Mechanism of the Photorearrangements of Phenylthiazoles

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Various arylthiazoles have been subjected to photolysis. The resulting photorearrangements have been classified as type A or B. Type A involves formal exchange of positions 2 and 4, or 3 and 5. Type B involves formal interchange of positions 2 and 3 with concomitant inversion of positions 4 and 5. The mechanistic aspects of the reaction are discussed and we present a mechanism involving a tricyclic sulphonium cation and subsequent formation of a more stable bicyclic intermediate leading to the rearrangement product. Strong support for our proposed mechanism has been provided by deuterium incorporation during the rearrangement of 2-phenylthiazole (17) or 4-phenylthiazole (19) to 3-phenylisothiazole (18).

PHOTOCHEMICAL ring-atom transposition reactions in five-membered hetero-aromatics have been extensively studied. Most of these reactions have been interpreted in terms of one of several conceivable pathways; a contraction–expansion mechanism,[1-4] valence-bond isomerisation,[4-6] bond twisting,[7] and a zwitterionic mechanism;[8,9] in some cases evidence has been provided for such a process. Also, the general outlines and analogies for the mechanism have been discussed with the hope of depicting the more general process.[10,11]

Photorearrangements in the thiazole series were initially reported by us in a preliminary communication.[12] Vernin *et al.*[13] have also systematically investigated the photorearrangements of various arylthiazoles, and have proposed a valence-bond isomerisation mechanism involving a Dewar-benzene type bicyclic intermediate on the basis of an analysis of the product and a π-bond order Hückel calculation.[13c,d] However, the mechanism of the rearrangement reported previously is still an open question.[14] The present paper gives evidence that carbanionic carbon is present in the intermediate in the photorearrangements of phenylthiazoles, and we propose a unified mechanism involving a zwitterionic species and subsequent formation of a more stable bicyclic isomer; this is capable of explaining a variety of the results.

RESULTS AND DISCUSSION

Photochemistry of Phenylthiazoles.—The products isolated from irradiation of several phenylthiazoles in benzene and/or ethanol are listed in Table 1 and the reactions studied can be represented as shown in Scheme 1. The structures were confirmed by elemental analyses as well as by their spectroscopic evidence, or by comparison with authentic samples.

Irradiation of 2,5-diphenylthiazole (1) in ethanol or benzene gave 3,4-diphenylisothiazole (2), 4,5-diphenylthiazole (3), and phenanthro[9,10-*d*]thiazole (4) as major products. The formation of an analogous pattern of rearrangement products was also observed on irradiation of the thiazoles (8) and (13), while similar irradiation of 2,4-diphenylthiazole (5) and 4-(*p*-methoxyphenyl)-2-phenylthiazole (15) led to a low consumption of the starting material and the formation of the isothiazoles (6) and (14), respectively. The 4,5-diarylthiazoles (3)

[1] R. Srinivasan, *Pure Appl. Chem.*, 1968, **16**, 65; E. E. van Tamelen and T. H. Whitesides, *J. Amer. Chem. Soc.*, 1968, **90**, 3894; H. Hiraoka and R. Srinivasan, *ibid.*, p. 2720; E. E. van Tamelen and T. H. Whitesides, *ibid.*, 1971, **93**, 6129; H. Hiraoka, *Tetrahedron*, 1973, **29**, 2955; E. Poquet, A. Dargelos, and M. Chaillet, *ibid.*, 1976, **32**, 1729.

[2] B. Singh and E. F. Ullman, *J. Amer. Chem. Soc.*, 1967, **89**, 6911; B. Singh, A. Zweig, and J. B. Gallivan, *ibid.*, 1972, **94**, 1199; D. W. Kurtz and H. Schechter, *Chem. Comm.*, 1966, 689.

[3] H. Tiefenthaler, W. Dörshlen, H. Göth, and H. Schmit, *Helv. Chim. Acta*, 1967, **50**, 244, and work cited therein.

[4] M. Maeda and M. Kojima, *J.C.S. Perkin I*, 1977, 239.

[5] P. Beak and W. Messer, *Tetrahedron*, 1969, **25**, 3287.

[6] H. Hiraoka, *Chem. Comm.*, 1970, 1306; 1971, 1610.

[7] R. M. Kellogg, *Tetrahedron Letters*, 1972, 1429.

[8] J. P. Catteau, A. Lablanche-Combier, and A. Pollet, *Tetrahedron*, 1972, **28**, 3141; M. Ohashi, A. Iio, and T. Yonezawa, *Chem. Comm.*, 1970, 1148; M. Maeda, A. Kawahara, M. Kai, and M. Kojima, *Heterocycles*, 1975, **3**, 389.

[9] H. Wynberg, *Accounts Chem. Res.*, 1971, **4**, 65, and works cited therein.

[10] A. Couture and A. Lablanche-Combier, *Tetrahedron*, 1971, **27**, 1059; A. Couture, A. Delevalle, A. Lablanche-Combier, and C. Parhanyi, *Tetrahedron*, 1975, **31**, 785.

