Enantiospecific Total Synthesis of (−)-D-Noviose[1])

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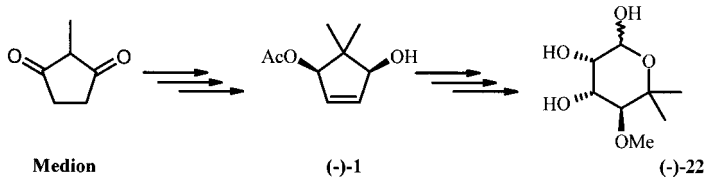
(−)-D-Noviose ((−)-**22**), a rare sugar, was synthesized starting from the optically active building block (−)-**1** in seven steps. The first step of this route, the introduction of a methyl-ether group under *Lewis*-acidic conditions, left the acetoxy group untouched and thereby preserved the absolute configuration in the product **2** (*Scheme 2*). Next, the double bond of methyl ether **2** was *cis*-dihydroxylated leading selectively to **3**. After saponification of the acetoxy group of **3** the two vicinal *cis* OH groups of **17** were selectively protected as the cyclic carbonate **18** (*Scheme 4*). This kind of protection was essential to achieve the proper regioselectivity in the *Baeyer-Villiger* rearrangement of the cyclopentanone derivative **19** that was obtained after oxidation of the remaining OH group of **18**. Lactone **20** was the major product of this rearrangement. Final reduction to the corresponding lactol (cyclic hemiacetal) with diisobutylaluminium hydride (DIBAH) at low temperature was accompanied by reductive cleavage of the protecting cyclic carbonate moiety thereby leading directly to (−)-D-noviose ((−)-**22**).

Introduction. – In the work presented here, (−)-D-noviose ((−)-**22**), the unnatural antipode, was synthesized for the first time *de novo* from building block (−)-**1** (*Scheme 1*). Both enantiomers of the latter were easily prepared from cheaply available medion as reported in 1996 [2].

Scheme 1



Medion **(-)-1** **(-)-22**

(+)-L-Noviose ((+)-**22**) has been identified as the sugar moiety of novobiocin, an antibiotic from *Streptomyces spheroides*, by *Hinman et al.* in 1957 [3]. It was first synthesized by *Kiss et al.* [4] in 1964 starting from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose, which was transformed into a 1,1-dimethyl-D-glucitol derivative, then oxidized to epi-noviose and isomerized to (+)-**22** in 15 steps. In 1976, *Achmatowicz Jr. et al.* [5] published a total synthesis in the racemic series starting from 2-acetylfuran, which, after *Grignard* reaction, acetylation, and hydrolysis yielded the keto-sugar derivative; reduction, methylation, and *cis*-hydroxylation led to the methyl glycoside of **22**. The most recent approach to noviose was reported by *Klemer et al.* [6] in 1986, involving a route of seven steps starting from L-rhamnose, which was oxidized after protection, then subjected to a *Grignard* reaction, and transformed to pyranose by deprotection; after renewed protection, methylation, and hydrolysis, (+)-L-noviose ((+)-**22**) was obtained. This short and efficient (overall yield 33%) synthesis, however, suffers from the high costs of the starting material and the fact that only one antipode is accessible.

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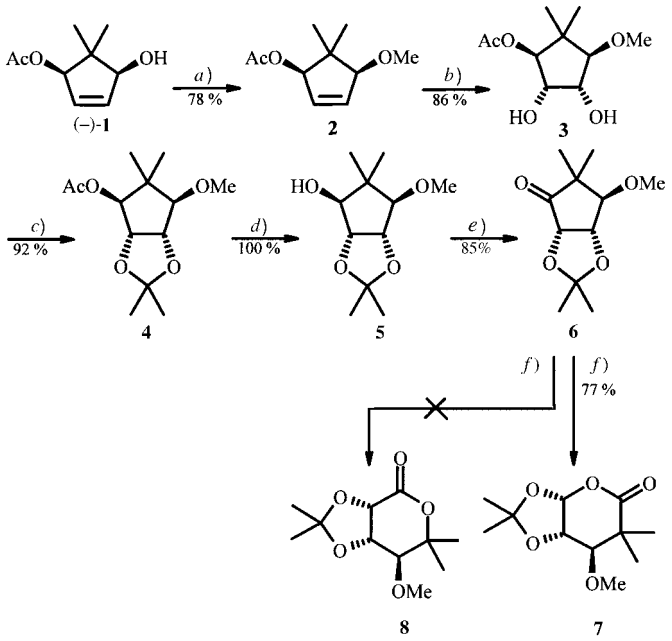
[1]) Preliminary communication [1].

