Facile and Highly Stereoselective Synthesis of the C_2-Symmetrical Diamino Diol Core-Unit of HIV-1 Protease Inhibitors and of Their Symmetrical and Unsymmetrical Analogs from Lithiated 2-(Dibenzylamino)alkyl Carbamates: Oxidative Dimerization

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

Abstract: The lithio derivatives of (*S*)- and (*R*)-2-(*N*,*N*-dibenzylamino)alkyl carbamates **3** and *ent*-**3**, generated by substrate-directed deprotonation from the precursors **2** and *ent*-**2**, add with high diastereoselectivity to (*S*)-2-(*N*,*N*-dibenzylamino)alkanals. The (*S*)-aminoaldehyde **5a**, derived from (*S*)-phenylalanine, is produced in situ from the lithium compound **3a** by the controlled addition of dioxygen to the reaction mixture affording the protected *anti*,*syn*,*anti*-α,δ-diamino-β,γ-diol **6aa** which is the core unit of anti-HIV 1 protease agents. Several symmetric and unsymmetric structure analogs, differing in the substitution pattern and the configurations, have been synthesized. A further approach to the title compound is given by the acylation of lithium derivatives **3**/**4**, followed by a hydride reduction. The reaction of the lithium derivatives **3a**/**4a** with CuCl leads to an eliminative oxidative coupling with formation of (3*E*/*Z*, 2*S*,5*S*)-2,5-dibenzylamino-1,6-diphenylhex-3-enes (*E*)- and (*Z*)-**26**.

Key words: 2,5,-diamino-1,6-diphenylhexane-3,4-diols, dioxygen, oxidative coupling, TMEDA-mediated deprotonation, lithiation, HIV-1 protease inhibitors

Introduction

C_2-Symmetric 2,5-diamino-1,6-diphenylhexane-3,4-diols **1** find application as core-units of pseudopeptides capable of very efficient HIV-1 protease inhibition.[1] Several approaches for their synthesis have been published,[2] among them pinacol-type homo- and cross-coupling reactions of α-aminoalkanals with low-valent metal salts[2a–c] or by elaboration of compounds from the "chiral pool" such as D-mannitol[2d,e] or D-tartrate.[2f,g]

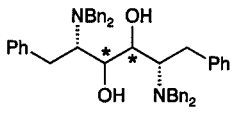


Figure 1 2,5-Diamino-1,6-diphenyl-3,4-hexanediols **1**

We found recently,[3] that the carbamates **2**, derived from (*S*)-2-(*N*,*N*-dibenzylamino)alkanols, are easily deprotonated by *sec*-butyllithium/TMEDA adjacent to the carbamate moiety[4] to form the epimeric lithium compounds **3** and **4** with good diastereoselectivities (90:10 for **2a**, $R^1 = CH_2Ph$, Scheme 1).[3b] From this observation, a general and simple route leading to C_2-symmetric diamino diols **10** and **13** ($R^1 = R^2$), to the configurational unsymmetrical diastereomers **11** and **12**, and as well, to the constitutional analogs **10–13** ($R^1 \neq R^2$) is obvious: It consists in the addition of the lithium reagents **3** and **4** onto (*S*)-2-(*N*,*N*-dibenzylamino)alkanals **5**.

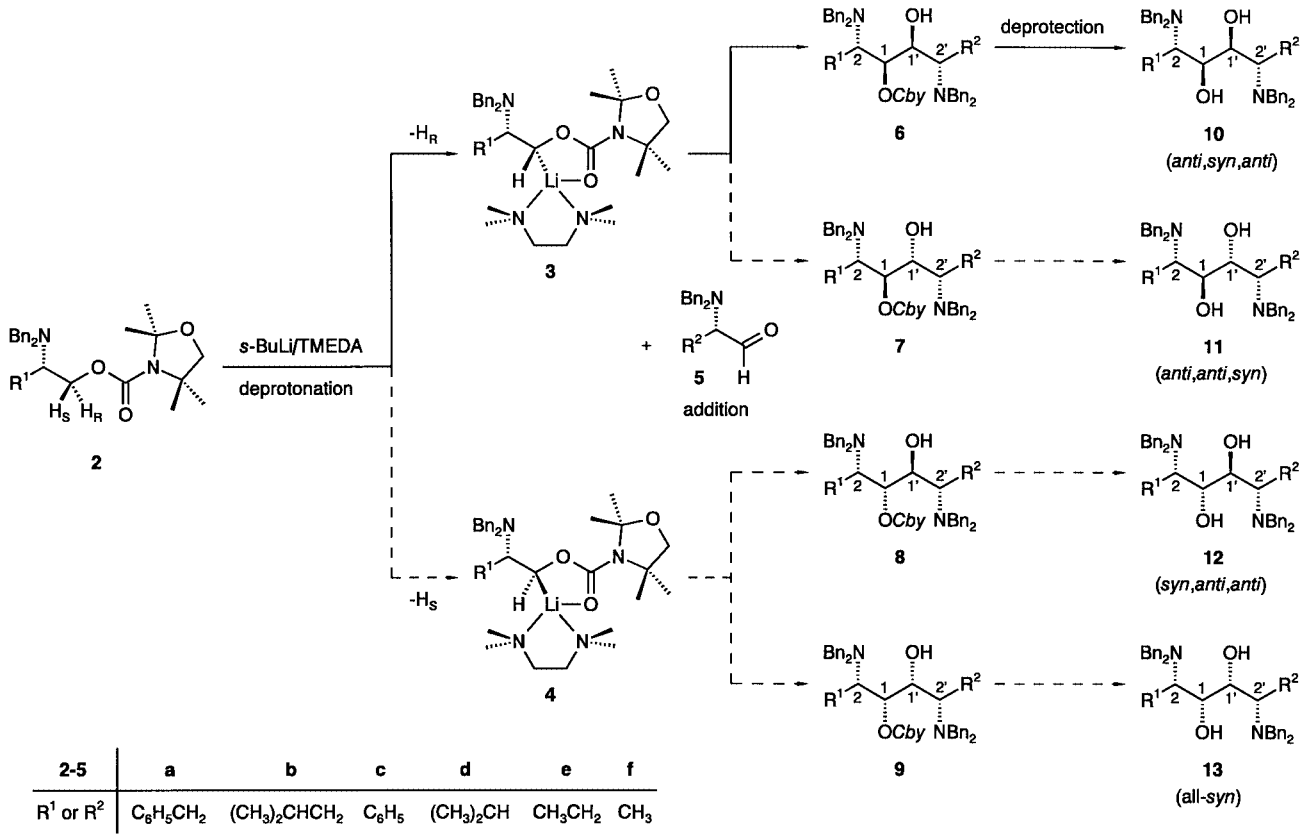
Taking into account the ratio of epimers **3** and **4** and the *Re*-facial selectivity predicted by the Felkin–Anh model[5] of (*S*)-2-(*N*,*N*-dibenzylamino)alkanals **5**, which are easily prepared from natural L-amino acids,[6] the adducts **6** and **8** are expected to be the major isomers. The efficient synthesis of the diastereomers **7** and **9**, which are not found as byproducts, should require more indirect approaches. We present in this paper a flexible brick-box system for the preparation of different stereoisomers and analogs of **1** by reliable and predictable routes, including oxidative dimerization of **3** and **4**.

Results and Discussion

Aldehyde Addition Reactions

The addition of **3a**/**4a** (approx. 90:10), prepared by the TMEDA-assisted deprotonation[3b] of the (*S*)-phenylalaninol carbamate **2a**, to the amino aldehyde **5a** yielded **6aa** as a single product in 61% yield, besides some starting material **2a** (Scheme 1, Table 1). Another diastereomer could not be detected. The same procedure for homo-coupling, starting from the (*S*)-leucinol derivatives **2b** (via **3b**/**4b**, 80:20) and **5b**, afforded a separable mixture of **6bb** and **8bb** (88:12) in 79% yield. The appropriate (*S*)-phenylglycinol pair **2c**/**5c** - via **3c**/**4c** (40:60) - yielded the epimers **6cc** and **8cc** (52%, 33:67). In the latter two examples, the diastereomer ratio roughly reflects the epimer ratio in the carbanionic intermediates **3**/**4**.

When performing cross-coupling reactions we were surprised when an apparently lower selectivity was observed. The reaction of **2a** and **5b** gave after usual workup, which includes warming-up the reaction mixture before neutralization to room temperature, in addition to the expected product **6ab** (48%), another unknown isomer in 25% yield (ratio 66:34) (Scheme 2). When the reaction mixture was neutralized by formic acid at −78°C, the ratio shifted to



For R^1 and R^2 in **6**, **8**, **10**, and **12** see Tables 1 and 2.

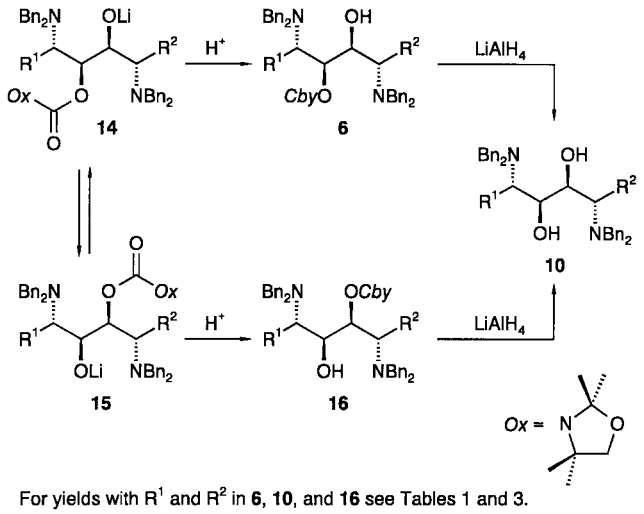
Scheme 1

83:17. After deblocking the hydroxy group in both isomers the same diol **10ab** was obtained. On the basis of these results it became clear, that the unknown compound differs from **6ab** only in the position of the *O*-carbamoyl group and has to be assigned the structure **16ab**. The rearrangement proceeds on the stage of the originally produced lithium alcoholates **14ab**/**15ab**. Further support comes from the deblocking of the constitutionally inverse mixture **6ba**/**16ba** [$R^1 = (CH_3)_2CHCH_2$, $R^2 = C_6H_5CH_2$] to give also the diol **10ab**. This feature already excludes the

Table 1 Coupling Products **6**, **8**, and **16** Prepared[a]