[11] J. Barltrop, A. C. Day, P. D. Moxon, and R. R. Ward, *J.C.S. Chem. Comm.*, 1975, 786.

[12] M. Kojima and M. Maeda, *Chem. Comm.*, 1970, 386.

[13] (*a*) G. Vernin, J.-C. Poite, J. Metzger, J.-P. Aune, and H. J. M. Dou, *Bull. Soc. chim. France*, 1971, 1103; (*b*) G. Vernin, R. Jauffred, C. Richard, H. J. M. Dou, and J. Metzger, *J.C.S. Perkin II*, 1972, 1145; (*c*) G. Vernin, C. Riou, H. J. M. Dou, L. Bouscasse, J. Metzger, and G. Loridan, *Bull. Soc. chim. France*, 1973, 1743; (*d*) C. Riou, J. C. Poite, G. Vernin, and J. Metzger, *Tetrahedron*, 1974, **30**, 879; (*e*) C. Riou, G. Vernin, H. J. M. Dou, and J. Metzger, *Bull. Soc. chim. France*, 1972, 2673; (*f*) G. Vernin, J.-C. Poite, H. J. M. Dou, and J. Metzger, *ibid.*, 1972, 3157.

[14] M. Maeda and M. Kojima, *Tetrahedron Letters*, 1973, 3523.

and (10) produced the 3,4-diarylisothiazoles (2) and (9). On the other hand, when a solution of the thiazole (3) or (10) was irradiated in the air, it underwent ring

The photorearrangements of phenylthiazoles studied here can be described as two modes of the transposition of ring atoms: (i) the formal exchange of positions 2 and

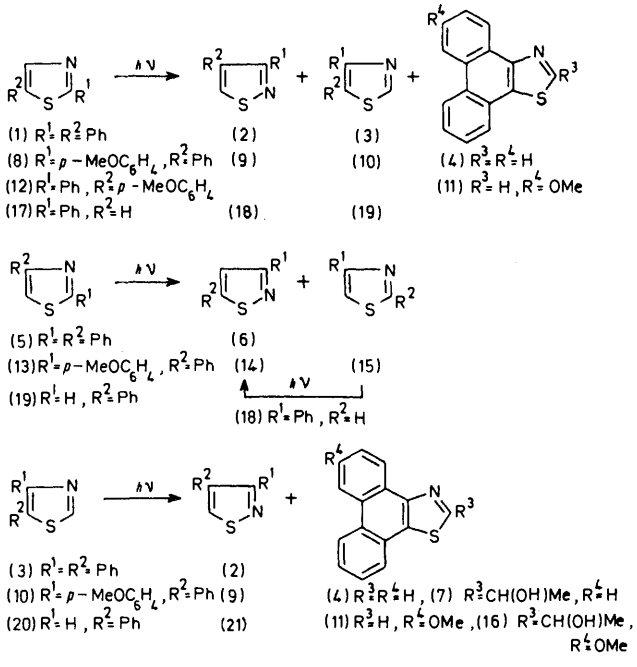
TABLE 1

Photolysis of phenylthiazoles [a]

Compound	Irradiation conditions: Conc. ($\times 10^{-2}$M)	Solvent	Time (h)	Recovery (%)	Products (% yield) [b]: Type A	Type B	Others
(1)	2.2	EtOH	42	10.0	(3) 26.4	(2) 13.1	(4) trace
	1.9	PhH	60	7.4	(3) 7.8	(2) 32.4	(4) 7.9
(3)	1.8	EtOH	90	1.8	(2) 20.6		(4) 13.8
							(7) 5.5
	1.9	PhH	90	7.1	(2) 22.7		(4) 17.6
	2.4	EtOH [c]	9.5				(4) 20.8
(5)	1.9	PhH	66	70.6		(6) 3.3	
	1.4	EtOH	56				(Decomp.)
(8)	1.9	EtOH	35	6.7	(10) 11.1	(9) 12.6	(11) 2.2
	1.6	PhH	49.5		(10) 6.3	(9) 31.1	(11) 0.4
(10)	1.9	EtOH	106.5	15.2	(9) 12.3		(11) 14.2,
							(16) 3.9
	1.5	PhH	97	10.3	(9) 19.2		(11) 25.9
	1.6	EtOH [c]	10				(11) 33.7
(12)	1.8	PhH	100	92.6			
(13)	1.8	PhH	63		(15) 46.1	(14) 5.8	
(15)	1.9	PhH	50	69.2	(14) 1.2		
(17)	2.7	EtOH	14		(19) 20.6	(18) 10.8	
	2.4	PhH	15	38.3	(19) 4.9	(18) 9.5	
(19)	2.6	EtOH	38.5	77.1	(18) 1.3		
	2.5	PhH	48	88.1	(18) 0.6		
(20)	2.5	EtOH	26	25.6		(21) 11.9	
	2.4	PhH	33	51.4		(21) 3.0	

