58. Glycosylidene Carbenes

Part 3

Synthesis of Spirocyclopropanes[1])

by **Andrea Vasella*** and **Christian A. A. Waldraff**

Organisch-chemisches Institut, Universität Zürich, Winterthurerstrasse 190, CH-8057 Zürich

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Thermolysis of the glycosylidene-derived *O*-benzylated diazirine **1** in the presence of *N*-phenylmaleimide (**2**), acrylonitrile (**3**), dimethyl fumarate (**4**), or dimethyl maleate (**5**) led in good yields to mixtures of the spirocyclopropanes **6**/**7**, **8**–**11**, **12**/**13**, and **12**/**13**/**16**/**17**. The diastereoselectivity depends upon the alkene. The cycloaddition of **1** to **5** is not diastereospecific, in keeping with previous results. Deprotection of **12**, **13**, **16**, and **17** yielded the tetrols **14**, **15**, **18**, and **19**, respectively.

1. Introduction. – Glycosylidene-derived diazirines (1-aziglycoses) such as **1** [1] are precursors of glycosylidene carbenes [2] which form glycosides by insertion into O–H bonds of phenols and alcohols [3] [4]. Glycosylidene carbenes are expected to be ambiphilic/nucleophilic [5] and to form spirocyclopropanes by cycloaddition to acceptor substituted alkenes [6]. *Descotes* and coworkers have indeed shown that photolysis of *O*-acylated 1,1-diazides in the presence of acrylonitrile leads to a mixture of diastereoisomeric spirocyclopropanes [7]. The scope of this method appears to be restricted to *O*-acylated diazides and to alkenes which are resistant to the conditions of photolysis. The restriction to acylated diazides is presumably due to a stepwise formation of carbenes *via* azidonitrenes, which lead to side reactions with *O*-benzylated diazides [8]. We have examined the reaction of the benzyl-protected aziglucose **1** with *N*-phenylmaleimide (**2**), acrylonitrile (**3**), dimethyl fumarate (**4**), and dimethyl maleate (**5**)[2]).

Results and Discussion. – 2.1. *Addition of* **1** *to* N-*Phenylmaleimide* (**2**; see *Scheme 1*). Treatment of the diazirine **1** with excess *N*-phenylmaleimide (**2**) in 1,4-dioxane at room temperature for 12 h yielded the two cyclopropanes **6** and **7** (80%) in a ratio of 9:1. The diastereoselectivity leading to the preferred formation of **6** is probably due to an unfavourable steric interaction in the transition state of the rate-determining step between the C(1) and C(5) substituents and the BnO group at C(3′).

Both **6** and **7** are pyrrolidine-2,5-diones, as evidenced by the typical C=O absorption at 1775 and 1710 cm^{-1} in their IR spectra and by the C=O *s*'s between 171.33 and 170.11 ppm in the ^{13}C-NMR spectra. In the IR spectra, the

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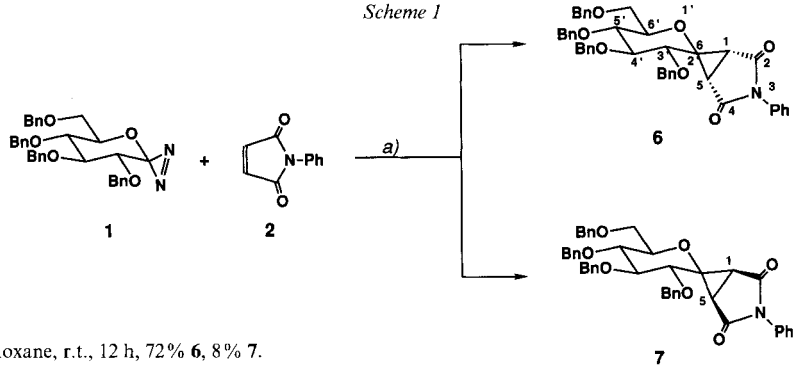
[2]) Pyranoses with a spirocyclopropane unit at C(2) [9], C(4) [10], or C(5) [11] have been prepared before, also known is a furanose with a spirocylopropane unit at C(4) [11]. Monosaccharides with annulated cyclopropyl groups are also known [11–15].

Scheme 1

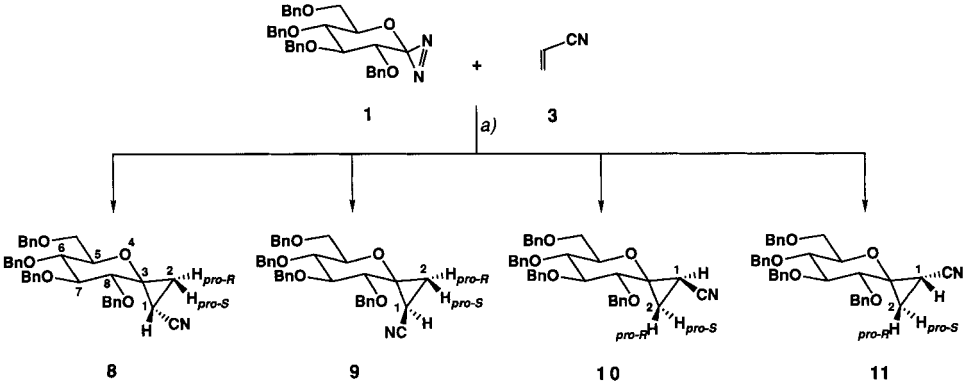


a) 1,4-Dioxane, r.t., 12 h, 72% **6**, 8% **7**.

characteristic cyclopropane C–H bands are detected at 3030 cm^{-1}. The ^{1}H-NMR spectra show the cyclopropane protons as *d*'s between 2.69 and 3.04 ppm with $^3J(1,5)$ of 5.8 and 6.7 Hz, in agreement with known values for similar compounds [16]. In the ^{13}C-NMR spectra, the cyclopropane C-atoms resonate between 32.68 and 29.36 ppm and the spiro C-atoms at 73.79 (**6**) and 73.67 ppm (**7**). The configuration of the minor product **7** was assigned on the basis of a NOE of H–C(6') on irradiation at H–C(5). The assignment is supported by a comparison of δ(H–C(3')) and δ(H–C(4')) of **6** and **7** (4.02 and 3.84 ppm for **6**; 4.17 and 4.01 ppm for **7**) showing the deshielding effect on H–C(3') and H–C(4') of **7** by the *cis*-oriented imide function. The conformation of the tetrahydropyran ring is not significantly affected by the spiro-annelation.

2.2. *Addition of* **1** *to Acrylonitrile* (**3**; see *Scheme 2*). The diazirine **1** reacted in excess **3** (room temperature, 12 h) to give a mixture of the four isomeric cyclopropanes **8**, **9**, **10**, and **11** (70%, 9:5.5:2:1). In the two major products (58%), the CN group is located below the average plane of the tetrahydropyran ring and, in the major product **8**, away from BnO–C(8). In the minor product **10** and **11**, the CN group is located above the average plane of the tetrahydropyran ring and, in the more abundant **10**, in the neighbourhood of BnO–C(8).

Scheme 2



a) R.t., 12 h, 36% **8**, 22% **9**, 8% **10**, 4% **11**.