Products	Starting Materials	R^1	R^2	Yield (%) (Ratio)	mp[b] (°C)	$[\alpha]_D^{22}$[c]
6aa	**2a,5a**	$C_6H_5CH_2$	$C_6H_5CH_2$	61	72–73	+17.7
6ab (=**16ba**),	**2a,5b**	$C_6H_5CH_2$	$(CH_3)_2CHCH_2$	48, 25 (66:34)[d]	58–62,	–28.5
16ab (=**6ba**)					56–61	–24.9
				77 (83:17)[e]		
6ac	**2a,5c**	$C_6H_5CH_2$	C_6H_5	45	71–75	+31.4
6ad,16ad	**2a,5d**	$C_6H_5CH_2$	$(CH_3)_2CH$	47, 36 (57:43)	49–51,	– 4.0
					51–54	–22.6
6bb,8bb	**2b,5b**	$(CH_3)_2CHCH_2$	$(CH_3)_2CHCH_2$	68, 11 (86:14)	48–50,	–53.8
					50–52	–23.4
6ba,16ba,8ba	**2b,5a**	$(CH_3)_2CHCH_2$	$C_6H_5CH_2$	44, 22, 17 (53:27:20)	48–50	–53.8
6cc,8cc	**2c,5c**	C_6H_5	C_6H_5	13, 39 (33:67)	–[f],	–[f],
					84–88	+63.4

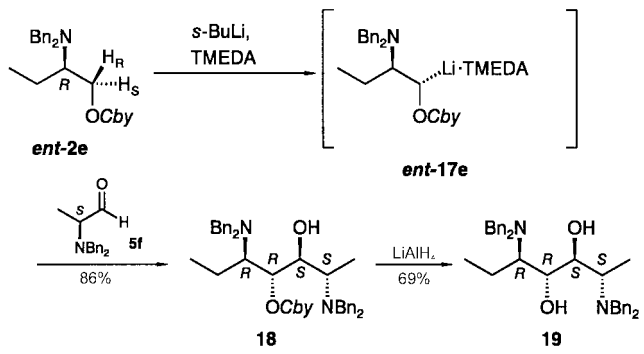
[a] All new compounds gave correct C,H-analyses (C ± 0.4, H ± 0.4).
[b] From Et_2O/pentane.
[c] (c = 1, CH_2Cl_2).
[d] Hydrolysis at room temperature.
[e] Hydrolysis at –78 °C.
[f] Mixture of **6cc** and **2c**, which is not separable by flash chromatography.



Scheme 2

structures **7** and **8** to be the major isomers, since here different diols must be formed from constitutionally inverse isomers.

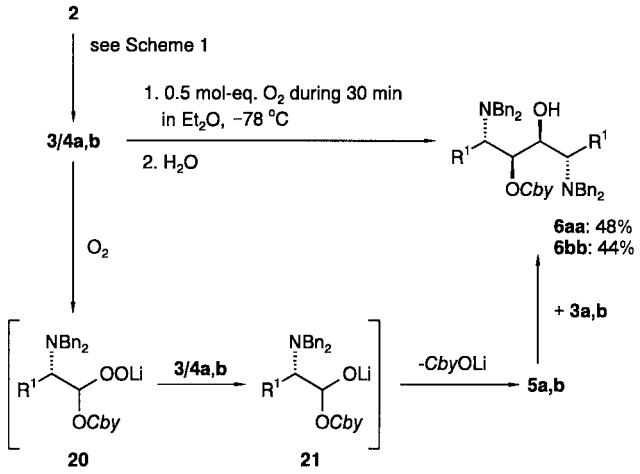
As Scheme 3 demonstrates, further series of diastereomers can be synthesized by selecting both starting materials with different absolute configurations. From the (*R*)-2-(*N*,*N*-dibenzylamino)butyl carbamate *ent*-**2e**,[3d] via TMEDA-mediated deprotonation and addition to (*S*)-*N*,*N*-dibenzylalaninal (**5f**), the adduct **18** was prepared to give a single all-*anti*-diol **19** on *O*-deprotection.



Scheme 3

Oxidative Coupling

When dioxygen was introduced to the ethereal solution of the lithium/TMEDA complexes **3a**/**4a** or **3b**/**4b** in a controlled way, the aldehyde adducts **6aa** (48%) or **6bb** (44%) could be isolated as the sole diastereomers besides some starting material **2a** (23%) or **2b** (14%) (Scheme 4). It is quite likely that the reaction starts with the formation of the lithium peroxides[7] **20,** which oxidize **3**/**4** to the lithium salts of hemiacetals **21**, and elimination of the lithium carbamate (LiO*Cby*) furnishes the intermediate aldehydes **5** which undergo addition to the remaining lithium compounds **3**. Surprisingly the diastereomeric purity of **6bb** is higher than in the two-step process described above. We assume that the minor epimer **4b** has a higher reactivity in the oxidation process and is removed preferentially.



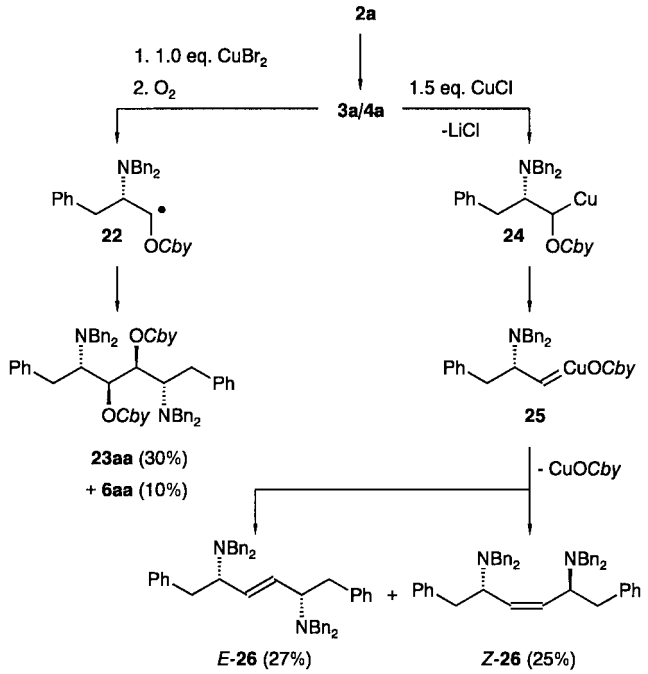
Scheme 4

We also undertook some experiments for accomplishing a "true" oxidative coupling of the carbanionic intermediates **3a**/**4a** by means of copper(II)[8] and copper(I)[9] salts (Scheme 5). After treating **3a**/**4a** with 1 equivalent of $CuBr_2$ and finally with dioxygen, from the multicomponent reaction mixture, the dimer **23aa** (30%) and again **6aa** (10%) could be isolated. Thus, minor amounts of further diastereomers can not be excluded. Presumably the (configurationally labile) radical **22** is the intermediate, which dimerizes with pronounced substrate-induced diastereoselectivity.

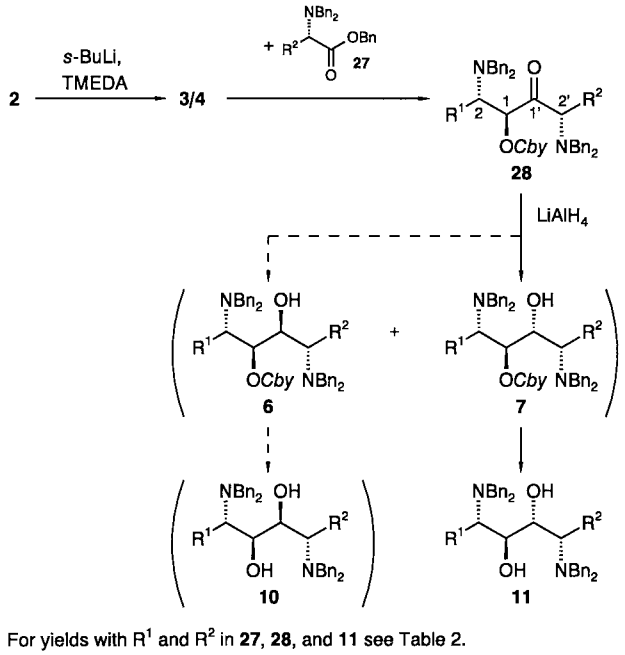
Using CuCl as the oxidation reagent, a surprising result was obtained. An *E*/*Z*-mixture of the diaminoalkenes **26** was isolated; the relative configuration of (*Z*)-**26** was elucidated by a single crystal X-ray analysis[10] (Figure 2). We assume the copper(I) carbene complex **25** to be the essential intermediate.[11]

anti,anti,syn-Diols 11 via Acylation/Reduction

An efficient, selective approach to the *anti*,*anti*,*syn*-diols **11** consists in the acylation of the lithiocarbamates **3**/**4** by (*S*)-*N*,*N*-dibenzylamino acid benzyl esters **27** and reduction of the ketones **28** (Scheme 6, Table 2). When the reduction is performed with $LiAlH_4$ in refluxing THF, the carbamate group is removed simultaneously to give directly the pure alcohols **11** via the carbamates **7**. Obviously, the stereodirecting power of the chiral centers in **3** and **28** is extremely high, since no other diastereomers could be detected by TLC or ^1H NMR spectroscopy. The prize



Scheme 5



Scheme 6

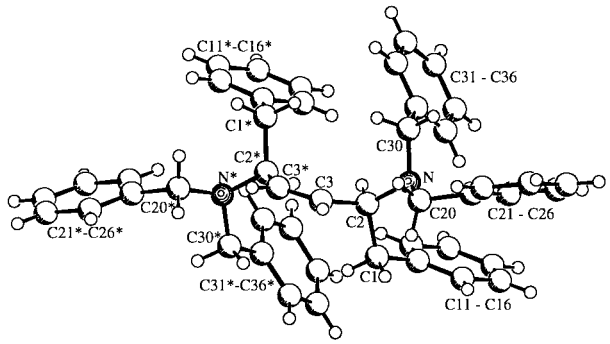
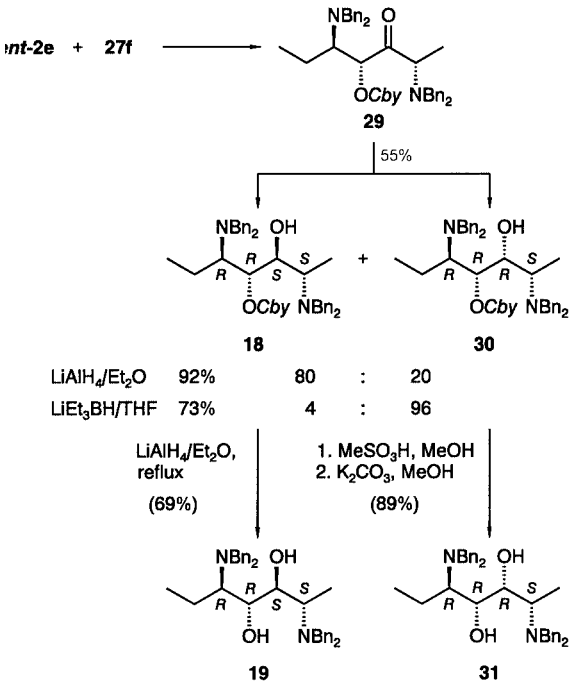


Figure 2 X-ray structure of (*Z*)-**26**[10]



Scheme 7

to pay for the high selectivity is in some cases the low yield, which arises from the low reactivity of the benzyl esters **27**.

