Photochemical Rearrangement of Fused 1λ⁴,2-Thiazines (2-Azathiabenzenes); Rapid Migration of Methylthio and Phenylthio Groups

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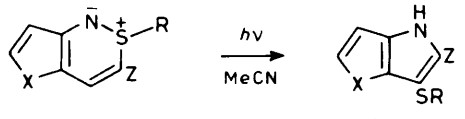
Irradiation of fused 1λ⁴,2-thiazines (**1**) gives the isomeric fused pyrroles (**2**). The structures of the thienopyrroles (**2a,b**) are assigned by decoupling and n.O.e. experiments on the thieno[3,2-*b*]pyrroles (**4a,b**) formed from them by hydrolysis and decarboxylation. A mechanism is proposed for conversion of thiazines (**1**) into pyrroles (**2**) (Scheme): nitrenes (**8**) are formed and cyclise to the 2*H*-pyrroles (**9**) which aromatise by [1,5] SR and H shifts. Surprisingly, the SR groups migrate faster than ester, acetyl, or formyl.

The chemistry of simple acyclic sulphur-nitrogen ylides (sulphimides) is well described.[1] In particular the known photochemical reactions of sulphimides almost invariably involve cleavage of the sulphur-nitrogen bond, as opposed to thermal reactions which usually result in rearrangement with participation of the sulphur substituents. In the previous papers we have reported the preparation of a series of novel cyclic sulphimides,[2] fused 1λ⁴,2-thiazines, which are derivatives of 2-azathiabenzenes, together with their thermal rearrangements,[3] which support their ylidic nature. We now report in detail the photochemical rearrangement of these heterocyclic systems.

Results and Discussion

The fused 1λ⁴,2-thiazines (**1**) were all found to be photo-labile, and decomposed on irradiation in acetonitrile at 300 or 350 nm to give products which were isomeric with the starting thiazines and were assigned the fused pyrrole structure (**2**) (Table).

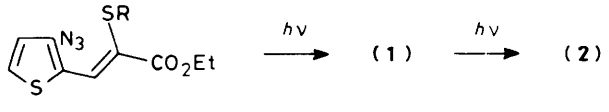
Irradiation of the azides (**3a,b**), precursors of the thiophene-fused sulphimides (**1a,b**), was also investigated. In contrast with thermolysis which gives the cyclic sulphimides (**1a**) and (**1b**) in 84 and 89% yield respectively, irradiation of the azides (**3a**) and (**3b**) for short times gives mixtures of the sulphimides (**1a**) and (**1b**), and the thienopyrroles (**2a**) and (**2b**). Thus irradiation of the azide (**3a**) in acetonitrile at 350 nm for 30 min gave the sulphimide (**1a**) (40%) and the thienopyrrole (**2a**) (53%). Similarly, the azide (**3b**) gave the sulphimide (**1b**) (56%) and the thienopyrrole (**2b**) (41%) after irradiation for 25 min. As expected, when the irradiation times were increased [120 min for (**3a**) and 180 min for (**3b**)] the thienopyrroles (**2a**) and (**2b**) were the only products isolated (79 and 80% respectively).



(**1**) (**2**)

Table. Photochemical rearrangement of fused 1λ⁴,2-thiazines

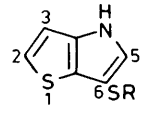
(1)/(2)	X	R	Z	Yield (%)
a	S	Me	CO_2Et	50
b	S	Ph	CO_2Et	83
c	S	Ph	COMe	77
d	S	Ph	CHO	75
e	O	Ph	CO_2Et	32
f	CH=CH	Ph	CO_2Et	75



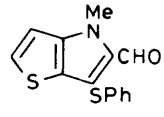
(**3**)

a, R = Me; **b**, R = Ph

The structures of the thienopyrroles (**2a**) and (**2b**) were confirmed by hydrolysis and decarboxylation to give the corresponding 6-substituted 4*H*-thieno[3,2-*b*]pyrroles (**4a**) and (**4b**). Decoupling experiments showed the presence in (**4a**) and (**4b**) of a proton at C-5 rather than C-6, due to its expected long-range coupling to 2-H (thiophene α-proton) (*J* 1.3 Hz) and to the NH, and the absence of any coupling to 3-H. Further confirmation was obtained from nuclear Overhauser effect (n.O.e.) difference experiments in which pre-saturation of the NH signals of (**4a**) and (**4b**) resulted in much larger enhancements (*ca.* 4:1) at 5-H than at 3-H.



