3-Amino-5,6-dihydro-4*H*-thiopyran 1,1-Dioxides. Reactivity with Diethyl Azodicarboxylate and Some α,β-Unsaturated Ketones

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The secondary enamines derived from 5,6-dihydro-2*H*-thiopyran-3(4*H*)-one 1,1-dioxide are in tautomeric equilibrium with their imine forms. With the title electrophiles, either they react at nitrogen or show the usual reactivity at the β-carbon atom of the enamine system. With electrophilic olefins carbocyclization compounds are also formed.

In connection with our studies of enamino sulphones,[1,2] we have turned our attention to secondary enamino sulphones derived from 5,6-dihydro-2*H*-thiopyran-3(4*H*)-one 1,1-dioxide (**1**). Interest in such compounds arises from the fact that in principle, two tautomeric equilibria may be present, that is the imine–enamine equilibrium[3,4] and the double bond isomerism[1,2] in the enamine form.

Secondary enamines derived from hydrocarbon aldehydes and ketones are in equilibrium with their corresponding imine forms, the latter prevailing over the former in most cases by amounts depending, *inter alia*, on the nature of the amine moiety and on the solvent.[3] In contrast, with the enamino ketones the enamine form predominates over the corresponding imine isomer, owing to the mesomeric effect of the carbonyl group.[5,6]

As to reactivity, almost all the above mentioned compounds react with electrophilic reagents at their β-carbon atom, that is in the enamine form. In some cases however, as for instance when the electrophile is an α,β-unsaturated acid chloride, the site of attack is nitrogen with formation of enamides.[7] In this case however, the reactive isomer seems to be the enamine.

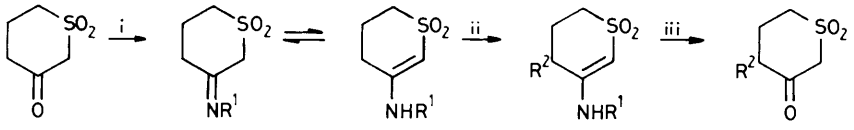
Results and Discussion

The primary amines chosen for condensation with the ketone (**1**) are listed in Scheme 1. t-Butylamine and *p*-nitroaniline did not react under the same conditions used for the other amines. Difficulties were also encountered for aniline for which yields were low.

Compounds (**2**) and (**3**), prepared from ketone (**1**) and cyclohexylamine and benzylamine respectively are imines when examined in the solid state and immediately after isolation, their i.r. spectra showing the presence of a strong band at 1 650 cm^{-1}, attributable to the C=N stretching absorption. However, the imine forms rapidly isomerize into the corresponding enamines, as indicated by disappearance of the band at 1 650 cm^{-1} and appearance of a strong band at 1 590 cm^{-1} for the C=C stretching band. Compounds (**2**) and (**3**) are also enamines in solution, their vinylic proton signals, both of area 1, resonating at 5.0 and 5.1 p.p.m. respectively.

Compounds (**4**)—(**8**), in which the amino moiety is aromatic, behave differently in different physical states. In the solid state, all but compound (**4**) are enamines, as indicated by the presence of the NH and C=C stretching bands, the latter at 1 610, 1 590, 1 600, 1 600, and 1 601 cm^{-1} respectively. Compound (**4**) is a mixture of enamine and imine forms, in contrast to the parallel derivative, in which the sulphone group is substituted for a carbonyl group, which is an enamine.[8] In chloroform solution, an equilibrium is rapidly established for all compounds (**4**)—(**8**), in which the imine form predominates over the corresponding enamine forms by amounts varying from 52 to 85% (see Table). Unfortunately measurements in apolar solvents were not possible, as the enamino sulphones were insoluble, whereas ^1H n.m.r. measurements in deuteriated polar solvents lead to perdeuteriation of the systems.

The i.r. spectra deserve a further comment. All the enamine forms show a strong band in the range 1 540—1 510 cm^{-1}, which is shifted towards lower wavenumber, 1 500—1 490 cm^{-1} in solution. Deuteriation of the NH group, although partial, decreases its intensity but it has no effect on its position. These data seem to be consistent with the assignment of this particular band to the NH bending vibration, coupled or not.



(**1**)

(**2**) R^1 = c-C_6H_{11}
(**3**) R^1 = CH_2Ph
(**4**) R^1 = 4-$H_2NC_6H_4$
(**5**) R^1 = 4-$MeOC_6H_4$
(**6**) R^1 = 4-MeC_6H_4
(**7**) R^1 = Ph
(**8**) R^1 = 4-ClC_6H_4

(**9**)* R^1 = c-C_6H_{11}
(**10**) R^1 = CH_2Ph
(**11**)* R^1 = 4-MeC_6H_4
(**12**)* R^1 = 4-ClC_6H_4
R^2 = $EtO_2C-\underset{|}{N}-NH-CO_2Et$

(**13**)

Scheme 1. *Reagents:* i, R^1NH_2, C_6H_6, 80 °C, 5 h; ii, $EtO_2C-N=N-CO_2Et$, EtOH, room temperature, 1 wk; iii, HCl-H_2O, room temperature, 24 h. * Compounds were not isolated.

