, 8H; CH_2), 1.42 (1.36) (s, 12H; $NC(CH_3)_2CH_2$), 1.56 (1.52) (s, 12H; $NC(CH_3)_2O$), 2.12 (m, 2H; CH), 3.72 (s, 4H, $CH_2OC(CH_3)_2$), 4.02–4.19 (m, 3H; CHDO*Cby*, CH_2OCby); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 23.11$ (2C; CH_2), 25.26 (24.10) (4C; $NC(CH_3)_2CH_2$), 25.40 (26.60) (4C; $NC(CH_3)_2O$), 26.31 (2C; CH_2), 36.70 (CH), 36.79 (CH), 59.54 (60.61) (2C; $NC(CH_3)_2CH_2$), 64.14 (t; CHDO*Cby*), 64.46 (CH_2OCby), 76.32 (76.05) (2C; $CH_2O(CH_3)_2$), 95.87 (94.56) (2C; $NC(CH_3)_2O$), 153.79 (152.08) (2C; NC=O); $C_{24}H_{41}DN_2O_6$ (455.61): calcd C 63.27, H 9.51, N 6.15; found C 63.31, H 9.36, N 6.15.

[1*S*,1(1*R*,2*S*)]-1-[2-(2,2,4,4-Tetramethyl-1,3-oxazolidine-3-carbonyloxymethyl)cyclohexyl]-1-(trimethylstannyl)methyl 2,2,4,4-tetramethyl-1,3-oxazolidine-3-carboxylate (11b): Compound **8** (433 mg, 0.95 mmol) was deprotonated with *sec*-BuLi (1.19M, 1.85 mL, 2.20 mmol) in the presence of **4** (563 mg, 2.41 mmol). After 4 h at −78°C, trimethyltin chloride (577 mg in 1.28 mL toluene, 2.90 mmol) was added. After workup and column chromatography (Et_2O/hexanes 1:4 then 1:2) 84 mg (19%) of **8** were recovered and **11b** (381 mg (65%), $dr = 98{:}1$, $ee > 95\%$) was isolated as a colorless solid. M.p. 98–100°C (hexanes); $[\alpha]_D^{21} = +2.2$ ($c = 1.02$ in CH_2Cl_2); IR (KBr): $\tilde{\nu} = 1680-1650$ cm^{-1} (C=O); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.09$ (s, $^2J(H,^{117}Sn) = 51.0$ Hz , $^2J(H,^{119}Sn) = 52.2$ Hz, 9H; $Sn(CH_3)_3$), 0.85–1.98 (m, 8H; CH_2), 1.40, 1.34 (s, 12H; $NC(CH_3)_2CH_2$), 1.50, 1.53 (s, 12H; $NC(CH_3)_2O$), 2.08–2.27 (m, 1H; CH), 2.40 (tt, $^3J(H,H) = 3.6$ Hz, $^3J(H,H) = 12.6$ Hz, 1H; CH), 3.70, 3.71 (s, 4H, $CH_2OC(CH_3)_2$), 4.06–4.40 (m, 3H, CHO*Cby*, CH_2OCby); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -8.53$ (3C; $Sn(CH_3)_3$), 20.39 (CH_2), 25.24 (24.09) (4C; $NC(CH_3)_2CH_2$), 25.40 (26.55, 26.89) (4C; $NC(CH_3)_2O$), 25.98 (CH_2), 26.39 (CH_2), 27.90 (CH_2), 33.97 (CH), 41.79 (CH), 59.48 (60.56) (2C; $NC(CH_3)_2CH_2$), 61.43 (CH_2OCby), 73.73 (CHO*Cby*), 76.06 (75.82) (2C; $CH_2OC(CH_3)_2$), 95.80 (94.59) (2C; $NC(CH_3)_2O$), 152.25 (153.02, 153.12) (2C; NC=O); $C_{27}H_{50}N_2O_6Sn$ (617.39): calcd C 52.53, H 8.16; found C 52.51, H 8.14.

12b: ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.12$ (s, $Sn(CH_3)_3$).

***rac*-11b**: The reaction of **8** (504 mg, 1.11 mmol) with *sec*-BuLi (1.27M, 2.00 mL, 2.54 mmol) in the presence of TMEDA (314 mg, 2.70 mmol) and trimethyltin chloride (518 mg in 2.60 mL hexane, 2.60 mmol) gave *rac*-**11b**. Yield: 510 mg (75%), $dr = 99{:}1$; m.p. 117–120°C (hexanes).

[1*S*,1(1*R*,2*S*)]-1-[2-(2,2,4,4-Tetramethyl-1,3-oxazolidine-3-carbonyloxymethyl)cyclohexyl]-1-(tributylstannyl)methyl 2,2,4,4-tetramethyl-1,3-oxazolidine-3-carboxylate (11c): To a solution of **8** (450 mg, 0.99 mmol) in toluene (10 mL) were added *sec*-BuLi (1.23M, 1.85 mL, 2.27 mmol), **4** (577 mg, 2.46 mmol), and tributyltin chloride (0.80 mL, 968 mg, 2.97 mmol) at −78°C to afford **8** (yield: 113 mg (25%)) and, after a second chromatographic purification (Et_2O/hexanes 1:4), **11c** as a viscous oil. Yield: 318 mg (43%); $[\alpha]_D^{21} = -0.35$ ($c = 1.14$ in CH_2Cl_2); IR (film): $\tilde{\nu} = 2940$, 2910, 2850 (C–H), 1680, 1665 (C=O), 1455, 1440 (δ-C–H), 1385, 1365 (δ-CH_3), 1090, 1065 cm^{-1} (C-O-C); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.80-0.89$ (m, 6H; $SnCH_2$), 0.89 (t, $^3J(H,H) = 7.3$ Hz, 9H; $Sn(CH_2)_3CH_3$), 1.22–1.62 (m, 18H; $SnCH_2(CH_2)_2$, CH_2), 1.35 (1.40, 1.41) (s, 12H; $NC(CH_3)_2CH_2$), 1.54 (1.49, 1.50) (s, 12H; $NC(CH_3)_2O$), 1.72–1.98 (m, 2H; CH_2) 2.08–2.25 (m, 1H; CH), 2.41 (ddt, $^3J(H,H) = 3.3$ Hz, $^3J(H,H) = 12.6$ Hz, 1H; CH), 3.71, 3.72 (s, 4H, $CH_2OC(CH_3)_2$), 4.19–4.39 (m, 3H, CHO*Cby*, CH_2OCby); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 10.31$ (3C; $SnCH_2$), 13.58 (3C; $Sn(CH_2)_3CH_3$), 20.32 (CH_2), 25.28 (24.06, 24.27) (4C; $NC(CH_3)_2CH_2$), 25.34 (26.46, 26.59) (4C; $NC(CH_3)_2O$), 26.13 (CH_2), 26.96 (CH_2), 27.47 (3C; $SnCH_2CH_2CH_2CH_3$), 27.87 (CH_2), 29.05 (3C; $Sn(CH_2)_2CH_2CH_3$), 33.90 (CH), 42.16 (CH), 59.38 (60.52) (2C; $NC(CH_3)_2CH_2$), 61.40 (CH_2OCby), 73.16 (CHO*Cby*), 76.32 (76.06) (2C; $CH_2OC(CH_3)_2$), 95.84 (94.60) (2C; $C(CH_3)_2$), 153.09 (152.42) (2C; NC=O); $C_{36}H_{68}N_2O_6Sn$ (743.66): calcd C 58.14, H 9.22, N 3.77; found C 58.22, H 9.38, N 3.85.

***rac*-11c** : The same reaction with **8** (512 mg, 1.13 mmol), TMEDA (332 mg, 2.86 mmol), *sec*-BuLi (1.27M, 2.05 mL, 2.60 mmol), and tributyltin chloride (0.79 mL, 956 mg, 2.94 mmol) gave *rac*-**11c**. Yield: 651 mg (77%).

Methyl [2*R*,1(1*R*,2*S*)]-2-{1-[2-(2,2,4,4-tetramethyl-1,3-oxazolidine-3-carbonyloxy-methyl)cyclohexyl]}-2-(2,2,4,4-tetramethyl-1,3-oxazolidine-3-carbonyloxy)acetate (11d): Dicarbamate **8** (244 mg, 0.54 mmol) was deprotonated with *sec*-BuLi (1.30M, 0.96 mL, 1.25 mmol) in the presence of **4** (319 mg, 1.36 mmol). Carboxylation was carried out by bubbling a stream of dry CO_2 through the reaction solution for 10 min. After warming the mixture, treatment with HCl/Et_2O, and extraction, the collected organic layers were dried over Na_2SO_4. The Et_2O was evaporated and the residue was treated with a solution of CH_2N_2 in diethyl ether until it remained yellow. The solution was stirred for 30 min, silica gel (100 mg) was added, and the mixture was stirred for a further 15 min to destroy the excess CH_2N_2. Chromatographic purification (Et_2O/hexanes 1:2 then 1:1) yielded **8** (58 mg (24%)) and **11d** (175 mg (63%), $dr = 96{:}4$, $ee > 95\%$) as a colorless solid. M.p. 124–126°C (hexanes); $[\alpha]_D^{21} = +16.3$ ($c = 1.00$ in CH_2Cl_2); IR (KBr): $\tilde{\nu} = 1750$ (OC=O), 1700, 1685 cm^{-1} (C=O); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.22-1.99$ (m, 8H; CH_2), 1.39 (1.41) (s, 12H; $NC(CH_3)_2CH_2$), 1.54, 1.55 (1.53) (s, 12H; $NC(CH_3)_2O$), 2.06–2.24 (m, 1H; CH), 2.24–2.40 (m, 1H; CH), 3.71, 3.72(s, 4H; $CH_2OC(CH_3)_2$), 3.74 (s, 3H; OCH_3), 3.93–4.24 (m, 1H; CH_2OCby), 4.33 (t, $^2J(H,H) = {}^3J(H,H) =$ 10.1 Hz, 1H; CH_2OCby), 4.78 (d, $^3J(H,H) = 9.8$ Hz, 1H; CHO*Cby*); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 20.29$ (CH_2), 24.04 (25.19) (4C; $NC(CH_3)_2CH_2$), 24.72 (CH_2), 25.46 (CH_2), 26.64 (25.68) (4C; $NC(CH_3)_2O$), 27.43 (CH_2), 34.22 (CH), 41.08 (CH), 51.81 (OCH_3), 59.49 (60.61), 59.86 (61.04) (2C; $NC(CH_3)_2CH_2$), 61.90 (CH_2OCby), 74.88 (CHO*Cby*), 76.29 (76.04), 76.39 (2C; $CH_2OC(CH_3)_2$), 95.85 (94.61), 96.21 (94.94) (2C; $NC(CH_3)_2O$), 151.99 (151.02), 152.77 (151.79) (2C; NC=O); $C_{26}H_{44}N_2O_8$ (512.64): calcd C 60.92, H 8.65, N 5.46; found C 60.96, H 8.83, N 5.56.

