Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 16 (2005) 1975–1981

New stable anomeric hydroperoxides derived from 2-deoxysugars; enantioselective epoxidation of 2-methyl-1,4-naphthoquinone

Wioletta Kośnik,[a] Andrew V. Stachulski[b] and Marek Chmielewski[a,*]

[a]*Institute of Organic Chemistry of the Polish Academy of Sciences, Kasprzaka 44/52, 01-224 Warsaw, Poland*
[b]*Robert Robinson Laboratories, Department of Chemistry, University of Liverpool, Liverpool L69 7ZD, UK*

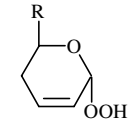
Received 9 March 2005; accepted 11 April 2005
Available online 23 May 2005

Abstract—3,5-Di- or 3,4,6-tri-*O*-substituted-2-deoxysugars or their glycosides can be oxidized with hydrogen peroxide in the presence of an acid catalyst to the corresponding anomeric hydroperoxides, which are relatively stable, can be separated into pure anomers by column chromatography and stored in a refrigerator without visible decomposition. The hydroperoxides thus obtained were used for the enantioselective epoxidation of 2-methyl-1,4-naphthoquinone with ees in the range 28–47%.

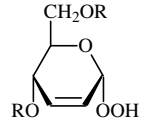
1. Introduction

Some time ago we reported the oxidation of 2,3-unsaturated hexopyranosides and 2-*C*-methylene glycosides with hydrogen peroxide in the presence of a molybdenum trioxide catalyst to give the corresponding anomeric hydroperoxides **1**–**10**.[1–4] Hydroperoxides **1**–**10** are relatively stable, can be purified on a silica gel column and stored in a refrigerator without visible decomposition. Hydroperoxides **5**–**10** can be used for the enantioselective oxidation of prochiral alcohols and sulfides in the presence of $Ti(O\text{-}i\text{-}Pr)_4$ with ees ranging from about 10% to 50%.[3–5]

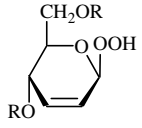
The catalytic asymmetric epoxidation of allylic alcohols by Sharpless[6] and of *Z*-alkenes by Jacobsen[7] are among the leading achievements of contemporary organic synthesis. In comparison to that, hydroperoxides **3**–**10** do not offer visible advantages. They are more expensive, provide significantly lower asymmetric induction, undergo self-oxidation and cannot be regenerated by subsequent reoxidation since the hemiacetals obtained from them are unstable and rearrange to α,β-unsaturated aldehydes.[8]



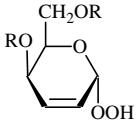
1: R = CO_2Bu
2: R = CH_2OAc



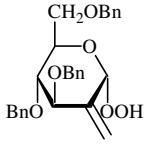
3: R = Ac
6: R = Bn



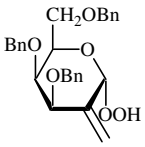
4: R = Ac
7: R = Bn



5: R = Ac
8: R = Bn



9



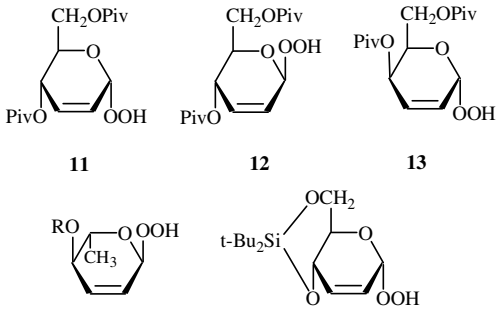
10

Considerable, if less spectacular, progress has been reported in the epoxidation of electrophilic olefins. The results of Wynberg,[9] Enders,[10] Shibasaki,[11] Jackson,[12] Lygo,[13] Adam,[14] Julia-Colonna,[15] Roberts[16] and others[17] are especially noteworthy. Enantioselective oxidation of α,β-unsaturated carbonyl compounds by enantiomerically pure hydroperoxides in the presence of bases has hardly been studied, with only a few hydroperoxides being used.[14,18–20] The crucial role of the base in these reactions has been noticed by Adam et al.[14,19] In the case of the epoxidation of chalcones using 1-phenylethyl

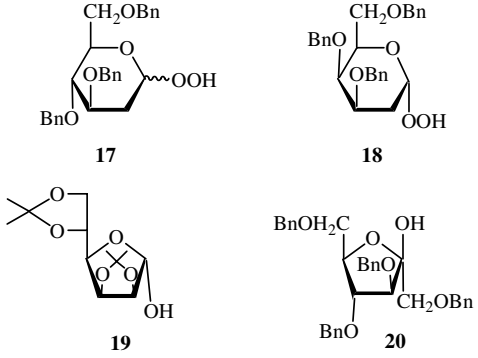
* Corresponding author. Tel.: +48 22 6318788; fax: +48 22 6326681; e-mail: chmiel@icho.edu.pl

0957-4166/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2005.04.009

hydroperoxide, the replacement of KOH by DBU changes the direction of asymmetric induction.



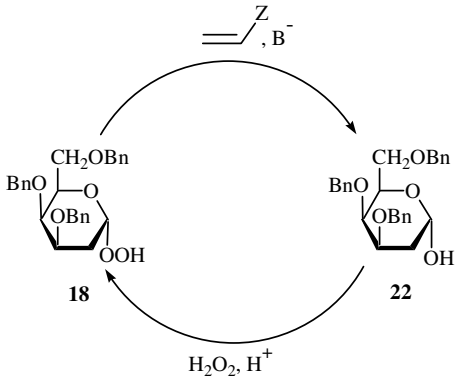
Taylor et al.[18,20] have used anomeric hydroperoxides **8** and **11**–**16** related to compounds **3**–**10** for the epoxidation of quinones. In the best case, an ee of 82% was obtained.[20] Compounds **8** and **11**–**16** were synthesized by a modification of the method of Fehlhaber, Snatzke and Vlahov.[21]



Epoxidation of electrophilic olefins with anomeric hydroperoxides derived from 2,3-unsaturated sugars **1**–**16** in the presence of a base in principle does not remove the drawbacks of the reagents mentioned above, particularly, the lack of possibility of regeneration of the hydroperoxide after oxidation.

