Tetrahedron Vol. 49, No. 23, pp. 5067-5078, 1993
Printed in Great Britain

0040-4020/93 $6.00+.00

Synthesis of α- and β- D,L-*ribo*-Carbahex-2-ulofuranose

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(*Received in Germany* 18 *February* 1993)

Abstract: *Both α- and β-D,L-ribo-carbahex-2-ulofuranose have been synthesized in racemic form starting from norbornen-2-one. In the course of the synthesis the reaction of sulfur ylides with α-alkoxyketones took an unexpected stereochemical pathway.*

INTRODUCTION

Carbocyclic analogues of carbohydrates[1,2] and nucleosides[3,4,5] have recently attracted considerable interest. Due to the absence of the acetal moiety these compounds lack sensitivity to hydrolysis which is of importance regarding their properties against biological systems. As part of our ongoing studies of syntheses in this field[6,7] we present results on the preparation of α- and β-carbapsicofuranose.

RESULTS AND DISCUSSION

Starting from (±)-norbornen-2-one[8] (1), a *Baeyer-Villiger* reaction with hydrogen peroxide[9] in a biphasic system (aqueous sodium hydroxide/diethyl ether) was performed. Excess of base was smoothly neutralized with gaseous carbon dioxide, which proved to be essential to achieve good yields, and the resulting carboxylate was reacted with iodomethane in DMF. Subsequent O-acetylation, *cis*-dihydroxylation with OsO_4/N-methylmorpholine-N-oxide (NMNO)[10] and protection of the diol led to *ribo*-hexofuranuronate **4**. This compound serves as a versatile intermediate for the synthesis of both carbocyclic nucleosides[7] and carbasugars[6]. Side chain degradation, which is required to obtain the desired carbapsicofuranose structure, was performed by the following sequence:

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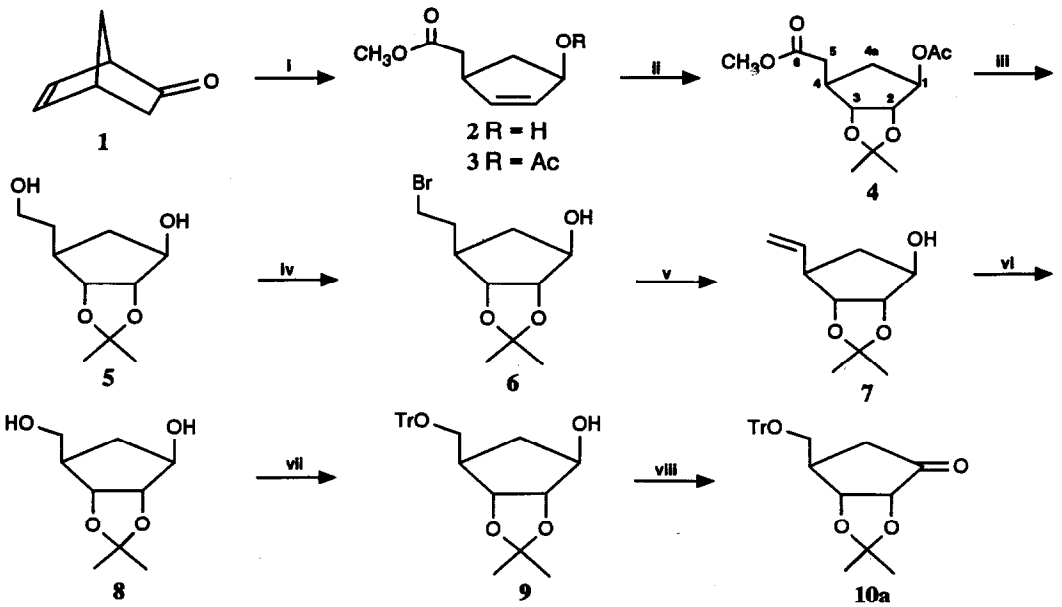
After $LiAlH_4$ reduction of intermediate **4** to give diol **5** the primary hydroxyl group was transformed selectively[11] into the bromide **6**. Reaction of **6** according to *Sharpless'* procedure[12] with 2-nitrophenylselenocyanate gave a selenide which was oxidized *in situ* with hydrogen peroxide to yield olefin **7**. Treatment of the latter with $OsO_4/NaIO_4$[13] followed by $NaBH_4$ reduction afforded diol **8**. Tritylation of the primary hydroxy group and subsequent PDC oxidation[14] gave ketone **10a** which is the central intermediate for the present study.

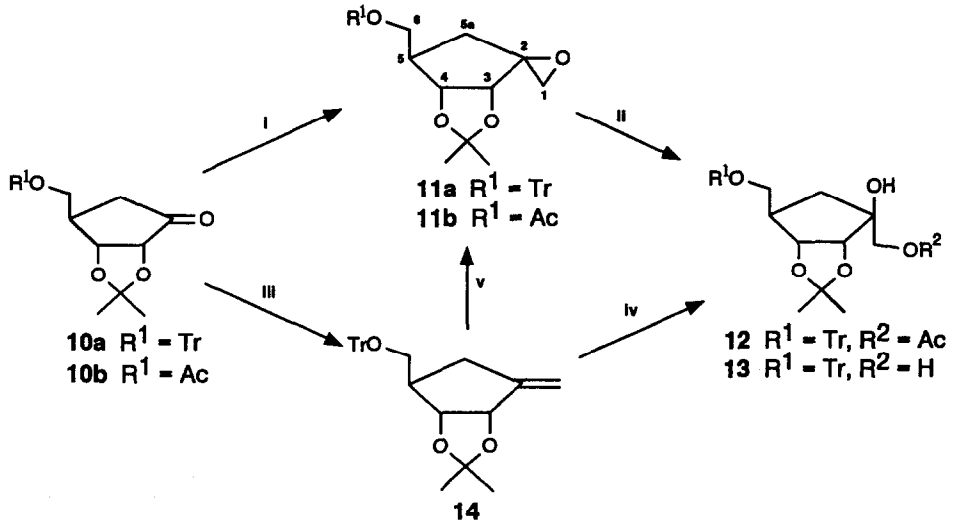


Reaction conditions: i a) $H_2O_2/NaOH/H_2O$/ether/0°C, b) CH_3I/DMF/r.t., c) Ac_2O/pyridine/DMAP/CH_2Cl_2/r.t.; ii a) OsO_4/NMNO/acetone/r.t., b) 2,2-dimethoxypropane/TosOH/r.t.; iii $LiAlH_4$/ether/0°C->r.t.; iv $Br_2/Ph_3P/Et_3N/CH_2Cl_2$/r.t.; v a) 2-nitrophenylselenocyanate/$NaBH_4$/THF/r.t., b) H_2O_2/THF/r.t.; vi a) $OsO_4/NaIO_4/H_2O$/ether/r.t., b) $NaBH_4$/methanol/r.t.; vii trityl chloride/pyridine/DMAP (N,N-dimethylaminopyridine)/CH_2Cl_2/r.t.; viii PDC/CH_2Cl_2/r.t.

