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Note

Photochemical access to alkyl 3-deoxyglycopyranosid-4-uloses

Janine Cossy *, Said Ibhi

Laboratoire de Chimie Organique, Associé au CNRS, ESPCI, 10 rue Vauquelin F-75231 Paris, France

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3-Deoxyaldos-4-uloses are suitable synthons in the synthesis of various natural products and analogues containing chiral diol subunits [1]. Moreover, 3,6-dideoxyhexoses are found in many biologically important compounds, for instance in lipopolysaccharides, conferring on them their serological specificity [2]. A general synthetic approach to these sugars involves the stereoselective reduction of aldose derived epoxides [3]. Alternatively they have been prepared from furfuryl alcohols [4] by deamination of methyl 3-amino-3-deoxy-β-D-allopyranoside [5] or from methyl 4,6-O-benzylidene-3-deoxy-α-D-*ribo*-hexopyranoside [6] in modest yields.

In connection with our studies [7] on the chemistry of radical-anions produced photochemically by electron transfer from triethylamine onto carbonyl compounds, we have found that the photoreduction of α,β-epoxyketones, derived from carbohydrates, results in selective Cα–O bond cleavage. This allows us to report here an efficient synthesis of alkyl 3-deoxyglycopyranosid-4-ulosides (Scheme 1). Furthermore, by using this methodology, a short synthesis of the methyl glycoside of cinerulose B, a rare sugar [8] present in the antibiotic Cinerubine B, has been achieved (Scheme 2).

The epoxyketones (−)-**2** and (+)-**2** were obtained by Swern oxidation of methyl 2,3-anhydro-β-L-ribopyranoside [9] (−)-**1** and of methyl 2,3-anhydro-β-D-ribopyranoside [9] (+)-**1**, respectively. Epoxyketone (+)-**5** was obtained by alkaline hydrogen peroxide oxidation of enone [10] (+)-**4**. The regiospecific ring opening of

* Corresponding author.

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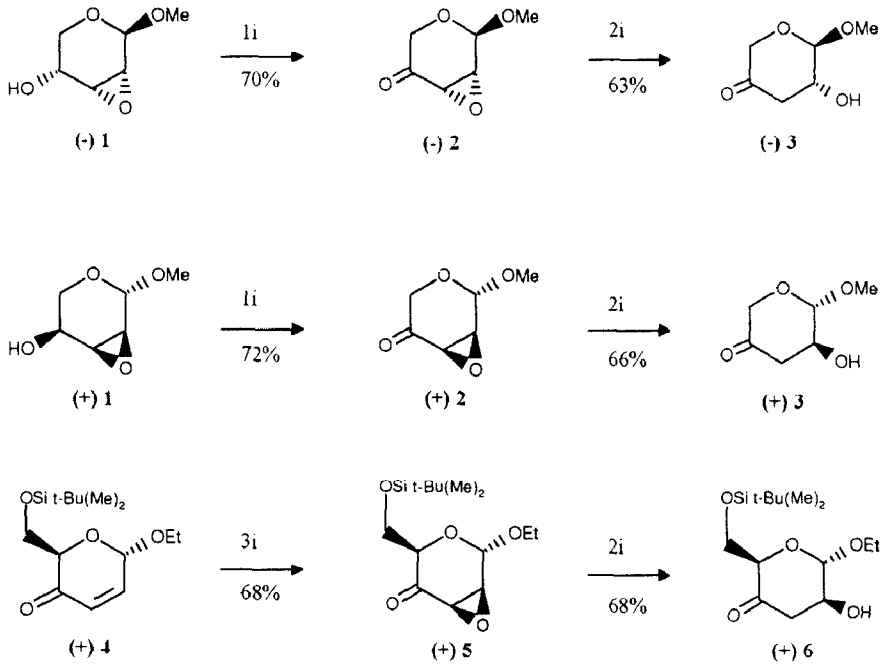
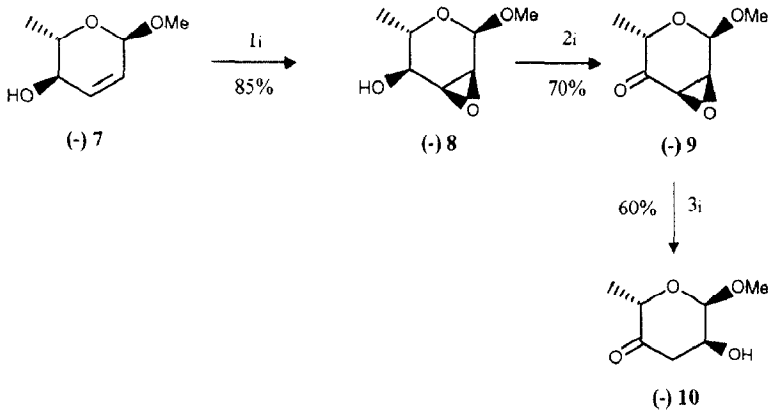