12d: ^1H NMR (300 MHz, $CDCl_3$): $\delta = 5.03$ (d, $^3J(H,H) = 6.2$ Hz, CHO-*Cby*).

***rac*-11d** : The racemic ester was prepared in 70% yield (160 mg, $dr = 98{:}2$) from **8** (225 mg, 0.48 mmol), TMEDA (127 mg, 1.09 mmol), *sec*-BuLi (0.88 mL, 1.30M, 1.14 mmol), and CO_2 as described above.

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The same reaction of **8** (236 mg, 0.52 mmol) with TMEDA (151 mg, 1.30 mmol) and *sec*-BuLi (1.30 M, 0.90 mL, 1.17 mmol), however with the introduction of CO_2 after 3 h at $-78\,^{\circ}C$ gave *rac*-**11d** in 85% yield (217 mg, *dr* = 91:9).

Without a diamine: The deprotonation of **8** (239 mg, 0.53 mmol) with *sec*-BuLi (1.30 M, 0.95 mL, 1.29 mmol) in Et_2O (10 mL), resulted in *rac*-**11d** (49 mg, *dr* = 40:60; 18% yield) and starting material **8** (171 mg; 72%).

Methyl chloroformate as the electrophile: According to the general procedure, **8** (441 mg, 0.97 mmol) was metallated with *sec*-BuLi (1.80 mL, 1.23 M, 2.21 mmol) and **4** (567 mg, 2.42 mmol) in toluene (10 mL). Addition of methyl chloroformate (0.22 mL, 274 mg, 2.90 mmol), workup, and purification gave **11d** (230 mg; 46%, *dr* = 96:4, *ee* > 95%) and **8** (157 mg; 36%).

By the use of the same procedure, *rac*-**11d** (206 mg; 40%, *dr* = 88:12) was formed by the reaction of **8** (453 mg, 1.00 mmol) with TMEDA (293 mg, 2.52 mmol), *sec*-BuLi (1.23 M, 1.87 mL, 2.30 mmol), and methyl chloroformate (0.23 mL, 281 mg, 2.97 mmol). Additionally, the starting material **8** (128 mg; 28%) was recovered.

Dimethyl carbonate as the electrophile: To a solution of **8** (452 mg, 0.99 mmol), **4** (583 mg, 2.49 mmol), and *sec*-BuLi (1.30 M, 1.75 mL, 2.28 mmol) in toluene (10 mL) was added dimethyl carbonate (0.25 mL, 267 mg, 2.97 mmol). Workup and purification afforded **11d** (125 mg; 25%, *dr* = 96:4, *ee* > 95%) and **8** (279 mg; 62%).

[1*S*,1(1*R*,2*S*)]-1-[2-(2,2,4,4-Tetramethyl-1,3-oxazolidine-3-carbonyloxymethyl)cyclohexyl]ethyl 2,2,4,4-tetramethyl-1,3-oxazolidine-3-carboxylate (11e): Dicarbamate **8** (2.03 g, 9.48 mmol) was deprotonated with *sec*-BuLi (1.03 M, 9.20 mL, 9.48 mmol) in the presence of **4** (2.31 g, 9.85 mmol). Addition of methyl iodide (1.67 g, 11.79 mmol), warming to room temperature for 16 h, workup, and column chromatography (Et_2O/hexanes = 1:4), gave the starting dicarbamate **8** (156 mg (8%)) and well as **11e** (1.47 g (70%), *ee* > 95%) as a colorless oil. $[\alpha]_D^{21} = +28.1$ (*c* = 0.79 in CH_2Cl_2); IR (film): $\tilde{\nu} = 1660\ cm^{-1}$ (C=O); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.08-2.36$ (m, 10H; 2CH, $4CH_2$), 1.24 (d, $^3J(H,H) = 6.2$ Hz, 3H; CH_3), 1.39 (1.34) (s, 12H; $NC(CH_3)_2CH_2$), 1.55 (1.50) (s, 12H; $NC(CH_3)_2O$), 3.71, 3.72, (s, 4H; $CH_2OC(CH_3)_2$), 3.98–4.20 (m, 1H; CH_2OCby), 4.29 (t, $^2J(H,H) = {}^3J(H,H) = 11.0$ Hz, 1H; CH_2OCby), 4.87 (dd, $^3J(H,H) = 9.1$ Hz, $^3J(H,H) = 6.2$ Hz, 1H; $CHOCby$); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 19.17$ (CH_3), 20.52 (CH_2), 24.77 (CH_2), 25.27 (24.09) (4C; $NC(CH_3)_2CH_2$), 25.27 (26.59) (4C; $NC(CH_3)_2O$), 25.78 (CH_2), 27.16 (CH_2), 34.47 (CH), 45.05 (CH), 59.44 (60.49) (2C, $NC(CH_3)_2CH_2$), 62.07 (CH_2OCby), 71.74 ($CHOCby$), 76.33 (76.12) (2C; $CH_2OC(CH_3)_2$), 94.62 (94.19), 95.87 (95.47) (2C; $NC(CH_3)_2O$), 152.75 (152.05) (2C; NC=O); $C_{25}H_{44}N_2O_6$ (468.63): calcd C 64.07, H 9.46; found C 64.08, H 9.47.

***rac*-11e**: The reaction of **8** (455 mg, 1.00 mmol) and *sec*-BuLi (2.00 mL, 1.25 M, 2.50 mmol) in the presence of TMEDA (295 mg, 2.54 mmol) and methyl iodide (0.19 mL, 431 mg, 3.04 mmol) gave *rac*-**11e** (238 mg, 51%).

[1*S*,1(1*R*,2*S*)]- and [1*R*,1(1*R*,2*S*)]-1-[2-(2,2,4,4-Tetramethyl-1,3-oxazolidine-3-carbonyl-oxymethyl)cyclohexyl]-but-3-enyl 2,2,4,4-tetramethyl-1,3-oxazolidine-3-carboxylate (11f and 12f): To a solution of **8** (1.025 g, 2.25 mmol) in toluene (20 mL) were added *sec*-BuLi (3.00 mL, 1.40 M, 4.20 mmol), **4** (1.140 g, 4.27 mmol), and allyl bromide (0.44 mL, 623 mg, 5.15 mmol). After flash chromatography (Et_2O/hexanes 1:4), **8** (241 mg; 24%) was recovered and a 68:32 mixture of **11f** and **12f** (651 mg, 59%) was obtained as a colorless oil. IR (film): $\tilde{\nu} = 3050$ (C=C–H), 1680 (C=O), 1630 cm^{-1} (C=C); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.08-2.00$ (m, 9H; CH, $4CH_2$), 1.39 (1.34) (s, 12H; $NC(CH_3)_2CH_2$), 1.54 (1.49) (s, 12H; $NC(CH_3)_2O$), 2.15–2.43 (m, 2H; $CH_2CH{=}CH_2$), 2.44–2.63 (m, 1H; CH), 3.71 (s, 4H; $CH_2OC(CH_3)_2$), 4.02–4.22 (m, 1H; CH_2OCby), 4.32 (t, $^2J(H,H) = {}^3J(H,H) = 11.1$ Hz, 1H; CH_2OCby), 4.94 (m, $^3J(H,H) = 6.3$ Hz, 1H; $CHOCby$), 5.01–5.13 (m, 2H; $CH_2CH{=}CH_2$), 5.81 (ddd, $^3J(H,H) = 11.1$ Hz, $^3J(H,H) = 17.5$ Hz, 1H; $CH_2CH{=}CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 20.14$ (CH_2), 24.50 (CH_2), 25.34 (24.14) (4C; $NC(CH_3)_2CH_2$), 25.90 (CH_2), 26.88 (25.36) (4C; $NC(CH_3)_2O$), 27.13 (CH_2), 34.89 (CH), 37.30 ($CH_2CH{=}CH_2$), 42.80 (CH), 59.55 (60.59) (2C; $NC(CH_3)_2CH_2$), 61.79 (CH_2OCby), 74.79 ($CHOCby$), 76.32 (76.05) (2C; $CH_2OC(CH_3)_2$), 95.78 (94.60) (2C; $NC(CH_3)_2O$), 117.67 ($CH_2CH{=}CH_2$), 133.95 ($CH_2CH{=}CH_2$), 152.72 (152.21) (2C; NC=O); $C_{27}H_{46}N_2O_6$, mixture (494.67): calcd C 65.56, H 9.37, N 5.66; found C 65.47, H 9.36, N 5.75.

