Cyclic Sulphones. Part XVII.[1] Probes for Conjugation of the Sulphonyl Group: Thiopyrano[3,2-*b*]-pyran, -pyridine, and -thiopyran *SS*-Dioxides

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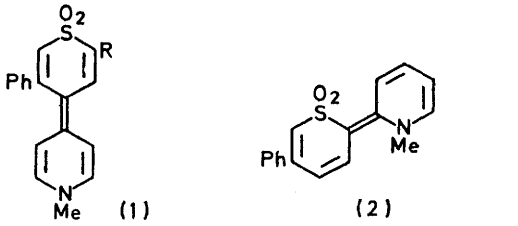
The thiopyran group in the title compounds, which have been synthesized, does not appear to reproduce the electronic situation present in thiopyran *SS*-dioxide anion. Thiopyrano[3,2-*b*]pyridine *SS*-dioxide shows striking spectroscopic analogies with 1-methyl-5-quinolone. I.r. stretching vibrations of the sulphonyl group in these molecules show a bathochromic shift; however the extent of this is small and indicates that little conjugation, if any, occurs through this group.

As part of a study of neutral compounds which could mimic the electron distribution in thiopyran *SS*-dioxide anion, we have recently described the thiopyranylidene-dihydropyridine *SS*-dioxide derivatives (1) and (2). In this and in the following paper[2] we report the synthesis and properties of compounds of type (3). As previously[1] we are concerned with the following questions. (i) Are compounds (3), through mesomerism [(3a) ⟷ (3b)], good models for thiopyran *SS*-dioxide anion? (ii) In what kind of conjugation is the sulphonyl group involved (' one-side ' or ' through ' conjugation †)? (iii) Are both S–O and C–S bond lengths altered by conjugation? (iv) Are sulphonyl stretching vibrations a measure[4] or at least an indication of the occurrence of conjugation of the sulphonyl



group? We shall show that, although compounds of type (3) might be viewed as sulphonyl homologues of pseudoazulenes, they have little in common with the latter. They can be better considered as sulphonyl analogues of ketonic compounds, *e.g.* of the quinolone-type structures (16) (when X = NR). Furthermore, whereas ' one-side ' conjugation of the sulphonyl group is appreciable, ' through ' conjugation does not occur. Although sulphonyl stretching vibrations are variously affected depending upon whether ' one-side ' or ' through ' conjugation occurs, carbon–sulphur and sulphur–oxygen bond lengths are perhaps the most dependable criterion[2] for distinguishing ' one-side ' and ' through ' conjugation.

† Basically one feature distinguishes ' through ' conjugation from ' one-side ' conjugation: in the former, mesomeric effects due to atom(s) present on one side of the group involved (in this case the sulphonyl group) can act through such a group and are transmitted to the other side, whereas in the latter they are not so transmitted, notwithstanding the fact that the group is capable of mesomeric interactions with such atom(s); see also the discussion by Jaffé.[3]

EXPERIMENTAL

I.r. spectra were recorded on a Perkin-Elmer 621 instrument, ^{1}H n.m.r. spectra on a Varian A60-A or HA-100D instrument, and u.v. spectra on a Beckman DB-GT instrument. Solutions were dried over Na_2SO_4.

2,4-Dimethyl-7-phenylthiopyrano[3,2-b]*pyran 5,5-Dioxide* (6).—A mixture of 5-phenyl-2*H*-thiopyran-3(6*H*)-one 1,1-dioxide (4)[5] (5·55 g, 25 mmol), 4-aminopent-3-en-2-one (5)[6] (2·75 g, 27·5 mmol), and toluene-*p*-sulphonic acid (0·2 g) in toluene (250 ml) was heated under reflux for 30 min. The reflux condenser was then replaced by a Claisen condenser, and toluene was slowly removed from the flask, to which fresh, anhydrous toluene was added dropwise in order to maintain the liquid level approximately constant (1 l of toluene added and removed during 18 h). The solution was then concentrated to *ca.* 50 ml, filtered, and evaporated to dryness. The residue was chromatographed on alumina (60 g; $CHCl_3$–AcOEt, 90 : 10) to give the *product* (20—30%), m.p. 104—105° (from benzene), which dissolved in 70% perchloric acid with discharge of the colour. Dilution with water gave the *perchlorate* (13), m.p. 247° (decomp.).