Scheme 1. 1i: Me_2SO, $(COCl)_2$, Et_3N. 2i: $h\nu$ /Et_3N/MeCN. 3i: H_2O_2 /NaOH.

the epoxyketones (−)-**2** and (+)-**2** was effected by irradiation at 254 nm, in a quartz vessel in the presence of 5 equiv of triethylamine in acetonitrile, resulting in the corresponding β-hydroxyketones (−)-**3** and (+)-**3** in 63 and 66% yields, respectively. In the same way, irradiation of the epoxyketone (+)-**5** gave the corresponding β-hydroxyketone (+)-**6** in comparable yield.

Following a similar procedure, a short synthesis of methyl 3,6-dideoxy-α-L-*erythro*-hexopyranosid-4-ulose **10** [methyl cineruloside B (−)-**10**] has been achieved



Scheme 2. 1i: *m*-CPBA. 2i: Pyridinium chlorochromate. 3i: $h\nu$ /Et_3N/MeCN.

from the commercialy available 3,4-di-*O*-acetyl-1,5-anhydro-2,6-dideoxy-L-*arabino*-hex-1-enitol (3,4-di-*O*-acetyl-6-deoxy-L-glucal). The α,β-epoxyketone (−)-**9** was obtained in two steps from the allylic alcohol (−)-**7**, which was obtained from the Ferrier [11] allylic rearrangement of 3,4-di-*O*-acetyl-6-deoxy-L-glucal. A first step involved the epoxidation of (−)-**7** by *m*-chloroperoxybenzoic acid (*m*-CPBA). It was followed by the oxidation of the epoxyalcohol (−)-**8** using pyridinium chlorochromate (PCC) in the presence of molecular sieves [12]. The regiospecific ring opening of the epoxyketone (−)-**9** under photoreductive conditions led to the formation of (−)-**10** in 60% yield.

The photoreductive ring opening of the oxirane ring of α,β-epoxyketones derived from carbohydrates is a very mild reaction, of interest for the preparation of β-hydroxyketones. The optically pure derivatives (+)-**3**, (−)-**3**, and (+)-**6** are potential chirons for the synthesis of natural products and compounds of biological interest.

1. Experimental

General methods.—All experiments were run under an Ar atmosphere. ^{1}H NMR and ^{13}C NMR spectra were obtained with a Bruker AC 300 instrument at 300 and 75 MHz, respectively, in $CDCl_3$ (Me_4Si as internal standard). IR spectra were recorded with a Perkin–Elmer Infracord 137 spectrometer. Mass spectra were run on ZAB HSQ Fisons instrument (EI mode at 70 eV). Preparative TLC were conducted on E. Merck Silica Kieselgel 60, $PF_{254+266}$ and flash chromatography was accomplished with E. Merck Silica 0.043–0.063 nm.

Preparative irradiations were conducted in a merry-go-round type system equipped with 12 low-pressure mercury Philips TUV 15 lamps (254 nm), using 10 mm o.d. quartz tubes. The solutions were degassed by bubbling Ar through them for 15 min. Solvents such as ether and THF were distilled from sodium benzophenone. Acetonitrile and Et_3N were distilled from CaH_2. In a typical experiment, a solution of epoxyketone (0.5 g, 1 equiv) in dry MeCN (5×10^{-2} M) was deoxygenated by bubbling Ar gas through it. Triethylamine (5 equiv) was added and the solution was irradiated at 254 nm for 1 h. Acetonitrile and Et_3N were evaporated and the crude mixture was purified by flash chromatography.

3,4-Di-*O*-acetyl-6-deoxy-L-glucal was purchased from Aldrich.