Scheme 1

From our synthesis of α-D-*ribo*-carbahexofuranose[6] we knew that ketone **10a** is attacked in a stereoselective manner by sodium borohydride. This led us to believe that nucleophilic attack with other nucleophiles could also be fairly selective. Epoxidation of ketone **10a** by means of dimethylsulfoxonium methylide[15] gave single product **11a**. Surprisingly, the structure of the isolated epoxide was found to be the result of sulfur ylide attack from the more hindered "lower" α-side. The stereochemistry was confirmed by chemical means as follows: Treatment of **11a** with sodium acetate in DMF gave a mixture of **12** and **13**. The formation of **13** may be a consequence of traces of water present and the drastic (DMF, reflux) reaction conditions required. Use of the more nucleophilic cesium acetate allows milder reaction conditions to be used and this resulted in the sole formation of **12**. Confirmation of the structure of **13** was provided by the independent synthesis of this compound from olefin **14**. Ketone **10a** was converted to **14** using *Tebbe's* reagent[16] or the more convenient

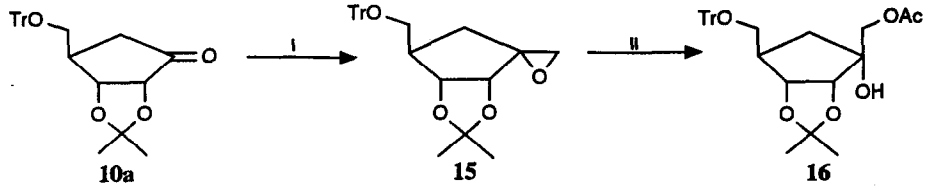
dimethyltitanocene[17]. *Wittig* methodology could not be successfully used for the synthesis of **14**. Treatment of **14** with OsO_4/NMNO in acetone gave a compound which was identical according to spectroscopic data with compound **13** resulting from the opening of epoxide **11**. To obtain additional information we epoxidized **14** with dimethyldioxirane[18] and MCPBA (*m*-chloroperbenzoic acid). This afforded a compound spectroscopically identical to **11**. These results support the assumption that ketone **10a** has been attacked by the sulfur ylide from the more hindered side.



Reaction conditions: i NaH/$((CH_3)_3SOI$/DMSO/THF/r.t.; ii NaOAc/DMF/140°C or CsOAc/DMF/80°C; iii $Cp_2Ti(CH_3)_2$/toluene/60-70°C; iv OsO_4/NMNO/acetone/r.t.; v oxone®/acetone/18-crown-6/$NaHCO_3/H_2O/CH_2Cl_2$/r.t. or MCPBA/benzene/reflux.

Scheme 2

In order to synthesize an epoxide resulting from carbanion attack from the "upper" β-side we used bromomethyllithium[19], a reagent which is also known to epoxidize ketones. **10a** reacted with $BrCH_2Li$ at -80°C to yield epoxide **15** which is different in both chromatographic and spectroscopic (see NMR: Tables 1 and 2) respects to epoxide **11a**.



Reaction conditions: i CH_2Br_2/n-BuLi/THF/-80°C->r.t.; ii CsOAc/DMF/90°C

Scheme 3

For further investigations on the unexpected stereochemical outcome of the sulfur ylide reaction we performed additional experiments. In order to exclude a possible influence of the trityl group we changed the protecting group to give acetate **10b** and repeated the reaction. Again the same outcome (**11b**) was observed. Also we reacted **10a** and **10b** with dimethylsulfonium methylide, in place of dimethylsulfoxonium methylide, which has been reported to exert different stereochemical preferences[15]. Nonetheless, the same products (**11a,11b**) were formed.

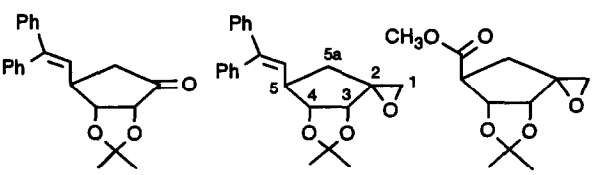
For a possible mechanistic interpretation of the steric course observed the isopropylidene moiety adjacent to the carbonyl group might be taken into consideration. Reaction of diazomethane with α-alkoxyketones is known to proceed from the sterically more hindered side[20] due to electrostatic attraction of the positively charged part of the reagent by the neighbouring oxygen atom. A few examples[21] are reported in the literature which suggest that, similar to diazomethane, sulfur ylides also exhibit the same behaviour.

In order to confirm this assumption we investigated the reaction behaviour of a number of carbohydrates possessing the α-alkoxyketo moiety[22]. According to this study we conclude that cyclic ketones possessing an axial α-alkoxy neighbouring group are attacked by both dimethylsulfoxonium methylide and dimethylsulfonium methylide from the side of the alkoxy substituent.

In a recently published paper[23] on the synthesis of protected carbapsicofuranoses a sulfur ylide was treated with ketone **17**, comparable in structure with substrate **10a** of the present study, to give compounds **18** and **19** (drawn in Scheme 4 as published). This outcome differs from our observations with ketone **10a**. Interestingly, comparison of the ^{1}H- and ^{13}C-NMR data of compounds **11a**, **11b**, and **15** with **18** and **19** (see Tables 1 and 2) shows that **11a** and **11b** are in almost perfect agreement with **18** and **19** while **15** is significantly different. This makes us believe that the effect observed by us also took place in the described synthesis but was not realized.

