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THIOPHENE CHEMISTRY—XVII*

THIO-CLAISEN-REARRANGEMENT OF ALLYL THIENYL SULPHIDES

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Abstract—Allyl 2-thienyl sulphide, allyl 3-thienyl sulphide, allyl 2-methyl-3-thienyl sulphide, and crotyl 2-thienyl sulphide undergo a typical thio-Claisen rearrangement, when heated in quinoline. The choice of solvent is crucial. The intermediates have been isolated or trapped as S-benzoyl derivatives and the ring-closure products formed identified.

INTRODUCTION

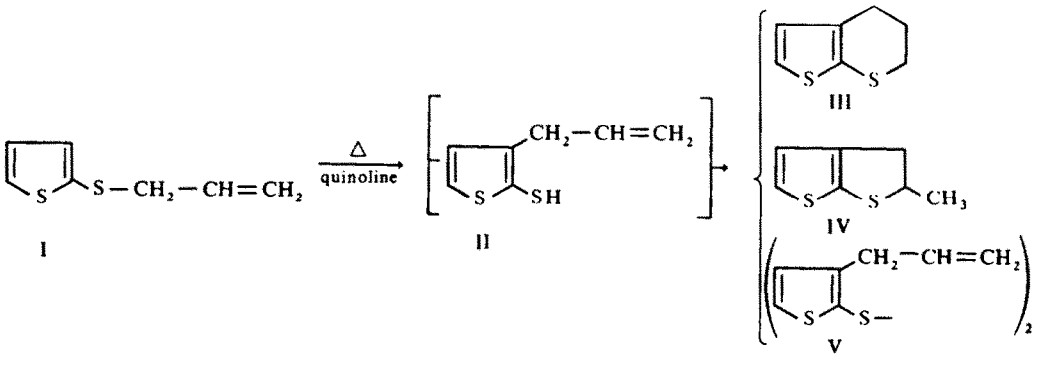
IT HAS been shown,[1–5] that allyl (or crotyl) aryl sulphides and aryl propargyl sulphides undergo a thio-Claisen rearrangement when heated in basic or acid solutions. The intermediates of the rearrangement can be trapped if acid halides or acid anhydrides are present. Thus, allyl 4-quinolyl sulphide, when heated in the presence of butyric anhydride, produces 3-allyl-4(1*H*)quinolinethione as its S-butyroyl derivative.[4] In the aryl propargyl sulphide rearrangements the intermediates have not been trapped, but believed to be of the expected type.

Attempts to rearrange allyl thienyl sulphides were made earlier by Brandsma,[3] but without success—only isomerization in the allyl group was observed.

Rearrangement procedure. In the general procedure quinoline was heated to 170–180° and then allyl thienyl sulphide added. After completion of the reaction, the quinoline was removed as the hydrochloride, and the products separated on a silica gel column (eluated with low boiling light petroleum) and by GLC.

In order to trap the intermediates of the sigmatropic rearrangements, the reactions were carried out in benzoyl chloride instead of quinoline.

Rearrangement of allyl 2-thienyl sulphide. Three main products (III, IV, and V) and a tarry residue (about 30%) were isolated from rearranged allyl 2-thienyl sulphide (I)



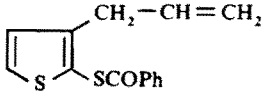
* Part XVI, E. B. Pedersen and S.-O. Lawesson, *Tetrahedron* **26**, 2959 (1970)

TABLE 1. PRODUCT-DISTRIBUTION OF THE REARRANGEMENT OF I, VI, AND IX

Conditions	I			XVIII			XIX			
	III	IV	V	XX	XXI	XIX	XX	XXI	XIX	XXII
	%	%	%	%	%	%	%	%	%	%
170°	17	50	33	38	19	43	24	1	47	28
140° peroxide	5	17	78	5	33	62				
170° peroxide				28	24	48				
190° quinone	22	22	56	16	11	73				

In Table 1 the product distributions and the various rearrangement conditions are reported. If the rearrangement of compound I is carried out in quinoline at 140° in the presence of traces of benzoyl peroxide, the main product is the disulphide (V) of the intermediate (II). The ratio III/IV is not changed by the presence of peroxide, which may be due to the lowering of the reaction temperature, because the formation of the dihydrothienothiophene (IV) is kinetically determined, while the formation of III is thermodynamically determined. This could also be the explanation why the radical quencher (*p*-quinone) has an effect opposite to that expected, which may be due to the higher temperature necessary when quinone is present. Concurrently it was observed that the peroxide accelerates the rearrangement while quinone slows it down.