[a] Reactions were carried out at 78—80 °C using a 100 W high-pressure mercury lamp (Pyrex or quartz filter) under nitrogen pressure. [b] Yields are based on the initial amount of the starting material. [c] Open to air.

closure to form a phenanthrene derivative analogous to those in the other heterocyclic system.[4,15] The monophenylthiazoles (17), (19), and (20) in benzene produced



SCHEME 1

rearrangement products identical with those independently reported by Vernin *et al.*[13e]

4, or 3 and 5 (type A), and (ii) the formal interchange of positions 2 and 3 with concomitant inversion of positions 4 and 5 (type B) (also see Table 1). The phenylthiazoles investigated here rearrange to give either one of type A and B products or both. This shows that the kind and position of the substituent on the thiazole ring significantly influences which type of product will be formed.

Quantum Yield Determination.—Ferrioxalate actinometry was used to measure the quantum yields of 3-phenylisothiazole (18) (ϕ_{3PIT}) and 4-phenylthiazole (19) (ϕ_{4PT}) production from (17) (ϕ_{2PT}) together with the rate of disappearance of the latter (see Table 2). The product distribution seems to be insensitive to the wavelength of light and the solvent used, and evidently the photolysis of 2-phenylthiazole (17) in the 280—310 nm range (the maximum absorption region) affords the rearrangement products, (18) and (19), in good yield.* Attempted generation of the triplet of (17) by sensitization with either benzophenone (E_T = 68.5 kcal mol^{-1}) or acetophenone (E_T = 73.6 kcal mol^{-1}) under conditions where the sensitizer absorbed the major portion of the incident irradiation failed to achieve the rearrangement to give (18) and (19); only a small

* The absorption spectrum of (17) in cyclohexane or ethanol showed an intense (π,π^*) band at 285—287 nm. The lowest excited singlet state of (17) is estimated to be at *ca.* 90 kcal mol^{-1} from its absorption and fluorescence spectra.

[15] A. Padwa and R. Hartman, *J. Amer. Chem. Soc.*, 1966, **88**, 3759; J. L. Cooper and H. H. Wasserman, *Chem. Comm.*, 1969, 200.

amount of (17) was consumed. Further, the rearrangement was not quenched by the addition of penta-1,3-diene. These results seem to indicate that the excited

TABLE 2

Quantum yield determination of irradiation of 2-phenylthiazole (17) [a]

Solvent	Wavelength	Additive	Quantum yield [b] ϕ_{2PT}	ϕ_{3PIT}	ϕ_{4PT}
EtOH	258	None	0.147	0.0012	0.0079
EtOH	285	None	0.147	0.0015	0.0241
EtOH	311	None	0.159	0.0027	0.0419
PhH	311	None	0.157	0.0049	0.0540
Cyclohexane	285	None	0.126	0.0019	0.0301
PhH	311	Penta-1,3-diene (0.25 M)		0.0042	0.0538
PhH	311	Penta-1,3-diene (0.68 M)		0.0047	0.0529
PhH [c]	360	Benzophenone (0.1 M)		0	0
PhH [c]	360	Acetophenone (0.1 M)		0	0

[a] Solutions (6.33×10^{-3}M) were irradiated with a JASCO CRM–FA spectro irradiator (±7.5 nm band width) and the products yields were determined by g.l.c. [b] Average from three runs. [c] 2-Phenylthiazole concentration were 1.8×10^{-2}M.

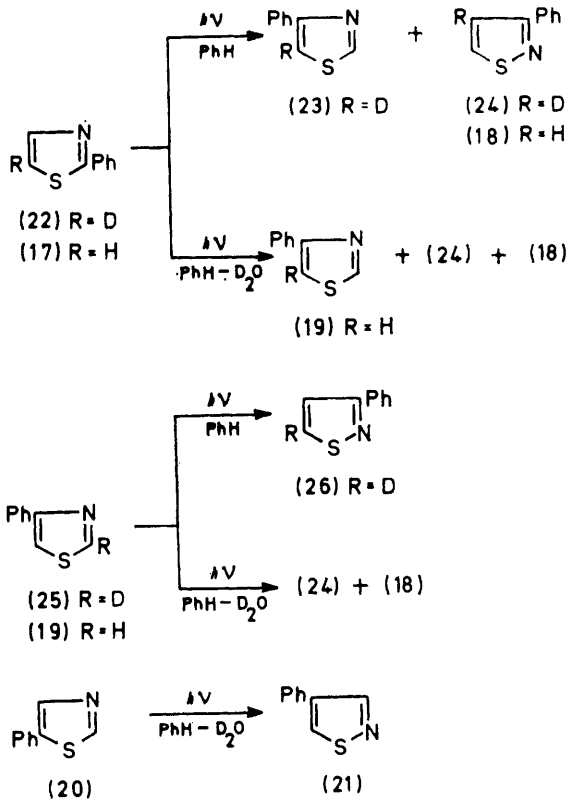
state involved in the photorearrangement of the thiazole (17) is the singlet (π,π^*) whereas the role of triplet state is apparently not significant.