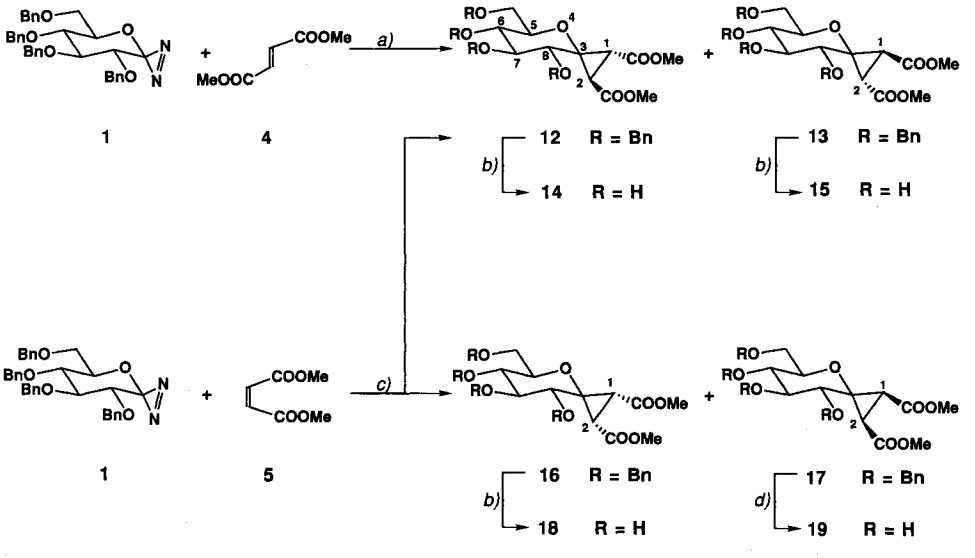
The CN function in **8**–**11** gives rise to a typical band at 2250 cm^{-1} in the IR spectra and to *s*'s in the ^{13}C-NMR spectra resonating between 118.96 and 117.94 ppm. The cyclopropane ring is evidenced by the IR band between 3030 and 3010 cm^{-1}. In the ^{1}H-NMR spectra, **8**, **10**, and **11** show three typical signals for the cyclopropane protons

between 1.88 and 1.13 ppm; the coupling constants are 10.6 or 9.9 Hz for $^3J_{cis}$, 7.2 or 6.4 Hz for $^3J_{trans}$, and 6.2–5.5 Hz for ^2J. Similar values for coupling constants in a cyclopropane ring have been reported [17]. In the ^{13}C-NMR spectra, the cyclopropane C-atoms give rise to signals between 16.30 and 14.78 ppm for C(2) and between 8.12 and 4.65 ppm for C(1). The spiro C-atoms resonate between 65.28 and 63.11 ppm.

The configurations were mainly assigned on the basis of NOE experiments. Compound **8** shows NOE's between H–C(7) and H–C(1), and between H–C(8) and $H_{pro\text{-}S}$–C(2). Both H–C(1) and $H_{pro\text{-}S}$–C(2) show a $^3J_{cis}$ of 9.9 Hz and a NOE between each other. The deshielding effect of the CN group on H–C(5) (δ = 3.78 ppm, as compared to 3.51, 3.43, and 3.52 ppm for **9**, **10**, and **11**, respectively) supports this assignment. The cyclopropane **10** shows NOE's between H–C(5) and $H_{pro\text{-}S}$–C(2) and between H–C(7) and $H_{pro\text{-}R}$–C(2) evidencing that the CN group is attached to the cyclopropane C-atoms located above the average plane of the tetrahydropyran ring. The orientation of the CN group is deduced from $^3J_{cis}$ = 10.6 Hz, as observed in the signals of H–C(1) and $H_{pro\text{-}S}$–C(2), and from a NOE between these two protons. With **11**, one finds all three possible NOE's, *i.e.* between H–C(8) and H–C(1), H–C(7) and $H_{pro\text{-}R}$–C(2), and between H–C(5) and $H_{pro\text{-}S}$–C(2). In this isomer, one finds $^3J_{cis}$ for H–C(1) and $H_{pro\text{-}R}$–C(2) and also a NOE between these protons. For **9**, one finds a NOE between H–C(1) and H–C(5). The signal of H–C(7) is shifted to lower fields (δ = 3.98 ppm, as compared to 3.70, 3.75, and 3.67 ppm for **8**, **10**, and **11**, respectively).

2.3. *Addition of* **1** *to Dimethyl Fumarate* (**4**) *and to Dimethyl Maleate* (**5**; see *Scheme 3*). Some cases of non-stereospecific cycloadditions of ambiphilic carbenes to electrophilic alkenes have been reported [18]. Glycosylidene carbenes are less reactive towards MeOH than methoxymethyl carbene [2], and this presumably on account of the BnO groups.

Scheme 3



a) 1,4-Dioxane, r.t., 12 h, 43% **12**, 29% **13**. *b*) 1.5 bar H_2, $Pd(OH)_2$/C, MeOH, r.t., 45 min, quant. *c*) 1,4-Dioxane, r.t., 12 h, 20% **16**, 17% **12**, 12% **13**, 11% **17**. *d*) With mixture of **12**/**13**/**16**/**17**, 4 h (2 bar), 10 h (1.2 bar) H_2, $Pd(OH)_2$/C, MeOH, r.t.; 98% **14**/**15**/**18**/**19**.

These electron-withdrawing substituents are expected to lower the nucleophilic properties of the carbene and to decrease the stability of the zwitterionic intermediate in a non-concerted cycloaddition (*cf.* [19] [20]) by interacting with the oxycarbenium center.

This could lead to a stereospecific addition to acceptor-substituted alkenes. We examined this question by exposing **1** to dimethyl fumarate (**4**) and to dimethyl maleate (**5**)[3]).

The reaction of **1** with excess **4** in 1,4-dioxane at room temperature for 12 h gave two crystalline cyclopropanes **12** and **13** (72%) in a ratio of 3:2 which were separated by HPLC[4]). The analogous reaction with **5**[5]) provided the four cyclopropanes **16**/**12**/**13**/**17** (60%; 1.8:1.5:1.1:1). HPLC gave pure **16** and a mixture of the other three compounds. The *cis*-configuration of the cyclopropane protons of **16** and **17** were assigned on the basis of large vicinal coupling constants (> 10 Hz).

To obtain the unprotected cyclopropanes, each of the benzyl ethers **12**, **13**, and **16** was hydrogenated in MeOH at room temperature for 45 min in the presence of $Pd(OH)_2/C$ at 1.5 bar H_2 pressure to give, in quantitative yield, the tetrols **14**, **15**, and **18**, respectively (*Scheme 3*), which were purified by flash chromatography. To assign the configuration of **19** and hence of **17**, the mixture **12**/**13**/**16**/**17** obtained from the addition to dimethyl maleate (**5**) was hydrogenated under similar conditions to give the cyclopropanes **14**/**15**/**18**/**19**. The desired compound **19** was isolated by flash chromatography.

The presence of the COOMe groups in the cyclopropanes **12**–**19** is readily detected in the IR, ^{1}H-, and ^{13}C-NMR spectra. The constitution of **12**, **13**, and **16**, the constitutional changes in the formation of **14**, **15**, **18**, and **19**, and particularly the presence of the cyclopropane ring are evident from the IR and NMR spectra. The cyclopropane protons of **12**, **13**, **14**, and **15** give rise to *d*'s between 3.26 and 2.55 ppm with $^3J(1,2) = 7.7$ Hz, in keeping with a *trans*-configuration. The compounds **16**, **18**, and **19** show *d*'s between 2.53 and 2.43 ppm with a $^3J(1,2)$ of 10.4 to 11.6 Hz, typical for *cis*-configurated cyclopropane protons[6]). This assignment is confirmed by NOE's between these protons (absent in the *trans*-configurated cyclopropanes). The orientation of the COOMe groups was determined by NOE's between H–C(8) and H–C(1) and between H–C(5) and H–C(2) of **12** and **14**. The cyclopropanes **13** and **15** show a NOE between H–C(7) and H–C(2). The same NOE was observed for **16** and **18**. A NOE between H–C(8) and H–C(1) of **16** was also observed. For compound **19**, one sees a NOE between H–C(5) and H–C(2). The downfield shift of H–C(7) of **12** ($\delta = 4.21$ ppm; for **13** and **16**, 3.36 and 3.73 ppm, respectively) and of **14** and **19** ($\delta = 3.60$ ppm, as compared to 3.36 and 3.32 ppm of **15** and **18**, respectively) support the assignments, and so does the downfield shift of H–C(8) of **19** ($\delta = 4.05$ ppm, in comparison with 3.82, 3.79, and 3.67 ppm of **15**, **16**, and **18**, respectively) and of H–C(5) of **16** ($\delta = 4.14$ ppm, as compared to 3.80 and 3.57 ppm for **12** and **13**, respectively).