(**4**)



(**5**)

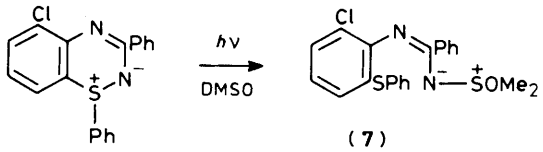
a, R = Me; **b**, R = Ph

The structures of the thienopyrroles (**2c**) and (**2d**) were also confirmed by n.O.e. difference experiments. For (**2c**) pre-irradiation of the NH signal caused enhancements of the acetyl methyl and of 3-H. In the case of the thienopyrrole (**2d**), the n.m.r. signals of the formyl group and the NH were too close, and therefore it was converted into the corresponding *N*-methyl derivative (**5**) by treatment with sodium hydride and iodomethane in dimethylformamide. Pre-irradiation of the aldehyde signal in (**5**) gave the expected large n.O.e. enhancement of the *N*-methyl protons. The furopyrrole structure (**2e**) was assigned by analogy with the corresponding thiophene derivative, but for the indole structure (**2f**) n.m.r. experiments, including n.O.e. difference, were inconclusive. Attempts to desulphurise to give a known indole derivative using either Raney nickel or nickel boride were unsuccessful, and therefore recourse was made to *X*-ray crystallography for final structure confirmation.†

Irradiation of the cyclic sulphimides (**1**) was expected to result

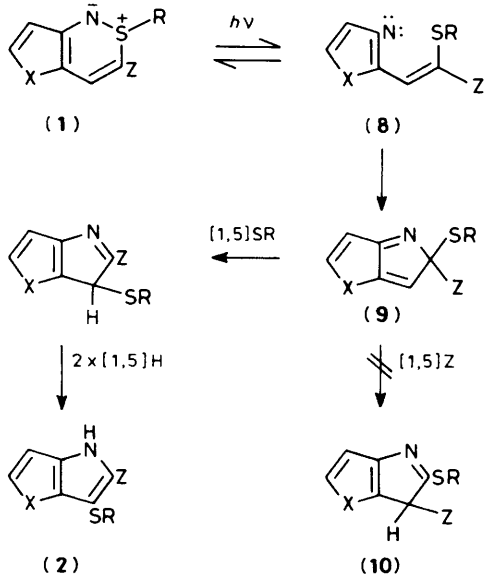
† Determined by Dr. D. J. Williams of this Department.

in cleavage of the sulphur-nitrogen bond and formation of the corresponding nitrene, in line with their acyclic counterparts.[1] Photochemical nitrene formation by cleavage of a sulphur-nitrogen bond has also been observed in the 1λ⁴,2,4-benzothiadiazine (**6**), and in the presence of dimethyl sulphoxide (DMSO), the nitrene was intercepted as the sulphoximide (**7**).[4] However, attempts to intercept the nitrene derived from the sulphimide (**1a**) by conducting the photolysis in DMSO were unsuccessful. Instead, a slightly higher yield (63%) of the thienopyrrole (**2a**) was observed.



(**6**) (**7**)

Despite this failure to intercept the nitrene intermediate the nitrenes (**8**) remain the most likely initial intermediates in the photolysis of the thiazines (**1**). Electrocyclic ring closure of the nitrene (**8**) would then lead to the non-aromatic 2*H*-pyrrole intermediate (**9**) (Scheme). The fused-pyrrole products (**2**) then arise by successive migrations of the RS group and hydrogen with concomitant aromatisation. It is not known whether these migrations are light induced or are subsequent 'dark' reactions, but one possible 'dark' reaction involving [1,5]-sigmatropic shifts is shown in the Scheme.



