Synthesis of Pyrano[3,2-c]pyranthiones; Characteristic Shifts in the ¹H Nuclear Magnetic Resonance Spectra of Thiones

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The behaviour of boron sulphide and silicon sulphide as sulphurization reagents varies according to batch and source. Silicon sulphide has now been used to convert 2-methylpyrano[3,2-c][1]benzopyran-4,5-dione (I) into 2-methyl-4H-thioxo-4-pyrano[3,2-c][1]benzopyran-5-one (II), characterised by further conversion into 8-methyl-5,10-dioxa-9,9a-dithia ($9\sigma S^{IV}$) pentaleno[2,1-a]naphthalen-6-one (III). Modification of this last step leads to 8-methyl-5,9,10-trioxa-9a-thia (S^{IV}) pentaleno[2,1-a]naphthalen-6-one (IV), identical with a substance previously obtained from a different reaction and tentatively assigned this structure.

4-Methylpyrano[3,2-c][1]benzopyran-2,5-dione (VI) was attacked only with difficulty by silicon sulphide but boron sulphide smoothly converted it into 4-methyl-2-thioxo-2H-pyrano[3,2-c][1]benzopyran-5-one (VII). In the first place, the thione group was located by stereochemical arguments, supported by the conversion of the lower homologue (VIII), pyrano[3,2-c][1]benzopyran-2,5-dione, under the same conditions into a mixture including pyrano[3,2-c][1]benzopyran-2,5-dithione (IX). This assignment was confirmed by a study of the ¹H n.m.r. shift differences between pyrones and the corresponding pyranthiones which gave unequivocal evidence favouring structure (VII). The method may have a wider utility.

Derivatives of pyrano[3,2-c][1]benzopyran-2,5-dione are accessible in very mild conditions by condensing the requisite 4-hydroxycoumarin with ethyl acetoacetate by means of potassium carbonate instead of an acid catalyst.

IN an earlier study we treated the pyranopyrone derivative (I) with boron sulphide or silicon sulphide but did not obtain the expected thione (II) because ring opening and further sulphurization gave the substituted oxadithiapentalene (III) instead.[1] We have repeated the treatment using different samples of the reagents and found that boron sulphide prepared by fusing together the elements and stored as lumps until use acts only with difficulty upon the pyranopyrone under the mild conditions normally employed. As the boron sulphide used originally had been kept for some time before use as a powder it seemed possible that the gradual access of air might have modified it slowly, at least superficially. We therefore exposed the fused (but powdered) reagent to the air or kept it for some time in damp benzene before use,
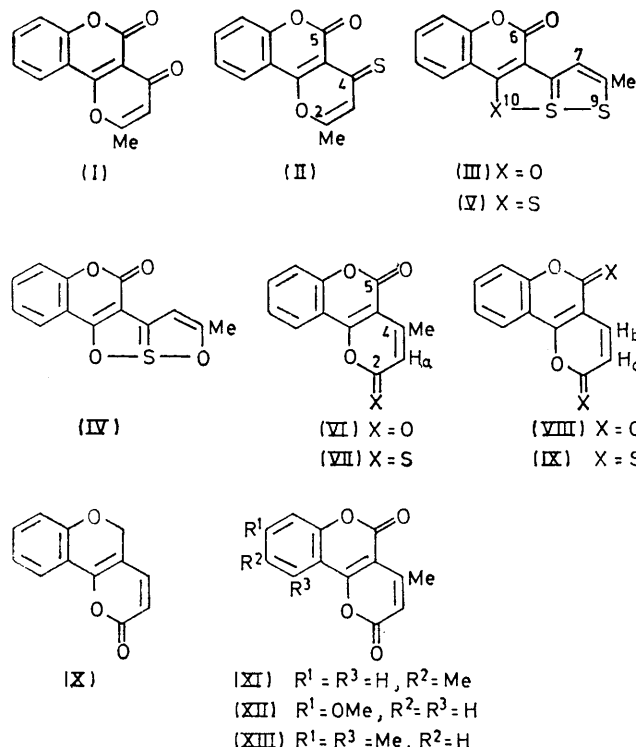
whereafter the formation of the oxadithiapentalene could be reproduced easily. General considerations[2] make it probable that the opening of the 4-pyrone ring is induced by the action of thiol groups present in a partially hydrolysed reagent.

