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CYCLOADDITION REACTIONS LEADING TO CARBOHYDRATE DERIVATIVES

PART I.

HETERO DIELS-ALDER REACTION OF MONOSACCHARIDE O-THIOFORMATES

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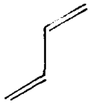
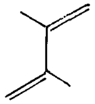
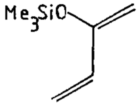
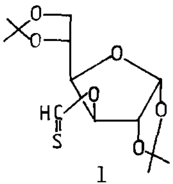
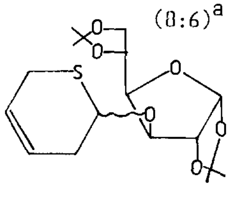
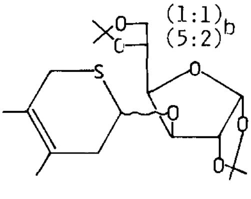
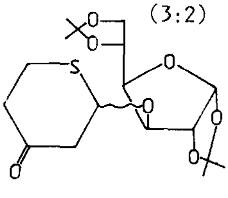
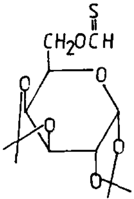
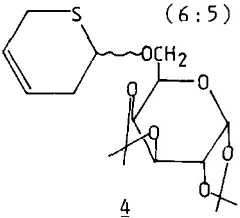
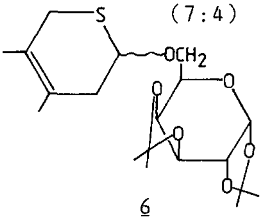
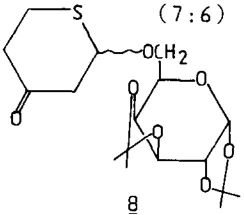
Summary: Monosaccharide O-thioformates under thermal or high-pressure conditions react with various dienes to give O-thiopyran-2-yl saccharides

In recent years substantial progress[1] has been made in making the pyranose framework of carbohydrates by means of the Diels-Alder reaction. Although cycloaddition reactions of thiocarbonyl compounds represent an intensely studied subject[2] only a single example[3] has been reported hitherto for the utilization of such process for the synthesis of carbohydrates containing sulphur in the pyranose ring. While thioketones and thioaldehydes are known as reactive dienophiles[2] the reactivity of dithioesters is considerably lower and thus their Diels-Alder reactions are much less studied. The dienophilic character of the latter compounds can be enhanced by an α-substitution with an electron withdrawing group and so the resulting cyanodithioformates[4], dithiooxalates[5] and dithiopyruvates[5] react more readily with dienes.

Alkyl- and aryl-dithiocarboxylates react with dienes only at an elevated temperature[6] and among such transformations of O-alkyl-thiocarboxylates the reaction[7] of di-O-methyl-dithiooxalate with dimethylbutadiene is the only known example.

With the goal of synthesizing thiosugar derivatives containing sulphur in the pyranose ring the cycloaddition reactions of two monosaccharide O-thioformates were studied. The starting materials (1 and 2) were prepared from 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose[8] and 1,2:3,4-di-O-isopropylidene-α-D-galactopyranose[9], respectively, according to the method of Barton and McCombie[10].

Treatment of 1 and 2 with butadiene or 2,3-dimethylbutadiene in toluene solution in sealed tube for 10-16 h at 150 °C gave the 2,3-dihydro-6H-thiopyran-2-yl saccharides 3, 4, 5 and 6. In the thermal reactions only low chiral induction occurs and an approximately 1:1 mixture of two diastereoisomeric products[11] is formed. As the stereoselectivity of the Diels-Alder additions can be generally enhanced by the application of high pressure[12] the reaction of 1 with 2,3-dimethylbutadiene was also performed at 2.5 kbar pressure for 6 days, and in this case the ratio of diastereoisomers produced was 5:2. Treatment of 1 and 2 with the 2-trimethylsilyloxybutadiene[13] and subsequent methanolysis of the resulting enolethers gave 7 and 8, respectively. NMR spectroscopic investigation[14] of the products demonstrated that the cycloaddition reactions had proceeded regioselectively and 2,3,5,6-

			
 1	 (8:6)[a] 3	 (1:1) (5:2)[b] 5	 (3:2) 7
 2	 (6:5) 4	 (7:4) 6	 (7:6) 8

[a] Ratio of diastereoisomers

[b] Ratio of diastereoisomers in cycloaddition reaction performed at 2.5 kbar

tetrahydrothian-4-on-2-yl-saccharides were obtained upon methanolysis.

The structures of the products were identified by means ^{1}H- and ^{13}C-NMR spectra, by mass spectrometry and by elemental analysis[15]. The diastereoisomeric mixtures 3, 5 and 7 have been separated on Kieselgel column, but separation of mixtures 4, 6 and 8 was unsuccesful in the solvent systems we used.

The prepared cycloadducts described here can be regarded as intermediates for the preparation of novel disaccharides. To our knowledge, no disaccharides carrying a monosaccharide unit with a sulphur in the ring have been hitherto synthesized.

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References and footnotes

1. S. David, A. Lubineau, A. Thieffry, Tetrahedron, 34, 299 (1978); S. David, A. Lubineau, A. Thieffry, Nouv. J. Chim., 1, 375 (1977); S. J. Danishefsky, C. J. Maring, J. Am. Chem. Soc., 107, 1269 (1985); S. J. Danishefsky, W. H. Pearson, B. E. Segmuller, ibid., 107, 1280 (1985); S. J. Danishefsky, E. Larson, J. P. Springer, ibid., 107, 1274 (1985); S. J. Danishefsky, W. H. Pearson, D. F. Harvey, C. J. Maring, J. P. Springer, ibid., 107, 1256 (1985) and references cited therein.
2. S. M. Weinreb, R. R. Staib, Tetrahedron, 38, 3087 (1982)
3. D. M. Vyas, G. W. Hay, J. Chem. Soc. Perkin Trans. I, 180 (1975)
4. D. M. Vyas, G. W. Hay, Canad. J. Chem., 49, 3755 (1971)
5. E. Vedejs, M. J. Arnost, J. M. Dolphin, J. Eustache, J. Org. Chem., 45, 2601 (1980)
6. P. Beslin, P. Metsner, Tetrahedron Lett., 4657 (1980)
7. K. Hartke, G. Henssen, T. Kissel, Liebigs Ann. Chem., 1665 (1980)
8. Methods on Carbohydrate Chemistry, Ed. R. L. Whistler, J. N. BeMiller, Vol. 2., p. 320., Academic Press, New York and London
9. ibid., p. 324.
10. D. H. R. Barton, S. W. McCombie, J. Chem. Soc. Perkin Trans. I, 1575 (1975)
11. The ratio of diastereoisomers was determined from the ratio of the integrated ^{1}H-NMR signals of H-2 of the thiane ring.
12. J. Jurczak, T. Bauer, S. Filipek, M. Tkatz, K. Zygo, J. Chem. Soc., Chem. Commun., 540 (1983)
13. J. Bélanger, N. L. Landry, J. R. J. Paré, K. Jankowski, J. Org. Chem., 47, 3649 (1982)

14. Detailed analyses of the spectra will be presented elsewhere.
15. All new compounds gave satisfactory elemental analyses for C, H and S.

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