27. C_2-Symmetrical Pyrrolidine Derivatives as Chiral Auxiliaries in Radical Chemistry

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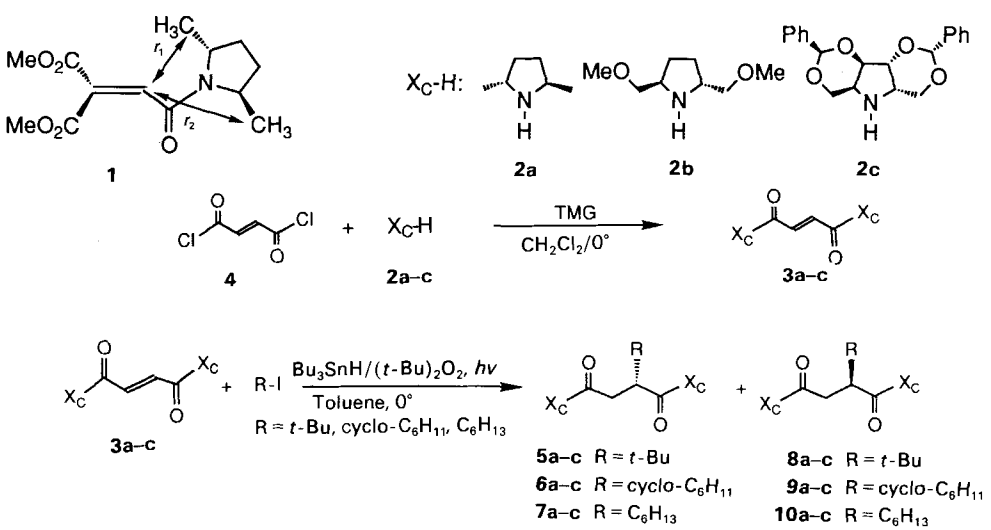
Fumaramides **3b** and **3c** bearing the C_2-symmetrical pyrrolidine moieties (2*R*,5*R*)-2,5-bis(methoxymethyl)pyrrolidine (**2b**) or 1,3:4,6-di-*O*-benzylidene-2,5-dideoxy-2,5-imino-L-idit (**2c**), respectively, as a chiral auxiliary lead to high diastereoselectivities in radical reactions ('tin method'; *Scheme 1*). Removal of the chiral auxiliaries affords the corresponding alkylated fumaric acids (*Scheme 2*). Single-crystal X-ray structures of **3b** and **3c** support arguments that lead to the model of 1,4-stereoinduction.

Introduction. – Recently *Porter* and *Giese et al.* demonstrated that radical additions to α,β-unsaturated amides derived from 2,5-dimethylpyrrolidine lead to stereoselective (C–C)-bond formation, the dimethylpyrrolidine moiety (X_c) acting as chiral auxiliary [1]. This stereoselectivity can be understood, because *a*) α,β-unsaturated amides adopt the s-*cis*-conformation [2], *b*) rotation by 180° of the bond between the carbonyl C-atom and the N-atom leads to an identical conformation (C_2 symmetry of the 2,5-dimethylpyrrolidine moiety), and *c*) the two Me groups of the dimethylpyrrolidine have different distances to the olefinic C-atom that is attacked by the radical. An X-ray analysis of α,β-unsaturated amide **1** showed that the distances r_1 and r_2 between the attacked olefinic C-atom and the two C-atoms of the Me groups on the pyrrolidine are 334 and 435 pm, respectively [3] (*Scheme 1*). This means, that only the adjacent Me group efficiently

Scheme 1



shields the olefinic C-atom from attack. The remote Me group is only necessary to make the amine part C_2-symmetrical. This picture predicts that the steric interaction should depend on the bulk of the attacking radical R˙ and of the two substituents at the C_2-symmetrical pyrrolidine. In accord to this, the stereoselectivity increases in going from primary to secondary and tertiary radicals R˙ [1]. We now show that also increase of the bulk of the pyrrolidine substituents in fumaramides **3a–c** dramatically increases the stereoselectivity of their reactions with radicals. Furthermore, the use of pyrrolidines with protected hydroxymethyl groups such as **2b** and **2c** allows an easy cleavage of the auxiliary X_c after the reaction.

Results and Discussion. – The two pyrrolidine derivatives **2b** and **2c** (*Scheme 1*) were prepared according to the procedures of *Ghosez et al.* [4] and *Shing* [5][1]), respectively. The diamides **3b** and **3c** were synthesized from fumaroyl chloride (**4**) and the corresponding amines **2b** and **2c** in the presence of tetramethylguanidine (TMG) in 74 and 64% yield, respectively (*Scheme 1*).

For both α,β-unsaturated amides **3b** and **3c**, X-ray structures were obtained (*Fig. 1* and *2*). The amide moieties adopt s-*cis*-conformations but are twisted against the olefinic plane[2]). The distances r_1 and r_2 between the olefinic C-atom and the two C-atoms at the shielding groups of the pyrrolidine part differ drastically from each other (*Table 1*). In going from **1** *via* **3b** to **3c**, the distance r_1 between the olefinic C-atom and the C-atom at the closer chiral center of the auxiliary decrease from 334 *via* 327 to 306 ppm.

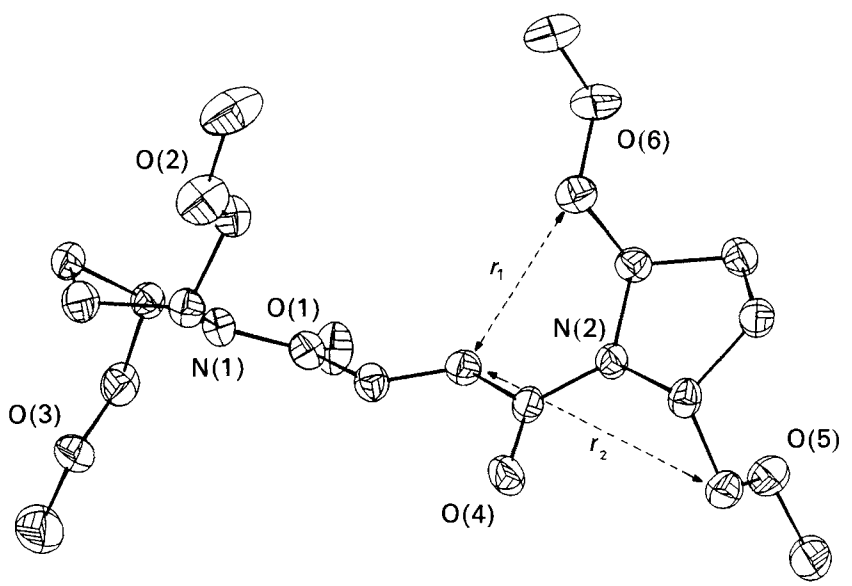


Fig. 1. *ORTEP Plot of alkene* **3b**

[1]) The synthesis was carried out with slight modifications according to [5b].

[2]) Although this twisting amounts to 4 to 31°, NMR spectra in different solvents show that the fumaramides **3a–c** must be C_2-symmetrical in solution. The twisting might be caused by packing effects in the crystals.

