10. Asymmetric *Diels-Alder* Cycloadditions with C_2-Symmetrical Chiral Carbamoylnitroso Dienophiles

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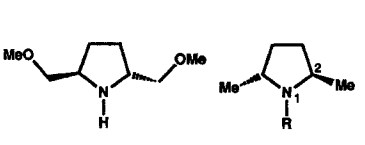
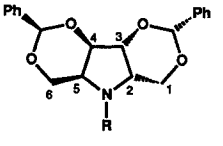
The C_2-symmetrical chiral pyrrolidines **2** and **3** are of opposite helicity. The corresponding *N*-acylnitroso dienophiles **6** and **7** react in good yield with cyclohexadiene, leading thereby with excellent diastereoisomeric excess to the expected *Diels-Alder* cycloadducts (see *Scheme*). The [2.2.2] bicyclic moieties of the major diastereoisomers **9** and **11** proved to be of opposite configuration, as expected. Their configuration is best explained by assuming the acylnitroso dienophile to be in the s-*cis* conformation in the transition state, the approach of the diene being *endo* (see *Fig.*).

Introduction. – Asymmetric *Diels-Alder* cycloadditions with chiral acylnitroso dienophiles are of recent vintage and have only been studied sparsely so far. For example, acylnitroso dienophiles which had been obtained either from chiral α-hydroxy acids (*e.g.* from D- and L-mandelic acids) [1–3] or from L-proline [4] were shown to react easily with cyclohexadiene, leading thereby in good yields to the expected cycloadducts. Nevertheless, in all these cases the diastereoisomeric excess proved to be only moderate.



1

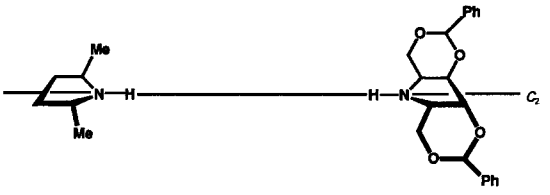
2 R = H
4 R = CONHOH
6 R = CON=O



3 R = H
5 R = CONHOH
7 R = CON=O

Quite recently, *Gouverneur* and *Ghosez* showed that the *Diels-Alder* reaction of cyclohexa-1,3-diene with the *N*-acylnitroso derivative of the chiral pyrrolidine **1** proceeded with excellent diastereoisomeric excess (d.e. > 98%) and in good yield (88%) [5]. The exceedingly high d.e. value which these authors observed is obviously due to the C_2 symmetry of the chiral pyrrolidine inductor [6].

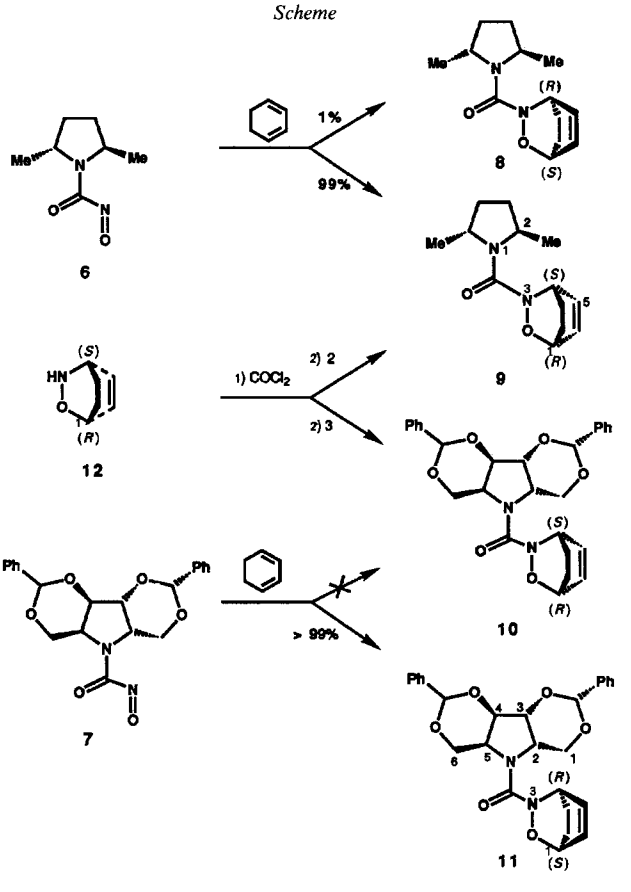
Asymmetric Hetero-*Diels-Alder* Cycloadditions. – We report herein on some novel asymmetric *Diels-Alder* reactions using *N*-acylnitroso derivatives of the chiral pyrrolidines **2** and **3**. Pyrrolidine **2** was prepared according to *Masamune*'s procedure [7], whereas pyrrolidine **3** was obtained from D-mannitol by a modified procedure (see *Exper. Part*) of *Shing*'s original methodology [8]. It should be noted that these chiral pyrrolidines also have C_2 symmetry and are of opposite helicity as indicated below.



