

The Circular Dichroism of the $n \rightarrow \pi^*$ Band of Cyclic Thionocarbonates. Part II.¹ Studies on the Thionocarbonates of Some Acyclic Vicinal Diols

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C.d. curves given by thionocarbonates of configurationally related vicinal diols can differ markedly. Thus the derivatives [(1)—(3)] of 1,4-di-*O*-methyl-*D*-threitol, 1,2:5,6-di-*O*-isopropylidene-*D*-mannitol and *D*-butane-2,3-diol show a composite two-band curve, a positively signed curve, and a negatively signed curve, respectively. For the thionocarbonate (4) of the *erythro*-diol 1,2:5,6-di-*O*-isopropylidene-*D*-altritol, the $\Delta\epsilon$ value approaches the magnitudes of those shown by conformationally rigid derivatives. The variation in the c.d. spectrum of compound (1) with solvent and temperature is best rationalized in terms of a two-conformer equilibrium. Analysis of the variable temperature results yields ΔG° for the interconversion, and also the rotational strengths of each conformer.

A RELATIONSHIP has been established between the chirality of the five-membered thionocarbonate ring and the sign of the Cotton effect associated with its $n \rightarrow \pi^*$ transition.¹ We have extended our studies to derivatives of acyclic diols, and now report on 1,4-di-*O*-methyl-*D*-threitol 2,3-thionocarbonate (1), 1,2:5,6-di-*O*-isopropylidene-*D*-mannitol 3,4-thionocarbonate (2), *D*-butane-2,3-diol thionocarbonate (3), and 1,2:5,6-di-*O*-isopropylidene-*D*-altritol 3,4-thionocarbonate (4).

Features of the unpolarized absorption and c.d. spectra of compounds (1)—(4) in dioxan and in methanol are recorded in Table I. Although compounds (1)—(3) are all derived from configurationally related *threo*-vicinal diols, their c.d. spectra differ considerably. The spectrum of compound (1) is composed of two

oppositely signed bands whereas spectra of compounds (2) and (3) show single bands with positive and negative signs, respectively.

TABLE I

Spectral properties of $n \rightarrow \pi^*$ band of thionocarbonates (1)—(4) in dioxan and in methanol

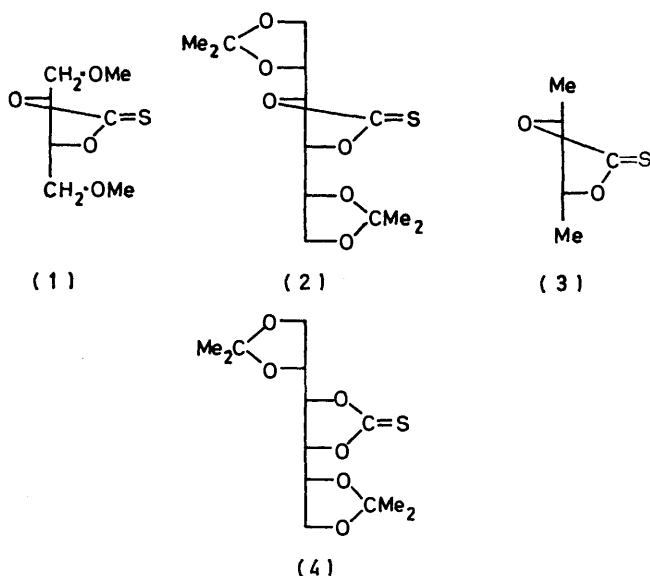
Compd.	Absorption				C.d.			
	Dioxan		Methanol		Dioxan		Methanol	
	$\lambda_{\max.}^a$	ϵ	$\lambda_{\max.}$	ϵ	$\lambda_{\max.}$	$\Delta\epsilon$	$\lambda_{\max.}$	$\Delta\epsilon$
(1)	311	24.5	302	29	{ 323 292	{ -0.11 +0.007	{ 323 292	{ -0.05 +0.12
(2)	313	23	312	25	316	+0.5	308	+0.4
(3)	300	30	298	33	313	-0.8	307	-0.55
(4)	311	30	309	32	313	-1.76	308	-1.45

^a In nm.