TABLE 1

Analytical data

Compound	Formula	Found (%) C	H	N	Required (%) C	H	N
(6)	$C_{16}H_{14}O_3S$	67·5	5·0		67·1	4·9	
(8)	$C_{22}H_{19}NO_2S$	72·9	5·2	3·7	73·1	5·3	3·9
(9)	$C_{16}H_{14}O_2S_2$	64·0	4·6		63·6	4·7	
(10)	$C_{16}H_{15}NO_2S$	66·9	5·4	4·7	67·3	5·3	4·9
(12)	$C_{17}H_{18}ClNO_2S$	60·3	5·5	3·95	60·8	5·4	4·2
(13)	$C_{16}H_{15}ClO_7S$	49·8	3·7		49·7	3·9	

6,8-Dimethyl-3-phenyl-2H-thiopyrano[3,2-b]*pyridine 1,1-Dioxide* (10).—A solution of compound (6) (102 mg) in acetic acid (3 ml) was treated with ammonium acetate (200 mg) and refluxed for 10 min. The solvent was evaporated off under reduced pressure and the residue was taken up in water (50 ml) and extracted with chloroform. The extract was washed with water, dried, and evaporated to give the *product* (10), m.p. 157° (from ethanol).

5,6,8-Trimethyl-3-phenyl-2H-thiopyrano[3,2-b]*pyridinium 1,1-Dioxide Chloride* (12).—A suspension of compound (10) (1·3 g) in dimethyl sulphate (12 ml) was heated at 100° for 30 min; after cooling anhydrous ether (30 ml)

[1] Part XVI, G. Pagani, *J.C.S. Perkin II*, 1973, 1184.
[2] Part XVIII, G. A. Pagani, following paper.
[3] H. H. Jaffé and M. Orchin in ' Theory and Applications of Ultra-violet Spectroscopy,' Wiley, New York, 1962, ch. 17.
[4] For leading references on S–O bonds see the review by H. H. Szmant in ' Sulphur in Organic and Inorganic Chemistry,' vol. 1, ed. A. Senning, Marcel Dekker, New York, 1971, ch. 5.
[5] G. Pagani, *Gazzetta*, 1967, **97**, 1518.
[6] A. Combes and C. Combes, *Bull. Soc. chim. France*, 1892, **7**, 779; J. Weinstein and G. M. Wyman, *J. Org. Chem.*, 1958, **23**, 1618.

was added to complete precipitation of the methosulphate (11). The salt was collected and dissolved in boiling 7% hydrochloric acid; the *chloride* (12) precipitated as a white solid, m.p. 203° (decomp.).

5,6,8-*Trimethyl*-3-*phenyl*-5H-*thiopyrano*[3,2-b]*pyridine* 1,1-*Dioxide* (7).—*Method A*. Aqueous potassium carbonate (10%; 100 ml) was added dropwise to a stirred suspension of the methosulphate (11) (800 mg) in ethyl acetate (100 ml). The precipitate was collected, washed with water and ethanol, and crystallized to give the *product* (7), m.p. 200—202° (decomp.) (from dioxan), characterized by conversion back into the chloride (12) by boiling in 10% hydrochloric acid.

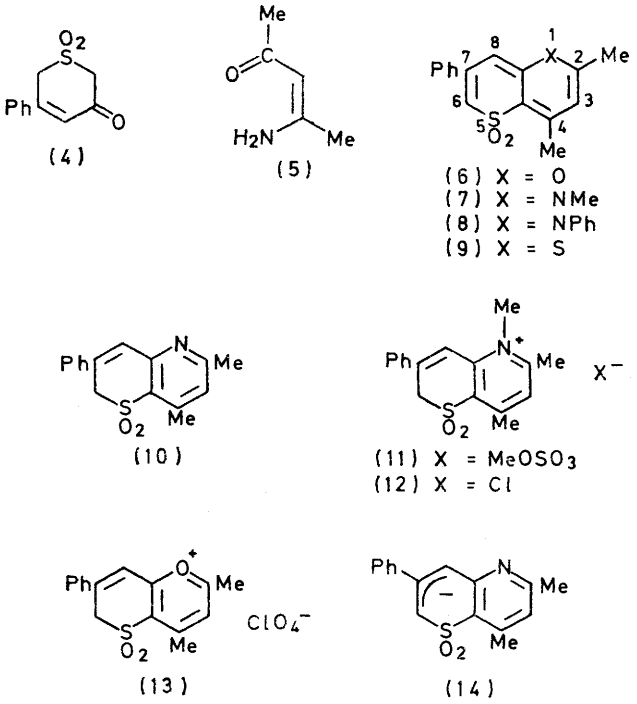
Method B. A solution of compound (6) (600 mg) in benzene (50 ml) was treated with an excess of gaseous methylamine. After 15 h at room temperature the solvent was evaporated off and the residue chromatographed, first on alumina (20 g; chloroform–ethyl acetate, 90 : 10) and then on silica gel (10 g; chloroform–ethyl acetate, 60 : 40). Fractions showing a single spot on t.l.c. afforded a crude product identical with that obtained by method A.

