1,2-Sulphur Shift in the Acid-catalysed Cyclisation of *o*-Arylthiophenyl-substituted Carbinols to Thioxanthen Derivatives

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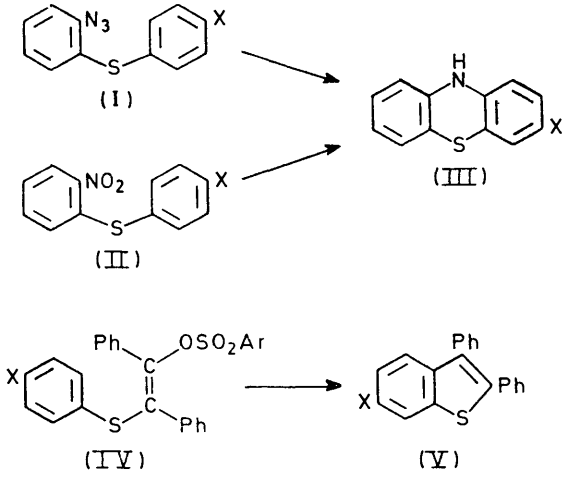
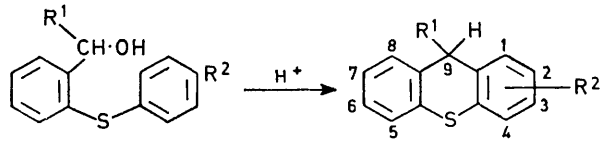
During the acid-catalysed cyclisation of some *o*-arylthiophenyl-substituted carbinols to thioxanthen derivatives, a rearrangement was observed with carbinols having a *para*-methyl substituent in the arylthio-group. Thus, 1-[*o*-(*p*-tolylthio)phenyl]ethanol gave 3,9-dimethylthioxanthen, while α-[*o*-(*p*-tolylthio)phenyl]benzyl alcohol gave a mixture of 3-methyl- and 2-methyl-9-phenylthioxanthen. The mechanism of the cyclisation is discussed in terms of a competition between ring-closure at the position *ortho* to the sulphur (*ortho*-substitution) and ring-closure at the position bearing the sulphur followed by a 1,2-sulphur shift (*ipso*-substitution).

EXAMPLES of 1,2-sulphur shifts in syntheses of sulphur heterocycles by electrophilic ring closure onto an aromatic nucleus have been reported recently, *e.g.* the cyclisation of 2-azidophenyl phenyl sulphides [1] (I) and 2-nitrophenyl phenyl sulphides [2] (II) to phenothiazines (III) and the cyclisation of 1,2-diaryl-2-arylthiovinyl sulphonates (IV) to benzo[*b*]thiophens [3] (V).



The mechanism suggested for these reactions involves attack by an electrophile at the position bearing the sulphur with formation of a spiro-intermediate,[4] followed by a 1,2-sulphur shift. This is an example of the so-called *ipso*-attack in electrophilic aromatic substitution.[5] Apart from sulphur-containing systems, migrations of this type have been observed in the cyclisations of sulphonyl-[6] and carbonyl-substituted [7] compounds.

Not all sulphur-substituted systems, however, give migration, and since all the factors underlying such rearrangements are still not clear, we have investigated some other systems in which the 1,2-sulphur shift could take place. We now report the results of the acid-catalysed cyclisation of some *o*-arylthiophenyl-substituted carbinols (VI) to thioxanthen derivatives (VII).



(VI)

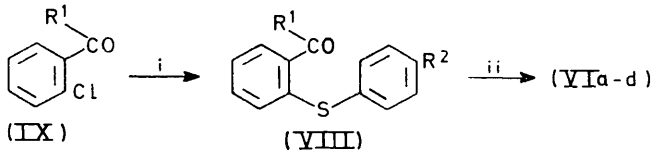
a; R^1 = Me, R^2 = H
b; R^1 = Me, R^2 = Me
c; R^1 = Ph, R^2 = H
d; R^1 = Ph, R^2 = Me

(VII)

a; R^1 = Me, R^2 = H
b; R^1 = Me, R^2 = 3-Me
c; R^1 = Ph, R^2 = H
d; R^1 = Ph, R^2 = 3-Me
e; R^1 = Ph, R^2 = 2-Me

RESULTS

Carbinols (VIa—d) were prepared by reduction with $LiAlH_4$ of the corresponding ketones (VIIIa—d), which were synthesised by reaction of the 2-chloro-substituted ketones (IXa and b) with the appropriately substituted copper(I) arenethiolates (see Scheme 1).



