Reaction of Prop-2-ene-1-sulphonyl Chloride with Enamines: Vinylthietan 1,1-Dioxides and Allylsulphonyl Enamines as Precursors of Thiopyran 1,1-Dioxides

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The reaction of prop-2-ene-1-sulphonyl chloride with enamines afforded 3-amino-2-vinylthietan 1,1-dioxides and/or allyl aminovinyl sulphones: no 1,4-cycloadducts were detected. Both the products were converted in the presence of base into 3-amino-3,4-dihydro-2*H*-thiopyran 1,1-dioxides, whose hydrochlorides underwent deamination to the corresponding thiopyran 1,1-dioxides. The intermediacy of the sulphones in the rearrangement of the vinylthietans to the thiopyrans is suggested; also it is suggested that the cyclisation of the sulphones proceeds through an allylsulphonyl carbanion.

αβ-UNSATURATED sulphones can react with electron-rich olefins to give 1,2-cycloadducts.[1] Vinylsulphen (CH_2=CH·CH=SO_2), produced *in situ* from prop-2-ene-1-sulphonyl chloride by treatment with triethylamine has been reported[2] to afford a 1,4-cycloadduct with 1,1-diethoxyethylene in low yield. The extension of this reaction to enamines would provide a ready synthesis of 3-amino-3,4-dihydro-2*H*-thiopyran 1,1-dioxides, which could alternatively be formed from a [1,3] sigmatropic rearrangement of 3-amino-2-vinylthietan 1,1-dioxides and from a concerted cyclisation of allyl vinyl sulphones.

Reaction of Prop-2-ene-1-sulphonyl Chloride with Enamines.—The reaction of α-morpholinostyrene with prop-2-ene-1-sulphonyl chloride in the presence of triethylamine gave only the sulphone (1), identified by its ^{1}H n.m.r. spectrum (Table 2). The reactions of 1-morpholinocyclo-octene and 1-morpholino-2-methylpropene with prop-2-ene-1-sulphonyl chloride gave only the 1,2-cyclo-adducts (9) and (10), respectively. In the case of 1-morpholinocyclopentene, 1-morpholinocyclohexene, and 1-morpholinocycloheptene, both the sulphones (2)—(4), and the 1,2-cycloadducts (6)—(8) were formed. The mixture of compounds (3) and (7) was the only one which could be successfully separated by fractional crystallisation. Compound (9) was thermally unstable and underwent isomerisation to the corresponding sulphone (5) during crystallisation. The signal at τ 4·92 in the ^{1}H n.m.r. spectrum of compound (5) confirms that the double bond is β to the sulphonyl group. The two series of isomers [(1)—(5) and (6)—(10)] behaved differently towards acid. The thietans (6)—(10) readily gave the corresponding hydrochlorides, from which they could be recovered quantitatively. The sulphones (1)—(5) were instead readily hydrolysed by acidic aqueous solutions to give the corresponding ketones (11)—(15). Physical, analytical, and spectroscopic data of compounds (1)—(15) are in Tables 1 and 2.

The multiplicity of the vinyl n.m.r. signal can be used to distinguish between the sulphones (1)—(5) and the

[1] For reviews see G. Opitz, *Angew. Chem. Internat. Edn.*, 1967, **6**, 117; T. J. Wallace, *Quart. Rev.*, 1966, **20**, 67; L. L. Muller and J. Hamer, '1,2-Cycloaddition Reactions,' Interscience, New York, 1967, p. 212.

[2] W. E. Truce and J. R. Norell, *J. Amer. Chem. Soc.*, 1963, **85**, 3231.

thietans (6)—(10). The sulphones (1)—(5) give rise to a signal at τ 5·5—5·8 (2H, m, C=C-CH_2), while in products (6)—(10) protons α and α' to the sulphonyl group give rise to two signals at τ 5·0—5·3 (m) and 5·6—5·8 (m), the allylic methine proton signal being at lower field. In the cyclic sulphones (6)—(10) the relatively large value of J_{AD} indicates a preferentially antiperiplanar conformation of the two C–H bonds.

In the case of compound (7) the proton α to the sulphonyl group (H_X) is preferentially equatorial, as revealed by the value of its coupling constants with H_M and H_N (J_{XM} 5·5, $J_{XN} < 1·5$ Hz), while for compound (9), on the basis of similar arguments, H_X is axial (J_{XM} 10·9; J_{XN} 2·4 Hz).[3]

[3] A. Ohno, Y. Ohnishi, and G. Tsuchihashi, *Tetrahedron Letters*, 1969, 283.