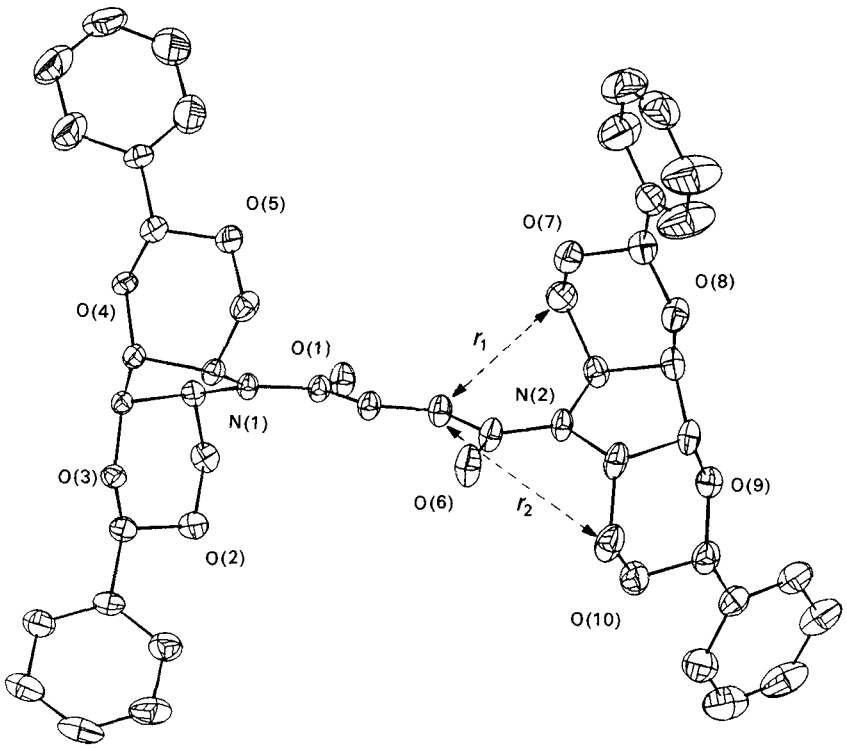


Fig. 2. *ORTEP Plot of alkene* **3c**

Table 1. *Distances* r_1 *and* r_2 *between the Shielding C-Atoms of the Pyrrolidine Moiety and the Adjacent Olefinic C-Atoms* (see *Fig. 1* and *2*)

Alkene	r_1 [ppm]	r_2 [ppm]
3b	327 (326)	440 (440)
3c	306 (317)	434 (425)

Addition of *tert*-butyl, cyclohexyl, and hexyl radicals to alkenediamides **3a–c**[3]) were carried out using the 'tin method' [6]. Products **5b**, **c**, **6b**, **c**, **7b**, **c**, and **10a** were formed as the major or only isomers (*Scheme 1*, *Table 2*). While in reactions with **3b**,

Table 2. *Product Ratios* **5–7/8–10** *during Addition of Radicals to Fumaramides* **3a–c** *at 0°* (see *Scheme 1*)

Radicals	Products	Product ratio[a]) (yield) from **3a**	Product ratio[a]) (yield) from **3b**	Product ratio[b]) (yield) from **3c**
t-C_4H_9	**5/8**	1:82 (53%) [1]	112:1 (80%)	> 200:1 (24%)
cyclo-C_6H_{11}	**6/9**	1:50 (70%) [1]	67:1 (78%)	> 200:1 (88%)
C_6H_{13}	**7/10**	1:16 (83%)[3])	35:1 (72%)	> 200:1 (89%)

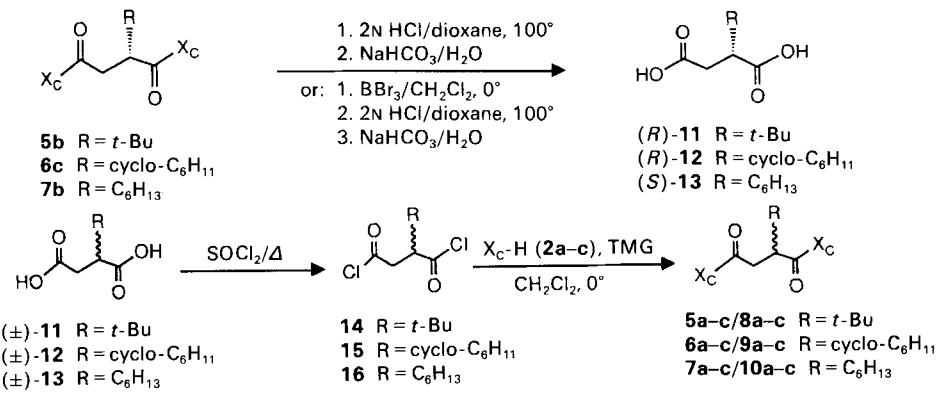
[a]) Determined by GC. [b]) Determined by HPLC.

[3]) In an additional experiment to our recent studies [1], hexyl radicals were added to alkenediamide **3a**.

slight amounts of the minor isomers **8b**, **9b**, and **10b** could be observed, with **3c** only the main isomers **5c**, **6c**, and **7c** were obtained (*Table 2*). Thus, the stereoselectivity considerably increases with increase of the bulk of substituents at the pyrrolidine moiety. In the addition of *t*-Bu radicals to **3c**, the steric interaction between the bulky *t*-Bu radical and the large pyrrolidine substituent reaches a maximum resulting in a low chemical yield.

Removal of the auxiliary group X_c requires the deprotection of the OH groups at the auxiliary [7] [8]. In case of diamide **6c**, this deprotection and the cleavage of X_c could be carried out in one operation by refluxing **6c** in dilute HCl/dioxane to give the free diacid (*R*)-**12** (*Scheme 2*). In case of diamides **5b** and **7b**, the methyl-ether functions of the pyrrolidine moiety were transformed into the corresponding free alcohols by treatment with BBr_3 [9]. Subsequently, the auxiliary was cleaved off by acidic hydrolysis to yield the free diacids (*R*)-**11** and (*S*)-**13**, respectively. The obtained R-substituted succinic acids (*R*)-**11**, (*R*)-**12**, and (*S*)-**13** showed no trace of racemisation.

Scheme 2



The minor isomers **7a**, **8b**, **9b**, **10b**, and **8c**, **9c**, **10c** were synthesized indepedently starting from the racemic diacids (±)-**11**–**13** *via* their dichlorides **14**–**16**. The resulting diastereoisomer pairs **5**/**8**, **6**/**9**, and **7**/**10** were separated by flash chromatography (*Scheme 2*).

The major products **5b**, **6b**, and **7b** of the addition of the *t*-Bu, cyclohexyl, and hexyl radical, respectively, to **3b** and the minor isomer **7a** of the addition of the hexyl radical to **3a** were identical to samples that were obtained by conversion of optically pure alkylsuccinic acids (*R*)-**11** [10], (*R*)-**12** [11], and (*S*)-**13** [12] to diamides **5b**, **6b**, **7b**, and **7a**, respectively, *via* their acyl chlorides. The major products **5c**, **6c**, and **7c** of the addition of the *t*-Bu, cyclohexyl, and hexyl radical, respectively, to **3c** showed chemical shifts and coupling constants in ^{1}H- and ^{13}C-NMR spectra that are, in the decisive parts, similar to those of **5b**, **6b**, and **7b**, respectively. The configurations were assigned on the basis of these similarities. In the case of cyclohexyl adduct **6c**, the configuration was also established by the formation of the corresponding free succinic acid (*R*)-**12** on cleavage of the auxiliary.

In the case of the *t*-Bu, cyclohexyl, and hexyl radical addition to fumaramide **3b**, measurements of the temperature dependence of the stereoselectivity over a range of 110° were carried out. *Arrhenius* plots from which the differences of the activation enthalpies ($\Delta\Delta H^{\neq}$) and of the activation entropies ($\Delta\Delta S^{\neq}$) were calculated (*Table 3*). While the values for $\Delta\Delta S^{\neq}$ are near to zero, the values for $\Delta\Delta H^{\neq}$ indicate that attack on the less hindered face of the alkene is favored by 2.0–2.6 kcal/mol compared to attack on the shielded alkene face.

Table 3. *Temperature Dependence and Activation Parameters for the Stereoselectivity of the Radical Addition to* **3b**

Radical	Product ratio				$\Delta\Delta H^{\neq}$ [kcal/mol]	$\Delta\Delta S^{\neq}$ [cal/K·mol]
	$T = 0°$	$T = 20°$	$T = 65°$	$T = 110°$		
t-Bu	112:1	88:1	43:1	33:1	2.6	0.1
cyclo-C_6H_{11}	67:1	51:1	33:1	25:1	2.0	−1.1
C_6H_{13}	35:1	27:1	17:1	10:1	2.3	−1.4

Conclusion. – As in ionic chemistry where the use of chiral auxiliaries for asymmetric (C–C)-bond formation has long been known, it was shown that this strategy is also applicable to radical chemistry. An explanation for the stereoselectivity is given by the model of 1,4-induction [1]. X-Ray analysis of fumaramides **3b** and **3c** and kinetic data of the addition of radicals to **3b** support this general model. Using bulky groups in the auxiliary or increasing the size of the attacking radical leads to higher stereoselectivities. The removal of the chiral auxiliary is easy and makes the use of stereoselective radical reactions in synthesis even more attractive.