Results. – The first step of our synthesis required the methylation of the free OH group of (−)-**1**. This goal was finally achieved by carbene insertion into the O−H bond of the allylic alcohol utilizing diazomethane in Et_2O catalyzed by $BF_3 \cdot Et_2O$. This somewhat peculiar procedure, being first introduced by *Chavis et al.* [7], had to be applied because of the lability of the acetate function towards alkaline conditions which did not allow a *Williamson* ether synthesis. Furthermore, migration of the acetate group could not safely be excluded in that latter synthesis. Thus, reaction of **1** with 5 equiv. of diazomethane in Et_2O and catalytic amounts of $BF_3 \cdot Et_2O$ led to **2** (*Scheme 2*) which was obtained as a colorless liquid with a very intense and typical smell in 78% yield after column chromatography. *cis*-Hydroxylation of **2** was then performed by catalytic amounts of OsO_4 and 4-methylmorpholine 4-oxide (NMO) as cooxidant in aqueous acetone, following a method described by *Deardorff et al.* [8]. These conditions selectively gave diol **3** in 86% yield due to the directing effect of the substituents on the β-face of the molecule. Diol **3** was then protected as an acetone ketal **4**, before the acetate function was hydrolyzed and the resulting cyclopentanol derivative **5** oxidized to ketone **6**. With this substrate, surprisingly, the *Baeyer-Villiger* rearrangement led selectively to the wrong lactone **7**, whereas no trace of the regioisomeric noviono-lactone derivative **8** could be detected.

The observed abnormal regioselectivity of the *Baeyer-Villiger* rearrangement of **6** (→ **7**) came unexpected to us since it appeared in conflict with well-known rules; but

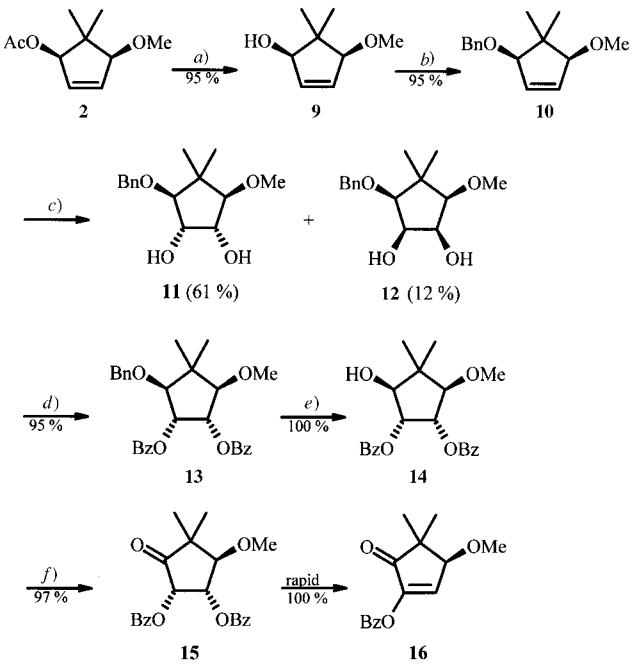
Scheme 2



a) CH_2N_2, $BF_3 \cdot Et_2O$, Et_2O, 0°. *b*) OsO_4, NMO, acetone/H_2O 8:1, 0°. *c*) $Me_2C(OMe)_2$, TsOH, acetone, r.t. *d*) KOH, MeOH/H_2O, r.t. *e*) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78°. *f*) 3-Chloroperbenzoic acid, CH_2Cl_2, r.t.

similar results have been reported very recently by *Chida* and *Ogawa* [9]. To achieve the desired normal regiochemistry, it was obviously necessary to choose different protecting groups for the vicinal *cis*-dihydroxy moiety of **3** which had to display a stronger electron-withdrawing effect. Thus, the protection by benzoate ester moieties was examined. Acetate **2** was first hydrolyzed to the alcohol **9** and then transformed to benzyl ether **10**, introducing a stable protective group towards alkaline conditions (*Scheme 3*). This material was subjected to *cis*-hydroxylation with OsO_4 and NMO as cooxidant leading to **11** in 61% yield. Surprisingly, the directing effect of the benzyloxy group turned out to be weaker than that of the acetoxy group in **2**; therefore, partly dihydroxylation at the β-face was observed too, leading in addition to **11** to the corresponding all-*cis* by-product **12** in 12% yield. The isolated diol **11** was then reacted with benzoyl chloride/pyridine in CH_2Cl_2 leading to **13**, which was transformed to the free mono-alcohol **14** by hydrogenolytic cleavage of the benzyl-ether group. Oxidation with pyridinium dichromate (PDC), a very mild method reported by *Corey* and *Schmidt* [10], yielded the cyclopentanone derivative **15** which, however, rapidly underwent β-elimination to the α,β-unsaturated ketone **16**. Such a behavior was not expected under neutral conditions, but in fact was even observed when **15** was stored neat at $-40°$. Within a few hours at that temperature, all the material was destroyed, which possibly may indicate an autocatalytic effect of benzoic acid, released during the process.

