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Reaction of 1-Deoxy-glyc-1-enopyranose Esters with Hydrogen Chloride and Hydrogen Bromide

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Reaction of tri-*O*-acetyl-1-deoxy-D-*threo*-pent-1-enopyranose, or the corresponding *erythro*-compound, with hydrogen chloride leads to the formation of di-*O*-acetyl-3-deoxy-D-*glycero*-pent-2-enopyranosyl chloride in high yield. Analogous results were obtained with tetra-*O*-acetyl-1-deoxy-D-*arabino*-hex-1-enopyranose and with the corresponding tri- and tetra-*O*-benzoates.

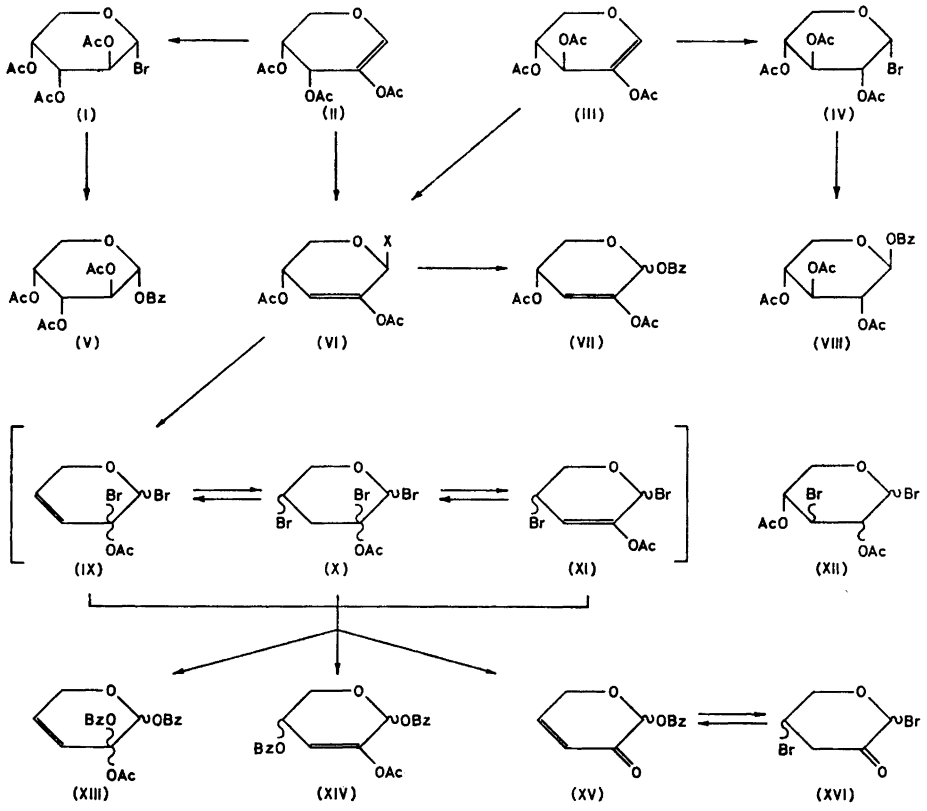
With one molar equivalent of hydrogen bromide 1-deoxy-pent-1-enopyranose esters behaved similarly, yielding 2,3-unsaturated glycosyl bromides. With excess hydrogen bromide, however, the latter compounds underwent further reaction to unstable products. Treatment of these with silver benzoate gave 1-*O*-benzoyl-3,4-dideoxy-pent-3-enopyranosulose as the major product. The mechanism of the reaction with hydrogen bromide is discussed. PMR spectral data of all products are given.

In view of the results obtained by treating glycal esters with hydrogen halides[1] it was of interest to study the behaviour of acetylated 1-deoxy-glyc-1-enopyranoses (2-hydroxy-glycal esters) towards hydrogen chloride and hydrogen bromide. A preliminary report on the reaction of these compounds with hydrogen fluoride has been published.[2]