A few years ago we reported on the synthesis of hydroperoxides **17** and **18** by direct oxidation of tri-*O*-benzyl-D-glucal and tri-*O*-benzyl-D-galactal, respectively, with the molybdenum trioxide–hydrogen peroxide mixture.[4] Compound **18** has been evaluated by Adam et al.[19] in asymmetric oxidation of α,β-unsaturated carbonyl compounds, giving preparatively useful ees.

The syntheses of **17** and **18** showed that the stability of hydroperoxides does not depend on an allylic acetal fragment and consequently has prompted us to search for other hydroperoxides of that kind. The particular target of our investigation was to find a sugar, which after oxidation of the anomeric centre would provide



Scheme 1.

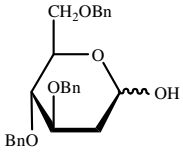
exclusively, or almost exclusively a single anomer and would offer a possible reuse of the reagent. It should be stressed that the particular proportion of α,β-anomers of a sugar hemiacetal does not necessary determine, after oxidation, similar proportion of anomeric hydroperoxides since the hydroperoxide group exhibits a much stronger anomeric effect than the hydroxyl.[2] The possibility of the regeneration of the hemiacetal and its reoxidation to the hydroperoxide would enhance significantly the economy of the process (Scheme 1).

2. Results and discussion

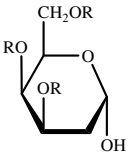
Oxidation of sugars **19** and **20**, which are known to exist as single anomers, failed. Hydrogen peroxide (50%) in the presence of molybdenum trioxide or sulfuric acid[18,20,21] did not convert either sugar into the corresponding anomeric hydroperoxide. On the other hand, oxidation of the readily available 2-deoxysugars or methyl glycosides **21**–**28** with 50% hydrogen peroxide in dioxane in the presence of sulfuric acid over 18 h–6 days provided the derived hydroperoxides **18** and **29**–**41** in 48–75% yields. In the case of **21** a mixture of anomers **29**:**30** in a ratio of about 2.1:1 was obtained; in the case of **22**, the ratio of **18**:**32** amounted to 16:1; in the case of **23**, the ratio of **31**:**33** amounted to 8:1; compound **24** gave one hydroperoxide **34** only.

Glycosides **25**–**27** were separated by chromatography into pure α- and β-anomers and used for anomeric oxidation separately, or as mixtures of both anomers. As was to be expected, in each case, the same ratio of anomeric hydroperoxides was obtained. Glycosides **25** and **26** afforded mixtures of hydroperoxides **35**:**38** and **36**:**39** in a similar ratio for both of about 1.6:1 whereas **27** afforded **37** and **40** in a ratio of about 1.2:1. In all cases, the α-anomers dominated. Except for hydroperoxides **18**:**32** and **31**:**33**, other mixtures of anomers were separated by chromatography. Glycoside **28** was obtained as a mixture of D-manno and D-gluco epimers in a ratio of about 3:2, respectively, which without separation was subjected to oxidation providing an even more complex mixture of hydroperoxides **41** (α-manno:α-gluco:β-gluco:β-manno as 8.7:5.8:1.2:1, respectively) that was not investigated further. Configurations at the anomeric centre of hydro-

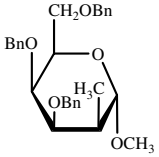
peroxides **18**, **29**–**31** and **35**–**41** were easily proved by ^{1}H NMR spectra. In the case of anomers **32** and **33**, their presence in the product was anticipated on the basis of characteristic downfield signals of their hydroperoxide protons. Except for acetates **35** and **38**, which can be separated by flash chromatography but cannot be stored, the other anomeric hydroperoxides **36**, **37**, **39** and **40** are relatively stable and can be kept in the refrigerator without visible decomposition.



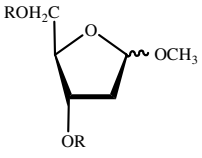
21



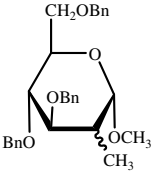
22:R=Bn
23: R=Piv



24

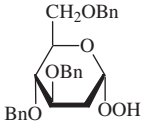


25:R=Ac
26: R=Bn
27; R=Piv

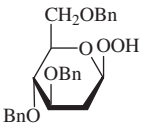


28: R=Bn

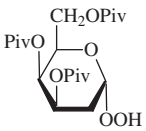
The easy synthesis of stable hydroperoxides from 2-deoxy- and from 2,3-unsaturated sugars, but not from fully hydroxylated sugars **19** and **20**, demonstrates that the crucial issue in the formation of anomeric hydroperoxides is the readiness of the sugar to expel alkoxyl or hydroxyl from the anomeric centre under mild acidic conditions and form a glycosyl cation to which hydrogen peroxide can add. 2-Deoxy- and 2,3-unsaturated-sugars are known to undergo hydrolysis easily.[8,22] The ring oxygen stabilizes the hydroperoxide; interaction between both groups is manifested by the strong anomeric effect.[2] A similar stability has been reported for related acetal hydroperoxides **42**.[23]



29

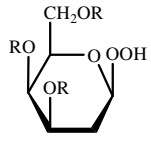


30

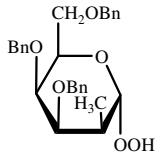


31

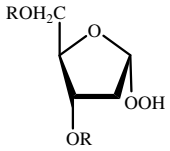
Epoxidations with the anomeric hydroperoxides **18**, **29**–**31**, **34**, **36**, **37**, **39** and **40** as chiral oxidants were performed on 2-methyl-1,4-naphthoquinone **43** under standard conditions used by Taylor et al.[18] (Scheme 2). The results obtained are summarized in Table 1. Asymmetric inductions are in the range of those reported for 2,3-unsaturated anomeric hydroperoxides by Taylor et al.[18,20] and for compound **18** by Adam et al.[19]



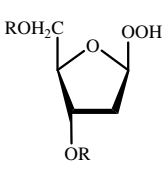
32: R=Bn
33: R=Piv



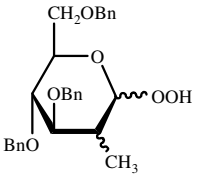
34



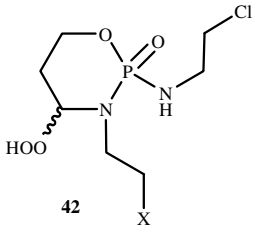
35: R=Ac
36: R=Bn
37: R=Piv



38: R=Ac
39: R=Bn
40: R=Piv

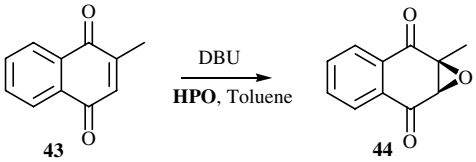


41



42

It is noteworthy that *O*-benzylated hydroperoxides display higher ees than related *O*-pivaloyl derivatives. As anticipated, the configuration of the anomeric carbon atom, to which the hydroxyperoxide group is bound, helps decide the direction of the asymmetric induction: compare the results found for the pairs of anomers **29**/**30**, **36**/**39** and **37**/**40**.