(IX)

a; R^1 = Me
b; R^1 = Ph

(VIII)

a; R^1 = Me, R^2 = H
b; R^1 = Me, R^2 = Me
c; R^1 = Ph, R^2 = H
d; R^1 = Ph, R^2 = Me

SCHEME 1 Reagents: i, $R^2C_6H_4SCu$ in quinoline–pyridine (10 : 1); ii, $LiAlH_4$ in ether

Two reagents were used for the cyclisation of carbinols (VI) to thioxanthens (VII): polyphosphoric acid at 100° mainly for the methyl-substituted compounds (VIa and b), and methanesulphonic acid in dichloromethane at room temperature for the phenyl-substituted compounds (VIc and d).†

The results obtained in these cyclisations are reported in Table 1.

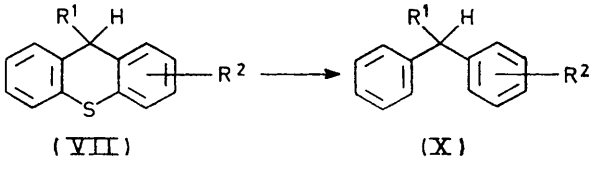
The structure of the cyclisation products (VIIIa and c) was determined by comparison of the physical constants

† Cyclisation of unsubstituted carbinols (VI; R^1 = H) was also attempted. With these and other common methods of ring-closure only extensive polymerisation was observed.

[1] M. Messer and D. Farge, *Bull. Soc. chim. France*, 1968, 2832; 1969, 4955.
[2] J. I. G. Cadogan, *Accounts Chem. Res.*, 1972, **5**, 303, and references therein.
[3] G. Capozzi, G. Melloni, and G. Modena, *J. Org. Chem.*, 1970, **35**, 1217; *J. Chem. Soc.* (*C*), 1970, 2621; G. Melloni, and G. Modena, *J.C.S. Perkin I*, 1972, 218.
[4] M. S. Newman, *Accounts Chem. Res.*, 1972, **5**, 534.
[5] C. L. Perrin, *J. Org. Chem.*, 1971, **36**, 420; C. L. Perrin and G. A. Skinner, *J. Amer. Chem. Soc.*, 1971, **93**, 3389.
[6] G. Melloni and G. Modena, *J.C.S. Perkin I*, 1972, 1355.
[7] H. Martens and G. Hoornaert, *Synthetic Comm.*, 1972, **2**, 147; *Tetrahedron Letters*, 1970, 1821.

with data reported in the literature. Thioxanthen (VIIb) and the mixture of thioxanthens (VIId and e) were characterised by elemental and ^{1}H n.m.r. analysis.

The position of the substituent R^2 in the thioxanthens (VIIb, d, and e) was established by reductive desulphurisation with Raney nickel [9] and comparison of the diaryl- and triaryl-substituted methanes (X) obtained with authentic samples synthesised independently. In the thioxanthens (VIIb and d) the position of the substituent



a; R^1 = Me, R^2 = 4-Me
b; R^1 = Me, R^2 = 3-Me
c; R^1 = Ph, R^2 = 4-Me
d; R^1 = Ph, R^2 = 3-Me

R^2 with respect to the sulphur was different from that in the starting compounds (VIb and d) (respectively), whereas it was maintained in the thioxanthen (VIIe).