Table. Percentage tautomeric forms and amino-group pK_a constant values

Entry	% of Enamine form	% of Imine form	pK_a of RNH_2 [a]
(2)	100	0	10.64
(3)	100	0	9.35
(4)	48	52	6.16
(5)	40	60	5.34
(6)	32	68	5.10
(7)	30	70	4.60
(8)	15	85	3.98

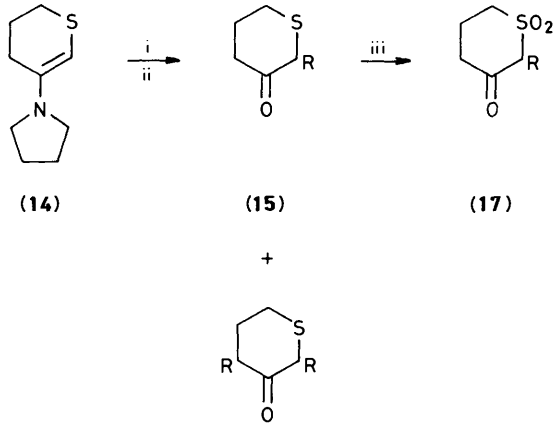
[a] J. W. Smith, in 'The Chemistry of the Amino Group,' ed. S. Patai, Interscience Publishers, John Wiley & Sons, London, 1968, p. 182.

The last column of the Table reports the pK_a values for the amine moiety, for comparison with the enamine/imine ratios in the resulting mixtures. The lower the pK_a value, the less the possibility for the nitrogen lone pair to conjugate with the enamine double bond and hence the reduced presence of the enamine form in the equilibrium mixture.

The reactivity of compounds (**2**)—(**8**) towards the same electrophiles used in our previous works[1,2] for the tertiary enamino sulphones has been examined.

No reactivity was observed at the β-carbon atom, except in the case of diethyl azodicarboxylate (DEAD). In this example the enamino sulphones (**2**), (**3**), (**6**), and (**8**) reacted at C-4, to yield, after hydrolyses of the reaction mixtures, the hydrazino oxo sulphone (**13**).[1] Of the enamine intermediates (**9**), (**10**), (**11**), and (**12**), only compound (**10**) was separated and characterized.

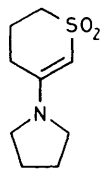
The structure of the oxo sulphone (**13**) was established by comparison with its regioisomer (**17**), obtained by reaction of 3-pyrrolidin-1-yl-5,6-dihydro-4*H*-thiopyran (**14**),[9,10] with DEAD, followed by hydrolysis of the reaction mixture and oxidation of the resulting oxo sulphide (**15**) (Scheme 2). In this reaction the double addition product (**16**) was also formed.



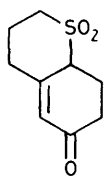
Scheme 2. *Reagents:* i, $EtO_2C-N=N-CO_2Et$, EtOH, room temperature, 1 week; ii, $HCl-H_2O$, room temperature, 24 h; iii, $ArCO_3H$, benzene, room temperature, 2 d; R = $EtO_2C-\underset{|}{N}-NH-CO_2Et$.

A series of reactions have also been performed on the secondary enamino sulphone (**3**) and on the tertiary enamino sulphone (**18**) with α,β-unsaturated ketones, such as methyl vinyl ketone, phenyl vinyl ketone, and phenyl styryl ketone.

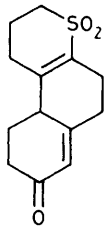
Cycloaddition products, (**19**) and (**20**), were isolated only



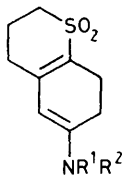
(**18**)



(**19**)



(**20**)



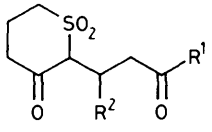
(**21**)* $R^1 = H$, $R^2 = CH_2Ph$

(**22**) $R^1R^2 = (CH_2)_4$

with methyl vinyl ketone, in buffer solution (see Experimental section, Procedure b). The bicyclic compound (**19**) derived from C-2 alkylation of the substrates, followed by intramolecular aldolization–crotonization reaction, whereas the tricyclic compound (**20**) was formed by the attack of methyl vinyl ketone onto the fully conjugated dienamines (**21**) and (**22**) respectively, formed in the reaction medium, and subsequent hydrolysis.

Unfortunately the dienamine (**21**) could not be prepared from compound (**19**) and benzylamine, whereas the dienamine (**22**) was easily prepared from pyrrolidine and the ketone (**19**). The latter dienamine was treated with methyl vinyl ketone to yield the expected tricyclic system (**20**), after work-up. The same is likely to occur with the secondary enamino sulphone (**3**).