43 **44**

Scheme 2. HPO = hydroperoxide.

3. Conclusion

In summary, we have demonstrated that 2-deoxysugars and their glycosides can be oxidized using hydrogen peroxide in the presence of acids to form anomeric hydroperoxides. Like hydroperoxides derived from 2,3-unsaturated hexopyranoses,[1–4,18,20] compounds **18** and **29**–**41** are relatively stable and can be purified or separated into anomers on a silica gel column and can be stored in a refrigerator without visible decomposition. The sugars can be isolated from the final reaction mixture, after asymmetric epoxidation of electrophilic olefins, as hemiacetals, which can be reoxidized to the corresponding hydroperoxides.

4. Experimental

Melting points were determined on a Koefler hot-stage apparatus. NMR spectra were recorded using Brucker Avance 500 and Varian Mercury 400 instruments. IR spectra were recorded on a Perkin–Elmer FTIR Spectrum 200 spectrophotometer. Mass spectra were recorded using AMD-604 Inectra GmbH and

Table 1. Asymmetric oxidation of quinone **43** with enantiomerically pure hydroperoxides **18**, **29**–**31**, **34**, **36**, **37**, **39**, **40** at 20 °C

Hydroperoxide	Proportion of HPO[a]:43	Time (h)	Yield (%)	ee[b] (%)	Absolute configuration of epoxide **44**
18	1.2	18	80	42.3	(2*R*,3*R*)
18	2.0	20	89	42.3	(2*R*,3*R*)
29	1.2	26	83	44.9	(2*R*,3*R*)
30	1.2	26	79	33.2	(2*S*,3*S*)
31	2.0	22	72	28.8	(2*R*,3*R*)
34	2.0	22.5	90	46.9	(2*R*,3*R*)
36	1.0	25	76	29.9	(2*R*,3*R*)
37	1.0	30	63	38.5	(2*R*,3*R*)
39	1.0	25	73	47.3	(2*S*,3*S*)
40	1.0	30	67	29.3	(2*S*,3*S*)

[a] HPO = hydroperoxide.
[b] Determined by HPLC on Daicel Chiralpak AD-H column.

HPLC–MS with Mariner and API 356 detectors. Optical rotations were measured using a JASCO P 3010 polarimeter at 22 ± 3 °C. Chiral HPLC was performed on a Daicel Chiralpak AD-H column, to measure the ee of 2-methyl-2,3-epoxy-1,4-naphthoquinone. Column chromatography was performed using E. Merck Kieselgel (230–400 mesh).

3,4,6-Tri-*O*-protected sugars **21**–**23** were obtained from corresponding glycals using the procedure of Takahashi and Vasella.[24] Methyl 2-deoxy-D-erythropentofuranosides were obtained by a standard method;[25] their acetylation and separation[26] provided **25α** and **25β**; benzylation and separation[27] gave **26α** and **26β**; pivaloylation and separation[28] afforded **27α** and **27β**.

4.1. Methyl 2-deoxy-3,5-di-*O*-pivaloyl-α-D-erythropentofuranoside 27α

Yield 85%; $[\alpha]_D$ = +55.1 (*c* 0.52 $CHCl_3$); IR (film): *ν* 2974, 1733 (C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): *δ* 5.09 (dd, 1H, *J* 5.3, 0.9 Hz, H-1), 5.03 (ddd, 1H, *J* 8.1, 2.1, 3.7 Hz, H-3), 4.30–4.26 (m, 1H, H-4), 4.23–4.18 (m, 2H, H-5a, H-5b), 3.36 (s, 3H, CH_3O), 2.37 (ddd, 1H, *J* 14.5, 5.3, 8.1 Hz, H-2a), 1.97 (ddd, 1H, *J* 14.5, 0.9, 2.1 Hz, H-2b), 1.21 (s, 9H, Piv), 1.20 (s, 9H, Piv); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 178.42 (Piv), 178.06 (Piv), 104.83 (C-1), 80.89 (C-3), 73.99 (C-4), 63.86 (C-5), 54.78 (*C*H_3O), 39.09 (C-2), 38.81 (Piv), 38.54 (Piv), 27.08 (Piv), 27.01 (Piv); HR-MS/ESI calcd for $C_{16}H_{28}O_6Na$ $(M+Na)^+$ 339.1778. Found: 339.1791. Anal. Calcd for $C_{16}H_{28}O_6$: C, 60.74; H, 8.92. Found: C, 60.80; H, 8.94.

4.2. Methyl 2-deoxy-3,5-di-*O*-pivaloyl-β-D-erythropentofuranoside 27β

Yield 85%; $[\alpha]_D$ = −44.0 (*c* 0.4 $CHCl_3$); IR (film): *ν* 2974, 1733 (C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): *δ* 5.21 (ddd, 1H, *J* 7.2, 4.6, 2.5 Hz, H-3), 5.14 (dd, 1H, *J* 2.4, 5.5 Hz, H-1), 4.23–4.15 (m, 3H, H-4, H-5a, H-5b), 3.34 (s, 3H, CH_3O), 2.40 (ddd, 1H, *J* 14.1, 2.4, 7.2 Hz, H-2a), 2.09 (ddd, 1H, *J* 14.1, 5.5, 4.6 Hz, H-2b), 1.23 (s, 9H, Piv), 1.22 (s, 9H, Piv); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 178.16 (Piv), 177.96 (Piv), 105.61 (C-1), 81.85 (C-3), 74.86 (C-4), 64.84 (C-5), 55.11 (*C*H_3O), 39.19 (C-2), 38.79 (Piv), 38.54 (Piv), 27.15 (Piv), 27.00 (Piv); HR-MS/ESI calcd for $C_{16}H_{28}O_6Na$ $(M+Na)^+$ 339.1778. Found: 339.1783. Anal. Calcd for $C_{16}H_{28}O_6$: C, 60.74; H, 8.92. Found: C, 60.61; H, 8.74.