Similarly, from the (*R*)-aminoalkyl carbamate *ent*-**2e** and benzyl (*S*)-*N*,*N*-dibenzylalaninate (**27f**), the "mixed" ketone **29** was obtained (Scheme 7). The reduction of **29** could be directed by the selection of the reducing agent: $LiAlH_4$ in diethyl ether at 0°C yielded the all-*anti*-monocarbamate **18** in excess, whereas lithium triethylboronate furnished the *anti*,*syn*,*syn*-diastereomer **31**. Monocarbamate **18**, on deprotection with excess $LiAlH_4$, led to the crystalline diol **19**, from which an X-ray analysis[12] was performed (Figure 3).

Deprotection and Configurational Assignment

The reductive decarbamoylation of monocarbamates **6**, **7**, or **8** to form the free bis(dibenzylamino)diols **10**, **11**, or **12** is the most convenient procedure on a laboratory scale[4] (Method A, Scheme 8, Table 3). The usual procedure, which consists in the acid-catalyzed cleavage of the oxazolidine ring and subsequent base-catalyzed cleavage of the intermediate *N*-hydroxyalkylcarbamate[4,13] was ap-

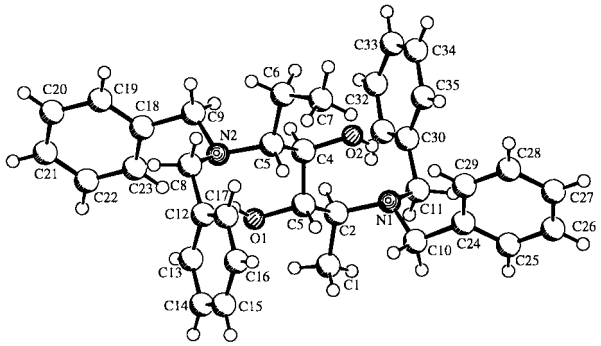
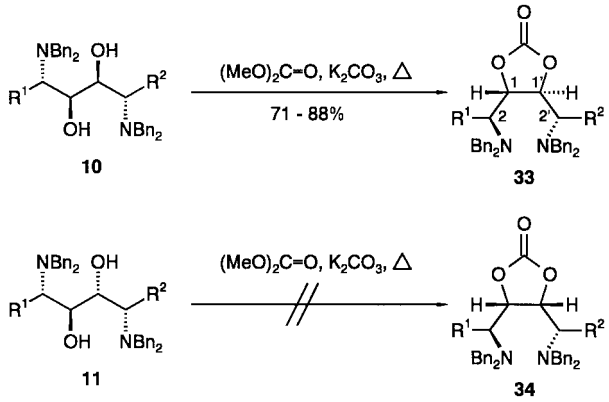


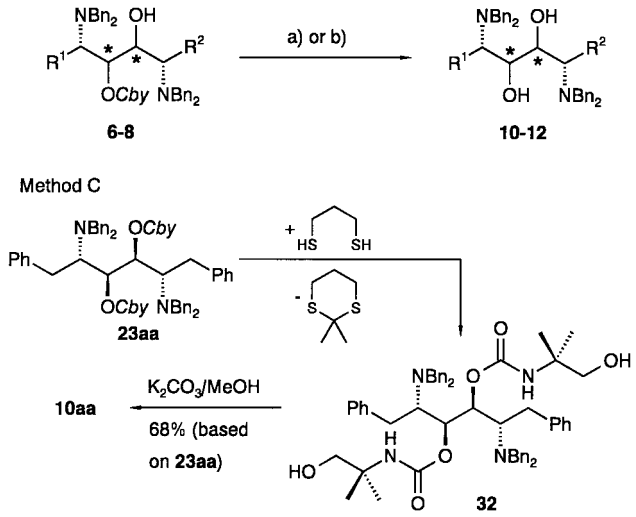
Figure 3 X-ray structure of diol **19**[12]



For examples and yields of **33** see experimental section.

Scheme 9

plied (Method B, Scheme 8). 1,3-Propanedithiol was used[14] for deblocking the dicarbamate **23aa** by transacetalization and the bis(*N*-monoalkyl)carbamate **32** formed was then treated with K_2CO_3/MeOH.



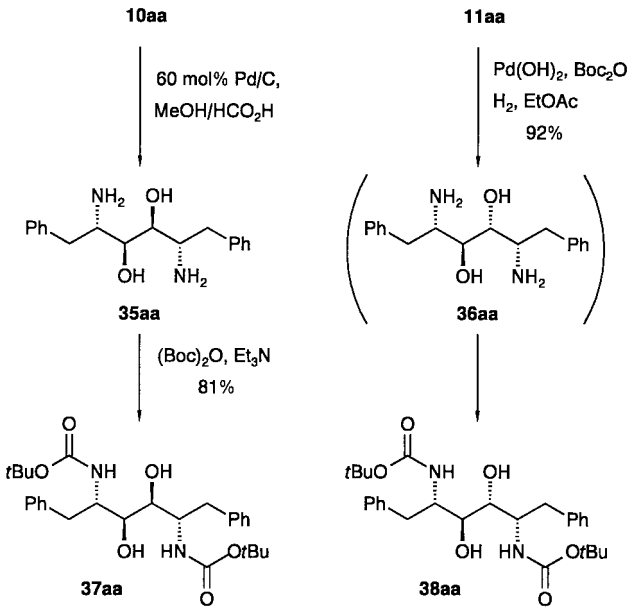
Examples and yields see Table 3.

Reagents and conditions: a) $LiAlH_4$ (4 equiv)/THF, reflux, 5 h (Method A); b) i. $MeSO_3H$ (5 equiv)/MeOH, reflux, ii. K_2CO_3 (8 equiv)/MeOH, reflux (Method B)

Scheme 8

Evidence for the correct stereochemical assignment of diols **10aa**, **10bb**, and **10cc**, in addition to the presented arguments, comes from the ^{1}H NMR spectra. As expected from their C_2-symmetry, the appropriate signals of the "left hand" and the "right hand" side coincide. Compounds **10aa**, **10bb**, **10ab** and **10ad**, bearing a *syn*-diol unit, easily cyclized on treatment with dimethyl carbonate[15] to give the *trans*-disubstituted 1,3-dioxolan-2-ones **33** ($J_{4,5}$ = 7.0–7.2 Hz)[3b,16], whereas the diastereomers **7** failed to give the highly stericly encumbered *cis*-isomers **34.**

Finally, diols **10aa** and **11aa** were separately converted to the known bis-Boc derivatives[2a] **37aa** and **38aa** via the diaminodiols **35aa** and **36aa**, respectively (Scheme 10).



Scheme 10

In conclusion, several methods are now available for the synthesis of the enantiopure title compounds, differing in the substitution pattern and the relative configuration by a simple "brick-box system".

All reactions which are sensitive to moisture were carried out under argon. All solvents were purified by distillation and dried, if necessary, prior to use. ^{1}H and ^{13}C NMR spectra were recorded on Bruker WM300, AM 360 or U600 spectrometer. Optical rotations were recorded on a Perkin-Elmer polarimeter 241 at 20°C. Mps were obtained on Gallenkamp melting point apparatus MFB-595 and are uncorrected. Products were purified by flash column chromatography on silica gel (40–63 μm).

Table 2 Acylation Products **28**, Diols **11**, and Derivatives **7** Prepared[a]

Product	Starting Materials	R^1	R^2	Yield (%)	mp (°C)[b]	$[\alpha]_D^{22c}$
28aa	**2a, 27a**	$C_6H_5CH_2$	$C_6H_5CH_2$	59	58–62	+35.1
28ab	**2a, 27b**	$C_6H_5CH_2$	$(CH_3)_2CHCH_2$	50	45–48	+43.0
28bb	**2b, 27b**	$(CH_3)_2CHCH_2$	$(CH_3)_2CHCH_2$	26	45–50	+14.3
28ba	**2b, 27a**	$(CH_3)_2CHCH_2$	$C_6H_5CH_2$	29	–[d]	–[d]
7aa	**28aa**	$C_6H_5CH_2$	$C_6H_5CH_2$	89[e]	68–72	–17.4
7bb	**28bb**	$(CH_3)_2CHCH_2$	$(CH_3)_2CHCH_2$	93[e]	46–49	–32.2
11aa	**28aa**	$C_6H_5CH_2$	$C_6H_5CH_2$	76	53–56	+48.6
11ab	**28ab**	$C_6H_5CH_2$	$(CH_3)_2CHCH_2$	77	47–50	+32.2
11bb	**28bb**	$(CH_3)_2CHCH_2$	$(CH_3)_2CHCH_2$	81	46–49	+17.9
11ba	**28ba**	$(CH_3)_2CHCH_2$	$C_6H_5CH_2$	86	57–59	+52.4

[a] All new compounds gave correct C,H-analyses (C ± 0.4, H ± 0.4).
[b] From Et_2O/pentane.
[c] (*c* = 1, CH_2Cl_2).
[d] Mixture of **28ba** and **2b**, which is not separable by flash column chromatography.
[e] Reduction with $NaBH_4$ in EtOH.

Deprotonation of Carbamates 2 and *ent*-2 with *s*-BuLi/TMEDA and Preparation of Substituted Products 6, 8, 16, 18, 28, and 29; General Procedure

Carbamate **2** or *ent*-**2** (1.00 mmol) and TMEDA (232 mg, 2.00 mmol) were dissolved in anhyd Et_2O (15 mL) under argon in a dry ice/acetone bath and *s*-BuLi (1.3 M) in cyclohexane/hexane (1.50 mL, 2.00 mmol) was added to the solution dropwise. After stirring for 4 h (*ent*-**2**) or 6 h (**2**) the electrophile (3.00 mmol) was slowly introduced with a syringe. The mixture was allowed to warm up to r. t. for 12 h and H_2O (10 mL) was added. The Et_2O layer was separated and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined Et_2O phases were dried ($MgSO_4$) and evaporated in vacuo. The residue was purified by flash chromatography (Et_2O/pentane, 1:1 to 1:8) to afford the substituted carbamate. For yields and physical data of substituted carbamates **6, 8** or **16** see Tables 1 and 4. For yields and physical data of substituted carbamates **28** see Tables 2 and 4.

(2*S*,3*S*,4*R*,5*R*)-2,5-Bis(*N*,*N*-dibenzylamino)-4-*O*-(2,2,4,4-tetramethyl-1,3-oxazolidine-3-carbonyl)-3,4-heptanediol (18)

The reaction of *ent*-**2e** with (*S*)-*N*,*N*-dibenzylalaninal as electrophile yielded **18** (583 mg, 86%, *dr* >95:<5) as a colorless solid; R_f 0.56 (Et_2O/pentane, 1:1); mp 54–56°C (Et_2O/pentane); $[\alpha]_D$ +28.6 (*c* = 1, acetone).

Anal. Calcd. for $C_{43}H_{55}N_3O_4$ (677.9): C, 76.18; H, 8.18; Found C, 76.13; H, 8.23.