Experimental Part

General. CH_2Cl_2 was distilled from CaH_2 and stored over molecular sieves. GC: *Carlo Erba 6000* with flame-ionization detector coupled to a *Shimadzu-C-R4*A integrator; 30-m *SE-30* column, temp. 150° (3 min) to 300° at 10°/min. HPLC: *Waters Delta Prep 3000* with UV detector (220 nm); *Lichrosphere SI 60* (5-μm column), hexane/AcOEt 4:6 (1.5 ml/min). FC: silica-gel flash chromatography *C-560KV*, 35–70 mm, *Chemische Fabrik Uetikon*. M.p.: *Büchi* apparatus, uncorrected. $[\alpha]_D^{25}$: *Perkin-Elmer-141* polarimeter. ^{1}H- and ^{13}C-NMR spectra: *Varian Gemini 300* (300 MHz) or *Varian VXR 400* (400 MHz); δ in ppm rel. to TMS as internal standard, *J* in Hz; if not noticed otherwise, $CDCl_3$ as solvent. MS: *VG 70-250*; Cl, NH_3 for chemical ionization; FAB = fast-atom bombardment.

Fumaramides **3b** *and* **3c**: *General Procedure.* To a stirred soln. of amine **2b** or **2c**[4]) (1.62–1.98 mmol) and 1 equiv. of tetramethylguanidine in dry CH_2Cl_2 (20 ml) at 0° was added fumaroyl chloride (**4**; 0.6 equiv. in dry CH_2Cl_2 (2 ml) within 30 min. Then the mixture was stirred 30 min at 0° and another 4 h at r.t., washed twice with dil. HCl soln., once with H_2O, dried (Na_2SO_4) and evaporated. The crude products **3b** or **3c**, respectively, were purified by FC.

N,N′-*Fumaroylbis[(2R,5R)-2,5-bis(methoxymethyl)pyrrolidine]* (**3b**). As described above, from **2b** (258 mg, 1.62 mmol), tetramethylguanidine (186 mg, 1.62 mmol), and **4** (149 mg, 0.97 mmol). FC (pentane/acetone 1:1) gave **3b** (137 mg, 74%). Colorless crystals. Suitable crystals for X-ray analysis were obtained by slow evaporation of the

[4]) When using the corresponding hydrochloride salts, the amine was liberated by the following procedure: a soln. of the hydrochloride salt in CH_2Cl_2 was washed twice with aq. 2N NaOH. The aq. phases were extracted twice with CH_2Cl_2 and the combined org. layers dried (KOH pellets). After filtration, the CH_2Cl_2 soln. was directly used for synthesis.

solvent (Et_2O) at r.t. M.p. 108–109°. ^{1}H-NMR (300 MHz): 7.26 (*s*, CH=CH); 4.26, 4.17 (2*m*, 2 × 2 H, H–C(2), H–C(5)); 3.52 (*dd*, *J* = 9.2, 6.9, 2 H, MeOC*H*$_2$); 3.38 (*dd*, *J* = 9.3, 3.0, 2 H, MeOC*H*$_2$); 3.28, 3.27 (2*s*, 2 × 6 H, *Me*OCH$_2$); 3.29–3.17 (*m*, 4 H, MeOC*H*$_2$); 2.15–1.88 (*m*, 8 H, CH_2(3), CH_2(4)). ^{13}C-NMR (75 MHz): 163.59, 132.10, 74.46, 71.28, 59.00, 58.88, 57.47, 57.33, 26.99, 25.23. CI-MS (NH_3): 399 (100), 353 (7), 240 (30), 114 (24), 82 (5). Anal. calc. for $C_{20}H_{34}N_2O_6$ (398.53): C 60.23, H 8.60, N 7.03; found: C 60.22, H 8.53, N 7.06.

N,N′-*Fumaroylbis(1,3:4,6-di-O-benzylidene-2,5-dideoxy-2,5-imino-*L*-iditol)* (= N,N′-*Fumaroylbis[(2*R*,4a*S*,5a*S*,8*R*,9a*R*,9b*R*)-4,4a,5a,6,9a,9b-hexahydro-2,8-diphenyl-2*H*,5*H*,8*H*-bis[1,3]dioxino[5,4-*b*:4′,5′-*d*]pyrrole]*; **3c**). As described above, from **2c** (1.12 g, 3.30 mmol), tetramethylguanidine (380 mg, 3.30 mmol), and **4** (303 mg, 1.98 mmol). FC (AcOEt) gave **3c** (793 mg, 64%). Colorless crystals. Suitable crystals for X-ray analysis were obtained by slow evaporation of the solvent (CH_2Cl_2/hexane) at r.t. M.p. 284–286°. ^{1}H-NMR (400 MHz): 7.45–7.33 (*m*, 20 H, Ph); 7.19 (*s*, CH=CH); 5.51, 5.47 (2*s*, 2 × 2 H, PhC*H*); 5.38 (*d*, *J* = 13.0, 2 H, CH_2O), 4.59 (*d*, *J* = 13.7, 2 H, CH_2O); 4.50 (*m*, 4 H, H–C(3), H–C(4)); 4.23 (*m*, 4 H, H–C(2), H–C(5)); 4.16 (*dd*, *J* = 13.7, 2.2, 2 H, CH_2O); 4.01 (*dd*, *J* = 13.1, 2.4, 2 H CH_2O). ^{13}C-NMR (101 MHz): 164.79, 137.47, 137.21, 132.84, 129.26, 129.18, 128.26, 126.08, 99.87, 99.57, 78.11, 77.56, 68.21, 64.09, 56.50, 54.76. FAB-MS: 760 (47), 759 (95), 758 (34), 757 (44), 654 (35), 653 (81), 547 (16), 420 (32), 338 (11), 234 (17), 105 (100), 77 (92), 55 (74). Anal. calc. for $C_{44}H_{42}N_2O_{10}$ (758.77): C 69.65, H 5.58, N 3.69; found: C 69.41, H 5.35, N 3.45.

Photolytical 'Tin Method'. The olefin and 5.0–7.5 equiv. of alkyl iodide (hexyl, cyclohexyl, or *t*-Bu) were dissolved in toluene (25–200 mM in olefin). The soln. was purged with Ar for 15 min and equilibrated to the reaction temp. A soln. of Bu_3SnH (3 equiv.) and di(*tert*-butyl)peroxide (0.05 equiv.) in toluene (0.5–2.0 ml) was added *via* a syringe pump within 3 h, while the mixture was irradiated with a 125-W Hg lamp. Then the mixture was stirred for another 3 h. The solvent and excess iodide were evaporated and the residue was taken up in Et_2O. The Et_2O solution was stirred for 12 h with an equal amount of sat. aq. KF soln. Bu_3SnF was removed by filtration, the org. layer dried (Na_2SO_4) and evaporated, and the product mixture separated by FC.

Thermal 'Tin Method'. The olefin and 15 equiv. of alkyl iodide (hexyl, cyclohexyl, or *t*-Bu) were dissolved in toluene (25–200 mM in olefin). The soln. was purged with Ar for 15 min and equilibrated to the reaction temp. A soln. of Bu_3SnH (7.5 equiv.) and 2,2′-azobis(isobutyronitrile) (= 2,2′-dimethyl-2,2′-azobis(propanenitrile); 0.5 equiv.) in toluene (0.5–2.0 ml) was added *via* a syringe pump within 2–3 h. Workup was carried out as described above.