4.3. Methyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-methyl-α-D-talohexopyranoside 24

Methyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-methylene-α-D-lyxohexopyranoside obtained following known procedure[29] was hydrogenated according to the procedure described by Hansen and Tagmose.[30] Yield 92%; $[\alpha]_D$ = +35.0 (*c* 0.62, $CHCl_3$); IR (film): *ν* 2909, 1078, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): *δ* 4.64 (br s, 1H, H-1), 4.97–4.44 (m, 6H, 3Bn), 3.96 (dt, 1H, *J* 6.2, 6.4, 1.3 Hz, H-5), 3.86–3.83 (m, 2H, H-4, H-3), 3.68 (dd, 1H, *J* 9.6, 6.2 Hz, H-6a), 3.65 (dd, 1H, *J* 9.6, 6.4 Hz, H-6b), 3.34 (s, 3H, CH_3O), 2.27 (m, 1H, H-2), 1.26 (d, 3H, *J* 7.4 Hz, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 103.92 (C-1), 76.38 (C-4), 74.74 (C-3), 74.13 (Bn), 73.48 (Bn), 70.20 (Bn), 69.80 (C-5), 69.77 (C-6), 54.82 (CH_3O), 36.37 (C-2), 12.57 (CH_3); HR-MS/ESI calcd for $C_{29}H_{34}O_5Na$ $(M+Na)^+$ 485.2298. Found: 485.2297. Anal. Calcd for $C_{29}H_{34}O_5$: C, 75.30; H, 7.41. Found: C, 75.24; H, 7.45.

4.4. Methyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-methyl-α-D-manno and α-D-glucohexopyranosides 28

Methyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-methyl-α-D-manno and α-D-glucohexopyranosides **28** were obtained from methyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-methylene-α-D-arabinohexopyranoside as a mixture of two epimers in a ratio of about 1:1, by the procedure described above.[25,26]

Compound **28α**-manno: Yield 55%; ^1H NMR (500 MHz, $CDCl_3$): selected signals taken for the mixture: *δ* 4.65 (d, 1H, *J* 1.4 Hz, H-1), 2.43 (qdd, 1H, *J* 1.4, 5.3, 7.3 Hz, H-2), 1.12 (d, 3H, *J* 7.3 Hz, CH_3).

Compound **28α**-gluco: Yield 35%; ^1H NMR (500 MHz, $CDCl_3$) selected signals taken for the mixture: *δ* 4.61 (d, 1H, *J* 3.3 Hz, H-1), 1.97 (m 1H, H-2), 1.12 (d, 3H, *J* 6.8 Hz, CH_3).

HR-MS/ESI taken for the mixture **28**, calcd for $C_{29}H_{34}O_5Na$ $(M+Na)^+$ 485.2298. Found: 485.2290.

4.5. Synthesis of hydroperoxides; general procedure

Methyl glycosides **23**–**30** (0.25 mM) were dissolved in 1,4-dioxane (1 mL) and 50% H_2O_2 (3 mL) and treated with concd H_2SO_4 (50 μL). The reaction was stirred at room temp until disappearance of the substrate was complete (TLC). Subsequently the mixture was treated with CH_2Cl_2 (50 mL) and the organic layer separated. Water solution was extracted with CH_2Cl_2 and the extracts combined, washed with water, dried and evaporated at room temperature. The crude product was purified or the products separated on a silica gel column using hexane–ethyl acetate 7.5:2.5 v/v as an eluent to afford hydroperoxides **18**, **29/30**, **32**, **34**, **35/38**, **36/39**, **37/40**, **41** in 50–90% overall yield.

4.6. 3,4,6-Tri-*O*-benzyl-2-deoxy-α-D-arabinohexopyranosyl hydroperoxide 29

Yield 45%; $[\alpha]_D = +66.7$ (*c* 0.5, $CHCl_3$); IR (film): *v* 3317.3 (OO–H) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): *δ* 9.22 (s, 1H, OO*H*), 5.35 (dd, 1H, *J* 1.5, 4.7 Hz, H-1), 4.87–4.50 (m, 6H, 3 × Bn), 3.89 (ddd, 1H, *J* 9.9, 2.1, 5.1 Hz, H-5), 3.78 (ddd, 1H, *J* 5.1, 11.5, 8.6 Hz, H-3), 3.77 (dd, 1H, *J* 10.5, 2.1 Hz, H-6a), 3.70 (dd, 1H, *J* 10.5, 5.1 Hz, H-6b), 3.51 (dd, 1H, *J* 9.9, 8.6 Hz, H-4), 2.26 (ddd, 1H, *J* 13.8, 1.5, 5.1 Hz, H-2a), 1.78 (ddd, 1H, *J* 13.8, 4.7, 11.5 Hz, H-2b); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 101.50 (C-1), 77.95 (C-5), 76.72 (C-3), 74.85 (Bn), 73.62 (Bn), 71.83 (Bn), 71.58 (C-4), 69.23 (C-6), 32.49 (C-2); HR-MS/LSIMS-NBA calcd for $C_{27}H_{30}O_6Na$ $(M+Na)^+$ 473.19401. Found: 473.19489. Anal. Calcd for $C_{27}H_{30}O_6$: C, 71.98; H, 6.71. Found: C, 72.00; H, 6.86.

4.7. 3,4,6-Tri-*O*-benzyl-2-deoxy-β-D-arabinohexopyranosyl hydroperoxide 30

Yield 21%; $[\alpha]_D = +7.2$ (*c* 0.5, $CHCl_3$); IR (film): *v* 3352.4 (O-H), 2869.2, 1085.9, 698.3 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): *δ* 9.64 (s, 1H, OO*H*), 5.02 (dd, 1H, *J* 2.8, 8.7 Hz, H-1), 4.83–4.51 (m, 6H, 3 × Bn), 3.81 (dd, 1H, *J* 10.6, 4.7 Hz, H-6a), 3.69 (dd, 1H, *J* 10.6, 1.7 Hz, H-6b), 3.72–3.58 (m, 3H, H-5, H-3, H-4), 2.30 (ddd, 1H, *J* 12.9, 2.8, 5.4 Hz, H-2a), 1.61 (ddd, 1H, *J* 12.9, 8.7, 10.1 Hz, H-2b); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 102.19 (C-1), 78.15 (C-5), 77.00 (C-3), 74.64 (C-4), 74.60 (Bn), 73.45 (Bn), 71.58 (Bn), 69.15 (C-6), 32.29 (C-2); HR-MS/LSIMS-NBA calcd for $C_{27}H_{30}O_6Na$ $(M+Na)^+$ 473.19401. Found: 473.19349. Anal. Calcd for $C_{27}H_{30}O_6$: C, 71.98; H, 6.71. Found: C, 71.69; H, 6.85.