For ^1H, ^{13}C NMR, and IR data of **18,** see Table 4.

Table 3 Deblocking of Monocarbamates **6**, **7**, **8**, **18**, and **30**[a]

Product	Starting Material	R^1	R^2	Method	Yield (%)	mp (°C)[b]	$[\alpha]_D^{20c}$
10aa	**6aa**	$C_6H_5CH_2$	$C_6H_5CH_2$	A	72	46–49	+ 2.0
11aa	**7aa**	$C_6H_5CH_2$	$C_6H_5CH_2$	B	75	–[d]	–[d]
10ab	**6ab**	$C_6H_5CH_2$	$(CH_3)_2CHCH_2$	B	91	43–47	–12.0
11ab	**7ab**	$C_6H_5CH_2$	$(CH_3)_2CHCH_2$	B	47	–[d]	–[d]
10ac	**6ac**	$C_6H_5CH_2$	C_6H_5	C	73	61–63	+43.4
10ad	**6ad**	$C_6H_5CH_2$	$(CH_3)_2CH$	A	74	39–43	–19.1
10da[e]	**6da**	$(CH_3)_2CH$	$C_6H_5CH_2$	B	90	–[e]	–[e]
10bb	**6bb**	$(CH_3)_2CHCH_2$	$(CH_3)_2CHCH_2$	A	83	36–41	–23.2
				B	94		
11bb	**7bb**	$(CH_3)_2CHCH_2$	$(CH_3)_2CHCH_2$	B	83	–[d]	–[d]
12bb[f]	**8bb**	$(CH_3)_2CHCH_2$	$(CH_3)_2CHCH_2$	A	43	–[d]	–[d]
10cc	**6cc**	C_6H_5	C_6H_5	B	86	77–81	+83.6
12cc	**8cc**	C_6H_5	C_6H_5	A	36	76–79	+83.2
				B	74		
19	**18**	–	–	A	69	212–214	+11.4
31	**30**	–	–	B	89	98–99	+50.5

[a] All new compounds gave correct C,H-analyses (C ± 0.4, H ± 0.4).
[b] From Et_2O/pentane.
[c] (*c* = 1, CH_2Cl_2).
[d] See Table 2.
[e] Compound **10da** corresponds to **10ad**.
[f] Compound **12bb** corresponds to **11bb** in Table 2.

(2*S*,4*R*,5*R*)-2,5-Bis(*N*,*N*-dibenzylamino)-4-*O*-(2,2,4,4-tetramethyl-1,3-oxazolidine-3-carbonyloxy)-3-heptanone (29)
Benzyl (*S*)-*N*,*N*-dibenzylalaninate **27f** was used as electrophile after deprotonation of *ent*-**2e**. Purification of the crude product by flash chromatography (Et_2O/pentane 1:10→1:6) gave **29** (372 mg, 55%, dr >95:<5) as a colorless solid; R_f 0.69 (Et_2O/pentane, 1:1); mp 124–126°C (Et_2O/pentane); $[\alpha]_D$ −106.0 (*c* = 1, acetone).

Anal. Calcd. for $C_{43}H_{53}N_3O_4$ (675.9): C, 76.41; H, 7.90; Found C, 76.39; H, 7.94.

For ^1H, ^{13}C NMR, and IR data of **29** see Table 4.

Dimerization of 2a in the Presence of $CuBr_2$; (2*S*,3*S*,4*S*,5*S*)-2,5-Bis(*N*,*N*-dibenzylamino)-1,6-diphenyl-3,4-bis(2,2,4,4-tetramethyl-1,3-oxazolidine-3-carbonyloxy)hexane (23aa)
To a solution of carbamate **2a** (486 mg, 1.00 mmol) and TMEDA (232 mg, 2.00 mmol) in anhyd Et_2O (15 mL) was added dropwise *s*-BuLi (1.3 M) in cyclohexane/hexane (1.50 mL, 2.00 mmol) at –78°C. Stirring was continued for 6 h and subsequently anhyd $CuBr_2$ (223 mg, 1.00 mmol) was added to the mixture under an argon stream. The slurry was allowed to warm up to r.t., oxygen (12 mL, 0.5 mmol) was introduced via syringe during 30 min, and finally H_2O (10 mL) was added. The two layers were separated and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with satd EDTA-solution, dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash chromatography (Et_2O/pentane, 1:6→1:3) to yield **23aa** (291 mg, 30%) as a colorless solid and **6aa** (82 mg, 10%) beside some starting material **2a** (44 mg, 9%); R_f 0.31 (Et_2O/pentane, 1:2); mp 94–98°C (Et_2O/pentane); $[\alpha]_D$ +22.2 (*c* = 1, CH_2Cl_2).

Anal. Calcd. for $C_{62}H_{74}N_4O_6$ (971.3): C, 76.67; H, 7.68; Found C, 76.67; H, 7.91.

For ^1H, ^{13}C NMR and IR data of **23aa** see Table 4.

Conversion of 2a in the Presence of CuCl; *cis*- and *trans*-(2*S*,5*S*)-2,5-Bis(*N*,*N*-dibenzylamino)-1,6-diphenyl-3-hexene (*Z*-26 and *E*-26)
To a solution of carbamate **2a** (486 mg, 1.00 mmol) and TMEDA (232 mg, 2.00 mmol) in anhyd Et_2O (15 mL) was added dropwise *s*-BuLi (1.3 M) in cyclohexane/hexane (1.50 mL, 2.00 mmol) at –78°C. After stirring for 5 h anhyd CuCl (150 mg, 1.50 mmol) was added under an argon stream and the mixture was allowed to warm up to r.t. Oxygen (12 mL, 0.5 mmol) was slowly introduced via syringe and then H_2O (10 mL) was added. The two layers were separated and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with satd EDTA-solution, dried ($MgSO_4$) and the solvents were evaporated in vacuo. Purification of the crude product by flash chromatography (Et_2O/pentane, 1:12) afforded a mixture of (*Z*)-**26** and (*E*)-**26** (170 mg, 54%) as colorless crystals; ratio 47:53. (*Z*)-**26** could be obtained as pure diastereomer by recrystallization from CH_2Cl_2/pentane.

(*Z*)-26
R_f 0.66 (Et_2O/pentane, 1:2); mp 165–167°C (Et_2O/pentane), colorless crystals; $[\alpha]_D$ +83.1 (*c* = 1, CH_2Cl_2).

Anal. [Mixture of (*Z*)-**26** and (*E*)-**26**] Calcd. for $C_{46}H_{46}N_2$ (626.9): C, 88.14; H, 7.40; Found C, 88.05; H, 7.40.

For ^1H, ^{13}C NMR, and IR data of ***Z*-26** and ***E*-26** see Table 4.

Reduction of Ketones 28aa and 28bb with $NaBH_4$ in EtOH; Preparation of Monocarbamates 7aa and 7bb
$NaBH_4$ (114 mg, 3.00 mmol) was added to a solution of ketone **28aa** (488 mg, 0.60 mmol) or **28bb** (448 mg, 0.60 mmol) in EtOH (10 mL). The solution was stirred for 3 h at r.t. and then refluxed for 24 h. After addition of H_2O (20 mL) the aqueous phase was extracted with Et_2O (3 × 20 mL). The combined organic layers were dried ($MgSO_4$) and the solvents were removed in vacuo. The residue was purified by flash chromatography (Et_2O/pentane, 1:8) to give **7aa** or **7bb** as pure product.

For yields and physical data of **7aa** and **7bb** see Tables 2 and 4.

Reduction of Ketone 29; Preparation of Monocarbamates 18 and 30
Reduction with $LiAlH_4$: A solution of ketone **29** (600 mg, 0.88 mmol) in anhyd Et_2O (20 mL) was added dropwise to a suspension of $LiAlH_4$ (57 mg, 1.50 mmol) in anhyd Et_2O (10 mL) at 0°C. The suspension was stirred for 1 h and then hydrolyzed with successively H_2O (57 μL), 15% NaOH solution (57 μL), and H_2O (171 μL). The precipitate was filtered off and washed with Et_2O (20 mL). The filtrate was dried ($MgSO_4$) and the solvent was evaporated in vacuo. The crude product was purified by flash chromatography (Et_2O/pentane, 1:8) to give **18** (440 mg, 74%) and **30** (110 mg, 18%) as colorless solids; diastereomeric ratio 80:20.

Reduction with $LiEt_3BH$: To a solution of **29** (450 mg, 0.67 mmol) in THF (20 mL) was added $LiEt_3BH$ (2.60 mL, 2.60 mmol, 1.0M in THF) at 0°C. The mixture was refluxed for 2 d and then hydrolyzed with H_2O (5 mL). The aqueous layer was separated and extracted with Et_2O (3 × 15 mL). The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. Purification of the residue by flash chromatography (EtOAc/cyclohexane, 1:15) afforded the diastereomers **18** (20 mg, 4%) and **30** (310 mg, 69%) in a ratio of 6:94 beside some starting material **29** (52 mg, 12%).

(2*S*,3*R*,4*R*,5*R*)-2,5-Bis(*N*,*N*-dibenzylamino)-4-*O*-(2,2,4,4-tetramethyl-1,3-oxazolidine-3-carbonyl)-3,4-heptanediol (30)
R_f 0.60 (Et_2O/pentane, 1:1); mp 134–135°C (Et_2O/pentane); colorless solid; $[\alpha]_D$ +64.2 (*c* = 1, acetone).

Anal. Calcd. for $C_{43}H_{55}N_3O_4$ (677.9): C, 76.18; H, 8.18; Found C, 75.93; H, 8.09.

For ^1H, ^{13}C NMR, and IR data of **30** see Table 4.

Simultaneous Reduction and Decarbamoylation of 28aa, 28bb, 28ab, and 28ba with $LiAlH_4$; Preparation of Diols 11aa, 11bb, 11ab, and 11ba
$LiAlH_4$ (0.5 mL, 0.5 mmol, 1M in Et_2O) was added dropwise to a solution of **28** (0.1 mmol) in THF or Et_2O (5 mL) at 0°C. The ice bath was removed and the suspension was refluxed for 24 h. After successive hydrolysis with H_2O (20 μL), aq NaOH (20 μL, 15%), and H_2O (60 μL) the slurry was heated under reflux for 30 min. The solid materials were filtered off and washed with CH_2Cl_2 (10 mL). The filtrate was dried ($MgSO_4$) and the solvents were evaporated in vacuo. Purification of the residue by flash chromatography (Et_2O/pentane, 1:8) yielded analytically pure diol **11**.

For yields and physical data of diols **11aa**, **11bb**, **11ab**, and **11ba** see Tables 2 and 4.