TABLE 1

Cyclisation of carbinols (VI) to thioxanthens (VII)

Compound	R^1	R^2	Cyclisation method	Yield (%) of (VII)	Product	R^1 in (VII)	R^2 in (VII)
(VIa)	Me	H	A [a]	50	(VIIa) [c]	9-Me	H
(VIa)	Me	H	B [b]	Trace	(VIIa) [c]	9-Me	H
(VIb)	Me	*p*-Me	A	62	(VIIb)	9-Me	3-Me
(VIc)	Ph	H	A	74	(VIIc) [d]	9-Ph	H
(VIc)	Ph	H	B	70	(VIIc) [d]	9-Ph	H
(VId)	Ph	*p*-Me	B	37	(VIId)	9-Ph	3-Me
				36	(VIIe)	9-Ph	2-Me

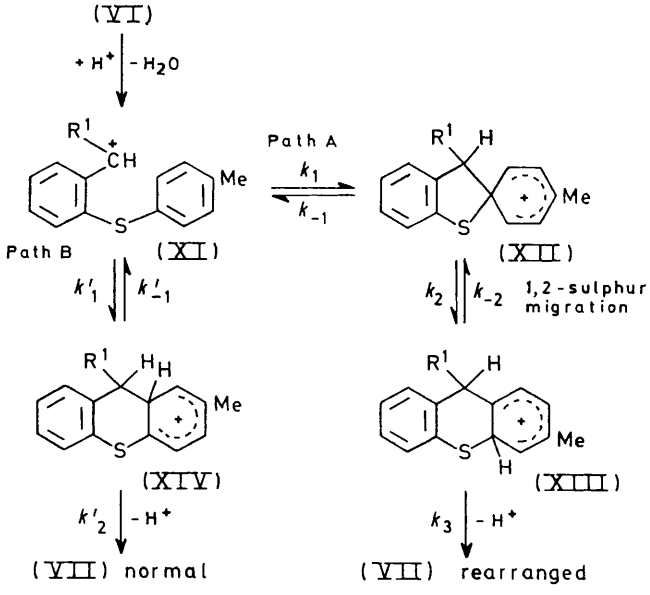
[a] Polyphosphoric acid at 100°. [b] Methanesulphonic acid in dichloromethane at room temperature. [c] M.p. 81—82° (from methanol) (lit.,[8] m.p. 84·5°). [d] M.p. 97—98° (from methanol) (lit.,[8] m.p. 99°).

DISCUSSION

The main feature of the cyclisation reaction described here is the dependence of the rearrangement on the substituent R^1. Thus, while methyl-substituted (VIb) gave only the rearranged thioxanthen (VIIb), the cyclisation of the phenyl-substituted (VId) gave a mixture (*ca.* 1 : 1) of the ' rearranged ' and ' normal ' thioxanthens (VIId and e). These results can be explained on the basis of the mechanism outlined in Scheme 2. The carbonium ion (XI) formed from the protonated carbinol (VI) may either attack the *ipso*-position of the arylthio-nucleus (path A) giving the spiro-intermediate (XII), which suffers a 1,2-sulphur shift to give the intermediate (XIII) leading to the ' rearranged ' product, or attack the positions *ortho* to the sulphur (path B) to give the ' normal ' product.

This mechanism is analogous to that suggested for the cyclisations to phenothiazines [1,2] and to benzo[*b*]thiophens [3] mentioned before. In such systems, however, the competition between paths A and B was analysed in terms of the nature of the substituent X in compounds (I), (II), and (IV) and its effect on the ratio $k_1 : k_1'$. In the present case the substituent R^2 is the same in both (VIb) and (VId) and on the basis of previous results *ipso*-substitution should be favoured ($k_1 \gg k_1'$).

The effect of phenyl *versus* methyl substitution at the electrophilic centre on the ratio $k_1 : k_1'$ should not be large unless steric effects are important. On the contrary, a variation of k_{-1} with the substituent R^1 can be anticipated. This could affect the balance between the 1,2-sulphur shift and the return of the spiro-intermediate (XII) to the initial intermediate (XI). Since it may be



SCHEME 2

assumed that loss of a proton from the intermediates (XIII) and (XIV) is faster than any other process (*i.e.*, $k_3 \gg k_{-2}$ and $k_2' \gg k_{-1}'$), the rates of formation of the ' rearranged ' and ' normal ' (VII) may be considered equal to the rates of formation of (XIII) and (XIV). According to Scheme 2, these rates are expressed by the equations (1) and (2), where r_{XIII} and r_{XIV} are the rates

[8] C. C. Price, M. Hori, T. Parasaran, and M. Polk, *J. Amer. Chem. Soc.*, 1963, **85**, 2278.