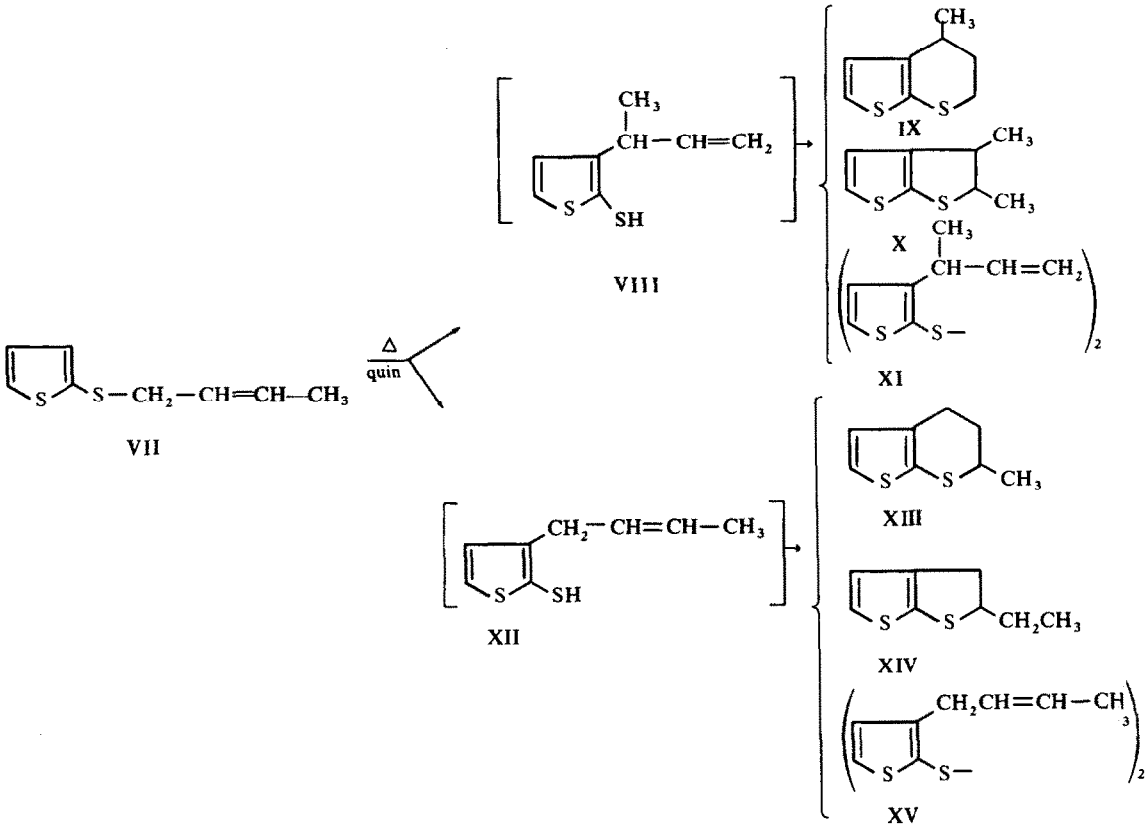
In order to confirm that II is an intermediate in the rearrangement of allyl 2-thienyl sulphide (I), the reaction was carried out in benzoyl chloride. Compound I then produces 3-allyl-2-benzoylthiothiophene (VI).



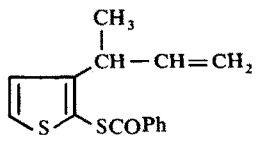
VI

Crotyl 2-thienyl sulphide (VII) is rearranged in quinoline at 200° and the only products isolated were IX, X, and XV. Consequently, both intermediates (VIII and XII) are involved in the rearrangement, and they are both trapped as 2-benzoylthiothiophenes (XVI and XVII), when the reactions are run in benzoyl chloride (or crotyl-) group.

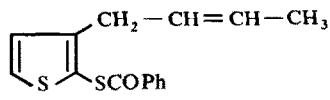
The first steps in these conversions are probably two competitive rearrangements, one—a Claisen-like sigmatropic shift, and another—a radical shift, of the allyl-



Rearrangement of allyl 3-thienyl sulphide. The products XIX, XX, and XXI (Table 1) and a tarry residue (about 20%) were isolated from rearranged allyl 3-thienyl sulphide (XVIII).