6,8-*Dimethyl*-3,5-*diphenyl*-5H-*thiopyrano*[3,2-b]*pyridine* 1,1-*Dioxide* (8).—A solution of compound (6) (570 mg) in benzene (40 ml) was treated with aniline (190 mg). After 36 h at room temperature, the solvent was evaporated off and the residue chromatographed on silica gel (10 g; chloroform–ethyl acetate 90 : 10) to give the *product* *ca.* 60%), m.p. 235—237° (from benzene).

2,4-*Dimethyl*-7-*phenylthiopyrano*[3,2-b]*thiopyran* 5,5-*Dioxide* (9).—A solution of compound (6) (730 mg) in benzene (50 ml) was saturated with hydrogen sulphide and set aside for 5 days in the dark. The solvent was evaporated off and the residue chromatographed on silica gel (100 g; chloroform–ethyl acetate, 90 : 10). Fractions giving a single spot on t.l.c. were collected to give the *product* (310 mg). This was dissolved in cold benzene; the solution was filtered and slow evaporation to one half volume gave almost black crystals, m.p. 142—144°.

RESULTS AND DISCUSSION

Treatment of 5-phenylthiopyran-3-one (4) with 4-aminopent-3-en-2-one (5) did not give the expected pyridine (10) as the major product, but instead gave the thiopyranopyran (6). The yields were poor (20—30%), and small amounts of the pyridine (10) could be detected by t.l.c. The detailed mechanism of this reaction has not been investigated, but it was ascertained that under the same conditions no reaction occurred when instead of (5) either acetylacetone or 4-morpholinopent-3-en-2-one was used. Strong acids protonated compound (6) in the thiopyran ring (^{1}H n.m.r.; see Table 2) affording the pyrylium salt (13), a pale yellow solid readily hydrolysed in water back to the purple anhydro-base (6). Conversion of compound (6) into the pyridine (10) was easily performed with ammonium acetate in acetic acid. Methylation of the pyridine (10) with dimethyl sulphate afforded the pyridinium methosulphate (11), and the crystalline, analytically pure chloride (12) was obtained from (11) with hydrochloric acid. The anhydro-base (7) was obtained from the pyridinium salt (11) or (12) with weak aqueous bases (*e.g.* Na_2CO_3). The anhydro-base (7) was also obtained directly from the pyran (6) with methylamine in benzene, but in lower yield.



The susceptibility of the pyran (6) to nucleophilic attacks was utilized to prepare the *N*-phenyl derivative (8) and the thiopyranothiopyran (9), by treatment with aniline and hydrogen sulphide, respectively. Whereas the pyran (6) and the thiopyran (9) are relatively unstable, especially in solution, the anhydro-base (8) is quite stable. Compound (8) is particularly useful for assignment of resonances in the ^{1}H n.m.r. spectra of compounds (6)—(9). Models show that the nitrogen-containing ring and the phenyl group cannot be coplanar, and shielding of protons adjacent to the latter is expected. In fact the signal of the methyl group in compound (7) which resonates at higher field is moved further upfield ($\Delta\tau$ 0·53 p.p.m.); thus the high field methyl group in compounds (6)—(10) must be in position 2.* In compound (8) the signal due to one of the two olefinic protons of the sulphur-containing ring is displaced to higher field by *ca.* 1 p.p.m. This must be the proton in position 8; thus the low-field proton (showing long-range coupling with the 8-proton) must be in position 6. It is apparent from the ^{1}H n.m.r. spectra that, relative to the precursor (10), the 8-proton in (7) resonates at considerably higher field. Also the 6-proton in both compounds (7) and (8) resonates at higher field than expected for an olefinic proton α to a sulphonyl group. The same trend is observed for the 6- and 8-protons in compounds (6) and (9). These protons show resonances similar to those of the anion (14), prepared from (10) and methylsulphinylmethanide in dimethyl sulphoxide. All this is consistent with what

* For convenience in discussion, compounds (6)—(14) are all numbered as illustrated in formula (6), although I.U.P.A.C. nomenclature requires a different numbering (as used in the Experimental section) for the pyridine derivatives.