[9] G. R. Pettitt and E. E. Van Tamelen, *Org. Reactions*, 1962, **12**, 356; W. A. Bonner and R. A. Grimm, in ' The Chemistry of Organic Sulphur Compounds,' eds. N. Kharasch and C. Y. Meyers, Pergamon, London, 1966, vol. 2, p. 35; see also ref. 8.

of formation of the intermediates (XIII) and (XIV) respectively.

$$r_{XIII} = k_1k_2[(XI)]/(k_{-1} + k_{-2}) \quad (1)$$

$$r_{XIV} = k_1'[(XI)] \quad (2)$$

The rate of the 1,2-sulphur shift (k_2) should not be much affected by the substituent R^1, whereas the rate of the return from the spiro-intermediate (XII) to the carbonium ion (XI) (*i.e.* k_{-1}) must depend on the stability of (XI) and hence be larger for (XI; R^1 = Ph), a diphenylmethyl cation, than for (XI; R^1 = Me), a 1-phenylethyl cation. It follows that r_{XIII} must be smaller in the former than in the latter case and must eventually be comparable with r_{XIV}, although k_1 might remain larger than k_1'.

The results discussed here are therefore consistent with those reported previously,[1-3] in the sense that *ipso*-attack is preferred over *ortho*-attack in *para*-methyl-substituted compounds. In this respect, the cyclisation of carbinols (VI) to thioxanthens (VII) is comparable with the cyclisation of sulphonates (IV) to benzo[*b*]thiophens (V),[3] in which, however, the cationic intermediate involved is a phenyl-substituted vinyl cation, for which k_{-1} is likely to be quite small.

EXPERIMENTAL

p-Methylacetophenone, *m*-bromotoluene, diphenylmethyl chloride, and benzophenone were commercial samples, and were purified by standard methods. *o*-Chloroacetophenone,[10] 2-chlorobenzophenone,[11] and copper(I) benzene- and toluene-*p*-thiolate [12] were prepared by literature methods.

The ^{1}H n.m.r. spectra were recorded with a Perkin-Elmer R12 spectrometer, or with a Bruker HFX high-resolution spectrometer operating at 90 MHz, with tetramethylsilane as internal standard.

o-Arylthioacetophenones (VIIIa *and* b).—A mixture of *o*-chloroacetophenone (IXa) (15·46 g, 0·1 mol), copper(I) benzenethiolate or toluene-*p*-thiolate (0·11 mol), quinoline (70 ml), and pyridine (7 ml) was heated to reflux (200—210°) until a homogeneous solution was obtained (*ca.* 10 h). The hot solution was slowly poured into concentrated hydrochloric acid containing cracked ice, and the mixture was stirred for 2 h. The gummy solid was extracted several times with ethyl acetate and the organic layer was washed with water and dried (Na_2SO_4). Evaporation gave a brown residue, which was chromatographed on silica gel. Elution with light petroleum (b.p. 40—70°)–benzene (1 : 1) gave *o-phenylthioacetophenone* (VIIIa) (11·4 g, 50%), m.p. 72—73° (from ethanol) (Found: C, 74·0; H, 5·3; S, 14·1. $C_{14}H_{12}OS$ requires C, 73·6; H, 5·2; S, 14·0%), or o-(p-*tolylthio*)-*acetophenone* (VIIIb) (15·0 g, 62%), m.p. 110—111° (from ethanol) (Found: C, 74·55; H, 5·9; S, 13·4. $C_{15}H_{14}OS$ requires C, 74·3; H, 5·8; S, 13·2%).

2-Arylthiobenzophenones (VIIIc *and* d).—These compounds were prepared by reaction of 2-chlorobenzophenone (IXb) with copper(I) benzenethiolate or toluene-*p*-thiolate in quinoline–pyridine for 15 h, as for the *o*-arylthioacetophenones (VIIIa and b). Chromatography of the reaction mixtures on silica gel with light petroleum (b.p. 40—70°)–ether (9 : 1) as eluant gave *o-phenylthiobenzophenone* (VIIIc) (58% yield), m.p. 51—52° (from ethanol) (Found: S, 9·95. $C_{19}H_{14}OS$ requires S, 11·05%), or o-(p-*tolylthio*)*benzophenone* (VIIId) (54% yield), m.p. 53—54° (from ethanol) (Found: S, 10·6. $C_{20}H_{16}OS$ requires S, 10·55%).