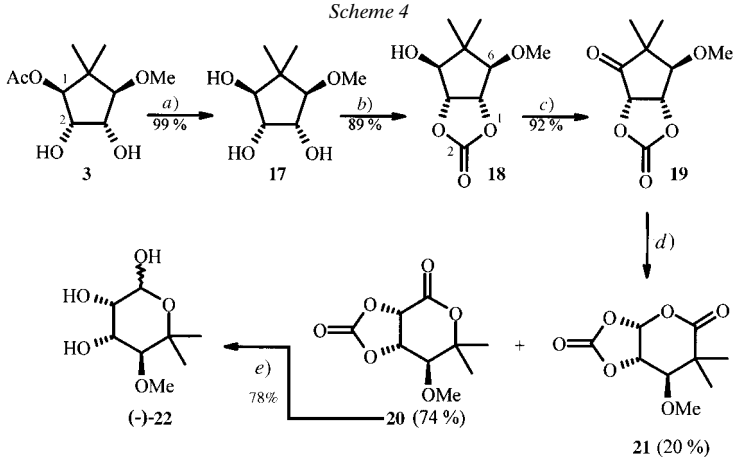
Scheme 3



a) KOH, MeOH, H_2O, r.t. *b*) BnBr, NaH, THF, 0°. *c*) OsO_4, NMO, acetone/H_2O 8:1, 0°. *d*) BzCl, pyridine, CH_2Cl_2, 0°. *e*) H_2, Pd/C, MeOH, r.t. *f*) PDC, CH_2Cl_2, r.t.

The benzoyl group having failed as a suitable protective group for the vicinal *cis*-dihydroxy moiety of **3** our next choice was a cyclic carbonate as a bidentate protection. In addition to its electron-withdrawing power and the reduced tendency for β-elimination, the cyclic carbonate ensures the conservation of the configuration at the OH-substituted C-atoms. Thus, the acetate function of diol **3** was first hydrolyzed yielding triol **17** which then was treated with triphosgene ($CO(OCCl_3)$) following a procedure described by *Burk* and *Roof* [11] (*Scheme 4*). The configuration of triol **17** only allowed for the introduction of the cyclic carbonate moiety at the *cis*-oriented OH groups, thereby rendering further protective groups unnecessary. Thus, alcohol **18** was obtained in 89% yield and easily oxidized by PDC to the cyclopentanone derivative **19** that was not prone to any β-elimination. *Baeyer-Villiger* oxidation of this new cyclopentanone derivative **19** was achieved with 3-chloroperbenzoic acid in CH_2Cl_2 at room temperature within 3 days and led to the novionolactone derivative **20** as the major product in 74% yield, whereas the unwanted regioisomeric lactone **21**, in this case, was only produced in 20% yield. The regioisomers could easily be separated by fractional crystallization from AcOEt. The target (−)-D-noviose ((−)-**22**) was accessible from the novionolactone derivative **20** in a single step by reduction with 5 equiv. of diisobutylaluminium hydride (DIBAH) at −70° [12] in CH_2Cl_2. Apart from the reduction of the lactone to the corresponding lactol (cyclic hemiacetal) under these conditions, also the protective cyclic carbonate group was cleaved, and (−)-**22** was isolated in 78% yield after recrystallization from cyclohexane/AcOEt, displaying a melting point of 128° ([3]: 128–130°).

Scheme 4



a) KOH, H_2O, MeOH, r.t. *b*) $CO(OCCl_3)_2$, pyridine, CH_2Cl_2, −70°. *c*) PDC, CH_2Cl_2; r.t. *d*) 3-Chloroperbenzoic acid, CH_2Cl_2, 3 d, r.t. *e*) DIBAH, CH_2Cl_2, −70°.