Compound	δ_{1a}	δ_{1b}	$J_{1a,1b}$
11a	2.81	2.94	4.5 Hz
11b	2.84	2.98	4.4 Hz
15	2.59	2.70	5.4 Hz
18	2.86	3.00	4.5 Hz
19	2.84	2.97	4.5 Hz

Table 1. Comparision of ^{1}H-NMR data



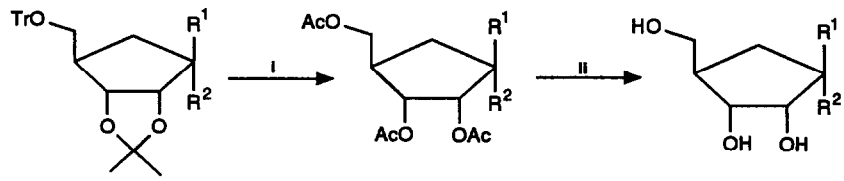
17 **18** **19**

Scheme 4

Compound	δ_1	δ_2	$\delta_{3/4}$	δ_5	δ_{5a}
11a	47.76	65.91	82.90 / 84.58	44.85	32.17
11b	47.63	65.73	82.77 / 84.88	43.81	31.90
15	54.60	63.68	80.47 / 82.54	42.30	30.91
18	47.41	65.02	81.59 / 84.30	48.43	32.64
19	47.41	65.64	84.68 / 85.55	44.25	35.62

Table 2: Comparison of ^{13}C-NMR data

In addition to the protected forms we also were interested in the synthesis of the free carbasugars. Epoxide **15** was treated with cesium acetate to give ring opened product **16**. Deprotection of compounds **12** and **16** proceeded smoothly with acidic ion exchange resin (Amberlite® IR-120) in a mixture acetonitrile/water. For the convenience of chromatographic purification the crude products were peracetylated (**20,21**) and subsequently deacetylated with sodium methoxide (**22,23**).



12 $R^1 = CH_2OAc$; $R^2 = OH$
16 $R^1 = OH$; $R^2 = CH_2OAc$

20a $R^1 = CH_2OAc$; $R^2 = OH$
20b $R^1 = CH_2OAc$; $R^2 = OAc$
21a $R^1 = OH$; $R^2 = CH_2OAc$
21b $R^1 = OAc$; $R^2 = CH_2OAc$

22 $R^1 = CH_2OH$; $R^2 = OH$
23 $R^1 = OH$; $R^2 = CH_2OH$

Reaction conditions: i a) Amberlite® IR-120/CH_3CN/H_2O/50°C, b) Ac_2O/pyridine/DMAP/CH_2Cl_2; ii CH_3OH/CH_3ONa/r.t.

Scheme 5

EXPERIMENTAL PART

General: Melting points were determined on a Tottoli (Büchi) apparatus and are uncorrected. For nomenclature the molecules have been treated as carbohydrate derivatives, where the furanose ring oxygen atom is formally replaced by CH_2 [24]. This additional C-Atom is numbered 4a, or 5a. Only one enantiomer is drawn. NMR spectra were recorded on a Bruker WH-90 or a Bruker MSL 300 spectrometer, chemical shifts are given in ppm from tetramethylsilane. Column chromatography was performed on silica gel 60 (0.040-0.063 mm, Merck). Extractive workup implies washing with 1M HCl and saturated aqueous sodium hydrogencarbonate solution.

(±)-*cis*-Methyl 4-acetoxycyclopent-2-enyl acetate (3)

A two phase system consisting of 20 g (185 mmol) of (±)-norbornen-2-one (**1**) in 100 ml diethyl ether and 11.5 g (500 mmol) of NaOH in 80 ml water was cooled to -5°C and under vigorous stirring 80 ml (787 mmol) of H_2O_2 (30%) were added maintaining the reaction temperature below 5°C. Stirring was continued for 120 min at ambient temperature followed by separation of the layers. The aqueous phase was extracted twice with diethyl ether to remove organic peroxides and subsequently treated with (CAUTION !) a catalytic amount of MnO_2 to destroy excess H_2O_2. After filtration over a Celite® pad the solution was neutralized with gaseous CO_2 to pH 8 and evaporated (0.5 mbar; bath temperature below 40°C) to dryness. The resulting salt was dissolved in 100 ml of DMF, reacted with 44 ml (706 mmol) of CH_3I and vigorously stirred for 16 h. The brown solution was evaporated, dissolved in 100 ml of water and extracted with 3 portions (50 ml) of CH_2Cl_2. The combined organic layers were dried over

Na_2SO_4 and molecular sieve (4Å) and reacted with 20 ml (212 mmol) of acetic anhydride, 25 ml (320 mmol) of pyridine and a catalytical amount of DMAP (N,N-dimethylaminopyridine). After completion of the reaction excess acetic anhydride was removed by reaction with 10 ml of methanol and extractive workup gave a solution of **3** and as a minor by-product a rearranged lactone[25]. Chromatographic purification (hexane/ethyl acetate 2:1 v/v) afforded 23.5 g (118 mmol, 64%) of **3** as a colorless oil which was distilled *in vacuo*, bp (0.1 mm) 85°C. ^{1}H-NMR: (300MHz) δ 1.34, dt, 14.3Hz, 4.2Hz, 1H; 1.90, s, 3H; 2.39, m, 2H; 2.47, dt, 14.4Hz, 7.1Hz, 1H; 2.95, m, 1H; 3.57, s, 3H; 5.50, m, 1H; 5.72, d, 2.0Hz, 1H; 5.91, d, 2.0Hz, 1H. ^{13}C-NMR: (23.0MHz) δ 21.2, 36.4, 40.4(2C), 51.5, 79.4, 130.3, 139.4, 170.6, 172.6. *Anal.* calcd for $C_{10}H_{14}O_4$: C 60.59; H 7.12%. Found: C 60.43; H 7.22%.

Methyl 1-O-acetyl-5-deoxy-2,3-O-isopropylidene-β-DL-*ribo*-carbahexofuranuronate (4)

16.0 g (80.7 mmol) of **3** were dissolved in 100 ml of acetone, treated with 22.5 g (192 mmol) of NMNO and 50 mg of OsO_4. Stirring for 16 h was followed by addition of 0.5 g of $NaHSO_3$, filtration and evaporation to dryness. The residue was dissolved in 50 ml of 0.5M H_2SO_4, saturated with sodium chloride and extracted with 5 portions (50 ml each) of dichloromethane. The combined extracts were evaporated to give 18.3 g (78.8 mmol) of the anticipated diol as a dark, highly viscous oil which was dissolved in 100 ml of 2,2-dimethoxypropane. Treatment with 0.5 g of TosOH for 60 min was followed by addition of 1 g of $NaHCO_3$. Filtration, evaporation and chromatographic purification (hexane/ethyl acetate 2:1 v/v) afforded 15.3 g (56.2 mmol, 71.6%) of **4** as a colorless oil which crystallized on storage at -30°C. mp 39-41°C. ^{1}H-NMR: (300MHz) δ 1.22, s, 3H; 1.40, s, 3H; 1.54, d, 14.5Hz, 1H; 2.01, s, 3H; 2.38, m, 3H; 2.56, t, 7.2Hz, 1H; 3.65, s, 3H; 4.42, d, 5.9Hz, 1H; 4.49, d, 5.9Hz, 1H; 4.99, dd, 2.2Hz, 5.2Hz, 1H. ^{13}C-NMR: (23.0MHz) δ 21.0, 24.2, 26.6, 34.0, 37.7, 41.1, 51.5, 79.7, 84.7, 84.9, 111.0, 169.8, 172.5. *Anal.* calcd for $C_{13}H_{20}O_6$: C 64.98; H 8.39%. Found: C 64.50; H 8.49%.