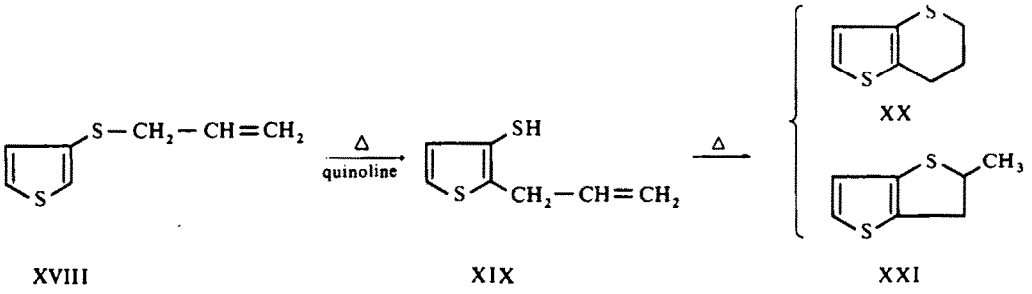
XVI

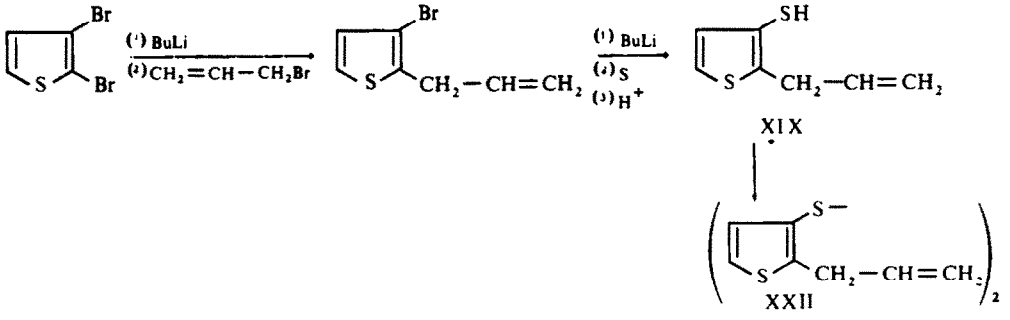


XVII

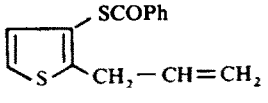
The intermediate, 2-allyl-3-mercaptothiophene (XIX) was isolated and also prepared from 2, 3-dibromothiophene.

Although not a trace of the disulphide (XXII) could be detected when XVIII was rearranged, if XIX is heated in quinoline (the same conditions as for the rearrangement reaction), a large amount of the disulphide XXII is formed, in addition to ring closure



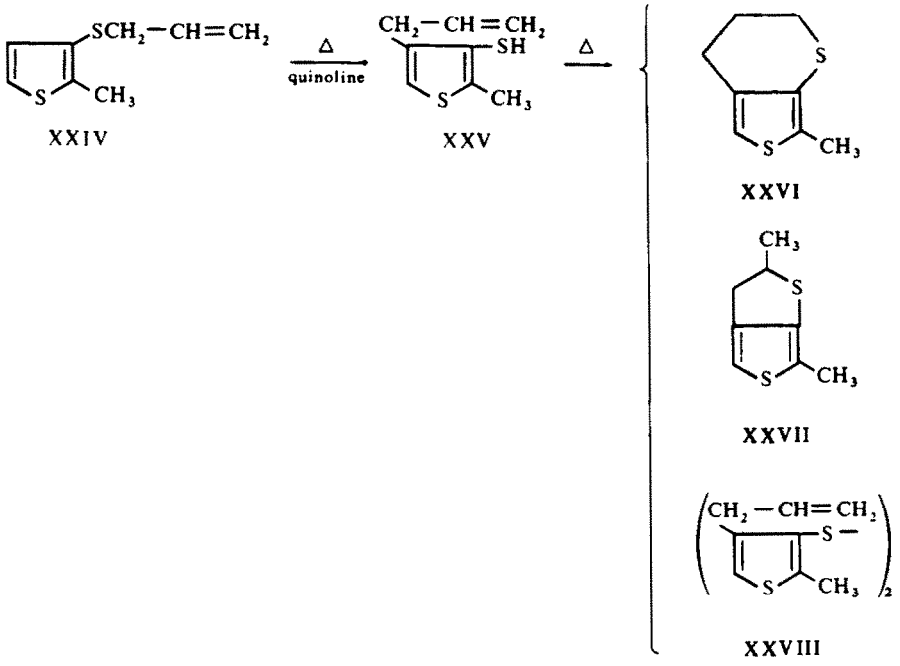


products (Table 1). The disulphide is also obtained from XIX by oxidation with iodine in ethanol. The suggested intermediate XIX was also trapped with benzoyl chloride as 2-allyl-3-benzoylthiothiophene (XXIII). In the rearrangement of XVIII (Table 1) the same temperature dependence was observed as for the rearrangement of I.