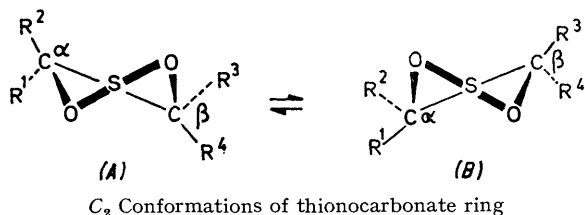
¹ Part I, A. H. Haines and C. S. P. Jenkins, *J. Chem. Soc. (C)*, 1971, 1438.

It is reasonable to assume that the most important conformations of the thionocarbonate ring will be the

two forms depicted* (Figure). Further, it is unlikely that the two oppositely signed bands in the spectrum of compound (1), and the variation in the spectrum



with solvent and temperature, can be rationalized satisfactorily in terms of solvation of the chromophore.^{4,5} Earlier study¹ showed thionocarbonates of fixed geometry to have apparently simple c.d. curves in different solvents, with similar $\Delta\epsilon$ values, and also that



temperature variation had little effect for solutions in methanol. Thus the spectrum most likely results from a superposition of two oppositely signed curves for conformers (A) and (B) (giving negative and positive effects respectively¹), in which the dichroic absorption maxima are not exactly coincident.[†] For compounds

* Models show that, apart from the planar form, maximum overlap between the p -orbitals of the thiocarbonyl group and the ring oxygen atoms (and thus maximum resonance interaction) is obtained in the C_2 forms shown, and in the envelope (C_3) forms in which each of the two ring carbon atoms contributed by the diol is in turn out of the plane of the other four ring atoms. In the C_2 forms, eclipsing interactions along the $C(\alpha)$ - $C(\beta)$ bond (Figure) are minimized, and calculations on cyclopentanone suggest² that the molecule exists in the C_2 form with maximum puckering at carbon atoms 3 and 4. Significantly, an X-ray diffraction study shows ethylene carbonate to exist in the C_2 form with the two-fold axis of symmetry along the $C=O$ bond.³

† A complex c.d. curve with two oppositely signed extrema separated by ca. 30 nm will arise whenever two Cotton effect curves of similar amplitude but opposite sign are superposed with their individual maxima separated by 1–20 nm.⁶ The observed amplitudes will be much smaller than the amplitudes of the contributing curves.

(2) and (3) the maxima must coincide. The ratio of (A) to (B) can be calculated if the rotational strengths of each chiral form are known. That these are not equal in magnitude for compound (1) is shown by variable-temperature measurements (see later), but it is apparent that the position of the conformational equilibrium (A) \rightleftharpoons (B) is significantly different for the compounds (1), (2), and (3).

The magnitude of $\Delta\epsilon$ for thionocarbonate (4) approaches that shown by the conformationally rigid compounds.¹ In either of the C_2 conformations shown (Figure; $R^1 = H$; $R^2 = C-2$; $R^3 = C-5$; $R^4 = H$) there is one quasi-axial and one quasi-equatorial substituent on the five-membered ring. Thus it might be expected that the chiralities of the two conformers (and thus the magnitudes of their $\Delta\epsilon$ values) would be similar, and therefore that the observed c.d. spectrum implies a preponderance of conformer (A). The bias is difficult to rationalize on purely steric grounds.