2 3

The pyrrolidines **2** and **3** reacted smoothly with *C*-phenoxycarbohydroxamic acid (PhOCONHOH) in pyridine solution [9], giving thereby the corresponding hydroxamic acids **4** and **5**. *In situ* oxidation of these latter ones, using $(Pr_4N)IO_4$ in CH_2Cl_2 solution, gave the short-lived carbamoylnitroso dienophiles **6** and **7**, respectively, which reacted at once with cyclohexadiene to the corresponding *Diels-Alder* adducts (*Scheme*). The dimethylpyrrolidine dienophile **6** led in good overall yield (81%) to a major cycloadduct **9** and to its minor diastereoisomer **8** (*ca.* 1%). This latter one could be isolated by TLC and characterized by ^{1}H-NMR. Consequently the d.e. is *ca.* 98%. As to the tricyclic

Scheme



6 8 9 12 10 7 11

pyrrolidine dienophile **7**, it led in good yield (90%) to cycloadduct **11**. Its diastereoisomer **10** could neither be isolated nor detected by the usual methods (HPLC, ^{1}H- or ^{13}C-NMR), so that the d.e. of this cycloaddition is > 99%.

The absolute configuration of these cycloadducts could be ascertained unequivocally by two independent syntheses starting from the already described bicyclic alkoxyamine **12** [10] whose absolute configuration is known to be (1*R*,4*S*) [11]. Reaction of **12** with phosgene led to the corresponding optically pure carbamoyl chloride which had already been described in the racemic series [12]. Acylation of the chiral pyrrolidines **2** and **3** with this (1*R*,4*S*)-carbamoyl chloride gave the corresponding cycloadducts whose configurations in their bicyclic alkoxyamine moieties are obviously (1*R*,4*S*). It turned out that, using dimethylpyrrolidine **3**, this synthetic procedure led to an optically active product which was identical with the major cycloadduct **9** obtained from **6**. Tricyclic pyrrolidine **2**, however, yielded a compound **10** which was different (physical properties; $[\alpha]_D$, ^{1}H- and ^{13}C-NMR data) from cycloadduct **11** (see *Exper. Part*). Clearly, **10** and **11** are diastereoisomers. *i.e.* **11** has (1*S*,4*R*)-configuration in the bicyclic alkoxyamine moiety (*Scheme*). Having synthesized diastereoisomers **10** and **11** by different routes, HPLC proved to be the method of choice for a precise quantitative determination, the retention times of **10** and **11** being notably different. Thus, HPLC confirmed that the asymmetric *Diels-Alder* cycloaddition of cyclohexadiene with the tricyclic dienophile **7** gave diastereoisomer **11** *as the only adduct*, whereas the reaction of pyrrolidine **3** with the carbamoyl chloride of **12** gave **10** (major) as well as trace amounts (*ca.* 0.5%) of **11**. This latter result was expected since *Kresze*'s methodology led to **12** in 99% optical purity, *i.e.* the (1*S*,4*R*)-enantiomer of **12** was also formed in trace amounts as reported by *Kresze* himself [11].