TABLE 1

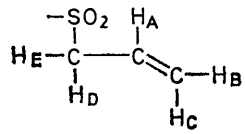
Physical and analytical data of compounds (1)—(15)

Compound	Yield (%)	M.p. (°C) (B.p.)	Found (%) C	Found (%) H	Found (%) N	Formula	Required (%) C	Required (%) H	Required (%) N
(1)	77 [a]	129 [b]	61·5	6·2	4·5	$C_{15}H_{19}NO_3S$	61·4	6·5	4·8
(2) + (6)	87 [a]	123 [b,c]	56·1	7·4	5·45	$C_{12}H_{19}NO_3S$	56·0	7·4	5·4
(3)	37 [a]	108—110 [b]	57·5	7·5	5·5	$C_{13}H_{21}NO_3S$	57·5	7·8	5·15
(4) + (8)	85 [a]	106 [b,c]	58·6	8·2	4·95	$C_{14}H_{23}NO_3S$	58·9	8·1	4·9
(5)	89 [d]	82 [b]	60·6	8·7	4·4	$C_{15}H_{25}NO_3S$	60·1	8·4	4·7
(7)	48 [a]	136 [b]	57·7	7·6	5·4	$C_{13}H_{21}NO_3S$	57·5	7·8	5·15
(9)	75 [a]	87—89 [b,e]	59·7	8·1	4·4	$C_{15}H_{25}NO_3S$	60·1	8·4	4·7
(10)	50 [a]	152—153 [b]	53·7	7·6	5·8	$C_{11}H_{19}NO_3S$	53·9	7·8	5·7
(11)	70	54—55 [b]	59·5	4·85		$C_{11}H_{12}O_3S$	58·9	5·4	
(12)	70	(210 at 1·5 mmHg) (110 at 0·1 mmHg)	51·0	6·4		$C_8H_{12}O_3S$	51·1	6·4	
(13)	70	(110—120 at 0·05 mmHg) 23 [f]	53·4	7·0		$C_9H_{14}O_3S$	53·4	7·0	
(14)	84	(150 at 0·8 mmHg)	55·1	7·4		$C_{10}H_{16}O_3S$	55·5	7·5	
(15)	70	41 [f]	57·0	7·8		$C_{11}H_{18}O_3S$	57·4	7·9	

[a] Yields refer to the products isolated from the reaction of prop-2-ene-1-sulphonyl chloride with enamines. [b] From anhydrous ethanol. [c] Figures refer to the highest m.p.s obtained for the mixtures. [d] Yields refer to the thermal isomerisation of thietan (9). [e] Crystallisation was performed as quickly as possible on a small amount of products (*ca.* 0·2 g). [f] From light petroleum (b.p. 80—120°).

TABLE 2

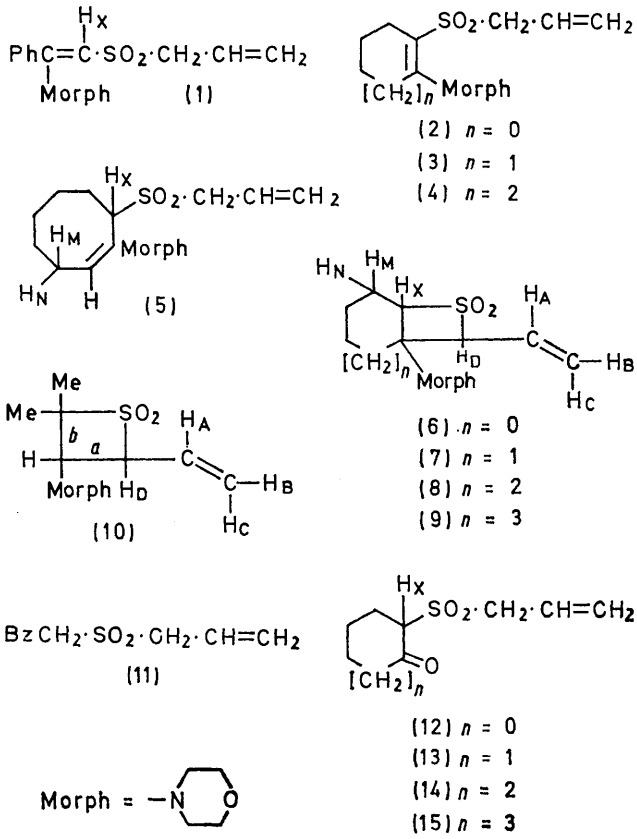
^{1}H N.m.r. data of compounds (1)—(15) [a]