The double Cotton effect c.d. spectrum shown by compound (1) in methanol and dioxan prompted a study of the relative band intensities for solutions in other solvents. The difference between the c.d. absorption spectra of solutions in water and in cyclohexane is particularly striking. In a study⁴ of conformationally fixed ketones, where asymmetric solvation was suggested as the cause of this type of curve, a dependence was noted between the magnitudes of the dichroic absorption maxima of the bands and the Z values⁷ of the solvents. Plots of $\Delta\epsilon$ for the band of compound (1) at ca. 320 nm against solvent Z values and also E_T values,⁸ showed that the absolute magnitudes of the intensities were inversely related to these measures of solvent polarity (correlation coefficients of 0.94 and 0.95, respectively). Therefore conformer (B) is favoured by an increase in solvent polarity if solvational effects are not operative.

The variation with temperature of the c.d. spectrum of compound (1) in methanol solution is recorded in Table 2 (see ref. 7 of Part I¹ for the determination of rotational strength R from the area of the c.d. band). Since the band at shorter wavelengths increases in intensity as the temperature is decreased, a solvational equilibrium cannot be ruled out. However if a simple two-conformer equilibrium exists (Figure; $R^1 = R^3 = CH_2 \cdot OMe$, $R^2 = R^4 = H$) and solvational changes are not important in the equilibrium then ΔS° for the process should be negligible. A plot of the observed rotational strength, R_0^T , at temperature T against the function $[1 + \exp(\Delta G^\circ/RT)]^{-1}$ for trial values of ΔG°

² K. S. Pitzer and W. E. Donath, *J. Amer. Chem. Soc.*, 1959, **81**, 3213.

³ C. J. Brown, *Acta Cryst.*, 1954, **7**, 92.

⁴ C. Coulombeau and A. Rassat, *Bull. Soc. chim. France*, 1966, **12**, 3752.

⁵ A. Moscovitz, K. M. Wellman, and C. Djerassi, *Proc. Nat. Acad. Sci. U.S.A.*, 1963, **50**, 799.

⁶ K. M. Wellman, P. H. A. Laur, W. S. Briggs, A. Moscovitz, and C. Djerassi, *J. Amer. Chem. Soc.*, 1965, **87**, 66.

⁷ E. M. Kosower, *J. Amer. Chem. Soc.*, 1958, **80**, 3253.

⁸ K. Dimroth, C. Reichardt, T. Siepmann, and F. Bohlmann, *Annalen*, 1963, **661**, 1.

yielded a straight line for $\Delta G^\circ = 1.1 \text{ kcal mol}^{-1} *$ (where ΔG° is the standard Gibbs free energy change for the conformer interconversion). The excellent correlation observed suggested that ΔG° is constant over the temperature range studied and supports the assumption that

TABLE 2

Variation in c.d. of thionocarbonate (1) in methanol with temperature

T/K	$\lambda_{\text{max.}}/\text{nm}$	$\Delta\epsilon$	$10^{40}R^a$
293	292	+0.12	+0.29
	323	-0.05	-0.069
273	296	+0.19	+0.44
	330	-0.047	-0.06
249	296	+0.23	+0.6
	332	-0.02	-0.02
229	298	+0.29	+0.75
	334	-0.02	-0.02
196	302	+0.4	+0.99
	333	-0.002	b

^a Determined from area of c.d. band; R in c.g.s. units.

^b Low intensity precludes calculation.

solvation is unimportant in this system. The slope and intercept of the plot yielded the rotational strengths of each conformer, $R_A = -8.42 \times 10^{-40}$ c.g.s. units, and $R_B = +1.53 \times 10^{-40}$ c.g.s. units. These results show (i) that conformer (B) with quasi-axial substituents is the more stable, (ii) the degree of skewness of conformer (A) is greater than that of (B), and (iii) the proportion of conformer (B) rises from 87% at 295 K to 94.5% at 196 K.