***rac*-11f**: The same reaction with **8** (421 mg, 0.93 mmol), TMEDA (275 mg, 2.37 mmol), *sec*-BuLi (1.70 mL, 1.25 M, 2.13 mmol), and allyl bromide (0.24 mL, 336 mg, 2.78 mmol) afforded *rac*-**11f** (311 mg; 68%, *dr* = 70:30) and **8** (14 mg; 3%).

[1*S*,1(1*R*,2*S*)]- and [1*R*,1(1*R*,2*S*)]-1-[2-(2,2,4,4-Tetramethyl-1,3-oxazolidine-3-carbonyl-oxymethyl)cyclohexyl]-2-phenylethyl 2,2,4,4-tetramethyl-1,3-oxazolidine-3-carboxylate (11g and 12g): Carbamate **8** (420 mg, 0.92 mmol) was deprotonated with *sec*-BuLi (1.63 mL, 1.30 M, 2.12 mmol) in the presence of **4** (544 mg, 2.32 mmol) and then benzyl bromide (0.34 mL, 496 mg, 2.90 mmol) was added. After purification (Et_2O/hexanes 1:4), **8** (105 mg; 25%) was recovered and a 74:26 mixture of **11g** and **12g** (223 mg; 44%) was obtained as a colorless oil. IR (film): $\tilde{\nu} = 3060$, 3040 (C=C–H), 1680 (C=O), 1590, 1480 (C=C), 750, 690 cm^{-1} (C=C–H); $C_{31}H_{48}N_2O_6$, mixture (544.73): calcd C 68.35, H 8.88, N 5.14; found C 68.13, H 8.81, N 5.07.

11g: ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.03-1.96$ (m, 9H; CH, $4CH_2$), 1.26 (1.31) (s, 12H; $NC(CH_3)_2CH_2$), 1.41 (1.44) (s, 12H; $NC(CH_3)_2O$), 2.18 (m, 1H; CH), 2.75 (dd, $^2J(H,H) = 14.1$ Hz, $^3J(H,H) = 8.4$ Hz, 1H; CH_2Ph), 3.04 (dd, $^3J(H,H) = 4.2$ Hz, 1H; CH_2Ph), 3.62 (3.53) (s, 4H; $CH_2OC(CH_3)_2$), 4.19–4.44 (m, 2H; CH_2OCby), 5.05 (dd, $^3J(H,H) = 8.4$ Hz, 1H; $CHOCby$), 7.08–7.38 (m, 5H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 20.08$ (CH_2), 24.50 (CH_2), 25.19 (23.98) (4C; $NC(CH_3)_2CH_2$), 25.33 (26.58) (4C; $NC(CH_3)_2O$), 25.90 (CH_2), 27.12 (CH_2), 33.93 (CH), 39.11 (CH_2Ph), 43.80 (CH), 59.30 (60.55) (2C, $NC(CH_3)_2CH_2$), 61.73 (CH_2OCby), 75.85 ($CHOCby$), 76.25 (76.00) (2C; $CH_2OC(CH_3)_2$), 95.70 (94.48) (2C; $NC(CH_3)_2O$), 126.09 (*p*-CH, arom.), 127.95 (*o*-CH, arom.), 129.43 (*m*-CH, arom), 137.58 (C_{quart}, arom.), 151.91 (152.68) (2C; NC=O).

12g: ^1H NMR (300 MHz, $CDCl_3$): $\delta = 4.00-4.19$ (m, 2H; CH_2OCby), 5.14 (dd, $^3J(H,H) = 5.5$ Hz, $^3J(H,H) = 7.6$ Hz, $CHOCby$); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 20.28$ (CH_2), 27.69 (CH_2), 35.91 (CH), 38.78 (CH_2Ph), 43.39 (CH), 128.04 (*o*-CH, arom.), 129.36 (*m*-CH, arom), 137.68 (C_{quart}, arom.).

***rac*-11g**: The reaction of **8** (391 mg, 0.86 mmol), TMEDA (248 mg, 2.13 mmol), *sec*-BuLi (1.52 mL, 1.30 M, 1.98 mmol), and benzyl bromide (0.32 mL, 460 mg, 2.69 mmol) gave the racemate in 58% yield (271 mg, *dr* = 85:15); **8** was recovered in 7% yield (27 mg).

[2*R*,1(1*R*,2*S*)]- and [2*S*,1(1*R*,2*S*)]-2-{1-[2-(2,2,4,4-Tetramethyl-1,3-oxazolidine-3-carbon-yloxymethyl)cyclohexyl]}-2-(2,2,4,4-tetramethyl-1,3-oxazolidine-3-carbonyloxy)ethanal (11h and 12h): To a solution of **8** (452 mg, 0.99 mmol) and **4** (581 mg, 2.48 mmol) in toluene (10 mL) was added *sec*-BuLi (1.80 mL, 1.26 M, 2.27 mmol). The mixture was treated with ethyl formate (0.24 mL, 221 mg, 2.98 mmol) and then with $H_2PO_4^-/HPO_4^{2-}$ buffer (1.0 mL, pH = 7). Workup and purification (silica gel, Et_2O/hexanes 1:4 to 1:1) afforded **8** (120 mg, 27%) and a 55:45 mixture of **11h** and **12h** (142 mg, 30%) as a viscous oil. IR (film): $\tilde{\nu} = 2960$, 2920, 2850 (C–H), 1730, 1700–1680 (C=O), 1460, 1440 (C–H), 1405, 1365 (-CH_3), 1090, 1060 cm^{-1} (C-O-C); $C_{25}H_{42}N_2O_7$, mixture (482.62): calcd C 62.22, H 8.77, N 5.80; found C 62.26, H 8.83, N 5.54.

11h: ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.18-2.44$ (m, 10H; 2CH, $4CH_2$), 1.41 (1.36) (s, 12H; $NC(CH_3)_2CH_2$), 1.55 (1.58) (s, 12H; $NC(CH_3)_2O$), 3.72 (3.73, 3.76, 3.78) (s, 4H; $CH_2OC(CH_3)_2$), 4.15 (m, 2H; CH_2OCby), 4.75 (d, $^3J(H,H) = 10.2$ Hz, 1H; $CHOCby$), 6.00 (s, 1H; CHO); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 20.25$ (CH_2), 24.73 (CH_2), 25.21 (24.03) (4C; $NC(CH_3)_2CH_2$), 25.41 (26.59) (4C; $NC(CH_3)_2O$), 25.78 (CH_2), 27.70 (CH_2), 34.20 (CH), 39.49 (CH), 59.51 (60.62), 59.98 (61.23) (2C; $NC(CH_3)_2CH_2$), 61.70 (CH_2OCby), 76.29 (75.99) (2C; $CH_2OC(CH_3)_2$), 79.39 ($CHOCby$), 95.87 (94.69), 96.31 (94.89) (2C; $NC(CH_3)_2O$), 151.77 (152.62) (2C; NC=O), 198.14 (CHO).

12h: ^1H NMR (300 MHz, $CDCl_3$): $\delta = 4.34$ (t, $^3J(H,H) = 10.5$ Hz, $^2J(H,H) = 10.5$ Hz; CH_2OCby), 5.07 (d, $^3J(H,H) = 5.2$ Hz; $CHOCby$), 6.02 (s, CHO); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 27.19$ (CH_2), 36.43 (CH), 39.70 (CH), 62.41 (CH_2OCby).

When the stirring time was reduced to 10 min after addition of the electrophile, the reaction of **8** (243 mg, 0.53 mmol) with **4** (313 mg, 1.33 mmol), *sec*-BuLi (1.25 M, 0.98 mL, 1.22 mmol), and ethyl formate (0.13 mL, 120 mg, 1.61 mmol) gave **8** (134 mg; 56%) and **11h** (41 mg; 16%, *dr* = 70:30). $[\alpha]_D^{21} = +17.8$ (*c* = 2.05 in CH_2Cl_2).

***rac*-11h**: Dicarbamate **8** (249 mg, 0.55 mmol) was treated with TMEDA (160 mg, 1.38 mmol), *sec*-BuLi (1.00 mL, 1.28 M 1.28 mmol), and ethyl formate (0.14 mL, 129 mg, 1.74 mmol). The mixture was stirred for 1 h, and then quenched with the $H_2PO_4^-/HPO_4^{2-}$ buffer to give ***rac*-11h** (120 mg; 45% yield, *dr* = 90:10).

[2*R*,1(1*R*,2*S*)]-2-{1-[2-(2,2,4,4-Tetramethyl-1,3-oxazolidine-3-carbonyloxymethyl)cyclohexyl]}-2-(2,2,4,4-tetramethyl-1,3-oxazolidine-3-carbonyloxy)-1-phenylethan-1-one (11i): Dicarbamate **8** (430 mg, 0.94 mmol) was deprotonated with *sec*-BuLi (1.25 M, 1.73 mL, 2.16 mmol) in the presence of **4** (554 mg, 2.36 mmol). After addition of methyl benzoate (0.33 mL, 360 mg, 2.64 mmol), workup, and column chromatography (Et_2O/hexanes 1:4 then 1:1), the dicarbamate **8** (142 mg; 33%) was recovered and **11i** (220 mg; 42%, *dr* = 85:15) was obtained as a colorless oil. $[\alpha]_D^{21} = +21.5$ ($c = 0.52$ in CH_2Cl_2); IR (film): $\tilde{\nu} = 3060$, 3040 (C=C−H), 1690–1670 (C=O), 1590, 1570 (C=C), 735, 700 cm^{-1} (C=C−H); $C_{31}H_{46}N_2O_7$ mixture (558.71): calcd C 66.64, H 8.30, N 5.01; found C 66.82, H 8.12, N 4.92.