The above described asymmetric syntheses of the major products **9** and **11** nicely complement those reported recently by *Gouverneur* and *Ghosez* who determined the absolute configuration of their major cycloadduct by an X-ray analysis [5]. The excellent facial diastereoselectivities which we observed show once more the powerful asymmetric inductions as exerted by chiral pyrrolidines having C_2 symmetry [6]. Even the relatively small Me groups of pyrrolidine **2** lead to a large d.e. value. When it comes to the sterically more crowded tricyclic pyrrolidine **3**, the asymmetric induction is even diastereospecific, since not even trace amounts of the expected cycloadduct **10** could be detected.

Interpretation. – Having determined the absolute configuration of the newly described cycloadducts, it follows that the geometry of the transition state leading to them must be as depicted, in the *Figure* for the cycloaddition of cyclohexadiene with the dimethylpyrrolidine dienophile **6**. If the cycloaddition proceeds according to the *'endo'* type – which is quite a reasonable hypothesis – the diene then approaches the dienophile from the least congested direction (*i.e.* the top-site). Such an *'endo'* approach implies that the acylnitroso moiety is in its s-*cis* conformation as indicated. *Gouverneur* and *Ghosez* reached the same conclusion in order to rationalize the absolute configuration of the major cycloadduct they had isolated after cycloaddition of cyclohexadiene and *N*-acylnitroso derivative **1** [5].

It should be noted that the absolute configuration of the bicyclic alkoxyamine moieties of the cycloadducts **9** and **11** correlate directly with the helicities of the C_2-symmetrical chiral inductors. Let us assume that **2** is right-handed; it follows that **3** is left-handed. As a consequence, the corresponding acylnitroso dienophiles **6** and **7** lead to

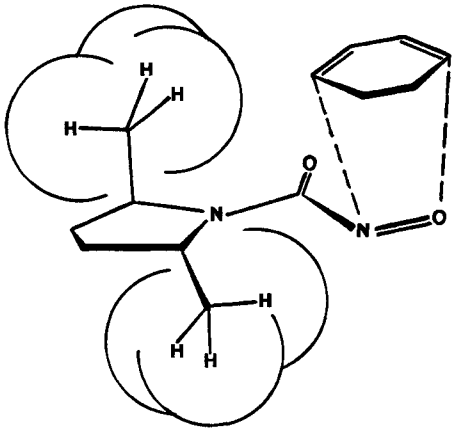


Figure. *Transition State of the* Diels-Alder *Reaction of* **6** *and Cyclohexa-1,3-diene*

a (1*R*,4*S*)- and (1*S*,4*R*)-cycloadduct (see **9** and **11**), respectively. In other words, the [2.2.2] bicyclic moieties of **9** and **11** are mirror images, hence enantiomers.

The support of the *Centre National de la Recherche Scientifique* (*URA-135*) is gratefully acknowledged. We also wish to thank *Rhône-Poulenc Company* for a PhD grant to one of us (*A. B.-P.*), Dr. *T. Tschamber* and *I. Tissot* for a preparative-scale synthesis of pyrrolidine **2**, and Prof. *B. Giese*, University of Basle, for his cooperation, particularly for the last step of the synthesis of **2**.

Experimental Part

General. D-Mannitol, cyclohexa-1,3-diene, trifluoromethanesulfonic anhydride, hydrazine (80% aq. soln.), *Raney* Ni (slurry in H_2O), and $(Pr_4N)IO_4$ were purchased from *Fluka*, acetonylacetone from *Aldrich*. Solvents were redistilled, chlorinated solvents were kept on Na_2CO_3. Flash chromatography (FC): silica gel (*Merck 60*; 230–400 mesh). TLC: alumina roll (*Merck 60 F_{254}*). M.p.: *Kofler* hot bench or *Büchi SMP 20* apparatus; corrected. $[\alpha]_D$ values: *Perkin-Elmer PE-241* polarimeter. IR spectra (cm^{-1}): *Perkin-Elmer 157-G*. ^1H- and ^{13}C-NMR spectra: *Bruker AC-F-250* using double-irradiation techniques; tetramethylsilane (TMS; ^1H-NMR) and $CDCl_3$ ($\delta(CDCl_3) = 77.00$ with respect to TMS; ^{13}C-NMR) as internal references; δ in ppm and J in Hz. High-resolution(HR) MS: were measured on a *MAT-311* spectrometer at the University of Rennes. Microanalyses were carried out by the Service Central de Microanalyses of the *CNRS*.