In contrast, a new sample of silicon sulphide proved superior to the old in that it converted the pyranopyrone (I) into the desired thione (II) without further consequences. Strong i.r. absorption at 1745 cm⁻¹ attests the presence of the lactonic carbonyl group, but it is not possible to show a corresponding loss of 4-pyrone carbonyl absorption because of the difficulty of identifying the appropriate mode in the parent compound;[3,4] bands originally at 1665 and 1610 appear to have moved to

¹ F. M. Dean, J. Goodchild, and A. W. Hill, *J.C.S. Perkin I*, 1973, 1022.

² R. Mayer, W. Broy, and R. Zahradník, *Adv. Heterocyclic Chem.*, 1967, **8**, 219.

³ D. Cook, *Canad. J. Chem.*, 1961, **39**, 1184.

⁴ A. R. Katritzky and R. A. Jones, *Spectrochim. Acta*, 1961, **17**, 64; A. R. Katritzky and A. P. Ambler, in ' Physical Methods in Heterocyclic Chemistry,' ed. A. R. Katritzky, Academic Press, New York, 1963, vol. 2, ch. 10.

1645 and 1615 cm⁻¹ in the spectrum of the thione and can be supposed to fall into line with those in simpler 4-pyrones[4] if contributions from the aromatic ring are not important. However, structure(II) is clearly supported by the n.m.r. spectrum (discussed below) and by the conversion of the compound by means of sodium sulphide and then ferricyanide[5] into the substituted oxadithiapentalene (III).

In the course of the previous work with silicon sulphide the pyranopyrone (I) furnished a very small amount of a substance tentatively assigned the dioxathiapentalene structure (IV). This assignment has now been confirmed. Dilute aqueous sodium sulphide opened the pyranthione ring in (II) without introducing another sulphur atom and ferricyanide oxidation then generated the dioxathiapentalene (IV) which was further characterised by sulphurization to the trithiapentalene (V). (Since these observations were made the dioxathiapentalene system has become readily accessible.[6])

We have already pointed out that, because sulphur is a more bulky atom than oxygen, a major steric factor would oppose the conversion of the dione (I) or the

thione (II) into the corresponding dithione and that introduction of a second sulphur atom would favour the ring opening reactions observed. We have tested this steric factor using a methyl group (van der Waals radius 2·0Å) to simulate the effect of a sulphur atom (van der Waals radius 1·9Å). Accordingly, boron sulphide readily converted the pyranopyrone derivative (VI) into the monothione (VII) which resisted further reaction, whereas the unhindered pyranopyrone (VIII) rapidly gave a mixture of products including the dithione (IX). Both these thiones are reconverted into their parent diones when treated with mercury(II) acetate, and this fact along with the absence of lactonic carbonyl absorption establishes structure (IX) completely. In (VII), however, the thione group has to be located independently otherwise the stereochemical argument would become circular.

At first an i.r. method seemed suitable. The pyrone (I) and the pyranthione (II) absorb in the range 1740—1745 cm⁻¹ whereas the pyrone (X) available from a different study absorbs at 1720 cm⁻¹. Several dilactones made in the course of this work showed maxima near both points (other authors record only one maximum[7]) so that it seemed reasonable to allocate the high frequency band to the 5- and the low frequency band to the 2-carbonyl group. But this approach failed. In the spectrum of the dilactone (VI) a twin maximum was observed at 1715 and 1705 cm⁻¹ with important inflections at about 1735 and 1690 cm⁻¹. The monothione showed a maximum at 1735 cm⁻¹ with several major inflections, so no conclusion could be drawn. It is possible that this complex behaviour originates in the flat, rigid, conjugated system connecting the two carbonyl groups which allows coupling and Fermi resonance effects to complicate the spectra.[8,9] Thiocarbonyl stretching bands are too difficult to recognise with certainty to be used diagnostically, and the u.v. spectra also seemed unsuitable.