5-Deoxy-2,3-O-isopropylidene-β-DL-*ribo*-carbahexofuranose (5)

10.0 g (36.7 mmol) of **4** in 60 ml diethyl ether were added at 0°C drop by drop to a stirred suspension of 3.0 g of $LiAlH_4$ in diethyl ether. The reaction mixture was stirred at room temperature for 15 min, refluxed for additional 15 min and the ice cold solution was quenched (CAUTION !) with 12 ml saturated aq. $MgSO_4$ solution. After filtration the solution was dried over Na_2SO_4 and evaporated affording 7.2 g (35.6 mmol, 97.0%) of **5** as a colorless oil, which crystallized on storage. An analytical sample was crystallized from pentane/diethyl ether 1:1 v/v, mp 58-59°C. ^{1}H-NMR: (300MHz) δ 1.28, s, 3H; 1.43, s, 3H; 1.53, td, 6.0Hz, 12.8Hz, 1.69, m, 2H; 2.09, ddt, 2.8Hz, 7.2Hz, 10.5Hz, 1H; 2.21, td, 6.6Hz, 12.0Hz, 1H; 2.89, bs, 1H; 3.38, bs, 1H; 3.70, t, 5.7Hz, 2H; 4.13, t, 2.8Hz, 1H; 4.38, m, 2H. ^{13}C-NMR: (23.0MHz) δ 24.7, 27.0, 36.4, 37.6, 41.8, 61.3, 77.3, 85.6, 87.5, 111.5. *Anal.* calcd for $C_{10}H_{18}O_4$: C 59.39; H 8.97%. Found: C 59.03; H 9.11%.

6-Bromo-5,6-dideoxy-2,3-O-isopropylidene-β-DL-*ribo*-carbahexofuranose (6)

A solution of 22.0 g (84.0 mmol) of Ph_3P in 500 ml of CH_2Cl_2 was titrated with Br_2 to yellow followed by addition of 14 ml of Et_3N. 14.0 g (69.2 mmol) of **5**, dissolved in 250 ml CH_2Cl_2, were added (exothermic reaction) and stirred for 15 min. After extractive workup the solution was evaporated, the residue treated with diethyl ether, filtrated from the precipitated Ph_3PO, evaporated and

subjected to chromatographic purification (hexane/ethyl acetate 2:1 v/v) yielding 16.0g (60.0 mmol, 87.0%) of **6** as a colorless oil. ^{1}H-NMR: (90MHz) 1.39, s, 3H; 1.45, s, 3H; 1.50, m, 1H; 1.92-2.14, m, 2H; 2.28, t, 2H; 2.44, bs, D_2O-exchangable, 1H; 3.45, t, 2H; 4.20, m, 1H; 4.39, AB-system, 2H. ^{13}C-NMR: (23.0MHz) δ 24.7, 27.1, 31.8, 35.8, 37.1, 43.5, 77.9, 85.4, 87.6, 111.6. *Anal.* calcd for $C_{10}H_{17}BrO_3$: C 45.30; H 6.46%. Found: C 45.17; H 6.57%.

5,6-Dideoxy-2,3-O-isopropylidene-β-DL-*ribo*-carbahex-5-enofuranose (7)

To a solution of 6.0 g (26.4 mmol) of 2-nitrophenylselenocyanate in 100 ml ethanol were added at 0°C 1.2g of $NaBH_4$, stirred for 15 min and allowed to warm up to room temperature. 6.6 g (24.9 mmol) of **6** dissolved in 50 ml ethanol were dropped to the brown solution and stirred for 16 h. The reaction was quenched with 100 ml of 0.2M HCl and extracted with 3 portions (100 ml) of CH_2Cl_2. After washing with aq. sat. $NaHCO_3$ solution the solution was evaporated to yield the crude selenide as an orange oil which was dissolved in 250 ml of THF and after addition of 24 ml of H_2O_2 (30%) stirred for 16 h at room temperature. Excess H_2O_2 was destroyed by addition of a catalytic amount of MnO_2 and after filtration the solution was extracted with 2 portions of CH_2Cl_2 (100 ml each), washed with aq. sat. $NaHCO_3$ solution, dried over Na_2SO_4 and evaporated. The residue was purified by column chromatography (hexane/ethyl acetate 2:1 v/v) and 3.01 g (20.2 mmol, 81.1%) of **6** were obtained as an orange oil. ^{1}H-NMR: (90MHz) δ 1.32, s, 3H; 1.46, s, 3H; 1.66, dt, 1H; 2.29, dt, 1H; 2.69, m, 1H; 2.90, bs, D_2O-exchangable, 1H; 4.20, dt, 1H; 4.48, AB-system, 2H; 5.04, dt, 1.2Hz, 8.7Hz, 1H; 5.13, t, 1.2Hz, 1H; 5.96, m, 1H. ^{13}C-NMR: (23.0MHz) δ 24.7, 27.0, 38.0, 48.5, 77.7, 85.2, 87.5, 111.5, 115.0, 140.4. *Anal.* calcd for $C_{10}H_{16}O_3$: C 65.19; H 8.75%. Found: C 64.79; H 8.92%.

2,3-O-Isopropylidene-β-DL-carbaribofuranose (8)

To a two phase system of 4.5 g (24.5 mmol) of **7** in 20 ml of diethyl ether and 20 ml of water, 11.5 g (53.8 mmol) of $NaIO_4$ and 40 mg of OsO_4 were added and vigorously stirred for 16 h. The etheric layer was separated, dried over Na_2SO_4 and subjected to $LiAlH_4$ reduction as described above for **5**. The reaction yielded 3.95 g (21.2 mmol, 86.8%) of diol **8** as a colorless oil, which crystallized on storage, mp 47-48°C ^{1}H-NMR: (300MHz) δ 1.22, s, 3H; 1.36, s, 3H; 1.50, d, 14.1Hz, 1H; 1.35, m, 2H; 3.46, dd, 2.6Hz, 10.2Hz, 1H; 3.74, dd, 3.2Hz, 10.2Hz, 2H (1H D_2O-exchangable); 4.07, d, 4.7Hz, 1H; 4.34, d, 5.7Hz, 1H; 4.60, d, 5.7Hz, 1H. ^{13}C-NMR: (75.4MHz) δ 24.2, 26.9, 35.6, 47.4, 64.3, 76.8, 84.7, 88.3, 110.4. *Anal.* calcd for $C_9H_{16}O_4$: C 57.43; H 8.57%. Found: C 57.18; H 8.71%.