*(2*R*,5*R*)-2,5-Dimethylpyrrolidine* (*trans*; **2**). The HCl salt of **2** was prepared from acetonylacetone according to [7] using minor modifications [13].

*(2*R*,4a*S*,5a*S*,8*R*,9a*R*,9b*R*)-Perhydro-2,8-diphenyl-2*H*,5*H*,8*H-bis[1,3]dioxino[5,4-*b*:4′,5′-*d*]pyrrole* (**3**) was synthesized according to [8] using some modifications: *i*) The bis-triflate of di-*O*-benzylidene-D-mannitol was prepared in CH_2Cl_2 soln. and led to colourless crystals which were washed with MeOH (yield: 52%). M.p. 114–115°, then dec. ([8]: 74–75°). These crystals were stored at −20° since they turned black at r.t. *ii*) The *N*-amino derivative of **3** was prepared as follows: a soln. of the preceding bis-triflate (6.4 g) in THF (60 ml) was reacted with aq. hydrazine (12 ml), leading thereby to the *N*-amino derivative of **3** as colourless leaflets which were washed with Et_2O. Yield 3.3 g (90%). M.p. 160–161° ([8]: 136–138°). $[\alpha]_D^{20} = +57.7$ ($c = 1.0$, $CHCl_3$; [8]: $[\alpha]_D^{20} = +58.2$ ($c = 0.96$, $CHCl_3$)). The crystals turned brown when standing at r.t.; they were stored at 0°. *iii*) Hydrogenolysis of the *N*-amino derivative of **3** (1.2 g) in EtOH (25 ml) for 4 h at r.t. with moist *Raney* Ni (5 g; washed several times with EtOH under H_2) led to **3** (1.08 g, 91%) as colourless crystals which were washed with chilled i-Pr_2O. M.p. 121–122° ([8]: 121–122°). $[\alpha]_D^{20} = +8.7$ ($c = 1.0$, $CHCl_3$; [8]: $[\alpha]_D^{20} = +15$ ($c = 0.5$, $CHCl_3$)).

(1R,4S)-2-Oxa-3-azabicyclo[2.2.2]oct-5-ene (**12**) was prepared as its HCl salt according to [10] (slightly modified procedure: the reaction mixture was diluted to twice its volume by adding anh. Et_2O whereby **12**·HCl precipitated). The colourless crystals were washed with anh. Et_2O (yield: 87%). M.p. 205–210° (dec.; [10]: 135° (dec.)). $[\alpha]_D^{20} = +27.5$ ($c = 1.0$, MeOH; [10]: $[\alpha]_D^{20} = +24.4$ ($c = 5.0$, MeOH)).

(2R,5R)-2,5-Dimethylpyrrolidine-1-carbohydroxamic Acid (*trans*; **4**). To a stirred soln. of **2**·HCl (0.50 g, 3.7 mmol) in pyridine (5 ml) under Ar were added PhOCONHOH [9] (0.79 g, 1.4 equiv.) and Et_3N (0.9 ml, 0.65 mmol, 1.7 equiv.). The mixture was left for 2 d at 40° and was then evaporated and separated by FC (AcOEt/cyclohexane 1:1, then pure AcOEt). The fraction which gave a positive colour test with $FeCl_3$ (1% MeOH soln.) was evaporated and crystallized in Et_2O: **4** (0.50 g, 85%). Colourless crystals. M.p. 150–151° (benzene). $[\alpha]_D^{20} = -40.6$ ($c = 0.8$, $CHCl_3$). $[\alpha]_D^{20} = -26.5$ ($c = 0.8$, H_2O). IR (KBr): 3310, 2960, 1620, 1480, 1370, 1205, 1165, 1030, 1005, 875, 820, 755, 720, 640. ^{1}H-NMR: *Table 1*. ^{13}C-NMR: *Table 2*. Anal. calc. for $C_7H_{14}N_2O_2$ (158.2): C 53.14, H 8.92, N 17.71; found: C 52.9, H 9.0, N 17.6.