Discussion. – The synthetic (−)-D-noviose ((−)-**22**) crystallized as almost pure β-D-anomer out of the equilibrium mixture of anomers, as shown by the ^{1}H-NMR spectrum measured immediately after dissolution of (−)-**22** in CD_3OD. After a short while, mutarotation was observed, leading to a double set of ^{1}H-NMR signals (*Fig. 1*). Our ^{1}H-NMR data, recorded at 400 MHz, complete those of *Angyal et al.* [13], measured at

60 MHz. The ^{13}C-NMR spectrum (*Table*) of (−)-**22** showed a double set of signals too, as reported earlier by *Achmatowicz et al.* [5].

Most interestingly, the synthetic (−)-D-noviose ((−)-**22**) displayed a surprisingly high optical rotation of $[\alpha]_D^{20} = -29.2$ (EtOH/H_2O 1:1, $c = 1.00$) (literature values:

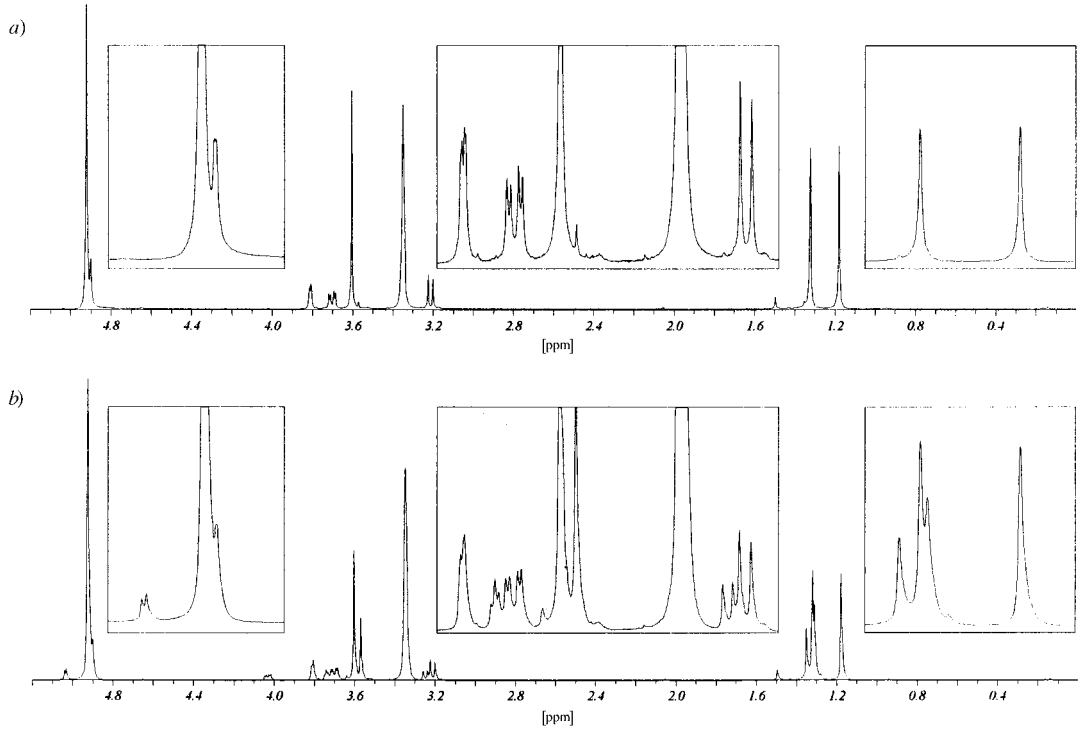


Fig. 1. *^{1}H-NMR Spectra* (CD_3OD) *of (−)-***22**: a) *recorded immediately after dissolution in CD_3OD and* b) *after 3 h at room temperature.* The insets show regions of most significant change during mutarotation. Besides the signals of (−)-**22**, strong signals of CD_3OH (*via* proton exchange) and CHD_2OD were registered, the latter one partially covering the signal of the acetal proton(s).

Table. *Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *of the α- and β-*D*-Anomer of* (−)-D-*Noviose* (−)-**22** *in CD_3OD* (tentatively assigned[a]))

	H−C(1)	H−C(2)	H−C(3)	H−C(4)	H−C(5)	Me	Me	MeO
^{13}C-NMR:								
β-D-anomer	91.24	74.09	70.01	86.07	76.02	29.25	18.95	62.50
α-D-anomer	95.91	72.79	73.57	85.47	78.42	28.83	25.37	61.84
^{1}H-NMR:								
β-D-anomer	4.90 ($d, J = 1.2$)	3.81 ($dd, J = 3.5, 1.2$)	3.72 ($dd, J = 9.8, 3.5$)	3.21 ($d, J = 9.8$)	–	1.32 (*s*)	1.18 (*s*)	3.60 (*s*)
α-D-anomer	5.03 ($d, J = 3.3$)	3.74 ($dd, J = 3.5, 3.3$)	4.04 ($dd, J = 3.3, 8.0$)	3.24 ($d, J = 8.0$)	–	1.31 (*s*)	1.35 (*s*)	3.57 (*s*)

[a]) Apparently due to different solvents, the ^{13}C-NMR data do not correspond to values reported by *Achmatowicz et al.* [5].