XXIII

Rearrangement of allyl (2-methyl)-3-thienyl sulphide (XXIV). The title compound (XXIV) in which the 2-position is blocked by a Me group, also undergoes a sigmatropic rearrangement when heated in quinoline. Four products, XXV–XXVIII, were isolated.



CONCLUSION

Allyl thienyl sulphides undergo a thio-Claisen-like rearrangement followed by a disulphide formation of the intermediates, or a ring-closure reaction of both Markownikoff and anti-Markownikoff type. The intermediates are stable when the mercapto-group is in the 3-position. It is well-known that 3-hydroxythiophenes predominantly exist as true hydroxythiophenes[6, 7] while 2-hydroxythiophenes exist as 3-thiolene-2-ones. It is concluded[6–8] that thiophenes with a functional group in the β-position rather than the α-position are stabilized as hydroxy (mercapto-etc) thiophenes.

In addition it is seen that an allyl group in the 2-position has less steric hindrance than an allyl group in the 3-position.

In the GLC some peaks were observed, with a retention-time a little longer than for the allyl thienyl sulphides. These compounds, which are not found in the NMR spectra of the crude mixture, were identified by MS as 1-propenyl thienyl sulphide isomers of the starting materials, and of compounds with isomerized double bonds of the intermediates. These products could only be formed during gas-chromatography as they were not present in the original products of the rearrangement reactions.

As we were unable to separate a mixture of III and IV; XXVI and XXVII; and IX and X, these compounds were detected in the mixtures by mixed C, H-analyses and NMR spectra.

EXPERIMENTAL

NMR spectra were recorded at 60 Mc/s on a Varian A-60 spectrometer. TMS was used as internal reference standard and the chemical shifts are express in δ-values (ppm) downfield from TMS.

A Perkin–Elmer F11 gaschromatograph, fitted with a S.E.30 column, was used for the GLC analyses, while a P.-E. F 21 gaschromatograph, fitted either with a S.E.30 or with a DEGS column, was used for the GLC separations. Mass spectra were recorded on a CEC 125 single-focusing mass-spectrometer.

Starting materials were prepared according to standard methods. the b.ps are uncorrected. Analyses were made by NOVO A/S, Copenhagen.

Allyl 2-thienyl sulphide (I). 1·5M n-BuLi (500 ml, 0·75 mole) was added to thiophene (63·1 g, 0·75 mole) thiophene in anhyd ether (400 ml) at room temp and refluxed for ½ hr. Sulphur (24·1 g, 0·75 mole) was added in 4 portions while the mixture was cooled on an ice–water bath. The mixture was then allowed to reach room temp, and allyl bromide (91·2 g, 0·75 mole) ether (100 ml) was added during ½ hr and stirred overnight. The mixture was poured into 1 l water, the organic layer separated, washed with water until neutral, and dried (Na_2SO_4). Distillation gave I, (80·3 g, 66%), b.p 87–88°, n_D^{20} = 1·5843. (Found: C, 53·93; H, 5·25; $C_7H_8S_2$ requires: C, 53·84; H, 5·16%); NMR (CCl_4): 7·2 (1H, m); 6·9 (2H, m); 5·7 (1H, m); 4·8 (2H, m); 3·3 (2H, m).