1,3:4,6-Di-O-benzylidene-2,5-dideoxy-2,5-[(N-hydroxycarbamoyl)imino]-L-iditol (= *(2R,4aS,5aS,8R,9aR,9bR)-Perhydro-2,8-diphenyl-2H,5H,8H-bis[1,3]dioxino[5,4-b:4′,5′-d]pyrrole-5-carbohydroxamic Acid*; **5**). To a stirred soln. of **3** (0.30 g, 0.9 mmol) in pyridine (0.5 ml) under Ar was added PhOCONHOH [9] (0.19 g, 1.25 mmol, 1.4 equiv.). The mixture was left for 7 d at 45–50° and was then evaporated. The residue was crystallized in i-PrOH (2 ml): pure **5** (134 mg, 35%). The mother liquors were evaporated and separated by FC (AcOEt/cyclohexane 1:1, then pure AcOEt). The fraction which gave a positive colour test with $FeCl_3$ (see above) was evaporated and recrystallized in i-PrOH leading to an additional crop of **5** (91 mg, 22%). Total yield: 225 mg (57%) of colourless crystals which proved to be solvated by some i-PrOH and became viscous when heated to 90–100° (evaporation of i-PrOH). $[\alpha]_D^{20} = +131.1$ ($c = 1.0$, $CHCl_3$). IR (KBr): 3240, 2900, 1630, 1450, 1390, 1345, 1300, 1140, 1130, 755, 700. ^{1}H-NMR: *Table 1*. ^{13}C-NMR: *Table 2*. Anal. calc. for $C_{21}H_{22}N_2O_6 \cdot 1\ H_2O \cdot \frac{2}{3}$ i-PrOH (456.4): C 60.6, H 6.5, N 6.1; found: C 60.8, H 6.3, N 6.0.

(1R,4S)-3-[(2R,5R)-2,5-Dimethylpyrrolidine-1-carbonyl]-2-oxa-3-azabicyclo[2.2.2]oct-5-ene (**9**) *and Its (1S,4R)-Diastereoisomer* **8**. a) Via *hetero*-Diels-Alder *Cycloaddition of* **6** *and Cyclohexadiene*. To a stirred soln. of cyclohexa-1,3-diene (41 µl, 0.43 mmol) in $CHCl_3$ (2 ml) containing *ca.* 10 beads of 4 Å molecular sieves were added portionwise $(Pr_4N)IO_4$ (72 mg, 0.19 mmol) and then **4** (68 mg, 0.43 mmol). The mixture was left at r.t. for 1 h, diluted with Et_2O (10 ml), and then washed with aq. 1N $NaHCO_3$ (1 ml) containing trace amounts of Na_2SO_3 and finally with brine. The aq. phase was extracted twice with Et_2O and the combined org. soln. dried over $MgSO_4$ and evaporated. The relative amounts of the minor **8** (1%) and the major **9** (99%) were determined by ^{1}H- and ^{13}C-NMR using this crude mixture. Prep. TLC (AcOEt/cyclohexane 1:1) gave **8** (*ca.* 1 mg, 1%) (^{1}H-NMR: *Table 1*) and **9** (82 mg, 81%) as colourless oils. **9**: $[\alpha]_D^{20} = -63$ ($c = 0.1$, $CHCl_3$). IR (film): 2960, 2870, 1680, 1630, 1610, 1395, 1365, 1160, 925. ^{1}H-NMR: *Table 1*. ^{13}C-NMR: *Table 2*. Anal. calc. for $C_{23}H_{20}N_2O_2$ (236.31): C 66.07, H 8.53, N 11.86; found: C 66.0, H 8.6, N 11.7.