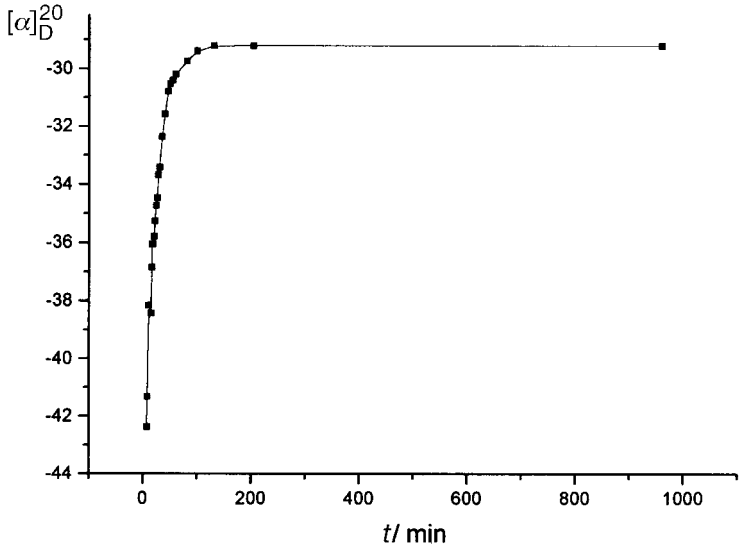


Fig. 2. *Mutarotation of (−)-*D*-noviose (−)-***22***.* Measured at 20° in EtOH/H_2O 1:1 with $c = 0.38$ g/100 ml.

$[\alpha]_D = +38$ [14] (in 0.5N aq. H_2SO_4), $+22.6$ [15], $+20.8$ [6], $+19.9$ [3], and $+19.35$ [4]). Our value of $[\alpha]_D^{20}$ is the final value, measured after several hours of equilibration in EtOH/H_2O 1:1 at 20°. The kinetics of the mutarotation is shown in *Fig. 2*.

Taking into account the reported cheap availability of both enantiomers of the building block **1**, the synthesis described herein is the most efficient approach to both enantiomers of noviose (**22**) which is achieved in 32% overall yield in seven steps.

Experimental Part

General. All reagents and solvents were commercially available and used without further purification. Abs. CH_2Cl_2 was freshly distilled from 4-Å molecular sieve. TLC: *Merck* silica gel *60* F_{254} plates (Art. No. 5554); detection with UV, I_2, or phosphomolybdic acid. Column chromatography (CC): silica gel *60* (230–400 mesh) of *Merck Co*. M.p.: *Büchi-571* instrument; not corrected. Optical rotations: *Perkin-Elmer-141* automatic polarimeter (10-cm, 1-ml cell); at 20°. IR Spectra: *Schimadzu-470* spectrometer; films or KBr discs; $\tilde{\nu}$ in cm^{-1}. NMR Spectra: *Bruker-DRX-400* spectrometer (^1H, 400.13 MHz; ^{13}C, 100.61 MHz); δ in ppm rel. to internal Me_4Si (= 0 ppm); J in Hz. MS: *Finnigan Mat-8230* spectrometer. (70 eV); *m/z* (rel. %).