N,N′-*[(2*R*)-2-(*tert*-Butyl)succinyl]bis[(2*R*,5*R*)-2,5-bis(methoxymethyl)pyrrolidine]* (**5b**). As described above, from **3b** (100 mg, 0.25 mmol), *t*-BuI (345 mg, 1.88 mmol), and Bu_3SnH (218 mg, 0.75 mmol) at 0° (photolytical cond.). FC (pentane/Et_2O/CH_2Cl_2 4:1:1) yielded **5b** (91 mg, 80%). Colorless oil. TLC: R_f 0.23. GC: t_R 14.38 min. ^{1}H-NMR (300 MHz): 4.19, 4.03 (2*m*, 4 H, H–C(2), H–C(5)); 3.88 (*dd*, *J* = 9.6, 3.6, 1 H, MeOC*H*$_2$); 3.55 (*m*, 3 H, MeOC*H*$_2$); 3.39, 3.36, 3.31, 3.29 (4*s*, 4 × 3 H, *Me*OCH$_2$); 3.40–3.18 (*m*, 4 H, MeOC*H*$_2$); 3.10 (*t*, *J* = 6.1, *t*-BuC*H*); 2.71 (*dd*, *J* = 16.2, 6.3, 1 H, CH_2); 2.57 (*dd*, *J* = 16.2, 5.9, 1 H, CH_2); 2.17–1.86 (*m*, 8 H, CH_2(3), CH_2(4)); 0.99 (*s*, *t*-Bu). ^{13}C-NMR (75 MHz): 173.38, 171.16, 73.49, 72.85, 71.60, 71.45, 58.99, 58.92, 58.80, 58.66, 58.24, 57.79, 57.01, 56.95, 48.34, 34.28, 33.86, 28.03, 27.29, 27.00, 25.22, 24.96. CI-MS (NH_3): 457 (28), 299 (17), 298 (100), 160 (18), 128 (10), 114 (8), 46 (25); Anal. calc. for: $C_{24}H_{44}N_2O_6$ (456.32): C 63.17, H 9.72, N 6.14; found: C 63.31, H 9.60, N 6.10.

N,N′-*[(2*R*)-2-(*tert*-Butyl)succinyl]bis(1,3:4,6-di-O-benzylidene-2,5-dideoxy-2,5-imino-*L*-iditol)* (= N,N′-*[(2*R*)-2-(*tert*-Butyl)succinyl]bis[(2*R*,4a*S*,5a*S*,8*R*,9a*R*,9b*R*)-4,4a,5a,6,9a,9b-hexahydro-2,8-diphenyl-2*H*,5*H*,8*H*-bis[1,3]dioxino[5,4-*b*:4′,5′-*d*]pyrrole]*; **5c**). As described above, from **3c** (146 mg, 0.19 mmol), *t*-BuI (177 mg, 0.96 mmol), and Bu_3SnH (173 mg, 0.59 mmol) at 0° (photolytical cond.). FC (pentane/Et_2O/CH_2Cl_2 1:1:1) yielded **5c** (37 mg, 24%). Colorless solid. TLC: R_f 0.30. M.p. 236–238° (MeOH). ^{1}H-NMR (300 MHz): 7.46–7.32 (*m*, 20 H, Ph); 5.49 (*m*, 5 H, CH_2O, PhC*H*); 5.42 (*d*, *J* = 12.9, 1 H, CH_2O; 5.32 (*d*, *J* = 13.8, 1 H, CH_2O); 4.83 (*d*, *J* = 12.9, CH_2O); 4.45 (*m*, 4 H, H–C(3), H–C(4)); 4.28 (*dd*, *J* = 13.8, 2.1, 1 H, CH_2O); 4.16 (*m*, 5 H, H–C(2), H–C(5), CH_2O); 3.98, 3.96 (2*dd*, *J* = 13.0, 2.2, 2 × 1 H, CH_2O); 3.37 (*m*, *t*-BuC*H*); 2.61 (*m*, CH_2); 1.07 (*s*, *t*-Bu). ^{13}C-NMR (75.5 MHz): 176.16, 172.67, 137.74, 137.69, 137.61, 137.31, 129.27, 129.15, 129.07, 128.54, 128.24, 127.35, 126.96, 126.26, 126.16, 100.50, 100.07, 99.77, 99.59, 78.69, 78.08, 78.00, 77.92, 68.16, 67.04, 64.67, 64.44, 56.67, 56.32, 55.69, 55.20, 50.17, 35.53, 35.06, 28.37. FAB-MS: 818 (6), 817 (13), 711 (10), 479 (32), 478 (100), 111 (19), 107 (15), 105 (28), 91 (15), 83 (15), 77 (15), 55 (22). Anal. calc. for $C_{48}H_{52}N_2O_{10}$ (816.89): C 70.57, H 6.41, N 3.43; found: C 70.43, H 6.42, N 3.21.

N,N′-*[(2*R*)-2-Cyclohexylsuccinyl]bis[(2*R*,5*R*)-2,5-bis(methoxymethyl)pyrrolidine]* (**6b**). As described above from **3b** (100 mg, 0.25 mmol), cyclohexyl iodide (394 mg, 1.88 mmol), and Bu_3SnH (218 mg, 0.75 mmol) at 0° (photolytical cond.). FC (pentane/Et_2O/CH_2Cl_2 3:1:1) yielded **6b** (92 mg, 76%). Colorless oil. TLC: R_f 0.27. GC: t_R 16.68 min. ^{1}H-NMR (300 MHz): 4.20, 4.03 (2*m*, 2 × 2 H, H–C(2), H–C(5)); 3.89 (*dd*, *J* = 9.6, 3.1, 1 H, MeOC*H*$_2$); 3.69 (*dd*, *J* = 9.6, 3.1, 1 H, MeOC*H*$_2$); 3.52 (*m*, 2 H, MeOC*H*$_2$); 3.39, 3.37, 3.27 (3*s*, 12 H, *Me*OCH$_2$);

3.46–3.18 (*m*, 4 H, MeOCH_2); 3.07 (*m*, cyclo-C_6H_{11}C*H*); 2.78 (*dd*, *J* = 16.1, 7.6, 1 H, CH_2); 2.47 (*dd*, *J* = 16.1, 5.5, 1 H, CH_2); 2.18–1.88 (*m*, 8 H, OH_2(3)); 1.76–0.86 (*m*, 11 H, cyclo-C_6H_{11}). ^{13}C-NMR (75 MHz): 173.97, 171.0, 73.26, 73.19, 71.53, 71.43, 59.05, 58.99, 58.88, 58.72, 57.68, 56.88, 56.76, 45.34, 41.52, 34.06, 31.14, 29.64, 27.21, 26.65, 26.27, 25.19. CI–MS (NH_3): 484 (14), 483 (56), 325 (14), 324 (83), 160 (100), 158 (17), 130 (10), 128 (86), 114 (39), 98 (20), 96 (11), 84 (9), 82 (7). HR-MS (EI): 482.3356 ($C_{26}H_{46}N_2O_6$, calc. 482.3376).

N,N′-*[(2*R*)-2-Cyclohexylsuccinyl]bis(1,3:4,6-di-*O*-benzylidene-2,5-dideoxy-2,5-imino-*L*-iditol)* (= N,N′-*[(2*R*)-2-Cyclohexylsuccinyl]bis[(2*R*,4a*S*,5a*S*,8*R*,9a*R*,9b*R*)-4,4a,5a,6,9a,9b-hexahydro-2,8-diphenyl-2*H*,5*H*,8*H*-bis[1,3]dioxino[5,4-*b*:4′,5′-*d*]pyrrole]*; **6c**). As described above, from **3c** (190 mg, 0.25 mmol), cyclohexyl iodide (263 mg, 1.25 mmol), and Bu_3SnH (218 mg, 0.75 mmol) at 0° (photolytical cond.). FC (pentane/Et_2O/CH_2Cl_2 1:1:1) yielded **6c** (184 mg, 88%). Colorless solid. TLC: R_f 0.33 HPLC: t_R 8.98 min. M.p. 239–240° (Et_2O/hexane 1:2). ^{1}H-NMR (400 MHz): 7.44–7.33 (*m*, 20 H, Ph); 5.52 (*m*, 5 H, CH_2O, PhC*H*); 5.43 (*d*, *J* = 12.9, 1 H, CH_2O); 5.16 (*d*, *J* = 13.7, 1 H, CH_2O); 4.81 (*d*, *J* = 13.7, 1 H, CH_2O); 4.47 (*m*, 4 H, H–C(3), H–C(4)); 4.25 (*d*, *J* = 1.38, 1 H, CH_2O); 4.20–4.12 (*m*, 5 H, CH_2O, H–C(2), H–C(5)); 3.95 (*d*, *J* = 13.0, 2 H, CH_2O); 3.21 (*m*, 1 H, cyclo-C_6H_{11}, C*H*); 2.65 (*m*, CH_2); 2.01, 1.62, 1.48, 1.00 (4*m*, 11 H, cyclo-C_6H_{11}). ^{13}C-NMR (75 MHz): 176.61, 172.07, 137.73, 137.51, 137.29, 129.19, 129.07, 129.04, 128.24, 128.18, 126.14, 126.10, 100.10, 99.93, 99.75, 99.57, 78.45, 78.24, 77.78, 77.72, 68.11, 66.96, 64.48, 64.38, 56.61, 56.44, 55.33, 55.06, 47.09, 42.73, 36.84, 30.67, 30.17, 26.28, 26.19, 26.06. FAB-MS: 844 (7), 843 (13), 737 (14), 505 (33), 504 (100), 105 (48), 77 (34), 55 (72). Anal. calc. for $C_{50}H_{54}N_2O_{10}$ (842.97): C 71.24, H 6.46, N 3.32; found: C 71.41, H 6.30, N 3.23.