2,3-O-Isopropylidene-5-O-trityl-β-DL-carbaribofuranose (9)

A solution of 188 mg (1.0 mmol) of **8**, 348 mg (1.25 mmol) of trityl chloride, 0.1 ml of pyridine and 5 mg of DMAP in 5 ml CH_2Cl_2 was stirred for 4 h. Extractive workup and chromatographic purification (hexane/ethyl acetate 3:1 v/v) gave 339 mg (78.8 mmol, 78.8%) of **9** as a white foam. ^{1}H-NMR: (300MHz) δ 1.31, s, 3H; 1.45, s, 3H; 1.68, bs, 1H; 2.34, m, 1H; 2.38, bs, 1H; 2.91, bs, 1H; 3.21, dd, 4.7Hz, 9.3Hz, 1H; 3.40, dd, 4.7Hz, 9.3Hz, 1H; 4.13, s, 1H; 4.44, d, 5.8Hz, 1H; 4.57, d, 5.8Hz, 1H; 7.30, m, 9H; 7.43, m, 6H. ^{13}C-NMR: (75.4MHz) δ 24.61, 27.05, 35.73, 45.96, 65.61, 76.84, 77.70, 83.57, 88.08, 110.88, 127.44, 128.14, 129.03, 144.16. *Anal.* calcd for $C_{28}H_{30}O_4$: C 78.11; H 7.02%. Found: C 78.20; H 6.92%.

2,3-O-Isopropylidene-5-O-trityl-DL-carbaribono-1,4-lactone (10a)

376 mg (2.0 mmol) of **8** were tritylated analogously as described above for **9** using 760 mg (2.8 mmol) of trityl chloride, 0.4 ml of pyridine and 10 mg of DMAP in 10 ml CH_2Cl_2 for 16 h. The reaction solution was treated with 1.5 g (4.0 mmol) of PDC and stirred vigorously for further 16 h. After filtration over a silica pad and extractive workup, chromatographic purification (hexane/ethyl acetate 4:1 v/v) afforded 609 mg (1.44 mmol, 77%) of **10a** as colorless crystals, mp 171-172°C ^{1}H-NMR: (300MHz) δ 1.32, s, 3H; 1.44, s, 3H; 2.24, d, 18.4Hz, 1H; 2.54, d, 9.4Hz, 1H; 2.80, dd, 9.4Hz, 18.4Hz, 1H; 3.30, m, AB-system, 2H; 4.40, d, 5.3Hz, 1H; 4.44, d, 5.3Hz, 1H; 7.30, m, 15H. ^{13}C-NMR: (75.4MHz) δ 24.97, 27.09, 37.89 (2xC), 65.17, 79.33, 81.70, 88.17, 111.68, 127.50, 128.04, 129.09, 143.71, 213.67. *Anal.* calcd for $C_{28}H_{28}O_4$: C 78.48; H 6.59%. Found: C 78.02; H 6.67%.

1,2-Anhydro-3,4-O-isopropylidene-6-O-trityl-β-DL-*ribo*-carbahex-2-ulofu ranose (11a)

a) Conversion of **10a** with sulfur ylides:

A solution of 38 mg (1.26 mmol) of NaH (80% suspension in mineral oil) in 1 ml DMSO was treated with 277 mg (1.26 mmol) of trimethylsulfoxonium iodide and stirred for 30 min. 360 mg (0.84 mmol) of **10a** in 1 ml THF were added and stirring was continued for 60 min. The reaction mixture was partitioned between water and CH_2Cl_2, the organic layer was evaporated and subjected to chromatographic purification (hexane/ethyl acetate 9:1 v/v) affording 320 mg (0.72 mmol, 86.1%) of **11a** as white foam.

30 mg of **10a** were also reacted in the same way as described above with trimethylsulfonium iodide affording 23 mg of **11a**. ^{1}H-NMR: (300MHz) δ 1.29, s, 3H; 1.41, d, 12.3Hz, 1H; 1.50, s, 3H; 2.56, m, 2H; 2.81, d, 4.5Hz, 1H; 2.94, d, 4.5Hz, 1H; 3.18, m, 2H; 4.04, d, 5.7Hz, 1H; 4.59, d, 5.7Hz, 1H; 7.30, m, 9H; 7.49, m, 6H. ^{13}C-NMR: (75.4MHz) δ 24.61, 26.84, 32.17, 44.85, 47.76, 64.27, 65.91, 82.90, 84.58, 87.07, 110.81, 127.25, 128.03, 129.03, 144.36. *Anal.* calcd for $C_{29}H_{30}O_4$: C 78.71; H 6.83%. Found: C 78.92; H 6.69%.

b) Epoxidation of olefin **14**:

A solution of 80 mg (0.189 mmol) of **14** in a mixture of 1 ml CH_2Cl_2, 1 ml acetone and 1 ml water was treated with 100 mg of $NaHCO_3$ and 5 mg 18-crown-6 and stirred in an ice bath while 0.78 ml (0.23 mmol) of a solution of Oxone® ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$, 0.29M) in water were added. After 30 min the reaction was allowed to warm up to room temperature and stirred for further 16 h. Treatment with 3 ml aqueous $Na_2S_2O_3$ solution (10%), 3 ml of aqueous saturated $NaHCO_3$ solution, followed by extraction with 3 portions CH_2Cl_2 (5 ml each) and evaporation yielded 61 mg (0.14 mmol, 72.9%) of **11a**.

Conversion of **10a** with MCPBA in refluxing benzene led to the same product.

6-O-Acetyl-1,2-anhydro-3,4-O-isopropylidene-β-DL-*ribo*-carbahex-2-ulofuranose (11b)

150 mg (0.66 mmol) of **10b** were treated in the same way as described above for **10a** and yielded after chromatography (hexane/ethyl acetate 3:1 v/v) 140 mg (0.58 mmol, 88.0%) of **11b** as a colorless oil. ^{1}H-NMR: (300MHz) δ 1.26, s, 3H; 1.47, m, 1H; 1.49, s, 3H; 2.09, s, 3H; 2.57, m, 2H; 2.84, d, 4.4Hz, 1H; 2.98, d, 4.4Hz, 1H; 4.08, m, 2H; 4.21, d, 5.7Hz, 1H; 4.64, d, 5.7Hz, 1H. ^{13}C-NMR: (75.4MHz) δ 21.14, 24.41, 26.70, 31.91, 43.82, 47.63, 64.99, 65.73, 82.77, 84.88, 111.02, 171.12. *Anal.* calcd for $C_{12}H_{18}O_5$: C 59.48; H 7.49%. Found: C 59.81; H 7.60%.