Decarbamoylation of Monocarbamates 6, 7, 8, 18, and 30; Preparation of Diols 10, 11, 12, 19, and 31; General Procedures
Method A: To a suspension of $LiAlH_4$ (76 mg, 2.00 mmol) in anhyd THF (7 mL), was added dropwise a solution of the monocarbamate **6** or **8** (0.50 mmol) in THF (8 mL) at 0°C. After heating under reflux for 6 h, the mixture was hydrolyzed successively with H_2O (76 μL), 15% NaOH solution (76 μL), and H_2O (228 μL) at 0°C. After heating under reflux for further 30 min the precipitate was filtered off and washed with THF (15 mL). The filtrate was dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography of the residue (Et_2O/pentane, 1:4 to 1:8) afforded the free diol **10** or **12**.

Method B: A solution of the monocarbamate **6**, **7**, or **8** (1.00 mmol) and $MeSO_3H$ (324 μL, 480 mg, 5.00 mmol) in MeOH (15 mL) was

Table 4 Selected Data of Compounds **6, 7, 8, 10, 11, 12, 18, 19, 23,** *Z*-**26,** *E*-**26, 28, 29, 30, 31,** and **33**[a]

Product	IR (KBr/film) ν (cm^{-1})	^{1}H NMR (300 MHz, $CDCl_3$), δ, *J* (Hz)						^{13}C NMR (75 MHz, $CDCl_3$), δ					
		1-H	1'-H	2-H	2'-H	N-CH_2Ph		C-1	C-1'	C-2	C-2'	N-CH_2 Ph	
6aa	3420, 1675	5.49 (dd, $^3J_{1,1'}$, $^3J_{1,2}$ = 5.4, 8.3)	4.42 (br s)	3.26–3.39 (m)	2.93–3.18[b] (m)	3.60, 3.82 (2 d, $^2J_{Bn}$ = 14.5), 3.68, 3.69 (2 d, $^2J_{Bn}$ = 10.4)	2.58–2.73 (m, 3'-H_a), 2.74–2.88 (m, 3-H_a), 2.93–3.18[b] (m, 3-H_b, 3'-H_b)	75.5	71.4	58.9	61.4	53.8, 54.6	32.7 (C-3'), 33.4 (C-3)
6bb	3430, 1680	5.36 (dd, $^3J_{1,1'}$, $^3J_{1,2}$ = 5.1, 10.1)	4.15 (br s)	2.83–2.97 (m)	2.62–2.74 (m)	3.61, 3.89 (2 d, $^2J_{Bn}$ = 14.3), 3.70, 3.82, 3.84 (2 d, $^2J_{Bn}$ = 13.8)	0.40, 0.49 (2 d, $^3J_{4,5,\ 4',5'}$ = 6.4, 5-H_3, 5'-H_3), 0.84, 0.89 (2 d, $^3J_{4,4\text{-}CH_3,\ 4'4'\text{-}CH_3}$ = 6.7, 4-CH_3, 4'-CH_3), 0.85–0.96, 1.67–1.88[b] (2 m, 3'-H_a, 3'-H_b), 0.97–1.12, 1.67–1.88[b] (2 m, 3-H_a, 3-H_b), 1.89–2.12 (m, 4-H, 4'-H)	75.8	71.8	55.6	57.2	54.0,, 54.7	20.8, 21.0, 23.8, 23.9 (C-5, C-5', 4-CH_3, 4'-CH_3), 23.8, 23.9 (C-4, C-4'), 34.9 (C-3'), 36.7 (C-3)
6ab (=16ba)	3430, 1685	5.40 (dd, $^3J_{1,1'}$, $^3J_{1,2}$ = 4.8, 7.4)	4.34 (br s)	1.83–2.00 (m)	2.65–2.85[b] (m)	3.55, 3.89 (2 d, $^2J_{Bn}$ = 14.3), 3.62-3.78[b] (m, 4 H)	0.34, 0.82 (2 d, $^3J_{4'4'\text{-}CH_3,\ 4',5'}$ = 6.4, 6.7, 5'-H_3, 4'-CH_3), 0.84–0.95, 1.65–1.80 (2 m, 3'-H_a, 3'-H_b), 1.83–2.00 (m, 4'-H), 2.65–2.85[b], 2.95–3.10 (2 m, 3-H_a, 3-H_b)	75.6	71.0	59.1	57.2	53.8, 54.7	20.6, 23.9 (C-5', 4'-CH_3), 23.8 (C-4'), 33.4 (C-3), 35.2 (C-3')
6ba (=16ab)	3430, 1680	5.46 (dd, $^3J_{1,1'}$, $^3J_{1,2}$ = 4.5, 9.1)	4.21 (br s)	2.90–3.10[b] (m)	2.90–3.10[b] (m)	3.55–3.90[b] (m, 8 H)	0.47, 0.89 (2 d, $^3J_{4,4\text{-}CH_3,\ 4,5}$ = 6.4, 6.9, 5-H_3, 4-CH_3), 1.00–1.20, 1.70–1.90[b] (2 m, 3-H_a, 3-H_b), 1.70–1.90[b] (m, OH), 1.90–2.05 (m, C-4), 2.60–2.73, 2.90–3.10[b] (2 m, 3'-H_a, 3'-H_b)	75.6	72.3	55.4	61.4	54.0, 54.7	21.0, 24.0 (C-5, 4-CH_3), 24.2 (C-4), 32.5 (C-3'), 36.7 (C-3)
6ad	3430, 1680	5.62 (dd, $^3J_{1,1'}$ = 6.8, $^3J_{1,2}$ = 3.5)	4.35 (dd, $^3J_{1',2'}$ = 7.4)	3.40–3.85[b] (m)	2.64 (dd, $^3J_{2',3'}$ = 3.3)	3.40–3.85[b] (m, 8 H)	0.96, 0.97 (2 d, $^3J_{3,3\text{-}CH_3}$ = $^3J_{3',4'}$ = 6.4, 4'-H_3, 3'-CH_3), 1.84–1.92 (m, 3'-H), 2.94 (dd, $^2J_{3a,3b}$ = 14.4, $^3J_{2,3a}$ = 3.4, 3-H_a), 3.22 (dd, $^3J_{2,3b}$ = 9.9, 3-H_b)	74.8	70.1	64.7	58.7	54.0, 55.6	20.3, 22.3 (C-4', 3'-CH_3), 28.4 (C-3'), 33.2 (C-3)
6da (=16ad)	3430, 1680	5.41 (br s)	4.34 (br s)	2.64 (br s)	3.12–3.24 (m)	3.45, 3.72 (2 d, $^2J_{Bn}$ = 13.8), 3.58, 3.88 (2 d, $^2J_{Bn}$ = 14.3)	1.09, 1.13 (2 d, $^3J_{3,3\text{-}CH_3}$ = $^3J_{3,4}$ = 6.7, 4-H_3, 3-CH_3), 1.98–2.16 (m, 3-H), 2.94 (dd, $^2J_{3'a,3'b}$ = 14.1, $^3J_{2',3'a}$ = 3.6, 3'-H_a), 3.07 (dd, $^3J_{2',3'b}$ = 9.5, 3'-H_b)	75.0	71.5	64.4	61.5	54.4, 56.0	21.2, 21.5 (C-4, 3-CH_3), 28.2 (C-3), 32.2 (C-3')
6cc[c]	–	5.93 (br s)	–	–	–	–	–	–	–	–	–	–	–
8cc	3450, 1680	5.90 (br s)	4.50–4.65 (m)	3.95–4.20[b] (m)	3.35 (d, $^3J_{1',2'}$ = 8.6)	2.94, 3.95-4.20[b] (d and m, $^2J_{Bn}$ = 13.6), 3.09, 3.80 (2 d, $^2J_{Bn}$ = 13.4)	6.49 (br s, OH)	75.1	74.4	63.4*	65.6*	54.7, 55.4	–

Table 4 (continued)

Product	IR (KBr/film) ν (cm^{-1})	^{1}H NMR (300 MHz, $CDCl_3$), δ, *J* (Hz)						^{13}C NMR (75 MHz, $CDCl_3$), δ					
		1-H	1'-H	2-H	2'-H	N-C*H*$_2$Ph		C-1	C-1'	C-2	C-2'	N-*C*H$_2$ Ph	
6ac	3400, 1680	5.49 (d, $^3J_{1,2}$ = 7.9)	4.55 (d, $^3J_{1',2'}$ = 7.2)	3.50–3.68 (m)	3.84/3.87 (d)	3.18, 3.94 (2 d, $^2J_{Bn}$ = 13.9), 3.42, 3.77 (2 d, $^2J_{Bn}$ = 13.8)	2.84 (bd, $^2J_{3a,3b}$ = 14.5, 3-H$_a$), 3.13 (dd, $^3J_{2,3b}$ = 12.6, 3-H$_b$)	74.0	70.8	59.7	65.5	54.0, 55.1	33.1 (C-3)
7aa	3380, 1680	5.66 (br s)	4.91 (br s)	3.30–3.42 (m)	2.80-3.26[b] (m)	3.35, 3.70–3.82[b] (d and m, $^2J_{Bn}$ = 13.6), 3.45, 3.70–3.82[b] (d and m, $^2J_{Bn}$ = 14.5)	2.80–3.26 (m, 3-H$_2$, 3'-H$_2$, 2'-H), 3.30–3.42 (m, 2-H)	72.7*	73.3*	60.5$^+$	61.6$^+$	53.8, 53.9	34.2, 35.2 (C-3, C-3')
7bb	3430, 1680	5.43 (br s)	3.32 (d, $^3J_{1',2'}$ = 8.1)	2.75–2.95[b] (m)	2.75-2.95[b] (m)	3.41, 3.97-4.18 (d + m, $^2J_{Bn}$ = 14.1), 3.69, 3.89 (2 d, $^2J_{Bn}$ = 14.6)	0.46, 0.84 (2 d, $^3J_{4,5}$ = $^3J_{4',5'}$ = 6.4, 5-H$_3$, 5'-H$_3$), 1.03 (d, 6H, $^3J_{4,4\text{-}CH_3,4'4'\text{-}CH_3}$ = 6.4, 4-CH$_3$, 4'-CH$_3$), 1.30–1.80 (m, 3-H$_2$, 3'-H$_2$), 1.80–2.10 (m, 4-H, 4'-H), 4.52 (br s, OH)	73.7	73.7	56.7*	59.0*	54.4, 54.4	21.2, 22.3, 24.4 (C-5, C'-5, 4-*C*H$_3$, 4'-CH$_3$), 24.5, 25.6 (C-4, C-4'), 38.3, 38.4 (C-3, C-3')
8bb	3430, 1680	5.08 (dd, $^3J_{1,2}$, $^3J_{1,1'}$ = 3.3, 7.6)	4.50–4.70 (m)	3.06–3.19 (m)	2.71 (br d, $^3J_{2',3b'}$ = 11.2)	3.41, 3.97-4.18 (d and m, $^2J_{Bn}$ = 14.1), 3.69, 3.89 (2 d, $^2J_{Bn}$ = 14.6)	0.70, 0.87 (2 d, $^3J_{4,5}$, $_{4',5'}$ = 6.7, 5-H$_3$, 5'-H$_3$), 0.86, 0.91 (2 d, $^3J_{4,4\text{-}CH_3,4'4'\text{-}CH_3}$ = 6.4, 4-CH$_3$, 4'-CH$_3$), 1.05–1.15 (m, 3'-H$_a$), 1.20–1.60[b] (m, 3-H$_2$), 1.63–1.79 (m, 4-H), 1.71 (ddd, $^2J_{3a',3b'}$ = 14.3, $^3J_{3b',4'}$ = 3.1, 3'-H$_b$), 1.90–2.05 (m, 4'-H)	73.8	71.2	56.1	57.2	55.3, 55.5	21.6, 21.8, 24.3, 24.4 (C-5, C'-5, 4-CH$_3$, 4'-CH$_3$), 24.1, 24.2 (C-4, C-4'), 31.6 (C-3'), 34.6 (C-3)
8ba[d]	–	5.15–5.28 (m)	4.45–4.65 (m)	–	–	–	–	–	–	–	–	–	–
23aa[e]	1680	6.01 (br s)		3.26 (br d, $^3J_{2,3b}$ = 12.0)		3.65, 3.87 (2 d, $^2J_{Bn}$ = 14.3)	2.66 (br d, $^2J_{3a,3b}$ = 14.5, 3-H$_a$), 3.02 (dd, 3-H$_b$)	71.8		58.0		52.3	33.2 (C-3)
28aa	1710, 1680	6.05 (br s)	-	3.57–3.68 (m)	3.70–3.88[b] (m)	3.43, 3.92 (2 d, $^2J_{Bn}$ = 14.3), 3.70-3.88[b] (m)	2.74 (dd, $^2J_{3a,3b}$ = 14.1, $^3J_{2,3a}$ = 3.3, 3-H$_a$), 2.77 (dd, $^2J_{3'a,3'b}$ = 15.0, $^3J_{2',3'a}$ = 8.4, 3'-H$_a$), 3.00–3.09 (m, 3-H$_b$), 3.19 (dd, $^3J_{2',3'b}$ = 6.9, 3'-H$_b$)	75.5	206.9	65.7	58.5	53.8, 53.8	33.8, 34.0 (C-3, C-3')
28bb	1710, 1680	6.05 (d, $^3J_{1,2}$ = 1.4)	-	3.18–3.29 (m)	3.47 (dd, $^3J_{2',3a'}$, $^3J_{2',3b'}$ = 5.3, 9.8)	3.50, 3.76 (2 d, $^2J_{Bn}$ = 14.3), 3.70-3.82[b] (m)	0.47, 0.48 (2 d, $^3J_{4,5}$, $_{4',5'}$ = 6.4, 5-H$_3$, 5'-H$_3$), 0.86, 0.93 (2 d, $^3J_{4,4\text{-}CH_3,4'4'\text{-}CH_3}$ = 6.7, 4-CH$_3$, 4'-CH$_3$), 0.79–1.11 (m, 3-H$_a$, 3'-H$_a$), 1.35–2.12 (m, 3-H$_b$, 3'-H$_b$, 4-H, 4'-H)	75.7	208.4	55.0	63.7	54.1, 54.6	20.9, 23.3, 24.2 (C-5, C-5', 4-CH$_3$, 4'-CH$_3$), 23.9, 24.3 (C-4, C-4'), 36.6, 37.5 (C-3, C-3')