Compound	H_A	H_B	H_C	H_D	H_E	H_X	Morpholine protons	Other groups	J_{AB}	J_{AC}	J_{BC}	J_{AD}
(1)		4·55(m)		5·53(m)		*ca.* 4·55(s)	6·3; 7·65(m)	2·65(m, Ph)				
(2) [b]	3·72(m)	4·65(m)		5·65(bd)			6·32; 7·48(m)	8·08(m, $[CH_2]_3$)				9
(3)	3·82(m)	4·66(dd)	4·82(dd)	5·78(d)			6·42; 7·44(m)	7·05—9(m, $[CH_2]_4$)	10	17	1·5	9
(4) [c]	3·98(m)	4·6(m)		5·45(m)			6·25; 7·3(m)	7·4—8·9(m, $[CH_2]_5$)	10	17	1·7	
(5)	4·1(m)	4·6(dm)	4·73(dm)	6·07(dq)	5·82(dq) [d]	6·25(m) [e]	6·28; 6·9; 7·4(m)	4·92(t, =CH) [f] 7·5—9(m, $[CH_2]_5$)	9	17	1	8·3
(6) [b]	4·04(m)	4·65(m)		5·05(dd) [g]		5·6	6·32; 7·48(m)	8·1(m, $[CH_2]_3$)				9
(7)	4·04(dt)	4·58(m)	4·6(m)	5·27(d)		5·8(bd) [h]	6·38; 7·44(m)	7·6—9(m, $[CH_2]_4$)	10·5	16·5		9
(8) [c]	3·98(m)	4·6(m)		5·0(bd)			6·25; 7·3(m)	7·4—8·9(m, $[CH_2]_5$)	10	17		9·5
(9) [i]	3·74(m)	4·61(m)	4·65(m)	5·6(d)		5·82(bd)	6·3; 6·9(m)	7·5—9(m, $[CH_2]_6$)	10	17·1	1·2	10·3
(10)	3·77(m)	4·52(dd)	4·67(dd)	5·36(t)			6·33; 7·6(m)	7·04(d, CH–Morph.) [k] 8·35(s, CH_3); 8·43(s, CH_3)	9	16·5	1·5	9
(11)	3·7—4·8(m)			5·95(m)				1·8—2·5(Ph) 5·35(s, $CO-CH_2-SO_2$)				
(12)	4·06(m)	4·45(dm)	4·40(dm)	6·16(m)		5·75(dd) [l]		7·2—8·3(m, $[CH_2]_3$)	10·5	16		
(13)	4·1(m)	4·50(m)	4·53(m)	6·16(m)		5·97(m) [m]		7·1—8·4(m, $[CH_2]_4$)	10·5	17		
(14)	4·15(m)	4·42(dm)	4·46(dm)	6·1(m)				6·9—8·8(m, $[CH_2]_5$)	9·5	17·5		
(15)	4·06(m)	4·46(dm)	4·50(dm)	6·1(m)				6·9—9(m, $[CH_2]_6$)	10	17		

[a] τ Values in $CDCl_3$ relative to tetramethylsilane; bd = broad doublet, d = doublet, dd = double doublet, dq = double quartet, dm = double multiplet, m = multiplet, s = singlet, t = triplet; $|J|$ in Hz. [b] 40:60 Mixture of (2) and (6). [c] 50:50 Mixture of (4) and (8). [d] J_{DE} 11·5; J_{AE} 6·5. [e] Covered by morpholine peaks. [f] J(=CH–CH_M) = J(=CH–CH_N) = 8·4. [g] J_{DB} 1·5. [h] H_M τ 7·75; H_N 8·05; J_{XM} 5·5. [i] Measured at −20 °C to avoid ring opening to (5). [j] H_M τ 7·8; H_N 8·04; J_{XM} 10·9; J_{XN} 2·4. [k] J(CH–CH) 8·5. [l] J_{XM} 13·5; J_{XN} 7·5. [m] J_{XM} 13·5; J_{XN} 7·5.