11i: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.06-2.53$ (m, 10H; 2CH, 4CH_2), 1.41 (1.34) (s, 12H; NC(CH_3)$_2$$CH_2$), 1.53 (1.50) (s, 12H; NC(CH_3)$_2$O), 3.72 (3.69) (s, 4H; CH_2OC(CH_3)$_2$), 3.93–4.47 (m, 2H; CH_2O*Cby*), 5.80 (d, ^3J(H,H) = 10.2 Hz, 1H; CHO*Cby*), 7.11–7.27 (m, ^3J(H,H) = 7.4 Hz, ^4J(H,H) = 1.4 Hz, 2H; *m*-CH, arom.), 7.43–7.58 (m, ^4J(H,H) = 1.4 Hz, 2H; *p*-CH, arom.), 7.96–8.02 (m, 2H; *o*-CH, arom.); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 19.98$ (CH_2), 23.08 (CH_2), 24.87 (24.09) (4C; NC(CH_3)$_2$$CH_2$), 25.44 (26.62) (4C; NC(CH_3)$_2$O), 26.35 (CH_2), 27.56 (CH_2), 33.87 (CH), 41.48 (CH), 59.51 (60.49) (2C; N*C*(CH_3)$_2$$CH_2$), 61.73 ($CH_2$O*Cby*), 74.84 (CHO*Cby*), 76.29 (76.06) (2C; *C*H_2OC(CH_3)$_2$), 94.62 (95.77) (2C; N*C*(CH_3)$_2$O), 128.39 (*o*-CH, arom.), 128.79 (*m*-CH, arom.), 133.21 (*p*-CH, arom.), 136.95 (C_{quart}, arom.), 151.94 (152.58) (2C; NC=O), 197.23 (C=O).

12i: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.97$ (d, ^3J(H,H) = 3.8 Hz; CHO*C-by*); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 24.57$ (CH_2), 26.05 (CH_2), 27.93 (CH_2), 37.03 (CH), 42.09 (CH), 62.10 (CH_2O*Cby*), 77.10 (CHO*Cby*), 199.05 (C=O).

***rac*-11i**: The reaction of **8** (423 mg, 0.93 mmol) with *sec*-BuLi (1.25 M, 1.71 mL, 2.14 mmol) in the presence of TMEDA (268 mg, 2.30 mmol) and methyl benzoate (0.32 mL, 354 mg, 2.60 mmol) yielded *rac*-**11i** (300 mg; 58%, *dr* = 90:10) and **8** (23 mg; 6%).

Methyl {2*R*,2[1*S*,2*R*(1*S*)]}- and {2*S*,2[1*S*,2*R*(1*S*)]}-{2[2(1D)]}-2-{1-[2-(2,2,4,4-tetramethyl-1,3-oxazolidine-3-carbonyloxymethyl)cyclohexyl]}-2-(2,2,4,4-tetramethyl-1,3-oxazolidine-3-carbonyloxy)acetate (13 and 14): The reaction of **11a** (125 mg, 0.27 mmol, $[D_1] = 99\%$, recovered from deprotonation reactions of **11a** ($[D_1] = 93\%$)), with *sec*-BuLi (1.30 M, 0.55 mL, 0.72 mmol), **4** (195 mg, 0.83 mmol), and CO_2 yielded **13** (5 mg (4%), *dr* of **13** ($[D_1] = 99\%$)/**14** ($[D_1] = 76\%$) = 73:27) as a colorless oil. **11a** was recovered in 75% yield (92 mg, $[D_1] > 99\%$). **13:** ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.03$ (d, ^3J(H,H) = 5.7 Hz; CHO*Cby*); **14:** ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 4.81$ (d, ^3J(H,H) = 9.8 Hz; CHO*Cby*).

Methyl {2*S*,2[1*S*,2*R*(1*S*)]}-{2[2(1D)]}-2-{1-[2-(2,2,4,4-tetramethyl-1,3-oxazolidine-3-carbonyloxymethyl)cyclohexyl]}-2-(2,2,4,4-tetramethyl-1,3-oxazolidine-3-carbonyloxy)-acetate (14): Compound **11a** (245 mg, 0.54 mmol, $[D_1] = 93\%$), derived from a second deprotonation and deuteration of **11a** ($[D_1] = 80\%$), was treated with *sec*-BuLi (1.27 M, 0.98 mL, 1.24 mmol) in the presence of TMEDA (157 mg, 1.35 mmol) and carboxylated with CO_2. After esterification and purification, **14** (218 mg (79%), *dr* = 96:4, *ee* > 95%, $[D_1] = 96\%$) was obtained as a colorless solid. M.p. 123–125 °C (hexanes); $[\alpha]_D^{21} = +16.9$ ($c = 1.04$ in CH_2Cl_2); IR (KBr): $\tilde{\nu} = 2960$, 2920, 2860, 2840 (C−H), 2160 (C-D), 1740 (OC=O), 1685, 1675 (C=O), 1405, (-CH_3), 1095, 1055 cm^{-1} (C-O-C); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.20-1.98$ (m, 8H; CH_2), 1.40 (1.41) (s, 12H; NC(CH_3)$_2$$CH_2$), 1.54, (1.53, 1.55) (s, 12H; NC(CH_3)$_2$O), 2.06–2.23 (m, 1H; CH), 2.24–2.41 (m, 1H; CH), 3.72 (s, 4H; CH_2OC(CH_3)$_2$), 3.74 (s, 3H; OCH_3), 4.13 (m, 1H; CHDO*Cby*), 4.81 (d, ^3J(H,H) = 9.8 Hz, 1H; CHO*Cby*); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta =$ 20.32 (CH_2), 24.02 (CH_2), 23.96 (24.06), 25.17 (25.04, 25.31), (4C; NC(CH_3)$_2$$CH_2$), 25.48 ($CH_2$), 26.66 (24.73, 25.68) (4C; NC(CH_3)$_2$O), 27.43 (CH_2), 34.14 (CH), 41.08 (CH), 51.83 (OCH_3), 59.51 (60.59), 59.88 (61.06) (2C; N*C*(CH_3)$_2$$CH_2$), 61.60 (CHDO*Cby*), 74.88 (CHO*Cby*), 76.29 (76.04), 76.60 (2C; *C*H_2OC(CH_3)$_2$), 95.87 (94.59), 96.21 (94.96) (2C; N*C*(CH_3)$_2$O), 151.98 (151.00), 152.72 (151.78) (2C; NC=O); $C_{26}H_{45}N_2O_8$ (513.65): calcd C 60.80, H 8.83, N 5.45; found C 60.86, H 8.70, N 5.58.

Kinetic resolution of *rac*-11a (*ent*-14): The reaction of *rac*-**11a** (205 mg, 0.45 mol, $[D_1] = 97\%$, derived from the lithiodestannylation and deuteration of **11c**) with *sec*-BuLi (1.31 M, 0.69 mL, 0.90 mmol) in the presence of (−)-sparteine (233 mg, 0.99 mmol), afforded, after carboxylation with CO_2, **11a** (130 mg (63%), $[D_1] = 97\%$, *dr* = 93:17, *ee* = 36%) and *ent*-**14** (58 mg (25%), $[D_1] = 94\%$, *dr* = 88:12, *ee* > 95%).

Lithiodestannylation of 11b and 11c: Preparation of the substituted carbamates 11a, 11d, and 11e: General procedure: To a stirred solution of carbamate **11b** or **11c** (*dr* > 98:2, *ee* > 95%, 0.50 mmol) in Et_2O (10 mL) under argon at −78 °C was added a solution of *n*-butyllithium (2.3 mmol, 1.6–3.0 M) with a syringe. The mixture was stirred for 1–2 h at −78 °C, the electrophile (2.5 mmol) was added, and the reaction mixture stirred for a further 1–2 h. HCl, (2 N, 1 mL) was added at −78 °C and the mixture was allowed to warm to room temperature. HCl (2 N, 5 mL) and Et_2O (5 mL) were added, the layers were separated, and the aqueous phase was extracted with Et_2O (3 × 5 mL). The combined extracts were stirred over $NaHCO_3$/Na_2SO_4, concentrated in vacuo, and the residue was purified by column chromatography on silica gel (Et_2O/hexanes 1:1) to yield the substituted carbamates **11**.

Lithiodestannylation of 11b: A mixture of **11b** (327 mg, 0.53 mmol) and *n*BuLi (0.41 mL, 3.0 M, 1.23 mmol) in Et_2O (7 mL) was stirred at −78 °C for 2 h. The mixture was treated with CO_2 and esterified to give **11d** (252 mg; 93%, *dr* = 98:2, *ee* > 95%). $[\alpha]_D^{21} = +17.0$ ($c = 1.01$ in CH_2Cl_2).

The reaction of **11b** (974 mg, 1.58 mmol) with *n*BuLi (2.00 mL, 1.6 M, 3.20 mmol) and methyl iodide (0.21 mL, 427 mg, 3.36 mmol) afforded **11e** (560 mg; 76%). $[\alpha]_D^{21} = +31.8$ ($c = 1.07$ in CH_2Cl_2).

Lithiodestannylation of 11c: Carbamate **11c** (271 mg, 0.36 mmol) was allowed to react with *n*BuLi (0.28 mL, 3.00 M, 0.84 mmol) for 2 h. The mixture was treated with CO_2 and esterified. Workup and purification gave tetrabutyltin (125 mg; 100%) and **11d** (171 mg; 93%, *dr* = 98:2, *ee* > 95%). $[\alpha]_D^{21} = +17.2$ ($c = 1.00$ in CH_2Cl_2).