(**1**) (**8**) (**9**) (**2**) (**10**)

Scheme.

Whatever the fine details of the mechanism, it is clear that the products arise by exclusive migration of the RS group in preference to the Z group (CO_2Et, COMe, or CHO); no products resulting from migration of the Z group to give (**10**) were isolated. Such Z groups, especially formyl groups, normally migrate readily in sigmatropic rearrangements.[5] On the other hand little is known about the sigmatropic shifts of alkyl- and aryl-thio groups,[6] although it has been shown that alkylthio groups migrate rapidly in what are formally [1,7]-shifts.[7,8]

Experimental

Photolysis of the Fused 1λ⁴,2-*Thiazines* (**1**): *General Procedure.*—The thiazine (**1**) was dissolved in acetonitrile in a quartz tube, and nitrogen was bubbled through the solution for 30 min. The solution was then irradiated at 300 or 350 nm in a Rayonet Photochemical reactor, the nitrogen flow being maintained, until t.l.c. indicated that the starting material had been consumed. The solvent was evaporated and the residue purified by chromatography on silica gel.

Photolysis of the Thiazine (**1a**).—(a) *In acetonitrile.* Irradiation of the thiazine (**1a**) (80 mg) in acetonitrile (55 ml) at 300 nm for 5 h gave *ethyl* 6-(*methylthio*)-4H-*thieno*[3,2-b]-*pyrrole-5-carboxylate* (**2a**) (40 mg, 50%), m.p. 115—116 °C (from aqueous ethanol) (Found: C, 49.9; H, 4.6; N, 5.8. $C_{10}H_{11}NO_2S_2$ requires C, 49.8; H, 4.6; N, 5.8%); $\nu_{max.}$(Nujol) 3 280, 1 675, and 1 665 cm^{-1}; δ (250 MHz, $CDCl_3$) 1.40 (3 H, t), 2.68 (3 H, s), 4.40 (2 H, q), 6.89 (1 H, d, *J* 5.5 Hz), 7.28 (1 H, d, *J* 5.5 Hz), and 9.65 (1 H, s); δ_C($CDCl_3$) 14.5, 16.5, 60.8, 111.3, 118.8, 122.9, 125.3, 129.8, 140.9, and 161.5; *m/z* 241 (M^+), 195 (base), 167, and 152.

(b) *In DMSO.* Irradiation of the thiazine (**1a**) (80 mg) in DMSO (60 ml) at 300 nm for 3 h gave the thienopyrrole (**2a**) (50 mg) (63%).

Photolysis of the Thiazine (**1b**).—A solution of the thiazine (**1b**) (180 mg) in acetonitrile (150 ml) was irradiated at 350 nm for 2 h to give *ethyl* 6-(*phenylthio*)-4H-*thieno*[3,2-b]*pyrrole-5-carboxylate* (**2b**) (150 mg, 83%), m.p. 136—137 °C (from aqueous ethanol) (Found: C, 59.2; H, 4.3; N, 4.6. $C_{15}H_{13}NO_2S_2$ requires C, 59.4; H, 4.3; N, 4.6%); $\nu_{max.}$(Nujol) 3 275 and 1 675 cm^{-1}; δ (250 MHz, $CDCl_3$) 1.38 (3 H, t), 4.43 (2 H, q), 6.88 (1 H, d, *J* 5.4 Hz), 7.21 (1 H, d, *J* 5.4 Hz), 7.30—7.55 (5 H, m), and 9.58 (1 H, br); δ_C($CDCl_3$) 14.5, 61.0, 110.9, 116.4, 123.4, 126.4, 127.9, 128.9, 130.6, 133.0, 140.3, 140.4, and 161.4; *m/z* 303 (M^+), 257 (base), 229, 152, and 105.