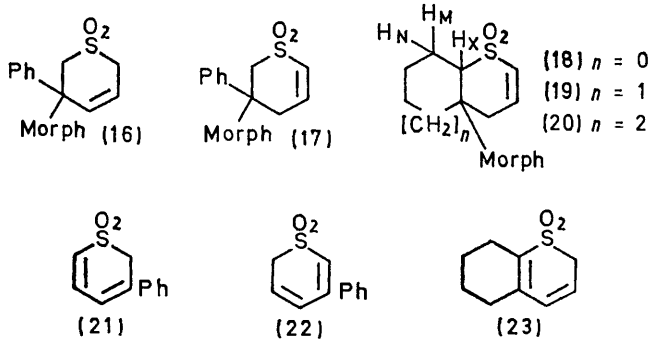
The present results show that the vinylsulphen intermediate does not undergo 1,4-cycloadditions with enamines; instead, as expected, it gives rise to acylation



and 1,2-cycloaddition products, the ratio of which strongly depends upon the nature of the enamine. The sulphone (3) was a primary product and was not formed from the dioxide (7), which was unchanged after treatment for several days with ether–triethylamine at 0°.

Interestingly, both for thietan 1,1-dioxide derivatives (6)—(10) and the sulphones (1)—(5) there was no evidence for isomerisation of the allylsulphonyl into the propenylsulphonyl group, even though such a [1,3] proton shift is known [5] to occur under basic conditions.

Aminodihydrothiopyran 1,1-Dioxides.—The sulphones (1) and (3) undergo cyclisation to the dihydrothiopyrans (17) and (19) when heated in dioxan in the presence of triethylamine. The 2-vinylthietan 1,1-dioxide (7) is also isomerised to the product (19) by analogous treatment. Similarly, the mixtures (2) + (6) and (4) + (8) give products (18) and (20) in 71 and 73% yield, respectively. Neither the cyclo-octene (5) nor the thietan (9) undergo cyclisation to the corresponding dihydrothiopyran under these conditions.



Although Δ^3-dihydrothiopyrans are known to be more stable than the Δ^2-dihydro-isomer,[6] the structures for the sulphones (17)—(20) are supported by their ^{1}H n.m.r. spectra. In the spectrum of the sulphone (17) the signal for the C-6 methylene group is present as an AB quartet at τ 6·33 while that for the allylic methylene is present as a distorted double doublet at τ 7·3. It was expected instead that for the isomer (16) the allylic methylene signal would be at lower field than the C-6 methylene signal. This expectation is also supported by the chemical shifts of the methylenes in some 3-amino-2,3-dihydrothiopyran 1,1-dioxide derivatives.[7] We have confidently assigned the Δ^2-dihydrothiopyran 1,1-dioxide structure to products (18)—(20) also, even though

TABLE 3

Physical and analytical data of the thiopyran 1,1-dioxides

Compound	Yield (%)	M.p. (°C)	Found (%) C	H	N	Formula	Requires (%) C	H	N	HCl salt M.p. (°C)
(17)	90	178—180 [a]	61·3	6·5	4·7	$C_{15}H_{19}NO_3S$	61·4	6·5	4·8	212 [a,e]
(18)	71	129 [a]	56·2	7·45	5·4	$C_{12}H_{19}NO_3S$	56·0	7·4	5·4	
(19)	50	180 [a]	57·7	7·7	5·3	$C_{13}H_{21}NO_3S$	57·5	7·8	5·15	191 [a]
(20)	73	156 [a]	59·0	8·0	4·7	$C_{14}H_{23}NO_3S$	58·9	8·1	4·9	
(21) + (22)	74	74—76 [b]								
(23)	84	83 [c,d]	58·6	6·7		$C_9H_{12}O_2S$	58·7	6·6		

[a] From ethanol. [b] Lit.,[9] 74—76°; after washing with ether and recrystallisation from MeOH pure (21) had m.p. 100—101° (lit.,[9] 100—101°). [c] From water. [d] $\lambda_{max.}$ (EtOH) 235 (log ε 3·24) and 268 nm (3·54). [e] From ethanol–ether.

No evidence is at present available to decide whether the acylation products (1), (2), and (4) are also primary products or if they originate from the base-induced ring opening (see ref. 4) of their corresponding cyclic isomers (5), (6), and (8).