*(1*R*,4*S*)-4-Methoxy-5,5-dimethylcyclopent-2-en-1-yl Acetate* (= *(1*R*,4*S*)-4-Methoxy-5,5-dimethylcyclopent-2-en-1-ol Acetate*; **2**). A soln. of 1.525 g (8.96 mmol) of (1*R*,4*S*)-4-hydroxy-5,5-dimethylcyclopent-2-en-1-yl acetate ((−)-(**1**)) in Et_2O was cooled to 0°, and 10 drops of $BF_3 \cdot Et_2O$ were added. Then an Et_2O soln. of diazomethane was added until the yellow color persisted for 1 min. Then the same amount of $BF_3 \cdot Et_2O$ soln. was added again, followed by addition of diazomethane soln. These operations were repeated until 50 mmol of diazomethane soln. had been consumed. Finally, the mixture was stirred for another 30 min, and the solid by-products were filtered off. The raw material was then purified by distillation under reduced pressure yielding 1.29 g (78%) of **2**. R_f 0.77 (cyclohexane/AcOEt 1:1). B.p. 38°/0.3 mbar. $[\alpha]_D^{20} = -21.67$ ($c = 2.52$, $CHCl_3$). IR (neat): 2822 (MeO), 1735 (C=O), 1370 (gem. dimethyl), 1363 (C–H, acetate), 1240 (C–O), 1035 (C–O), 716 (H–C=C). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.95 (*s*, Me–C(5)); 1.18 (*s*, Me–C(5)); 2.08 (*s*, MeCOO); 3.43 (*s*, MeO); 3.73 (*s*, H–C(4)); 5.22 (*s*, H–C(1)); 5.87 (*d*, $^3J(3,2) = 5.0$, H–C(3)); 6.11 (*d*, $^3J(2,3) = 5.0$, H–C(2)). ^{13}C-NMR (100 MHz, $CDCl_3$): 16.70 (*q*, *Me*–C(5)); 21.00 (*q*, *Me*COO); 27.51 (*q*, *Me*–C(5)); 46.06 (*s*, C(5)); 58.16 (*q*, MeO); 83.68 (*d*, C(1)); 91.37 (*d*, C(4)); 131.77 (*d*, C(2)); 134.64 (*d*, C(3)); 170.79 (*s*, Me*C*OO). MS: 184 (3, M^+), 153(21), 141(2), 125(35), 95(29), 59(19), 43(100).

*(1*S*,2*S*,3*R*,4*R*)-2,3-Dihydroxy-4-methoxy-5,5-dimethylcyclopent-1-yl Acetate* (= *(1*S*,2*S*,3*R*,4*R*)-4-Methoxy-5,5-dimethylcyclopentane-1,2,3-triol 1-Acetate*; **3**). To a soln. of **2** (12.6 g, 68.4 mmol) and NMO (17.9 g, 151 mmol) in H_2O (500 ml) and acetone (60 ml), OsO_4 (60 mg) was added and the mixture stirred for 3 days at r.t. The major part of the solvent was then removed by distillation and the residue extracted with AcOEt (4 × 200 ml). Usual workup gave 14.2 g of crude yellow oil which was crystallized from AcOEt yielding in several crops a total of 12.7 g (86%) of pure **3**. R_f 0.16 (cyclohexane/AcOEt 1:1). M.p. 84° (AcOEt). $[\alpha]_D^{20} = -26.09$ ($c = 2.2$, $CHCl_3$). IR (KBr): 3375 (O–H), 2945 (C–H), 2833 (MeO), 1739 (C=O), 1376 (gem. dimethyl), 1232 (C–O), 1079 (C–O), 1058 (C–O). ^{1}H-NMR ($CDCl_3$): 0.86 (*s*, Me–C(5)); 1.10 (*s*, Me–C(5)); 2.15 (*s*, MeCOO); 3.23 (*d*, $^3J(4,3) = 5.0$, H–C(4)); 3.52 (*s*, MeO); 3.54 (br. *s*, OH–C(3)*); 4.00–4.02 (*m*, H–C(2), H–C(3)); 4.08 (br. *s*, OH–C(2)*); 4.58 (*d*, $^3J(1,2) = 5.8$, H–C(1)). ^{13}C-NMR (100 MHz, $CDCl_3$): 14.06 (*q*, *Me*–C(5)); 20.88 (*q*, *Me*COO); 25.91 (*q*, *Me*–C(5)); 40.48 (*s*, C(5)); 58.85 (*q*, MeO); 72.14 (*d*, C(3)); 73.08 (*d*, C(2)); 85.66 (*d*, C(1)); 92.11 (*d*, C(4)); 172.67 (*s*, Me*C*OO). MS: 218 (30, M^+), 200 (5), 186 (45), 169 (50), 159 (5), 43 (100).

