Studies on the Synthesis of Novel Carbohydrates with Sulphur in the Ring. Part II.[1,2] Analogues of Derivatives of Unsaturated Deoxy-ulopyranosidonic Acids *via* Diels–Alder Reactions with Methyl Cyanodithioformate

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3,6-Dihydro-2-methylthio-2*H*-thiopyran-2-carbonitrile (5) and its 3-methoxy-derivative (11) were obtained directly from the Diels–Alder reactions of methyl cyanodithioformate (4) with buta-1,3-diene and *trans*-1-methoxybuta-1,3-diene, respectively. The regioselectivity of the reagent (4) is opposite to that of carbonyl dienophiles with 1-alkoxybuta-1,3-dienes. The structure of compound (11) was established by ^{1}H n.m.r. studies involving compounds (5) and (11) and their selectively oxidized and/or reduced derivatives. The results indicated that (11) exists predominantly in the $^0H_2$ conformation in chloroform.

THE synthesis [3] of 5-amino-5,6-dideoxy-DL-hexonic acids from a Diels–Alder adduct precursor demonstrated the usefulness of 1,4-cycloaddition reactions in carbohydrate chemistry. Subsequently, additional applications of the Diels–Alder reaction have been documented [4-6] in the syntheses of a variety of monosac-

[1] Part I, D. M. Vyas and G. W. Hay, *Canad. J. Chem.*, 1971, **49**, 3755.

[2] Preliminary reports, (*a*) D. M. Vyas and G. W. Hay, *Chem. Comm.*, 1971, 1411; (*b*) D. M. Vyas and G. W. Hay, Abstracts, Amer. Chem. Soc. 162nd National Meeting, Washington, D.C., 1971, CARB. 036.

[3] B. Belleau and Yum-Kin Au-Young, *J. Amer. Chem. Soc.*, 1963, **85**, 64.

[4] F. Sweet and R. K. Brown, *Canad. J. Chem.*, 1968, **46**, (*a*) p. 2289; (*b*) p. 2283; (*c*) T. P. Murray, C. S. Williams, and R. K. Brown, *J. Org. Chem.*, 1971, **36**, 1311; (*d*) R. M. Srivastava and R. K. Brown, *Canad. J. Chem.*, 1971, **49**, 1339; (*e*) T. P. Murray, U. P. Singh, and R. K. Brown, *ibid.*, p. 2132; (*f*) U. P. Singh and R. K. Brown, *ibid.*, 1970, **48**, 1791; (*g*) U. P. Singh and R. K. Brown, *ibid.*, 1971, **49**, 1179; (*h*) R. M. Srivastava and R. K. Brown, *ibid.*, 1970, **48**, 830.

[5] A. Banaszek and A. Zamojski, *Carbohydrate Res.*, 1972, **25**, 453 and references cited therein.

[6] V. B. Mochalin, Y. N. Porshev, and G. I. Samokhalov, *J. Gen. Chem.* (*U.S.S.R.*), 1969, **39**, 395.

charides, and certain sugar systems present in antibiotics.

Zamojski and his co-workers [5] generated the anomeric centre in their initial step by a regiospecific Diels–Alder addition between 1-methoxybuta-1,3-diene and glyoxylic acid esters to afford the structure (2), whereas Brown and his co-workers modified the heterocyclic 1,4-adduct (1) to form compounds which were structurally related to derivatives of hex-2-enopyranoses [4a] and hex-3-enopyranoses.[4c] Mochalin *et al.*[6] employed the regiospecific 1,4-cycloaddition product (3) formed from formaldehyde and a 1-alkoxybuta-1,3-diene to synthesize 3-aminopentoses.

Previously the synthesis of sugars with sulphur [7] in the ring had been achieved mainly from chemical modifications of readily available carbohydrate precursors. No attempt to synthesize a sugar ring containing a heteroatom other than oxygen by means of the Diels–Alder reaction had been reported, although compounds of the type CH_2=NR [8] and R^1R^2C=S [9] were known to possess dienophilic properties.

Methyl cyanodithioformate (MCDF) (4), a highly dienophilic compound,[1] is a particularly useful reagent for synthesizing a sulphur-containing sugar ring because it can be converted readily, in one step, into a cyclic dithioacetal (5);[10,11] this reaction should be capable of extension to a wide variety of dienes since the anomeric centre of (5) arises from the MCDF.

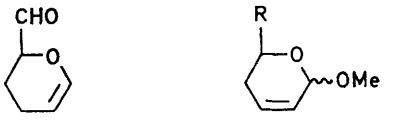
This paper describes the synthesis, *via* Diels–Alder reactions with MCDF, of some novel carbohydrate analogues containing sulphur in the ring. Conformational studies on one product are presented.