4.8. 3,4,6-Tri-*O*-benzyl-2-deoxy-α-D-lyxohexopyranosyl hydroperoxide 18

Yield 75%; $[\alpha]_D = +32.3$ (*c* 1, $CHCl_3$); IR (film): *v* 3341.2 (O-H), 2873.3, 1092.9, 698.3 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): *δ* 9.08 (s, 1H, OO*H*), 5.41 (d, 1H, *J* 4.7 Hz, H-1), 4.92–4.42 (m, 6H, 3 × Bn), 3.97 (m, 1H, H-5), 3.85 (br s, 1H, H-4), 3.72 (ddd, 1H, *J* 12.4, 4.7, 2.5 Hz, H-3), 3.65 (dd, 1H, *J* 9.6, 6.6 Hz, H-6a), 3.51 (dd, 1H, *J* 9.6, 5.6 Hz, H-6b), 2.29 (ddd, 1H, *J* 13.4, 4.7, 12.4 Hz, H-2a), 2.03 (m, 1H, *J* 13.4, 4.7, 1.2 Hz, H-2b); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 102.11(C-1), 74.27 (Bn), 73.95 (C-5), 73.67 (Bn), 72.76 (C-4), 70.90 (C-3), 70.47 (Bn), 70.09 (C-6), 28.23 (C-2); HR-MS/LSIMS-NBA calcd for $C_{27}H_{31}O_6$ $(M+H)^+$ 451.21206. Found: 451.21298. Anal. Calcd for $C_{27}H_{30}O_6$: C, 71.98; H, 6.71. Found: C, 71.89; H, 6.68. Compound **32**: ^1H NMR (500 MHz, $CDCl_3$): 9.31 (s, 1H, OO*H*).

4.9. 2-Deoxy-3,4,6-tri-*O*-pivaloyl-α-D-lyxohexopyranosyl hydroperoxide 31

Yield 70%; $[\alpha]_D = +79.8$ (*c* 0.35, $CHCl_3$); IR (film): *v* 3395 (O–H), 2974, 1737 (C=O), 1155 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): *δ* 8.95 (s, 1H, OO*H*), 5.47 (d, 1H, *J* 4.6 Hz, H-1), 5.37 (br d, 1H, *J* 2.9 Hz, H-4), 5.12 (ddd, 1H, *J* 12.7, 5.1, 2.9 Hz, H-3), 4.35 (br t, 1H, H-5), 4.20 (dd, 1H, *J* 11.1, 6.7 Hz, H-6a), 4.03 (dd, 1H, *J* 11.1, 7.1 Hz, H-6b), 2.12 (dt, 1H, *J* 13.4, 12.7, 4.6 Hz, H-2a), 1.97 (dd, 1H, *J* 13.4, 5.1 Hz, H-2b), 1.25 (s, 9H, Piv), 1.20 (s, 9H, Piv), 1.19 (s, 9H, Piv); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 178.21 (Piv), 177.37 (Piv), 176.89 (Piv), 101.23 (C-1), 67.73 (C-4), 65.81 (C-3), 65.54 (C-5), 61.76 (C-6), 39.12 (Piv), 38.78 (Piv), 38.67 (Piv), 27.67 (C-2), 27.21 (Piv), 27.09 (Piv), 27.01 (Piv); HR-MS/ESI calcd for $C_{21}H_{36}O_9Na$ $(M+Na)^+$ 455.2252. Found: 455.2259. Anal. Calcd for $C_{21}H_{36}O_9$: C, 58.32; H, 8.39. Found: C, 56.48; H, 8.55. Compound **33**: ^1H NMR (500 MHz, $CDCl_3$): 9.36 (s, 1H, OO*H*).

4.10. 3,4,6-Tri-*O*-benzyl-2-deoxy-2-*C*-methyl-α-D-talohexopyranosyl hydroperoxide 34

Yield 48%; $[\alpha]_D = +2.1$ (*c* 1.19, $CHCl_3$); IR (film): *v* 3326 (O–H), 2874, 1061, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): *δ* 9.46 (s, 1H, OO*H*), 5.19 (br s, 1H, H-1), 4.93–4.44 (m, 6H, 3 × Bn), 4.06 (ddd, 1H, *J* 7.1, 4.8, 1.8 Hz, H-5), 3.78 (br s, 1H, H-4), 3.76 (dd, 1H, *J* 9.9, 7.1 Hz, H-6a), 3.65 (dd, 1H, *J* 5.5, 3.0 Hz, H-3), 3.59 (dd, 1H, *J* 9.9, 4.8 Hz, H-6b), 2.31 (m, 1H, H-2), 1.29 (d, 3H, *J* 7.4 Hz, C*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 106.74 (C-1), 75.85 (C-4), 74.51 (C-3), 74.03 (Bn), 73.70 (Bn), 71.05 (C-5), 70.38 (Bn), 70.28 (C-6), 33.79 (C-2), 12.63 (*C*H$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 106.74 (C-1), 75.85 (C-4), 74.51 (C-3), 74.03 (Bn), 73.70 (Bn), 71.05 (C-5), 70.38 (Bn), 70.28 (C-6), 33.79 (C-2), 12.63 (*C*H$_3$); HR-MS/ESI calcd for $C_{28}H_{32}O_6Na$ $(M+Na)^+$ 487.2091. Found: 487.2063. Anal. Calcd for $C_{28}H_{32}O_6$: C, 72.39; H, 6.94. Found: C, 72.31; H, 6.96.