Deuterium Incorporation.—Photolyses of the deuteriated compounds (22) and (25) in benzene were carried out under the conditions used for the unlabelled series. The deuteriated products were isolated and their n.m.r. spectra were determined.

The n.m.r. spectra of the recovered starting thiazoles were identical with those recorded prior to irradiation. The n.m.r. analysis of the isothiazole isolated from irradiation products of 5-deuterio-2-phenylthiazole (22) showed it to be a mixture of 3-phenylisothiazole (18) and 4-deuterio-3-phenylisothiazole (24) in a ratio of 31 : 69, thus indicating that deuterium–hydrogen exchange had occurred.* Although the origin of the hydrogen is uncertain it may arise from traces of water in the solvent. In a previous report on the photochemical behaviour of the deuteriated thiazole (22) by Vernin *et al.*,[13e] however, deuterium–hydrogen exchange was not described.

Thus 2-, 4-, and 5-phenylthiazole [(17), (19), and (20)] were irradiated in benzene containing deuterium oxide, and the n.m.r. spectra of the recovered starting material and the products, 4-phenylthiazole and 4-phenylisothiazole, were recorded. There was no incorporation of deuterium within the limits of n.m.r. detection. In contrast, 3-phenylisothiazole produced by irradiation of 2-phenylthiazole (17) was formed with substantial deuterium incorporation. The n.m.r. analysis showed that deuterium had been incorporated at the 4-position in 3-phenylisothiazole in 22%. Similarly, the isolated 3-phenylisothiazole resulting from 4-phenylthiazole (19) was also formed with 33% deuterium incorporation at the 4-position. On the other hand, since no deuterium incorporation in the isothiazole (18) was observed when the sample in benzene containing deuterium oxide was either refluxed in the dark or irradiated, deuterium incorporation must occur before the formation of the final product (18) on irradiation.

Mechanistic Considerations.—A proposal made both by us at the initiation of this work [12] and by Vernin *et al.*[13] was that a bicyclic intermediate analogous to the Dewar benzene valence-bond isomer may be involved in the photorearrangements of phenylthiazoles. This valence-bond isomerisation mechanism (see Scheme 3),



SCHEME 2

involves an initial disrotatory formation [17] of the isomer (27) followed by a 1,3-shift of a sulphur atom [18] to give either (28) or (29); the latter lead to the thiazole (31) and the isothiazole (32), respectively. The same treatment of (28) or (29) affords the bicyclic compound (30) which gives access to the isothiazole (33). A similar bicyclic compound has been isolated after irradiation of tetrakis(trifluoromethyl)thiophen.[19] In fact, this

* It has been reported [16] that the proton at the position 5 of 3-phenylisothiazole (18) undergoes exchange of this proton for deuterium in the presence of methoxide in CH_3OD.

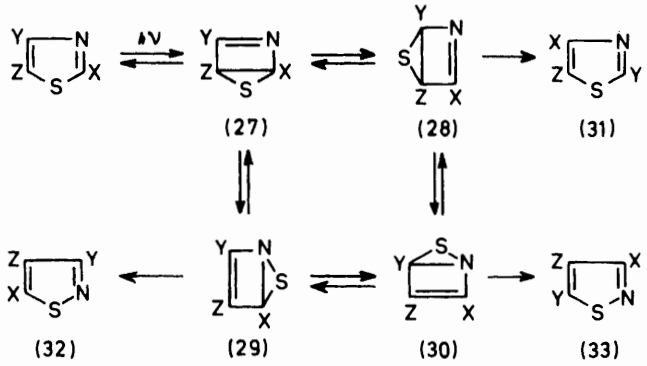
[16] R. A. Olofson, J. M. Landesberg, R. O. Berry, D. Leaver, W. A Robertson, and D. M. McKinnon, *Tetrahedron*, 1966, **22**, 2119.

[17] R. B. Woodward and R. Hoffman, *Angew. Chem.*, 1969, **81**, 797.

[18] P. Brownbridge and S. Warren, *J.C.S. Perkin I*, 1977, 2125, and works cited therein.

[19] H. A. Wiebe, S. Braslavsky, and J. Heicklen, *Canad. J. Chem.*, 1972, **50**, 2721; Y. Kobayashi, I. Kumadaki, A. Ohsawa, and Y. Sekine, *Tetrahedron Letters*, 1975, 1639.