RESULTS AND DISCUSSION

The reaction of MCDF with an excess of buta-1,3-diene gave a high yield of 3,6-dihydro-2-methylthio-2*H*-thiopyran (5).[2a] Compound (5) afforded 60 MHz p.m.r. data (Table 1) similar to those of analogous heterocyclic Diels–Alder products, and possessed a vinylic proton pattern diagnostic of a 3,6-dihydro-2*H*-thiopyran.[12] This confirmed that (5) was a 1,4-cycloaddition product rather than a 1,2-adduct.[13]

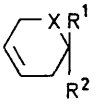
Treatment of the thiopyran (5) with *m*-chloroperbenzoic acid (MCPBA) gave the *SSS'S'*-tetraoxide (6). The 6-acetamido-derivative (7) of compound (6) was obtained by reduction of (5) with lithium aluminium hydride followed by *N*-acetylation of the product (8) and oxidation of the *N*-acetate (9) with MCPBA. Oxidation of (5) with peracetic acid afforded the *SSS'*-trioxide (10).

The 100 MHz n.m.r. spectrum of (5) showed an AB quartet (J_{AB} 12 Hz) centred at τ 4·10 which was split into a complex pattern due to allylic and vicinal coupling with the vinylic protons (H-4 and -5). The continued presence of the ring double bond in each of the derivatives (6), (7), and (10) was indicated by the two-proton multiplet centred at τ 4·12, 4·23, and 4·15, respectively, in the n.m.r. spectra.



(1) (2) R=CO_2Me (3) R=H

(4) (5)



(6) R^1 = CN, R^2 = SO_2Me, X = SO_2
(7) R^1 = CH_2·NHAc, R^2 = SO_2Me, X = SO_2
(8) R^1 = CH_2·NH_2, R^2 = SMe, X = S
(9) R^1 = CH_2·NHAc, R^2 = SMe, X = S
(10) R^1 = CN, R^2 = SOMe, X = SO_2

(11) (12)

In 3,6-dihydrothiopyrans analogous to (5) it has been established [12] that the C-6 methylene protons are deshielded relative to those of C-3. Also, protons on a carbon atom adjacent to a sulphonyl [14] or a sulphinyl group resonate at lower field than the corresponding protons in the unoxidized analogue. Comparison of the n.m.r. data for (5) with those for (6), (7), and (10), lead to the provisional assignment of the signals as reported in Table 1.

Methylene protons α to sulphonyl groups undergo base-catalysed hydrogen–deuterium exchange readily; the resulting changes in the n.m.r. spectra permit ready identification of such groups.[15] Deuteriation of compound (7) in 1,4-dioxan–D_2O–K_2CO_3 afforded a white,

[7] H. Paulsen and K. Todt, *Adv. Carbohydrate Chem.*, 1968, **23**, 115 and references cited therein.
[8] M. P. Cava and C. K. Wilkins, jun., *Chem. and Ind.*, 1964, 1422; W. J. Middleton and C. C. Krespan, *J. Org. Chem.*, 1965, **30**, 1398.
[9] W. J. Middleton, *J. Org. Chem.*, 1965, **30**, 1390.
[10] J. K. N. Jones and W. A. Szarek, in 'The Total Synthesis of Natural Products,' ed. J. ApSimon, Wiley–Interscience, New York, 1973, p. 27.
[11] D. M. Vyas and G. W. Hay, unpublished data.
[12] P. Y. Johnson, E. Koza, and R. E. Kohrman, *J. Org. Chem.*, 1973, **38**, 2967.
[13] N. J. Turro and P. D. Bartlett *J. Org. Chem.*, 1965, **30**, 1849.
[14] A. Ohno, Y. Ohnishi, and G. Tsuchihashi, *Tetrahedron*, 1969, **25**, 871.
[15] C. R. Johnson, J. E. Keiser, and J. C. Sharp, *J. Org. Chem.*, 1969, **34**, 860.

crystalline product the 60 MHz n.m.r. spectrum of which lacked the multiplet at τ 6·00. A decrease in the complexity of the multiplet at τ 6·95 was observed; this

TABLE 1

60 MHz ^{1}H N.m.r. data (τ values; Me_4Si internal standard; $CDCl_3$) for the Diels–Alder adduct (5) and its derivatives

Compound	$C(6)H_2$ *	$C(3)H_2$ *	HC(4)=C(5)H *	Other signals
(5)	6·66	7·27	4·10	7·57 (3H, s, SCH_3)
(6)	5·88	6·48	4·12	6·48 (3H, s, $SO_2{\cdot}CH_3$)
(7)	6·00	6·95	4·23	3·63 (1H, m, $NH{\cdot}COCH_3$), 6·73 (3H, s, $SO_2{\cdot}CH_3$), 7·97 (3H, s, $NH{\cdot}COCH_3$) 5·78 (2H $CH_2{\cdot}NHAc$)
(8)	6·81	7·56	4·18	7·15 (2H, s, $CH_2{\cdot}NH_2$), 7·95 (3H, s, SCH_3), 8·46 (2H, s, $CH_2{\cdot}NH_2$)
(9)	6·90	7·60	4·27	3·0 (1H, m, $NH{\cdot}COCH_3$), 6·48 (2H, $CH_2{\cdot}NHAc$), 7·96 (3H, s), 8·06 (3H, s)
(10)	5·97	6·95	4·15	6·57 (3H, s, $SO{\cdot}CH_3$)

* Two-proton multiplets.