N,N′-*[(2*R*)-2-Hexylsuccinyl]bis[(2*R*,5*R*)-2,5-dimethylpyrrolidine]* (**10a**). As described above, from **3a** [1] (150 mg, 0.54 mmol), hexyl iodide (855 mg, 4.05 mmol) and Bu_3SnH (855 mg, 1.89 mmol) at 0° (photolytical cond.). FC (pentane/Et_2O 1:40) yielded **10a** (163 mg, 83%). Colorless oil. TLC: R_f 0.21. GC: t_R 12.97 min. ^{1}H-NMR (300 MHz): 4.23, 4.10 (2*m*, 2 × 2H, H–C(2), H–C(5)); 3.19 (*m*, 1 H, C_6H_{13}C*H*); 2.65 (*dd*, *J* = 15.4, 7.5, 1 H, CH_2); 2.47 (*dd*, *J* = 15.4, 6.4, 1 H, CH_2); 2.27–2.03 (*m*, 4 H, CH_2(3), CH_2(4)), 1.68–1.42 (*m*, 6 H, CH_2(3), CH_2(4), C_6H_{13}); 1.34 (*d*, *J* = 6., 3 H, Me-Pyr.); 1.26 (*m*, 8 H, C_6H_{13}); 1.24, 1.16, 1.15 (3*d*, *J* = 6.4, 3 × 3 H, *Me*-Pyr.); 0.89 (*m*, 3 H, C_6H_{13}). ^{13}C-NMR (75 MHz): 174.08, 170.06, 53.65, 52.84, 40.02, 36.90, 33.12, 31.65, 30.79, 30.71, 29.40, 28.97, 28.88, 26.94, 22.47, 21.92, 21.50, 19.10, 18.89, 14.02. CI-MS (NH_3): 366 (24), 365 (100), 266 (20), 240 (6), 238 (8), 142 (5), 100 (22), 99 (5), 98 (63), 84 (10). Anal. calc. for $C_{22}H_{40}N_2O_2$ (364.57): C 72.48, H 11.06, N 7.68; found: C 72.38, H 11.29, N 7.47.

N,N′-*[(2*S*)-2-Hexylsuccinyl]bis[(2*R*,5*R*)-2,5-bis(methoxymethyl)pyrrolidine]* (**7b**). As described above, from **3b** (100 mg, 0.25 mmol), hexyl iodide (400 mg, 1.88 mmol), and Bu_3SnH (218 mg, 0.75 mmol) at 0° (photolytical cond.). FC (pentane/Et_2O/CH_2Cl_2 3:1:1) yielded **7b** (88 mg, 72%). Colorless oil. TLC: R_f 0.19. GC: t_R 15.16 min. ^{1}H-NMR (300 MHz): ^{1}H-NMR (300 MHz): 4.20, 4.02 (2*m*, 2 × 2 H, H–C(2), H–C(5)); 3.82 (*dd*, *J* = 9.6, 3.1, 1 H, MeOCH_2); 3.38, 3.36, 3.32, 3.31 (4*s*, 4 × 3 H, *Me*OCH_2O); 3.41–3.08 (*m*, 8 H, MeOCH_2, C_6H_{13}C*H*); 2.76 (*dd*, *J* = 15.8, 7.4, 1 H, CH_2); 2.51 (*dd*, *J* = 15.8, 6.3, 1 H, CH_2); 2.18–1.85 (*m*, 8 H, CH_2(3), CH_2(4)); 1.59–1.23 (*m*, 10 H, C_6H_{13}); 0.88 (*t*, *J* = 6.9, 3 H, C_6H_{13}). ^{13}C-NMR (75 MHz): 174.68, 170.74, 73.46, 73.30, 71.46, 71.31, 58.98, 58.83, 58.71, 57.68, 57.45, 56.87, 56.72, 40.38, 36.84, 33.19, 31.62, 29.43, 29.21, 27.19, 27.08, 26.86, 25.17, 22.48, 13.98. CI-MS (NH_3): 486 (30), 485 (100), 455 (7), 327 (5), 326 (25), 160 (11), 128 (10), 114 (17). Anal. calc. for $C_{26}H_{48}N_2O_6$ (484.71): C 64.43, H 9.98, N 5.78; found: C 64.39, H 10.16, N 5.91.

N,N′-*[(2*S*)-2-Hexylsuccinyl]bis(1,3:4,6-di-*O*-benzylidene-2,5-dideoxy-2,5-imino-*L*-iditol)* (= N,N′-*[(2*S*)-2-Hexylsuccinyl]bis[(2*R*,4a*S*,5a*S*,8*R*,9a*R*,9b*R*)-4,4a,5a,6,9a,9b-hexahydro-2,8-diphenyl-2*H*,5*H*,8*H*-bis[1,3]dioxino[5,4-*b*:4′,5′-*d*]pyrrole]*; **7c**). As described above, from **3c** (150 mg, 0.20 mmol), hexyl iodide (210 mg, 1.0 mmol), and Bu_3SnH (173 mg, 0.59 mmol) at 0° (photolytical cond.). FC (pentane/Et_2O/CH_2Cl_2 1:1:1) yielded **7c** (410 mg, 89%). Colorless solid. TLC: R_f 0.39. HPLC: t_R 9.60 min. M.p. 219–221° (MeOH). ^{1}H-NMR (300 MHz): 7.43–7.32 (*m*, 20 H, Ph); 5.51 (*m*, 5 H, CH_2O, PhC*H*); 5.43 (*d*, *J* = 13.1, 1 H, CH_2O); 5.07, 4.67 (2*d*, *J* = 14.0, 2 × 1 H, CH_2O); 4.47 (*m*, 4 H, H–C(3), H–C(4)); 4.25 (*d*, *J* = 13.9, 1 H, CH_2O); 4.15 (*m*, 5 H, H–C(2), H–C(5), CH_2O); 3.98, 3.96 (2*dd*, *J* = 13.1, 2.5, 2 × 1 H, CH_2O); 3.22 (*m*, C_6H_{13}C*H*); 2.61 (*m*, CH_2); 1.72–0.99 (*m*, 10 H, C_6H_{13}); 0.68 (*t*, *J* = 6.7, 3 H, C_6H_{13}). ^{13}C-NMR (75 MHz): 176.47, 172.05, 137.77, 137.73, 137.42, 137.33, 129.29, 129.22, 129.18, 129.12, 128.231, 128.24, 128.20, 126.19, 126.14, 100.23, 100.11, 99.89, 99.65, 78.25, 77.98, 77.82, 77.74, 67.82, 67.68, 64.43, 64.18, 56.64, 56.41, 55.41, 55.02, 42.94, 38.46, 33.40, 31.52, 29.46, 27.18, 22.57, 13.97. FAB-MS: 845 (13), 843 (11), 739 (16), 508 (7), 507 (35), 506 (100), 294 (8), 139 (7), 128 (6), 110 (9), 105 (45), 77 (24), 55 (37). Anal. calc. for $C_{50}H_{56}N_2O_{10}$ (845.01): C 71.07, H 6.68, N 3.32; found: C 70.85, H 6.84, N 3.22.