Photolysis of the Thiazine (**1c**).—A solution of the thiazine (**1c**) (100 mg) in acetonitrile (150 ml) was irradiated at 350 nm to give 5-*acetyl*-6-(*phenylthio*)-4H-*thieno*[3,2-b]*pyrrole* (**2c**) (77 mg, 77%), m.p. 127—129 °C (Found: C, 61.5; H, 4.3; N, 5.1. $C_{14}H_{11}NOS_2$ requires C, 61.5; H, 4.1; N, 5.1%); $\nu_{max.}$(CCl_4) 3 440 and 1 630 cm^{-1}; δ (90 MHz, $CDCl_3$) 2.74 (3 H, s), 6.93 (1 H, d, *J* 5 Hz), 7.20—7.37 (6 H, m), and 10.09 (1 H, br s); δ_C($CDCl_3$) 28.0, 111.4, 112.2, 126.8, 129.1, 129.2, 129.7, 131.5, 134.6, 135.6, 140.8, and 189.1; *m/z* 273 (M^+, base), 258, and 231.

Photolysis of the Thiazine (**1d**).—A solution of the thiazine (**1d**) (100 mg) in acetonitrile (150 ml) was irradiated at 350 nm to give 6-(*phenylthio*)-4H-*thieno*[3,2-b]*pyrrole-5-carbaldehyde* (**2d**) (75 mg, 75%), m.p. 189—191 °C (Found: C, 60.0; H, 3.5; N, 5.2. $C_{13}H_9NOS_2$ requires C, 60.0; H, 3.5; N, 5.4%); $\nu_{max.}$(CCl_4) 3 440 and 1 645 cm^{-1}; δ (90 MHz, $CDCl_3$) 6.98 (1 H, d, *J* 5.6 Hz), 7.26—7.31 (5 H, m), 7.42 (1 H, d, *J* 5.6 Hz), 9.55 (1 H, s), and 9.92 (1 H, s); *m/z* 259 (M^+) and 243 (base).

Photolysis of the Thiazine (**1e**).—A solution of the thiazine (**1e**) (132 mg) in acetonitrile (20 ml) was irradiated at 300 nm for 2 h to give *ethyl* 6-(*phenylthio*)-4H-*furo*[3,2-b]*pyrrole-5-carboxylate* (**2e**) (42 mg, 32%), m.p. 70—72 °C (Found: C, 62.9; H, 4.6; N, 4.9. $C_{15}H_{13}NO_3S$ requires C, 62.7; H, 4.6; N, 4.9%); $\nu_{max.}$(Nujol) 3 300 and 1 670 cm^{-1}; δ (90 MHz, $CDCl_3$) 1.30 (3 H, t), 4.40 (2 H, q), 6.4 (1 H, d, *J* 2 Hz), 7.1—7.4 (5 H, m), 7.4 (1 H, d, *J* 2 Hz), and 9.0 (1 H, br): *m/z* 287 (M^+), 241, 186, and 105.

Photolysis of the Thiazine (**1f**).—A solution of the thiazine (**1f**) (100 mg) in acetonitrile (150 ml) was irradiated at 300 nm to

give *ethyl* 3-(*phenylthio*)*indole*-2-*carboxylate* (**2f**) (75 mg, 75%), m.p. 135 °C (Found: C, 68.8; H, 5.1; N, 4.7. $C_{17}H_{15}NO_2S$ requires C, 68.7; H, 5.1; N, 4.7%); $\nu_{max.}$(CCl_4) 3 450 and 1 690 cm^{-1}; δ (90 MHz, $CDCl_3$) 1.30 (3 H, t), 4.36 (2 H, q), 7.38—7.60 (9 H, m), and 9.35 (1 H, br); *m/z* 297 (M^+) and 251 (base).

Photolysis of the Azide (**3a**).—A solution of the azide (**3a**) (100 mg) in acetonitrile (90 ml) was irradiated at 350 nm for 30 min to give (i) the thienopyrrole (**2a**) (47 mg, 53%) and (ii) the thienothiazine (**1a**) (36 mg, 40%).

When the experiment was repeated and the irradiation continued for 120 min, the only product isolated was the thienopyrrole (**2a**) (79%).