An n.m.r. study provided the necessary proof of structure (VII). Studies on the thiocarbonyl group have established that the deshielding cones are much like those in the carbonyl group but more effective;[10] limited use of the phenomenon has been made in some fields (e.g. refs. 11—13) though not yet in pyrone chemistry where, however, it seems particularly suitable. As models for the structural features now under investigation we used some thiones derived from an earlier study[14] and combined the results with data from the literature for pyran-4-thione[15,16] to form the Table. By far the most marked effect is the downfield shift in the α-vinylic proton signal when the oxygen atom of a carbonyl group

[5] D. H. Reid and R. G. Webster, *J.C.S. Perkin I*, 1972, 1447.

[6] D. H. Reid and R. G. Webster, *J.C.S. Chem. Comm.*, 1972, 1283.

[7] V. N. Dholakia, M. G. Parekh, and K. N. Trivedi, *Austral. J. Chem.*, 1968, **21**, 2345.

[8] R. H. Wiley and J. G. Esterle, *J. Org. Chem.*, 1957, **22**, 1257; R. H. Wiley and S. C. Slaymaker, *J. Amer. Chem. Soc.*, 1956, **78**, 2393.

[9] L. J. Bellamy, 'Advances in Infrared Group Frequencies,' Methuen, London, 1968, ch. 5.

[10] P. V. Demarco, D. Doddrell, and E. Wenkert, *Chem. Comm.*, 1969, 1418.

[11] S. McKenzie and D. H. Reid, *J. Chem. Soc. (C)*, 1970, 145.

[12] G. W. Gribble and F. P. Bousquet, *Tetrahedron*, 1971, **27**, 3785.

[13] D. Lichtenberg, F. Bergmann, and Z. Neimann, *J. Chem. Soc. (C)*, 1971, 1939.

[14] F. M. Dean, J. Goodchild, and A. W. Hill, *J. Chem. Soc. (C)*, 1969, 2192.

[15] N. M. D. Brown and P. Bladon, *Spectrochim. Acta*, 1965, **21**, 1277.

[16] J. Jonas, W. Derbyshire, and H. S. Gutowsky, *J. Phys. Chem.*, 1965, **69**, 1.

is replaced by sulphur. Probably this shift is partly a function of the deshielding cone, whereas the smaller shift in the opposite direction at the β-vinylic proton is mainly a consequence of the smaller electronegativity of the sulphur atom. It also appears that the thione group deshields an *ortho* aromatic proton more strongly than does carbonyl, in line with related effects noted amongst thionanilides [12] and indolizines.[11] Other shifts are relatively small, and although there is some evidence that the effects of a thione group can be felt over a long range [13] we have encountered none of importance for the present context.

First we noted that the resonances of the pyran-4-thione (II) for the methyl group (τ 8·00) and the adjacent proton (2·96) are in line with this structure but not

provided that the related thione is accessible, and we are therefore extending this investigation into other series.

Dilactones related to (VI) have been made by condensing ethyl acetoacetate with an appropriately substituted 4-hydroxycoumarin either thermally [17] at 260° or at lower temperatures but with an acid catalyst (sulphuric acid,[18] trifluoroacetic acid,[7] aluminium chloride[19]). An observation by Tan [20] suggested that these condensations, which can be regarded as modified aldol condensations, should be amenable to catalysis by mild bases; and the dilactone (VI) required for this work was therefore prepared from the appropriate reactants in a smooth, convenient reaction conducted at 100° in the presence of potassium carbonate. Similar syntheses of the dilactones (XI), (XII), and (XIII) indicate that the method

N.m.r. bands [a] and shift differences for pyrones and pyranthiones

	A		B		C		D		E	
Pyrone (pyranthione)	X = O	X = S	X = O	X = S	X = O	X = S	X = O	X = S	X = O	X = S
Pyran-4-one			2·12	2·48	3·63	2·85				
2,6-Dimethylpyran-4-one [b]	7·72	7·78			3·92	3·05				
Flavone					3·25	2·31	1·81	1·42		
5,7-Dimethylflavone					3·33	2·41			7·18	7·03
7-Methoxy-2-methylchromone	7·73	7·72			4·02	3·00	2·04	1·52		
Xanthone							1·69	1·29		
Coumarin			2·29	2·52	3·62	2·82				
7-Methoxy-4-methylcoumarin	7·69	7·69			3·94	3·00				
Dibenzo[b,d]pyran-6-one							1·69	1·10		
Average shift difference (τ_{C:S} − τ_{C:O})	+0·03		+0·29		−0·89		−0·48		−0·15	