4.11. 3,4,6-Tri-*O*-benzyl-2-deoxy-2-*C*-methyl-α-D-gluco-, β-D-gluco-, α-D-manno- and β-D-mannohexopyranosyl hydroperoxide 41

Compound was obtained from **28** according to general procedure. ^1H NMR (500 MHz, $CDCl_3$) taken for the mixture: α-D-gluco-, (21%) *δ* 9.09 (s, 1H, OO*H*), 5.18 (d, 1H, *J* 4.2 Hz, H-1), 2.03 (m, 1H, Σ*J* 36.4 Hz, H-2), 1.10 (d, 1H, *J* 7.0 Hz, C*H*$_3$); α-D-manno-, (32%) *δ* 9.22 (s, 1H, OO*H*), 5.14 (d, 1H, *J* 1.9 Hz, H-1), 2.03 (m, 1H, Σ*J* 30.0 Hz, H-2), 1.10 (d, 1H, *J* 7.2 Hz, C*H*$_3$); β-D-manno- (3.5%) *δ* 9.52 (s, 1H, OO*H*), 5.00 (d, 1H,

J 2.5 Hz, H-1), 2.49 (m, 1H, Σ*J* 27.0 Hz, H-2), 1.11 (d, 1H, *J* 6.7 Hz, C*H*$_3$); β-D-gluco-, (4.5%) δ 9.49 (s, 1H, OO*H*), 4.72 (d, 1H, *J* 7.8 Hz, H-1), 2.49 (m, 1H, Σ*J* 36.4 Hz, H-2), 1.11 (d, 1H, *J* 7.0 Hz, C*H*$_3$); HR-MS/ESI taken for the mixture **41** calcd for $C_{28}H_{32}O_6Na$ $(M+Na)^+$ 487.2091. Found: 487.2093.

4.12. 2-Deoxy-3,5-di-*O*-acetyl-α-D-erythropentofuranosyl hydroperoxide 35

Yield 34%; IR (film): *v* 3362 (O–H), 1741 (C=O), 1238 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.88 (s, 1H, OO*H*), 5.67 (dd, 1H, *J* 6.5, 0.9 Hz, H-1), 5.03 (ddd, 1H, *J* 7.8, 2.7, 3.4 Hz, H-3), 4.37 (m, 1H, H-4), 4.33 (dd, 1H, *J* 11.8, 3.5 Hz, H-5a), 4.17 (dd, 1H, *J* 11.7, 4.6 Hz, H-5b), 2.49 (ddd, 1H, *J* 14.7, 6.5, 7.8 Hz, H-2a), 2.09 (s, 3H, Ac), 2.08 (s, 3H, Ac) 1.99 (br d, 1H, *J* 15.0 Hz, H-2b); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.71 (Ac), 170.60 (Ac), 107.67 (C-1), 81.38 (C-3), 73.34 (C-4), 63.62 (C-5), 35.95 (C-2), 20.88 (Ac), 20.74 (Ac); HR-MS/ESI calcd for $C_9H_{14}O_7Na$ $(M+Na)^+$ 257.0632. Found: 257.0624. Compound **35** did not give consistent elemental analysis and since contaminations were found in its NMR spectrum, $[\alpha]_D$ was not provided.

4.13. 2-Deoxy-3,5-di-*O*-acetyl-β-D-erythropentofuranosyl hydroperoxide 38

Yield 21%; IR (film): *v* 3361 (O–H), 1739 (C=O) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.05 (s, 1H, OO*H*), 5.63 (dd, 1H, *J* 1.7, 6.1 Hz, H-1), 5.09 (ddd, 1H, *J* 7.9, 5.6, 3.2 Hz, H-3), 4.71 (dd, 1H, *J* 11.5, 8.7 Hz, H-5a), 4.26–4.19 (m, 2H, H-4, H-5b), 2.41 (ddd, 1H, *J* 14.7, 1.7, 7.9 Hz, H-2a), 2.21 (dt, 1H, *J* 14.7, 6.1, 5.7 Hz, H-2b), 2.14 (s, 3H, Ac), 2.06 (s, 3H, Ac); ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.55 (Ac), 170.72 (Ac), 108.04 (C-1), 83.96 (C-3), 74.08 (C-4), 65.44 (C-5), 35.88 (C-2), 21.19 (Ac), 20.80 (Ac); DEPT 135 (125 MHz, $CDCl_3$): δ 108.04 (C-1), 83.96 (C-3), 74.08 (C-4), 65.44 (C-5), 35.88 (C-2), 21.19 (Ac), 20.80 (Ac); HR-MS/ESI calcd for $C_9H_{14}O_7Na$ $(M+Na)^+$ 257.0632. Found: 257.0639. Compound **38** did not give consistent elemental analysis and since contaminations were found in its NMR spectrum, $[\alpha]_D$ was not provided.

4.14. 3,5-Di-*O*-benzyl-2-deoxy-α-D-erythropentofuranosyl hydroperoxide 36

Yield 42%; $[\alpha]_D$ 66.2 (*c* 0.74, $CHCl_3$); IR (film): *v* 3328 (O–H), 2863, 1095, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.94 (s, 1H, OO*H*), 5.61 (dd, 1H, *J* 6.5, 2.1 Hz, H-1), 4.57–4.42 (m, 4H, 2 × Bn), 4.33 (m, 1H, *J* 4.4, 3.8, 4.5 Hz, H-4), 4.01 (ddd, 1H, *J* 7.7, 3.2, 4.4 Hz, H-3), 3.58 (dd, 1H, *J* 10.6, 3.8 Hz, H-5a), 3.42 (dd, 1H, *J* 10.6, 4.5 Hz, H-5b), 2.32 (ddd, 1H, *J* 14.6, 6.5, 7.7 Hz, H-2a), 1.96 (ddd, 1H, *J* 14.6, 2.1, 3.2 Hz, H-2b); ^{13}C NMR (125 MHz, $CDCl_3$): δ 107.77 (C-1), 82.85 (C-4), 78.16 (C-3), 73.56 (Bn), 71.67 (Bn), 69.94 (C-5), 35.68 (C-2); HR-MS/ESI calcd for $C_{19}H_{22}O_5Na$ $(M+Na)^+$ 353.1359. Found: 353.1365. Anal. Calcd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 69.15; H, 6.85.