*Methyl 2,3-anhydro-β-*L*-(-*D*-)-*erythro*-pentopyranosid-4-ulose* [(−)-**2** *and* (+)-**2**]. —To a solution of Me_2SO (0.17 mL, 2.35 mmol) in dry CH_2Cl_2 (1 mL) was added a solution of oxalyl chloride (0.10 mL, 1.26 mmol) in CH_2Cl_2 (1 mL) at −60°C. After 10 min a solution of (−)-**1** or (+)-**1** (ref 9, 0.15 g, 1.05 mmol) in CH_2Cl_2 (1 mL) was added followed by the addition of triethylamine (0.70 mL, 0.52 mmol). After 15 min, the temperature was raised up to ambient temperature. The mixture was extracted with CH_2Cl_2. The organic phase was evaporated. The crude product was purified by flash chromatography with 3:7 EtOAc–hexane as the eluent, to give (−)-**2** or (+)-**2**, (0.10 g, 70%) as a syrup; $[\alpha]_D$ +244.0° (*c* 2.0, $CHCl_3$) and $[\alpha]_D$ −245.0° (*c* 2.1, $CHCl_3$), respectively; IR ($CHCl_3$): 1720 cm^{-1}; ^{1}H NMR: δ

3.40 (d, 1 H, $J_{2,3}$ 4.1 Hz, H-3); 3.50 (s, 3 H, OMe); 3.60 (dd, 1 H, $J_{1,2}$ 1.3 Hz, H-2), and 4.15 (d, 2 H, $J_{5a,5b}$ 3.2 Hz, H-5a, H-5b); 5.10 (s, 1 H, H-1); ^{13}C NMR: δ 202.0 (C-4), 94.9 (C-1), 65.7 (C-5), 56.4 (OMe), 53.04 (C-3), and 53.1 (C-2); MS: *m/z* 162 (M^+, 65%), 144 (32), 130 (42), 119 (100), 102 (72). Anal. Calcd for $C_6H_8O_4$: C, 50.00; H, 5.59. Found: C, 50.03; H, 5.55.

*Methyl 3-deoxy-β-*D*-(-*L*-)-glycero-pentopyranosid-4-ulose* [(−)-**3** *or* (+)-**3**].—Purification of the crude material after the irradiation of (−)-**2** (0.5 g) or (+)-**2** (0.5 g) by flash chromatography with 1:1 EtOAc–hexane as the eluent gave (−)-**3** (0.31 g, 63%), $[\alpha]_D$ −152.1° (*c* 0.6 $CHCl_3$), and (+)-**3** (0.33 g, 66%), $[\alpha]_D$ +153.0° (*c* 0.6 $CHCl_3$), respectively; IR ($CHCl_3$): 3450, 1750 cm^{-1}; ^{1}H NMR: δ 2.25 (s, 1 H, OH), 2.60 (dd, H; $J_{2,3a}$ 4.4, Hz, $J_{3a,3b}$ 12.1 Hz, H-3a), 2.90 (dd, 1 H, $J_{2,3b}$ 4.6 Hz, H-3b), 3.55 (s, 3 H, OMe), 3.90–4.20 (m, 3 H, H-2, H-5a, H-5b), and 4.65 (d, 1 H, $J_{1,2}$ 3.0 Hz, H-1); ^{13}C NMR: δ 206.0 (C-4), 102.0 (C-1), 70.0 (C-2), 68.0 (C-5), 56.0 (OMe), and 44.0 (C-3). MS: *m/z* 164 ($M^{+\cdot}$, 100%), 132 (10), 74 (70). Anal. Calcd for $C_6H_{10}O_4$: C, 49.31; H, 6.89. Found: 49.35; H, 6.92.