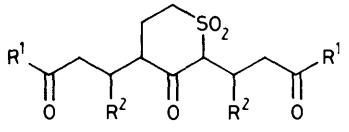
Slightly different behaviour between the two enamine systems was observed when condensation between the reagents was carried out in benzene, with elimination of the water formed (see Experimental section, Procedure a). After hydrolysis of the reaction mixture, enamine (**3**) yielded the same compounds (**19**) and (**20**) as above, whereas enamine (**18**) furnished the cyclic adduct (**19**), together with the open-chain diketone (**23**).



(**23**) R^1 = Me, R^2 = H

(**24**) R^1 = Ph, R^2 = H

(**25**) $R^1 = R^2$ = Ph



(**26**) R^1 = Me, R^2 = H

(**27**) R^1 = Ph, R^2 = H

With phenyl vinyl ketone and styryl vinyl ketone neither a cyclic product nor a dihydropyran type compound, the latter usually formed when the substrate is a cycloalkanone enamine,[3] were isolated. Instead, only the 1,4-diketones (**24**) and (**25**) were obtained and with phenyl vinyl ketone the double addition product (**27**) was also formed.

Reactions were also performed on the ketone (**1**) with the same electrophiles, to make a comparison with the reactivities of the substrates (**3**) and (**18**). In all cases, only open chain products were obtained, namely the ketones (**23**) and (**26**) with methyl vinyl ketone, the diketone (**24**) with phenyl vinyl ketone, and the diketone (**25**) with phenyl styryl ketone.

Experimental

^{1}H N.m.r. spectra were recorded on a Bruker WP-80 spectrometer, with tetramethylsilane as internal standard, using $CDCl_3$ solutions, unless otherwise stated. I.r. spectra were recorded on a Perkin-Elmer 297 spectrophotometer for Nujol mulls. The mass spectra were recorded at 70 eV on a WG-77 double focusing spectrometer. For chromatographic columns extra pure silica (Merck 70—230 mesh ATMS) was used as stationary phase. Light petroleum was in the b.p. range 30—50 °C unless otherwise stated.

Preparation of 3-*Amino*-5,6-*dihydro*-4H-*thiopyran* 1,1-*Dioxides: General Procedure.*—The enamines (**2**)—(**8**) were prepared by Stork condensation[3] of 5,6-dihydro-2*H*-thiopyran-3(4*H*)-one 1,1-dioxide (**1**) and the respective primary amines, in benzene under reflux for 5 h. After elimination of the solvent, the crude product was purified by crystallization.

3-*Cyclohexylamino*-5,6-*dihydro*-4H-*thiopyran* 1,1-*dioxide* (**2**) (86%), m.p. 143 °C (light petroleum) (Found: C, 58.0; H, 8.7; N, 6.0. $C_{11}H_{19}NO_2S$ requires C, 57.6; H, 8.3; N, 6.1%); $\nu_{max.}$(Nujol) 3 320, 1 540 (NH), 1 590 (C=C), 1 260, 1 240 (C–N), and 1 305 and 1 100 cm^{-1} (SO_2); $\nu_{max.}$($CHCl_3$) 3 430, 1 500 (NH), 1 600 (C=C), and 1 310 and 1 100 cm^{-1} (SO_2); δ_H 5.0 (1 H, s, vinyl H), 4.1 (1 H, br t, NH), 3.8—2.8 (3 H, m, NCH and CH_2SO_2), 2.8—2.2 (4 H, m, $CH_2CH_2CH_2SO_2$), and 2.2—0.8 [10 H, m, $(CH_2)_5$].

3-*Benzylamino*-5,6-*dihydro*-4H-*thiopyran* 1,1-*dioxide* (**3**) (89%), m.p. 160—161 °C (EtOH) (Found: C, 60.3; H, 6.2; N, 5.8. $C_{12}H_{15}NO_2S$ requires C, 60.7; H, 6.4; N, 5.9%); $\nu_{max.}$ 3 335, 1 540 (NH), 1 605 (C=C), 1 595, 1 495, 725 (Ph), 1 235 (C–N), and 1 305, 1 100, and 1 085 cm^{-1} (SO_2); $\nu_{max.}$($CDCl_3$) 3 430, 1 495 (NH), 1 610 (C=C), 1 600 (Ph), and 1 305 and 1 100 cm^{-1} (SO_2); δ_H 7.35 (5 H, s, Ph), 5.1 (1 H, s, vinyl H), 4.6 (1 H, br t, NH), 4.1 (2 H, d, CH_2Ph), 3.1 (2 H, m, CH_2SO_2), and 2.4 (4 H, m, $CH_2CH_2CH_2SO_2$).

3-(4-*Aminophenyl*)*amino*-5,6-*dihydro*-4H-*thiopyran* 1,1-*dioxide* (**4**) (15%), m.p. 160 °C (EtOH–light petroleum) (Found: C, 56.0; H, 5.6; N, 11.3. $C_{11}H_{14}N_2O_2S$ requires C, 55.5; H, 5.9; N, 11.7%); $\nu_{max.}$(Nujol) 3 400, 3 370, 3 320, 1 510 (NH), 1 610 (C=C), 1 600, 1 585 (Ar), 1 300, 1 090 (SO_2), and 1 230 cm^{-1} (C–N); δ_H ($CDCl_3$ + CD_3CN) 7.25—6.50 (4 H, m, ArH), 6.2 (0.5 H, br s, NH), 5.4 (0.5 H, s, vinyl H), 4.1, 4.0 (1 H, 2 m, N=C–CH_2SO_2), and 3.9—2.0 (8 H, m, $CH_2CH_2CH_2SO_2$ and NH_2).