*(1*S*,2*R*,3*R*,4*R*)-4-Methoxy-5,5-dimethylcyclopentane-1,2,3-triol* (**17**). A soln. of **3** (4.2 g, 19 mmol) in MeOH (60 ml) was treated with a soln. of KOH (6.0 g) in H_2O (10 ml) for 2 h at r.t. MeOH was then removed by distillation and the residue extracted overnight with Et_2O utilizing a perforator apparatus. Usual workup yielded 3.4 g (quant.) of pure **17**. Colorless crystals. R_f 0.71 (MeOH/AcOEt 1:1). M.p. 55–56° (Et_2O). $[\alpha]_D^{20} = +9.3$ ($c = 1.72$, $CHCl_3$). IR (KBr): 3345 (O–H), 2944 (C–H), 2832 (MeO), 1367 (gem. dimethyl), 1195 (C–O), 1173 (C–O), 1134 (C–O), 1089 (C–O), 1061 (C–O). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.79, 1.11 (2*s*, 2 Me–C(5)); 3.14 (*d*, $^3J(4,3) = 4.0$, H–C(4)); 3.46 (*d*, $^3J(1,2) = 7.0$, H–C(1)); 3.49 (*s*, MeO); 3.91 (*m*, H–C(3)*); 4.88 (*m*, H–C(2)*). ^{13}C-NMR (100 MHz, $CDCl_3$): 15.69 (*q*, 1 *Me*–C(5)); 26.15 (*q*, 1 *Me*–C(5)); 40.75 (*s*, C(5)); 58.94 (*q*, MeO); 72.80 (*d*, C(3)*); 73.78 (*d*, C(2)*); 82.2 (*d*, C(1)); 93.32 (*d*, C(4)).

*(3a*R*,4*S*,6*R*,6a*S*)-3a,5,6,6a-Tetrahydro-4-hydroxy-6-methoxy-5,5-dimethyl-4*H*-cyclopenta[*d*]-1,3-dioxol-2-one* (**18**). At −70°, a soln. of triphosgene (6.6 g, 22.3 mmol) in CH_2Cl_2 (20 ml) was added dropwise within 20 min to a stirred soln. of **17** (3.93 g, 22.3 mmol) in CH_2Cl_2 (200 ml). The mixture was stirred for additional 16 h at −70° and then quenched with sat. aq. NH_4Cl soln. (100 ml). After warming to r.t. stirring was continued for another 30 min. The aq. layer was extracted with AcOEt (3 ×) and the combined org. phase washed with HCl and $NaHCO_3$ soln. and worked up as usual: 4.81 g (89%) of **18**. Slightly yellow solid. R_f 0.56 (cyclohexane/AcOEt 1:1). M.p. 79° (AcOEt). $[\alpha]_D^{20} = +11.0$ ($c = 2.6$, $CHCl_3$). IR (KBr): 3473 (O–H), 2970 (C–H), 2938 (C–H), 2878 (C–H), 2837 (MeO), 1828 (C=O, carbonate), 1790 (C=O, carbonate), 1770 (C=O, carbonate), 1373 (gem. dimethyl), 1267 (C–O), 1207 (C–O), 1158 (C–O), 1108 (C–O), 1039 (C–O), 1009 (C–O). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.84, 1.26 (2*s*, 2 Me–C(5)); 3.37 (*d*, $^3J(6,6a) = 4.3$, H–C(6)); 3.48 (*s*, MeO); 3.81 (*d*, $^3J(4,3a) = 4.8$, H–C(4)); 4.80 (*m*, H–C(3a), H–C(6a)). ^{13}C-NMR (100 MHz, $CDCl_3$): 15.25 (*q*, 1 *Me*–C(5)); 24.26 (*q*, 1 *Me*–C(5)); 43.43 (*s*, C(5)); 58.58 (*q*, MeO); 81.49 (*d*, C(4)); 82.50 (*d*, C(6a)*); 83.84 (*d*, C(3a)*); 90.44 (*d*, C(6)); 154.96 (*s*, C(2)). MS: 202 (2, M^+), 170 (41), 101 (11), 98 (23), 84 (56), 43 (100).

*(3a*S*,6*R*,6a*S*)-3a,5,6,6a-Tetrahydro-6-methoxy-5,5-dimethyl-4*H*-cyclopenta[*d*]-1,3-dioxole-2,4-dione* (**19**). PDC (30.0 g, 40 mmol) was added to a soln. of **18** (4.01 g, 20 mmol) in CH_2Cl_2 (200 ml) and the resulting suspension stirred for 3 d at r.t. Thereafter, it was filtrated through a plug of *ca.* 2 cm of silica gel and washed with more CH_2Cl_2 (500 ml). Evaporation yielded 3.7 g (92%) of almost pure **19** which was recrystallized from AcOEt. R_f 0.61 (cyclohexane/AcOEt 1:1). M.p. 72° (AcOEt). $[\alpha]_D^{20} = +32.13$ ($c = 2.68$, $CHCl_3$). IR (KBr): 2984 (C–H), 2962 (C–H), 2842 (C–H, MeO), 1861, 1844, 1834, 1824, 1810, 1791, 1784, 1768, 1759 (all C=O), 1376 (gem. dimethyl), 1262, 1112, 1102, 1091, 1079, 1063 (all C–O). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.99, 1.16 (2*s*, 2 Me–C(5)); 3.48 (*s*, MeO); 3.55 (*d*, $^3J(6,6a) = 3.5$, H–C(6)); 4.97 (*dd*, $^3J(6a,6) = 3.5$, $^3J(6a,3a) = 9.0$, H–C(6a)); 5.03 (*d*, $^3J(3a,6a) = 9.0$, H–C(3a)). ^{13}C-NMR (100 MHz, $CDCl_3$): 20.44 (*q*, 1 Me–C(5)); 23.14 (*q*, 1 Me–C(5)); 51.90 (*s*, C(5)); 60.57 (*q*, MeO); 78.33 (*d*, C(3a)); 81.20 (*d*, C(6a)); 90.80 (*d*, C(6)); 155.14 (*s*, C(2)); 209.68 (*s*, C(4)). MS: 200 (70, M^+), 149 (5), 97 (14), 86 (100), 71 (71).