TABLE 2

N.m.r. data (τ values) *

Compound	Solvent	Ph	3-H	6-H	8-H	2-Me	4-Me	J/Hz	
(6)	$CDCl_3$	2·45—2·70	4·22br (s)	3·77 (d)	4·08 (d)	7·76	7·35	$J_{6,8}$ 1·20	
	$CDCl_3$–CF_3·CO_2H	2·37—2·61	*a*	5·12br (s)	*a*	7·08 [b]	6·98 [b]		
(10)	$(CD_3)_2CO$	2·10—2·60	*a*	5·37 (d)	2·83 (d)	7·48	7·33	$J_{6,8}$ 1·25	
(14)	$(CH_3)_2SO$	2·25—2·80	3·72br (s)	5·08 (d)	4·25 (d)	*c*	*c*	$J_{6,8}$ *ca.* 1·50	
(7)	$(CD_3)_2SO$ [d]	2·00—2·70	3·55br (s)	4·05 (d)	4·40 (d)	7·45	7·30	$J_{6,8}$ *ca.* 1·50	
	$(CD_3)_2SO$–CF_3·CO_2H [e]	2·00—2·70	*a*	4·90br (s)	*a*	7·10	7·10		
(8)	$(CD_3)_2SO$ [f]	2·20—2·60	3·40br (s)	4·04 (d)	5·39 (d)	7·98	7·27	$J_{6,8}$ 1·25	
	CF_3CO_2H [g]	2·26—2·40	*h*	5·40br (s)	3·56br (s)	7·68	7·19		
		2·61—3·03							
(9)	$CDCl_3$	2·55	3·72 (q)	2·78 (d)	3·66 (d)	7·75	7·30	$J_{6,8}$ 1·20	$J_{2,2\text{-Me}}$ 1·00
	$CDCl_3$–CF_3·CO_2H	2·45	1·87br (s)	5·18br (s)	2·50br (s)	6·9	6·88 [b]		

* Compounds numbered as in formula (6).

[a] Covered by phenyl resonances. [b] Assignments of 2- and 4-Me might be reversed. [c] Covered by solvent peaks. [d] At 100 °C; NMe at τ 6·35. [e] NMe at τ 5·70. [f] NPh at τ 2·70. [g] Me of $MeCO_2H$ was added as internal reference; Me at τ 8. [h] Covered by aromatic signals at 2·61—3·03.

TABLE 3

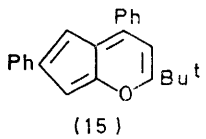
U.v. and visible spectral data [a]

Compound	Solvent	$\lambda_{max.}$/nm (log ε)						
(6)	MeOH	487 (3·63)			323 (4·02)		250 (4·12)	
	MeOH–H_2O (50 : 50)	487 (3·57)			323 (4·03)		250 (4·12)	
	MeOH–N-HCl (50 : 50)	487 (3·28)		402 (3·78)	323 (3·94)		250 (3·98)	
(10)	MeOH				313 (4·29)		225 (4·21)	
	1·032N-MeONa in MeOH		*426*	398 (3·73)	*307*	281 (4·21)	234 (4·13)	
(7)	MeCN	480 (3·81)		367 (3·87)		284 (4·13)	230 (4·20)	
	MeCN–H_2O (20 : 80)	476 (3·71)		362 (4·02)	301 (4·02)	286 (4·01)	*242*	
	MeCN–2N-HCl (20 : 80)			353 (4·33)			*243*	
(8)	MeCN	498 (3·77)		372 (3·88)	*300*	288 (4·11)	*243*	*232*
	MeCN–H_2O (20 : 80)	493 (3·76)		369 (3·93)	*298*	*288*	*246*	
	MeCN–2N-HCl (20 : 80)			354 (4·34)	*298*		*246*	
(9)	MeCN	524 (3·63)		352 (4·00)			259 (4·20)	
	MeCN–H_2O (20 : 80)	536 (3·63)		351 (4·03)			261 (4·18)	
	MeCN–2N-HCl (20 : 80)		427 (4·29)	342 (3·87)		285 (3·89)	240 (4·19)	
(15) [b]	Dioxan	462 (2·92)		393 (4·34)			248 (4·46)	
(16) [c]	pH 8·5	462 (3·58)		332 (3·06)	318 (3·09)	273 (4·52)	237 (4·06)	
	pH 3			376 (3·50)	318 (3·26)	254 (4·62)	222 (3·90)	
					305 (3·20)			

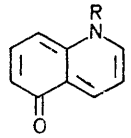
[a] Figures in italics refer to inflections. [b] Ref. 7. [c] Ref. 8.

is known [7] for protons bonded to electron-rich trigonal carbon atoms. However the situations depicted in (3b) and (3c), where the carbon framework C(6)C(7)C(8)C(8a) is dienaminic in nature (X = NR), can both accommodate the high-field resonances for the 6- and 8- protons. Comparison of the chemical shifts of the 3-protons in compounds (6)—(9) with those of the precursor (10) and the anion (14) suggests that little positive charge is present on the X-containing ring (X = O, S, NMe, or NPh), and favours the hypothesis that the negative charge present on the SO_2-containing ring is due to the mesomerism (3a) ⟷ (3c).