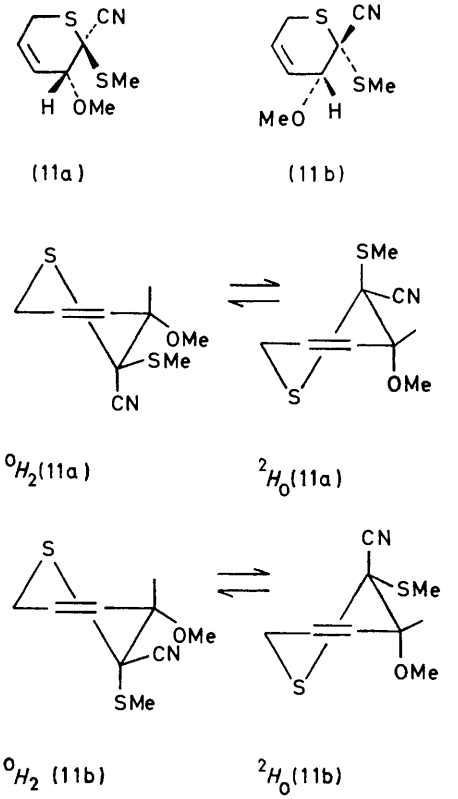
appeared as a simple AB pattern of an ABX system due to the removal of homoallylic coupling. Similarly, the olefinic proton resonance at τ 4·23 was simplified by the loss of allylic and vicinal proton couplings. These data give unequivocal support to the assignments of the C-3 and -6 protons cited in Table 1.

Methoxylated analogues are attainable by Diels–Alder reactions of MCDF with alkoxybutadienes. Thus, *trans*-1-methoxybuta-1,3-diene underwent ready addition with MCDF to afford the 3-methoxy-dihydrothiopyran (11) * as a white crystalline solid. The n.m.r. spectrum of the mother liquor revealed only traces of the regioisomer (12), although variations in experimental conditions could increase the proportion of this to as high as 20% (based on n.m.r. integration data). The conclusion that (11) and (12) are regioisomers and not geometric isomers was based solely upon n.m.r. data.

By comparison with the n.m.r. spectrum of (5), the integration, chemical shift, and coupling patterns in the 60 MHz n.m.r. spectrum of (11) allowed the identification of the vinylic [HC(4)=C(5)H: τ 4·08 (m)], methylene [$C(6)H_2$: τ 6·67 (unresolved ABq)], methine [C(3)H: τ 5·98], methylthio [τ 7·50 (s)], and methoxy (τ 6·42) protons. The complex multiplet of the methylene protons was almost identical with that of the $C(6)H_2$ signal of (5); consequently, the methylene group of (11) was judged to be adjacent to the ring sulphur atom.

A comparison of the 60 MHz n.m.r. spectrum of (11) with that of the residual mixture of (11) and (12) revealed distinct diagnostic signals due to (12) at τ 7·58 (s, SMe) and 6·41 (s, OMe). The multiplet at τ 5·64 was assigned to the acetal C-6 proton of (12). This conclusion was substantiated by the fact that the chemical shift of the multiplet at τ 7·38 was similar to that of the C-3 methylene protons in compound (5). The i.r. spectrum of (11) and that of the mixture containing (11) and (12) were identical. These results established compound (12) to be a regioisomer of (11). Thus the regioselectivity of MCDF is opposite to that of the carbonyl dienophiles with 1-methoxybuta-1,3-diene.[5]

The relative stereochemistry at C-2 and -3 could be presumed on the basis of adherence to the '*endo*-rule'[16,17] demonstrated by open-chain dienes at low temperatures.[17] In addition, theoretical calculations by Hoffmann and Woodward[18] support the predominance of *endo* approach products with dienophiles possessing a conjugated π-system in a kinetically controlled reaction. For compound (11), the *endo*- and *exo*-products are represented by structures (11a) and (11b), respectively.



The predominant conformation of (11) was uncertain. A preferred boat conformation has been proposed[19] for 3,6-dihydro-2*H*-thiopyran, and established for a number of unsaturated, six-membered sulphur heterocycles by *X*-ray studies.[20] Conformational informa-

* Compound (11) can be regarded as a new type of carbohydrate: an alternative designation would be methyl 4,5-dideoxy-3-*O*-methyl-2,6-dithio-β-DL-*glycero*-hex-4-en-2-ulopyranosidononitrile.