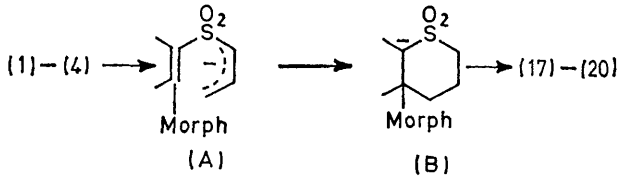
[4] J. N. Wells and F. S. Abbott, *J. Medicin. Chem.*, 1966, **9**, 489; J. J. Looker, *J. Org. Chem.*, 1966, **31**, 2973.
[5] H. J. Backer and G. J. De Jong, *Rec. Trav. chim.*, 1948, **67**, 884.
[6] E. A. Fehnel and P. A. Lackey, *J. Amer. Chem. Soc.*, 1951, **73**, 2473; E. A. Fehnel, *ibid.*, 1952, **74**, 1569.
[7] G. Opitz and F. Schweinsberg, *Angew. Chem.*, 1965, **77**, 811.

signals due to the methine proton α to the sulphonyl group and the allylic methylene protons are not always easily distinguished from resonances due to the morpholine and cycloaliphatic protons. However, by analogy with the sulphone (17), the integration shows that the methine proton signal is present at lower field than that of the allylic methylene.

The sulphonyl group of the thiopyran ring occupies an equatorial position in (19) as deduced from the J_{aa} and J_{ae} values of H_X with H_M and H_N (10·5 and 5·5 Hz, respectively).

Confirmation of the six-membered ring structure of the sulphones (17)—(20) was obtained by deamination of the hydrochlorides of (17) and (19) to the corresponding thiopyran derivatives (21)—(23). The thiopyran (23) is a single pure isomer whose structure was assigned on the basis of ^{1}H n.m.r. and u.v. spectra.[8] Deamination of the sulphone (17) gave a 70 : 30 mixture of the isomers (21) and (22), the properties of which have been previously described.[9]

The conversion of the sulphones (1)—(4) into the β-morpholinothiopyrans (17)—(20) can be interpreted as a thermally allowed electrocyclic reaction between the *termini* of the enaminic double bond and the allylsulphonyl portion in the intermediate anion (A). This reaction is similar to the recently reported cyclisations of pentadienyl, nonatetraenyl,[10] and other allylic anions.[11]



Conversion of the thietans (6)—(8) into the thiopyrans (18)—(20) might proceed (i) *via* the intermediacy of the sulphones (2)—(4) or (ii) *via* a thermal concerted [1,3] sigmatropic rearrangement. Few thermal [1,3] sigmatropic shifts are known and such processes generally involve such high activation energies that a non-concerted path is not thermodynamically unreasonable.[12]

3-Aminothietan 1,1-dioxides are known [4] to undergo a ready ring cleavage in basic media, and we have further observed that compounds (6), (7), and (9) are thermally unstable even in the absence of added base, while the 2-vinylthietan (10), which was expected not to undergo ring opening to the corresponding sulphone (*a* bond breaking),* was recovered unchanged after 22 h under reflux in dioxan and in the presence of triethylamine.

Thus, the intermediacy of the sulphones (1)—(4) in the conversion of 2-vinylthietan 1,1-dioxides into morpholinodihydrothiopyran 1,1-dioxides is reasonable.

EXPERIMENTAL

Enamines.—1-Morpholinocyclopentene,[14] 1-morpholinocyclohexene,[14] 1-morpholinocycloheptene,[14] and 1-morpholinocyclo-octene [15] were prepared as previously. 1-Morpholino-2-methylpropene was prepared, as for other aldehyde enamines,[16] from 2-methylpropanal (1 mol. equiv.), morpholine (2 mol. equiv.), and anhydrous potassium carbonate (1 mol. equiv.) (overnight at room temperature). The *product* (63%) had b.p. 68—70° at 20 mmHg; to avoid polymerisation the distillation was performed below 120°. Morpholinostyrene was prepared by slowly adding at 0° and under nitrogen, titanium tetrachloride (1 mol. equiv.) to a stirred solution of acetophenone (1 mol. equiv.) and morpholine (1 mol. equiv.) in light petroleum (800 ml). After 24 h at room temperature the solution was filtered, evaporated, and distilled; b.p. 98° at 0·2 mmHg (lit.,[14] 89° at 0·3 mmHg).