3-(4-*Methoxyanilino*)-5,6-*dihydro*-4H-*thiopyran* 1,1-*dioxide* (**5**) (87%), m.p. 171—172 °C (benzene) (Found: C, 56.7; H, 5.5; N, 5.1. $C_{12}H_{15}NO_3S$ requires C, 56.9; H, 5.9; N, 5.5%); $\nu_{max.}$(Nujol) 3 300, 1 510 (NH), 1 590 (C=C), 1 605, 1 580 (Ar), 1 300, 1 090 (SO_2), and 1 230 cm^{-1} (C–N); $\nu_{max.}$($CDCl_3$) 3 420, 3 150, 1 500 (NH), 1 655 (C=N), 1 615 (C=C), 1 605 (Ar), and 1 315, 1 120, and 1 100 cm^{-1} (SO_2); δ_H (CD_3CN) 7.2—6.6 (4 H, m, ArH), 5.7 (0.4 H, br s, NH), 5.4 (0.4 H, s, vinyl H), 4.1, 4.0, 3.9 (4.2 H, 2 m and 2 s, N=C–CH_2SO_2 and OMe), 3.3 (2 H, m, CH_2SO_2), and 3.0—2.0 (4 H, m, $CH_2CH_2SO_2$).

3-(p-*Toluidino*)-5,6-*dihydro*-4H-*thiopyran* 1,1-*dioxide* (**6**) (98%), m.p. 172 °C (Found: C, 60.4; H, 6.4; N, 5.5. $C_{12}H_{15}NO_2S$ requires C, 60.7; H, 6.4; N, 5.9%); $\nu_{max.}$(Nujol) 3 280, 1 510 (NH), 1 600 (C=C), 1 590, 1 585, 720 (Ar), 1 305, 1 090 (SO_2), and 1 235 cm^{-1} (C–N); $\nu_{max.}$($CDCl_3$) 3 380, 3 180, 1 490 (NH), 1 660 (C=N), 1 610 (C=C), 1 590 (Ar), and 1 320 and 1 120 cm^{-1} (SO_2); δ_H 7.45—6.5 (4 H, m, ArH), 6.0 (0.3 H, br s, NH), 5.6 (0.3 H, s, vinyl H), 4.1 (0.65 H, m, syn N=C–CH_2SO_2), 4.0 (0.75 H, m, *anti* N=C–CH_2SO_2), 3.25 (2 H, m, CH_2SO_2), and 3.0—1.9 (7 H, m and s, $CH_2CH_2CH_2SO_2$ and Me).

3-*Anilino*-5,6-*dihydro*-4H-*thiopyran* 1,1-*dioxide* (**7**) (40%), m.p. 75 °C (EtOH–light petroleum) (Found: C, 56.2; H, 6.0; N, 6.3. $C_{11}H_{13}NO_2S$ requires C, 56.9; H, 6.2; N, 6.6%); $\nu_{max.}$(Nujol) 3 300, 1 510 (NH), 1 655 (C=N), 1 600 (C=C), 1 585, 700 (Ph), 1 235 (C–N), and 1 310 and 1 120 cm^{-1} (SO_2); $\nu_{max.}$($CDCl_3$) 3 420, 3 360, 1 500 (NH), 1 660 (C=N), 1 615 (C=C), 1 590 (Ph), and 1 310 and 1 120 cm^{-1} (SO_2); δ_H 7.6—7.0 (3 H, m, *m*- and *p*-ArH), 7.0—6.5 (2 H, m, *o*-ArH), 6.15 (0.3 H, br s, NH), 5.6 (0.3 H, s, vinyl H), 4.1 (0.65 H, m, *syn* N=C–CH_2SO_2), 3.9 (0.75 H, m, *anti* N=C–CH_2SO_2), 3.25 (2 H, br m, CH_2SO_2), and 2.95—1.80 (4 H, m, $CH_2CH_2CH_2SO_2$).