Treatment of tri-*O*-acetyl-1-deoxy-D-*erythro*-pent-1-enopyranose (II), or the corresponding D-*threo*-derivative (III), with hydrogen chloride in benzene solution led to the formation of di-*O*-acetyl-3-deoxy-D-*glycero*-pent-2-enopyranosyl chloride (VI, X = Cl) in almost quantitative yield. Similarly, tetra-*O*-acetyl-1-deoxy-D-*arabino*-hex-1-enopyranose (XVII) gave the 2,3-unsaturated chloride (XVIII, X = Cl). The products, (VI) and (XVIII), did not react further with excess hydrogen chloride in the course of several hours. Ferrier *et al.*[3,4] have discussed the PMR spectra of a number of 3-deoxy-glyc-2-enopyranoses and, using their results, the pentose-derivative (VI) was found to consist almost entirely of the β-chloride (Table 1). Similarly, the chloride (XVIII) was shown by the PMR spectrum to be the known[5] α-anomer. Treatment of the chloride (VI) with silver benzoate gave a mixture of the

anomeric 1-*O*-benzoyl-derivates (VII). The products were separated and the anomeric structures were assigned on the basis of PMR spectroscopy (Table 1). Similar treatment of the chloride (XVIII) with silver acetate gave the anomeric tetra-*O*-acetates (XIX), characterized through their PMR spectra.

Reaction of (III) with one molar equivalent of hydrogen bromide in benzene solution proceeded similarly to give the 2,3-unsaturated bromide (VI, X = Br) which was converted to the 1-*O*-benzoyl-derivatives (VII). With excess hydrogen bromide, however, both (II) and (III) underwent further reaction



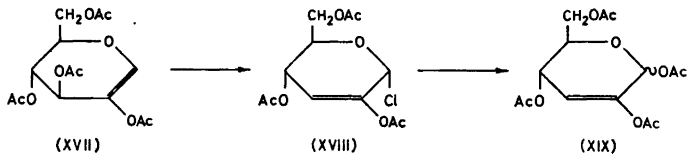


Table 1. δ Values and observed first order coupling constants (cps) of compounds shown in Fig. 1.

	H_1	H_3	H_4	H_{5a}	H_{5e}	H_6	J_{34}	J_{35a}	J_{35e}	J_{45a}	J_{45e}	J_{5a5e}	J_{13}	J_{14}
VI, Cl	6.33	5.95	5.30	4.25	4.05		6.0		1.0	2.8	1.0	13.0		
VI, Br	6.76	5.95	5.35	3.95—4.30			6.1							
XVIII	6.25	5.75	5.60	4.10—4.50			2.0			9.0				
VII, α	6.50	5.98	5.62	3.89	4.08		2.4		1.1	9.3	6.0	11.0	0.6	1.1
VII, β	6.58	6.11	5.30	4.24	4.01		6.0		0.9	2.6	1.0	13.1		
VII, α*	6.72	6.30	5.91	4.13	4.21		2.4		0.8	9.2	6.0	10.8	0.5	1.1
VII, β*	6.78	6.42	5.62	4.40	4.20		6.2		0.9	2.5	1.0	13.0		
XV	6.38	6.31	7.18	4.66	4.40		10.2	2.2	1.8	2.0	3.6	18.8	0.8	
XIV	6.66	6.25	5.60	4.40	4.20		6.1		1.0	2.3	1.0	13.0		
XIII	7.32	6.15	6.70	4.05—4.45			10.6	2.6	2.3	2.0	2.1		1.5	
XIII*	7.33	6.22	6.90	4.10—4.50			10.6	2.4	2.2					
XIX, α	6.30	5.85	5.50	4.05—4.40			2.1			9.0				
XIX, β	6.38	5.95	5.30	4.05—4.45			5.5				1.5			
II	6.61	5.68	5.23	3.86	3.97		4.0		1.0	9.0	4.6	11.0		
III	6.72	5.35	4.96	4.22	4.00		2.5	1.5	0.5	2.4	1.8	12.5	J_{15a} 0.5	

* Tribenzoates.

to a mixture of products, too unstable to be isolated. Hence, the crude reaction mixture was treated with silver benzoate to give a mixture of products which were separated by chromatography into (XIII), (XIV), and (XV). In addition to these three products a small amount of 1-*O*-benzoyl-tri-*O*-acetyl-α-D-arabinopyranose (V) was obtained when (II) was the starting material. When (III) was used, a low yield of 1-*O*-benzoyl-tri-*O*-acetyl-β-D-*xylo*pyranose (VIII) was isolated in addition to (XIII), (XIV), and (XV). The products (V) and (VIII) are presumably formed *via* the corresponding 1,2-adducts, (I) and (IV), respectively. Of the three products (XIII), (XIV), and (XV), the unsaturated ketone (XV) was the major product, obtained in 50 % yield. Its structure was evident from the PMR spectrum (Table 1) and from the IR spectrum which shows the band of an α, β-unsaturated ketone at 1690 cm^{-1}. The product was a racemic modification as seen on the basis of lack of optical rotation at the D-line. Compound(s) (XIII) had a PMR spectrum which was very similar to that of (XV) except that it contained two *O*-benzoyl and one *O*-acetyl groups, and on this basis the structure is proposed. The product is optically active but its stereochemistry is not known. The third product (XIV) was isolated as the β-anomer which had a PMR spectrum identical with that of the β-anomer of (VII) except that one acetyl group was replaced by a benzoyl group. The stereochemistry at C-4 remains unestablished.