The present approach appears to offer considerable advantages over n.m.r. spectroscopy in investigating the conformational properties of this type of system. An attempt by Anet to relate the conformer population of the closely related (\pm)-butane-2,3-diol carbonate with the measured coupling constant $J_{AA'}$ of the $X_3AA'X_3$ system was not entirely successful, and led that author to advocate caution in applying the Karplus equation to five-membered ring systems.¹⁰

EXPERIMENTAL

The c.d. measurements were made as described previously.¹ Compounds (2) and (4) were available from earlier work.¹¹

2,3-O-Isopropylidene-D-threitol.—A stirred solution of 3,4-O-isopropylidene-D-mannitol¹² (4.44 g) in water (20 ml) was cooled in ice and a solution of sodium periodate (8.56 g) in water (50 ml) was added dropwise. After 15 min a solution of barium chloride dihydrate (4.9 g) in water (15 ml) was added, and the mixture was stirred for 5 min. Barium iodate was filtered off through kieselguhr, and the solution was treated with sodium hydrogen carbonate (0.2 g) followed by potassium borohydride (2.2 g). The

* This method of analysis has been applied to the conformational equilibrium of (+)-*trans*-2-chloro-5-methylcyclohexanone.⁹ In cases where asymmetric solvation is thought to occur, no temperature-independent values of ΔG° yield a straight line.

⁹ A. Moscovitz, K. Wellman, and C. Djerassi, *J. Amer. Chem. Soc.*, 1963, **85**, 3515.

¹⁰ F. A. L. Anet, *J. Amer. Chem. Soc.*, 1962, **84**, 747.

mixture was stored for 24 h and then excess of hydride was destroyed with glacial acetic acid. The solution was then brought to pH 8 by addition of sodium hydrogen carbonate, concentrated to ca. 50 ml, and continuously extracted with chloroform. Evaporation of the dried chloroform extract yielded a syrup, which was distilled to yield the product (3.0 g, 92%), b.p. 110° at 0.25 mmHg, n_D^{26} 1.4573, $[\alpha]_D^{19}$ -1.6° (c 0.32 in CHCl_3) {lit.,¹³ b.p. 91–93° at 0.01 mmHg, n_D^{25} 1.4547, $[\alpha]_D^{26}$ -0.5° (c 2.09 in CHCl_3)}. (Found: C, 51.7; H, 8.6. Calc. for $\text{C}_7\text{H}_{14}\text{O}_4$: C, 51.8; H, 8.7%).

2,3-O-Isopropylidene-1,4-di-O-methyl-D-threitol.—To 2,3-O-isopropylidene-D-threitol (2.3 g) in chloroform (20 ml) and methyl iodide (25 ml), silver oxide (16 g) was added with stirring during several hours. The mixture was then heated under reflux for 24 h. Chloroform was added and the mixture was filtered through kieselguhr. The filtrate was concentrated and the residue distilled to yield the ether (2.1 g, 77%), b.p. 89–92° at 12 mmHg, $[\alpha]_D^{19}$ $+8.7^\circ$ (c 0.29 in CHCl_3) (Found: C, 56.8; H, 9.6. $\text{C}_9\text{H}_{18}\text{O}_4$ requires C, 56.8; H, 9.5%).

1,4-Di-O-methyl-D-threitol.—The foregoing ether (2 g) was stirred for 18 h with *N*-sulphuric acid (25 ml), and the mixture was then heated under reflux for 1 h, neutralized with sodium hydrogen carbonate, and extracted continuously with chloroform for 48 h. Concentration of the extract gave an oil which after distillation solidified to yield the diol (1.3 g, 79%), b.p. 89–94° at 0.25 mmHg, $[\alpha]_D^{19}$ $+4^\circ$ (c 2.8 in CHCl_3) (Found: C, 48.2; H, 9.4. $\text{C}_6\text{H}_{14}\text{O}_4$ requires, C, 48.0; H, 9.4%).