A solution of **11c** (30 mg, 0.50 mmol) in Et_2O was treated with *n*BuLi (0.50 mL, 3.0 M, 1.50 mmol) and the mixture was stirred for 3 h at −78 °C. CH_3CO_2D (0.09 mL, 1.55 mmol) dissolved in Et_2O (5 mL) was added and the reaction mixture was allowed to warm to room temperature and stirred for 16 h. Column chromatography yielded **11a** (222 mg; 98%, $[D_1] = 97\%$) and tetrabutyltin (139 mg; 80%).

Kinetic resolution of the tributylstannane 11c: Stannane **11c** (0.38, 0.41, or 0.87 mmol, respectively) was dissolved in Et_2O (7 mL) and treated with MeLi (1.64 M, 0.74 mmol, 0.82 mmol, and 1.47 mmol) and (−)-sparteine (0.83 mmol, 0.91 mmol, and 1.80 mmol) for 30 min, 60 min, and 140 min, respectively. The mixture was treated with CO_2 and the crude acid was then esterified. Workup, as described for the preparation of **11d**, and column chromatography (silica gel, Et_2O/hexanes 1:3) gave tributylmethyltin, stannane *ent*-**11c**, and ester **11d** (*dr* > 99:1) (Table 3).

Deprotection of the dicarbamates 11: Method A:[7, 24] A solution of a dicarbamate **11** (1.00 mmol) and methanesulfonic acid (1.00 mmol) in methanol (10 mL) was refluxed for 3 h. The solvent was removed under reduced pressure and the residue purified on silica gel (90 g, EtOAc/cyclohexane 1:2 to pure EtOAc) to yield the bisurethanes **15**. The diols **16** were obtained by refluxing **15** (1.00 mmol) with K_2CO_3 (0.50 mmol) in methanol (10 mL) for 3 h or by adding K_2CO_3 or NaOH (0.50 mmol) to the above reaction mixture and refluxing for a further 3 h. Concentration and column chromatography (silica gel, Et_2O/hexanes 2:1 to pure EtOAc) afforded the analytically pure diols.

Table 3. Kinetic resolution of the tributylstannane **11c**.

11c [mg]	MeLi [mL] (equiv)	**4** [mg] (equiv)	Time [min]	Yield **11d** [%] (*ee* [%])[a]	Yield *ent*-**11c** [%] (*ee* [%])[b]	Bu_3MeSn yield [%]
282	0.45 (1.9)	194 (2.2)	30	16 (52)	63 (13)	16
308	0.82 (2.0)	214 (2.2)	60	32 (48)	54 (27)	45
651	0.92 (1.7)	422 (2.1)	140	53 (44)	33 (60)	67

[a] Determined by ^{1}H NMR shift experiments with (+)-Eu(hfc)$_3$ (32 mol%). [b] Determined by comparing the $[\alpha]_{365}^{21}$ with that of **11c**.

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***cis*-1,2-Cyclohexanedimethyl bis[*N*-(2-hydroxy-1,1-dimethylethyl)carbamate] (15a)**: The reaction of **8** (314 mg, 0.69 mmol) with methanesulfonic acid (69 mg, 0.72 mmol) for 3 h yielded **15** (231 mg (89%)) as a colorless solid. M.p. 93–95 °C (EtOAc); IR (KBr): $\tilde{\nu}$ = 3470, 3420 (N–H), 3355, 3310 (O–H), 2980, 2940, 2870 (C–H), 1695 (C=O), 1550 (N–H), 1365 (-CH_3), 1105, 1070 cm^{-1} (C-O); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27, 1.28 (s, 12H; $C(CH_3)_2$), 1.32–1.64 (m, 8H; CH_2), 1.94–2.09 (m, 2H; CH), 3.24–3.51 (br, 2H; NH), 3.57 (d, ^3J(H,H) = 11.3 Hz, 2H; $C(CH_3)_2CH_2OH$), 3.63 (d, 2H; $C(CH_3)_2CH_2OH$), 3.92 (dd, ^2J(H,H) = 11.0 Hz, ^3J(H,H) = 6.4 Hz, 2H; CH_2OH), 4.12 (dd, ^3J(H,H) = 7.6 Hz, 1H; CH_2OH), 4.84–5.16 (br, 2H; OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.42 (2C; CH_2), 24.36 (24.20) (4C; $C(CH_3)_2$), 26.82 (2C; CH_2), 38.60 (2C; CH), 54.19 (2C; $C(CH_3)_2$), 65.34 (2C; CH_2OH), 69.73 (2C; $C(CH_3)_2CH_2OH$), 156.23 (2C; NC=O); $C_{18}H_{34}N_2O_6$ (374.48): calcd C 57.73, H 9.15, N 7.48; found C 58.04, H 9.26, N 7.64.

Methyl [1*R*,1(1*R*,2*S*)]-{2-[*N*-(2-hydroxy-1,1-dimethylethyl)carbamoyloxymethyl]cyclohexyl]}-2-[*N*-(2-hydroxy-1,1-dimethylethyl)carbamoyloxy]-acetate (15d): A mixture of **11d** (312 mg, 0.61 mmol, *dr* = 96:4) and methanesulfonic acid (44 mg, 0.46 mmol) in methanol was refluxed for 6 h to afford **15d** (248 mg; 94%, *dr* > 98:2) as a colorless solid. M.p. 94–96 °C (EtOAc); $[\alpha]_D^{21}$ = –0.7 (*c* = 1.02 in CH_2Cl_2), +23.3 (*c* = 1.01 in MeOH); IR (KBr): $\tilde{\nu}$ = 3400 (N–H), 3300 (O–H), 2985, 2940, 2880 (C–H), 1750 (OC=O), 1700 (C=O), 1545 (N–H), 1375 (-CH_3), 1060 cm^{-1} (C–O); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.17–1.54 (m, 6H; CH_2), 1.28 (1.27), 1.29 (1.30) (s, 12H; $C(CH_3)_2$), 1.67–1.91 (m, 1H; CH), 1.95–2.24 (m, 1H; CH), 3.55 (3.36, 3.40, 3.57) (s, 4H; $C(CH_3)_2CH_2OH$), 3.76 (s, 3H; OCH_3), 3.87 (m, 1H; CH_2OH), 4.35 (dd, ^2J(H,H) = 11.0 Hz, ^3J(H,H) = 7.1 Hz, 1H; CH_2OH), 5.13 (d, ^3J(H,H) = 6.9 Hz, 1H; CHOH), 5.57 (br, 2H, OH) 6.09 (br, 2H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.96 (2C; CH_2), 23.84 (23.56), 23.96 (25.23) (4C; $C(CH_3)_2$), 24.50 (CH_2), 25.48 (CH_2), 27.83 (CH_2), 34.37 (CH), 41.04 (CH), 52.13 (OCH_3), 54.29, 54.52 (2C; $C(CH_3)_2$), 63.52 (CH_2OH), 68.37 (69.05), 69.82 (69.42) (2C; $C(CH_3)_2CH_2OH$), 74.20 (CHOH), 154.87, 156.39 (2C; NC=O), 171.52 (OC=O); $C_{20}H_{36}N_2O_8$ (432.51): calcd C 55.54, H 8.39, N 6.48; found C 55.80, H 8.76, N 6.20.

[1*S*,1(1*R*,2*S*)]-15d: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.05 (d, ^3J(H,H) = 7.6 Hz; CHOH).

[1*S*,1(1*R*,2*S*)]-1-{2[*N*-(2-Hydroxy-1,1-dimethylethyl)carbamoyloxymethyl]-cyclohexyl}-ethyl *N*-(2-hydroxy-1,1-dimethylethyl)carbamate (15e): The methyl-substituted bisurethane **15e** was obtained as a colorless solid in 80% yield (325 mg) by heating **11e** (504 mg, 1.07 mmol) with methanesulfonic acid (131 mg, 1.36 mmol) for 3 h. M.p. 91–92 °C (EtOAc); $[\alpha]_D^{21}$ = +26.8 (*c* = 1.03 in CH_2Cl_2); IR (KBr): $\tilde{\nu}$ = 3400 (N–H), 3300 (O–H), 2970, 2935, 2870 (C–H), 1720, 1700, 1680 (C=O), 1545, 1510 (N–H), 1390 (-CH_3), 1100, 1060 cm^{-1} (C-O); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.13–1.56 (m, 6H; CH_2), 1.18 (d, ^3J(H,H) = 6.2 Hz, 3H; CH_3), 1.27 (1.26), 1.29 (s, 12H; $C(CH_3)_2$), 1.56–1.86 (m, 3H; CH, CH_2), 2.15–2.34 (m, 1H; CH), 3.31–3.81 (m, 4H; $C(CH_3)_2CH_2OH$), 3.87 (dd, ^2J(H,H) = 11.0 Hz, ^3J(H,H) = 7.0 Hz, 1H; CH_2OH), 3.96 (br, 2H; OH), 4.26 (dd, ^3J(H,H) = 7.9 Hz, 1H; CH_2OH), 4.72 (dq, ^3J(H,H) = 3.8 Hz, 1H; CHOH), 4.98, 5.36 (s, 2H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.38 (CH_3), 21.36 (CH_2), 24.28 (CH_2), 24.36 (24.19, 24.84) (4C; $C(CH_3)_2$), 25.61 (CH_2), 28.31 (CH_2), 33.66 (CH), 44.82 (CH), 54.19 (2C; $C(CH_3)_2$), 64.31 (CH_2OH), 69.38, 69.86 (2C; $C(CH_3)_2CH_2OH$), 72.08 (CHOH), 156.12, 156.49 (2C; NC=O); $C_{19}H_{36}N_2O_6$ (388.51): calcd C 58.74, H 9.34, N 7.21; found C 58.36, H 9.60, N 6.92.

