Carbohydrate Research, 165 (1987) 111–115
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

Note

Stable, enantiomerically pure hydroperoxides derived from sugars

MAREK CHMIELEWSKI*, JANUSZ JURCZAK, AND SYLWESTER MACIEJEWSKI
Institute of Organic Chemistry, Polish Academy of Sciences, 01-224 Warsaw (Poland)
(Received May 17th, 1986; accepted for publication, January 27th, 1987)

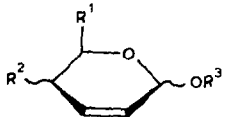
We have reported[1] the transformation of 2,3-unsaturated glycosides **1** into the respective 2,3-dideoxyhex-2-enono-1,5-lactones **2** by oxidation with 30% hydrogen peroxide in the presence of molybdenum trioxide as catalyst, followed by dehydration of the resulting hydroperoxide **3**. Other syntheses of **2** have since been published[2]. We now report on the oxidation of the 2,3-unsaturated glycosides **4–6** and on the intermediate hydroperoxides.

The oxidation of **4–6** with hydrogen peroxide, when catalysed by molybdenum trioxide (1% mol), required several days. Thus, **4** and **5** afforded the corresponding α-hydroperoxides **7** and **8**; ~5% of the β-anomer **9** of **8** was also detected. Oxidation of **6** gave a 2:1 α,β-mixture of the hydroperoxides **10** and **11**.

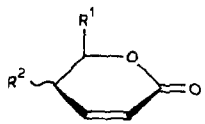
The structures of the hydroperoxides **7–11** were determined on the basis of spectral data (i.r., ^{1}H- and ^{13}C-n.m.r.), elemental analysis, and iodometric titration (see Experimental). A characteristic spectral feature of **7–11**, when compared with the 2,3-unsaturated hemiacetals **12** and **13** (ref. 3), was the down-field shift of 10 p.p.m. of the C-1 signal. The configuration at C-1 in **7–11** was deduced from the $J_{1,2}$, $J_{3,4}$, and $J_{4,5}$ values, and the α configuration of **8** was confirmed by optical rotation data[4]. In solution, **11** occurs almost exclusively in the $^5H_0$ conformation with the $AcOCH_2$ group axial, and AcO-4 and OOH pseudo-axial. This inference was confirmed by the relatively small $J_{4,5}$ value as well as by large $J_{1,2}$ and $J_{3,4}$ values[5]. Some participation of the $^5H_0$ conformation can also be postulated for the *β-threo* hydroperoxide **9**. The conformational behaviour of **11** reflects the allylic effect[6] of the secondary acetoxyl substituent and the anomeric effect of the hydroperoxide group. The exceptionally large anomeric effect operating in **7–11** is caused by the more effective interaction of the lone pair of the ring oxygen atom and the lowest unoccupied orbital of the glycosidic C–O bond. This effectiveness can be explained in terms of the so-called α-effect[7] which, for the hydroperoxide group, leads to a low-lying LUMO, and hence makes its overlapping with the *p*-type lone-pair orbital more energy-lowering.

Compounds **7–11**, which are the first examples of stable hydroperoxides of potential biological importance, were stable under the conditions of flash

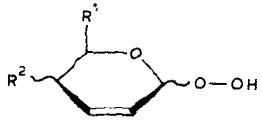
0008-6215/87/$ 03.50



1

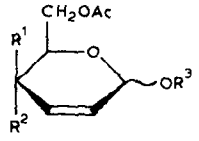


2

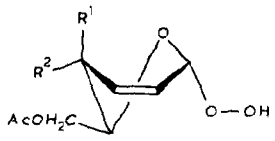


3

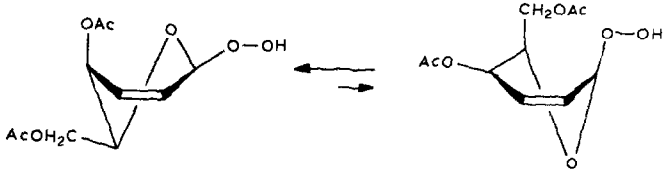
R^1 = CH_2OAc, CO_2Bu, CH_2NHAc, $CH_2N(CO)_2C_6H_4$; R^2 = H, Ac;
R^3 = Me, Et