Table 4 (continued)

Product	IR (KBr/film) ν (cm^{-1})	^{1}H NMR (300 MHz, $CDCl_3$), δ, *J* (Hz)						^{13}C NMR (75 MHz, $CDCl_3$), δ					
		1-H	1'-H	2-H	2'-H	N-CH_2Ph		C-1	C-1'	C-2	C-2'	N-CH_2 Ph	
28ab	1710, 1680	6.08 (d, $^3J_{1,2}$ = 1.4)	-	3.45–3.63[b] (m)	3.45–3.63[b] (m)	3.54, 3.99 (2 d, $^2J_{Bn}$ = 14.6), 3.70–3.85[b] (m)	0.50 (d, $^3J_{4',5'}$ = 6.4, 5'-H_3), 0.85 (d, $^3J_{4'4'\text{-}CH_3}$ = 6.7, 4'-CH_3), 1.40–1.95[b] (m, 3'-H_2, 4'-H), 2.83 (d, $^2J_{3a,3b}$ = 13.2, 3-H_a), 3.06, 3.15 (d, 3-H_b)	75.6	207.9	58.6	63.4	53.9, 54.4	21.1, 23.1 (C-5', 4'-CH_3), 24.4 (C-4'), 34.0 (C-3), 37.2 (C-3')
28ba[f]	–	6.05 (br s)	-	–	–	–	–	–	–	–	–	–	–
10aa[e]	3540, 3440	4.05 (d, $^3J_{1,2}$ = 5.7)		2.90–3.12[b] (m)		3.53, 3.66 (2 d, $^2J_{Bn}$ = 13.8)	2.03 (br s, OH), 2.90–3.12[b] (m, 3-H_2)	72.1		61.5		54.6	33.0 (C-3)
11aa	3420	4.07 (dd, $^3J_{1,1'}$ = $^3J_{1,2}$ = 8.5)	2.85–3.24[b] (m)	2.85–3.24[b] (m)	2.85–3.24[b] (m)	3.38, 3.79 (2 d, $^2J_{Bn}$ = 13.0), 3.52, 4.31 (d and br s, $^2J_{Bn}$ = 13.6)	2.18 (br s, OH), 2.85–3.24[b] (m, 3-H_2, 3'-H_2), 5.78 (br s, OH)	70.1	74.7	64.2	59.2	54.8, 55.7	28.2 (C-3'), 32.6 (C-3)
10ab	3550, 3440	4.01 (dd, $^3J_{1,1'}$ = 1.9, $^3J_{1,2}$ = 4.8)	3.92 (dd, $^3J_{1',2'}$ = 6.7)	2.98–3.13[b] (m)	2.72 (ddd, $^3J_{2',3'a}$ = $^3J_{2',3'b}$ = 6.4)	3.54, 3.72 (2 d, $^2J_{Bn}$ = 13.8), 3.58, 3.65 (2 d, $^2J_{Bn}$ = 13.6)	0.76 (d, $^3J_{4',5'}$ = 6.7, 5'-H_3), 0.88 (d, $^3J_{4'4'\text{-}CH_3}$ = 6.7, 4'-CH_3), 1.37 (ddd, $^2J_{3'a,3'b}$ = 13.8, $^3J_{3'a,4'}$ = 6.7, 3'-H_a), 1.58 (ddd, $^3J_{3'b,4'}$ = 6.7, 3'-H_b), 1.79 (ddqq, 4'-H), 2.18 (br s, 2 H, OH), 2.98–3.13[b] (m, 3-H_2)	72.0*	72.1*	62.0	57.4	54.6, 54.6	23.0, 23.1 (4'-CH_3, C-5'), 25.5 (C-4'), 32.8 (C-3), 36.4 (C-3')
11ab (=12ba)	3380	3.99 (dd, $^3J_{1',1'}$ = $^3J_{1,2}$ = 8.0)	2.88–3.08[b] (m)	3.09–3.24[b] (m)	2.68–2.80 (m)	3.39, 4.15 (d and br s, $^2J_{Bn}$ = 13.1), 3.43, 3.77 (2 d, $^2J_{Bn}$ = 12.9)	0.77 (d, $^3J_{4',5'}$ = 5.7, 5'-H_3), 0.98 (d, $^3J_{4'4'\text{-}CH_3}$ = 6.0, 4'-CH_3), 1.35–1.55 (m, 3'-H_a, 4'-H), 1.88 (dd, $^2J_{3'a,3'b}$ = 9.9, $^3J_{2',3'b}$ or $^3J_{3'b,4'}$ = 9.9, 3'-H_b), 2.88–3.08[b] (m, 3-H_a), 3.09–3.24[b] (m, 3-H_b)	70.6	75.2	64.1	54.7	54.8, 55.6	21.9, 24.4 (4'-CH_3, C-5'), 24.8 (C-4'), 30.5 (C-3'), 32.7 (C-3)
10ac	3550, 3400	4.49 (d, $^3J_{1,2}$ = 7.2)	4.56 (d, $^3J_{1',2'}$ = 10.0)	3.13–3.25[b] (m)	3.76 (d)	3.00, 3.75 (2 d, $^2J_{Bn}$ = 13.8), 3.58, 3.72 (2 d, $^2J_{Bn}$ = 13.8)	2.27, 2.55 (2 br s, OH), 3.02–3.12 (m, 3-H_a), 3.13–3.25[b] (m, 3-H_b)	71.0	70.4	61.5	64.0	54.6, 54.7	–
10ad	3550, 3430	4.20 (d, $^3J_{1,2}$ = 8.1)	4.20 (d, $^3J_{1',2'}$ = 9.6)	3.00–3.22[b] (m)	2.54 (dd, $^3J_{2',3'}$ = 1.9)	3.43, 3.55 (2 d, $^2J_{Bn}$ = 13.4), 3.46, 3.66 (2 d, $^2J_{Bn}$ = 13.8)	1.06 (d, $^3J_{3',4'}$ = 7.2, 4'-H_3), 1.08 (d, $^3J_{3'3'\text{-}CH_3}$ = 7.7, 3'-CH_3), 3.00–3.22[b] (m, 3-H_2)	71.4*	69.8*	61.8[+]	61.0[+]	54.6, 54.7	19.3, 24.2 (3'-CH_3, C-4'), 24.9 (C-3'), 33.2 (C-3)
10bb[e]	3550, 3430	3.91 (d, $^3J_{1,2}$ = 5.9)		2.72 (ddd, $^3J_{2,3a}$ = $^3J_{2,3b}$ = 6.2)		3.69, 3.71 (2 d, $^2J_{Bn}$ = 13.6)	0.76 (d, $^3J_{4,5}$ = 6.4, 5-H_3), 0.89 (d, $^3J_{4,4\text{-}CH_3}$ = 6.7, 4-CH_3), 1.40 (ddd, $^2J_{3a,3b}$ = 13.6, $^3J_{3a,4}$ = 6.5, 3-H_a), 1.61 (ddd, $^3J_{3b,4}$ = 6.5, 3-H_b), 1.79 (ddqq, 4-H), 2.49 (br s, OH)	71.6		57.9		54.6	22.9, 23.1 (4-CH_3, C-5), 25.3 (C-4), 36.0 (C-3)

Table 4 (continued)