Treatment of tri-O-benzoyl-1-deoxy-D-*threo*-pent-1-enopyranose with hydrogen bromide followed by reaction with silver benzoate gave products analogous to those described above, although in somewhat different yields (see Experimental).

The mechanism of the reaction of (II) or (III) with excess hydrogen bromide is not known with certainty because the bromo-compounds formed are too unstable to be isolated. However, since reaction of (II) or (III) with one equivalent of hydrogen bromide gives the 2,3-unsaturated bromide (VI, X = Br) this must be an intermediate in the reaction with excess hydrogen bromide. This is further confirmed by the fact that treatment of (VII) with hydrogen bromide in benzene gives the same products as those obtained from (II) or (III) with the exception, of course, of the products, (V) and (VIII). PMR spectra of the crude benzene solution, resulting from the treatment of (VII) with excess hydrogen bromide, show that more than one product is present. However, only weak signals corresponding to vinylic protons were seen in the spectra, whereas a rather strong signal was present at *ca.* 3 δ. This indicates that the tribromo-derivative (X) is the major product present in the benzene solution. This product may be formed by addition of hydrogen bromide to the 3,4-unsaturated compound (IX) which can, in its turn, arise by attack of a bromide ion at C-2 of (VI), accompanied by acid catalyzed displacement of the *O*-acetyl group at C-4. Treatment of the benzene solution, containing (X), with silver benzoate may then account for the formation of the final products (XIII), (XIV), and (XV) by substitution or elimination of the bromine atoms of (X).

When the crude benzene solution, presumed to contain (X), was evaporated, elimination of hydrogen bromide took place. A PMR spectrum of the residue thus obtained showed a rather strong signal corresponding to a vinylic proton. The spectrum was quite similar to that of (VI) except that the signal of H-4

was shifted upfield to *ca.* 4.9 δ, and only one *O*-acetyl group remained. This indicates that (X) is converted to (XI) by evaporation of the benzene solution. Treatment of the crude solution of (XI) with silver benzoate gave a mixture of (XIII), (XIV), and (XV).

When the unsaturated ketone (XV) was treated with hydrogen bromide in benzene solution a quantitative conversion to a mixture of the isomeric dibromides (XVI) took place, as seen from the PMR spectra. These products are too unstable to be isolated. On treatment of the crude solution of (XVI) with silver benzoate (XV) was recovered in good yield.

Reaction of tetra-*O*-acetyl-1-deoxy-D-*arabino*-hex-1-enopyranose (XVII) with one molar equivalent of hydrogen bromide in benzene gave a high yield of the 2,3-unsaturated α-bromide (XVIII). With excess hydrogen bromide, followed by reaction of the crude product with silver benzoate, (XVII) was converted into a very complex mixture of products which were not investigated further.

Katsuhara *et al.*[6] studied the reaction of 1,3,4,5-tetra-*O*-acetyl-2-deoxy-L-*threo*-hex-2-enopyranulose with hydrogen bromide and found results similar to those described above. However, they also found products resulting from addition of hydrogen bromide to a 2,3-unsaturated intermediate, analogous to (VI). A reaction of this type would, in the present case, have led to the formation of the 3-bromo-3-deoxy-compound (XII); products of this type were, however, not observed.

EXPERIMENTAL

Melting points are uncorrected. Chromatography was performed as described previously.[1] PMR spectra were obtained in deuteriochloroform solution on Varian A-60 or HA-100 instruments using tetramethylsilane as an internal standard.

