Diels–Alder Reactions with Methyl Cyanodithioformate. An Approach to the Synthesis of Novel Carbohydrates with Sulphur in the Ring

By D. M. VYAS and G. W. HAY*

(*Department of Chemistry, Queen's University, Kingston, Ontario, Canada*)

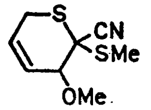
Summary Sulphur analogues of unsaturated deoxysugars were synthesized by Diels–Alder reactions with methyl cyanodithioformate.

WE report the synthesis of the first unsaturated, deoxy sulphur analogues of ketoses[1] *via* simple Diels–Alder reactions with methyl cyanodithioformate (I).[2] This dienophile has been demonstrated in this laboratory[3] to give heterocyclic adducts with a wide variety of dienes. The Diels–Alder condensation of acraldehyde previously was used to form the precursor to a series of carbohydrates leading to DL-glucose.[4]

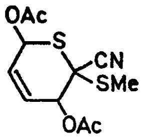
6-Cyano-6-methylthio-Δ^3-dihydrothiopyran (II)† was obtained in 75% yield as colourless crystals, m.p. 32—33°, by adding (I) in CH_2Cl_2 to an excess of liquid buta-1,3-diene at −78°, and allowing the mixture to stand at room temperature for ½ h in a pressure bottle. The 60MHz n.m.r. spectrum (Bruker HX-60, internal $SiMe_4$ lock, $CDCl_3$) disclosed the vinylic protons (3-H, 4-H) as an unresolved, 2-proton multiplet at τ 4·10, the methylene protons as two discrete, unresolved 2-proton multiplets at τ 6·66 (C-2) and 7·27 (C-5), and the methyl protons as a sharp singlet at τ 7·57. This spectrum is comparable to those of analogous heterocyclic Diels–Alder adducts,[5] and clearly obviates the possibility of 1,2-adduct formation.[6] The assignments of the methylene signals were corroborated by the n.m.r. spectra of derivatives of (II) in which selective oxidation of the sulphur atoms was effected. A nearly quantitative yield of the aminomethyl derivative of (II) was obtained by reduction with $LiAlH_4$ in anhydrous ether.

In a similar manner (I) reacted with 1-methoxybuta-1,3-diene in 1 h at atmospheric pressure to give a quantitative yield of 6-cyano-5-methoxy-6-methylthio-Δ^3-dihydrothiopyran (III), a portion of which crystallized (m.p. 54—56°). The relative simplicity of the n.m.r. spectrum suggested a high degree of specificity in the orientation of the reactants during adduct formation. Resonances were observed at τ 4·07 (multiplet, 2H; vinyl), 6·02 (multiplet, 1H; C–H), 6·46 (singlet, 3H; OCH_3), 6·75 (multiplet 2H; S–CH_2), and 7·56 (singlet, 3H; S–CH_3). Comparison of this spectrum with that of (II) indicated that the methoxy-group was not on the carbon atom adjacent to sulphur.

2,5-Diacetoxy-6-cyano-6-methylthio-Δ^3-dihydrothiopyran (IV) was obtained in 20% yield as colourless crystals, m.p. 68—69°, after heating (I) for 24 h under reflux with *trans,trans*-1,4-diacetoxybuta-1,3-diene in benzene containing a drop of acetic acid. The n.m.r. spectra (Varian A-60 and T-60, internal $SiMe_4$ standard) of (IV) indicated resonance at τ 3·88 (multiplet, 1H; 4-H), 7·55 (singlet, 3H; SCH_3), 7·76 (singlet, 3H; acetoxy), and 7·83 (singlet, 3H; acetoxy).



(III)



(IV)

Compounds (III) and (IV) are methylthio glycosidic analogues of deoxythiopyranuloses and it is feasible to

---

† The elemental analyses and i.r. spectra of (II), (III), and (IV) were in agreement with the structures assigned. Each compound gave a distinct molecular ion in the mass spectrum.

name them by carbohydrate conventions. However, heterocyclic nomenclature has been employed pending the results of current studies to resolve and define their stereochemistry.

This work was supported by an Operating Grant from the National Research Council of Canada.

(*Received, July 26th,* 1971; *Com.* 1298.)

[1] M. S. Feather and R. L. Whistler, *J. Org. Chem.*, 1963, **28**, 1567.
[2] H. E. Simmons, D. C. Blomstrom, and R. D. Vest, *J. Amer. Chem. Soc.*, 1962, **84**, 4756.
[3] D. M. Vyas and G. W. Hay, *Canad. J. Chem.*, 1971, **49**, in the press.
[4] U. P. Singh and R. K. Brown, *Canad. J. Chem.*, 1970, **48**, 1791.
[5] A. Ohno, Y. Ohnishi, and G. Tsuchihashi, *Tetrahedron*, 1969, **25**, 871, and refs therein.
[6] N. J. Turro and P. D. Bartlett, *J. Org. Chem.*, 1965, **30**, 1849.

Printed by W Heffer & Sons Ltd Cambridge England