[16] K. Alder and G. Stein, *Angew. Chem.*, 1937, **50**, 510.
[17] J. Sauer, *Angew. Chem. Internat. Edn.*, 1967, **6**, 16.
[18] R. Hoffmann and R. B. Woodward, *J. Amer. Chem. Soc.*, 1965, **87**, 4388.
[19] C. A. R. Baxter and D. A. Whiting, *J. Chem. Soc.* (*C*), 1968, 1174.
[20] D. A. Pulman and D. A. Whiting, *Chem. Comm.*, 1971, 831.

tion was not available from the Karplus [21] equation because of the unsaturation in (11). However, Garbisch [22] has developed an empirical relationship between conformation and n.m.r. coupling constants in unsaturated systems somewhat analogous to those studied here. Therefore this equation [22] was used to obtain an estimate of the angles between the ring C–H bonds and the plane of the ring double bond of (11) from the vicinal coupling constants. Vicinal and allylic coupling constants were extracted from a 220 MHz spectrum of (11) (Figure 1) by analysis of the vinylic pattern obtained after decoupling from the signal at τ 5·98 (Figure 1b). Analysis of the multiplets centred at τ 6·67 (C-6) and 5·98 (C-3) yielded the geminal ($J_{6,6'}$) and homoallylic ($J_{3,6}$) coupling constants. These data are summarized in Table 2.

The validity and accuracy of these values were corroborated by employing them to generate a computer-simulated 220 MHz n.m.r. spectrum of (11) (omitting the OMe and SMe singlets) by using the Laocoon II program (Figure 2).[23] The authentic and simulated spectra were closely similar.

The homoallylic coupling constants were found to be 2·5 ($J_{3qa,6qa}$) and 2·1 Hz ($J_{2qa,6qe}$), whereas the vinylic and allylic constants were 2·6 ($J_{5,6qa}$) and 4·6 Hz ($J_{5,6qe}$) (Table 2). From the allylic and vinylic coupling constants the Garbisch equation indicated torsion angles of *ca.* 45 and 90° between the plane of the ring double

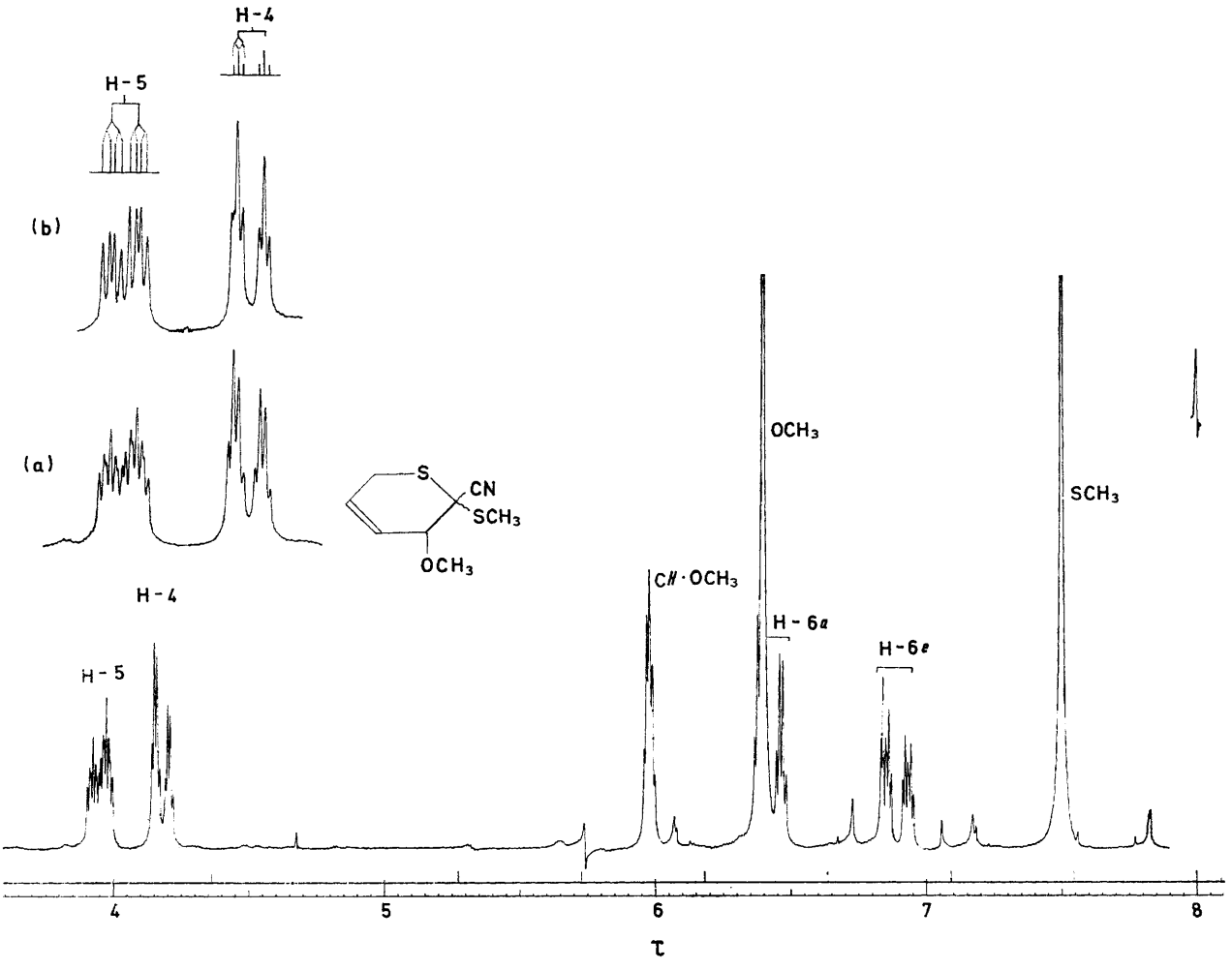


FIGURE 1 220 MHz ^{1}H N.m.r. spectrum of compound (11) in $CDCl_3$; (a) expansion of signal attributed to H-4 and -5; (b) expansion of signal attributed to H-4 and -5 with simultaneous irradiation of signal at τ 5·98