Product	IR (KBr/film) ν (cm^{-1})	^{1}H NMR (300 MHz, $CDCl_3$), δ, *J* (Hz)						^{13}C NMR (75 MHz, $CDCl_3$), δ					
		1-H	1'-H	2-H	2'-H	N-CH_2Ph		C-1	C-1'	C-2	C-2'	N-CH_2 Ph	
11bb (=12bb)	3550, 3400	3.94 (dd, $^3J_{1',1'}$ = $^3J_{1,2}$ = 8.2)	3.13 (dd, $^3J_{1',2'}$ = 3.8)	2.70–2.80[b] (m)	2.70–2.80[b] (m)	3.39, 4.22 (d and br s, $^2J_{Bn}$ = 13.4), 3.49, 3.75 (2 d, $^2J_{Bn}$ = 13.6)	0.79, 1.00 (2 d, $^3J_{4,5}$ = $^3J_{4',5'}$ = 6.2, 5-H_3, 5'-H_3), 0.83, 0.88 (2 d, $^3J_{4,4\text{-}CH_3}$ = $^3J_{4'4'\text{-}CH_3}$ = 6.5, 4-CH_3, 4'-CH_3), 1.35–1.65 (m, 3-H_2, 3'-H_2), 1.80–1.95 (m, 4-H, 4'-H)	71.3	75.5	59.8	54.6	54.4, 55.6	22.1, 23.2, 23.3, 24.4 (C-5, C-5', 4-CH_3, 4'-CH_3), 25.1, 26.0 (C-4, C-4'), 30.6 (C-3'), 36.8 (C-3)
11ba	3550, 3410	4.02 (dd, $^3J_{1,1'}$ = $^3J_{1,2}$ = 8.4)	2.88–3.27[b] (m)	2.57–2.68[b] (m)	2.88–3.27[b] (m)	3.39, 4.32 (d and br s, $^2J_{Bn}$ = 13.1), 3.52, 3.77 (2 d, $^2J_{Bn}$ = 13.4)	0.75–0.85 (m, 5-H_3, 4-CH_3), 1.35–1.58 (m, 3-H_2), 1.70–1.80 (m, 4-H), 2.08, 6.04 (2 br s, OH), 2.88–3.27[b] (m, 3'-H_2)	71.3	75.1	59.2	60.2	54.3, 55.8	22.9, 23.6 (4-CH_3, C-5) 26.3 (C-4), 28.2 (C-3'), 36.8 (C-3)
10cc[e]	3550, 3400	5.03 (d, $^3J_{1,2}$ = 9.8)	–	3.83 (d)	–	2.96, 3.82 (2 d, $^2J_{Bn}$ = 13.8)	4.12 (br s, OH)	69.2		64.1		54.4	–
12cc	3550, 3400	4.02 (dd, $^3J_{1,1'}$ = 7.0, $^3J_{1,2}$ = 3.9)	4.29 (dd, $^3J_{1',2'}$ = 8.0)	3.82 (d)	3.72 (d)	2.94, 4.09 (2 d, $^2J_{Bn}$ = 13.4), 3.09, 3.80 (2 d, $^2J_{Bn}$ = 13.6)	–	70.3*	74.7*	63.2[+]	66.7[+]	54.7, 54.9	–
33aa[e]	1790	4.27 (br s)		2.87–3.10[b] (m)		3.43, 3.63 (2 d, $^2J_{Bn}$ = 14.2)	2.79 (dd, $^2J_{3a,3b}$ = 12.9, $^3J_{2,3a}$ = 6.2, 3-H_a), 2.87–3.10[b] (m, 3-H_b)	80.7		61.7		54.7	31.0 (C-3), 154.5 (C=O)
33ab	1795	4.52 (dd, $^3J_{1,1'}$ = 7.2, $^3J_{1,2}$ =1.2)	4.26 (dd, $^3J_{1',2'}$ = 1.7)	3.06 (ddd, $^3J_{2,3a}$ = 6.7, $^3J_{2,3b}$ = 6.4)	2.53 (ddd, $^3J_{2',3a'}$ = 3.3, $^3J_{2',3b'}$ = 9.8)	3.10, 3.68 (2 d, $^2J_{Bn}$ = 14.0), 3.68, 3.80 (2 d, $^2J_{Bn}$ = 14.3)	0.61 (d, $^3J_{4',5'}$ = 6.4, 5'-H_3), 0.90 (ddd, $^2J_{3'a,3'b}$ = 13.9, $^3J_{3'a,4'}$ = 9.8, 3'-H_a), 0.91 (d, $^3J_{4'4'\text{-}CH_3}$ = 6.7, 4'-CH_3), 1.67 (ddd, $^3J_{3'b,4'}$ = 3.7, 3'-H_b), 1.75–1.95 (m, 4'-H), 2.89 (dd, $^2J_{3a,3b}$ = 13.4, 3-H_a), 3.15 (dd, 3-H_b)	80.7	78.2	61.8	57.9	54.5, 54.7	21.5, 23.7 (4'-CH_3, C-5') 24.2 (C-4'), 30.9 (C-3), 34.0 (C-3'), 154.7 (C=O)
33ad	1790	4.73 (d, $^3J_{1,1'}$ = 7.0)	4.14 (dd, $^3J_{1',2'}$ = 3.3)	3.08–3.21[b] (m)	2.38 (dd, $^3J_{2',3'}$ = 6.9)	3.14, 3.60 (2 d, $^2J_{Bn}$ = 14.1), 3.76 (br s)	0.74 (d, $^3J_{3',4'}$ = 6.7, 4'-H_3), 0.98 (d, $^3J_{3'3'\text{-}CH_3}$ = 6.7, 3'-CH_3), 1.96 (dqq, 3'-H), 2.94 (dd, $^2J_{3a,3b}$ = 15.5, $^3J_{2,3a}$ = 9.3, 3-H_a), 3.08–3.21[b] (m, 3-H_b)	82.4	78.2	64.9	62.7	54.7, 55.1	20.4, 22.0 (3'-CH_3, 4'-H_3), 26.6 (C-3'), 30.7 (C-3), 154.8 (C=O)
33bb[e]	1800	4.53 (br s)		2.68 (dd, $^3J_{2,3a}$ = 3.0, $^3J_{2,3b}$ = 10.2)		3.40, 3.90 (2 d, $^2J_{Bn}$ = 14.2)	0.68 (d, $^3J_{4,5}$ = 6.4, 5-H_3), 0.98 (d, $^3J_{4,4\text{-}CH_3}$ = 6.7, 4-CH_3), 0.99 (ddd, $^2J_{3a,3b}$ = 14.3, $^3J_{3a,4}$ = 10.0, 3-H_a), 1.81 (ddd, $^3J_{3b,4}$ = 3.6, 3-H_b), 2.00 (ddqq, 4-H)	78.2		57.9		54.5	21.6, 23.8 (4-CH_3, C-5), 24.2 (C-4), 34.0 (C-3), 154.8 (C=O)
***Z*-26**[e]	1590[g]	5.87 (dd, $^3J_{1,2}$ = 9.3, $^4J_{1,2'}$ = 2.4)		3.57 (dddd, $^3J_{2,3a}$ = 5.7, $^3J_{2,3b}$ = 9.3)		3.28, 3.71 (2 d, $^2J_{Bn}$ = 14.3)	2.71 (dd, $^2J_{3a,3b}$ = 14.1, 3-H_a), 2.97 (dd, 3-H_b)	131.6		57.2		53.6	39.8 (C-3)

Table 4 (continued)

Product	IR (KBr/film) ν (cm^{-1})	^{1}H NMR (300 MHz, $CDCl_3$), δ, *J* (Hz)						^{13}C NMR (75 MHz, $CDCl_3$), δ					
		1-H	1'-H	2-H	2'-H	N-CH_2Ph		C-1	C-1'	C-2	C-2'	N-CH_2 Ph	
E-**26**[e]	–[g]	5.40 (dd, $^3J_{1,2}$ = 5.0, $^4J_{1,2'}$ = 2.4)		3.34–3.48 (m)		3.42, 3.82 (2 d, $^2J_{Bn}$ = 13.8)	2.68 (dd, $^2J_{3a,3b}$ = 13.9, $^3J_{2,3a}$ = 7.6, 3-H_a), 2.96 (dd, $^3J_{2,3b}$ = 6.8, 3-H_b)	130.9		61.6		53.8	38.7 (C-3)
18	3300–3510, 1680	5.23 (dd, $^3J_{1,1'}$, $^3J_{1,2}$ = 4.8, 7.9)	3.45–3.90[b] (m)	2.98–3.10 (m)*	2.73–2.98 (m)*	3.45–3.90[b] (m)	1.01 (d, $^3J_{2',3'}$ = 7.4, 3'-H_3), 1.18 (t, $^3J_{3,4}$ = 7.2, 4-H_3), 1.40–1.60 (m, 3-H_a), 1.60–1.80 (m, 3-H_b)	72.1$^+$	71.9$^+$	61.2	54.4	55.0, 54.0	8.5 (C-4), 12.9 (C-3'), 19.9 (C-3)
19	3250–3550	3.40 (dd, $^3J_{1,1'}$ = 8.7, $^3J_{1,2}$ = 9.3)	3.25 (dd, $^3J_{1',2'}$ = 9.3)	2.77 (ddd, $^3J_{2,3a}$ = $^3J_{2,3b}$ = 4.5)	2.98 (dq, $^3J_{2',3'}$ = 6.7)	3.28, 3.82 (2 d, $^2J_{Bn}$ = 12.9), 3.41, 3.80 (2 d, $^2J_{Bn}$ = 12.9)	1.15 (t, $^3J_{3,4}$ = 7.4, 4-H_3), 1.16 (d, 3'-H_3), 1.53 (br s, OH), 1.63–1.85 (m, 3-H_2)	74.5*	74.4*	59.8	64.9	54.1, 54.5	7.9 (C-4), 14.4 (C-3'), 18.4 (C-3)
29	1700, 1680	5.88 (br s)	–	2.60–2.70 (m)	3.56 (q, $^3J_{2',3'}$ = 6.7)	3.13, 3.72–3.84[b] (d and m, $^2J_{Bn}$ = 13.8), 3.72–3.84[b] (m, 4 H)	0.75–0.90 (m, 3'-H_3, 4-H_3), 1.20–1.34 (m, 3-H_a), 1.70–1.75 (m, 3-H_b)	77.5	208.9	58.2	56.4	54.0, 54.1	12.2, 12.8 (C-4, C-3'), 20.2 (C-3)
30	3340-3520, 1680	5.01 (dd, ($^3J_{1,1'}$ = 12.2, $^3J_{1,2}$ = 5.6)	3.50–3.77[b] (m)	3.02 (ddd, $^3J_{2,3}$ = 9.7, 5.6)	2.55 (dq, $^3J_{1',2'}$ = $^3J_{2',3'}$ = 6.6)	3.18, 3.71 (2 d, $^2J_{Bn}$ = 13.2), 3.50-3.77[b] (m, 4H)	1.00/1.01 (t, $^3J_{3,4}$ = 7.3, 4-H_3), 1.08, 1.10 (d, 3'-H_3), 1.60–1.85 (m, 3-H_2), 4.15 (br s, OH)	71.9, 72.1*	70.0, 70.2*	62.4	55.2, 55.4	53.0, 54.5	7.6 (C-4), 12.6 (C-3'), 20.8 (C-3)
31	3300–3520	3.38 (d, $^3J_{1,2}$ = 7.1)	3.57 (d, $^3J_{1',2'}$ = 9.7)	2.62 (ddd, $^3J_{2,3a}$ = $^3J_{2,3b}$ = 7.1)	2.87 (dq, $^3J_{2',3'}$ = 6.6)	3.31, 3.78 (2 d, $^2J_{Bn}$ = 12.9), 3.62, 3.68 (2 d, $^2J_{Bn}$ = 13.4)	1.01 (t, $^3J_{3,4}$ = 7.1, 4-H_3), 1.03 (d, 3'-H_3), 1.62–1.75 (m, 3-H_2)	70.6*	69.7*	54.6	62.3	53.4, 54.6	8.2 (C-4), 13.3 (C-3'), 19.7 (C-3)

[a] NMR data of the *Cby* group and the aromatic rings are omitted. * or $^+$ NMR data, signed by these symbols, are interchangeable.
[b] As part of a multiplett.
[c] Data from a mixture of **6cc** and **2c**.
[d] Data from a mixture of **8ba** and **8b**.
[e] Compound is C_2-symmetrical. The ^{1}H and ^{13}C NMR data are only given for one half of the molecule.
[f] Data from mixture of **28ba** and **2b**.
[g] *Z*-**26** could be obtained diastereomerically pure from a diastereomeric mixture of *E*-**26** and *Z*-**26** by recrystallization.

refluxed for 12 h. After the addition of solid K_2CO_3 (1.11 g, 8.00 mmol) the suspension was refluxed for 4 h. The inorganic salts were removed by filtration over silica gel (1 g) and washed with MeOH (30 mL). The solvent was evaporated in vacuo and the residue was purified by flash chromatography (Et_2O/pentane, 1:4 to 1:8) to give the pure diol.