Rearrangement of I. Quinoline (45 ml) was heated to 170° and I (20·0 g, 0·13 mole) was added at once and stirred for 15 min. The mixture was cooled and poured into 200 ml light petroleum (b.p. 40–60°) and washed 4 times with 0·1M HCl (200 ml) and with water until neutral. The organic layer was dried (Na_2SO_4), the solvent stripped off, and the crude product (17·5 g) analysed by GLC (Table 1). The crude product (1·2 g) was separated in small portions by GLC on a S.E.30 column. Three main fractions were obtained, the first containing pure IV. (Found; C, 53·81; H, 5·24; $C_7H_8S_2$ requires; C, 53·84; H, 5·16%); NMR (CCl_4): 6·89 (1H, d, J = 5·1 cs); 6·63 (1H, d, J = 5·1 cs); 4·39 (1H, sextet, J = 6·9 cs); 2·88 (2H, m); 1·48 (3H, d, J = 6·9 cs). The second fraction was an equimolar mixture of III and IV (NMR determined). (Found: C, 53·83; H, 5·06; $C_7H_8S_2$ requires: C, 53·84; H, 5·16%); NMR of III (CCl_4): 6·88 (1H, d, J = 5·1 cs); 6·61 (1H, d, J = 5·1 cs); 2·7 (4H, m); 2·1 (2H, m), and the third fraction a mixture of III and V (1:5, resp.), for V see below.

Rearrangement of I *with traces of benzoyl peroxide.* The procedure above was followed in the presence of benzoyl peroxide (0·5 g) and the temp kept at 140° for 5 min. By GLC the third fraction was found to contain pure V. (Found: 54·25; H, 4·31; $C_{14}H_{14}S_4$ requires: C, 54·19; H, 4·55%); NMR (CCl_4): 7·19 (1H, d, J = 5·3 cs); 6·80 (1H, d, 5·3 cs); 5·7 (1H, m); 4·9–5·1 (2H, m); 3·4 (2H, m).

Rearrangement of I *with traces of* p*-quinone.* The procedure above was followed, with ½ g of *p*-quinone present and the temp raised to 190° to start the reaction and stirring continued for another 20 min. The product distribution was analysed by GLC (Table 1).

Rearrangement of I *in benzoyl chloride.* The usual rearrangement procedure was followed, but with benzoyl chloride instead of quinoline as solvent. The product was washed with NaOH and water until neutral, the organic layer dried (Na_2SO_4), the solvent and the residual benzoyl chloride distilled off. After further purification by GLC with a S.E.30 column, VI was obtained. (Found: C, 64·35; H, 4·66; $C_{14}H_{12}OS_2$ requires: C, 64·61; H, 4·65%); NMR (CCl_4): 7·4–7·9 (6H, m); 6·93 (1H, d, J = 5·1 cs); 5·7 (1H, m); 4·9–5·1 (2H, m); 3·3 (2H, m).

Crotyl 2-thienyl sulphide (VII). The synthetic route to I was via thiophene (42·0 g, 0·5 mole) in ether (200 ml), 1·5M n-BuLi (0·5 mole, 330 ml), S (17·0 g, 0·53 mole) and crotyl bromide (68·1 g, 0·5 mole) yielding VII, b.p. 100°, n_D^{20} = 1·5757, yield 58·5 g (65%). (Found: C, 55·98; H, 5·87; $C_8H_{10}S_2$ requires: C, 56·46; H, 5·92%); NMR (CCl_4): 7·2 (1H, m); 6·9 (2H, m); 5·4 (2H, m); 3·2–3·3 (2H, m); 1·6 (3H, m).

Rearrangement of VII. The procedure for rearrangement of I was followed, but heating to 200° was necessary. Distillation gave two fractions, A: B.p.$_{0·1}$ 72–74°, and B: B.p.$_{0·1}$ 90–92°. Fraction A contained IX and X, fraction B contained pure XV. Compounds IX and X could not be separated, mixtures with ratios from 90/1 to 1/90, respectively, were obtained on attempted separation on a silica gel column. ($C_8H_{10}S_2$ requires: C, 56·46; H, 5·92; mixture 90/1 (IX/X): C, 56·06; H, 5·99; mixture 1/90 (IX/X): C, 56·04; H, 5·76%); NMR (CCl_4), IX: 6·86 (1H, d, J = 5·1 cs); 6·70 (1H, d, J = 5·1 cs); 2·83 (1H, sextet, J = 7.0 cs); 2·0 (4H, m); 1·23 (3H, d, J = 7·0 cs); a broadening in the signals at 2·83 and 1·23 is observed; X: 6·86 (1H, d, J = 5·0 cs); 6·58 (1H, d, J = 5·0 cs); 3·91 (1H, quintet, J = 7·0 cs); 2·90 (1H, quintet, J = 7·0 cs); 1·49 (3H, d, J = 7·0 cs); 1·24 (3H, d, J = 7·0 cs); the signals at 3·91 and 2·90 are broad; XV: (Found: C, 56·86; H, 5·44; $C_{16}H_{18}S_4$ requires: C, 56·80; H, 5·36%); NMR (CCl_4): 7·12 (2H, d, J = 5·1 cs); 6·77 (2H, d, J = 5·1 cs); 5·3–5·5 (4H, m); 3·2–3·4 (4H, m); 1·5–1·7 (6H, m).