3-(4-*Chloroanilino*)-5,6-*dihydro*-4H-*thiopyran* 1,1-*dioxide* (**8**) (88%), m.p. 182 °C (Found: C, 50.9; H, 4.7; N, 4.8. $C_{11}H_{12}ClNO_2S$ requires C, 51.2; H, 4.7; N, 5.4%); $\nu_{max.}$(Nujol) 3 260, 1 510 (NH), 1 601 (C=C), 1 590, 1 585, 1 485, 725 (Ar), 1 310, 1 090 (SO_2), and 1 240 cm^{-1} (C–N); $\nu_{max.}$($CDCl_3$) 3 360, 3 140, 1 490 (NH), 1 650 (C=N), 1 615 (C=C), 1 595 (Ar), and 1 320 and 1 120 cm^{-1} (SO_2); δ_H 7.75—6.5 (4 H, m, ArH), 5.75 (0.15 H, br s, NH), 5.6 (0.15 H, s, vinyl H), 4.1 (0.85 H, br s, *syn* N=C–CH_2SO_2), 3.85 (0.85 H, br s, *anti* N=C–CH_2SO_2), 3.25 (2 H, m, CH_2SO_2), and 2.9—1.8 (4 H, m, $CH_2CH_2CH_2SO_2$).

Reaction of 3-*Amino*-5,6-*dihydro*-4H-*thiopyran* 1,1-*Dioxides with Diethyl Azodicarboxylate: General Procedure.*—Diethyl azodicarboxylate (1.7 mmol) was added to a solution of the enamine (1.7 mmol) in anhydrous EtOH and the mixture was set aside at room temperature for 5 days. After elimination of the solvent, the residue was crystallized from EtOH. When the residue was an oil, it was hydrolysed in EtOH with 10% hydrochloric acid, at room temperature for 24 h. The mixture was then extracted with chloroform to give the already known ketone (**13**),[1] in the following yields: 90% from (**2**) and (**3**), 73% from (**6**), and 32% from (**8**).

4-(N,N′-*Diethoxycarbonylhydrazino*)-3-*benzylamino*-5,6-*dihydro*-4H-*thiopyran* 1,1-*dioxides* (**10**) (96%), m.p. 138 °C (EtOH) (Found: C, 52.8; H, 5.8; N, 10.2. $C_{18}H_{25}N_3O_6S$ requires C, 52.5; H, 6.1; N, 10.2%); $\nu_{max.}$(Nujol) 3 320, 3 240, 1 540 (NH), 1 710 (CO), 1 595, 1 490, 730 (Ph), 1 600 (C=C), 1 285, 1 090 (SO_2), and 1 250 and 1 230 cm^{-1} (C–N, C–O); δ_H 7.3 (6 H, s and br s, ArH and NH), 6.3 (1 H, br s, NH), 5.1, 4.6 (2 H, s and br m, vinyl H and C*H*–N–CO_2Et), 4.4—3.95 (6 H, q and d, CH_2Me and CH_2Ph), 4.2 (q, CH_2Me), 3.2 (2 H, m, CH_2SO_2), 3.0—2.0 (2 H, m, $CH_2CH_2SO_2$), and 1.25 (6 H, dt, Me).

2-(N,N′-*Diethoxycarbonylhydrazino*)-5,6-*dihydro*-2H-*thiopyran*-3(4H)-*one* (**15**). Diethyl azodicarboxylate (0.83 g, 4.8 mmol) was added to a solution of 3-pyrrolidin-1-yl-5,6-dihydro-4*H*-thiopyran (**14**)[10] (0.81 g, 4.8 mmol). After hydrolysis, the oily residue was chromatographed on silica gel to give compound (**15**) (0.28 g, 20%), m.p. 56—58 °C (EtOH–light petroleum) (Found: C, 45.0; H, 6.5; N, 9.3. $C_{11}H_{18}N_2O_5S$ requires C, 45.5; H, 6.2; N, 9.6%); $\nu_{max.}$(Nujol) 3 270, 1 510 (NH), and 1 690 cm^{-1} (CO); δ_H 6.7 (1 H, br s, NH), 6.1 (1 H, s, CHS), 4.3 (4 H, q, 2 CH_2Me), 3.5—2.3 (4 H, m, CH_2CH_2S), 2.1—1.6 (2 H, m, CH_2CO), and 1.25 (6 H, t, 2 Me). The last fraction furnished 2,4-*bis*(N,N′-*diethoxycarbonyl-hydrazino*)-5,6-*dihydro*-2H-*thiopyran*-3(4H)-*one* (**16**) (0.5 g, 22%), m.p. 188 °C (EtOH) (Found: C, 43.4; H, 5.9; N, 11.9. $C_{17}H_{28}N_4O_9S$ requires C, 43.9; H, 6.1; N, 12.1%); $\nu_{max.}$(Nujol) 3 240, 1 520 (NH), and 1 740 and 1 695 cm^{-1} (CO); δ_H 7.1, 7.0 (2 H, 2 br s, NH), 5.7—5.1 (2 H, s and m, CO–CH–S and CH_2CHCO), 4.6—4.0 (8 H, 4 q, 2 CH_2Me), 3.0—2.5 (4 H, m, CH_2CH_2S), and 1.5—1.0 (12 H, 4 t, 4 Me).