Method C: Monocarbamate **6ac** (120 mg, 0.15 mmol) or dicarbamate **23aa** (78 mg, 0.08 mmol), 1,3-propanedithiol (59 μL, 64 mg, 0.60 mmol), and $MeSO_3H$ (48 μL, 72 mg, 0.75 mmol) were dissolved in CH_2Cl_2 (3 mL) and the solution was stirred for 24 h at r.t. After addition of solid K_2CO_3 (207 mg, 1.50 mmol) stirring was continued for 30 min and subsequently the inorganic salts were filtered off and washed with CH_2Cl_2 (10 mL). The solvent was removed in vacuo and the residue was dissolved in MeOH (10 mL). Solid K_2CO_3 (207 mg, 1.50 mmol) was added and the suspension was refluxed for 24 h. The solid materials were filtered off and washed with CH_2Cl_2 (10 mL). The filtrate was dried ($MgSO_4$) and concentrated in vacuo. Purification of the crude product by flash chromatography (Et_2O/pentane, 1:6 to 1:8) yielded the diol **10ac** (71 mg, 73%) or **10aa** (36 mg, 68%).

For yields and physical data of diols **10**, **11**, **12**, **19**, and **31** see Tables 3 and 4.

Cyclic Carbonates 33aa, 33ab, 33ad, and 33bb; General Procedure[15]

A suspension of diol **10** (0.40 mmol) in excess dimethyl or diethyl carbonate (10 mL) and K_2CO_3 (280 mg, 2.00 mmol) was heated at 80 °C, until the substrate could not longer be detected by TLC (approx. 2–3 d). The solids were filtered off and washed with Et_2O (30 mL). The filtrate was concentrated in vacuo and the residue was purified by flash chromatography (Et_2O/pentane, 1:6 to 1:10) to give the cyclic carbonate **33** as pure compound. For ^{1}H, ^{13}C NMR, and IR data of **33aa**, **33ab**, **33ad**, and **33bb**, see Table 4.

[4*S*,4*S*(1*S*),5*S*,5*S*(1*S*)]-4,5-Bis[1-(*N*,*N*-dibenzylamino)-2-phenylethyl]-1,3-dioxolan-2-one (33aa)
Yield: 193 mg (72%); colorless crystals; mp 199–201°C (Et_2O/pentane); R_f 0.52 (Et_2O/pentane, 1:2); $[\alpha]_D$ –32.2 (*c* = 1, CH_2Cl_2).

Anal. Calcd. for $C_{47}H_{46}N_2O_3$ (686.9): C, 82.18; H, 6.75; Found C, 82.29; H, 8.78.

[4*S*,4*S*(1*S*),5*S*,5*S*(1*S*)]-5-[1-(*N*,*N*-dibenzylamino)-3-methylbutyl]-4-[1-(*N*,*N*-dibenzylamino)-2-phenylethyl]-1,3-dioxolan-2-one (33ab)
Yield: 225 mg (88%); colorless solid; mp 138–140°C (Et_2O/pentane); R_f 0.57 (Et_2O/pentane, 1:2); $[\alpha]_D$ –66.0 (*c* = 0.5, CH_2Cl_2).

Anal. Calcd. for $C_{44}H_{48}N_2O_3$ (652.9): C, 80.95; H, 7.41; Found C, 80.98; H, 7.61.

[4*S*,4*S*(1*S*),5*S*,5*S*(1*S*)]-5-[1-(*N*,*N*-dibenzylamino)-2-methylpropyl]-4-[1-(*N*,*N*-dibenzylamino)-2-phenylethyl]-1,3-dioxolan-2-one (33ad)
Yield: 209 mg (83%); colorless solid; mp 53–55°C (Et_2O/pentane); R_f 0.55 (Et_2O/pentane, 1:2); $[\alpha]_D$ –50.0 (*c* = 1, CH_2Cl_2).

Anal. Calcd. for $C_{43}H_{46}N_2O_3$ (638.8): C, 80.48; H, 7.40; Found C, 80.63; H, 7.36.

[4*S*,4*S*(1*S*),5*S*,5*S*(1*S*)]-4,5-Bis[1-(*N*,*N*-dibenzylamino)-3-methylbutyl]-1,3-dioxolan-2-one (33bb)
Yield: 176 mg (71%); colorless solid; mp 147–150°C (Et_2O/pentane); R_f 0.77 (Et_2O/pentane, 1:2); $[\alpha]_D$ –112.3 (*c* = 1, CH_2Cl_2).

Anal. Calcd. for $C_{41}H_{50}N_2O_3$ (618.9): C, 79.57; H, 8.14; Found C, 79.57; H, 8.34.

Debenzylation[17] of Diol 10aa and Subsequent Conversion to the Bis-*N*-Boc-Protected Derivative 37; (2*S*,3*S*,4*S*,5*S*)-2,5-Bis{[(*tert*-butyloxy]carbonyl)amino}-3,4-dihydroxy-1,6-diphenylhexane
A suspension of diol **10aa** (182 mg, 0.27 mmol) and palladium (180 mg, 60 mol%, 10% on charcoal) in MeOH/HCO_2H (20 mL, 95:5) was stirred under a H_2 atmosphere for 48 h at r.t. The solids were filtered over Celite (500 mg) and washed with MeOH (10 mL). The solvents were removed in vacuo and the residue was dissolved in MeOH (10 mL) without any further purification. After addition of di-*tert*-butyl dicarbonate (219 mg, 1.00 mmol) and Et_3N (0.17 mL, 121 mg, 1.20 mmol) the solution was stirred for 4 d at r.t. The solvent was evaporated in vacuo and the residue was purified by flash chromatography (Et_2O/pentane, 1:8→1:3) to give **37** (110 mg, 81%, two steps) as a colorless solid. The ^1H NMR data were identical to those from the literature;[2a] $[\alpha]_D$ –6.0 (*c* = 1, $CHCl_3$); mp 211°C (Et_2O/pentane) (Lit.[2a] mp 172–173°C).

Debenzylation of Diol 11aa and Conversion to the Bis-*N*-Boc-Protected Derivative 38 in a One-Pot Synthesis;[18] (2*S*,3*S*,4*R*,5*S*)-2,5-Bis{[(*tert*-butyloxy]carbonyl)amino}-3,4-dihydroxy-1,6-diphenylhexane
A suspension of diol **11aa** (80 mg, 0.12 mmol), di-*tert*-butyl dicarbonate (33 mg, 0.33 mmol), and $Pd(OH)_2$ (32 mg, 20% on charcoal, 50% neat) in EtOAc (3 mL) was stirred under a H_2 atmosphere for 24 h at r.t. The solid materials were filtered off and washed with EtOAc (10 mL). The filtrate was concentrated in vacuo and the crude product was purified by flash chromatography (Et_2O/pentane, 1:6) to afford **38** (54 mg, 92%) as a colorless solid. The ^1H NMR data are identical to those from the literature;[2a] $[\alpha]_D$ –53.2 (*c* = 1, $CHCl_3$); mp 171°C (Et_2O/pentane).

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(10) X-ray crystal structure analysis of ***Z*-26**: formula $C_{46}H_{46}N_2$, M = 626.85, colourless crystal, 0.25 × 0.20 × 0.10 mm, a = 9.608(1), c = 40.315(3) Å, V = 969.0(2) Å^3, ρ_{calc} = 1.119 g cm^{-3}, F(000) = 1344 e, μ = 4.85 cm^{-1}, empirical absorption correction via φ scan data ($0.954 \le C \le 0.999$), Z = 4, tetragonal, space group $P4_12_12$o. 92), λ = 1.54178 Å, T = 223 K, ω scans, 4260 reflections collected (+h,+k,+l), [(sinθ)/λ] = 0.62 Å^{-1}, 3771 independent and 2208 observed reflections [$I \ge 2\,\sigma(I)$], 218 refined parameters, R = 0.046, wR^2 = 0.106, max. residual electron density 0.14 (–0.14) e Å^{-3}, hydrogens calculated and refined as riding atoms.

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(12) X-ray crystal structure analysis of **19**: formula $C_{35}H_{42}N_2O_2$, M = 522.71, colourless crystal, 0.7 × 0.3 × 0.1 mm, a = 9.510(1), b = 9.649(1), c = 16.386(2) Å, β = 91.84(1)°, V = 1502.8(3) Å^3, ρ_{calc} = 1.155 g cm^{-3}, F(000) = 564 e, μ = 5.49 cm^{-1}, no absorption correction, Z = 2, monoclinic, space group $P2_1$ (No. 4), λ = 1.54178 Å, T = 223 K, $\omega/2\theta$ scans, 3436 reflections collected (+h, –k, ±l), [(sinθ)/λ] = 0.62 Å^{-1}, 3240 independent and 2713 observed reflections [$I \ge 2\,\sigma(I)$], 357 refined parameters, R = 0.052, wR^2 = 0.131, max. residual electron density 0.37 (–0.32) e Å^{-3}, hydrogens calculated and refined as riding atoms.
Data sets were collected with an Enraf Nonius CAD4 diffractometer. Programs used: data reduction MolEN, structure solution SHELX*S*-86, structure refinement SHELXL-97, graphics SCHAKAL-92.
Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-114412 (**19**) and CCDC-114413 (***Z*-26**). Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, CambridgeCB2 1EZ, UK [fax +44(1223)336033, e-mail: deposit@ccdc.cam.ac.uk].

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