4.15. 3,5-Di-*O*-benzyl-2-deoxy-β-D-erythropentofuranosyl hydroperoxide 39

Yield 27%; $[\alpha]_D$ −9.8 (*c* 0.60, $CHCl_3$); IR (film): *v* 3369 (O–H), 2866, 1089, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.16 (s, 1H, OO*H*), 5.61 (br d, 1H, *J* 5.8 Hz, H-1), 4.61–4.44 (m, 4H, 2 × Bn), 4.30 (m, 1H, *J* 5.0, 6.7, 7.2 Hz, H-3), 4.20 (m, 1H, *J* 4.5, 4.2, 5.0 Hz, H-4), 3.71 (dd, 1H, *J* 10.3, 4.5 Hz, H-5a), 3.57 (dd, 1H, *J* 10.3, 4.2 Hz, H-5b), 2.37 (ddd, 1H, *J* 13.9, 1.3, 7.2 Hz, H-2a), 2.16 (dt, 1H, *J* 13.9, 5.8, 6.7 Hz, H-2b); ^{13}C NMR (125 MHz, $CDCl_3$): δ 107.44 (C-1), 83.16 (C-4), 78.32 (C-3), 73.46 (Bn), 72.04 (Bn), 70.24 (C-5), 36.70 (C-2); HR-MS/ESI calcd for $C_{19}H_{22}O_5Na$ $(M+Na)^+$ 353.1359. Found: 353.1348. Anal. Calcd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 69.41; H, 6.86.

4.16. 2-Deoxy-3,5-di-*O*-pivaloyl-α-D-erythropentofuranosyl hydroperoxide 37

Yield 44%; $[\alpha]_D$ 95.4 (*c* 0.73, $CHCl_3$); IR (film): *v* 3388 (O–H), 2973, 1730 (C=O), 1157 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.69 (s, 1H, OO*H*), 5.67 (dd, 1H, *J* 6.3, 1.3 Hz, H-1), 5.05 (ddd, 1H, *J* 7.7, 2.1, 3.3 Hz, H-3), 4.35 (q, 1H, *J* 3.6, 3.9, 3.3 Hz, H-4), 4.29 (dd, 1H, *J* 11.9, 3.6 Hz, H-5a), 4.19 (dd, 1H, *J* 11.9, 3.9 Hz, H-5b), 2.48 (ddd, 1H, *J* 15.3, 6.3, 7.7 Hz, H-2a), 1.97 (dt, 1H, *J* 15.3, 1.3, 2.1 Hz, H-2b), 1.21 (s, 9H, Piv), 1.20 (s, 9H, Piv); ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.24 (Piv), 178.00 (Piv), 107.82 (C-1), 81.99 (C-3), 73.40 (C-4), 63.62 (C-5), 38.81 (Piv), 38.56 (Piv), 36.18 (C-2), 27.17 (Piv), 26.93 (Piv); HR-MS/ESI calcd for $C_{15}H_{26}O_7Na$ $(M+Na)^+$ 341.1571. Found: 341.1575. Anal. Calcd for $C_{15}H_{26}O_7$: C, 56.59; H, 8.23. Found: C, 56.85; H, 8.32.

4.17. 2-Deoxy-3,5-di-*O*-pivaloyl-β-D-erythropentofuranosyl hydroperoxide 40

Yield 36%; $[\alpha]_D$ = −97.0 (*c* 0.81, $CHCl_3$); IR (film): *v* 3369 (O–H), 2973, 1731 (C=O), 1154 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.32 (s, 1H, OO*H*), 5.63 (d, 1H, *J* 1.2, 6.1 Hz, H-1), 5.05 (ddd, 1H, *J* 7.9, 5.8, 3.3 Hz, H-3), 4.81 (dd, 1H, *J* 12.1, 9.9 Hz, H-5a), 4.20–4.15 (m, 2H, H-4, H-5b), 2.43 (ddd, 1H, *J* 14.6, 1.2, 7.9 Hz, H-2a), 2.20 (dt, 1H, *J* 14.6, 6.1, 7.9 Hz, H-2b), 1.24 (s, 9H, Piv), 1.20 (s, 9H, Piv); ^{13}C NMR (125 MHz, $CDCl_3$): δ 180.35 (Piv), 178.49 (Piv), 108.07 (C-1), 84.36 (C-3), 73.94 (C-4), 65.62 (C-5), 39.19 (Piv), 38.57 (Piv), 35.95 (C-2), 27.13 (Piv), 27.01 (Piv); HR-MS/ESI calcd for $C_{15}H_{26}O_7Na$ $(M+Na)^+$ 341.1571. Found: 341.1581. Anal. Calcd for $C_{15}H_{26}O_7$: C, 56.59; H, 8.23. Found: C, 56.81; H, 8.02.

4.18. Epoxidation of 43; general procedure[18,20]

Hydroperoxide **18**, **29**–**31**, **34**, **36**, **37**, **39** or **40** (0.103 mM) in toluene (20 mL) was treated with DBU (16 μL, 0.103 mM). After 10 min at room temperature the mixture was treated with quinone **43** (molar equivalents, see Table 1) in toluene (10 mL). The progress of the reaction was monitored by TLC. After the disappearance of quinone, the mixture was washed with

water. The water layer was extracted with CH_2Cl_2 (3×15 mL). Organic layers were combined and filtered through silica gel to afford epoxide **44**. Ees were assigned by chiral HPLC (see above).

Acknowledgements

This work was supported by the State Committee for Scientific Research Grant No. 3 T09A 024 28.