Methyl and Phenyl o-Arylthiophenyl Carbinols (VIa—d).—These compounds were prepared by reduction with $LiAlH_4$ (0·1 mol) of the corresponding ketones (VIIIa—d) (0·1 mol) in refluxing ether for 5—7 h (80—90% yields), and purified by recrystallisation from light petroleum (b.p. 75—120°).

Physical constants and analytical data of the *carbinols* (VIa—d) are reported in Table 2.

Cyclisation of Carbinols (VI) *to Thioxanthens* (VII).—While Method A could be used both for the methyl-substituted (VI; R^1 = Me) and the phenyl-substituted compounds (VI; R^1 = Ph), Method B gave satisfactory results only for the latter (see Table 1).

Method A. The appropriate carbinol (VI) (20 mmol) was added in small portions to polyphosphoric acid (120 g) [from phosphoric acid (*d* 1·75; 30 ml) and phosphorus pentoxide (48 g)] with vigorous stirring, and the mixture was stirred and heated at 100° for 2 h. The mixture was then cooled, poured on cracked ice, and extracted with ether. The extracts were washed with water and dried (Na_2SO_4), and evaporated to give a reddish residue, which was chromatographed on silica gel. Elution with light petroleum (b.p. 40—70°) gave, as indicated in Table 1, the crystalline thioxanthens (VII).

Method B. The appropriate carbinol (VI) (20 mmol) was dissolved in dichloromethane (60 ml), methanesulphonic acid (*d* 1·48; 10 ml) was added, and the mixture was stirred at room temperature for 1 h. The dichloromethane solution was then washed with water, dried (Na_2SO_4), and evaporated. The pink residue was then purified as described in method A.

9-Methylthioxanthen [8] (VIIa) and *9-phenylthioxanthen* [8] (VIIc) were identified by comparison of their physical constants with reported data. *3,9-Dimethylthioxanthen* (VIIb) had m.p. 49—50° (from methanol) (Found: C, 79·75; H, 6·3; S, 14·1. $C_{15}H_{14}S$ requires C, 79·5; H, 6·2; S,

TABLE 2

Physical constants and analytical data of carbinols (VI)

				Found (%)				Required (%)		
Compound	R^1	R^2	M.p. (°C)	C	H	S	Formula	C	H	S
(VIa)	Me	H	35—37			13·75	$C_{14}H_{14}OS$			13·9
(VIb)	Me	Me	58—59	73·5	6·65	13·2	$C_{15}H_{16}OS$	73·7	6·6	13·1
(VIc)	Ph	H	45—46			11·15	$C_{19}H_{16}OS$			10·95
(VId)	Ph	Me	79—80	78·3	5·85	10·35	$C_{20}H_{18}OS$	78·4	5·9	10·45

[10] H. G. Walker and C. R. Hauser, *J. Amer. Chem. Soc.*, 1946, **68**, 1386.

[11] G. Pfister-Guillouzo, M. Grimaud, and J. Deschamps, *Bull. Soc. chim. France*, 1969, 1203.

[12] R. Adams, W. Reifschneider, and M. D. Nair, *Croat. Chem. Acta*, 1957, **29**, 277.

14·1%), τ (CCl_4) 2·50—3·25 (7H, m), 6·10 (1H, q, *J* 7 Hz), 7·72 (3H, s), and 8·6 (3H, d, *J* 7 Hz).

The isomeric 3-*methyl*-9-*phenylthioxanthen* (VIId) and 2-*methyl*-9-*phenylthioxanthen* (VIIe) formed in the cyclisation of carbinol (VId) could not be satisfactorily separated either by chromatography or by fractional recrystallisation. The mixture (VIId and e) had m.p. 68—73° (Found: C, 83·2; H, 5·55; S, 11·1. $C_{20}H_{16}S$ requires C, 83·3; H, 5·6; S, 11·1), τ (CS_2) 2·65—3·20 (12H, m), 4·91 (1H, s), and 7·70 (3H, s).