Lack of any notable analogy between the electronic spectra of compounds (6)—(9) and that of the anion (14) further supports the foregoing hypothesis. Electronic absorptions of compounds (6)—(9) show close similarities to those of compounds (1) and (2),[1] no doubt due to the presence in both series of the fulvene-like structure of the thiopyran ring conjugated to one or two additional double bonds, respectively. Since previous investigations [1,8] showed that for compounds (1) and (2) there is tenuous evidence for 'through' conjugation of the sulphonyl group associated with the dipolar structure of the molecules, we must conclude that, at least qualitatively, electronic spectra are an insufficiently sensitive tool for detecting subtle changes in delocalization mechanisms. Although exact pseudo-azulene analogues of compounds (6)—(9) are not known, comparison of electronic spectra of compounds (6) and (15) [9] shows no particular similarity; a closer analogy seems to exist instead between the spectra of compound (7) and 1-methyl-5-quinolone (16) [10] (Table 3). As expected this analogy breaks down on protonation: in compound (7) protonation occurs



(15)



(16)

at C-6 (^1H n.m.r.; see Table 2), whereas in compound (16) protonation occurs on oxygen to give a phenolic pyridinium cation. The analogy between compounds (7) and (16) extends to the i.r. bathochromic shifts (relative to normal values) experienced by the sulphonyl and carbonyl groups, respectively.

Table 4 shows that asymmetric sulphonyl stretching

[7] T. Shaeffer and W. G. Schneider, *Canad. J. Chem.*, 1968, **41**, 966; J. W. Burley and R. N. Young, *J.C.S. Perkin II*, 1972, 1006, and references cited therein.

[8] G. D. Andreetti, G. Bocelli, and P. Sgarabotto, *J.C.S. Perkin II*, 1973, 1189.

[9] G. V. Boyd, *J. Chem. Soc.*, 1958, 1978.

[10] D. J. Brown and S. F. Mason, *J. Chem. Soc.*, 1956, 3443.

TABLE 4

I.r. data

Compound	Phase	ν_{SO_2}/cm^{-1} asym	sym
(6)	$CDCl_3$	1270s	1119vs
		1265s	
	Nujol	1255s	1112vs
		1248s	
(13)	Nujol	1305s	1135s
(10)	$CDCl_3$	1308vs	1154s
			1133vs
	Nujol	1297vs	1147s
			1127vs
(7)	$CDCl_3$	1257s	1098vs
(8)	$CDCl_3$	1275m	1112vs
		1252s	1093vs
		1239s	
(9)	$CDCl_3$	1267s	1103vs
	Nujol	1259vs	1103vs

vibrations for compounds (6)—(9) are bathochromically shifted, relative to the appropriate precursor [*e.g.* (10)], by *ca.* 35—50 cm^{-1}; such a shift, although significant, is far less pronounced than that observed in the thiopyranylidenedihydropyridines (1) and (2) [1] (*ca.* 100 cm^{-1}). This result favours the conclusion that in compounds (6)—(9), in contrast with compounds (1) and (2), there is little involvement, if any, of the sulphonyl group in ' through ' conjugation. The extent of bathochromic shift exhibited by the C=O group in the quinolone (16) [10] ($\nu_{C=O}$ 1648, $\Delta\nu$ *ca.* 40 cm^{-1}) is strikingly analogous to that observed in compound (7).

If one accepts the foregoing interpretation, the following conclusions can be drawn: (i) the thiopyran *SS*-dioxide system in compounds (6)—(9) is electron-rich but is a poor model for the thiopyran *SS*-dioxide anion; (ii) if the sulphonyl group interacts with the C=C–C=C–X system, little, if any, involvement of the sulphur–oxygen bonds is associated with such an interaction (' one-side ' conjugation); and (iii) structures (6)—(9) show more similarities to quinolone-type structures than to pseudoazulene structures. Further details and support for this conclusion are given in the following paper.

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