References

1. Mieczkowski, J.; Jurczak, J.; Chmielewski, M.; Zamojski, A. *Carbohydr. Res.* **1977**, *56*, 180–182.
2. Chmielewski, M.; Jurczak, J.; Maciejewski, S. *Carbohydr. Res.* **1987**, *165*, 111–115.
3. Hamann, H.-J.; Höft, E.; Mostowicz, D.; Mishnev, A.; Urbańczyk-Lipkowska, Z.; Chmielewski, M. *Tetrahedron* **1997**, *53*, 185–192.
4. Mostowicz, D. M.; Jurczak, M.; Hamann, H.-J.; Höft, E.; Chmielewski, M. *Eur. J. Org. Chem.* **1998**, 2617–2621.
5. Hamann, H.-J.; Höft, E.; Chmielewski, M.; Maciejewski, S. *Chirality* **1990**, *5*, 338–340.
6. Katsuki, T.; Martin, V. S. *Org. React.* **1996**, *48*, 1–299.
7. Jacobsen, E. N. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993, pp 159–202.
8. (a) Fraser-Reid, B.; Radatrus, B. J. *J. Am. Chem. Soc.* **1970**, *92*, 5288–5290; (b) Gonzales, F.; Lesage, S.; Perlin, A. S. *Carbohydr. Res.* **1975**, *42*, 267–274; (c) Torsel, K.; Tyagi, M. P. *Acta Chem. Scand.* **1977**, *B31*, 297–301; (d) Tatsuta, K.; Yamauchi, T.; Kinoshita, M. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 3035–3038; (e) Chmielewski, M. *Pol. J. Chem.* **1980**, *54*, 1913–1921.
9. (a) Helder, R.; Hummelen, J. C.; Laane, R. W. P. M.; Wiering, J. S.; Wynberg, H. *Tetrahedron Lett.* **1976**, *17*, 1831–1834; (b) Wynberg, H.; Greijdanus, B. *J. Chem. Soc., Chem. Commun.* **1978**, 427–428; (c) Wynberg, H.; Marsman, B. *J. Org. Chem.* **1980**, *45*, 158–161.
10. Enders, D.; Zhu, J.; Kramps, L. *Liebigs Ann./Recueil* **1997**, 1101–1113.
11. (a) Watanabe, S.; Kobayshi, Y.; Arai, T.; Sasai, H.; Bougauchi, M.; Shibasaki, M. *Tetrahedron Lett.* **1998**, *39*, 7353–7356; (b) Watanabe, S.; Arai, T.; Sasai, H.; Bougauchi, M.; Shibasaki, M. *J. Org. Chem.* **1998**, *63*, 8090–8091.
12. Elston, C. L.; Jackson, R. F.; MacDonald, S. J. F.; Murray, P. J. *Angew. Chem., Int. Ed.* **1997**, *36*, 410–412.
13. Lygo, B.; Wainwright, P. G. *Tetrahedron* **1999**, *55*, 6289–6300.
14. (a) Adam, W.; Fell, T. R.; Hoch, U.; Schreier, P. *Tetrahedron: Asymmetry* **1995**, *6*, 1047–1050; (b) Adam, W.; Hoch, U.; Lazarus, M.; Saha-Möller, C. R.; Schreier, P. *J. Am. Chem. Soc.* **1995**, *117*, 11898–11901.
15. Julia, S.; Guixer, J.; Masana, J.; Rocas, J.; Colonna, S.; Annuziata, R.; Molinari, H. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1317–1324.
16. (a) Adger, B. M.; Barkley, J. V.; Bergeron, S.; Cappi, M. W.; Flowerdew, B. E.; Jackson, M. P.; McCague, R.; Nugent, T. J.; Roberts, S. M. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3501–3508; (b) Porter, M. J.; Roberts, S. M.; Skidmore, J. *Bioorg. Med. Chem.* **1999**, *7*, 2145–2156; (c) Allen, J. V.; Drauz, K.-H.; Flood, R. W.; Roberts, S. M.; Skidmore, J. *Tetrahedron Lett.* **1999**, *40*, 5417–5420; (d) Cappi, M. W.; Chen, W.-P.; Flood, R. W.; Liao, Y.-W.; Roberts, S. M.; Skidmore, J. *J. Chem. Soc., Chem. Commun.* **1998**, 1159–1160; (e) Lauret, Ch.; Roberts, S. M. *Aldrichim. Acta* **2002**, *35*, 47–51.
17. (a) Porter, M. J.; Skidmore, J. *Chem. Commun.* **2000**, 1215–1225; (b) Arai, S.; Tsuge, H.; Shioiri, T. *Tetrahedron Lett.* **1998**, *39*, 7563–7566; (c) MacDonald, G.; Alcaraz, L.; Lewis, N. J.; Taylor, R. J. K. *Tetrahedron Lett.* **1998**, *39*, 5433–5436; (d) Pu, L. *Tetrahedron: Asymmetry* **1998**, *9*, 1457–1477; (e) Ebrahim, S.; Wills, M. *Tetrahedron: Asymmetry* **1997**, *8*, 3163–3173; (f) Yu, H.-B.; Zheng, X.-F.; Lin, Z.-m.; Hu, Q.-S.; Huang, W.-S.; Pu, L. *J. Org. Chem.* **1999**, *64*, 8149–8155; (g) Hamann, H.-J.; Höft, E.; Liebscher, J. In *Peroxide Chemistry*; Adam, W., Ed.; Wiley-VCH: Weinheim, 2000, pp 381–405.
18. Dwyer, C. L.; Gill, Ch. D.; Ichikawa, O.; Taylor, R. J. K. *Synlett* **2000**, 704–706.
19. Adam, W.; Rao, P. B.; Degen, H.-G.; Saha-Möller, C. R. *Eur. J. Org. Chem.* **2002**, 630–639.
20. Bundu, A.; Berry, N. G.; Gill, Ch. D.; Dwyer, C. L.; Stachulski, A.; Taylor, R. J. K.; Whittall, J. *Tetrahedron: Asymmetry* **2005**, *16*, 283–293.
21. Fehlhaber, H.-W.; Snatzke, G.; Vlahov, I. *Liebigs Ann. Chem.* **1987**, 637–638.
22. Gomez, A. M.; Lopez, J. C. In *Glycoscience; Chemistry and Chemical Biology*; Fraser-Reid, B., Tatsuta, K., Thiem, J., Eds.; Springer: Berlin, Heidelberg, New York, 2001; Vol. 1, pp 467–500.
23. Hohorst, H. J.; Peter, G.; Struck, R. F. *Cancer Res.* **1976**, *36*, 2278–2281; Takamizawa, A.; Matsumoto, S.; Iwata, T.; Makino, I. *Chem. Pharm. Bull.* **1977**, *25*, 1877–1891; Misiura, K.; Szymanowicz, D.; Kuśnierczyk, H.; Wietrzyk, J.; Opolski, A. *Il Farmaco* **2002**, *57*, 315–319.
24. Takahashi, Y.; Vasella, A. *Helv. Chim. Acta* **1992**, *75*, 1563–1571.
25. Hansen, P.; Pedersen, E. B. *Acta Chem. Scand.* **1990**, *44*, 522–523.
26. Binder, W. H.; Prenner, R. H.; Schmid, W. *Tetrahedron* **1994**, *50*, 749–758.
27. Dyson, M. R.; Coe, P. I.; Walker, R. T. *Carbohydr. Res.* **1991**, *216*, 237–248.
28. Kassou, M.; Castillon, S. *Tetrahedron Lett.* **1994**, *35*, 5513–5516.
29. Booma, C.; Balasubramian, K. K. *J. Chem. Soc., Chem. Commun.* **1993**, 1394–1395.
30. Hansen, A.; Tagmose, T. M. *Tetrahedron* **1997**, *53*, 697–706.