1,4-Di-O-methyl-D-threitol 2,3-Thionocarbonate (1).—The foregoing diol (1.2 g) in dry tetrahydrofuran (15 ml) was treated successively with *n*-butyl-lithium in hexane, carbon disulphide, and methyl iodide in the usual manner,¹¹ and the mixture was poured into ice-water. The product was extracted with chloroform (4 \times 30 ml) and the combined extracts were washed with water, then dried (Na_2SO_4), and finally concentrated. The residue so obtained was subjected to chromatography on silica gel (100 g; BDH) [chloroform-ether (4 : 1 v/v) as eluant]. The first fractions yielded a small amount of a yellow oil which was discarded. Later fractions yielded crystalline material on concentration, and all of these fractions were combined to yield the crude material (0.5 g). T.l.c. in the same solvent system showed the material to be homogeneous, R_F 0.4. Two recrystallizations from ethyl acetate-light petroleum yielded the thionocarbonate, m.p. 38–40°, $[\alpha]_D^{25}$ $+38^\circ$ (c 1.1 in CHCl_3) (Found: C, 44.0; H, 6.2; S, 16.8. $\text{C}_{17}\text{H}_{32}\text{O}_4$ requires C, 43.7; H, 6.25; S, 16.65%).

D-Butane-2,3-diol Thionocarbonate (3).—D-Butane-2,3-diol was prepared by fermentation of D-glucose in a nutrient medium with *Bacillus polymyxa*, essentially as already described.¹⁴ The product had b.p. 75–78° at 12 mmHg, $[\alpha]_D^{22}$ -15.8° (c 1.6 in CHCl_3) {lit.,¹⁵ $[\alpha]_D^{26}$ -13.34° (neat)}.

The diol (0.1 g) in anhydrous benzene (20 ml) was heated under reflux in a stream of dry nitrogen with bis(imidazol-1-yl) thione (0.154 g) for 1 h. The mixture was concentrated to an oil, which was partitioned between chloroform (30 ml) and water (30 ml), and the chloroform

¹¹ A. H. Haines, *Carbohydrate Res.*, 1965, **1**, 214.

¹² L. F. Wiggins, *J. Chem. Soc.*, 1946, 13.

¹³ L. J. Rubin, H. A. Lardy, and H. O. L. Fischer, *J. Amer. Chem. Soc.*, 1952, **74**, 425.

¹⁴ A. C. Neish and G. A. Ledingham, *Canad. J. Res.*, 1949, **B**, 27, 694.

¹⁵ A. C. Neish, *Canad. J. Res.*, 1945, **B**, 23, 10.

layer was separated. After extraction of the aqueous layer with more chloroform, the organic extracts were dried and concentrated to yield a yellow oil, which was subjected to p.l.c. (chloroform as developer). The main band was removed from the plate, and material extracted from the silica gel yielded the oily *thionocarbonate* (0.063 g, 40%), $[\alpha]_D^{22} +16.3^\circ$ (*c* 2.3 in CHCl_3) (Found: C, 45.0; H, 6.21. $\text{C}_5\text{H}_8\text{O}_2\text{S}$ requires C, 45.4; H, 6.1%).

C.d. Spectral Details for 1,4-Di-O-methyl-D-threitol 2,3-Thionocarbonate (1) in Various Solvents.—Details are given in the following order: solvent, λ_{max} ($\Delta\epsilon$) of long-wavelength band (*ca.* 323 nm), λ_{max} ($\Delta\epsilon$) of short wavelength band (at *ca.* 292 nm.).

Cyclohexane, 323 (−0.186); carbon tetrachloride, 323 (−0.15); chloroform, 318 (−0.14); ethyl acetate, 323 (−0.13); dioxan, 323 (−0.11), 292 (+0.007); butan-1-ol, 323 (−0.096), 292 (+0.04); propan-2-ol, 323 (−0.09), 292 (+0.06); 2-methylpropan-2-ol, 323 (−0.09), 292 (+0.086); propan-1-ol, 323 (−0.08), 292 (+0.07); ethanol, 323 (−0.06), 292 (+0.12); methanol, 323 (−0.05), 292 (+0.12); ethylene glycol, 328 (−0.03), 292 (+0.179); water, 331 (−0.001), 290 (+0.14).

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