TABLE 2

Coupling constants (Hz) for compound (11) obtained from the 220 MHz n.m.r. spectrum

$J_{3,4}$	$J_{3,5}$	$J_{3,6}$	$J_{4,5}$	$J_{4,6}$	$J_{5,6}$ *	$J_{6,6'}$
2	2	2·1	11	2	4·6 (*ca.* 45°)	18
		2·5		2	2·6 (*ca.* 90°)	

* The values in parentheses denote the torsion angle corresponding to that coupling constant, as obtained by employing the Garbisch equation.

[21] M. Karplus, *J. Chem. Phys.*, 1959, **30**, 11.
[22] E. W. Garbisch, *J. Amer. Chem. Soc.*, 1964, **86**, 5561.
[23] S. Castellano and A. A. Bother-By, *J. Chem. Phys.*, 1964, **41**, 3863.

bond and the C–H bonds on C-5 and -6. The Garbisch equation is very sensitive to variations in coupling constants in the range 2·6—2·8 Hz and probably requires modification for accurate application to sulphur

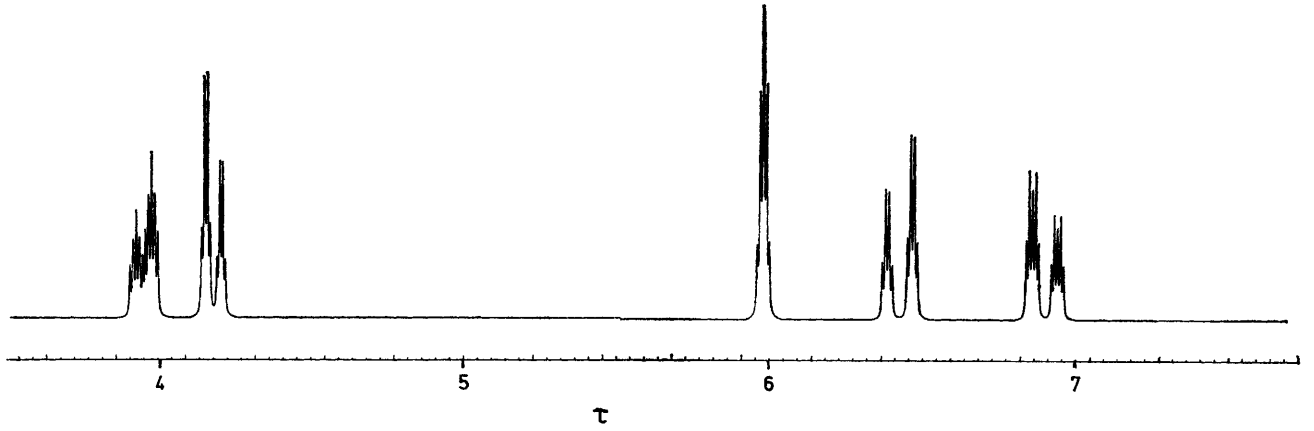
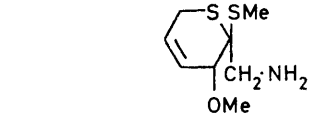


FIGURE 2 Computer-simulated 220 MHz spectrum of compound (11) (with singlets for OCH_3 and SCH_3 omitted) based upon coupling constants and chemical shifts obtained from Figure 1

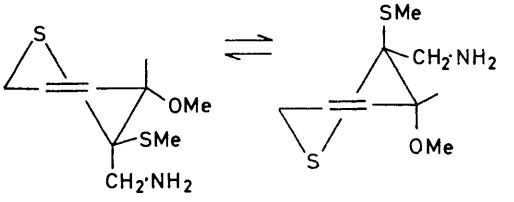
heterocycles. Nevertheless it is clear that (11) does not exist in a boat conformation. Drieding models of cyclohexene revealed torsion angles close to 45 and 75° between the quasi-equatorial (*qe*) and quasi-axial (*qa*) C–H bonds and the plane of the ring in the stable half-chair conformer.[24] The corresponding bonds have been reported to have torsion angles of 30 and 90° in some unsaturated carbohydrates.[25,26] Thus the data suggest that (11) exists in a half-chair conformer in $CDCl_3$.

