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Note

The synthesis of 2,3-dideoxyhex-2-enono-1,5-lactones

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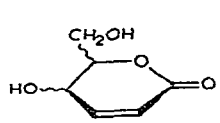
2,3-Dideoxyhex-2-enono-1,5-lactones (**1**) represent a class of simple sugar compounds that are of potential interest in preparative carbohydrate chemistry. Until now, only four representatives (**2**–**5**) of this class have been described[1].



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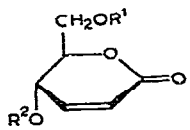
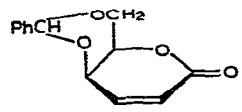


2 R^1, R^2 = PhCH

3 $R^1 = R^2$ = Ac



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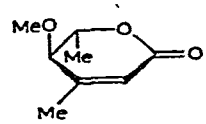

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Compounds of type **1** can be easily obtained from alkyl 2,3-dideoxyhex-2-enopyranosides by oxidation with 30% hydrogen peroxide in the presence of molybdenum trioxide as a catalyst, followed by dehydration of the resulting hydroperoxide with, for example, acetic anhydride and pyridine. Thus, ethyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**6**) gave the corresponding 1,5-lactone (**3**) in 41% yield, and ethyl 4,6-di-*O*-acetyl-2,3-dideoxy-αβ-D-*threo*-hex-2-enopyranoside (**7**) afforded the 1,5-lactone **13** in 39% yield. A series (**8**–**11**) of 6-substituted 2-alkoxy-5,6-dihydro-2*H*-pyrans gave the corresponding lactones (**14**–**17**) in 60–70% yield.

One intermediate hydroperoxide was isolated (**12** from **8**). The oxidation of glycosides described herein is analogous to the oxidation[5] of dialkyl acetals of simple aldehydes with anhydrous hydrogen peroxide at 70–80° to give hydroperoxides of the type RO–CHR'–OOH. No oxidation occurred at the anomeric centre when methyl 3,6-di-*O*-acetyl-2,4-dideoxy-α-DL-*threo*- and -*erythro*-hexopyranosides were used as substrates.

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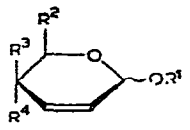
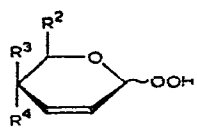


6–11



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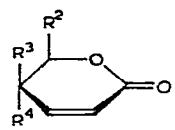

3, 13–17

6 and **3** : $R^1 = Et$, $R^2 = CH_2OAc$, $R^3 = H$, $R^4 = OAc$
7 and **13**: $R^1 = Et$, $R^2 = CH_2OAc$, $R^3 = OAc$, $R^4 = H$
8, **12**, and **14**: $R^1 = Me$, $R^2 = CO_2Bu$, $R^3 = R^4 = H$
9 and **15**: $R^1 = Me$, $R^2 = CH_2OAc$, $R^3 = R^4 = H$
10 and **16**: $R^1 = Me$, $R^2 = CH_2NHAc$, $R^3 = R^4 = H$
11 and **17**: $R^1 = Me$, $R^2 = CH_2N(CO)_2C_6H_4$, $R^3 = R^4 = H$

EXPERIMENTAL

Melting points are not corrected. Boiling points refer to bath temperatures. ^{1}H-N.m.r. spectra were recorded for solutions in $CDCl_3$ (internal Me_4Si) with JEOL JNM-4H-100 (100 MHz) and Varian HA-60/IL (60 MHz) spectrometers. I.r. spectra were recorded on a Unicam SP-200 spectrophotometer. Optical rotations were measured at 18 $\pm 2°$ (*c* 1, chloroform) with a Perkin–Elmer 141 automatic polarimeter. T.l.c. was performed with Silica Gel G Merck, and column chromatography with Silica Gel 60 Merck (70–230 mesh).