2-Alkylsuccinyl Chlorides **14–16**. Racemic 2-(*tert*-butyl)succinyl chloride (**14**) and 2-cyclohexylsuccinyl chloride (**15**) are known [1]. Racemic 2-hexylsuccinyl chloride (**16**) was prepared analogously to **14** and **15** [1] starting from 2-hexylsuccinic acid (±)-**13**; (706 mg, 3.49 mmol) in 68% yield (568 mg) as a yellowish liquid. Diacid (±)-**13** was synthesized like the 2-alkylsuccinic acids (±)-**11** and (±)-**12** [1]. **16**: B.p. 105°/0.05 mbar. ^{1}H-NMR (300 MHz): 3.39 (*dd*, *J* = 17.7, 8.6, 1 H, CH_2); 3.33–3.25 (*m*, C_6H_{13}C*H*); 3.09 (*dd*, *J* = 17.7, 4.3, 1 H, CH_2); 1.82–1.29 (*m*, 10 H,

C_6H_{13}); 0.89 (*t*, *J* = 6.7, 3 H, C_6H_{13}). ^{13}C-NMR (75 MHz): 175.03, 171.82, 52.43, 47.87, 31.36, 30.84, 28.80, 26.15, 22.45, 13.96.

N,N′-*[(2S)-2-(*tert*-Butyl)succinyl]bis[(2R,5R)-2,5-bis(methoxymethyl)pyrrolidine]* (**8b**). As described above for **3b** and **3c**, from **2b** (142 mg, 0.89 mmol), tetramethylguanidine (103 mg, 0.89 mmol), and **14** [1] (129 mg, 0.53 mmol). The diastereoisomers were separated by FC (pentane/acetone/CH_2Cl_2 4:1:1): **8b** (75 mg, 37%; R_f 0.36, t_R 15.12 min (GC)) and **5b** (60 mg, 30%; R_f 0.23, t_R 14.38 min (GC); identical to **5b** obtained from **3b**) as oils. **8b**: ^{1}H-NMR (300 MHz): 4.48, 4.19, 4.05 (3*m*, 4 H, H–C(2), H–C(5)); 3.71 (*dd*, *J* = 9.0, 3.2, 1 H, MeOCH_2); 3.58 (*dd*, *J* = 8.6, 3.1, 1 H, MeOCH_2); 3.53 (*dd*, *J* = 7.11, 3.8, 1 H, MeOCH_2); 3.37, 3.34, 3.33, 3.32 (4*s*, 4 × 3 H, *Me*OCH$_2$); 3.42–3.08 (*m*, 5 H, MeOCH_2); 3.01 (*dd*, *J* = 10.2, 2.5, *t*-BuC*H*); 2.79 (*dd*, *J* = 15.4, 10.2, 1 H, CH_2); 2.53 (*dd*, *J* = 15.4, 2.5, 1 H, CH_2); 2.04–1.87 (*m*; 8 H, CH_2(3), CJ_2(4)); 1.06 (*s*, *t*-Bu). ^{13}C-NMR (75 MHz): 175.01, 171.27, 74.83, 74.25, 71.55, 70.70, 59.10, 58.90, 58.84, 58.71, 57.60, 57.48, 57.16, 56.59, 47.67, 35.99, 33.35, 28.17, 27.34, 27.10, 25.25, 25.11. CI-MS (NH_3): 457 (4), 299 (24), 298 (100), 160 (5). Anal. calc. for $C_{24}H_{44}N_2O_6$ (456.32): C 63.17, H 9.72, N 6.14; found: C 63.25, H 9.88, N 6.07.

N,N′-*[(2S)-2-Cyclohexylsuccinyl]bis[(2R,5R)-2,5-bis(methoxymethyl)pyrrolidine]* (**9b**). As described above for **3b** and **3c**, from **2b** (163 mg, 1.02 mmol), tetramethylguanidine (117 mg, 1.02 mmol), and **15** [1] (165 mg, 0.61 mmol). The diastereoisomers were separated by FC (pentane/acetone/CH_2Cl_2 3:1:1): **9b** (84 mg, 30%; R_f 0.37, t_R 17.59 min (GC)) and **6b** (70 mg, 28%; R_f 0.27, t_R 16.68 min (GC); identical to **6b** obtained from **3b**) as oils. **9b**: ^{1}H-NMR (300 MHz): 4.39, 4.18, 4.04 (3*m*, 4 H, H–C(2), H–C(5)); 3.65 (*dd*, *J* = 9.0, 3.2, MeOCH_2); 3.57 (*dd*, *J* = 8.7, 3.2, 1 H, MeOCH_2); 3.41 (*dd*, *J* = 9.6, 3.8, 1 H, MeOCH_2); 3.36, 3.35, 3.34, 3.32 (4*s*, 4 × 3 H, *Me*OCH$_2$); 3.36–3.08 (*m*, 5 H, MeOCH_2); 2.91 (*ddd*, *J* = 9.6, 6.2, 3.5, cyclo-C_6H_{11}C*H*); 2.72 (*dd*, *J* = 15.5, 9.6, 1 H, CH_2); 2.57 (*dd*, *J* = 15.5, 3.5, 1 H, CH_2); 2.18–1.92 (*m*, 8 H, CH_2(3), CH_2(4)); 1.88–1.52, 1.33–0.83 (2*m*, cyclo-C_6H_{11}). ^{13}C-NMR (75 MHz): 174.89, 171.11, 74.63, 74.06, 71.35, 70.54, 59.06, 58.91, 58.85, 58.64, 57.38, 57.13, 57.04, 56.66, 45.19, 40.47, 35.93, 32.09, 29.53, 26.96, 26.85, 26.56, 26.48, 25.16, 25.01. CI-MS (NH_3): 484 (28), 483 (100), 325 (18), 324 (97), 160 (23), 158 (5), 128 (22), 114 (11), 98 (7). HR-MS (EI): 482.3356 ($C_{26}H_{46}N_2O_6$; calc. 482.3376).

N,N′-*[(2S)-2-Cyclohexylsuccinyl]bis(1,3:4,6-di-*O*-benzylidene-2,5-dideoxy-2,5-imino-*L*-iditol)* (= N,N′-*[(2S)-2-Cyclohexylsuccinyl]bis[(2R,4aS,5aS,8R,9aR,9bR)-4,4a,5a,6,9a,9b-hexahydro-2,8-diphenyl-2*H,*5*H,*8*H-bis[1,3]dioxino[5,4-*b*:4′,5′-*d*]pyrrole*; **9c**). As described for **3b** and **3c**, from **2c** (200 mg, 0.59 mmol), tetramethylguanidine (68 mg, 0.59 mmol), and **16** [1] (53 mg, 0.22 mmol). The diastereoisomers were separated by FC (pentane/Et_2O/CH_2Cl_2 1:1:1): **9c** (46 mg, 24%). Colorless solid. TLC: R_f 0.41, HPLC: t_R 5.42 min. M.p. 210–212° (MeOH). ^{1}H-NMR (300 MHz): 7.56–7.29 (*m*, 20 H, Ph); 5.49, 5.47 (2*s*, 2 × 1 H, PhC*H*); 5.46 (*d*, *J* = 13.0, 1 H, CH_2O); 5.30 (*d*, *J* = 12.9, 1 H, CH_2O); 5.20, 5.18 (2*s*, 2 × 1 H, PhC*H*); 4.63 (*d*, *J* = 13.4, 1 H, CH_2O); 4.46 (*d*, *J* = 13.0, 1 H, CH_2O); 4.30, 4.05 (2*m*, 2 × 2 H, H–C(3), H–C(4)); 3.94 (*d*, *J* = 12.9, 2 H, CH_2O); 3.85 (*m*, 4 H, H–C(2), H–C(5)); 3.55 (*d*, *J* = 13.2, 2 H, CH_2O); 2.95–2.89 (*m*, cyclo-C_6H_{11}C*H*); 2.72–2.57 (*m*, CH_2); 1.94–1.13 (*m*, cyclo-C_6H_{11}). ^{13}C-NMR (75 MHz): 176.49, 172.64, 138.14, 138.03, 137.58, 137.35, 129.27, 128.22, 128.93, 128.71, 128.28, 128.18, 126.12, 99.68, 99.42, 99.31, 99.08, 78.55, 78.04, 77.93, 77.42, 68.00, 66.74, 65.21, 64.68, 56.97, 56.66, 54.54, 54.20, 46.37, 39.65, 36.96, 32.37, 29.91, 26.74, 26.64, 26.52. FAB-MS: 844 (8), 843 (14), 738 (10), 737 (21), 505 (34), 504 (100), 105 (43), 77 (19), 55 (44). Anal. calc. for $C_{50}H_{54}N_2O_{10}$ (842.97): C 71.24, H 6.46, N 3.32; found: C 71.50, H 6.27, N 3.52.