***rac*-1-{2-[*N*-(2-Hydroxy-1,1-dimethylethyl)carbamoyloxymethyl]cyclohexyl}-2-phenyl-ethyl *N*-(2-hydroxy-1,1-dimethylethyl)carbamate (*rac*-15g)**: Carbamate *rac*-**11g** (464 mg, 0.85 mmol) was heated with methanesulfonic acid (148 mg, 1.54 mmol) for 6 h to give *rac*-**15g** (241 mg, (61%)) as a colorless solid. It was converted into the diol *rac*-**16g** without further identification. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.14–1.52 (m, 4H; CH_2), 1.26, 1.27 (s, 12H; $C(CH_3)_2$), 1.54–1.86 (m, 5H; 1CH, 2CH_2), 2.22 (m, 1H; CH), 2.76 (dd, ^2J(H,H) = 14.1 Hz, ^3J(H,H) = 6.7 Hz, 1H; CH_2Ph), 3.02 (dd, ^3J(H,H) = 4.5 Hz, 1H; CH_2Ph), 2.8–3.2 (br, 2H; NH), 3.55 (d, ^2J(H,H) = 11.3 Hz, 2H; $C(CH_3)_2CH_2OH$), 3.61 (d, 2H; $C(CH_3)_2CH_2OH$), 3.88 (dd, ^2J(H,H) = 11.0 Hz, ^3J(H,H) = 7.4 Hz, 1H; CH_2OH), 4.36 (dd, ^3J(H,H) = 6.9 Hz, 1H; CH_2OH), 4.83 (s, 1H; OH), 4.96 (ddd, ^3J(H,H) = 9.1 Hz, 1H; CHOH), 5.17 (br, 1H; OH).

***cis*-1,2-Cyclohexanedimethanol (1a)**: To a solution of **15a** (207 mg, 0.55 mmol) in methanol (5 mL) was added K_2CO_3 (40 mg, 0.29 mmol). This mixture was heated under reflux for 3 h and then purified to give diol **1a** (78 mg; 98%) and oxazolidin-2-one **17** (113 mg; 89%).

17: M.p. 54–56 °C (EtOAc) (ref.:[41a] 56–58 °C); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.35 (s, 6H; CH_3), 4.07 (s, 2H; CH_2), 6.24–6.39 (br, 1H; NH); $C_5H_9NO_2$ (115.13): calcd C 52.16, H 7.88; found C 52.10, H 7.97.

[1*S*,1(1*R*,2*S*)]-1-[2-(Hydroxymethyl)cyclohexyl]ethanol (16e): Refluxing of **15e** (124 mg, 0.32 mmol) with K_2CO_3 (23 mg, 0.17 mmol) in MeOH (6 mL) for 17 h gave incomplete conversion. Addition of further K_2CO_3 (22 mg, 0.16 mmol) and refluxing for a further 3 h gave **17** (53 mg; 73%) along with **16e** (51 mg; 100%, *dr* = 99:1) as a colorless oil. $[\alpha]_D^{21}$ = +23.2 (*c* = 1.37 in MeOH); IR (film): $\tilde{\nu}$ = 3680–3020 (O–H), 2970, 2935, 2870 (C–H), 1390 (-CH_3), 1100, 1060 cm^{-1} (C-O); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.14–1.78 (m, 9H; 1CH, 4CH_2), 1.24 (d, ^3J(H,H) = 6.2 Hz, 3H; CH_3), 2.14–2.25 (m, 1H; CH), 2.69 (s, 2H; OH), 3.54 (dd, ^2J(H,H) = 10.8 Hz, ^3J(H,H) = 3.5 Hz, 1H; CH_2OH), 3.77 (dq, ^3J(H,H) = 7.9 Hz, 1H; CHOH), 3.93 (dd, ^3J(H,H) = 9.3 Hz, 1H; CH_2OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.40 (CH_3), 22.58 (CH_2), 25.44 (CH_2), 25.98 (CH_2), 29.65 (CH_2), 37.44 (CH), 46.40 (CH), 63.25 (CH_2OH), 69.25 (CHOH); $C_9H_{18}O_2$ (158.13): calcd C 68.31, H 11.46; found C 68.40, H 11.19.

The one-pot reaction of **11e** (1.97 g, 4.2 mmol) with methanesulfonic acid (148 mg, 1.54 mmol) and then with NaOH (638 mg, 15.95 mmol) in methanol (20 mL), followed by chromatographic purification (Et_2O/hexanes 2:1, then pure Et_2O) yielded **16e** (610 mg, 92%, *dr* = 95:5) and **17** (208 mg, 21%).

[1*S*,1(1*R*,2*S*)]- and [1*R*,1(1*R*,2*S*)]-1-[2-(Hydroxymethyl)cyclohexyl]-2-phenyl-ethan-1-ol (16g): Carbamate **11g** (703 mg, 1.29 mmol) was converted into the diol by treatment with methanesulfonic acid (111 mg, 1.16 mmol), K_2CO_3 (164 mg, 1.19 mmol), and NaOH (105 mg, 2.62 mmol). Purification (Et_2O/hexanes 2:1 to neat Et_2O) yielded the two diastereomeric diols **16g** as colorless solids (140 mg; 46% and 64 mg; 21%); *dr* = 70:30).

[1*S*,1(1*R*,2*S*)]-16g: M.p. 58–59 °C (hexanes); $[\alpha]_D^{21}$ = –12.0 (*c* = 1.03 in MeOH); IR (KBr): $\tilde{\nu}$ = 3560–3100 (O–H), 3090, 3060, 3035 (C=C–H), 2930, 2860 (C–H), 1610, 1500 (C=C), 1110, 1030 (C-O), 745, 695 cm^{-1} (=C–H); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.03–1.78 (m, 9H; 1CH, 4CH_2), 2.21 (m, 1H; CH), 2.67 (dd, ^2J(H,H) = 13.6 Hz, ^3J(H,H) = 9.2 Hz, 1H; CH_2Ph), 2.93 (dd, ^3J(H,H) = 3.6 Hz, 1H, CH_2Ph), 3.05–4.02 (br, 2H; OH), 3.45 (dd, ^2J(H,H) = 10.8 Hz, ^3J(H,H) = 3.3 Hz, 1H; CH_2OH), 3.74 (ddd, ^3J(H,H) = 6.6 Hz, 1H; CHOH), 3.87 (dd, ^3J(H,H) = 9.5 Hz, 1H; CH_2OH), 7.08–7.41 (m, 5H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.41 (CH_2), 25.68 (CH_2), 25.91 (CH_2), 29.89 (CH_2), 37.44 (CH), 41.41 (CH_2Ph), 44.18 (CH), 63.05 (CH_2OH), 74.71 (CHOH), 126.16 (*p*-CH, arom.), 128.35 (*o*-CH, arom.), 129.30 (*m*-CH, arom.), 139.21 (C_{quart}, arom.); $C_{12}H_{22}O_2$ (234.34): calcd C 76.88, H 9.46; found C 76.35, H 9.52.

[1*R*,1(1*R*,2*S*)]-16g: M.p. 109–112 °C (hexanes); $[\alpha]_D^{21}$ = +7.2 (*c* = 1.03 in MeOH); IR (KBr): $\tilde{\nu}$ = 3525–3100 (O–H), 3085, 3065, 3025 (C=C–H), 2930, 2850 (C–H), 1610, 1500 (C=C), 1110, 1030 (C-O), 735, 695 cm^{-1} (=C–H); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.02–1.96 (m, 10H; 2CH, 4CH_2), 2.80 (d, ^3J(H,H) = 7.0 Hz, 2H; CH_2Ph), 3.02–4.12 (br, 2H; OH), 3.48 (dd, ^2J(H,H) = 11.1 Hz, ^3J(H,H) = 4.0 Hz, 1H; CH_2OH), 3.90 (ddd, ^3J(H,H) = 1.9 Hz, 1H; CHOH), 3.98 (dd, ^3J(H,H) = 9.4 Hz, 1H; CH_2OH), 7.07–7.39 (m, 5H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.15 (CH_2), 21.80 (CH_2), 26.62 (CH_2), 31.17 (CH_2), 41.28 (CH), 41.75 (CH_2Ph), 44.62 (CH), 62.48 (CH_2OH), 75.58 (CHOH), 126.33 (*p*-CH, arom.), 128.52 (*o*-CH, arom.), 129.30 (*m*-CH, arom.), 139.07 (C_{quart}, arom.); $C_{12}H_{22}O_2$ (234.34): calcd C 76.88, H 9.46; found C 76.07, H 9.48.

***rac*-16g**: Bisurethane *rac*-**15g** (241 mg, 0.52 mmol) was cleaved with K_2CO_3 (168 mg, 1.22 mmol). Column chromatography (Et_2O/hexanes 2:1, then pure EtOAc) afforded **17** (126 mg, 100%) and *rac*-**16g** (118 mg; 96%, *dr* = 81:19) as a colorless solid.

[2*RS*,2(1*S*,2*R*)]-2-Hydroxy-2-[2-(hydroxymethyl)cyclohexyl]-*N*-(2-hydroxy-1,1-dimethyl-ethyl)acetamide (18): The reaction of **11d** (345 mg, 0.67 mmol) with methanesulfonic acid (22 mg, 0.23 mmol) and K_2CO_3 (43 mg, 0.31 mmol), followed by purification (EtOAc/cyclohexane 2:1, then neat EtOAc) yielded **18** (112 mg (64%), *dr* = 51:49) as a viscous oil. The two diastereomers were separated by a second purification by column chromatography (EtOAc/EtOH 10:1).