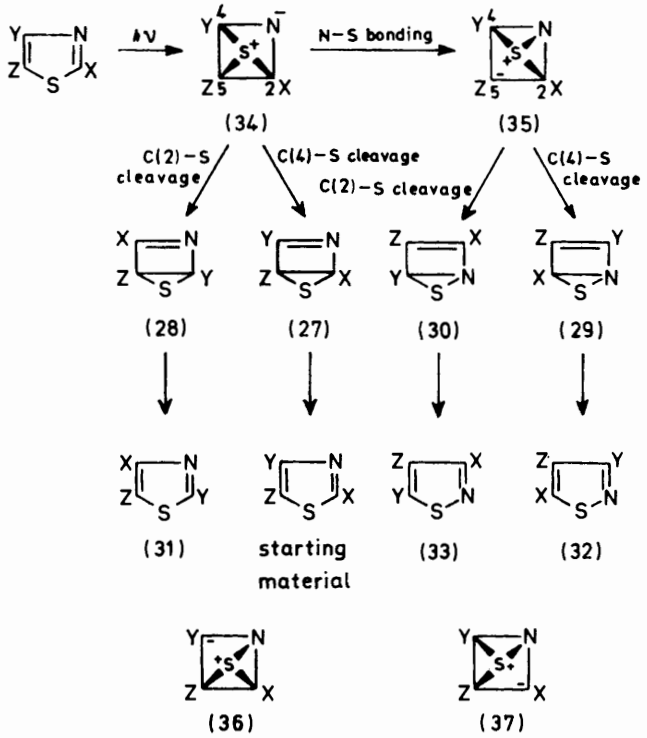
mechanism seems to provide a useful qualitative description of the species leading to the rearrangement products, but is inconsistent with the results of deuterium incorporation experiments. If the bicyclic intermediate shown in Scheme 3 undergoes deuterium incorporation to give a deuteriated compound, the resulting product



SCHEME 3

(19), in the case of 2-phenylthiazole (17), should also undergo deuteriation. Such a phenomenon, however, was not observed. Our results demonstrate that carbanionic carbon is present in the intermediate in the transformation of (17) or (19) into (18).

An attractive mechanism we propose here is outlined in Scheme 4. This postulated pathway involves a



SCHEME 4

tricyclic sulphonium cation [(34) and (35)] and subsequent formation of a bicyclic isomer leading to re-aromatization. Thus, deuterium incorporation into the 4-position in the product (18) is expected for an intermediate corresponding to (35; X = Ph, Y = Z = H). Further, the above mechanism avoids the necessity of having unsymmetrical zwitterionic species (36) and (37) on the basis that the incorporation of deuterium does not occur on irradiation of 5-phenylthiazole (20). In the photorearrangement of 2,3-dihydro-4,5-diphenylpyrazine to *N*-methyl-4,5-diphenylimidazole, the presence of a zwitterionic species as an intermediate has been demonstrated by the deuterium incorporation from C_2H_5OD.[20]

One of the most important hypotheses is that the zwitterionic species (34) and (35) may not itself re-aromatize but re-open through a more stable bicyclic intermediate which could then rearomatize to the product. The same view of a zwitterionic-bicyclic species transformation has been found in the photolysis of *N*-imidazoles.[5] The tricylic sulphonium cations (34) and (35) can thus re-open as shown to give either type A or type B products, or the starting material. However, the preferred formation of a given bicyclic isomer should take place in such a fashion as to place the aryl group on the double bond of the bicyclic isomer formed, as suggested by Vernin *et al.*[13c] Hence the preferred mode of bond cleavage in (34) and (35) may be controlled by the substituents at the 2-, 4-, and 5-positions.

In the light of the above considerations, each zwitterionic species (34) and (35) (X = H, Y = Z = Ph) formed by the photolysis of 4,5-diphenylthiazole (3) leads to the formation of the starting thiazole and 3,4-diphenylisothiazole (2) by the cleavage of the C(4)–S bond *via* the bicyclic compounds (27) and (29) (X = H, Y = Z = Ph). Also the bicyclic compounds (28) and (30) (X = Z = Ph, Y = H), resulting from the preferred cleavage of the C(2)–S bond in the zwitterionic species (34) and (35) (X = Z = Ph, Y = H) for 2,5-diphenylthiazole (1), give the thiazole (3) and the isothiazole (2), respectively. It should be noted that the bicyclic compound (28) and (30) resulting from the thiazole (1) are identical with those (27) and (29) involved in the rearrangement of the thiazole (3). Similarly, the photorearrangement of *p*-methoxyphenyl derivatives can be easily explained in the same terms. On the other hand, both the zwitterionic intermediates (34) and (35) become specific symmetrical species when the two substituents, X and Y, of (34) and (35) are the same. In this case, therefore, the two possible processes [C(2)–S and C(4)–S bond cleavages] become identical. Thus irradiation of 2,4-diphenylthiazole (5) or 5-phenylthiazole (20) gives rise to the starting thiazole and the isothiazoles (6) or (21), respectively. In the same manner, this mechanism provides a satisfactory explanation for all the results obtained. In a formal sense, the photorearrangements of methylisothiazoles that more closely resemble those of the thiazole system have been interpreted by the formation of all possible zwitterionic intermediates.[8a] Also Labhart has pointed out, on the

[20] P. Beak and J. L. Miesel, *J. Amer. Chem. Soc.*, 1967, **89**, 2375.

basis of CNDO calculations, the strong possibility that immonium species, analogous to (34), are intermediates in the photochemistry of pyrazole.[21] A new mechanistic approach reached in this paper gives an interesting result but the above considerations seem to be the only one so far which can account for phenylthiazoles investigated here.