*Ethyl 2,3-anhydro-6-*O*-[(*tert*-butyldimethyl)silyl]-*D*-lyxo-hexopyranosid-4-ulose* (+)-**5**.—To a well stirred solution of (+)-**4** (ref 10, 0.21 g, 0.73 mmol) in MeOH (5 mL) cooled to 0°C, was added dropwise a mixture of 30% H_2O_2 (0.22 mL) and aq 6 N NaOH (0.10 mL). The mixture was stirred for 2 h at 0°C, and then for 1 h at room temperature. The mixture was diluted with water (10 mL) and extracted with EtOAc (3 × 20 mL). The combined extracts were washed with brine, dried over anhyd $MgSO_4$, filtered, and concentrated. Purification of the crude material by flash chromatography with 2:8 EtOAc–hexane as the eluent afforded (+)-**5** as a syrup, (0.14 g, 68%); $[\alpha]_D$ +125.0° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$): 1750, 1450, 820 cm^{-1}; ^{1}H NMR: δ 0.00 (s, 6 H, Si*t*BuMe_2), 0.80 (s, 9 H, Si*tBu*Me_2), 1.20 (t, 3 H, *J* 7.1 Hz, OCH_2CH_3), 3.45–3.50 (m, 1 H, H-3), 3.60–3.64 (m, 2 H, OCH_2CH_3), 4.00–4.10 (m, 4 H, H-2, H-5, H-6a, H-6b), and 5.15 (d, 1 H, $J_{1,2}$ 1.1 Hz, H-1); ^{13}C NMR: δ 201.4 (C-4), 93.5 (C-1), 77.2 (C-5), 64.6 (C-6), 63.1 (OCH_2CH_3), 53.7 (C-3), 53.3 (C-2), 25.7 (OCH_2CH_3), 18.2 (Si$C[CH_3]_3[CH_3]_2$), and 14.9 (SiC$[CH_3]_3[CH_3]_2$); MS: *m/z* 320 ($M^{+\cdot}$, 3%), 289 (100), 257 (12). Anal. Calcd for $C_{14}H_{26}O_5Si$: C, 55.59; H, 8.66. Found: C, 55.54; H, 8.63.

*Ethyl 6-*O*-[(*tert*-butyldimethyl)silyl]-3-deoxy-α-*D*-threo-hexopyranosid-4-ulose* (+)-**6**.—The mixture resulting from the irradiation of (+)-**5** (0.5 g) was purified by flash chromatography with 4:6 EtOAc–hexane as the eluent to give (+)-**6** as a syrup (0.34 g, 68%); $[\alpha]_D$ +128.0° (*c* 2, $CHCl_3$); IR ($CHCl_3$): 3440, 1730 cm^{-1}: ^{1}H NMR: δ 0.00 (s, 6 H, Si*t*BuMe_2), 0.80 (s, 9 H, Si*tBu*Me_2), 1.15 (t, 3 H, *J* 7.1 Hz, OCH_2CH_3), 2.40 (m, 1 H, H-6a), 2.80 (dd, 1 H, $J_{5,6}$ 13.9, $J_{6a,6b}$ 4.9 Hz, H-6b), 3.60 (m, 1 H, H-2), 3.80–3.86 (m, 6 H, CH_2CH_3, H-3a, H-3b, H-5, OH), and 4.90 (d, 1 H, $J_{1,2}$ 2.5 Hz, H-1); ^{13}C NMR: δ 207.9 (C-4), 97.5 (C-1), 78.3 (C-2), 66.1 (C-5), 65.2 (C-3), 63.7 (OCH_2CH_3), 42.4 (C-6), 25.6 (OCH_2CH_3), 18.2 [(Si$C[CH_3]_3[CH_3]_2$], 14.8 (SiC$[CH_3]_3[CH_3]_2$); MS: *m/z* 322 ($M^{+\cdot}$, 76%), 293 (100), 294 (42). Anal. Calcd for $C_{14}H_{28}O_5Si$: C, 55.22; H, 9.27. Found: C, 55.27; H, 9.20.

*Methyl 2,3-trideoxy-α-*L*-erythro-hex-2-enopyranoside* (−)-**7**.—Boron trifluoroetherate (1.98 mL, 14.1 mmol) was added dropwise at room temperature to a

solution of 3,4-di-*O*-acetyl-6-deoxy-L-glucal (2 g, 9.34 mmol) and MeOH (0.37 mL, 18.7 mmol) in benzene [11] (50 mL). After 25 min, the mixture was neutralized with $NaHCO_3$ (2 g) and filtered through Celite. The solvent was removed under reduced pressure. The residue (1 g, 5.4 mmol) was stirred with Amberlite® resin (IRN-78 OH^-) (0.15 g) in MeOH (20 mL) for 16 h at room temp (to give (−)-**7**. Since (−)-**7** was unstable, it was used without further purification.