The MS of **14**, **15**, **18**, and **19** show a peak at m/z 275, corresponding to $[M + 1 - \text{MeOH}]^+$, but M^+ was only found in the MS of **15** and **18**. The greater ease with which **14** and **19** lose MeOH may be rationalized by a facile lactonization involving OH–C(8). This constitutes an additional, albeit weak evidence for the proposed configurations and hints at a way to differentiate the ester functions in **14** and **19**.

Thus, *O*-benzyl-protected glycosylidene-derived diazirines form spiro[cyclopropane-tetrahydropyrans] under very mild thermal conditions. While the addition to *N*-phenylmaleimide (**2**) shows a satisfactory degree of diastereoselectivity, this is not so for the

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[3]) Conceivably, the diazirine **1** may undergo isomerization to a diazo compound [3]. A 1,3-dipolar cycloaddition [22] of this diazo compound to **4** and to **5** could form 4,5-dihydro-3*H*-pyrazoles [23], which might yield cyclopropanes by extrusion of N_2. Both cases are known, *i.e.* reactions, where 4,5-dihydro-3*H*-pyrazoles were isolated or observed [12b] [16a] [23] and reactions, where these intermediates evaded detection [25]. We found no evidence for the formation of diazo ethers or 4,5-dihydro-3*H*-pyrazoles in the reactions of **1** with **2**, **3**, **4**, or **5** (but *cf.* [4]).

[4]) Both photolysis (−15°, *HPK125 Philips* high-pressure Hg lamp with a *Solidex* filter) and thermal decomposition (room temperature) of **1** in the presence of **4** in CH_2Cl_2 yielded **12** and **13** in a ratio of 2.5:1, besides several by-products, in markedly lower yields as compared to the thermal reaction in 1,4-dioxane.

[5]) The dimethyl maleate (**5**) contained less than 1% of dimethyl fumarate (**4**; GLC: *SE-25*, 80°).

[6]) The cyclopropane protons of **17** (spectrum of a mixture **12**/**13**/**17** in $CDCl_3$) appear as two *d*'s at 2.47 and 2.34 ppm with $^3J(1,2) = 11.1$ Hz.

additions to the other alkenes we examined. It remains to be seen if this lack of selectivity is restricted to glycosylidene-derived diazirines with an equatorial substituent at C(2).

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Experimental Part

General. See [2]. Solvents and liquid reagents were destilled, solid reagents were recrystallized; 1,4-dioxane was dried over Na and MeOH over Mg, both were kept under N_2. Powdered 4-Å molecular sieves (*Union Carbide*) were activated for 6 h at 280° and kept under N_2. Qual. TLC: detection by treating with a soln. of 5% $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ and 0.1% $Ce(SO_4)_2\cdot 4H_2O$ in 10% H_2SO_4 or with a soln. of 5% vanillin in conc. H_2SO_4.

Cyclopropanation of **1** *with* N-*Phenylmaleimide* (**2**). Under N_2, a soln. of 471 mg (2.7 mmol) of **2** in 1 ml of 1,4-dioxane was stirred in the presence of 0.1 g of 4-Å molecular sieves for 30 min at r.t. Then, 150 mg (0.27 mmol) of **1** were added quickly, the mixture was stirred at r.t. for 12 h, diluted with 5 ml of CH_2Cl_2, and filtered through *Celite*. The *Celite* was washed several times with CH_2Cl_2. The combined filtrates were evaporated. FC (hexane/AcOEt 9:1) of the residue gave 137 mg (72%) of **6** and 15 mg (8%) of **7**.

(1R,3'R,4'S,5S,5'R,6'R)-3',4',5'-Tris(benzyloxy)-6'-[(benzyloxy)methyl]-3',4',5',6'-tetrahydro-3-phenylspiro[3-azabicyclo[3.1.0]hexane-6,2'-[2H]pyran]-2,4-dione (**6**): R_f (hexane/AcOEt 1:1) 0.82. $[\alpha]_D^{25} = +67.8$ (c = 1.05, $CHCl_3$). IR: 3090*w*, 3070*w*, 3030*w*, 3010*w*, 2910*w*, 2870*w*, 1775*w*, 1710*s*, 1600*w*, 1495*w*, 1450*w*, 1385*m*, 1360*m* (sh), 1175*m* (sh), 1145*m*, 1120*m*, 1085*s*, 1025*m*, 1005*m* (sh), 690*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.37–7.16 (*m*, 25 arom. H); 4.93 (*d*, J = 10.9, PhC*H*); 4.92 (*d*, J = 11.3, PhC*H*); 4.87 (*d*, J = 10.9, PhC*H*); 4.86 (*d*, J = 11.0, PhC*H*); 4.62 (*d*, J = 11.0, PhC*H*); 4.61 (*d*, J = 11.3, PhC*H*); 4.46 (*s*, PhCH_2); 4.02 (*m*, H–C(3')); 3.84 (*m*, H–C(5'), H–C(4')); 3.66–3.60 (*m*, H–C(6'), CH–C(6')); 3.48 (*m*, CH–C(6')); 3.04 (*d*, J = 5.8, H–C(5 or 1); irrad. at 2.81: NOE (weak)); 2.81 (*d*, J = 5.8, H–C(1 or 5); irrad. at 3.04: NOE (weak)). ^{13}C-NMR (50 MHz, $CDCl_3$): 171.33 (*s*, C=O); 170.92 (*s*, C=O); 138.07 (*s*); 137.92 (*s*); 137.63 (*s*); 137.16 (*s*); 131.84 (*s*); 129.11–126.70 (*m*); 86.24 (*d*); 78.87 (*d*); 77.75 (*d*); 77.51 (*d*); 75.83 (*t*); 75.63 (*t*); 75.04 (*t*); 73.79 (*s*, C(6)); 73.11 (*t*); 67.91 (*t*); 30.56 (*d*); 29.36 (*d*). CI-MS: 698 (15), 697 (51), 696 (100, $[M+1]^+$), 604 (10), 516 (12), 498 (11), 480 (19), 181 (13), 107 (16), 91 (30). Anal. calc. for $C_{44}H_{41}NO_7$ (695.82): C 75.95, H 5.94, N 2.01; found: C 76.05, H 6.04, N 2.19.

(1S,3'R,4'S,5R,5'R,6'R)-3',4',5'-Tris(benzyloxy)-6'-[(benzyloxy)methyl]-3',4',5',6'-tetrahydro-3-phenylspiro[3-azabicyclo[3.1.0]hexane-6,2'-[2H]pyran]-2,4-dione (**7**): R_f (hexane/AcOEt 1:1) 0.70. $[\alpha]_D^{25} = +3.0$ (c = 1.0, $CHCl_3$). IR: 3090*w*, 3070*w*, 3030*w*, 3010*w*, 2920*w*, 2860*w*, 1775*w*, 1710*s*, 1600*w*, 1490*w*, 1450*w*, 1380*m*, 1360*m* (sh), 1170*m*, 1130*m* (sh), 1100*s* (sh), 1085*s*, 1060*m* (sh), 1025*m*, 690*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.38–7.28 (*m*, 13 arom. H); 7.26–7.10 (*m*, 6 arom. H); 7.04–6.97 (*m*, 6 arom. H); 4.88 (*d*, J = 11.5, PhC*H*); 4.85 (*d*, J = 11.6, PhC*H*); 4.80 (*d*, J = 11.0, PhC*H*); 4.64 (*d*, J = 10.8, PhC*H*); 4.59 (*d*, J = 12.2, PhC*H*); 4.52 (*d*, J = 11.3, PhC*H*); 4.51 (*d*, J = 10.8, PhC*H*); 4.49 (*d*, J = 12.2, PhC*H*); 4.17 (*d*, J = 8.5, H–C(3')); 4.01 (*t*, J = 8.3, H–C(4')); 3.89 (*dd*, J = 8.3, 9.4, H–C(5')); 3.72 (*m*, H–C(6'); irrad. at 2.69: NOE (weak)); 3.69 (*m*, CH–C(6')); 3.61 (*m*, CH–C(6')); 3.01 (*d*, J = 6.7, H–C(1); irrad. at 2.69: NOE (weak)); 2.69 (*d*, J = 6.7, H–C(5); irrad. at 3.01: NOE (weak)). ^{13}C-NMR (50 MHz, $CDCl_3$): 170.11 (*s*, C=O); 170.07 (*s*, C=O); 137.94 (*s*); 137.85 (*s*); 137.69 (*s*); 135.89 (*s*); 131.60 (*s*); 129.03–125.61 (*m*); 84.52 (*d*); 78.40 (*d*); 77.97 (*d*); 77.11 (*d*); 75.78 (*t*); 74.74 (*t*); 73.67 (*s*, C(6)); 73.45 (*t*); 68.18 (*t*); 32.68 (*d*); 30.83 (*d*). CI-MS: 696 (2, $[M+1]^+$), 181 (5), 147 (4), 108 (8), 107 (37), 105 (6), 92 (16), 91 (100). Anal. calc. for $C_{44}H_{41}NO_7$ (695.82): C 75.95, H 5.94, N 2.01; found: C 75.67, H 6.07, N 2.12.