Reaction of Prop-2-ene-1-sulphonyl Chloride with Enamines.—Prop-2-ene-1-sulphonyl chloride [17] (4·2 g, 3 mmol) in anhydrous ether (10 ml) was added dropwise to a stirred and cooled (−2° to 0°) solution of the appropriate enamine (3 mmol) and triethylamine (3 mmol) in ether (150 ml). After 1 h at room temperature the products were isolated. In the case of the sulphone (1) the solid was taken up in water (30 ml) and extracted with chloroform. The ethereal mother liquors and the chloroform extract were evaporated, the residue was washed with ether, and was crystallised. For compounds (2), (4), (6), (8), and (9) the solvent was evaporated and the residue was taken up in water (30 ml), collected, and crystallised. The mixture of (3) and (7) was collected and washed with anhydrous ether (*ca.* 300 ml) and then with water; crystallisation afforded compound (7). The ether extract and the reaction solution were combined and evaporated to leave a solid, m.p. 99—107°, which was shown by ^{1}H n.m.r. analysis to be (3) contaminated by (7). The sulphone (3) could be obtained by cooling a saturated ethereal solution of this product for 2 days. Compound (10) was collected, washed with water, and crystallised; another crop was obtained from the mother liquors.

Hydrolysis of the Sulphones (1)—(5).—The sulphones (1)—(5) were hydrolysed at room temperature with 10% hydrochloric acid: reaction times were 6, 5, 21, 6, and 24 h, respectively. Extraction with ether of the acidic solutions and distillation of the residue afforded pure allylsulphonyl ketones (11)—(15).

Morpholinodihydrothiopyran 1,1-Dioxides.—A solution of the sulphones (1) or (3) or (7), or of the mixtures [(2) + (6), and (4) + (8)] (2 mmol) and triethylamine (2 mmol) in anhydrous dioxan was heated under reflux for 7 h. Compound (17) was obtained by evaporating the solvent to half

* *b* Bond breaking was not observed, as in other cases [13] where the required incipient carbanion could be stabilised by electronegative substituents.

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[9] G. Pagani, *Gazzetta*, 1967, **97**, 1518; S. Bradamante, A. Mangia, and G. Pagani, *Tetrahedron Letters*, 1970, 3381.

[10] R. B. Bates and D. A. McCombs, *Tetrahedron Letters*, 1969, 977; D. H. Hunter and S. K. Sim, *J. Amer. Chem. Soc.*, 1969, **91**, 6202; P. J. Garratt and K. A. Knapp, *Chem. Comm.*, 1970, 1215.

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[12] R. B. Woodward and R. Hoffmann, 'The Conservation of Orbital Symmetry,' Academic Press, New York, 1970, p. 120.

[13] S. Maiorana and G. Pagani, *Chimica e Industria*, 1971, **53**, 358.

[14] G. Domschke, *J. prakt. Chem.*, 1966, **32** (3—4), 144.

[15] J. Kennedy, A. Lewis, N. J. McCorkindale, and R. A. Raphael, *J. Chem. Soc.*, 1961, 4945.

[16] R. Dulov, E. Elkik, and A. Veillard, *Bull. Soc. chim. France*, 1960, 970.

[17] M. A. Belous and I. Ya. Postovskii, *Zhur. obshchei Khim.*, 1950, **20**, 1701.

volume under reduced pressure and adding an equal volume of 15% hydrochloric acid. The resulting solution was extracted with ether and then made alkaline with ammonia; the oil which separated readily crystallised on washing with ether, affording a crude product which could be recrystallised. Compounds (18)—(20) were obtained by removing the solvent under reduced pressure and crystallising the residue. The hydrochloride of (17) was prepared by bubbling anhydrous hydrogen chloride into acetone solution of the corresponding base and was isolated (80%) by collection of the precipitated solid. The hydrochloride of (19) was prepared similarly and was isolated (88%) by diluting the acetone solution with ether (ratio 2 : 3), decanting the solution, and taking up the residue in dry acetone.

Pyrolysis of Morpholinothiopyran 1,1-*Dioxide Hydrochlorides.*—The hydrochlorides of (17) and (19) were sublimed for 3 min at 220° and 0·5 mmHg and at 190—195° and 15 mmHg, respectively. The product and the residue were treated with 10% hydrochloric acid (7—8 ml) and the collected solid was washed with water and crystallised.

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