Methyl 2,3-anhydro-6-deoxy-α-L-allopyranoside (−)-**8**.—To a solution of *m*-CPBA (1.8 g, 10.35 mmol) in CH_2Cl_2 (3 mL), (−)-**7** (0.5 g, 3.45 mmol) was added. The mixture was stirred at room temperature for 15 h and then filtered on Celite. Magnesium sulfate (2.0 g) was added to the filtrate, followed by the addition of $Ca(OH)_2$ (3.6 g). After a further 2-h stirring, the mixture was filtered through Celite. The solvent was evaporated and the residue was purified by flash chromatography with 7:3 EtOAc–hexane as the eluent to give (−)-**8** as a syrup (0.46 g, 85%); $[\alpha]_D$ −182.0° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$): 3400, 1500, 1100 cm^{-1}; ^1H NMR: δ 1.25 (d, 3 H, $J_{5,Me}$ 6.2 Hz, CCH_3), 1.80–1.90, (m, 2 H, OH, H-4), 3.45 (s, 3 H, OMe), 3.60–3.65 (m, 3 H, H-2, H-3, H-5), and 4.85 (d, 1 H, $J_{1,2}$ 3.2 Hz, H-1); ^{13}C NMR: δ 94.4 (C-1), 71.3 (C-4), 68.2 (C-5), 64.9 (OMe), 56.0 (C-3), 55.6 (C-2), and 17.4 (C-6); MS: *m/z* 178 ($M^{+\cdot}$, 15%), 160 (100), 120 (56). Anal. Calcd for $C_7H_{12}O_4$: C, 52.49; H, 7.55. Found: C, 52.43; H, 7.57.

Methyl 2,3-anhydro-6-deoxy-α-L-ribo-hexopyranosid-4-ulose (−)-**9**.—A solution of (−)-**8** (0.7 g, 4.37 mmol) in CH_2Cl_2 (20 mL) was stirred with pyridinium chlorochromate (4.7 g, 21.87 mmol) in the presence of 4A molecular sieves for 16 h at room temperature. After removal of the solvent under reduced pressure, chromatography on silica gel with 1:1 EtOAc–hexane as the eluent and distillation, (−)-**9** was obtained as a syrup (0.48 g, 70%); $[\alpha]_D$ −206.0° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$): 1740, 1450 cm^{-1}. ^1H NMR: δ 1.15 (d, 3 H, $J_{5,Me}$ 6.1 Hz, CCH_3), 3.40 (d, 1 H, $J_{2,3}$ 3.8 Hz, H-3), 3.55 (s, 3 H, OMe), 3.85 (dd, 1 H, $J_{1,2}$ 3.7 Hz, H-2), 4.65 (q, 1 H, H-5), and 5.00 (d, 1 H, H-1); ^{13}C NMR: δ 201.9 (C-4), 94.3 (C-1), 66.2 (C-5), 60.1 (OMe), 56.2 (C-3), 51.7 (C-2), and 13.6 (C-6). MS: *m/z* 176 ($M^{+\cdot}$, 17%), 148 (100), 101 (55). Anal. Calcd for $C_7H_{10}O_4$: C, 53.16; H, 6.37. Found: C, 53.13; H, 6.35.

Methyl 3,6-dideoxy-α-L-erythro-hexopyranosid-4-ulose (−)-**10**.—Purification of the crude material after irradiation of (−)-**9** (0.5 g) by flash chromatography with 6:4 EtOAc–hexane as the eluent gave (−)-**10** (0.3 g, 60%); $[\alpha]_D$ −176.0° (*c* 2, $CHCl_3$); IR ($CHCl_3$): 3440, 1720 cm^{-1}; ^1H NMR: δ 1.25 (d, 3 H, $J_{5,Me}$ 6.3 Hz, CCH_3), 2.65–2.70 (m, 3 H, H-3a, H-3b, OH), 3.50 (s, 3 H, OMe), 4.10–4.20 (m, 2 H, H-2, H-5), and 4.60 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-1); ^{13}C NMR: δ 206.7 (C-4), 97.9 (C-1), 70.3 (C-2), 67.8 (C-5), 55.7 (OMe), 42.9 (C-3), and 14.5 (C-6). MS: *m/z* 178 ($M^{+\cdot}$, 56%), 147 (100), 150 (35). Anal. Calcd for $C_7H_{12}O_4$: C, 52.49; H, 7.55. Found: C, 52.53; H, 7.51.

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