Photolysis of the Azide (**3b**).—A solution of the azide (**3b**) (161 mg) in acetonitrile (120 ml) was irradiated at 350 nm for 25 min to give (i) the thienopyrrole (**2b**) (60 mg, 41%) and (ii) the thienothiazine (**1b**) (83 mg, 56%).

When the experiment was repeated and the irradiation continued for 180 min, the only product isolated was the thienopyrrole (**2b**) (80%).

Hydrolysis and Decarboxylation of the Thienopyrrole (**2a**).—A mixture of the thienopyrrole (**2a**) (70 mg) and aqueous potassium hydroxide (1M; 0.35 ml) in dioxane (0.5 ml) was heated under reflux for 1 h. The mixture was acidified to pH 5 and extracted with ethyl acetate. The organic extracts were dried and evaporated to give 6-(methylthio)-4*H*-thieno[3,2-b]-pyrrole-5-carboxylic acid (60 mg, 97%), m.p. 140—143 °C. The acid (30 mg) was heated at 130—145 °C for a few minutes. Chromatography of the residue gave 6-(*methylthio*)-4H-*thieno*[3,2-b]*pyrrole* (**4a**) (13 mg, 55%), as an oil, $\nu_{max.}$(neat) 3 400 cm^{-1}; δ (250 MHz, $CDCl_3$) 2.42 (3 H, s), 6.95 (1 H, d, *J* 5.3 Hz), 7.05 (1 H, dd, *J* 2.3, 1.3 Hz), 7.13 (1 H, dd, *J* 5.3, 1.3 Hz), and 8.25 (1 H, br, D_2O exch.); *m/z* 169 (M^+) and 154 (base).

Hydrolysis and Decarboxylation of the Thienopyrrole (**2b**).—A mixture of the thienopyrrole (**2b**) (50 mg) and aqueous potassium hydroxide (1M; 0.2 ml) in dioxane (0.5 ml) was heated under reflux for 1 h. Work-up as above gave 6-(phenylthio)-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylic acid (45 mg, 99%), m.p. 134—136 °C (decomp.). The acid (20 mg) was heated at 145 °C for 30 s. Chromatography gave 6-(*phenylthio*)-4H-*thieno*[3,2-b]*pyrrole* (**4b**) (12 mg, 73%), m.p. 131—132 °C, $\nu_{max.}$(Nujol) 3 420 cm^{-1}; δ (250 MHz, $CDCl_3$), 6.98 (1 H, d, *J* 5.2 Hz), 7.05—7.25 ([7 H, m, which includes 7.14 (1 H, dd, *J* 5.2, 1.3 Hz) and 7.24 (1 H, dd, *J* 2.5, 1.3 Hz)], and 8.48 (1 H, br, D_2O exch.); *m/z* 231 (M^+, base).

N-*Methylation of the Thienopyrrole* (**2d**).—A solution of the thienopyrrole (**2d**) (21.4 mg, 0.08 mmol) in dry DMF (0.5 ml) was added to a stirred suspension of sodium hydride (2.4 mg, 0.1 mmol) in DMF (3 ml) at 0 °C. After 5 min, iodomethane (34 mg, 0.24 mmol) was added, and the mixture stirred for a further 30 min. Aqueous work-up and chromatography gave 4-*methyl*-6-(*phenylthio*)-4H-*thieno*[3,2-b]*pyrrole*-5-*carbaldehyde* (**5**) (16 mg, 70%), m.p. 123—125 °C (Found: C, 61.3; H, 4.1; N, 5.2. $C_{14}H_{11}NOS_2$ requires C, 61.5; H, 4.05; N, 5.1%); $\nu_{max.}$(CCl_4) 1 655 cm^{-1}; δ (250 MHz, $CDCl_3$) 4.11 (3 H, s), 6.95 (1 H, d, *J* 5.6 Hz), 7.18—7.30 (5 H, m), 7.41 (1 H, d, *J* 5.6 Hz), and 10.3 (1 H, s); *m/z* 273 (M^+, base).

Acknowledgements

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