The relative stereochemistry at C-5 and -6 could be approximated by any of the structures (11a) $^0H_2$, (11b) $^0H_2$, (11a) $^2H_0$, and (11b) $^2H_0$. However, the observation that $J_{3qa,4}$ is 2 Hz (Table 2) indicated that the methoxy-group occupies a quasi-equatorial position; hence the preferred conformation is more similar to $^0H_2$. The Drieding model for the (11a) $^0H_2$ conformer indicated that the C-6 quasi-axial proton probably was in the deshielding zone of the axially disposed C≡N group, which should cause it to resonate at lower field than the C-6 quasi-equatorial proton. Such non-equivalence would not arise in the (11b) $^0H_2$ conformer since the diamagnetic anisotropy of the equatorial C≡N group should have little influence on either of the C-6 protons. The 220 MHz n.m.r. spectrum of (11) showed clearly the non-equivalence of the C-6 protons, which gave rise to an AB quartet centred at τ 6·67 (Table 2). These results demonstrated that the '*endo*-rule' was obeyed with respect to the cyano-group in the reaction, and that conformer (11a) $^0H_2$ is the best approximation in $CDCl_3$ solution.

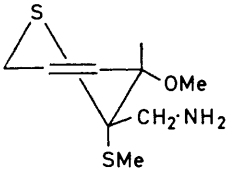
The 60 MHz n.m.r. spectrum of the reduction product (13) from (11) indicated that a stereoisomeric mixture was present, presumably owing to thermal isomerization. Modification of the conditions of reduction afforded pure (13) as evidenced by the presence of only one singlet for each of the OMe and SMe groups in the n.m.r. spectrum. The i.r. spectrum of the isomeric mixture was indistinguishable from that of pure (13) which subsequently was characterized as the *N*-acetyl derivative. The thermal isomerization appears to be restricted to the amino-compound (and certain of its



(13)



$^0H_2$ (13) $^2H_0$ (13)



$^0H_2$ (14)

derivatives): prolonged heating of (11) in dilute solutions of either hydrogen chloride or sodium methoxide

[24] E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, 'Conformational Analysis,' Wiley, New York, 1965, p. 111.

[25] R. J. Ferrier and G. H. Sankey, *J. Chem. Soc.* (*C*), 1966, 2345.

[26] K. Bock and C. Pedersen, *Acta Chem. Scand.*, 1971, **25**, 1021.

in methanol caused no change. However, n.m.r. evidence was obtained which indicated that the *N*-acetyl derivative of (13) had undergone isomerization during high vacuum distillation.

Thermodynamic considerations indicated that either the $^2H_0$ or the $^0H_2$ conformer of (11) would be less stable than the $^0H_2$ conformer of the isomerized product (14) in which there occurs both a minimization of non-bonded interactions, and stabilization of the axial methylthio-group by the anomeric effect.[27] The presence of an axial cyano-group in the predominant ($^0H_2$) conformer of (11) may be another example of the effect of electronegativity on conformational equilibria,[28] and reflect the greater electronegativity of C≡N as compared with SMe. This difference would be reduced by reduction of (11) to (13), thus allowing the subsequently isomerized product (14) to achieve an $^0H_2$ conformation.

EXPERIMENTAL

M.p.s were determined with a Fisher–Johns apparatus. B.p.s were measured with a Büchi Kugelrohr-type distillation apparatus. Evaporations were conducted at 40° and 25 mm Hg. I.r. spectra were recorded on a Perkin-Elmer 180 spectrometer. ^{1}H N.m.r. spectra were obtained with a Varian T60, a Bruker HX-60, a Varian HA-100, or a Varian HR 200 spectrometer, with tetramethylsilane as internal standard. Mass spectra were determined with a JEOL-JMS-OISC double-focusing spectrometer at 75 eV and 100 mA. G.l.c. was conducted with a Gow-Mac 69—700 chromatograph (flame ionization detector; helical 6 ft copper tube packed with 10% Carbowax 4500 on acid-washed Chromosorb P).

Methyl cyanodithioformate (MCDF) (4) was prepared as described by Simmons *et al.*[29] and used without subsequent purification.

3,6-*Dihydro*-2-*methylthio*-2H-*thiopyran*-2-*carbonitrile* (5).—MCDF [from tetra-*N*-ethylammonium cyanodithioformate (23 g)] was dissolved in dichloromethane (20 ml) and added to an excess of liquid buta-1,3-diene at −78° (Me_2CO–CO_2 bath) in a pressure bottle. The purple colour of the MCDF disappeared during 0·5 h at room temperature. Evaporation left a yellow syrup (17 g) which afforded colourless *crystals*, m.p. 32—33° [from acetone–petroleum (b.p. 30—60°)] (Found: C, 49·05; H, 5·35; S, 37·65. $C_7H_9NS_2$ requires C, 49·1; H, 5·25; S, 37·45%); $\nu_{max.}$ (film) 3125 (C=CH), 2222 (C≡N), and 1653 cm^{-1} (C=C); τ ($CDCl_3$) see Table 1; *m/e* 171 (M^+), 124, 123 (base peak), 122, 97, and 45.