N,N′-*[(2S)-2-Hexylsuccinyl]bis[(2R,5R)-2,5-dimethylpyrrolidine]* (**7a**). As described for **3b** and **3c**, from **2a** (219 mg, 2.21 mmol), tetramethylguanidine (255 mg, 2.21 mmol), and **16** (300 mg, 1.11 mmol). The diastereoisomers were separated by FC (pentane/Et_2O *1:40*): **7a** (*131* mg, 32%; R_f *0.31*, t_R *13.38 min (GC)*) and **10a** (*110* mg, 27%; R_f 0.12, t_R 12.97 min (GC); identical to **10a** obtained from **3a**) as oils. **7a**: ^{1}H-NMR (300 MHz): 4.40, 4.22–4.06 (2*m*, 1 × 1 H, 1 × 3 H, H–C(2), H–C(5)); 3.11 (*m*, C_6H_{13}C*H*); 2.72 (*dd*, *J* = 14.4, 10.0, 1 H, CH_2); 2.32 (*dd*, *J* = 14.4, 3.8, 1 H, CH_2); 2.11 (*m*, 4 H, CH_2(3), CH_2(4)); 1.71–1.21 (*m*, 14 H, CH_2(3), CH_2(4), C_6H_{13}); 1.18, 1.15, 1.14, 1.12 (4*d*, *J* = 6.4, 4 × 3 H, Me-Pyr.); 0.87 (*t*, *J* = 6.4, 3 H, C_6H_{13}). ^{13}C-NMR (75 MHz): 174.17, 170.08, 53.55, 53.15, 53.00, 40.49, 38.22, 31.58, 30.74, 30.54, 29.41, 29.02, 28.98, 27.36, 22.48, 13.94. CI-MS (NH_3): 366 (25), 365 (100), 266 (13) 238 (5), 142 (6), 100 (17), 99 (4), 98 (53), 84 (6). Anal. calc. for $C_{22}H_{40}N_2O_2$ (364.57): C 72.48, H 11.06, N 7.68; found: C 72.33, H 11.13, N 7.73.

N,N′-*[(2R)-2-Hexylsuccinyl]bis[(2R,5R)-2,5-bis(methoxymethyl)pyrrolidine]* (**10b**). As described for **3b** and **3c** from **2b** (221 mg, 1.39 mmol), tetramethylguanidine (160 mg, 1.39 mmol), and **16** (172 mg, 0.63 mmol). The diastereoisomers were separated by FC (pentane/acetone/CH_2Cl_2 (3:1:1) to yield **10b** (84 mg, 28%; R_f 0.29, t_R 16.04 min (GC)) and **7b** (80 mg, 23%; R_f 0.19, t_R 15.16 min (GC); identical to **7b** obtained from **3b**) as oils. **10b**: ^{1}H-NMR (100 MHz): 4.38, 4.19, 4.02 (3*m*, 4 H, H–C(2), H–C(5)); 3.63 (*dd*, *J* = 9.1, 3.1, 1 H, MeOCH_2); 3.58 (*dd*, *J* = 8.7, 3.0, 1 H, MeOCH_2); 3.35, 3.34, 3.33, 3.32 (4*s*, 4 × 3 H, *Me*OCH$_2$); 3.38–3.11 (*m*, 6 H, MeOCH_2); 3.08 (*m*, C_6H_{13}C*H*); 2.69 (*dd*, *J* = 15.7, 8.8, 1 H, CH_2); 2.55 (*dd*, *J* = 15.7, 4.6, 1 H, CH_2); 2.17–1.86 (*m*, 8 H, CH_2(3), CH_2(4)); 1.65–1.26 (*m*, 10 H, C_6H_{13}); 0.88 (*t*, *J* = 6.3, 3 H, C_6H_{13}). ^{13}C-NMR (75 MHz): 175.34, 170.77, 74.55,

71.36, 70.74, 59.01, 58.90, 58.83, 58.65, 57.42, 57.01, 56.94, 56.80, 40.29, 38.50, 32.74, 31.69, 29.47, 27.48, 26.99, 26.84, 25.17, 25.0, 22.54, 13.98. CI-MS (NH_3): 486 (29), 485 (100), 455 (5), 327 (12), 326 (62), 202 (8), 160 (28), 128 (19), 114 (25). Anal. calc. for $C_{26}H_{48}N_2O_6$ (484.71): C 64.43, H 9.98, N 5.78; found: C 64.61, H 10.15, N 5.76.

*N,N'-[(2R)-2-Hexylsuccinyl]bis(1,3:4,6-di-O-benzylidene-2,5-dideoxy-2,5-imino-*L*-iditol)* (= *N,N'-[(2R)-2-Hexylsuccinyl]bis[(2R,4aS,5aS,8R,9aR,9bR)-4,4a,5a,9a,9b-hexahydro-2,8-diphenyl-2H,5H,8H-bis[1,3]dioxino[5,4-b,4',5'-d]pyrrole]*; **10c**). As described for **3b** and **3c**, from **2c** (1.17 g, 3.44 mmol), tetramethylguanidine (396 mg, 3.44 mmol), and **16** (309 mg, 1.29 mmol). The diastereoisomers were separated by FC (pentane/Et_2O/CH_2Cl_2 1:1:1): **10c** (360 mg, 33%). Colorless solid. TLC: R_f 0.45. HPLC: t_R 5.69 min. M.p. 127–129° (MeOH). ^{1}H-NMR (300 MHz): 7.57–7.34 (*m*, 20 H, Ph); 5.51 (*s*, 2 H, PhC*H*); 5.46 (*d*, *J* = 12.7, 1 H, CH_2O); 5.34 (*d*, *J* = 13.1, 1 H, CH_2O); 5.10 (*s*, 2 H, PhCH); 4.51 (*d*, *J* = 13.8, 1 H, CH_2O); 4.31, 4.05 (2*m*, 5 H, CH_2O, H–C(3), H–C(4)); 3.97 (*m*, 2 H, H–C(2), H–C(5)); 3.89 (*d*, *J* = 12.9, 2 H, CH_2O); 3.81–3.69 (*m*, H–C(2), H–C(5)); 3.52 (*m*, 1 H, CH_2O); 3.31 (*dd*, *J* = 13.8, 1.7, 1 H, CH_2O); 2.84 (*m*, $C_6H_{13}CH$); 2.54 (*dd*, *J* = 14.9, 2.4, 1 H, CH_2); 2.39 (*dd*, *J* = 14.9, 7.6, 1 H, CH_2); 1.99–1.19 (*m*, 10 H, C_6H_{13}); 0.83 (*t*, *J* = 6.5, 3 H, C_6H_{13}). ^{13}C-NMR (75 MHz): 176.46, 172.73, 138.15, 137.50, 137.37, 129.24, 128.94, 128.76, 128.36, 128.28, 128.17, 126.05, 99.40, 99.27, 99.22, 99.03, 78.29, 77.98, 77.62, 77.56, 68.20, 67.03, 64.81, 64.53, 56.66, 56.38, 55.54, 54.16, 42.57, 39.93, 32.10, 31.61, 29.58, 27.92, 22.59, 14.05. FAB-MS: 845 (10), 843 (13), 739 (31), 508 (7), 507 (34), 506 (100), 139 (5), 128 (6), 110 (14), 105 (53), 77 (29), 55 (44). Anal. calc. for $C_{50}H_{56}N_2O_{10}$ (845.01): C 71.07, H 6.68, N 3.32; found: C 70.81, H 6.82, N 3.21.