[2*R*,2(1*S*,2*R*)]-18: Viscous oil; R_f = 0.18 (EtOAc); IR (film): $\tilde{\nu}$ = 3500–3200 (O–H, N–H), 2935, 2860 (C–H), 1655 (C=O), 1545 (N–H), 1125, 1030 cm^{-1} (C–O); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.04–1.38 (m, 4H;

CH_2), 1.29, 1.31 (s, 6H; $C(CH_3)_2$), 1.38–1.86 (m, 4H; CH_2), 2.01 (m, 1H; CH), 2.17 (dq, $^3J(H,H) = 3.0$ Hz, $^3J(H,H) = 5.8$ Hz, $^3J(H,H) = 12.2$ Hz, 1H; CH), 3.59 (d, $^2J(H,H) = 2.6$ Hz, 2H; $C(CH_3)_2CH_2OH$), 3.62 (dd, $^2J(H,H) = 11.0$ Hz, $^3J(H,H) = 2.9$ Hz, 1H; CH_2OH), 4.00 (t, $^3J(H,H) = 11.0$ Hz, 1H; CH_2OH), 4.11 (d, $^3J(H,H) = 2.4$ Hz, 1H, $CHOH$), 7.11 (s, 1H; NH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 20.36$ (CH_2), 21.53 (CH_2), 24.95, 25.15 (2C; $C(CH_3)_2$), 26.38 (CH_2), 31.26 (CH_2), 40.67 (CH), 43.25 (CH), 55.69 ($C(CH_3)_2$), 62.78 (CH_2OH), 70.52 ($C(CH_3)_2CH_2OH$), 75.04 (CHOH), 174.58 (NC=O); HRMS (EI) calcd for $C_{13}H_{25}NO_4$ [M^+]: 259.1783; found: 259.1786.

[2*S*,2(1*S*,2*R*)]-18: Viscous oil; $R_f = 0.11$ (EtOAc); IR (film): $\tilde{\nu} = 3500-3200$ (O–H, N–H), 2935, 2860 (C–H), 1655 (C=O), 1545 (N–H), 1125, 1030 cm^{-1} (C–O); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.08-1.87$ (m, 8H; CH_2), 1.27, 1.35 (s, 6H; $C(CH_3)_2$), 2.03 (dt, $^3J(H,H) = 3.6$ Hz, $^3J(H,H) = 6.9$ Hz, 1H; CH), 2.25 (dq, $^3J(H,H) = 8.4$ Hz, $^3J(H,H) = 11.8$ Hz, 1H; CH), 3.43 (d, $^2J(H,H) = 11.2$ Hz, 2H; $C(CH_3)_2CH_2OH$), 3.54 (dd, $^2J(H,H) = 11.2$ Hz, $^3J(H,H) = 3.3$ Hz, 1H; CH_2OH), 3.86 (t, $^3J(H,H) = 11.2$ Hz, 1H; CH_2OH), 3.96 (d, $^3J(H,H) = 5.0$ Hz, 1H; CHOH), 6.79 (s, 1H; NH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 21.70$ (CH_2), 23.79 ($C(CH_3)_2$), 25.05 (CH_2), 25.10 ($C(CH_3)_2$), 26.42 (CH_2), 30.43 (CH_2), 37.17 (CH), 42.66 (CH), 55.20 ($C(CH_3)_2$), 62.41 (CH_2OH), 68.91 ($C(CH_3)_2CH_2OH$), 75.92 (CHOH), 174.42 (NC=O); $C_{13}H_{25}NO_4$ (259.35): calcd C 60.21, H 9.72, N 5.40; found C 60.15, H 9.78, N 5.53.

Deprotection of the Dicarbamates 11. Method B:[38] **Methyl (1*S*,6*R*,7*R*)-8-oxabicyclo[4.3.0]nonan-7-carboxylate (19)**: Compound **11d** (1.83 g, 3.6 mmol) was refluxed in HCl (5N, 30 mL) for 14 h. The reaction mixture was extracted with Et_2O (4 × 30 mL), dried over $MgSO_4$, the solvent was evaporated, and the residue esterified with diazomethane, as described for **11d**. Column chromatography afforded **19** (539 mg (82%), $dr > 98:2$, $ee =$ 94%) as a slightly yellow liquid. IR (film): $\tilde{\nu} = 1750$ cm^{-1} (C=O); $[\alpha]_D^{21} = -42.2$ ($c = 0.85$ in CH_2Cl_2); ^1H NMR (200 MHz, $CDCl_3$): $\delta = 1.20-1.80$ (m, 8H, CH_2), 2.10–2.50 (m, 2H; CH), 3.75 (s, 3H, OCH_3), 3.76 (dd, $^2J(H,H) = 7.9$ Hz, $^3J(H,H) = 4.7$ Hz, 1H, CH_2O), 4.03 (dd, $^3J(H,H) =$ 5.9 Hz, 1H, CH_2O), 4.27 (d, $^3J(H,H) = 6.1$ Hz, 1H, CHO); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 22.36$ (CH_2), 23.11 (CH_2), 25.35 (CH_2), 25.49 (CH_2), 37.89 (CH), 43.12 (CH), 51.90 (OCH_3), 73.44 (CH_2O), 79.88 (CHO), 174.19 (OC=O); HRMS (EI) calcd for $C_{10}H_{16}O_3$ [M^+]: 184.1099; found: 184.1096.

Method C1:[38b, 39] A solution of the carbamates **11** (1.00 mmol) in dry THF (5 mL) was added dropwise to a stirred suspension of $LiAlH_4$ (156 mg, 4.1 mmol) in dry THF (10 mL). The reaction mixture was refluxed for 4–5 h and then worked up with water (0.16 mL), aqueous NaOH (0.16 mL, 15%), and water (0.48 mL). Column chromatography (silica gel, EtOAc/cyclohexane 2:1) gave the diols **16** and 2,2,3,4,4-pentamethyl-1,3-oxazolidine.

***rac*-16e**: ***rac*-11e** (467 mg, 1.00 mmol) was diluted in THF (6 mL) and added to a suspension of $LiAlH_4$ (158 mg, 4.16 mmol) in THF (10 mL). The mixture was heated for 5 h, worked up, and purified to give ***rac*-16e** (137 mg; 87%, $dr = 99:1$) as well as *N*-2,2,3,4,4-pentamethyloxazolidine as a colorless liquid. IR (film): $\tilde{\nu} = 2940$, 2910, 2840 (C–H), 2780 (N-CH_3), 1450 (C–H), 1365, 1355 (-CH_3), 1260 (-C-N), 1110, 1050 cm^{-1} (C-O-C); ^1H NMR (360 MHz, $CDCl_3$): $\delta = 1.09$ (s, 6H; $NC(CH_3)_2CH_2$), 1.24 (s, 6H; $NC(CH_3)_2O$), 2.24 (s, 3H; NCH_3), 3.64 (s, 2H; CH_2O); ^{13}C NMR (90 MHz, $CDCl_3$): $\delta = 22.71$ (2C; $NC(CH_3)_2CH_2$); 26.02 (2C; $NC(CH_3)_2O$), 27.49 (NCH_3), 59.38 ($NC(CH_3)_2CH_2$), 76.35 (CH_2O), 94.95 ($NC(CH_3)_2O$); HRMS (EI) calcd for $C_8H_{17}NO$ [M^+]: 143.1310; found: 143.1329.

[1*S*,1(1*R*,2*S*)]- and [1*R*,1(1*R*,2*S*)]-1-[2-(Hydroxymethyl)cyclohexyl]-but-3-en-1-ol (16f): The 68:32 mixture of **11f** and **12f** (203 mg, 0.41 mmol) was treated with $LiAlH_4$ (72 mg, 1.90 mmol) in THF (10 mL) to give **16f** (49 mg; 67%, $dr = 65:35$) as a viscous colorless oil. IR (film): $\tilde{\nu} = 3400-3200$ (O–H), 3085 (C=C–H), 2935, 2860 (C–H), 1645 (C=C), 1045 (C-O), 1005, 920 cm^{-1} (=C–H); $C_{11}H_{20}O_2$ (184.28), mixture: calcd C 71.70, H 10.94; found C 71.57, H 11.05.

[1*S*,1(1*R*,2*S*)]-16f: ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.12-1.98$ (m, 9H; 1CH, $4CH_2$), 2.11–2.27 (m, 2H; $CH_2CH=CH_2$), 2.41 (ddt, $^3J(H,H) =$ 1.4 Hz, $^3J(H,H) = 6.2$ Hz, $^3J(H,H) = 3.6$ Hz, 1H; CH), 3.32–4.12 (br, 2H; OH), 3.50 (dd, $^2J(H,H) = 11.0$ Hz, $^3J(H,H) = 3.6$ Hz, 1H; CH_2OH), 3.61 (ddd, $^3J(H,H) = 8.1$ Hz, $^3J(H,H) = 1.7$ Hz, 1H; $CHOH$), 3.90 (dd, $^3J(H,H) = 9.3$ Hz, 1H; CH_2OH), 5.12 (dd, $^2J(H,H) = 1.1$ Hz, $^3J(H,H) = 10.3$ Hz, 1H; $CH_2CH=CH_2$), 5.13 (dd, $^3J(H,H) = 16.9$ Hz, 1H; $CH_2CH=CH_2$), 5.87 (dddd, $^3J(H,H) = 7.7$ Hz, $^3J(H,H) = 6.5$ Hz, 1H; $CH_2CH=CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 22.54$ (CH_2), 25.57 (CH_2), 25.76 (CH_2), 29.76 (CH_2), 37.49 (CH), 39.42 ($CH_2CH=CH_2$), 43.94 (CH), 63.20 (CH_2OH), 72.40 (CHOH), 117.60 ($=CH_2$), 135.38 ($CH=CH_2$).