2-(N,N′-*Diethoxycarbonylhydrazino*)-5,6-*dihydro*-2H-*thiopyran*-3(4H)-*one* 1,1-*dioxide* (**17**). Compound (**15**) (0.2 g, 0.7 mmol) was treated with monoperphthalic acid in dry benzene. After 2 d at room temperature, the phthalic acid was filtered off and the solvent eliminated. The oily residue solidified in ethanol to give the ketone (**17**), m.p. 120—122 °C (0.15 g, 68%) (Found: C, 40.8; H, 5.6; N, 8.5. $C_{11}H_{18}N_2O_7S$ requires C, 41.0; H, 5.6; N, 8.7%); $\nu_{max.}$(Nujol) 3 340, 3 300, 1 500 (NH), 1 760—1 680 (CO), and 1 310, 1 295, and 1 140 cm^{-1} (SO_2); δ_H 6.3 (1 H, s, $COCHSO_2$), 4.6—4.2 (6 H, m, 2 CH_2Me and CH_2SO_2), 3.8—

3.0 (2 H, m, CH_2CO), 3.0—1.9 (2 H, m, $CH_2CH_2SO_2$), and 1.3 (6 H, t, 2 Me).

Reaction of 3-*Benzylamino*-5,6-*dihydro*-4H-*thiopyran* 1,1-*Dioxide with Methyl Vinyl Ketone.—Procedure* (*a*). Methyl vinyl ketone (3.5 g, 5.0 mmol) was added to a solution of the enamine (**3**) (1.2 g, 5.0 mmol) in benzene, in a Dean and Stark apparatus, to remove the water formed. After 24 h, the solvent was removed and the mixture hydrolysed in ethanol with 10% hydrochloric acid, at room temperature. After a further 24 h, elimination of ethanol and extraction with chloroform left an oil which was chromatographed on silica gel to furnish 3,4,8,8a-*tetrahydro*-2H-1-*benzothiopyran*-6(7H)-*one* 1,1-*dioxide* (**19**) (0.1 g, 10%), m.p. 123—125 °C (EtOH–light petroleum) (Found: C, 54.5; H, 6.1. $C_9H_{12}O_3S$ requires C, 54.0; H, 6.0%); $\nu_{max.}$(Nujol) 1 660 (CO), 1 630 (C=C), and 1 310 and 1 130 cm^{-1} (SO_2); δ_H 6.1 (1 H, s, vinyl H), 3.8 (1 H, m, $CHSO_2$), 3.3 (2 H, m, CH_2SO_2), and 3.1—2.1 (8 H, m, $CH_2CH_2CH_2SO_2$ and CH_2CH_2CO). The compound 2,3,5,6,10,10a-*hexahydro*-1H-*naphtho*[2,1-b]-*thiopyran*-8(9H)-*one* 4,4-*dioxide* (**20**) was also separated (0.12 g, 10%), m.p. 168 °C (Found: C, 61.0; H, 6.45; S, 12.1. $C_{13}H_{16}O_3S$ requires C, 61.9; H, 6.33; S, 12.6%); $\nu_{max.}$(Nujol) 1 660 (CO), 1 615 (C=C), and 1 300 and 1 120 cm^{-1} (SO_2); δ_H 5.9 (1 H, s, vinyl H), 3.8 (2 H, m, CH_2SO_2), 3.5—1.8 (13 H, m, 6 CH_2 and CH); δ_C 192.6 (s, C-8), 153.2 (s, C-6a), 143.0 (s, C-4a), 132.2 (s, C-10b), 125.4 (d, C-7), 63.4 (d, C-10a), 52.6 (t, C-3), 36.9, 29.6, 28.1, 26.2, 22.9, 18.1 (t, C-1, C-2, C-5, C-6, C-9, C-10); *m/z* 252 (M^+, 13%), 188 (67, M − SO_2), 173 (11), 160 (51, 188 − CO), 146 (100, 188 − CH_2CO), 132 (25), 131 (69), 117 (84), 115 (37), 104 (23), 91 (57), 77 (27), 65 (24), 53 (16), 51 (18), 41 (20), 39 (31); m* 140.3 (252 − 188), 136.2 (188 − 160), 113.4 (188 − 146). An amount of the parent ketone (**1**) was also recovered (0.25 g, 33%).

Procedure (*b*). Methyl vinyl ketone (0.21 g, 3 mmol) was added to a solution of the enamine (**3**) (0.7 g, 3 mmol) in benzene (15 ml) containing acetic acid (0.4 ml, 6.7 mmol), sodium acetate (0.4 g, 3 mmol), and water (1 ml). The mixture was then refluxed for 24 h, the organic layer separated and the residue chromatographed on silica gel, to give compounds (**19**) (0.12 g, 20%) and (**20**) (0.12 g, 18%).