Tri-O-*acetyl-1-deoxy*-D-erythro-*pent-1-enopyranose* (II) was prepared according to the general procedure of Ferrier.[7] Tri-*O*-acetyl-α-D-arabino-pyranosyl bromide (50 g) was dissolved in dry acetone (200 ml) containing sodium iodide (25 g) and the mixture was stirred at room temperature for 15 min. Dry diethylamine (50 ml) was then added and the stirring was continued for 1 h. The solution was diluted with water and methylene chloride and the organic phase was washed twice with 1 N hydrochloric acid and with water and dried over magnesium sulfate. Evaporation of the solvent and crystallization from ethanol gave 19.5 g (51 %) of (II), m.p. 55–60°C. Two additional recrystallizations from ethanol gave an analytical specimen, m.p. 59–60°C, $[\alpha]_D^{23} = +202°$ (*c* 2.5, $CHCl_3$). (Found: C 51.15; H 5.37. Calc. for $C_{11}H_{14}O_7$: C 51.17; H 5.47). The product was further characterized through its PMR spectrum (Table 1) together with that of the corresponding *threo*-derivative (III).[7]

Reaction of acylated 2-hydroxy-glycals with hydrogen halides. The following general procedure was used: the 2-hydroxy-glycal (2 mequiv.) was dissolved in dry benzene (10 ml) and hydrogen chloride or hydrogen bromide was passed through the solution under ice-cooling. After 30 min the solvent was removed *in vacuo* at 25°C. The remaining crude halide was stirred with silver benzoate (2.0 g) in acetonitrile (35 ml) for 2 h at room temperature. The silver salts were then removed by filtration through charcoal and the solvent was evaporated; the residue was dissolved in methylene chloride (50 ml) and filtered. The filtrate was washed twice with saturated aqueous sodium hydrogen carbonate, dried and evaporated, leaving the crude product.

Tri-O-acetyl-1-deoxy-D-threo-*pent-1-enopyranose (III) and hydrogen chloride.* Treatment of (III)[7] (500 mg) with hydrogen chloride as described above gave the syrupy chloride (VI, X=Cl) (484 mg) which could not be induced to crystallize. Reaction with silver benzoate gave 571 mg of a crude product which was separated into two fractions by preparative TLC, eluting twice with ether-pentane (1:2). The fastest moving fraction

gave the α-anomer of (VII) as a syrup, 134 mg (21 %), $[\alpha]_D^{23} = -18.8°$ (*c* 3.4, $CHCl_3$). (Found: C 59.95; H 4.86. Calc. for $C_{16}H_{16}O_7$: C 60.00; H 5.04). The second fraction gave 190 mg (31 %) of the corresponding β-anomer of (VII), $[\alpha]_D^{23} = +134.5°$ (*c* 1.7, $CHCl_3$). (Found: C 59.97; H 5.03).

Tri-O-*acetyl-1-deoxy*-D-erythro-*pent-1-enopyranose* (II) was treated with hydrogen chloride and silver benzoate in the same manner, yielding 24 % of (α-VI) and 35 % of (β-VI), identical with the products described above.

Treatment of 1-O-*benzoyl-2,4-di*-O-*acetyl-3-deoxy*-D-glycero-*pent-2-enopyranose* (VII) with hydrogen chloride gave (VI) as the sole product. Reaction of the latter with silver benzoate gave (VII) as an α: β-mixture in a 2:3 ratio, as estimated from the PMR spectrum.

Tri-O-*benzoyl-1-deoxy*-D-threo-*pent-1-enopyranose* (1.02 g) was treated with hydrogen chloride followed by reaction with silver benzoate. The crude product (1.24 g) thus obtained was separated into two fractions by preparative TLC using ether-pentane (1:1) as the eluent. The fastest moving fraction gave 681 mg (66 %) of a mixture of anomers of 1,2,4-tri-*O*-benzoyl-3-deoxy-D-*glycero*-pent-2-enopyranose. The a: β ratio was 2:1 as seen from a PMR spectrum. The second fraction gave 184 mg (14 %) of tetra-*O*-benzoyl-β-D-xylopyranose, which was recrystallized from acetone-water, m.p. 160–161°C, $[\alpha]_D^{23} = -41.6°$ (*c* 2.7, $CHCl_3$) (recorded,[8] m.p. 173°C, $[\alpha]_D = -42.1°$). A PMR spectrum showed that the product was pure.