b) Via *Acylation of* **12**. To a soln. of **12**·HCl (0.1 g, 0.68 mmol, 1.9 equiv.) and Et_3N (0.11 ml, 0.81 mmol, 2.1 equiv.) in $CHCl_3$ (3 ml) was added dropwise a 0.45M soln. of phosgene in toluene (1.8 ml, 0.81 mmol, 2.1 equiv.). The mixture was left to react overnight at r.t. under Ar. After evaporation, the residue was taken up in CCl_4 (3 ml), the mixture filtered, and the soln. evaporated. The resulting resin was dissolved in AcOEt (2 ml) to which were added successively H_2O (20 µl), **2**·HCl (49 mg, 0.36 mmol), and solid K_2CO_3 (89 mg, 0.65 mmol, 1.2 equiv.). This soln. was stirred overnight at r.t. under Ar and filtered. The filtrate was evaporated and separated by prep. TLC (AcOEt): **9** (R_f 0.7) as a colourless resin (80 mg, 94%). $[\alpha]_D^{20} = -68.6$ ($c = 1.0$, $CHCl_3$). IR: identical to the one described above. ^{1}H-NMR ($CDCl_3$, 250 MHz): 4.19 (*m*, H–C(1)); 4.71 (*m*, H–C(4)); 6.26 (*ddd*, H–C(5)); 6.13 (*ddd*, H–C(6)); 1.89 (*m*, H_a–C(7)); 2.23 (*m*, H_a–C(8)); 0.98 (*m*, H_b–C(7), H_b–C(8)); 4.30 (*m*, H–C(2′), H–C(5′)); 1.76, 1.12 (2*m*, 2 H–C(3′), 2 H–C(4′)); 1.12 (*d*, $J = 6.2$, 2 Me).

1,3:4,6-Di-O-benzylidene-2,5-dideoxy-2,5-{[(1R,4S)-2-oxa-3-azabicyclo[2.2.2]oct-5-ene-3-carbonyl]imino}-L-iditol (= *(2R,4aS,5aS,8R,9aR,9bR)-Perhydro-5-[(1R,4S)-2-oxa-3-azabicyclo[2.2.2]oct-5-ene-3-carbonyl]-2,8-diphenyl-2H,5H,8H-bis[1,3]dioxino[5,4-b:4′,5′-d]pyrrole*; **10**). To a soln. of **12**·HCl (0.1 g, 0.68 mmol) and Et_3N (0.1 ml, 0.72 mmol, 1.1 equiv.) in CH_2Cl_2 (2 ml) was added dropwise a 0.45M soln. of phosgene in toluene (1.7 ml, 0.76 mmol, 1.1 equiv.). The mixture was left overnight at r.t. under Ar. After evaporation, the residue was taken up in CCl_4 (3 ml), the mixture filtered, and the soln. evaporated. The remaining resin was dissolved in Et_2O (3 ml) and H_2O (0.1 ml) and stirred overnight after addition of powdered K_2CO_3 (54 mg, 0.39 mmol, 1.1 equiv.) and **3** (0.23 g, 0.68 mmol, 1 equiv.). The mixture was then diluted with AcOEt and filtered and the org. filtrate evaporated. The resulting resin was separated by FC (AcOEt/cyclohexane 1:1) leading to **10** (0.23 g, 71%) and **3** (15 mg, 7%) in that order of elution. **10**: Colourless crystals. M.p. 195–196° (AcOEt/cyclohexane). $[\alpha]_D^{20} = +181.3$ ($c = 1.0$, $CHCl_3$). IR (KBr): 2930, 1637, 1422, 1400, 1340, 1132, 1088, 1020, 998, 986, 927, 752, 697. ^{1}H-NMR:

Table 1. *^{1}H-NMR Data of the Hydroxamic Acids* **4** *and* **5** *and of the Cycloadducts* **8–11**[a]). 250 MHz, 300 K; δ in ppm and J in Hz, internal standard TMS.