*Butyl 5,6-dihydro-2-hydroperoxy-2*H*-pyran-6-carboxylate* (**12**). — A mixture of butyl 5,6-dihydro-2-methoxy-2*H*-pyran-6-carboxylate[6] (**8**) (532 mg, 2.4 mmol), molybdenum trioxide (20 mg), and 30% hydrogen peroxide (20 ml) was stirred at room temperature for 16 h. The reaction was then complete (t.l.c.; hexane–ether, 7:3). The product was extracted with chloroform, the extract was dried ($MgSO_4$) and concentrated, and the crude, oily product (425 mg, 79%) was eluted from silica gel with hexane–ether (9:1) to give **12**; ν_{max}^{film} 3400 (OOH), 1730 (C=O), and 1660 cm^{-1} (C=C). ^{1}H-N.m.r. data: δ 6.15 (m, 1 H, H-4), 5.74 (m, 1 H, H-3), 5.61 (s, 1 H, H-2), 4.59 (t, 1 H, ΣJ 15.5 Hz, H-6), 4.21 (t, 2 H, ΣJ 13.0 Hz, OCH_2), 2.48–2.19 (m, 2 H, CH_2), 2.0–0.7 (m, 7 H, C_3H_7).

Anal. Calc. for $C_{10}H_{16}O_5$: C, 55.6; H, 7.4. Found: C, 55.7; H, 7.6.

Butyl 5,6-dihydro-2-pyrone-6-carboxylate (**14**). — A mixture of crude **12** (425 mg) and acetic anhydride–pyridine (1:4, 10 ml) was kept overnight at room temperature, and then concentrated under diminished pressure. Elution of the oily residue from silica gel with hexane–ether (9:1) gave **14** (260 mg, 65%) as a colourless oil, b.p. 105°/0.3 mmHg; ν_{max}^{film} 1750 (C=O), 1630 cm^{-1} (C=C); λ_{max}^{EtOH} 205 nm. ^{1}H-N.m.r. data: δ 6.75 (dt, 1 H, $J_{3,4}$ 9.7, $J_{4,5}+J_{4,5'}$ 8.8 Hz, H-4), 5.96 (dt, 1 H, $J_{3,5}+J_{3,5'}$ 3.8 Hz, H-3), 4.97 (t, 1 H, ΣJ 11.4 Hz, H-6), 4.15 (t, 2 H, OCH_2), 2.78 (m, 2 H, CH_2), 2.0–0.7 (m, 7 H, C_3H_7).

Anal. Calc. for $C_{10}H_{14}O_4$: C, 60.6; H, 7.1. Found: C, 60.7; H, 7.1.

According to the above procedure, the following compounds were prepared:

4,6-Di-*O*-acetyl-2,3-dideoxy-D-*erythro*-hex-2-enono-1,5-lactone (**3**, from **6**[7], 41%), b.p. 160°/0.3 mmHg, $[\alpha]_{578}$ +129°; ν_{max}^{film} 1745 (C=O), 1640 (C=C), and

1225 cm^{-1} (C–O–C); lit.[3] 1740 cm^{-1}. ^{1}H-N.m.r. data: δ 6.67 (dd, 1 H, $J_{2,3}$ 9.7, $J_{3,4}$ 3.0 Hz, H-3), 6.00 (dd, 1 H, $J_{2,4}$ 1.5 Hz, H-2), 5.43 (dq, 1 H, $J_{4,5}$ 7.4 Hz, H-4), 4.57 (m, 1 H, $J_{5,6} \approx J_{5,6'} \approx 4$ Hz, H-5), 4.23 (m, 2 H, H-6,6'), 2.11 and 2.06 (2 s, 6 H, 2 OAc).

Anal. Calc. for $C_{10}H_{12}O_6$: C, 52.6; H, 5.3. Found: C, 52.7; H, 5.4.