*(2R-)-2-(*tert*-Butyl)succinic Acid* ((*R*)-**11**). A soln. of **5b** (175 mg, 0.38 mmol) in dry CH_2Cl_2 (0.2 ml) under Ar was cooled to 0°. Then 1M BBr_3 in CH_2Cl_2 (1.52 ml, 1.52 mmol) was added with a syringe within 15 min. After stirring for 1 h at 0° and 5 h at r.t., the mixture was quenched by addition of ice-water (3 ml) and stirred for another 15 min. The org. layer was separated, the aq. soln. saturated with NaCl and extracted 4 times with CH_2Cl_2. The combined org. layer was dried (Na_2SO_4) and evaporated. The resulting brown oil (129 mg) was dissolved in a dioxane (6.0 ml)/2N HCl (5.0 ml) and refluxed for 12 h. The mixture was cooled to r.t., the org. solvent evaporated, and the resulting aq. soln. neutralized with sat. aq. $NaHCO_3$ soln. After stirring for another 3 h at r.t, the mixture was washed 2 times with Et_2O, acidified with conc. HCl soln., saturated with NaCl and extracted 6 times with CH_2Cl_2. The combined org. layers were dried (Na_2SO_4) and evaporated: 33 mg (50%) of (*R*)-**11**. Waxy solid. $[\alpha]^{24} = -22.5$ (*c* = 3.30, acetone; [10]: $[\alpha]^{20} = -26.5$ (*c* = 5.0, acetone)). ^{1}H-NMR (300 MHz): 2.80 (*dd*, *J* = 15.6, 12.2, 1 H, CH_2); 2.66 (*dd*, *J* = 12.2, 2.3, 1 H, CH_2); 2.52 (*dd*, *J* = 15.6, 2.3, *t*-BuC*H*); 1.02 (*s*, *t*-Bu). ^{13}C-NMR (75 MHz, DMSO): 175.57, 174.43, 50.91, 31.77, 27.74, 27.59. CI-MS (NH_3): 192 (100), 174 (14).

(2R)-2-Cyclohexylsuccinic Acid ((*R*)-**12**). A soln. of **6c** (894 mg, 1.06 mmol) in dioxane (15 ml)/2N HCl (10 ml) was heated under reflux for 24 h. Workup as described for (*R*)-**11** gave (*R*)-**12** (168 mg, 80%). Colorless solid. M.p. 91–93° ([11]: 96°). $[\alpha]_D^{23} = -37.4$ (*c* = 1.66, acetone; [11]: $[\alpha]_D^{25} = -38.2$ (*c* = 2.60, acetone)). ^{1}H-NMR (300 MHz): 10.4–10.2 (br. *s*, 2 COOH); 2.75 (*m*, CH_2), 2.50 (*m*, cyclo-$C_6H_{11}CH$); 1.78–1.03 (*m*, cyclo-C_6H_{11}). CI-MS (NH_3): 218 (100), 200 (67), 186 (64), 184 (25), 166 (8), 150 (7), 52 (14), 46 (20).

(2S)-2-Hexylsuccinic Acid ((*S*)-**13**). As described above for (*R*)-**11**; treatment of **7b** (143 mg, 0.30 mmol) with 1M BBr_3 in CH_2Cl_2 (1.18 ml, 1.18 mmol) and subsequent reflux in dioxane (5 ml)/2N HCl (4 ml) yielded 54 mg (90%) of (*S*)-**13**. Colorless solid. M.p. 81–82° ([12]: 82–83°). $[\alpha]_D^{25} = -26.1$ (*c* = 3.50, EtOH; [12]: $[\alpha]_D^{23} = -26.0$ (*c* = 4, EtOH)). ^{1}H-NMR (300 MHz): 11.8 (br. *s*, 2 COOH); 2.91–2.81 (*m*, $C_6H_{13}CH$); 2.72 (*dd*, *J* = 16.8, 10.9, 1 H, CH_2), 2.51 (*dd*, *J* = 16.8, 3.5, 1 H, CH_2); 1.72–1.28 (*m*, 10 H, C_6H_{13}); 0.88 (*t*, *J* = 6.5, 3 H, C_6H_{13}).

*Resolution of (±)-2-(*tert*-Butyl)succinic Acid* ((±)-**11**). A soln. of (±)-**11** [1] (1.69 g, 9.70 mmol) and (–)-(*S*)-1-phenylethylamine (1.18 g, 9.70 mmol) in EtOH (20 ml) was refluxed for 1 h. After cooling Et_2O (50 ml) was added and the precipitate (2.38 g) that was formed during 24 h at 8° collected and recrystallized twice from boiling EtOH. A third recrystallisation did not change the optical rotation anymore. The collected salt (1.08 g; $[\alpha]_D^{23} = -13.4$ (*c* = 1.00, MeOH)) was dissolved in H_2O (20 ml), the resulting soln. acidified with conc. HCl soln. and extracted eight times with Et_2O. The combined org. layers were dried (Na_2SO_4) and evaporated: pure (*R*)-**11** (509 mg, 30%). Colorless solid. M.p. 124–126° ([10]: 122–123°). $[\alpha]_D^{20} = -26.1$ (*c* = 5.05, acetone; [10]: $[\alpha]_D^{20} = -26.5$ (*c* = 5.0, acetone)).

5b *from (*R*)-***11***.* As described for **5b**/**8b**, (*R*)-**11** (80 mg, 0.46 mmol) gave, *via* its dichloride (61 mg, 55%), **5b** (43 mg, 51%), identical with **5b** obtained from **3b**.

*(*R*)-***12*** from (2R)-Phenylsuccinic Acid.* A mixture of (2*R*)-2-phenylsuccinic acid (250 mg, 1.29 mmol) in MeOH (15 ml) and 5% Rh/Al_2O_3 (550 mg) was hydrogenated in a *Parr* apparatus (4.7 atm initial pressure) for 16 h at r.t. The mixture was filtered through a plug of *Celite* and the cake washed several times with MeOH. Evaporation gave 250 mg of crude product as a yellowish waxy solid. Crystallisation from benzene at 0° yielded pure (*R*)-**12** (200 mg, 77%). White solid. M.p. 91–92° ([11]: 96°). $[\alpha]_D^{25} = -39.5$ (*c* = 1.66, acetone; [11]: $[\alpha]_D^{25} = -38.2$ (*c* = 2.60, acetone)).

6b *from (*R*)-***12***.* As described for **6b**/**9b**, (*R*)-**12** (120 mg, 0.6 mmol) gave *via* its dichloride (84 mg, 52%), **6b** (15 mg, 48%), identical with **6b** obtained from **3b**.

Resolution of (±)-2-Hexylsuccinic Acid ((±)-**13**) as described by *Wren* and *Burns* [12] starting with 5.40 g (26.7 mmol) of racemic diacid: (*S*)-**13** (770 mg, 14%; [12]: 9%). M.p. 76–79° ([12]: 82–83°). $[\alpha]_D^{25} = -24.2$ ($c = 4.14$, EtOH; [12]: $[\alpha]_D^{23} = -26.0$ ($c = 4$, EtOH)).

7a *from (*S*)-***13***.* As described for **7a**/**10a**, (*S*)-**13** (300 mg, 1.48 mmol) gave, *via* its dichloride (334 mg, 83%), **7a** (43 mg, 54%) identical with **7a** obtained from racemic dichloride **16**.

7b *from (*S*)-***13***.* Analogously to **7a**, (*S*)-**13** gave, *via* its dichloride (200 mg, 0.74 mmol), **7b** (208 mg, 58%) identical with **7b** obtained from **3b**.

Diastereoselectivity at Different Temperatures. General Procedure. Reactions were carried out using the 'tin' or 'mercury method' [6] [13]. When using the 'tin method', the alkenediamide **3a–c** (10–20 mg, 26.4–50.2 μmol) was reacted as described above (photolytical: 0°, 20°; thermal: 65°, 110°). After workup, the diastereoisomer ratio was determined by GC or HPLC.

The 'mercury method' consisted in treating a vigorously stirred soln. of alkenediamide **3a–c** (10–20 mg, 26.4–50.2 μmol; 35–100 mM) and 10–50 equiv. of alkylmercuric chloride in CH_2Cl_2 or toluene with $NaBH_4$ (3 equiv. rel. to the mercury salt) that was dissolved in a minimum of H_2O. At 0 and 20°, CH_2Cl_2, while at 65 and 110°, toluene was used as solvent. The mixture was stirred for additional 30 min at the adjusted temp. and the diastereoisomer ratio determined by GC or HPLC directly from the reaction mixture.

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