The anomeric pair was separated by preparative TLC using benzene as an eluent. The fastest moving fraction consisted of 1,2,4-tri-*O*-benzoyl-3-deoxy-α-D-*glycero*-pent-2-enopyranose which was a syrup, $[\alpha]_D^{23} = +43.0°$ (*c* 3.0, $CHCl_3$). (Found: C 70.10; H 4.85. Calc. for $C_{26}H_{20}O_7$: C 70.30; H 4.50). The second fraction was crystallized from ethanol to give the corresponding β-anomer, m.p. 132–134°C, $[\alpha]_D^{23} = +65.9°$ (*c* 1.5, $CHCl_3$), in agreement with the reported values.[9]

Tetra-O-*acetyl-1-deoxy*-D-arabino-*hex-1-enopyranose (XVII) and hydrogen chloride.* Reaction of this compound (500 mg) with hydrogen chloride in benzene for 3 h gave the pure chloride (XVIII) as seen from a PMR spectrum (Table 1).[5] Treatment of the chloride with silver acetate afforded (XIX) as a mixture of anomers. The anomers were not separated, but characterized through their PMR spectra,[4,5] which showed that the α: β ratio was 27:63.

An analogous result was obtained when (XVII) was treated with one molar equivalent of hydrogen bromide in benzene for 5 h.

Tri-O-*acetyl-1-deoxy*-D-threo-*pent-1-enopyranose (III) and hydrogen bromide.* Treatment of (III) (1.03 g) with excess hydrogen bromide in benzene, as described above, followed by reaction with silver benzoate gave 1.23 g of crude product. The material was separated into three fractions by preparative TLC using ether-pentane (1:1) as the eluent. The slowest moving fraction gave 140 mg (9 %) of (β–VIII), m.p. 144–145°C, $[\alpha]_D^{23} = -66.7°$ (*c* 3.6, $CHCl_3$). (Found: C 56.80; H 5.36. Calc. for $C_{18}H_{20}O_9$: C 56.85; H 5.28). The PMR spectrum was identical with that of an authentic sample prepared from acetobromoxylose and silver benzoate. The next fraction gave 400 mg (47 %) of (XV), which was recrystallized from ether-pentane, m.p. 74–75°C, $[\alpha]_D = 0°$ ($CHCl_3$). (Found: C 66.07; H 4.75. Calc. for $C_{12}H_{10}O_4$: C 66.06; H 4.62). An IR spectrum in potassium bromide showed a weak absorption at 1635 cm^{-1} (conjugated C=C) and two strong bands at 1690 and 1710 cm^{-1} corresponding to the conjugated keto group and the ester carbonyl group, respectively. The third fraction gave 300 mg (21 %) of a 2:1 mixture of (XIII) and (XIV). The two compounds were separated by preparative TLC, eluting several times with benzene. The fastest moving fraction was the 3,4-unsaturated compound (XIII), which was recrystallized from ether-pentane, m.p. 113–115°C, $[\alpha]_D^{23} = -96.9°$ (*c* 1.3, $CHCl_3$). (Found: C 65.68; H 4.51. Calc. for $C_{21}H_{18}O_7$: C 65.95; H 4.74). The slower moving fraction was (XIV) which was recrystallized from ethanol, m.p. 107–110°C, $[\alpha]_D^{23} = -70.0°$ (*c* 0.7, $CHCl_3$). (Found: C 65.70; H. 4.80. Calc. for $C_{21}H_{18}O_7$: C 65.95; H 4.74).

Reaction of (III) with 1 molar equivalent of hydrogen bromide gave (VI, X=Br) as the main product as seen from the PMR spectrum. Treatment of this product with silver benzoate gave a mixture of anomers of (VII). In addition (VIII) was obtained in 8 % yield.

Tri-O-*acetyl-1-deoxy*-D-erythro-*pent-1-enopyranose* (II) (525 mg) was treated with excess hydrogen bromide followed by reaction with silver benzoate. The crude product (598 mg) was separated into three fractions by preparative TLC using ether-pentane

(1:1) as the eluent. The fastest moving fraction consisted of 155 mg (25 %) of a 2:1 mixture of (XIII) and (XIV), identical with the products obtained in the preceding experiment. The next fraction gave 176 mg (40 %) of (XV), m.p. 70–71°C. The slowest moving fraction gave 90 mg (12 %) of 2,3,4-tri-*O*-acetyl-1-*O*-benzoyl-α-D-arabinopyranose (V), m.p. 149–150°C, $[\alpha]_D^{23} = +11.9°$ (*c* 2.8, $CHCl_3$). (Found: C 56.80; H 5.40. Calc. for $C_{18}H_{20}O_9$: C 56.85; H 5.28). The product was identical with an authentic sample prepared from acetobromoarabinose and silver benzoate.