Cyclopropanation of **1** *with Acrylonitrile* (**3**). Under N_2, 3 ml (78.5 mmol) of **3** were stirred in the presence of 0.5 g 4-Å molecular sieves for 30 min at r.t. Then, 690 mg (1.25 mmol) of **1** were added quickly, the mixture was stirred at r.t. for 12 h, diluted with 5 ml of CH_2Cl_2, and filtered through *Celite*. The *Celite* was washed several times with CH_2Cl_2. The combined filtrates were evaporated. FC (pentane/Et_2O 4:1) of the residue yielded 506 mg (70%) of a mixture of products, which, upon a second FC (pentane/Et_2O 10:1→4:1), gave **8** (36%), **9** (22%), **10** (8%), and **11** (4%) as colourless oils.

(1R,3R,5R,6R,7S,8R)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-4-oxaspiro[2.5]octane-1-carbonitrile (**8**): R_f (pentane/Et_2O 1:1) 0.86. $[\alpha]_D^{25} = +108.7$ (c = 2.4, $CHCl_3$). IR: 3120*w*, 3100*w*, 3070*w*, 3040*w*, 3010*w*, 2920*w*, 2880*w*, 2800*w*, 2250*m*, 1500*w*, 1455*m*, 1365*m*, 1265*m*, 1250–1200*w* (br.), 1150*m* (sh), 1130*m* (sh), 1090*s*, 1060*s* (sh), 1030*s*, 1010*m* (sh), 990*m* (sh), 870*w*, 810*w*, 715*m* (sh), 700*s*, 665*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.36–7.26 (*m*, 16 arom. H); 7.20–7.14 (*m*, 4 arom. H); 4.92 (*d*, J = 10.9, PhC*H*); 4.85 (*d*, J = 11.0, PhC*H*); 4.85 (*d*, J = 10.7, PhC*H*); 4.84 (*d*, J = 11.3, PhC*H*); 4.68 (*d*, J = 12.1, PhC*H*); 4.59 (*d*, J = 10.8, PhC*H*); 4.53 (*d*, J = 11.3, PhC*H*); 4.47 (*d*, J = 12.1, PhC*H*); 3.93 (*t*, J = 9.4, H–C(6)); 3.91 (*d*, J = 9.1, H–C(8); irrad. at 1.29: NOE (weak)); 3.84 (*dd*,

J = 2.5, 10.8, CH–C(5)); 3.78 (*td*, J = 2.2, 9.8, H–C(5)); 3.73 (*dd*, J = 2.0, 10.8, CH–C(5)); 3.70 (*t*, J = 9.1, H–C(7); irrad. at 1.79: NOE (weak)); 1.79 (*dd*, J = 6.4, 9.9, H–C(1); irrad. at 1.29: NOE (weak)); 1.48 (*t*, J = 6.4, $H_{pro\text{-}R}$–C(2); irrad. at 1.29: NOE (strong)); 1.29 (*dd*, J = 6.2, 9.9, $H_{pro\text{-}S}$–C(2); irrad. at 1.79: NOE (strong), irrad. at 1.48: NOE (weak)). ^{13}C-NMR (50, MHz, $CDCl_3$): 138.16 (*s*); 137.96 (*s*); 137.64 (*s*); 137.18 (*s*); 128.52–127.64 (*m*); 118.96 (*s*, CN); 86.34 (*d*); 77.78 (*d*); 77.38 (*d*); 76.10 (*d*); 75.69 (*t*); 75.37 (*t*); 74.99 (*t*); 73.54 (*t*); 67.85 (*t*); 64.36 (*s*, C(3)); 16.30 (*t*, C(2)); 4.65 (*d*, C(1)). CI-MS: 577 (41), 576 (100, $[M + 1]^+$), 486 (14), 484 (14), 181 (50), 107 (34), 91 (63). Anal. calc. for $C_{37}H_{37}NO_5$ (575.71): C 77.19, H 6.48, N 2.43; found: C 77.44, H 6.37, N 2.46.

(1S,3R,5R,6R,7S,8R)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-4-oxaspiro[2.5]octane-1-carbonitrile (**9**): R_f (pentane/Et_2O 1:1) 0.65. $[\alpha]_D^{25} = -2.5$ (c = 2.0, $CHCl_3$). IR: 3120*w*, 3090*w*, 3070*w*, 3040*w*, 3010*m*, 2910*m*, 2880*m*, 2820*w*, 2250*w*, 1500*w*, 1455*m*, 1360*m*, 1320*w*, 1260*m*, 1150*m* (sh), 1130*s* (sh), 1090*s*, 1050*s* (sh), 1030*s*, 1010*m* (sh), 695*m*, 670*m* (sh). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.39–7.27 (*m*, 18 arom. H); 7.17–7.15 (*m*, 2 arom. H); 4.96 (*d*, J = 12.0, PhC*H*); 4.94 (*d*, J = 10.9, PhC*H*); 4.89 (*d*, J = 10.8, PhC*H*); 4.49 (*d*, J = 10.8, PhC*H*); 4.72 (*d*, J = 12.1, PhC*H*); 4.57 (*d*, J = 12.2, PhC*H*); 4.52 (*d*, J = 10.8, PhC*H*); 4.45 (*d*, J = 12.2, PhC*H*); 4.03 (*d*, J = 9.4, H–C(8)); 3.98 (*t*, J = 8.9, H–C(7)); 3.81 (*dd*, J = 8.5, 9.7, H–C(6)); 3.67 (*dd*, J = 3.9, 10.8, CH–C(5)); 3.58 (*dd*, J = 1.9, 10.8, CH–C(5)); 3.51 (*ddd*, J = 1.9, 3.9, 9.8, H–C(5)); 1.50–1.42 (*m*, 3 H). ^{1}H-NMR (400 MHz, CD_3OD): 7.35–7.15 (*m*, 20 arom. H); 4.84 (*d*, J = 12.2, PhC*H*); 4.84 (*d*, J = 11.2, PhC*H*); 4.81 (*d*, J = 12.8, PhC*H*); 4.80 (*d*, J = 10.7, PhC*H*); 4.73 (*d*, J = 11.9, PhC*H*); 4.55 (*d*, J = 11.1, PhC*H*); 4.48 (*d*, J = 12.0, PhC*H*); 4.42 (*d*, J = 12.0, PhC*H*); 3.98 (*d*, J = 9.5, H–C(8); irrad. at 1.50–1.44: NOE (weak)); 3.84 (*t*, J = 9.1, H–C(7)); 3.69 (*t*, J = 9.3, H–C(6)); 3.61 (*dd*, J = 4.5, 11.0, CH–C(5)); 3.56 (*dd*, J = 1.9, 11.0, CH–C(5)); 3.51 (*ddd*, J = 1.9, 4.4, 9.8, H–C(5); irrad. at 1.75: NOE (strong)); 1.75 (*dd*, J = 7.7, 10.1, H–C(1)); 1.50–1.44 (*m*, 2 H–C(2)). ^{13}C-NMR (50 MHz, $CDCl_3$): 138.07 (*s*); 137.87 (*s*); 137.60 (*s*); 137.50 (*s*); 128.84–127.14 (*m*); 117.94 (*s*, CN); 85.16 (*d*); 78.91 (*d*); 77.79 (*d*); 77.16 (*d*); 75.78 (*t*); 75.41 (*t*); 75.13 (*t*); 73.47 (*t*); 68.12 (*t*); 65.28 (*s*, C(3)); 16.04 (*t*, C(2)); 6.32 (*d*, C(1)). CI-MS: 577 (41), 576 (100, $[M + 1]^+$), 486 (13), 419 (12), 391 (11), 338 (39), 181 (23), 147 (15), 108 (16), 107 (77), 92 (13), 91 (90). Anal. calc. for $C_{37}H_{37}NO_5$ (575.71): C 77.19, H 6.48, N 2.43; found: C 76.99, H 6.57, N 2.73.