Structural elements [c]
(X = O or S)

A	B	C	D	E

[a] τ values; spectra examined at 100 Hz. [b] See also ref. 15. [c] Planarity assumed.

with any isomeric arrangement (the parent pyrone is not soluble enough for study). Next we tested the shift increments for the dithione (IX); since the parent dipyrone (VIII) shows signals at 3·27 (H_a) and 1·64 (H_b), calculation requires the dithione (IX) to exhibit corresponding signals at 2·37 and 1·44. The values found were 2·35 and 1·47, which is satisfactorily close. (Measurements were made on dioxan solutions and all bands were doublets, J 10 Hz.) With these assurances, we could complete the structural proof for thione (VII). The parent dilactone (VI) shows signals at 7·32 (Me) and 3·71 (H_a), so calculation for the thione (VII) gives 7·32 and 2·81, respectively. Corresponding values for the alternative thione would be 7·17 and 3·71. The observed values are 7·48 and 2·95 (slight splitting occurs) and are obviously compatible only with structure (VII). In principle, the method can be employed for investigating protons in the neighbourhood of any carbonyl group

is general, though it cannot be extended to simple phenols as 2-naphthol does not react. The success of base-catalysed reactions in a related field [21] indicates that phloroglucinol derivatives would be amenable, and this point is being tested. The four dilactones now fully reported were used for detailed mass spectral studies reported earlier.[22]

EXPERIMENTAL

U.v. spectra were determined using *ca.* 10⁻³M-solutions in ethanol. I.r. spectra were usually determined on KBr discs or mulls in paraffin, and only significant bands are reported. Molecular weights were determined mass spectroscopically.

4-Methylpyrano[3,2-c][1]benzopyran-2,5-dione (VI).—4-Hydroxycoumarin (1·0 g) was heated on a steam-bath with ethyl acetoacetate (50 ml) and potassium carbonate (0·1 g) for 7 h. Upon cooling, the solution deposited the dione as long needles (0·9 g), identical with samples prepared by

[17] C. Mentzer, D. Molho, and P. Vercier, *Compt. rend.*, 1951, **232**, 1488.
[18] A. Mustafa, O. H. Hsimat, S. M. A. D. Zayed, and A. Ahmed Nawar, *Tetrahedron*, 1963, **19**, 1831.
[19] J. Patell and R. N. Usgaonker, *J. Indian Chem. Soc.*, 1965, **42**, 215.

[20] A. K. Kiang and S. F. Tan, *J. Chem. Soc.*, 1965, 2283.
[21] J. C. Macleod and B. R. Worth, *Tetrahedron Letters*, 1972, **237**, 241.
[22] R. A. W. Johnstone, B. J. Millard, F. M. Dean, and A. W. Hill, *J. Chem. Soc. (C)*, 1966, 1712.

thermal condensation or by the acid catalysis methods.[7] Omission of the base led to recovery of the initial coumarin. This dione had $\lambda_{max.}$ 238sh, 257, 267, 275sh, 317sh, 328, 344, and 355sh nm (log ε 3·38, 3·90, 3·90, 3·50, 3·47, 3·67, 3·72, and 3·44) and $\nu_{max.}$ (KBr) 1745, 1726, and 1627 cm⁻¹.

4,9-Dimethylpyrano[3,2-c][1]*benzopyran-2,5-dione* (XI).—Prepared from 4-hydroxy-6-methylcoumarin (1·0 g) in the above manner, this dione (0·9 g) separated from acetic acid as needles, m.p. 196°, identical with a sample prepared by acid catalysis.[7] This dione was very similar to the lower homologue but some of the u.v. absorption maxima showed slight shifts, as follows: 238sh, 259, 267, 278sh, 323sh, 337, 348, and 357sh nm.