EXPERIMENTAL

Unless otherwise noted, Mallinckrodt silica ARCC-4 (100 mesh) was used for column chromatography [monitored by t.l.c. (Wakogel B-0 silca gel)]. U.v. spectra were taken on a Hitachi 139 UV-VIS or a Shimazu SV-50 A spectrometer. I.r. spectra were obtained on a JASCO DS-701G instrument and n.m.r. spectra on a JNM-60H spectrometer with $SiMe_4$ as internal standard. Mass spectral determinations were performed with a JEOL JMS-OISG spectrometer. Analytical g.l.c. was carried out with a Hitachi 063 chromatograph equipped with a flame-ionisation detector and preparative g.l.c. was done with a Varian A-700 Autoprep gas chromatograph using thermal conductivity detection.

Large-scale photolyses were performed with a Riko UVL-700P or UVL-100HP 100-W high-pressure mercury lamp, with a Pyrex or quartz filter. All photolyses were monitored by t.l.c. or periodic scanning of the u.v. spectra. Monochromatic light (*ca.* ±7.5 nm band width) was obtained from a concave radiating monochromator (2 kW xenon discharge lamp, JASCO CRM-FA). In the monochromatic irradiations, solutions were purged initially with nitrogen for at least 30 min and the quartz sample cells (4 ml) were sealed during irradiation. All solvents used for irradiation were purified according to known methods. Penta-1,3-diene, acetophenone, and benzophenone were obtained from commercial sources and purified by distillation or recrystallisation before use.

2-(p-*Methoxyphenyl*)-5-*phenylthiazole* (8).[22]—A mixture of 2-(anisoylamino)acetophenone (6 g) and P_2S_5 (5 g) was heated in an oil-bath until evolution of a gas ceased. After cooling, the mixture was made basic (2N-NaOH), refluxed for 5 min, and extracted with ether. After drying (Na_2SO_4) and removal of the ether, chromatography on silica gel (benzene) gave the thiazole (8) (3.4 g, 57%) as needles (from ethanol), m.p. 129—130 °C; $\lambda_{max.}$(EtOH) 332 nm (log ε 4.36); *m/e* 267 (M^+) (Found: C, 71.7; H, 4.65; N, 5.25. $C_{16}H_{13}NOS$ requires C, 71.91; H, 4.93; N, 5.24%).

5-(p-*Methoxyphenyl*)-2-*phenylthiazole* (12).—The thiazole (12) was prepared similarly from 2-(benzoylamino)-4′-methoxyacetophenone and P_2S_5. Chromatography on silica gel (benzene) gave the thiazole (12) (15%) as needles (from ethanol), m.p. 102—103 °C; $\lambda_{max.}$(EtOH) 334 nm (log ε 4.39); *m/e* 267 (M^+) (Found: C, 72.0; H, 4.8; N, 5.25. $C_{16}H_{13}NOS$ requires C, 71.91; H, 4.93; N, 5.24%).

4-(p-*Methoxyphenyl*)-5-*phenylthiazole* (10).[23]—A mixture of 2-chloro-4′-methoxy-2′-phenylacetophenone (160 mg),[4] formamide (67 mg), and P_2S_5 (67 mg) was heated in a water-bath until the evolution of a gas ceased. After cooling, the mixture was made basic (2N-NaOH), diluted with water, and extracted with ether. The ether was removed and the residue was chromatographed on silica gel (chloroform) to give the thiazole (10) (67 mg, 41%) as needles (from ethanol), m.p. 95 °C; $\lambda_{max.}$(EtOH) 239 (log ε 4.27) and 289 nm (4.02); δ($CDCl_3$) 3.80 (3 H, s, OCH_3), 6.6—7.6 (9 H, A_2B_2 m and five other aromatic), and 8.77 (1 H, s, ring proton); *m/e* 267 (M^+) (Found: C, 71.65; H, 4.7; N, 5.35. $C_{16}H_{13}NOS$ requires C, 71.91; H, 4.93; N, 5.24%).