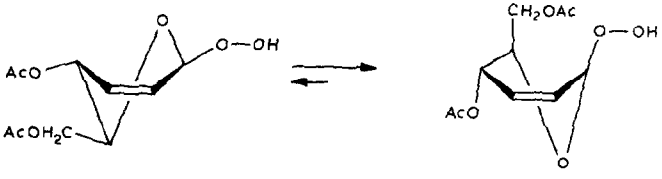
4 R^1 = R^2 = H, R^3 = Me
5 R^1 = OAc, R^2 = H, R^3 = OEt
6 R^1 = H, R^2 = OAc, R^3 = OEt



7 R^1 = R^2 = H
8 R^1 = OAc, R^2 = H
10 R^1 = H, R^2 = OAc



9

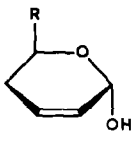


11

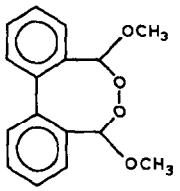
chromatography on silica gel and the pure compounds could be stored at ~5° for several months without marked decomposition.

The presence of the 2,3-double bond in **4–6** facilitates oxidation to give **7–11**; the saturated glycosides could not be oxidised by this procedure. The peroxide **14**, which is related structurally to **7–11**, exhibits exceptional stability[8].

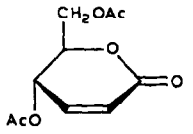
The hydroperoxides **7–11** can be utilised in organic synthesis[9] and as chiral peroxy reagents for asymmetric synthesis. Preliminary experiments showed that



12 R = CH_2OAc
13 R = CO_2Bu



14



15

oxidation of methyl *p*-tolyl sulfide by **8** to the sulfoxide gave the low (5%) asymmetric induction which is typical of the oxidation of sulfides with chiral peroxy acids[10].

The simplicity and cheapness of the preparation of the lactones **2** *via* the hydroperoxide stage makes the method more advantageous than others which have been reported[2]. Therefore, an improved general procedure for preparation of the lactones **2** was devised, and exemplified by the preparation of the *erythro*-lactone **15**, which eliminates the hazard involved in rapid decomposition of peroxyacetic acid possibly generated in the second step of the synthesis.

EXPERIMENTAL

General. — The ^1H- and ^{13}C-n.m.r. spectra were recorded for solutions in $CDCl_3$ with a Bruker 300-MHz spectrometer. I.r. spectra were recorded as films with a Unicam SP-200 spectrophotometer. Optical rotations were measured with a Perkin–Elmer 141 spectropolarimeter. Mass spectra were recorded with an LKB GC-MS 2091 mass spectrometer.

Iodometric titrations of chromatographically pure **7**, **8**, and **10–11** were carried out according to the known procedure[11]; the contents of hydroperoxide were in the range 93–99%.

4,6-Di-O-acetyl-2,3-dideoxy-α- (**10**) *and -β-*D-erythro-*hex-2-enopyranosyl hydroperoxide* (**11**). — To a suspension of **6** (ref. 12) (20.8 g, 0.08 mol) in aqueous 30% hydrogen peroxide (250 mL) was added molybdenum trioxide (0.2 g). The mixture was stirred at room temperature for 6 days; the initial two-phase mixture slowly became homogeneous. The reaction was monitored by t.l.c. After disappearance of the substrate, water (250 mL) was added, the mixture was extracted with dichloromethane (4 × 50 mL), and the combined extracts were washed twice with water, dried, and concentrated to dryness, to afford a mixture (15.7 g, 79%) of **10** and **11**. A portion (1 g) of the mixture was eluted from a column of silica gel (20 g) with hexane–ethyl acetate (7:3), to give a 2:1 mixture of **10** and **11**, isolated as a colourless syrup, $[\alpha]_D$ +154° (*c* 1, chloroform); ν_{max}^{film} 3380, 1735, 1365, 1230, 860 cm^{-1}. N.m.r. data ($CDCl_3$): ^1H, δ 2.11 (s, 6 H, 2 OAc of both anomers), 4.1–4.4 (m, 3 H, H-5,6,6′ of both anomers), 5.12 (dt, 0.33 H, $J_{2,4}$ 1.5, $J_{3,4}$ 4.1, $J_{4,5}$ 3.0 Hz, H-4β), 5.38 (dt, 0.66 H, $J_{2,4}$ 1.9, $J_{3,4}$ 1.2, $J_{4,5}$ 9.6 Hz, H-4α), 5.54 (bs, 0.66 H,