(1R,3S,5R,6R,7S,8R)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-4-oxaspiro[2.5]octane-1-carbonitrile (**10**): R_f (pentane/Et_2O 1:1) 0.76. $[\alpha]_D^{25} = +50.2$ (c = 0.77, $CHCl_3$). IR: 3120*w*, 3090*w*, 3070*w*, 3030*w*, 3010*w*, 2910*m*, 2870*m*, 2800*w*, 2250*w*, 1495*w*, 1450*w*, 1360*m*, 1260*m*, 1145*m* (sh), 1120*s* (sh), 1090*s*, 1025*s*, 1010*s* (sh), 690*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.37–7.24 (*m*, 18 arom. H); 7.16–7.12 (*m*, 2 arom. H); 4.95 (*d*, J = 10.1, PhC*H*); 4.93 (*d*, J = 10.9, PhC*H*); 4.88 (*d*, J = 10.1, PhC*H*); 4.87 (*d*, J = 11.1, PhC*H*); 4.83 (*d*, J = 10.8, PhC*H*); 4.60 (*d*, J = 12.2, PhC*H*); 4.55 (*d*, J = 10.8, PhC*H*); 4.49 (*d*, J = 12.2, PhC*H*); 4.07 (*d*, J = 8.6, H–C(8)); 3.82 (*t*, J = 9.4, H–C(6)); 3.75 (*t*, J = 8.9, H–C(7); irrad. at 1.65: NOE (weak)); 3.68 (*dd*, J = 3.9, 10.9, CH–C(5)); 3.58 (*dd*, J = 1.9, 10.9, CH–C(5)); 3.43 (*ddd*, J = 1.9, 3.9, 9.5, H–C(5); irrad. at 1.21: NOE (weak)); 1.88 (*dd*, J = 7.2, 10.6, H–C(1); irrad. at 1.21: NOE (strong)); 1.65 (*dd*, J = 5.8, 7.1, $H_{pro\text{-}R}$–C(2); irrad. at 1.21: NOE (strong)); 1.21 (*dd*, J = 5.6, 10.6, $H_{pro\text{-}S}$–C(2); irrad. at 1.65: NOE (strong), irrad. at 1.88: NOE (weak)). ^{13}C-NMR (50 MHz, $CDCl_3$): 138.15 (*s*); 137.81 (*s*); 137.68 (*s*); 137.64 (*s*); 128.42–127.42 (*m*); 118.27 (*s*, CN); 87.53 (*d*); 77.83 (*d*); 77.70 (*d*); 75.69 (*d*); 75.45 (*t*); 75.03 (*t*); 74.55 (*t*); 73.57 (*t*); 68.20 (*t*); 65.14 (*s*, C(3)); 14.57 (*t*, C(2)); 8.12 (*d*, C(1)). CI-MS: 577 (28), 567 (70, $[M + 1]^+$), 486 (10), 419 (13), 181 (16), 108 (10), 107 (100), 97 (10), 93 (14), 91 (38). Anal. calc. for $C_{37}H_{37}NO_5$ (575.71): C 77.19, H 6.48, N 2.43; found: C 77.14, H 6.42, N 2.60.

(1S,3S,5R,6R,7S,8R)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-4-oxaspiro[2.5]octane-1-carbonitrile (**11**): R_f (pentane/Et_2O 1:1) 0.84. IR: 3090*w*, 3070*w*, 3030*w*, 3010*w*, 2960*m*, 2920*m*, 2870*m*, 2250*w*, 1730*w*, 1495*w*, 1455*m*, 1360*m*, 1260*s*, 1260–1200*m* (br.), 1150*m* (sh), 1090*s*, 1050*s* (sh), 1030*s* (sh), 1010*s*, 910*w*, 865*w*, 810–700*m* (br.). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.37–7.25 (*m*, 16 arom. H); 7.21–7.14 (*m*, 4 arom. H); 4.91 (*d*, J = 10.9, PhC*H*); 4.86 (*d*, J = 11.5, PhC*H*); 4.85 (*d*, J = 10.7, PhC*H*); 4.84 (*d*, J = 11.0, PhC*H*); 4.65 (*d*, J = 12.2, PhC*H*); 4.62 (*d*, J = 10.7, PhC*H*); 4.56 (*d*, J = 12.3, PhC*H*); 4.55 (*d*, J = 11.5, PhC*H*); 3.91 (*d*, J = 9.1, H–C(8); irrad. at 1.60: NOE (weak)); 3.86 (*t*, J = 9.4, H–C(6)); 3.73 (*m*, 2 CH–C(5)); 3.67 (*t*, J = 9.1, H–C(7); irrad. at 1.43: NOE (weak)); 3.52 (*td*, J = 2.8, 9.8, H–C(5); irrad. at 1.13: NOE (strong)); 1.60 (*dd*, J = 6.4, 9.9, H–C(1); irrad. at 1.43: NOE (strong)); 1.43 (*dd*, J = 5.5, 9.9, $H_{pro\text{-}R}$–C(2); irrad. at 1.60: NOE (strong), irrad. at 1.13: NOE (strong)); 1.13 (*t*, J = 5.9, $H_{pro\text{-}S}$–C(2); irrad. at 1.43: NOE (strong)). ^{13}C-NMR (50 MHz, $CDCl_3$): 138.14 (*s*); 137.97 (*s*); 137.89 (*s*); 137.29 (*s*); 128.67–127.64 (*m*); 118.09 (*s*, CN); 86.62 (*d*); 79.21 (*d*); 78.12 (*d*); 76.20 (*d*); 75.73 (*t*); 75.27 (*t*); 75.18 (*t*); 73.55 (*t*); 67.97 (*t*); 63.11 (*s*, C(3)); 14.78 (*t*, C(2)); 6.81 (*d*, C(1)).

Cyclopropanation of **1** *with Dimethyl Fumarate* (**4**). Under N_2, a soln. of 1 g (7 mmol) of **4** in 5 ml of 1,4-dioxane was stirred in the presence of 1.5 g of 4-Å molecular sieves for 30 min at r.t. Then, 400 mg (0.7 mmol) of **1** were added quickly, the mixture was stirred at r.t. for 12 h, diluted with 5 ml of CH_2Cl_2, and filtered through *Celite*. The *Celite* was washed several times with CH_2Cl_2. The combined filtrates were evaporated. FC (pentane/Et_2O 3:1) of the residue yielded 338 mg (72%) of **12**/**13** 3:2. In contact with MeOH, some **12** crystallized. The isomers were

separated completely by prep. HPLC (pentane/Et_2O 7:3, 16 ml/min). Crystallization of pure **13** from Et_2O/hexane at −25° afforded colourless needles; **12** was recrystallized in MeOH to give a white powder.