Photolysis of 2,5-*Diphenylthiazole* (1).—(*a*) A solution of the thiazole (1) (2.656 g) in refluxing benzene (600 ml) was irradiated through a Pyrex filter for 60 h. The mixture was evaporated and the residue was chromatographed on silica gel (benzene) to give four fractions. The first fraction, in order of elution, after rechromatography [benzene–light petroleum (2 : 1)] and recrystallisation from ethanol, gave 3,4-diphenylisothiazole (2) (872 mg) as needles, m.p. 82—83.5 °C; $\lambda_{max.}$(EtOH) 277 nm (log ε 4.07); $\nu_{max.}$(KBr) 1 445, 1 025, 810, 806, 725, and 695 cm^{-1}; δ($CDCl_3$) 7.2—7.6 (10 H, m, Ar) and 8.53 (1 H, s, ring proton); *m/e* 237 (M^+), 135 (C_7H_5NS), 134 (C_8H_6S), 103 (C_7H_5N), and 77 (C_6H_5)[24] (Found: C, 75.7; H, 4.9; N, 5.8. $C_{15}H_{11}NS$ requires C, 75.94; H, 4.64; N, 5.90%). The second fraction, after recrystallisation from ethanol, gave unchanged (1) (208 mg). The third fraction, after rechromatography [benzene–light petroleum (2 : 1)] and recrystallisation from ethanol, gave phenanthro[9,10-*d*]thiazole (4) (210 mg) as needles, m.p. 135—137 °C; $\lambda_{max.}$(EtOH) 233sh (log ε 4.44), 254 (4.77), 260sh (4.64), 283 (4.03), 300 (3.92), and 312 nm (3.89); $\nu_{max.}$(KBr) 1 500, 907, 814, 747, and 720 cm^{-1}; δ($CDCl_3$) 7.5—8.9 (8 H, m, phenanthrene) and 8.99 (1 H, s, thiazole ring proton) (Found: C, 76.6; H, 3.85; N, 5.75. $C_{15}H_9NS$ requires C, 76.56; H, 3.85; N, 5.96%). The fourth fraction, after recrystallisation from light petroleum, gave 4,5-diphenylthiazole (3) (208 mg) as needles, m.p. 60—61 °C, identical with an authentic sample.[25]

(*b*) The thiazole (1) (3.000 g) was similarly irradiated in ethanol (600 ml) for 42 h. Work-up as above and chromatography [benzene–light petroleum (2 : 1)] led to the isothiazole (2) (392 mg), starting material (1) (300 mg), the phenanthrene (4) (trace), and the thiazole (3) (729 mg).

Photolysis of 4,5-*Diphenylthiazole* (3).—(*a*) A solution of the thiazole (3) (2.816 g) in refluxing benzene (600 ml) was irradiated through a Pyrex filter for 90 h. The benzene was removed and the residue was chromatographed on silica gel [benzene–light petroleum (2 : 1)] to give two fractions. The first, after recrystallisation from ethanol, afforded 3,4-diphenylisothiazole (2) (760 mg) as needles, m.p. 82—83 °C. The second fraction, after rechromatography on silica gel [benzene–light petroleum (2 : 1)] and recrystallisation from ethanol, gave the phenanthrene (4) (506 mg) and unchanged (3) (201 mg), respectively.

(*b*) A solution of the thiazole (3) (2.622 g) in ethanol (600 ml) was similarly irradiated for 90 h. Work-up as above and chromatography on silica gel [benzene–light petroleum (2 : 1)] led to the isothiazole (2) (541 mg), unchanged (3) (48 mg), the phenanthrene (4) (366 mg), and a final fraction which, after sublimation (130 °C and 10^{-5} mmHg), gave 2-(1-hydroxyethyl)phenanthro[9,10-*d*]thiazole (7) (170 mg) as needles, m.p. 151—152 °C; $\lambda_{max.}$(EtOH) 254 (log ε 4.83), 261sh (4.72), 274sh (4.25), 284 (4.15), 302 (4.06), and 315 nm (4.03); $\nu_{max.}$(KBr) 3 225 cm^{-1}; δ($CDCl_3$) 1.75

[21] H. Labhart, W. Heinzelmann, and J. P. Dubois, *Pure Appl. Chem.*, 1970, **24**, 495.
[22] S. Gabriel, *Ber.*, 1910, **43**, 137.
[23] H. Bredereck, R. Gompper, and F. Reich, *Chem. Ber.*, 1960, **93**, 1389.
[24] T. Naito, *Tetrahedron*, 1968, **24**, 6237.
[25] M. Ohta, *J. Pharm. Soc. Japan*, 1951, **71**, 869.

(3 H, d, *J* 7 Hz, CH_3), 3.37 (1 H, s, OH), 5.31 (1 H, q, *J* 7 Hz, CH), and 7.4—8.8 (8 H, m, phenanthrene ring protons); *m/e* 279 (M^+) (Found: C, 73.0; H, 4.75; N, 4.9. $C_{17}H_{13}NOS$ requires C, 73.11; H, 4.69; N, 5.02%).

(*c*) A solution of the thiazole (3) (346 mg) in refluxing ethanol (600 ml), open to air, was irradiated for 9.5 h. Work-up as above and chromatography (benzene) led to the phenanthrothiazole (4) (70 mg), m.p. 152—153 °C.