	Solvent	H_a–C(1), H_a–C(6)	H_b–C(1), H_b–C(6)	H–C(2), H–C(5)	H–C(3), H–C(4)	H–C(1′)	H–C(4′)	H–C(5′)	H–C(6′)	H_a–C(7′)	H_b–C(7′)	H_a–C(8′)	H_b–C(8′)	Others
4	$CDCl_3$			3.97	2.14, 1.56									1.19 (Me); 6.59, 6.45 (NHOH)
5	$CDCl_3$	4.00	5.16	4.03	4.46									5.51 (C*H*Ph); 7.40, 7.34 (arom. H); 6.45, 6.75 (NHOH); 1.19 (Me_2CH); 4.01 (Me_2CH)
8	C_6D_6			4.50	1.35, 1.19	4.12	4.86	6.65	6.08	1.84	0.92	1.77	1.10	1.19 (Me)
9	C_6D_6			4.33	1.75, 1.13	4.16	4.76	6.26	6.10	1.88	0.96	2.26	0.96	1.13 (Me)
10	$CDCl_3$	3.98	5.03	4.14	4.39	4.60	4.87	6.71	6.51	2.13	1.36	2.09	1.54	5.47 (C*H*Ph); 7.41, 7.34 (arom. H)
11	$CDCl_3$	3.97	4.89	4.13	4.43	4.66	4.75	6.61	6.57	2.21	1.33	2.41	1.47	5.48 (C*H*Ph); 7.44, 7.35 (arom. H)

	Solvent	J(1a,1b)	J(1a,2)	J(1b,2)	J(2,3)	J(1′,5′)	J(1′,6′)	J(1′,7a)	J(1′,7b)	J(4′,5′)	J(4′,6′)	J(4′,8′a)	J(4′,8′b)	J(5′,6′)
5	$CDCl_3$	13.2	2.2	[b])	2.3									
8[c])	C_6D_6					1.6	5.8	[b])	[b])	5.6	1.8	[b])	[b])	8.2
9[c])	C_6D_6					1.7	5.6	3.7	1.7	6.3	1.7	2.8	3.7	8.2
10	$CDCl_3$	13.0	2.4	1.0	2.4	1.6	5.8	4.0	1.6	5.6	1.8	2.8	2.8	8.4
11	$CDCl_3$ or C_6D_6	13.2	2.3	1.0	2.4	1.7	5.4	3.5	1.8	6.6	1.7	3.6	1.8	8.2

[a]) Primed numbers refer to the [2.2.2]bicyclic moieties. [b]) Not determined. [c]) J(2, Me) = 6.2.

Table 2. *^{13}C-NMR Data* ($CDCl_3$) *of the Hydroxamic Acids* **4** *and* **5** *and of the Cycloadducts* **9–11**[a]). δ in ppm; 300 K, internal standard $CDCl_3$ (= 77.0 ppm).

	Frequency	C(1), C(6)	C(2), C(5)	C(3), C(4)	C(1′)	C(4′)	C(5′)	C(6′)	C(7′)	C(8′)	C=O	Others
4	62.9 MHz		53.0	29.9								19.6 (Me)
5	62.9 MHz	65.0	55.1	77.9							160.6	137.7, 129.0, 128.2, 126.1 (arom. C); 99.6 (*C*HPh)
9	100.6 MHz		54.4	30.1	70.2	50.7	131.8[b])	131.7[c])	23.7	20.5	160.2	20.7 (Me)
10	62.9 MHz	65.4	55.9	78.2	70.7	49.4	135.2	130.9	24.7	20.1	162.3	138.3, 129.0, 128.2, 126.3 (arom. C); 99.9 (*C*HPh)
11	100.6 MHz	65.5	55.8	78.2	70.7	49.8	132.4[b])	132.2[c])	22.9	20.1	159.9	138.9, 129.0, 128.2, 126.2 (arom. C); 99.9 (*C*HPh)

[a]) Primed numbers refer to the [2.2.2]bicyclic moieties. [b]) Or C(6′). [c]) Or C(5′).