1-O-*Benzoyl-2,4-di*-O-*acetyl-3-deoxy*-D-glycero-*pent-2-enopyranose* (VII) was treated with excess hydrogen bromide and worked up as described above. This gave 10 % of (XIII), 7 % of (XIV), and 49 % of (XV).

Tri-O-*benzoyl-1-deoxy*-D-threo-*pent-1-enopyranose* (513 mg) was treated with excess hydrogen bromide and silver benzoate and the crude product thus obtained was separated into four fractions by preparative TLC using benzene as an eluent. The fastest moving fraction gave 125 mg (25 %) of the tri-*O*-benzoyl analogue of (XIII), which was recrystallized from ether, m.p. 155–156°C, $[\alpha]_D = 0°$ ($CHCl_3$). (Found: C 69.76; H 4.65. Calc. for $C_{26}H_{20}O_7$: C 70.30; H 4.50). The next fraction gave 54 mg (11 %) of a mixture of 1,2,4-tri-*O*-benzoyl-3-deoxy-β-D-*glycero*-pent-2-enopyranose and the corresponding L-epimer (the tribenzoyl analogue of (XIV)), m.p. 130°C, $[\alpha]_D^{23} = -16.0°$ (*c* 2.3, $CHCl_3$). The PMR spectrum was identical with that of the pure D-compound described above, the latter, however, had $[\alpha]_D = +65.9°$ and it is therefore concluded that a partial epimerization has taken place at C-4. The third fraction (183 mg) was a mixture of tetra-*O*-benzoyl-β-D-xylopyranose (21 %) and unequal amounts of 1,2,4-tri-*O*-benzoyl-3-deoxy-α-D-*glycero*-pent-2-enopyranose and the corresponding L-epimer (10 %). The two compounds were separated by preparative TLC using acetone-water (2:1) as eluent. The unsaturated compound had $[\alpha]_D^{23} = +15.2$ and it is therefore a mixture of enantiomers as seen by comparison with the pure D-compound described above. The last fraction obtained by chromatography with benzene as eluent gave 7 mg (2.8 %) of (XV), characterized through its PMR spectrum.

1,2,4-Tri-O-*benzoyl-3-deoxy-β*-D-glycero-*pent-2-enopyranose* was treated with hydrogen bromide and silver benzoate as described above. This gave 29 % of the tribenzoyl analogue of (XIII), 31 % of an α, β-mixture of 1,2,4-tri-*O*-benzoyl-3-deoxy-D(L)-*glycero*-pent-2-enopyranose, and 12 % of (XV). Tetra-*O*-benzoyl-β-D-xylopyranose was of course not formed.

1-O-*Benzoyl-3,4-dideoxy-pent-3-enopyranosulose (XV) and hydrogen bromide.* Hydrogen bromide was passed through a solution of (XV) (60 mg) in benzene-d_6 (0.5 ml) for a few min at +5°C. A PMR spectrum of this solution showed that the vinylic protons of (XV) had disappeared completely. The anomeric proton was observed as a broad singlet at 6.2 δ. A complex 2 proton signal at 2.2–3.0 δ probably represents the protons at C-3 of (XVI). The three protons at C-4 and C-5 were observed as a group of signals at 3.1–4.0 δ. Treatment of this solution with silver benzoate (1.0 g) in acetonitrile (10 ml) followed by isolation as described above gave pure (XV) (42 mg, 70 %), identified through its PMR spectrum.

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REFERENCES

1. Bock, K., Lundt, I. and Pedersen, C. *Acta Chem. Scand.* **23** (1969) 2083.
2. Bock, K. and Pedersen, C. *Tetrahedron Letters* **1969** 2983.
3. Ferrier, R. J. and Sankey, G. H. *J. Chem. Soc.* **C 1966** 2345.
4. Ferrier, R. J., Prasad, N. and Sankey, G. H. *J. Chem. Soc.* **C 1969** 587.
5. Lemieux, R. U. and Bose, R. J. *Can. J. Chem.* **44** (1966) 1855.
6. Katsuhara, M., Wakahara, S. and Tokuyama, K. *Bull. Chem. Soc. Japan* **41** (1968) 1208.
7. Ferrier, R. J. and Sankey, G. H. *J. Chem. Soc.* **C 1966** 2339.
8. Fletcher, H. G., Jr. and Hudson, C. S. *J. Am. Chem. Soc.* **69** (1947) 921.
9. Ferrier, R. J., Prasad, N. and Sankey, G. H. *J. Chem. Soc.* **C 1968** 974.

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