4,8,10-Trimethylpyrano[3,2-c][1]*benzopyran-2,5-dione* (XIII).—Prepared by the foregoing method from 4-hydroxy-5,7-dimethylcoumarin (1·0 g), this *dione* crystallised from acetic acid as needles (1·0 g), m.p. 197°, $\lambda_{max.}$ 245, 265sh, 2·71, 2·80sh, 3·26sh, 336, 348, and 356sh nm (log ε 3·97, 4·15, 4·16, 4·10, 4·11, 4·17, 4·20, and 4·02), $\nu_{max.}$ (KBr) 1750, 1735, and 1615 cm⁻¹ (Found: C, 70·2; H, 4·9. $C_{15}H_{12}O_4$ requires C, 70·0; H, 4·7%).

8-Methoxy-4-methylpyrano[3,2-c][1]*benzopyran-2,5-dione* (XII).—Prepared by the foregoing method from 4-hydroxy-7-methoxycoumarin (1·0 g), this dione crystallised from acetic acid as faintly yellow plates (1·0 g), m.p. 234°, identical with a specimen from acid catalysis.[7] It had $\lambda_{max.}$ 243sh, 252, 279, 346, 352, and 360sh nm (log ε 3·98, 4·01, 4·25, 4·47, 4·51, and 4·40), $\nu_{max.}$ (KBr) 1735, 1710, and 1615 cm⁻¹ (Found: C, 65·2; H, 3·8. $C_{14}H_{10}O_5$ requires C, 65·1; H, 3·9%).

2-Methyl-4-thioxo-4H-pyrano[3,2-c][1]*benzopyran-5-one* (II).—Silicon disulphide (5 g) was added to 2-methylpyrano-[3,2-c][1]benzopyran-4,5-dione[1] (1 g) in chloroform (dried over P_2O_5) contained in a flask (flame-dried; 250 ml) fitted for distillation with all outlets guarded by drying tubes. The solvent was removed by distillation and the residue heated on a steam-bath for 5 h. The product was repeatedly extracted with chloroform and the soluble materials were recovered and re-extracted with a little benzene to remove sulphur. The residue was not very soluble in benzene but could be purified from a large volume of solvent on a silica column. Thus obtained, the *thione* crystallised from chloroform–benzene as dark brown prisms (0·64 g), m.p. 206—210°, $\lambda_{max.}$ 264, 297, and 335 nm (log ε 4·23, 4·21, and 4·35) (Found: C, 63·7; H, 3·4; S, 13·3%; *M*, 244. $C_{13}H_8O_3S$ requires C, 63·9; H, 3·3; S, 13·1%; *M*, 244).

8-Methyl-5,10-dioxa-9,9a-dithia(9aS^{VI})pentaleno[2,1-a]-naphthalen-6-one (III).—Sodium sulphide (1·7 g) in water (0·8 ml) was added to a stirred solution of the thione (II) (430 mg) in dimethyl sulphoxide (36 ml). Benzene (70 ml) was added to the deeply red solution after 35 min, and then potassium ferricyanide (3 g) in water (25 ml) was stirred in during 30 min. The benzene layer was decanted from the viscous mixture which was extracted several times with ether. The combined benzene and ether solutions were washed with water, dried (Na_2SO_4), and concentrated to give the crude dithiapentalene (ca. 370 mg). Chromatography on silica gave the pure dithiapentalene (ca. 310 mg), dark yellow needles, m.p. and mixed m.p. 219—220°, further identified spectroscopically.

8-Methyl-5,9,10-trioxa-9a-thia(S^{IV})pentaleno[2,1-a]naph-thalen-6-one (IV).—The foregoing experiment was repeated but with the use of more dilute aqueous sodium sulphide, *i.e.* sodium sulphide (260 mg) in water (4·2 ml), and the reaction mixture was filtered through Celite. The orange benzene

layer formed by the filtrate was augmented by ethereal extracts of the aqueous layer and the solutes were purified by t.l.c. on silica. This gave the dioxadithiapentalene (III) (79 mg) but mainly the trioxathiapentalene, which separated from ethanol as yellowish needles (190 mg), m.p. and mixed m.p. 230—235° (browning above 200°), spectroscopically identical with an earlier sample.[1]