4,6-Di-*O*-acetyl-2,3-dideoxy-D-*threo*-hex-2-enono-1,5-lactone (**13**, from **7**[7], 39%), b.p. 160°/0.3 mmHg, $[\alpha]_{578}$ −350°; ν_{max}^{film} 1740 (C=O), 1640 (C=C), and 1230 cm^{-1} (C–O–C). ^{1}H-N.m.r. data: δ 6.87 (dd, 1 H, $J_{2,3}$ 9.5, $J_{3,4}$ 5.7 Hz, H-3), 6.10 (d, 1 H, H-2), 5.20 (dd, 1 H, $J_{4,5}$ 2.6 Hz, H-4), 4.67 (dq, 1 H, $J_{5,6} \sim 7.0$, $J_{5,6'} \sim$ 5.4 Hz, H-5), 4.27 (d, 2 H, H-6,6'), 2.04 (2 s, 6 H, 2 OAc).

Anal. Calc. for $C_{10}H_{12}O_6$: C, 52.6; H, 5.3. Found: C, 52.7; H, 5.4.

6-Acetoxymethyl-5,6-dihydro-2-pyrone (**15**, from **9**[8], 59%), b.p. 140°/0.5 mmHg; ν_{max}^{film} 1740 (C=O) and 1630 cm^{-1} (C=C). ^{1}H-N.m.r. data: δ 6.91 (dt, 1 H, $J_{3,4}$ 10.0, $J_{4,5}+J_{4,5'}$ 8.6 Hz, H-4), 6.00 (dt, 1 H, $J_{3,5}+J_{3,5'}$ 3.8 Hz, H-3), 4.64 (m, 1 H, ΣJ 25.0 Hz, H-6), 4.25 (d, 2 H, CH_2O), 2.44 (m, 2 H, H-5,5'), 2.10 (s, 3 H, OAc).

Anal. Calc. for $C_8H_{10}O_4$: C, 56.5; H, 5.9. Found: C, 56.3; H, 5.9.

6-Acetamidomethyl-5,6-dihydro-2-pyrone (**16**, from **10**[9], 65%), b.p. 153°/0.2 mmHg, m.p. 79°; ν_{max}^{KBr} 1720 (C=O), 1650, and 1570 cm^{-1} (amide). ^{1}H-N.m.r. data: δ 6.90 (dt, 1 H, $J_{3,4}$ 10.0, $J_{4,5}+J_{4,5'}$ 8.5 Hz, H-4), 5.98 (dt, 1 H, $J_{3,5}+J_{3,5'}$ 3.6 Hz, H-3), 4.52 (m, 1 H, ΣJ 26.5 Hz, H-6), 3.60 and 3.50 (2 m, 2 H, CH_2–N), 2.37 (m, 2 H, ΣJ 14.0 Hz, CH_2), 2.02 (s, 3 H, NAc).

Anal. Calc. for $C_8H_{11}NO_3$: C, 56.8; H, 6.6; N, 8.3. Found: C, 56.8; H, 6.5; N, 8.2.

5,6-Dihydro-6-phthalimidomethyl-2-pyrone (**17**, from **11**[10], 70%), m.p. 164°; ν_{max}^{KBr} 1770, 1720, 1620 (phthalimide), and 1735 cm^{-1} (lactone). ^{1}H-N.m.r. data: δ 8.0–7.6 (m, 4 H, aromatic), 6.85 (dt, 1 H, $J_{3,4}$ 10.0, $J_{4,5}+J_{4,5'}$ 8.7 Hz, H-4), 6.00 (dt, 1 H, $J_{3,5}+J_{3,5'}$ 3.8 Hz, H-3), 4.79 (m, 1 H, ΣJ 27.5 Hz, H-6), 4.10 (dd, 1 H, J_{gem} −14.1, J 7.5 Hz), 3.84 (dd, 1 H, J 5.6 Hz, N–CH_2), 2.47 (m, 2 H, ΣJ 14.5 Hz, H-5,5').

Anal. Calc. for $C_{14}H_{11}NO_4$: C, 65.4; H, 4.3; N, 5.4. Found, C, 65.5; H, 4.2; N, 5.3.

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