1-O-Acetyl-3,4-O-isopropylidene-6-O-trityl-β-DL-*ribo*-carbahex-2-ulofuranose (12) and 3,4-O-Isopropylidene-6-O-trityl-β-DL-*ribo*-carbahex-2-ulofuranose (13)

a) A solution of 180 mg (0.41 mmol) of **11a** and 150 mg (1.83 mmol) of NaOAc in 2 ml of DMF was refluxed for 16 h, subjected to extractive workup and separated by chromatography affording 36 mg (0.08 mmol) of starting material **11a**, 93 mg (0.19 mmol) of **12** and 50 mg (0.11 mmol) of **13**.

The use of CsOAc allowed the reduction of the reaction temperature to 90°C which resulted in complete conversion and the sole formation of 146 mg (0.29 mmol, 71.2%) of **12**. Chromatographic purification was done with hexane/ethyl acetate 2:1 v/v.

12: ^{1}H-NMR: (300MHz) δ 1.32, s, 3H; 1.46, s, 3H; 1.55, d, 14.0Hz; 2.11, s, 3H; 2.11, m, 1H; 2.45, dd, 7.0Hz, 14.6Hz, 1H; 2.80, s, 1H; 3.32, AB-system, 2H; 4.21, 2xd, AB-system, 11.4Hz, 2H; 4.29, d, 5.5Hz, 1H; 4.62, d, 5.5Hz, 1H; 7.30, m, 9H; 7.48, d, 6H. ^{13}C-NMR: (75.4MHz) δ 21.09, 24.54, 26.87, 36.37, 45.66, 65.35, 67.82, 81.43, 84.08, 86.44, 87.33, 110.84, 127.19, 127.93, 128.90, 143.97, 171.25. *Anal.* calcd for $C_{31}H_{34}O_6$: C 74.08; H 6.82%. Found: C 73.82; H 6.93%.

13: ^{1}H-NMR: (300MHz) δ 1.29, s, 3H; 1.46, s, 3H; 1.52, d, 14,3Hz, 1H; 2.11, m, 1H; 2.41, m, 1H; 2.50, bs, 1H; 3.28, m, 1H; 3.39, m, 1H; 2.47, bs, 1H; 3.57, d, 11.1Hz, 1H; 3.81, d, 11.1Hz, 1H; 4.34, d, 5.8Hz, 1H; 4.62, d, 5.8Hz, 1H; 7.31, m, 9H; 7.46, d, 6H. ^{13}C-NMR: (75.4MHz) δ 24.44, 26.78, 36.41, 45.28, 65.44, 66.35, 82.22, 83.93, 87.47, 87.52, 111.04, 127.25, 127.99, 128.90, 143.81. *Anal.* calcd for $C_{29}H_{32}O_5$: C 75.63; H 7.00%. Found: C 75.23; H 7.08%.

b) *cis*-dihydroxylation of olefin **14**: 80 mg (0.19 mmol) of **14** were treated with 52 mg (0.38 mmol) of NMNO and 5 mg of OsO_4 in 2 ml of acetone as described above for **4** affording after chromatography (hexane/ethyl acetate 2:1 v/v) 41 mg (0.09 mmol, 47.1%) of **13** as a colorless oil.

2,5-Anhydro-1-deoxy-3,4-O-isopropylidene-6-O-trityl-DL-*ribo*-carbahex-1-enitol (14)

A solution of 100 mg (0.23 mmol) of **10a** and 0.47 ml of dimethyltitanocene (1M solution in THF) in 5 ml toluene was protected from light and heated to 60°C for 16 h. The reaction mixture was evaporated to dryness, dissolved in 0.5 ml of toluene and subjected to chromatographic purification (hexane/ethyl acetate 9:1 v/v) affording 81 mg (0.189 mmol, 81.0%) of **14** as an orange oil. A second chromatography of an analytical sample gave **14** as a colorless oil. ^{1}H-NMR: (300MHz) δ 1.34, s, 3H; 1.50, s, 3H; 2.22, d, 15.5Hz, 1H; 2.48, dd, 1H; 2.82, dd, 7.5Hz; 15.3Hz, 1H; 2.98, AB-system, 2H; 4.42, d, 5.6Hz, 1H; 4.64, d, 5.6Hz, 1H; 5.10, s, 1H; 5.19, s, 1H; 7.29, m, 9H; 7.46, d, 6H. ^{13}C-NMR: (75.4MHz) δ 24.66, 26.90, 33.18, 33,63, 64.06, 81.86, 83.09, 87.27, 110.49, 113.01, 127.05, 127.86, 128.83, 144.17, 149.76. *Anal.* calcd for $C_{29}H_{30}O_3$: C 81.66; H 7.09%. Found: C 81.34; H 7.20%.

1,2-Anhydro-3,4-O-isopropylidene-6-O-trityl-α-DL-*ribo*-carbahex-2 -ulofuranose (15)

A solution of 300 mg (0.7 mmol) of **10a** and 0.49 ml (7.0 mmol) of CH_2Br_2 in 5 ml THF was cooled to -80°C and 3.5 ml (5.6 mmol) of a solution of n-BuLi (1.6M in hexane) were slowly added. The cooling bath was allowed to warm up to room temperature while stirring was continued for 16 h. After extractive workup chromatographic purification (hexane/ethyl acetate 9:1 v/v) gave 250 mg (0.56 mmol, 80.7%) of **15** as a colorless oil. ^{1}H-NMR: (300MHz) δ 1.30, s, 3H; 1.48, d, 11.6Hz, 1H; 1.54, s, 3H; 2.52, m, 3H; 2.59, d, 5.4Hz, 1H; 2.70, d, 5.4Hz, 1H; 3.09, m, 2H; 4.15, d, 5.6Hz, 1H; 4.48, d, 5.6Hz, 1H; 7.31, m, 9H; 7.47, m, 6H. ^{13}C-NMR: (75.4MHz) δ 24.64, 26.61, 30.91, 42.30, 54.60, 63.68, 64.22, 80.47, 82.54, 87.07, 111.40, 127.37, 128.06, 128.90, 144.05. *Anal.* calcd for $C_{29}H_{30}O_4$: C 78.71; H 6.83%. Found: C 78.92; H 6.88%.