Dimethyl (1R,2R,5R,6R,7S,8R)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-4-oxaspiro[2.5]octane-1,2-dicarboxylate (**12**): Prep. HPLC: t_R 13.4 min. R_f (pentane/Et_2O 1:1) 0.44. M.p. 92°. $[\alpha]_D^{25} = +14.7$ ($c = 1.2$, $CHCl_3$). IR: 3090*w*, 3070*w*, 3040*w*, 3010*w*, 2960*w*, 2910*w*, 2870*w*, 1735*s*, 1450*m*, 1440*m* 1306*m*, 1320–1190*m* (br.), 1290*m*, 1150*m*, 1120*m* (sh), 1090*s*, 1030*m*, 1010*m* (sh). ^{1}H-NMR (400 MHz, C_6D_6): 7.30–7.01 (*m*, 20 arom. H); 4.86 (*d*, $J = 11.3$, PhC*H*); 4.81 (*m*, PhCH_2); 4.64 (*d*, $J = 11.2$, PhC*H*); 4.55 (*d*, $J = 10.9$, PhC*H*); 4.37 (*d*, $J = 11.0$, PhC*H*); 4.36 (*d*, $J = 12.1$, PhC*H*); 4.29 (*d*, $J = 12.1$, PhC*H*); 4.21 (*t*, $J = 8.8$, H–C(7)); 3.96 (*dd*, $J = 8.8$, 9.8, H–C(6)); 3.91 (*d*, $J = 8.8$, H–C(8); irrad. at 2.92: NOE (weak)); 3.80 (*ddd*, $J = 1.9$, 3.5, 9.9, H–C(5); irrad. at 2.84: NOE (weak)); 3.63 (*dd*, $J = 3.6$, 11.2, CH–C(5)); 3.58 (*dd*, $J = 1.9$, 11.2, CH–C(5)); 3.35 (*s*, MeO); 3.15 (*s*, MeO); 2.92 (*d*, $J = 7.5$, H–C(1)); 2.84 (*d*, $J = 7.5$, H–C(2)). ^{13}C-NMR (50 MHz, $CDCl_3$): 167.63 (*s*, C=O); 167.49 (*s*, C=O); 138.29 (*s*); 138.08 (*s*); 138.01 (*s*); 137.24 (*s*); 128.33–127.56 (*m*); 84.63 (*d*); 78.87 (*d*); 78.18 (*d*); 78.08 (*d*); 75.66 (*t*); 75.32 (*t*); 74.89 (*t*); 73.34 (*t*); 68.05 (*t*); 67.90 (*s*, C(3)); 52.08 (*q*, MeO); 51.77 (*q*, MeO); 30.30 (*d*); 27.65 (*d*). CI-MS: 668 (25), 667 (57, $[M + 1]^+$), 635 (5), 575 (13), 559 (18), 451 (13), 437 (13), 361 (11), 307 (16), 271 (19), 239 (19), 181 (45), 179 (13), 167 (55), 92 (15), 91 (100). Anal. calc. for $C_{40}H_{42}O_9$ (666.78): C 72.06, H 6.35; found: C 72.09, H 6.57.

Dimethyl (1S,2S,5R,6R,7S,8R)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-4-oxaspiro[2.5]octane-1,2-dicarboxylate (**13**): Prep. HPLC: t_R 11 min. R_f (pentane/Et_2O 1:1) 0.49. M.p. 80°. $[\alpha]_D^{25} = +73.3$ ($c = 1.05$, $CHCl_3$). IR: 3090*w*, 3070*w*, 3040*w*, 3010*w*, 2960*w*, 2910*w*, 2870*w*, 1730*s*, 1455*m*, 1440*m*, 1360*w*, 1320*m*, 1300–1180*m* (br.), 1150*m*, 1120*m* (sh), 1090*s*, 1050*s* (sh), 1030*m* (sh). ^{1}H-NMR (400 MHz, C_6D_6): 7.31–7.30 (*m*, 2 arom. H); 7.19–7.00 (*m*, 18 arom. H); 4.89 (*d*, $J = 11.7$, PhC*H*); 4.81 (*d*, $J = 11.2$, PhC*H*); 4.66 (*d*, $J = 11.3$, PhC*H*); 4.62 (*d*, $J = 11.2$, PhC*H*); 4.51 (*d*, $J = 11.3$, PhC*H*); 4.46 (*d*, $J = 11.7$, PhC*H*); 4.45 (*d*, $J = 11.9$, PhC*H*); 4.31 (*d*, $J = 11.9$, PhC*H*); 4.09 (*d*, $J = 8.1$, H–C(8)); 3.98 (*t*, $J = 9.2$, H–C(6)); 3.89 (*t*, $J = 8.5$, H–C(7); irrad. at 3.07: NOE (weak)); 3.69 (*m*, 2 CH–C(5)); 3.57 (*td*, $J = 2.7$, 9.8, H–C(5)); 3.34 (*s*, MeO); 3.26 (*d*, $J = 7.6$, H–C(1)); 3.07 (*d*, $J = 7.6$, H–C(2)); 2.99 (*s*, MeO). ^{13}C-NMR (50 MHz, $CDCl_3$): 168.72 (*s*, C=O); 167.26 (*s*, C=O); 137.95 (*s*); 137.87 (*s*, 2 C); 137.80 (*s*); 128.38–126.26 (*m*); 86.75 (*d*); 78.05 (*d*); 77.42 (*d*); 75.44 (*d*); 75.35 (*t*); 75.00 (*t*); 73.51 (*t*); 73.43 (*t*); 68.65 (*s*, C(3)); 68.08 (*t*); 52.17 (*q*, MeO); 51.82 (*q*, MeO); 31.45 (*d*); 25.67 (*d*). CI-MS: 668 (15), 667 (40, $[M + 1]^+$), 635 (3), 181 (16), 107 (19), 92 (12), 91 (100). Anal. calc. for $C_{40}H_{42}O_9$ (666.78): C 72.06, H 6.35; found: C 71.86, H 6.24.

Cyclopropanation of **1** *with Dimethyl Maleate* (**5**). Under N_2, a soln. of 5 ml (40 mmol) of **5** (containing < 1% **4**) in 5 ml of 1,4-dioxane was stirred in the presence of 1.2 g of 4-Å molecular sieves for 30 min at r.t. Then, 1.0 g (1.82 mmol) of **1** was added quickly, the mixture was stirred at r.t. for 12 h, diluted with 5 ml of CH_2Cl_2, and filtered through *Celite*. The *Celite* was washed several times with CH_2Cl_2. The combined filtrates were evaporated. FC (pentane/Et_2O 3:1) of the residue afforded 725 mg of **16**/**12**/**13**/**17** (60%, 1.8:1.5:1.1:1, according to HPLC). Prep. HPLC (pentane/Et_2O 7:3, 16 ml/min) gave pure **16** and a mixture **12**/**13**/**17**.