Table 1. ^{13}C-NMR: *Table 2.* Anal. calc. for $C_{27}H_{28}N_2O_6$ (476.51): C 68.05, H 5.92, N 5.88; found: C 67.8, H 6.0, N 6.0.

1,3:4,6-Di-O-benzylidene-2,5-dideoxy-2,5-{[(1S,4R)-2-oxa-3-azabicyclo[2.2.2]oct-5-ene-3-carbonyl]imino}-L-iditol (**11**). To a stirred soln. of cyclohexa-1,3-diene (0.14 µl, 0.14 mmol, 1.5 equiv.) in CH_2Cl_2 (0.4 ml) containing a few beads of 4 Å molecular sieves were added $(Pr_4N)IO_4$ (15 mg, 0.04 mmol) and **5** (40 mg, 0.09 mmol). The mixture was left for 2 h at r.t., then diluted with Et_2O (10 ml), and washed with aq. 1N $NaHCO_3$ (1 ml) containing trace amounts of Na_2SO_3 and finally with brine. The aq. phase was extracted twice with Et_2O, the combined org. soln. dried ($MgSO_4$) and evaporated, and the residue crystallized in Et_2O: **11** as colourless crystals (40 mg, 90%). M.p. 182–184° (AcOEt/cyclohexane). $[\alpha]_D^{20} = +193.3$ ($c = 1.0$, $CHCl_3$). IR (KBr): 1657, 1390, 1343, 1330, 1296, 1136, 1010, 750, 698. ^{1}H-NMR: *Table 1.* ^{13}C-NMR: *Table 2.* Anal. calc. for $C_{27}H_{28}N_2O_6$ (476.51): C 68.05, H 5.92, N 5.88; found: C 68.1, H 6.0, N 6.0.

Isomer **10** was not detected in the mother liquors (residue: 7 mg) by NMR or HPLC.

REFERENCES

[1] A. Defoin, H. Fritz, Ch. Schmidlin, J. Streith, *Helv. Chim. Acta* **1987,** *70,* 554.
[2] G.W. Kirby, M. Nazeer, *Tetrahedron Lett.* **1988,** *29,* 6173.
[3] A. Miller, T. McC. Paterson, G. Procter, *Synlett* **1989,** 32.
[4] A. Brouillard-Poichet, A. Defoin, J. Streith, *Tetrahedron Lett.* **1989,** *30,* 7061.
[5] V. Gouverneur, L. Ghosez, *Tetrahedron: Asymmetry* **1990,** *1,* 363.
[6] J.K. Whitesell, *Chem. Rev.* **1989,** *89,* 1581.
[7] R.P. Short, R.M. Kennedy, S. Masamune, *J. Org. Chem.* **1989,** *54,* 1755.
[8] T.K.M. Shing, *Tetrahedron* **1988,** *44,* 7261.
[9] A. Brouillard-Poichet, A. Defoin, J. Streith, to be published.
[10] H. Felber, G. Kresze, H. Braun, A. Vasella, *Tetrahedron Lett.* **1984,** *25,* 5381; H. Felber, G. Kresze, R. Prewo, A. Vasella, *Helv. Chim. Acta* **1986,** *69,* 1137.
[11] H. Braun, R. Charles, G. Kresze, M. Sabuni, J. Winkler, *Liebigs Ann. Chem.* **1987,** 1129; this paper is a corrigendum to [10].
[12] St.F. Nelsen, J.A. Thompson-Colon, B. Kirste, A. Rosenhouse, M. Kaftory, *J. Am. Chem. Soc.* **1987,** *109,* 7128.
[13] B. Giese, A. Veit, University of Basle, private communication.