1-O-Acetyl-3,4-O-isopropylidene-6-O-trityl-α-DL-*ribo*-carbahex-2-ulofuranose (16)

A solution of 200 mg (0.45 mmol) of **15** and 260 mg (1.36 mmol) of CsOAc in 2 ml of DMF was heated to 90°C for 48 h. Extractive workup and chromatographic purification (hexane/ethyl acetate 3:1 v/v) yielded 152 mg (0.30 mmol, 66.9%) of **16** as a colorless oil. ^{1}H-NMR: (300MHz) δ 1.33, s, 3H, 1.58, s, 3H, 1.64, dt, 1.1Hz, 13.7Hz, 1H; 2.12, s, 3H; 2.16, dd, 7.1Hz, 13.7Hz, 1H; 2.68, m, 1H; 3.08, bs, 1H; 3.12, dd, 6.5Hz, 8.9Hz, 1H; 3.23, dd, 5.8Hz, 8.9Hz, 1H; 3.99, d, 11.2Hz, 1H; 4.09, d, 11.2Hz, 1H; 4.34, d, 7.6Hz, 4.41, dd, 5.0Hz, 7.7Hz, 1H; 7.28, m, 9H; 7.43, d, 6H. ^{13}C-NMR: (75.4MHz) δ 21.12, 25.11, 26.71, 38.68, 43.67, 64.66, 68.79, 76.30, 82.19, 83.35, 86.75, 114.67, 127.25, 128.05, 128.99, 144.33, 171.07. *Anal.* calcd for $C_{31}H_{34}O_6$: C 74.08; H 6.82%. Found: C 73.79; H 6.88%.

1,3,4,6-Tetra-O-acetyl-β-DL-*ribo*-carbahex-2-ulofuranose (20a) and **1,2,3,4,6-Penta-O-acetyl-β-DL-*ribo*-carbahex-2-ulofuranose (20b)**

A solution of 146 mg (0.29 mmol) of **12** in 2 ml of MeCN/H_2O 1:1 was treated with strong acidic ion exchange resin (Amberlite® IR-120) and stirred at 50°C for 60 min. After filtration and evaporation the crude product was treated with 0.5 ml of acetic anhydride, 1 ml of pyridine and a catalytic amount of DMAP. After stirring for 16 h tetraacetylated compound **20a** and a minor by-product, pentaacetylated compound **20b**, were formed. Chromatographic separation (hexane/ethyl acetate 1:1 v/v) yielded 63 mg (0.18 mmol) of **20a** and 16 mg (0.04 mmol) of **20b**.

20a: ^{1}H-NMR: (300MHz) δ 1.58, dd, 6.2Hz, 14.25Hz, 1H; 1.99, s, 3H; 2.04, s, 3H; 2.07, s, 6H; 2.14, dd, 11.0Hz, 14.25Hz, 1H; 2.49-2.63, m, 1H; 2.92, brs, 1H; 4.00, d, 11.6Hz, 1H; 4.07-4.20, AB-system 2dd, 6.3Hz, 11.05Hz, 6.5Hz, 11.05Hz, 2H; 4.30, d, 11.6Hz, 1H; 5.22, d, 4.3Hz, 1H; 5.34, dd, 4.3Hz, 8.3Hz, 1H. ^{13}C-NMR: (75.4MHz) δ 20.83, 20.98, 34.96, 39.39, 65.63, 66.43, 74.84, 77.08, 79.57, 169.79, 170.21, 171.06. *Anal.* calcd for $C_{15}H_{22}O_9$: C 52.02; H 6.40%. Found: C 51.88; H 6.47%.

20b: ^{1}H-NMR: (300MHz) δ 2.03, s, 3H; 2.04, s, 3H; 2.06, s, 3H; 2.07, s, 3H; 2.09, s, 3H; 2.13-2.33, AB-system 2dd, 10.3Hz, 15.4Hz, 8.3Hz, 15.4Hz, 2H; 2.53-2.66, m, 1H; 4.01-4.14, AB-system 2dd, 5.6Hz, 11.4Hz, 5.9Hz, 11.4Hz, 2H; 4.43, d, 12.3Hz, 1H; 4.76, d, 12.2Hz, 1H; 5.24, dd, 4.4Hz, 8.8Hz, 1H; 5.48, d, 4.4Hz, 1H. ^{13}C-NMR: (75.4MHz) δ 20.83, 20.96, 22.18, 32.82, 39.58, 62.10, 64.69, 73.62, 75.46, 87.46, 169.26, 170.01, 170.12, 170.57, 170.95. *Anal.* calcd for $C_{17}H_{24}O_{10}$: C 52.58; H 6.23%. Found: C 52.33; H 6.29%.

1,3,4,6-Tetra-O-acetyl-α-DL-*ribo*-carbahex-2-ulofuranose (21a) and **1,2,3,4,6-Penta-O-acetyl-α-DL-*ribo*-carbahex-2-ulofuranose (21b)**

135 mg (0.27 mmol) of **16** were treated and purified as described above for **20** and yielded 67 mg (0.20 mmol) of **21a** and 12 mg (0.03 mmol) of **21b**.

21a: ^{1}H-NMR: (300MHz) δ 1.55, dd, 9.8Hz, 14.1Hz, 1H; 2.07, s, 3H; 2.08, dd, 9.1Hz, 14.1Hz, 1H; 2.09, s, 6H; 2.12, s, 3H; 2.62, brs, 3H; 2.73, m, 1H; 4.08, AB-system 2d, 11.65Hz, 2H; 4.13, d, 5.45Hz, 2H; 5.08, d, 6.6Hz, 1H; 5.15, dd, 5.6Hz, 6.6Hz. ^{13}C-NMR: (75.4MHz) δ 20.73, 20.92, 20.98, 34.63, 41.13, 64.69, 67.42, 73.51, 73.71, 78.47, 169.59, 170.09, 170.75, 170.99. *Anal.* calcd for $C_{15}H_{22}O_9$: C 52.02; H 6.40%. Found: C 51.90; H 6.49%.