The trioxathiapentalene (30 mg) was heated with phosphorus pentasulphide (0·2 g) in refluxing toluene for 35 min. Filtration and removal of the solvent from the filtrate under reduced pressure left an orange solid (30 mg) that was shown by t.l.c. to be nearly pure 8-methyl-5-oxa-9,9a,10-tri-thia(9aS^{VI})pentaleno[2,1-a]naphthalen-6-one (V); as before, crystallisation of this compound was not easy but furnished orange-red needles, m.p. and mixed m.p. 219°, further identified spectroscopically.

4-Methyl-2-thioxo-2H-pyrano[3,2-c][1]*benzopyran-5-one* (VII).—Boron sulphide (0·2 g) and 4-methylpyrano[3,2-[c]1]benzopyran-2,5-dione (VI) (50 mg) were heated together in refluxing xylene for 7 h. Filtration of the hot mixture and concentration of the filtrate under reduced pressure gave a residue that was separated by chromatography on silica. Light petroleum removed sulphur, then increasing proportions of benzene were employed to remove small amounts of various coloured impurities. The last fractions supplied the *thione*, which formed orange-yellow needles (40 mg), m.p. 185—187°, $\lambda_{max.}$ 264, 297, 324sh, 336, and 350sh nm (log ε 4·27, 4·25, 4·37, 4·39, and 4·35), $\nu_{max.}$ (CHCl₃) 1735, 1720sh, and 1695 cm⁻¹ (Found: C, 63·7; H, 3·3; S, 13·1%; *M*, 244·0187. $C_{13}H_8O_3S$ requires C, 63·9; H, 3·3; S, 13·1%; *M*, 244·0194).

The same thione resulted (25% yield) when the reagent was silicon sulphide, used at 140° for 15 h; most of the initial pyranopyrone was recovered.

The thione (20 mg) in acetone (4 ml) was treated with mercury(II) acetate (80 mg) in acetic acid (2 ml), and 20 min later the precipitate was removed and the product isolated from the solvent by standard methods giving the dione (VI) (almost quantitatively), indistinguishable chromatographically or spectroscopically from an authentic specimen.

Pyrano[3,2-c][1]*benzopyran-2,5-dithione* (IX).—The interaction of boron sulphide (5 g) and pyrano[3,2-c][1]benzopyran-2,5-dione[23] (VIII) (1·25 g) in refluxing xylene appeared to be complete after 36 h, so the solvent was removed *in vacuo* and the residue warmed with chloroform. The solution was filtered and evaporated onto silica, which was then placed on a silica column. Elution with light petroleum removed sulphur, and then gradually increasing proportions of benzene in the eluant developed several discrete bands from which four substances were isolated: A, dark wine-red needles, m.p. 204—206°; B, purple-red needles, m.p. 240° (decomp.); C, orange needles, m.p. 178—178·5°; and D, dark brown-red needles, m.p. 195·5—196·5°.

Preliminary investigations showed that substance C was the compound sought although the yield (37 mg after crystallisation from benzene—light petroleum) was poor. The *dithione* obtained in this way had $\lambda_{max.}$ (EtOH—CH₂Cl₂) 218, 252, 283, 299, 377, and 392 nm (log ε 4·49, 4·02, 4·07, 4·01, 4·35, and 4·39), $\nu_{max.}$ (mull) 1613, 1568, 1541, 1307, 1292, 1137, 1069, and 767 cm⁻¹ (Found: C, 58·5; H, 2·7; S, 25·6. $C_{12}H_6O_2S_2$ requires C, 58·5; H, 2·5; S, 26·05%), *m/e*

[23] V. N. Dholakia and K. N. Trivedi, *J. Indian Chem. Soc.*, 1966, **43**, 804.

246 ($C_{12}H_6O_2S_2$), 202 (246—CS), and 174 (202—CO) (substantiated by appropriate metastable ions).

Treatment of this dithione with mercury(II) acetate as described for the thione (VII) gave the parent dione. None of the other three substances behaved thus, and their chemistry will form part of a separate communication.