[1*R*,1(1*R*,2*S*)]-16f: ^1H NMR (300 MHz, $CDCl_3$): $\delta = 2.26-2.36$ (m, 2H; $CH_2CH=CH_2$), 2.46 (ddt, $^3J(H,H) = 1.4$ Hz, $^3J(H,H) = 6.3$ Hz, $^3J(H,H) =$ 3.6 Hz, 1H; CH), 3.52 (dd, $^2J(H,H) = 11.4$ Hz, $^3J(H,H) = 4.0$ Hz, 1H; CH_2OH), 3.72 (ddd, $^3J(H,H) = 8.1$ Hz, $^3J(H,H) = 1.7$ Hz, 1H; $CHOH$), 3.99 (dd, $^3J(H,H) = 9.3$ Hz, 1H; CH_2OH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta =$ 26.62 (CH_2), 31.19 (CH_2), 39.85 ($CH_2CH=CH_2$), 41.54 (CH), 44.76 (CH), 62.35 (CH_2OH), 73.49 (CHOH), 135.61 ($CH=CH_2$).

***rac*-16f**: ***rac*-11f** (255 mg, 0.51 mmol) was treated with $LiAlH_4$ (83 mg, 2.19 mmol) to give, after chromatography (Et_2O/hexanes 1:1), ***rac*-16f** (63 mg; 67%, $dr = 77:23$).

Method C2:[40] ***rac*-16e**: Carbamate ***rac*-11e** (211 mg, 0.45 mmol) was dissolved in dry THF (5 mL) and cooled to 0°C. Then a solution of DIBAH in THF (7.40 mL, 7.40 mmol, 1.0M) was added and the reaction mixture was allowed to warm to room temperature. After stirring for 18 h, the reaction was quenched with HCl (5N, 20 mL) and ***rac*-16e** (69 mg; 97%, $dr = 98:2$) was isolated by column chromatography.

Methyl (3*R*,3a*R*,7a*S*)-3-oxo-octahydrobenzofuran-1-carboxylate (20): Tetrahydrofuran **19** (87 mg, 0.47 mmol) was oxidized by the method described by Sharpless,[42] by using a solvent mixture of tetrachloromethane (1.0 mL), acetonitrile (1.0 mL), and water (1.5 mL) to which was added sodium periodate (786 mg, 3.7 mmol) and ruthenium trichloride hydrate (69 mg, 0.33 mmol). The mixture was stirred at room temperature for 12.5 h, washed with dichloromethane (5 × 10 mL), and dried over Na_2SO_4. Column chromatography (Et_2O/hexanes 1:2) afforded **20** (58 mg; 62%) as a colorless solid. M.p. 66°C (hexanes); IR (KBr): $\tilde{\nu} = 1775$ and 1750 cm^{-1} (C=O); $[\alpha]_D^{21} = -11.4$ ($c = 0.52$ in CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.11-1.36$ (m, 3H, CH_2), 1.52–1.77 (m, 3H; CH_2), 1.91–2.19 (m, 2H; CH_2), 2.61 (ddt, $^3J(H,H) = 1.4$ Hz, 6.3 Hz, 11.0 Hz, 1H, CH), 2.77–2.82 (m, 1H, CH), 3.79 (s, 3H, OCH_3), 4.50 (d, $^3J(H,H) = 1.4$ Hz, 1H, HCO); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 22.21$ (CH_2), 22.58 (CH_2), 23.22 (CH_2), 28.07 (CH_2), 37.24 (CH), 39.36 (CH), 51.50 (OCH_3), 78.92 (HCO), 169.87 (OC=O), 177.02 (CO_2CH_3); $C_{10}H_{14}O_4$ (198.22): calcd C 60.59, H 7.12; found C 60.44, H 7.35.

Methyl [1*R*,1(1*R*,2*S*)]-2-acetoxy-2-{2-[1-(acetoxy)methyl]cyclohexyl}acetate (21): Following the method of Ganem and Small, Jr.,[44] the tetrahydrofuran **19** (222 mg, 1.2 mmol) was stirred in dry acetic anhydride (3 mL) with a suspension of iron(III) chloride (419 mg, 2.6 mmol) in dry acetic anhydride (2 mL) for 43 h at 80°C. The mixture was worked up with HCl (2N, 10 mL) and Et_2O (20 mL), extracted with Et_2O (3 × 20 mL), and the combined organic layers were dried over $NaHCO_3/Na_2SO_4$. Chromatographic purification (silica gel, Et_2O/hexanes 1:3, then 1:1) afforded **21** (202 mg; 59%) as a slightly yellow oil. IR (film): $\tilde{\nu} = 1740-1715$ cm^{-1} (C=O); $[\alpha]_D^{21} = +31.2$ ($c = 0.87$ in CH_2Cl_2); ^1H NMR (200 MHz, $CDCl_3$): $\delta = 1.20-1.90$ (m, 8H, CH_2), 2.02 and 2.13 (s, 6H, $O(CO)CH_3$), 2.05–2.29 (m, 2H, CH), 3.76 (s, 3H, OCH_3), 4.08 (dd, $^2J(H,H) = 11.3$ Hz, $^3J(H,H) =$ 7.7 Hz, 1H, CH_2OAc), 4.28 (dd, $^3J(H,H) = 6.4$ Hz, 1H, CH_2OAc), 4.89 (d, $^3J(H,H) = 8.4$ Hz, 1H, CHOAc); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 20.45$, 20.84 (2C; $O(CO)CH_3$), 21.10 (CH_2), 24.40 (CH_2), 25.27 (CH_2), 27.88 (CH_2), 34.20 (CH), 40.36 (CH), 52.02 (OCH_3), 63.31 (CH_2OAc), 74.74 (CHOAc), 170.89, 170.48, 170.33 (3C; OC=O); HRMS (EI) calcd for $C_{12}H_{19}O_4$ [$M - CO_2CH_3$]: 227.1283; found: 227.1290.

Methyl [1*R*,1(1*R*,2*S*)]-2-acetoxy-2-{2-[1-(trifluoromethylsulfonyloxymethyl)cyclohexyl]}acetate (22): According to the method described by Effenberger et al.,[45] the mixed acetic acid (trifluormethanesulfonic acid) anhydride was generated from silver trifluoromethanesulfonate (912 mg, 3.6 mmol) and acetyl chloride (283 mg, 3.6 mmol) in dry dichloromethane (10 mL) at −78°C. The mixture was stirred for 17.5 h at this temperature, then a solution of **19** (420 mg, 2.3 mmol) in dry dichloromethane (8 mL) was added. The reaction mixture was stirred for 4 h at room temperature. HCl (2N, 20 mL) was added and the mixture was filtered. The aqueous layer was extracted and the solvent evaporated to give crude **22** (846 mg) as a brown oil, which was used without further purification in the preparation of **23**.

(1*S*,5*R*,6*R*)-3-Benzyl-5-hydroxy-3-azabicyclo[4.4.0]decan-4-one (23): Benzylamine (10 mL) was added dropwise at room temperature to neat, crude **22** (1.68 g, 4.5 mmol). The reaction mixture was stirred for 13 h and was then poured into saturated aqueous $NaHCO_3$ (20 mL) and Et_2O (20 mL). The aqueous layer was extracted with Et_2O (3 × 20 mL) and the combined

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organic layers were dried over $MgSO_4$. Chromatographic purification (silica gel, Et_2O/hexanes 1:2) yielded **23** (867 mg; 74% from **19**, $dr > 98:2$) as a colorless solid. M.p. 118 °C (hexanes); IR (KBr): $\tilde{\nu} = 3310\ cm^{-1}$ (OH), 1645 cm^{-1} (C=O); $[\alpha]_D^{20} = +3.0$ ($c = 0.83$ in CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.16-1.93$ (m, 8H, CH_2), 2.14–2.25 (m, 1H, CH), 2.39 (quint., $^3J(H,H) = 6.1$ Hz, 1H, CH), 3.73 (dd, $^2J(H,H) = 8.1$ Hz, $^3J(H,H) = 5.5$ Hz, 1H, CH_2N), 3.87 (dd, $^3J(H,H) = 6.2$ Hz, 1H, CH_2N), 4.20 (d, $^3J(H,H) = 6.1$ Hz, 1H, C*H*OH), 4.44 (d, $^2J(H,H) = 6.0$ Hz, 2H; CH_2Ph), 6.95–7.10 (br., 1H; OH), 7.23–7.38 (m, 5H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta =$ 22.34 (CH_2), 22.98 (CH_2), 25.11 (CH_2), 25.88 (CH_2), 37.84 (CH), 42.70 (CH_2Ph), 42.86 (CH), 72.75 (CH_2N), 80.94 (CHOH), 127.34, 127.55 and 128.59 (CH, arom.), 138.23 (C_{quart}, arom.); $C_{16}H_{21}NO_2$ (259.35): calcd C 74.10, H 8.16, N 5.40; found C 73.95, H 8.17, N 5.49.

***rac*-3-Methyl-octahydrobenzofuran-1-one (*rac*-24)**: According to the method described by Ley et al.[46a, 46c] and Bloch et al.,[46b] tetrapropylammonium perruthenate (35 mg, 0.10 mmol) was added at room temperature to a stirred suspension of molecular sieve (498 mg, 4 Å), diol **16e** (161 mg, 1.02 mmol), and *N*-methylmorpholine *N*-oxide (358 mg, 3.06 mmol) in dry CH_2Cl_2 (10 mL). The reaction mixture was stirred for 4 h, the solvent evaporated, and the residue purified by column chromatography (CH_2Cl_2) to afford *rac*-**24**[47] (113 mg (72%)) as a colorless oil.

Acknowledgments

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