Reductive Desulphurisation of Thioxanthens (VIIb) *and* (VIId and e).—Raney nickel [13] (*ca.* 20 g) was added to a solution of compound (VII) (10 mmol) in absolute ethanol (100 ml) and the mixture was refluxed for 4 h. More Raney nickel (*ca.* 10 g) was added, and refluxing was continued for 3 h. The suspension was filtered and evaporated. The residue was then chromatographed on silica gel.

From thioxanthen (VIIb) elution with light petroleum (b.p. 40—70°) gave 1-phenyl-1-*p*-tolylethane (Xa) (85% yield), which was compared with an authentic sample and also with a sample of 1-phenyl-1-*m*-tolylethane (Xb), synthesised independently.

From the mixture of thioxanthens (VIId and e) elution with light petroleum (b.p. 40—70°)–ether (9 : 1) gave a mixture of diphenyl-*p*-tolymethane (Xc) and diphenyl-*m*-tolylmethane (Xd) (92% total yield), which was compared with authentic samples synthesised independently. The mixture showed τ (CS_2) 2·60—3·35 (14H, m), 4·65 (1H, s), and 7·75 and 7·80 (total 3H, 2s integral ratio *ca.* 1 : 1).

1-*Phenyl*-1-p-*tolylethane* (Xa).—This was prepared by hydrogenation over 5% palladium–carbon of 1-phenyl-1-*p*-tolylethylene.[14] The latter was prepared by dehydration with dilute sulphuric acid of 1-phenyl-1-*p*-tolylethanol (obtained by reaction of phenylmagnesium bromide with *p*-methylacetophenone in ether) and chromatographed on silica gel, with light petroleum (b.p. 40—70°) as eluant. Compound (Xa) was purified by distillation; b.p. 97—100° (0·3 mmHg),[15] τ (CCl_4) 2·80—3·20 (9H, m), 6·03 (1H, q, *J* 7 Hz), 7·81 (3H, s), and 8·48 (3H, d, *J* 7 Hz).

1-*Phenyl*-1-m-*tolylethane* (Xb).—This was prepared by catalytic hydrogenation of 1-phenyl-1-*m*-tolylethylene.[14] The latter was prepared by dehydration with dilute sulphuric acid of 1-phenyl-1-*m*-tolylethanol (obtained by reaction of *m*-tolylmagnesium bromide with acetophenone), and chromatographed on silica gel, with light petroleum (b.p. 40—70°) as eluant. Compound (Xb) was purified by distillation; b.p. 104—106° (0·2 mmHg),[16] τ (CCl_4) 2·70—3·30 (9H, m), 6·04 (1H, q, *J* 7 Hz), 7·85 (3H, s), and 8·49 (3H, d, *J* 7 Hz).

Diphenyl-p-*tolylmethane* (Xc).—This was prepared by Friedel–Crafts reaction of diphenylmethyl chloride with toluene in the presence of tin(IV) tetrachloride and purified by chromatography on silica gel, with light petroleum (b.p. 40—70°)–ether (9 : 1) as eluant, followed by recrystallisation from ethanol, m.p. 69—70°,[17] τ (CS_2) 2·70—3·35 (14H, m), 4·65 (1H, s), and 7·75 (1H, s).

Diphenyl-m-*tolylmethane* (Xd).—This compound was prepared by reduction with zinc powder in glacial acetic acid of diphenyl-*m*-tolylmethanol [18,19] (obtained by reaction of *m*-tolylmagnesium bromide with benzophenone in ether), and purified by chromatography on silica gel, with light petroleum (b.p. 40—70°)–ether (9 : 1) as eluant, followed by recrystallisation from absolute ethanol, m.p. 60—61°,[19] τ (CS_2) 2·60—3·20 (14H, m), 4·65 (1H, s), and 7·80 (3H, s).

We thank Mr. Roberto Salmaso for technical assistance in recording the high-resolution n.m.r. spectra.

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