*2,3-*O*-Carbonyl-*D*-noviono-1,5-lactone* (= *(3a*S*,7*S*,7a*S*)-3a,6,7,7a-Tetrahydro-7-methoxy-6,6-dimethyl-4*H*-1,3-dioxolo[4,5-*c*]pyran-2,4-dione*; **20**). A soln. of **19** (3.3 g, 16.5 mmol) and 3-chloroperbenzoic acid (14.16 g, 65.5 mmol) in CH_2Cl_2 (250 ml) was stirred for 3 d at r.t. Then more CH_2Cl_2 (200 ml) was added and the mixture washed with 100 ml of aq. $Na_2S_2O_3$ and $NaHCO_3$ soln. (100 ml each), dried ($MgSO_4$), and evaporated. The crude yellowish oil was crystallized from AcOEt: 2.64 g (74%) of pure **20**. Colorless crystals. R_f 0.53 (cyclohexane/AcOEt 1:1). M.p. 107° (AcOEt). $[\alpha]_D^{20} = +12.36$ ($c = 1.44$, $CHCl_3$). IR (KBr): 2982 (C–H), 2966 (C–H), 1835, 1818, 1806, 1793 (all C=O), 1748 (C=O, lactone), 1393, 1377 (gem. dimethyl), 1261, 1106, 1098, 1087 (all C–O). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.39, 1.52 (2*s*, 2 Me–C(6)); 3.46 (*d*, $^3J(7,7a) = 5.3$, H–C(7));

3.61 (*s*, MeO); 5.16 (*dd*, *J*(7a,7) = 5.3, ^3J(7a,3a) = 7.3, H–C(7a)); 5.29 (*d*, ^3J(3a,7a) = 7.3, H–C(3a)). ^{13}C-NMR (100 MHz, $CDCl_3$): 22.27 (*q*, 1 *Me*–C(6)); 26.97 (*q*, 1 *Me*–C(6)); 59.6 (*q*, MeO); 70.27 (*d*, C(3a)); 77.99 (*d*, C(7a)); 82.26 (*s*, C(6)); 82.85 (*d*, C(7)); 152.28 (*s*, C(2)); 163.39 (*s*, C(4)). MS: 216 (2, M^+), 201(6), 128(10), 99(19), 86(100), 71(92).

(–)-D-*Noviose* (= *(–)-6-Deoxy-5*-C,*4*-O-*dimethyl*-D-lyxo-*hexopyranose*; (–)-**22**). Within 30 min, 1M DIBAH in hexane (25 ml, 25 mmol) was added dropwise at –70° to a soln. of **20** (1.1 g, 5.09 mmol) in abs. CH_2Cl_2 (50 ml). The mixture was stirred for another 3.5 h, then quenched with sat. aq. Na_2SO_4 soln. (25 ml), and allowed to warm up to r.t. After evaporation, the residue was dried *in vacuo* leading to a white powder which was submitted to *Soxhlet* extraction with CH_2Cl_2 (14 h). This yielded a slightly yellow solid which was recrystallized from cyclohexane/AcOEt: 764 mg (78%) of pure (–)-**22**. R_f 0.18 (CH_2Cl_2/AcOEt/EtOH 6:3). M.p. 128°. $[\alpha]_D^{20} = -29.2$ ($c = 1.0$, EtOH/H_2O 1:1). IR (KBr): 3418 (O–H), 2981 (C–H), 1385, 1371 (gem. dimethyl), 1198, 1164, 1112, 1070, 1023 (all C–O). ^{1}H- and ^{13}C-NMR: *Table.* MS: 192 (1, M^+), 145(9), 99(2), 87(52), 74(100), 71(26).

Compounds **4**–**16** are described in [16].

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