3,6-*Dihydro*-2-*methylsulphonyl*-2H-*thiopyran*-2-*carbonitrile* 1,1-*Dioxide* (6).—MCPBA (30 g) in anhydrous dichloromethane (100 ml) was added to a cold solution of the thiopyran (5) (5 g) in dichloromethane (30 ml) which was then stirred for 24 h at room temperature. The solution was washed sequentially with saturated aqueous sodium hydrogen sulphite, saturated aqueous sodium hydrogen carbonate, and water, dried ($MgSO_4$), and evaporated to give *crystals* (5·1 g), m.p. 159—160° [from dichloromethane–petroleum (b.p. 65—110°)] (Found: C, 35·3; H, 3·75. $C_7H_9NS_2O_4$ requires C, 35·65; H, 3·85%); $\nu_{max.}$ (KBr) 3030 (C=CH), 2222 (C≡N), 1667 (C=C), 1342, and 1136 cm^{-1} (SO_2); τ ($CDCl_3$) see Table 1; *m/e* 235 (M^+).

2-*Acetamidomethyl*-3,6-*dihydro*-2-*methylsulphonyl*-2H-*thiopyran* 1,1-*Dioxide* (7).—Compound (5) (5 g) in anhydrous diethyl ether (20 ml) was added dropwise with stirring to lithium aluminium hydride (1 g) suspended in the same solvent (30 ml) at ice-bath temperature, and the mixture was stirred for 0·5 h at room temperature. The excess of hydride was removed in the usual manner (water; aqueous sodium potassium tartrate) and the organic phase was dried ($MgSO_4$). Evaporation afforded 2-aminomethyl-3,6-dihydro-2-methylthio-2*H*-thiopyran (8) as a pale yellow syrup. Distillation at 1 mmHg gave a colourless oil (0·7 g), b.p. 55—60°; $\nu_{max.}$ 3333 (NH), 3030 (C=CH), 1667 (C=C), and 1613 cm^{-1} (NH); τ ($CDCl_3$) see Table 1.

Aqueous sodium hydroxide (5%) was added to a solution of the amine (8) (2 g) in aqueous 5% hydrochloric acid (15 ml) until an incipient cloudiness was observed. A small amount of ice and acetic anhydride (3 ml) were added, followed immediately by sodium acetate (6 g) in water (12 ml). The solution was extracted with chloroform. The extract was washed with saturated aqueous sodium hydrogen carbonate and water, and dried ($MgSO_4$). Evaporation gave a light orange syrup (1·8 g) which slowly solidified at room temperature. After crystallization from dichloromethane–petroleum (b.p. 60—110°), 2-acetamido-3,6-dihydro-2-methylthio-2*H*-thiopyran (9) was obtained as colourless needles, m.p. 66—67°; $\nu_{max.}$ (KBr) 3279 (NH), 3077 (C=CH), 1653 (C=O), and 1550 cm^{-1} (NH); τ ($CDCl_3$) see Table 1. MCPBA (7 g) in dichloromethane (30 ml) was added in portions to the amide (9) (1 g) in dichloromethane (10 ml) at ice-bath temperature. The solution was kept at room temperature for 48 h. Work-up as before gave a white solid (0·8 g) which, upon crystallization from chloroform–petroleum (b.p. 60—110°), afforded the *amide* (7) as colourless crystals, m.p. 147—148° (Found: C, 38·1; H, 5·45. $C_9H_{15}NS_2O_5$ requires C, 38·45; H, 5·35%); $\nu_{max.}$ (KBr) 3390 (NH), 3030 (C=CH), 1667 (C=O), 1527 (NH), and 1299 and 1136 cm^{-1} (SO_2); τ ($CDCl_3$) see Table 1.

Hydrogen–Deuterium Exchange in Compound (7).—Compound (7) (60 mg) was dissolved in anhydrous 1,4-dioxan (5 ml), and D_2O (15 ml) and anhydrous potassium carbonate (*ca.* 20 mg) were added. After 20 h at room temperature, the solution was acidified with dilute hydrochloric acid, and evaporated to dryness. The solid residue was extracted with hot chloroform. On cooling, white crystals were obtained; m.p. 148—149°, mixed m.p. with (7) undepressed.

3,6-*Dihydro*-2-*methylsulphinyl*-2H-*thiopyran*-2-*carbonitrile* 1,1-*Dioxide* (10).—Compound (5) (0·6 g) dissolved in glacial acetic acid (10 ml) was shaken with 30% hydrogen peroxide (5 ml) at room temperature for *ca.* 15 h. During this period crystalline material (0·9 g) formed in the solution. Recrystallization of this from 95% ethanol gave (10) as *needles*, m.p. 138—139°; $\nu_{max.}$ (KBr) 3058 (C=CH), 2222 (C≡N), 1653 (C=C), 1316 and 1136 (SO_2), and 1058 cm^{-1} (S=O) (Found: C, 38·4; H, 4·05. $C_7H_9NS_2O_3$ requires C, 38·3; H, 4·1%); τ ($CDCl_3$) see Table 1; *m/e* 219 (M^+).