H-1α), 5.60 (bs, 0.33 H, H-1β), 5.75 (ddd, 0.66 H, $J_{1,2}$ 2.7, $J_{2,3}$ 10.2 Hz, H-2α), 6.04 (ddd, 0.33 H, $J_{1,2}$ 2.4, $J_{2,3}$ 10.3 Hz, H-2β), 6.07 (dd, 0.66 H, H-3α), 6.10 (ddd, 0.33 H, $J_{3,5}$ 1.4 Hz, H-3β); ^{13}C, δ 62.90 (C-6α), 63.40, 63.89 (C-5,6β), 65.09 (C-5α), 67.53 (C-4α), 73.19 (C-4β), 97.90 (C-1β), 98.51 (C-1α), 123.23 (C-2α), 125.97 (C-2β), 128.33 (C-3β), 132.92 (C-3α). Mass spectrum: *m/z* 213 ($M^+ - 33$).

Anal. Calc. for $C_8H_{14}O_7$: C, 48.8; H, 5.7. Found: C, 48.4; H, 5.6.

*6-O-Acetyl-2,3,4-trideoxy-α-*DL-glycero-*hex-2-enopyranosyl hydroperoxide* (**7**). — Compound **7**, obtained from **4** (ref. 13) by using the procedure described above, was isolated (72%) as a colourless syrup; ν_{max}^{film} 3380, 1730, 1365, 1240, 855 cm^{-1}. N.m.r. data ($CDCl_3$): ^{1}H, δ 1.9–2.2 (m, 5 H, H-4,4′ and OAc), 4.0–4.3 (m, 3 H, H-5,6,6′), 5.42 (bs, 1 H, H-1), 5.62 (bd, 1 H, $J_{2,3}$ 10.0 Hz, H-2), 6.10 (bdd, 1 H, $J_{3,4}$ 5.7 Hz, H-3); ^{13}C, δ 26.63 (C-4), 65.17 (C-6), 66.13 (C-5), 98.85 (C-1), 121.11 (C-2), 131.83 (C-3). Mass spectrum: *m/z* 171 ($M^+ - 17$), 155 ($M^+ - 33$).

Anal. Calc. for $C_8H_{12}O_5$: C, 51.1; H, 6.4. Found: C, 51.5; H, 6.7.

*4,6-Di-O-acetyl-2,3-dideoxy-α-*D-threo-*hex-2-enopyranosyl hydroperoxide* (**8**). — Compound **8**, obtained from **5** (ref. 12) by the procedure described above, was isolated (67%) as a colourless syrup, $[\alpha]_D$ −180° (*c* 1, chloroform); ν_{max}^{film} 3400, 1740, 1375, 1240, 870 cm^{-1}. N.m.r. data ($CDCl_3$): ^{1}H, δ 2.10 (s, 6 H, 2 OAc), 4.2–4.4 (m, 2 H, H-6,6′), 4.41 (dt, 1 H, $J_{4,5}$ 2.4, $J_{5,6} + J_{5,6'}$ 12.8 Hz, H-5), 5.04 (dd, 1 H, $J_{3,4}$ 5.5 Hz, H-4), 5.58 (m, 1 H, H-1), 5.99 (dd, 1 H, $J_{1,2}$ 3.1, $J_{2,3}$ 10.0 Hz, H-2), 6.27 (ddd, 1 H, $J_{1,3}$ 1.0 Hz, H-3); ^{13}C, δ 62.16, 62.62 (C-5,6), 67.45 (C-4), 97.99 (C-1), 126.16 (C-2), 128.49 (C-3). Mass spectrum: *m/z* 213 ($M^+ - 33$).

Anal. Calc. for $C_{10}H_{14}O_7$: C, 48.8; H, 5.7. Found: C, 48.3; H, 5.9.

The following ^{1}H-n.m.r. signals, due to ~5% of the *β-*D-*threo* anomer **9**, were visible in the spectra of **8**: ^{1}H, δ 5.94 (bd, 1 H, $J_{2,3}$ 10.2 Hz, H-2), 6.16 (ddd, 1 H, $J_{1,3}$ 1.6, $J_{3,4}$ 4.5 Hz, H-3); ^{13}C, δ 62.73 (C-6), 64.02 (C-5), 57.54 (C-4), 99.48 (C-1), 127.30 (C-2), 129.01 (C-3).