Rearrangement of VII *in benzoyl chloride.* The procedure of the rearrangement of compound I in benzoyl chloride was followed. Distillation gave three fractions, the first one containing a mixture of IX and X, the second pure XV, and the third an equimolar mixture (NMR determined) of XVI and XVII, which could not be separated. Analyses of the mixture: (Found: C, 65·60; H, 6·12; $C_{15}H_{14}OS_2$ requires: C,

65·69; H, 6·15%). The NMR-spectrum (CCl_4) contained 10 groups of signals which were identified as: 7·8–8·0, 7·3–7·5, and 6·93 (broad, d, J = 5 cs) which are signals from the benzoyl and thienyl groups; the remaining signals could be due to either compound XVI or compound XVII; XVI: 5·7–6·3 (1H, m); 5·05 (1H, m); 4·8 (1H, m); 3·4–3·8 (1H, m); 1·29 (3H, d, J = 7·0 cs); XVII: 5·4–5·5 (2H, m); 3·2 (2H, m); 1·6 (3H, m).

Allyl 3-thienyl sulphide (XVIII). 1·5M n-BuLi (333 ml, 0·5 mole) was added to 3 bromothiophene (81·5 g, 0·5 mole) in anhyd ether (350 ml) at −70°. After stirring for 15 min, S (16·0 g, 0·5 g atom) was added in 3 portions. The mixture was then allowed to reach room temp, and allyl bromide (60·5 g, 0·5 mole) in ether (75 ml) was added during 15 min and stirred overnight. The mixture was poured into 500 ml water, the organic layer separated and washed with water until neutral and dried (Na_2SO_4). Distillation gave XVIII (43·5 g, 56%), b.p.$_{12}$ 104°, n_D^{20} = 1·5897. (Found: C, 53·70; H, 5·20; $C_7H_8S_2$ requires: C, 53·84; H, 5·16%); NMR (CCl_4): 6·9–7·2 (3H, m); 5·7 (1H, m); 4·8–5·1 (2H, m); and 3·3 (2H, m).

Rearrangement of XVIII. Quinoline (45 ml) was heated to 170° and VI (20·0 g, 0·13 mole) was added at once and stirred for 15 min. The mixture was cooled and poured into light petroleum (200 ml) (b.p. 40–60°) and washed 4 times with 0·1M HCl (200 ml) and water until neutral. The organic layer was dried (Na_2SO_4), the solvent stripped off, and the crude product (18·3 g) analysed by GLC (Table 1). The crude product (3·4 g) was separated on a 2·5 cm wide column, packed with 45 g silica gel, and eluated with light petroleum (b.p. <50°). Two main fractions were obtained, the first one containing XIX, (Found: C, 53·24; H, 5·01; $C_7H_8S_2$ requires: C, 53·84; H, 5·16%) and the second a mixture of XX and XXI, which was separated on a Perkin–Elmer F21 gaschromatograph, fitted with a 3 × 0·9 m S.E.30 column kept at 130°. XX: (Found: C, 53·59; H, 5·10; $C_7H_8S_2$ requires: C, 53·84; H, 5·16%); NMR (CCl_4) of XIX: 7·00 (1H, d, J = 5·3 cs), 6·79 (1H, d, J = 5·3 cs), 5·7 (1H, m), 4·9–5·2 (2H, m), 3·5 (2H, m), 2·88 (1H, s). XX: 6·99 (1H, d, J = 5·2 cs), 6·64 (1H, d, J = 5·2 cs), 4·30 (1H, m), 3·23 (2H, m), 1·48 (3H, d, J = 7·0 cs). XXI: 6·96 (1H, d, J = 5·2 cs), 6·55 (1H, d, J = 5·2 cs), 2·8 (4H, m), 2·2 (2H, m).