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Reaction of MCDF with trans-1-*Methoxybuta*-1,3-*diene*.—A solution of MCDF [from tetra-*N*-ethylammonium cyanodithioformate (11·5 g)] in dichloromethane (20 ml) was added to *trans*-1-methoxybuta-1,3-diene (5 g) in dichloromethane (5 ml) at ice-bath temperature. The reaction was complete after 1 h at room temperature, as evidenced by the complete discharge of the deep purple colour. Evaporation afforded a light yellow syrup (8 g), which, upon crystallization from dichloromethane–petroleum (b.p. 30—60°), yielded 3,6-*dihydro*-3-*methoxy*-2-*methylthio*-2H-*thiopyran*-2-*carbonitrile* (11) as colourless crystals (5 g), m.p. 54—56° (Found: C, 47·75; H, 5·35; N, 6·95; S, 31·95. $C_8H_{11}NOS_2$ requires C, 47·75; H, 5·45; N, 6·95; S, 31·85%); $\nu_{max.}$ (KBr) 3030 (C=CH), 2817 (–OCH_3), 2222 (C≡N), 1658 (C=C) and 1111 cm^{-1} (C–O–C); τ ($CDCl_3$; 60 MHz) 4·08 (2H, m, H-4 and -5), 5·97 (1H, m, *H*C·OCH_3), 6·67 (2H, m), 6·42 (3H, s, OCH_3), and 7·50 (3H, s, SCH_3); the product gave one symmetrical peak on g.l.c.

The 60 MHz n.m.r. spectrum of the residual syrup showed the presence of (11) with a trace (<5%) of impurity, which gave discernible n.m.r. signals at τ 5·64 (m), 6·41 (s), 7·57 (s), and 7·38 (m). The i.r. spectrum of the residual syrup was identical with that of (11). The mixture showed two peaks in the g.l.c. trace.

In a separate experiment, in which an excess of the diene was added dropwise to the dienophile in dichloromethane, the reaction was complete in less than 15 min. Moreover the n.m.r. spectrum of the syrup obtained after the usual work-up revealed the presence of the same impurity as before but in 20% yield (calculated from peak integrations).

Reduction of Compound (11) *to Methyl* 1-*Amino*-1,4,5-*trideoxy*-3-O-*methyl*-2,6-*dithio*-β-DL-glycero-*hex*-4-*en*-2-*ulopyranoside* (13).—Compound (11) (1 g) was reduced with lithium aluminium hydride in anhydrous diethyl ether to afford compound (13) as a light yellow oil (0·9 g); $\nu_{max.}$ (film) 3333 (NH), 3030 (C=CH), 2801 (OCH_3), and 1667 cm^{-1} (broad doublet, NH); τ ($CDCl_3$) 4·00 (2H, m, vinyl protons), 6·25 (1H, m, *H*C·OCH_3), 6·50 (3H, s, OCH_3), 6·87 (2H, m), 7·08 (2H, ABq), 7·90 (3H, s, SCH_3), and 8·37br (2H, s, CH_2·N*H*$_2$).

In a separate experiment, in which compound (13) was added to the hydride in relatively large portions at room temperature, sufficient heat was generated to cause refluxing. The 60 MHz n.m.r. spectrum of the product indicated the presence of (13) and an isomeric product which gave additional singlets at τ 6·47 and 7·87. The i.r. spectrum of this mixture was identical with that of pure (13).

Attempted Isomerization of Compound (11).—Compound (11) (0·5 g) was refluxed for 24 h in 5% methanolic hydrogen chloride (6 ml). The solution was diluted with water (20 ml) and extracted with chloroform, and the extract was washed with aqueous sodium hydrogen carbonate and water, dried $(MgSO)_4$, and evaporated. The product (0·45 g) was indistinguishable from (11) (n.m.r. and i.r. spectroscopy).

Similar results were obtained when (11) was refluxed for 4 h in methanolic sodium methoxide.

Methyl 1-*Acetamido*-1,4,5-*trideoxy*-3-*methoxy*-2,6-*dithio*-β-DL-glycero-*hex*-4-*en*-2-*ulopyranoside* (15).—Compound (13) (1 g) was acetylated as described for (8). The *N*-acetyl derivative was a light orange syrup which failed to crystallize. The 60 MHz n.m.r. spectrum revealed sharp diagnostic signals at τ ($CDCl_3$) 7·85 (3H, s, SCH_3), 6·58 (3H, s, OCH_3), 8·08 (3H, s, OAc), and 4·18 (2H, m, vinyl). Distillation of (15) gave a yellow *oil*, b.p. 95—97° at 0·1 mmHg (Found: C, 48·55; H, 7·2; S, 25·3. $C_{10}H_{17}NO_2S_2$ requires C, 48·55; H, 6·95; S, 25·9%); $\nu_{max.}$ (film) 3320 (NH), 1660 (C=O), and 1550 cm^{-1} (NH). The 60 MHz n.m.r. spectrum of the distilled product revealed some broadening of singlets and increased complexity of the vinyl protons signal.

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