Dimethyl (1R,2S,5R,6R,7S,8R)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-4-oxaspiro[2.5]octane-1,2-dicarboxylate (**16**): Prep. HPLC: t_R 8.0 min. R_f (pentane/Et_2O 1:1) 0.30. $[\alpha]_D^{25} = +47.2$ ($c = 1.18$, $CHCl_3$). IR: 3090*w*, 3070*w*, 3030*w*, 3010*w*, 2950*m*, 2910*w*, 2870*w*, 1740*s*, 1450*m*, 1440*m*, 1350*s*, 1270–1190*m* (br.), 1155*s*, 1125*s*, 1090*s*, 1070*s* (sh), 1030*m*, 1010*m*, 690*w*. ^{1}H-NMR (400 MHz, C_6D_6): 7.36–6.98 (*m*, 20 arom. H); 4.87 (*d*, $J = 11.2$, PhC*H*); 4.81 (*d*, $J = 11.3$, PhC*H*); 4.71 (*d*, $J = 11.2$, PhC*H*); 4.69 (*d*, $J = 11.4$, PhC*H*); 4.65 (*d*, $J = 11.4$, PhC*H*); 4.53 (*d*, $J = 12.1$, PhC*H*); 4.39 (*d*, $J = 12.0$, PhC*H*); 4.18 (*d*, $J = 11.4$, PhC*H*); 4.14 (*ddd*, $J = 1.8$, 3.1, 10.1, H–C(5)); 4.04 (*m*, H–C(6)); 3.92 (*dd*, $J = 1.8$, 11.4, CH–C(5)); 3.84 (*dd*, $J = 3.1$, 11.4, CH–C(5)); 3.73 (*m*, H–C(7), H–C(8); irrad. at 2.52: NOE (weak), irrad. at 2.34: NOE (weak)); 3.46 (*s*, MeO); 3.40 (*s*, MeO); 2.52 (*d*, $J = 10.6$, H–C(1 or 2); irrad. at 2.34: NOE (strong)); 2.34 (*d*, $J = 10.6$, H–C(2 or 1); irrad. at 2.52: NOE (strong)). ^{13}C-NMR (50 MHz, $CDCl_3$): 167.66 (*s*, C=O); 166.53 (*s*, C=O); 138.31 (*s*); 138.28 (*s*); 138.01 (*s*); 137.38 (*s*); 128.51–127.50 (*m*); 86.28 (*d*); 79.45 (*d*); 77.85 (*d*); 77.39 (*d*); 75.68 (*t*); 75.53 (*t*); 75.07 (*t*); 73.50 (*t*); 68.00 (*t*); 66.18 (*s*, C(3)); 52.02 (*q*, MeO); 51.94 (*q*, MeO); 26.78 (*d*); 24.19 (*d*). CI-MS: 669 (10), 668 (44), 667 (100, $[M + 1]^+$), 635 (14), 575 (14), 559 (33), 527 (19), 451 (24), 437 (13), 361 (12), 271 (12), 181 (23), 91 (16). Anal. calc. for $C_{40}H_{42}O_9$ (666.78): C 72.06, H 6.35; found: C 71.78, H 6.28.

General Procedure for the Debenzylations. Hydrogenation at 1.5 bar H_2 pressure of a soln. of the benzyl ether in MeOH in the presence of $Pd(OH)_2$/C (20% Pd) at r.t. for 45 min, followed by filtration through *Celite* and evaporation of the solvent yielded the crude product, which was purified by FC (CH_2Cl_2/MeOH 7:1).

Dimethyl (1R,2R,5R,6R,7S,8R)-6,7,8-Trihydroxy-5-(hydroxymethyl)-4-oxaspiro[2.5]octane-1,2-dicarboxylate (**14**). Hydrogenation of 32 mg (0.048 mmol) of **12** in 2 ml of MeOH in the presence of 52 mg of $Pd(OH)_2$/C gave 15 mg (100%) of **14**. R_f (CH_2Cl_2/MeOH 4:1) 0.42. $[\alpha]_D^{25} = +13.1$ ($c = 1$, MeOH). IR (KBr): 3490*s* (br.), 3340*s* (br.), 3040*w*, 2960w, 2930*m*, 2880*w*, 1735*s*, 1450*m*, 1440*m*, 1385*m*, 1330*s*, 1290*m*, 1270*m*, 1215*s*, 1190*m* (sh), 1160*s*,

1130*m*, 1110*m*, 1080*s*, 1070*m*, 1060*m*, 1035*s*, 1020*m* (sh), 1000*w*, 960*w*, 950*m*, 930*w*, 910*w*, 890*w*, 860*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 5.44 (*d*, J = 4.4, exchanged with D_2O, OH); 5.06 (br. *s*, exchanged with D_2O, 2 OH); 4.27 (*t*, J = 5.4, exchanged with D_2O, OH); 3.62 (*s*, MeO); 3.54 (*s*, MeO); 3.59–3.24 (*m*, 6 H); 2.58 (*d*, J = 7.7, H–C(1 or 2)); 2.35 (*d*, J = 7.7, H–C(2 or 1)). ^{1}H-NMR (400 MHz, CD_3OD): 3.79 (*d*, J = 9.2, H–C(8); irrad. at 2.73: NOE (3%)); 3.76 (*dd*, J = 1.3, 12.0, CH–C(5)); 3.71 (*s*, MeO); 3.66 (*s*, MeO); 3.65 (*dd*, J = 4.5, 11.9, CH–C(5)); 3.60 (*t*, J = 8.7, H–C(7)); 3.44 (*m*, H–C(6), H–C(5); irrad. at 2.55: NOE (7.5%)); 2.73 (*d*, J = 7.7, H–C(1); irrad. at 3.79: NOE (3%)); 2.55 (*d*, J = 7.7, H–C(2)). ^{13}C-NMR (50 MHz, CD_3OD): 170.11 (*s*, C=O); 170.06 (*s*, C=O); 82.11 (*d*); 77.70 (*d*); 71.64 (*d*); 71.54 (*d*); 70.75 (*s*, C(3)); 62.23 (*t*, *C*–C(5)); 52.77 (*q*, MeO); 52.69 (*q*, MeO); 31.69 (*d*); 28.30 (*d*). CI-MS: 275 (21), 257 (26), 244 (18), 243 (100), 225 (14), 217 (16), 215 (13), 197 (10), 181 (10), 139 (14), 137 (11). Anal. calc. for $C_{12}H_{18}O_9$ (306.27): C 47.06, H 5.92; found: C 46.81, H 5.71.

Dimethyl (1S,2S,5R,6R,7S,8R)-6,7,8-Trihydroxy-5-(hydroxymethyl)-4-oxaspiro[2.5]octane-1,2-dicarboxylate (**15**). Hydrogenation of 28 mg (0.042 mmol) of **13** in 2 ml of MeOH in the presence of 50 mg of $Pd(OH)_2/C$ yielded 13 mg (100%) of **15**. R_f (CH_2Cl_2/MeOH 4:1) 0.43. $[\alpha]_D^{25}$ = +96.4 (c = 0.7, MeOH). IR (KBr): 3480*s* (br.), 3440*s* (br.), 3350*s* (br.), 3030*m*, 2980*m*, 2930*w*, 2910*m*, 2860*w* (sh), 1710*s*, 1450*w* (sh), 1440*s*, 1410*m*, 1390*m*, 1355*m*, 1340*s*, 1300*s*, 1250*s*, 1200*m*, 1180*m*, 1170*m* (sh), 1155*s* (sh), 1105*s*, 1075*s*, 1060*s*, 1045*s*, 1020*s*, 1000*s*, 930*m*, 900*w*, 870*w*, 815*w*, 780*w*, 760*w*, 630*m*, 600*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 5.38 (br. *d*, J = 5.2, exchanged with D_2O, OH); 5.10 (br. *s*, exchanged with D_2O, OH); 5.01 (br. *s*, exchanged with D_2O, OH); 4.32 (br. *s*, exchanged with D_2O, OH); 3.61 (*s*, MeO); 3.54 (*s*, MeO); 3.61–3.35 (*m*, 3 H); 3.26 (br. *t*, J = 9.4, 1 H); 3.15 (br. *t*, J = 8.9, 1 H); 2.74 (*td*, J = 3.2, 9.4, H–C(5)); 2.65 (*d*, J = 7.5, H–C(1 or 2)); 2.43 (*d*, J = 7.5, H–C(2 or 1)). ^{1}H-NMR (400 MHz, CD_3OD): 3.82 (br. *d*, J = 8.5, H–C(8)); 3.71 (*s*, MeO); 3.67 (*dd*, J = 2.5, 12.1, CH–C(5)); 3.67 (*s*, MeO); 3.58 (*dd*, J = 5.2, 12.1, CH–C(5)); 3.41 (*t*, J = 8.8, H–C(6)); 3.36 (*t*, J = 8.9, H–C(7)); 2.94 (*ddd*, J = 2.5, 5.2, 9.4, H–C(5)); 2.79 (*d*, J = 7.5, H–C(1)); 2.65 (*dd*, J = 0.6, 7.7; irrad. at 3.82: *d*, J = 7.7, H–C(2); irrad. at 3.36: NOE (3%)). ^{13}C-NMR (50 MHz, CD_3OD): 170.76 (*s*, C=O); 170.13 (*s*, C=O); 81.47 (*d*); 79.29 (*d*); 70.85 (*d*); 70.60 (*s*, C(3)); 70.14 (*d*); 62.21 (*t*, *C*–C(5)); 52.87 (*q*, MeO); 52.81 (*q*, MeO); 32.18 (*d*); 26.52 (*d*). CI-MS: 307 (29, $[M+1]^+$), 275 (31), 257 (28), 244 (12), 243 (100), 239 (11), 215 (10), 197 (11), 195 (16), 183 (14), 181 (10), 172 (10), 171 (78), 157 (29), 117 (25), 107 (53), 105 (14), 103 (61), 91 (38), 85 (14), 75 (12). Anal. calc. for $C_{12}H_{18}O_9$ (306.27): C 47.06, H 5.92; found: C 46.78, H 5.78.