*4,6-Di-O-acetyl-2,3-dideoxy-*D-erythro-*hex-2-enono-1,5-lactone* (**15**). — A solution of the mixture (15.0 g, 0.06 mol) of **10** + **11** in dichloromethane (25 mL) was added dropwise to a cooled and stirred mixture of acetic anhydride and pyridine (1:1, 50 mL) at <30°. The reaction was stored at room temperature for 2 h, then poured onto crushed ice, and extracted with dichloromethane (3 × 30 mL). The combined extracts were washed with aqueous sodium hydrogencarbonate, aqueous sodium hydrogensulfite, and water, dried, and concentrated to dryness, to afford **15** (10.0 g, 71%). Column chromatography (ether) on silica gel gave pure **15**, b.p. 160°/0.3 mmHg, $[\alpha]_D$ +129° (*c* 1, chloroform); ^{1}H-n.m.r. data, *inter alia*: 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, $J_{5,6} + J_{5,6'}$ 4 Hz, H-5), identical with that obtained previously[1].

ACKNOWLEDGMENTS

This work was supported by the Polish Academy of Sciences (grant CPBP-01.13.2.15).

REFERENCES

1 J. MIECZKOWSKI, J. JURCZAK, M. CHMIELEWSKI, AND A. ZAMOJSKI, *Carbohydr. Res.*, 56 (1977) 180–182.
2 S. LESAGE AND A. S. PERLIN, *Can. J. Chem.*, 56 (1978) 2889–2896; C. BERNASCONI, L. COTTIER, G. DESCOTES, AND G. REMY, *Bull. Soc. Chim. Fr.*, (1979) 332–336; P. ROLIN AND P. SINAŸ, *Carbohydr. Res.*, 98 (1981) 139–142; P. JARGLIS AND F. W. LICHTENTHALER, *Tetrahedron Lett.*, 23 (1982) 3781–3784.
3 M. CHMIELEWSKI, *Pol. J. Chem.*, 54 (1980) 1913–1921.
4 D. M. CIMENT, R. J. FERRIER, AND W. G. OVEREND, *J. Chem. Soc. C*, (1966) 446–449; G. GRYNKIEWICZ, W. PRIEBE, AND A. ZAMOJSKI, *Carbohydr. Res.*, 68 (1979) 33–41.
5 E. W. GARBISCH, JR., *J. Am. Chem. Soc.*, 86 (1964) 5561–5564; R. J. FERRIER, *Adv. Carbohydr. Chem. Biochem.*, 24 (1969) 199–266; O. ACHMATOWICZ, JR., P. BUKOWSKI, B. SZECHNER, Z. ZWIERZCHOWSKA, AND A. ZAMOJSKI, *Tetrahedron*, 27 (1971) 1973–1996.
6 R. J. FERRIER AND G. H. SANKEY, *J. Chem. Soc. C*, (1966) 2345–2349; A. ZAMOJSKI, M. CHMIELEWSKI, AND S. JAROSZ, *Pol. J. Chem.*, 55 (1981) 1459–1467.
7 I. FLEMING, *Frontier Orbitals and Organic Chemical Reactions*, Wiley, New York, 1978, pp. 77–78.
8 P. S. BAILEY AND R. E. ERICKSON, *Org. Synth.*, Coll. Vol. 5 (1973) 489–495; A. H. ANDRIST AND M. J. KOVELAN, *Spectrosc. Lett.*, 8 (1975) 547–550; J. N. BROWN, R. L. R. TOWNS, M. J. KOVELAN, AND A. H. ANDRIST, *J. Org. Chem.*, 41 (1976) 3756–3757.
9 E. J. COREY, S. G. PYNE, AND WEI-GUO SU, *Tetrahedron Lett.*, 24 (1983) 4883–4886; I. PANFIL AND M. CHMIELEWSKI, *Tetrahedron*, 41 (1985) 4713–4716; I. PANFIL, M. CHMIELEWSKI, AND C. BEŁZECKI, *Heterocycles*, 24 (1986) 1609–1617; J. JURCZAK, T. BAUER, AND K. ANKNER, *ibid.*, 24 (1986) 1531–1534.
10 M. MIKOŁAJCZYK AND J. DRABOWICZ, *Top. Stereochem.*, 13 (1982) 333–468.
11 J. H. SKELLON AND E. D. WILLS, *Aanalyst*, 73 (1948) 78–86.
12 R. J. FERRIER, *Methods Carbohydr. Chem.*, 6 (1972) 307–311.
13 J. JURCZAK, A. KONOWAŁ, AND A. ZAMOJSKI, *Rocz. Chem.*, 44 (1970) 1587–1590.