Rearrangement of XVIII *in benzoyl chloride.* The rearrangement of compound I in benzoyl chloride was followed, and XXIII obtained by GLC. (Found: C, 64·54; H, 4·68; $C_{14}H_{12}OS_2$ requires: C, 64·61; H, 4·65%); NMR (CCl_4): 7·4–7·9 (5H, m); 7·11 (1H, d, J = 5·1 cs); 6·88 (1H, d, J = 5·1 cs); 5·7 (1H, m); 4·9–5·1 (2H, m); 3·5 (2H, m).

2-Allyl-3-bromothiophene. 1·5M n-BuLi (0·27 mole, 170 ml) was added to 2,3-dibromothiophene (66·1 g, 0·27 mole) in anhyd ether (200 ml) at −70°. The mixture was allowed to reach room temp, and allyl bromide (32·6 g, 0·27 mole) in ether (50 ml) was added during 15 min and stirred overnight. The mixture was poured into 500 ml water, the organic layer was separated, and washed with water until neutral, and dried (Na_2SO_4). Distillation gave 2-allyl-3-bromothiophene, b.p.$_{10}$ 83–84°; n_D^{20} = 1·5711, yield 27·2 g (49%). (Found: C, 40·86; H, 3·29; Br, 40·04; S, 15·83; C_7H_7BrS requires: C, 41·37; H, 3·49; Br, 39·35; S, 15·79%); NMR (CCl_4): 7·03 (1H, d, J = 5·0 cs); 6·81 (1H, d, J = 5·0 cs); 5·6–6·2 (1H, m); 4·9–5·2 (2H, m); 3·45 (2H, m).

2-Allyl-3-mercaptothiophene (XIX). 1·5M n-BuLi (70 ml, 0·11 mole) was added to 2-allyl-3-bromothiophene (21·9 g, 0·11 mole) in anhyd ether (90 ml) at −70°. The mixture was allowed to rise to 0° and S (3·9 g, 0·12 mole) was added in 3 portions, and the mixture stirred overnight. The mixture was poured into 300 ml water and carefully acidified, the organic layer was washed with water until neutral, dried (Na_2SO_4), and the solvent stripped off. Distillation gave 8·5 g (50%) of XIX; b.p.$_{10}$ 94–97°; n_D^{20} = 1·5849, and 1·4 g (25%) of XXII; b.p.$_{10}$ 144–145°; n_D^{20} = 1·5971. (Found: C, 54·52; H, 4·90; $C_{14}H_{14}S_4$ requires: C, 54·19; H, 4·55%); NMR (CCl_4): 7·05 (1H, d, J = 5·2 cs); 6·93 (1H, d, J = 5·2 cs); ≈ 5·7 (1H, m); 4·9–5·1 (2H, m); 3·3 (2H, m).

Preparation of XXII. Compound XIX (1·3 g, 0·008 mole) was treated with I_2 (2 g) in EtOH (2 ml). Ether (10 ml) was added, the mixture washed with water, dried (Na_2SO_4), and the ether stripped off, yield 1·1 g (85%) of XXII.

Allyl (2-methyl)-3-thienyl sulphide (XXIV). The procedure for preparing XVIII was followed starting with 3-bromo-2-methylthiophene (35 g, 0·2 mole) b.p.$_{12}$ 93–95°; n_D^{20} = 1·5780, yield 26·1 g (67%). The rearrangement of XVIII was followed and the same separation methods used. Three fractions were obtained, the first containing XXV, the second a mixture of XXVI and XXVII, and the third pure XXVII (see Table 1 for GLC analyses). XXV: (Found: C, 56·07; H, 5·90; $C_8H_{10}S_2$ requires: C, 56·46; H, 5·92%); NMR (CCl_4); 6·88 (1H, s); ≈ 5·4 (1H, m); 4·8–5·0 (2H, m); 3·3 (2H, m); 3·05 (1H, broad s); 2·48 (3H, broad s). XXVIII: (Found: C, 56·68; H, 5·47; $C_{16}H_{18}S_4$ requires: C, 56·80; H, 5·36%); NMR (CCl_4): 6·89 (1H, s); ≈ 5·4 (1H, m); 4·8–5·0 (2H, m); 3·3 (2H, m); 2·30 (3H, s). Mixture of XXVI and XXVII: (Found: C, 55·75; H, 5·73; $C_8H_{10}S_2$ requires: C, 56·46; H, 5·92%); NMR (CCl_4): 6·97 (s); 6·99 (s); 4·28 (XXVI, sextet); 2·8–3·2 (XXV and XXVI, m); 2·2 (XXV, m); 1·50 (d, J = 6·8 cs, XXVI).

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