Reaction of 3-*Pyrrolidin*-1-*yl*-5,6-*dihydro*-4H-*thiopyran* 1,1-*Dioxide* (**18**) *with Methyl Vinyl Ketone.*—Methyl vinyl ketone (0.34 g, 4.9 mmol) was treated with enamine (**18**) 1.0 g, 4.9 mmol) following Procedure (a). Compound (**19**) (0.16 g, 16%) was separated, together with 2-(3-*oxobutyl*)-5,6-*dihydro*-2H-*thiopyran*-3(4H)-*one* 1,1-*dioxide* (**23**) (0.18 g, 16%), m.p. 88—90 °C (EtOH–light petroleum) (Found: C, 49.4; H, 6.4; S, 14.6. $C_9H_{14}O_4S$ requires C, 49.5; H, 6.5; S, 14.7%); $\nu_{max.}$(Nujol) 1 720sh, 1 700 (CO), and 1 300 and 1 130 cm^{-1} (SO_2); δ_H 4.2 (1 H, t, $COCHSO_2$), 3.35 (2 H, dd, CH_2SO_2), 3.0—2.0 (11 H, m and s, 4 CH_2 and Me), and 2.15 (s, Me). The parent ketone (**1**) was also separated (0.1 g, 14%). When the reaction was carried out following Procedure b, starting from 6.2 mmol of enamine (**18**), a small amount of the tricyclic compound (**20**) (0.15 g, 9%) was isolated together with the ketone (**19**) (0.15 g, 12%), and the parent ketone (**1**) (0.44 g, 60%).

Preparation of 3,4,7,8-*Tetrahydro*-6-*pyrrolidin*-1-*yl*)-2H-1-*benzothiopyran* 1,1-*Dioxide* (**22**).—The enamine (**22**) was prepared by Stork condensation[3] of the ketone (**19**) and pyrrolidine in benzene. After elimination of the solvent, the crude product was crystallized from acetone–light petroleum (53%), m.p. 132—134 °C (Found: C, 60.0; H, 7.0; N, 5.2. $C_{13}H_{19}NO_2S$ requires C, 61.6; H, 7.6; N, 5.5%); $\nu_{max.}$($CHCl_3$) 1 610, 1 520 (C=C), and 1 300 and 1 100 cm^{-1} (SO_2); δ_H 4.35 (1 H, s, vinyl H), 3.6—3.3 (6 H, m, CH_2NCH_2 and CH_2SO_2), 2.8—2.2 (8 H, m, $CH_2CH_2CH_2SO_2$ and $NCCH_2CH_2$), and 1.95 (4 H, m, $NCH_2CH_2CH_2$).

Reaction of the Enamine (**22**) *with Methyl Vinyl Ketone.*—Methyl vinyl ketone (0.17 g, 2.5 mmol) was added to the enamine (**22**) (0.6 g, 2.5 mmol) in benzene and the mixture was refluxed for 16 h. After elimination of the solvent, the residue was washed with water and hydrolysed with 10% hydrochloric acid. Extraction with chloroform left an oil which was found to be a 2:1 mixture of (**19**) and (**20**) (0.21 g, 33%).

Reaction of 3-*Benzylamino*-5,6-*dihydro*-4H-*thiopyran* 1,1-*Dioxide with Phenyl Vinyl Ketone.*—Phenyl vinyl ketone (0.26 g, 1.9 mmol) was added to a suspension of the enamine (**3**) (0.5 g, 1.9 mmol) in benzene, under stirring. The mixture was kept at room temperature for 24 h. After elimination of the solvent, the crude product was hydrolysed in acetone with 10% hydrochloric acid and the mixture was chromatographed on silica gel, to furnish 2-(3-*phenyl*-3-*oxopropyl*)-5,6-*dihydro*-2H-*thiopyran*-3(4H)-*one* 1,1-*dioxide* (**24**) (0.6 g, 10%), m.p. 118—120 °C (EtOH) (Found: C, 59.8; H, 5.79. $C_{14}H_{16}O_4S$ requires C, 60.0; H, 5.7%); $\nu_{max.}$(Nujol) 1 715, 1 675 (CO), 1 595, 1 580, 740, 690 (Ph), and 1 300, 1 280, and 1 135 cm^{-1} (SO_2); δ_H 8.0 (2 H, m, *o*-ArH), 7.5 (3 H, m, *m*- and *p*-ArH), 4.35 (1 H, t, $COCHSO_2$), 3.6—3.2 (4 H, m, CH_2SO_2 and CH_2COPh), and 2.9—2.0 (6 H, m, $CH_2CH_2SO_2$ and $COCHCH_2CH_2Ph$). The remainder was 2-benzylaminoethyl phenyl ketone (0.15 g, 30%) and the parent ketone (**1**) (0.03 g, 12%). When the reaction was carried out at 80 °C, the product (**24**) (27%) was obtained.