21b: ^{1}H-NMR: (300MHz) δ 1.88, dd, 8.9Hz, 14.8Hz, 1H; 2.04, s, 3H; 2.06, s, 3H;2.09, s, 3H; 2.10, s, 3H; 2.12, s, 3H; 2.48, dd, 10.4Hz, 14.8Hz, 1H; 2.69, m, 1H; 4.08, dd, 5.1Hz, 11.2Hz, 1H; 4.13, dd, 4.6Hz, 11.3Hz, 1H; 4.41, d, 11.9Hz, 1H; 4.54, d, 11.9Hz, 1H; 5.12, dd, 4.9Hz, 8.3Hz, 1H; 5.49, d, 4.9Hz, 1H. ^{13}C-NMR: (75.4MHz) δ 20.62, 20.72, 20.79, 21.53, 33.38, 39.33, 63.85, 63.94, 72.48, 73.49, 84.28, 169.34, 169.76, 170.02, 170.81. *Anal.* calcd for $C_{1724}H_{10}O$: C 52.58; H 6.23%. Found: C 52.30; H 6.27%.

β-DL-*ribo*-Carbahex-2-ulofuranose (22)

A solution of 63 mg (0.18 mmol) of **20a** in 2 ml of methanol was treated with a catalytic amount of NaOMe and stirred for 120 min. After neutralization with weakly acidic ion exchange resin (Amberlite® IRC-84) the solution was evaporated to give 32 mg (0.18 mmol, 98%) of **22**, as colorless oil. TLC indicated complete conversion of substrate **20b**, affording the anticipated compound **22**. ^{1}H-NMR: (CD_3OD) (300MHz) δ 1.40, dd, 5.0Hz, 13.0Hz, 1H; 2.10, dd, 10.5Hz, 13.0Hz, 1H; 2.15, m, 1H; 3.56, d, 11.6Hz, 1H; 3.60, dd, 6.6Hz, 10.4Hz, 1H; 3.72, d, 11.7Hz, 1H; 3.74, d, 10.4Hz, 1H; 3.79, d, 4.5Hz, 1H; 4.08, dd, 4.5Hz, 7.1Hz, 1H. ^{13}C-NMR: (CD_3OD) (75.4MHz) δ 36.16, 46.44, 65.80, 66.72, 76.03, 79.65, 82.25. *Anal.* calcd for $C_7H_{14}O_5$: C 47.19; H 7.92%. Found: C 46.92; H 8.01%.

α-DL-*ribo*-Carbahex-2-ulofuranose (23)

67 mg (0.20 mmol) of **21a** were treated in the same way as shown above for **20a** and yielded 33 mg (0.19 mmol, 95%) of **23**, a colorless oil, likewise **21b** showed the same conversion to **23**. ^{1}H-NMR: (CD_3OD) (300MHz) δ 1.51, dd, 9.5Hz, 14.0Hz, 1H; 1.84, dd, 8.9Hz, 14.0Hz, 1H; 2.92, m, 1H; 3.44 and 3.51, 2xd AB-system, 11.1Hz, 2H; 3.56, dd, 6.2Hz, 10.8Hz, 1H; 3.63, dd, 5.3Hz, 10.7Hz, 1H; 3.80, m, 2H. ^{13}C-NMR: (CD_3OD) (75.4MHz) δ 35.62, 47.11, 64.70, 67.42, 74.56, 75.44, 80.78. *Anal.* calcd for $C_7H_{14}O_5$: C 47.19; H 7.92%. Found: C 46.97; H 7.98%.

Acknowedgement: Financial support by *Fonds zur Förderung der wissenschaftlichen Forschung* (Project P8238-CHE) is gratefully acknowledged.

REFERENCES

1. Suami, T. *Topics Curr. Chem.* **1990**, *154*, 257.
2. Gaudino, J. J.; Wilcox, C. S. *Carbohydr. Res.* **1990**, *206*, 233.
3. Borthwick, A. D.; Biggadike, K. *Tetrahedron* **1992**, *48*, 571.
4. Marquez, V. E.; Lim, M. I. *Med. Res. Rev.* **1986**, *6*, 1.
5. Roberts, S. M.; Biggadike, K.; Borthwick, A. D.; Kirk, B. E. *Spec. Publ. R. Soc. Chem.* **1988**, *65*, 172.
6. Marschner, Ch.; Penn, G.; Griengl, H. *Tetrahedron Lett.* **1990**, *31*, 2873.
7. Baumgartner, H.; Marschner, Ch.; Pucher, R.; Singer, M.; Griengl, H. *Tetrahedron Lett.* **1992**, *33*, 6443.
8. Corey, E. J.; Weinshenker, N. M.; Schaaf, T. K.; Huber, W. *J. Am. Chem. Soc.* **1969**, *91*, 5675.
9. Cheng, P. T. W.; McLean, S. *Can. J. Chem.* **1989**, *67*, 261.
10. Schröder, M. *Chem. Rev.* **1980**, *80*, 187.
11. Wiley, G. A.; Hershkowitz, R. L.; Rein, B. M.; Chung, B. C. *J. Am. Chem. Soc.* **1964**, *86*, 964.
12. Sharpless, K. B.; Young, M. W. *J. Org. Chem.* **1975**, *40*, 947.
13. Stetter, H. in *Houben-Weyls Handbuch der organischen Chemie* [Müller, E. ed.], Thieme, Stuttgart, **1976**, Vol. *VII*/2b, p1316. Verlag Thieme Stuttgart **1976**
14. Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* **1979**, 399.
15. Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353.
16. Tebbe, F. N.; Parshall, G. W.; Reddy, G. S. *J. Am. Chem. Soc.* **1978**, *100*, 3611.
17. Petasis, N. A.; Bzowej, E. I. *J. Am. Chem. Soc.* **1990**, *112*, 6392.
18. Jenniskens, L. H. D.; Wijnberg, J. B. P. A; de Groot, A. *J. Org. Chem.* **1991**, *56*, 6585.
19. Michnick, T. J.; Matteson, D. S. *Synlett* **1991**, 631.
20. Sato, K.-I.; Yoshimura, J. *Carbohydr. Res.* **1982**, *103*, 221.
21. Paulsen, H.; Heiker, F. R. *Angew. Chem.* **1980**, *92*, 930; *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 904.
22. Marschner, Ch.; Baumgartner, J.; Griengl, H., presented in part at the *9th International Conference on Organic Synthesis*, **1992**, Montreal, Canada.
23. Bodenteich, M.; Marquez, V. E. *Tetrahedron* **1992**, *29*, 5961.
24. Balzarini, J.;Baumgartner, H.; Bodenteich M.; De Clercq, E.; Griengl, H. *Nucleosides & Nucleotides* **1989**, *8*, 855.
25. Meinwald, J.; Seidel, M.C.; Cadoff, B.C. *J. Am. Chem. Soc.* **1958**, *80*, 6303.