Dimethyl (1R,2S,5R,6R,7S,8R)-6,7,8-Trihydroxy-5-(hydroxymethyl)-4-oxaspiro[2.5]octane-1,2-dicarboxylate (**18**). Hydrogenation of 30 mg (0.045 mmol) of **16** in 2 ml of MeOH in the presence of 50 mg of $Pd(OH)_2/C$ afforded 14 mg (100%) of **18**. R_f (CH_2Cl_2/MeOH 4:1) 0.38. $[\alpha]_D^{25}$ = +137.9 (c = 0.7, MeOH). IR (KBr): 3500–3300*s* (br.), 3020*m* (br.), 2950*m*, 2900*m*, 2880*m*, 1735*s*, 1450*s*, 1360*s*, 1270*s*, 1240*s*, 1200*s*, 1165*s*, 1105*s*, 1070*s*, 1055*s* (br.), 1030*s*, 955*m*, 945*m* (br.), 895*w* (sh), 880*w*, 800*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 5.70 (br. *s*, exchanged with D_2O, OH); 5.45 (br. *s*, exchanged with D_2O, OH); 5.14 (br. *s*, exchanged with D_2O, OH); 3.99 (*t*, J = 5.3, exchanged with D_2O, OH); 3.57 (br. *s*, 2 MeO); 3.51–3.45 (*m*, 3 H); 3.35 (*m*, 1 H); 3.13 (*m*, 2 H); 2.37 (*d*, J = 10.4, H–C(1 or 2)); 2.20 (*d*, J = 10.4, H–C(2 or 1)). ^{1}H-NMR (400 MHz, CD_3OD): 3.71–3.63 (*m*, 2*CH*–C(5), H–C(8)); 3.70 (*s*, MeO); 3.67 (*s*, MeO); 3.48 (*t*, J = 9.4, H–C(6)); 3.32 (*t*, J = 9.1, H–C(7); irrad. at 2.40: NOE (3%)); 3.23 (*ddd*, J = 2.4, 4.5, 9.9, H–C(5)); 2.48 (*d*, J = 10.4, H–C(1)); 2.40 (*d*, J = 10.4, H–C(2)). ^{13}C-NMR (50 MHz, CD_3OD): 169.80 (*s*, C=O); 169.36 (*s*, C=O); 82.31 (*d*); 78.48 (*d*); 70.88 (*d*); 70.69 (*d*); 68.78 (*s*, C(3)); 62.06 (*t*, *C*–C(5)); 52.63 (*q*, MeO); 52.50 (*q*, MeO); 27.41 (*d*); 24.94 (*d*). CI-MS: 308 (12), 307 (82, $[M+1]^+$), 276 (11), 275 (85), 272 (11), 257 (46), 244 (13), 243 (100), 239 (28), 229 (14), 225 (13), 209 (32), 197 (12), 195 (13), 185 (10), 183 (10), 169 (10), 157 (31), 145 (11), 127 (10), 107 (11), 99 (10), 85 (45), 75 (19), 73 (15), 65 (17). Anal. calc. for $C_{12}H_{18}O_9 \cdot H_2O$ (324.29): C 44.45, H 6.21; found: C 44.54, H 6.32.

Dimethyl (1S,2R,5R,6R,7S,8R)-6,7,8-Trihydroxy-5-(hydroxymethyl)-4-oxaspiro[2.5]octane-1,2-dicarboxylate (**19**). Hydrogenation of 620 mg (0.9298 mmol) of the crude mixture, obtained from the reaction of **1** with **5**, in 20 ml of MeOH in the presence of 800 mg of $Pd(OH)_2/C$ yielded, after 4 h at 2 bar and 10 h at 1.2 bar H_2 pressure, 280 mg (98%) of **14**/**15**/**18**/**19**. FC (CH_2Cl_2/MeOH 9:1) afforded pure **19** and a mixture **14**/**15**/**18**. **19**: R_f (CH_2Cl_2/MeOH 4:1) 0.48. $[\alpha]_D^{25}$ = –3.3 (c = 0.6, MeOH). IR (KBr): 3500–3300*s* (br.), 3030*w*, 2960*w*, 2920*w*, 1730*s*, 1445*m*, 1420*m* (br.), 1360*m*, 1320*m* (sh), 1290*m*, 1260*m* (sh), 1210*m*, 1170*m*, 1160*m* (sh), 1080*s*, 1020*m* (sh), 990*m* (sh), 955*w* (sh), 935*w*, 860*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 5.08 (br. *s*, exchanged with D_2O, 2 OH); 4.63 (*d*, J = 5.7, exchanged with D_2O, OH); 4.39 (br. *s*, exchanged with D_2O, OH); 3.86 (*dd*, J = 5.6, 8.4; after addn. of D_2O: *d*, J = 8.5, H–C(8)); 3.64 (*s*, MeO); 3.60 (*s*, MeO); 3.63–3.55 (*m*, 2 H); 3.42–3.36 (*m*, 3 H); 3.21 (*m*, 1 H); 2.48 (*d*, J = 11.6, H–C(1 or 2)); 2.38 (*d*, J = 11.6, H–C(2 or 1)). ^{1}H-NMR (400 MHz, CD_3OD): 4.05 (*d*, J = 8.9, H–C(8)); 3.78 (*dd*, J = 1.8, 12.1, CH–C(5)); 3.75 (*s*, MeO); 3.68 (*s*, MeO); 3.64 (*t*, J = 8.9, H–C(7)); 3.58 (*dd*, J = 6.0, 12.0, CH–C(5)); 3.39 (*t*, J = 9.1, H–C(6)); 3.37 (*m*, H–C(5); irrad. at 2.53–2.49: NOE (6%)); 2.53 (*d*, J = 11.6, H–C(1 or 2)); 2.49 (*d*, J = 11.7, H–C(2 or 1)). ^{13}C-NMR (50 MHz, CD_3OD): 171.93 (*s*, C=O); 170.01 (*s*, C=O); 81.13 (*d*); 77.77 (*d*); 71.50 (*d*); 70.90 (*d*); 69.02 (*s*, C(3)); 62.49 (*t*, *C*–C(5)); 53.26 (*q*, MeO); 52.92 (*q*, MeO);

32.18 (*d*); 31.25 (*d*). CI-MS: 275 (12), 258 (17), 257 (32), 245 (16), 244 (52), 243 (100), 225 (19), 218 (20), 217 (25), 215 (15), 200 (11), 199 (18), 197 (12), 182 (11), 181 (26), 171 (10), 157 (10), 156 (11), 155 (18), 153 (13), 140 (14), 139 (33), 138 (19), 83 (12). Anal. calc. for $C_{12}H_{18}O_9$ (306.27): C 47.06, H 5.92; found: C 47.17, H 6.04.

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