Reaction of 3-*Pyrrolidin*-1-*yl*-5,6-*dihydro*-4H-*thiopyran* 1,1-*Dioxide with Phenyl Vinyl Ketone.*—The reaction between phenyl vinyl ketone (0.46 g, 3.8 mmol) and the enamine (**18**) (0.76 g, 3.8 mmol) was carried out as described for the enamine (**3**). Separation of the reaction mixture on silica gel gave the ketone (**1**) (0.21 g, 38%), the already mentioned ketone (**24**) (0.32 g, 30%), and 2,4-*bis*(3-*phenyl*-3-*oxopropyl*)-5,6-*dihydro*-2H-*thiopyran*-3(4H)-*one* 1,1-*dioxide* (**27**) (0.14 g, 9%), m.p. 98—100 °C (EtOH) (Found: C, 66.7; H, 5.8. $C_{23}H_{24}O_5S$ requires C, 66.9; H, 5.9%); $\nu_{max.}$(Nujol) 1 708, 1 675 (CO), 1 595, 1 580, 740, 725, 690 (Ph), and 1 310, 1 290, and 1 120 cm^{-1} (SO_2); δ_H 7.95 (4 H, m, *o*-ArH), 7.5 (6 H, m, *m*- and *p*-ArH), 4.4 (1 H, t, $COCHSO_2$), 3.75—2.95 (6 H, m, CH_2COPh and CH_2SO_2), and 2.95—1.55 (7 H, m, $CHCH_2CH_2SO_2$ and $2CH_2COPh$). When the reaction was performed in refluxing benzene for 24 h, compounds (**24**) (34%) and (**27**) (16%) were formed.

Reaction of 3-*Benzylamino*-5,6-*dihydro*-4H-*thiopyran* 1,1-*Dioxide with Phenyl Styryl Ketone.*—Phenyl styryl ketone (0.17 g, 0.8 mmol) was added to a solution of the enamine (**3**) (0.2 g, 0.8 mmol) in anhydrous ethanol and the mixture refluxed for 72 h. Addition of 10% hydrochloric acid, elimination of ethanol, and extraction with chloroform left an oil which was chromatographed on silica gel. 2-(1,3-*Diphenyl*-3-*oxopropyl*)-5,6-*dihydro*-2H-*thiopyran*-3(4H)-*one* 1,1-*dioxide* (**25**) was separated (0.09 g, 30%), m.p. 200 °C (EtOH) (Found: C, 66.5; H, 5.4; S, 7.8. $C_{20}H_{20}O_4S$ requires C, 67.4; H, 5.6; S, 8.9%). $\nu_{max.}$(Nujol) 1 720, 1 678 (CO), 1 595, 1 585, 750, 700, 690 (Ph), and 1 315, 1 310, and 1 120 cm^{-1} (SO_2); δ_H 8.0 (2 H, m, *o*-ArH), 7.8—7.1 (8 H, m, *m*- and *p*-ArH, ArH), 4.6—4.3 (2 H, m, $CHCHPh$), 3.9—3.0 (4 H, m, CH_2SO_2 and CH_2COPh), 2.6—1.8 (4 H, m, $COCH_2CH_2$). The parent ketone (**1**) (0.08 g, 64%) and phenyl styryl ketone (0.13 g, 64%) were also recovered.

Reaction of 3-*Pyrrolidin*-1-*yl*-5,6-*dihydro*-4H-*thiopyran* 1,1-*Dioxide with Phenyl Styryl Ketone.*—The reaction between phenyl styryl ketone (0.15 g, 0.7 mmol) and the enamine (**18**) (0.15 g, 0.7 mmol) was carried out as described for enamine (**3**). The ketone (**25**) (0.06 g, 23%) was separated.

Reaction of 5,6-*Dihydro*-2H-*thiopyran*-3(4H)-*one* 1,1-*Dioxide with Methyl Vinyl Ketone.*—Methyl vinyl ketone (0.18 g, 2.5 mmol) was added to a suspension of the ketone (**1**) (0.4 g, 2.5 mmol) in methanol and 10% potassium hydroxide (1 ml). The mixture was heated for 4 h, the solvent was eliminated and the crude reaction mixture extracted with chloroform. Elimination of the solvent left an oil which was chromatographed on silica gel to yield compound (**23**) (0.2 g, 37%) and 2,4-*bis*(3-*oxobutyl*)-5,6-*dihydro*-2H-*thiopyran*-3(4H)-*one* 1,1-*dioxide* (**26**) (0.1 g, 14%), m.p. 145 °C (EtOH) (Found: C, 53.5; H, 6.9. $C_{13}H_{20}O_5S$ requires C, 54.2; H, 7.0%); $\nu_{max.}$($CHCl_3$) 1 705, 1 695 (CO), and 1 310, 1 305, and 1 130 cm^{-1} (SO_2).

Reaction of 5,6-*Dihydro*-2H-*thiopyran*-3(4H)-*one* 1,1-*Dioxide with Phenyl Vinyl Ketone.*—Phenyl vinyl ketone (0.1 g, 0.8 mmol) was added to a suspension of the ketone (**1**) (0.12 g, 0.8 mmol) in methanol and 10% potassium hydroxide (1 ml). The mixture was heated for 24 h. After elimination of the solvent and chromatographic separation, the compound (**24**) (0.13 g, 59%) was isolated, besides the parent ketone (**1**).

Reaction of 5,6-*Dihydro*-2H-*thiopyran*-3(4H)-*one* 1,1-*Dioxide with Phenyl Styryl Ketone.*—The reaction was performed as described above for the reaction between the ketone (**1**) and methyl vinyl ketone. The ketone (**25**) (0.35 g, 39%) was separated after the usual work-up.

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