Photolysis of 2,4-*Diphenylthiazole* (5).—(*a*) A solution of the thiazole (5) (2.879 g) in refluxing benzene (600 ml) was irradiated through a Pyrex filter for 66 h. The benzene was removed and the residue was chromatographed on silica gel [benzene–light petroleum (2 : 3)] to give two fractions. The first, after recrystallisation from ethanol, gave unchanged (5) (2.033 g). The second fraction, after recrystallisation from ethanol, afforded needles. Sublimation (90 °C and 5 mmHg) gave pure 3,5-diphenylisothiazole (6) (97 mg), m.p. 79—80 °C (lit.,[16] 81 °C); $\lambda_{max.}$(EtOH) 252 (log ε 4.43) and 278 nm (4.34); δ($CDCl_3$) 7.3—8.1 (10 H, m, Ar) and 7.76 (1 H, s, ring proton); *m/e* 237 ($C_{15}H_{11}NS$, M^+), 135 (C_7H_5NS), 134 (C_8H_6S), 121 (C_7H_5S), 103 (C_7H_5N), and 77 (C_6H_5) as reported [16] (Found: C, 76.25; H, 4.6; N, 5.7. $C_{15}H_{11}NS$ requires C, 75.94; H, 4.64; N, 5.90%).

(*b*) A solution of the thiazole (5) (2.673 g) in refluxing ethanol (600 ml) was similarly irradiated for 56 h. Only decomposition occurred; attempts to isolate rearrangement products failed.

Photolysis of 2-(p-*Methoxyphenyl*)-5-*phenylthiazole* (8).—(*a*) A solution of the thiazole (8) (2.627 g) in refluxing benzene (600 ml) was irradiated through a Pyrex filter for 49.5 h. The solvent was removed and the residue was chromatographed on silica gel (benzene) to give three fractions. The first, after rechromatography (chloroform) and recrystallisation from ethanol, gave 3-(*p*-methoxyphenyl)-4-phenylisothiazole (9) (818 mg) as needles from ethanol, m.p. 125—127 °C; $\lambda_{max.}$(EtOH) 283 nm (log ε 4.07); $\nu_{max.}$(KBr) 1 610, 1 510, 1 405, 1 130, 810, 770, 750, and 700 cm^{-1}; δ($CDCl_3$) 3.77 (3 H, s, OCH_3), 6.7—7.5 (9 H, A_2B_2 m and five other aromatic), and 8.50 (1 H, s, isothiazole ring proton); *m/e* 267 ($C_{16}H_{13}NOS$, M^+), 165 (C_8H_7NOS), 134 (C_8H_6S), 133 (C_8H_7NO), and 77 (C_6H_5) (Found: C, 72.05; H, 4.75; N, 5.25. $C_{16}H_{13}NOS$ requires C, 71.91; H, 4.93; N, 5.24%). The second fraction, after repeated chromatography [benzene–light petroleum (4 : 1)] and recrystallisation from ethanol, gave 4-(*p*-methoxyphenyl)-5-phenylthiazole (10) (178 mg) as needles, m.p. 95—96 °C, identical with material synthesised independently. The last fraction, after being twice recrystallised from ethanol, gave 6-methoxyphenanthro[9,10-*d*]thiazole (11) (12 mg) as needles, m.p. 152—153 °C; $\lambda_{max.}$(EtOH) 247sh (log ε 4.71), 254 (4.84), 278 (4.25), 291 (4.09), and 315 nm (3.83); δ($CDCl_3$) 4.00 (3 H, s, OCH_3), 7.3—8.8 (7 H, m, phenanthrene), and 8.88 (1 H, s, thiazole ring proton); *m/e* 265 (M^+) (Found: C, 72.7; H, 4.25; N, 5.15. $C_{16}H_{11}NOS$ requires C, 72.44; H, 4.18; N, 5.28%).

(*b*) The thiazole (8) (3.017 g) was similarly irradiated in ethanol (600 ml) for 35 h. Work-up as above led to the isothiazole (9) (490 mg), unchanged (8) (205 mg), (10) (335 mg), and (11) (67 mg).

Photolysis of 4-(p-*Methoxyphenyl*)-5-*phenylthiazole* (10).—(*a*) A solution of the thiazole (10) (3.108 g) in refluxing ethanol (600 ml) was irradiated through a Pyrex filter for 106.5 h. The solvent was removed and the residue was chromatographed on silica gel (chloroform) to give four fractions. The first, after rechromatography (chloroform) and recrystallisation from ethanol, gave the isothiazole (9) (398 mg), m.p. 127—128 °C. The second fraction gave unchanged (10) (473 mg), m.p. 95—96 °C. The third fraction gave the phenanthrene (11) (454 mg) as needles, m.p. 152—153 °C, after recrystallisation from ethanol. The last fraction, after rechromatography (chloroform) and sublimation (130—140 °C and 2 × 10^{-5} mmHg), gave 2-(1-hydroxyethyl)-6-methoxyphenanthro[9,10-*d*]thiazole (16) (141 mg), m.p. 148—149 °C; $\lambda_{max.}$(EtOH) 248sh (log ε 4.70), 256 (4.81), 262sh (4.69), 280 (4.28), 291 (4.22), and 316 nm (3.92); $\nu_{max.}$(KBr) 3 350 cm^{-1} (OH); δ($CDCl_3$) 1.76 (3 H, d, *J* 7 Hz, CH_3), 3.05br (1 H, OH), 3.98 (3 H, s, OCH_3), 5.32 (1 H, q, *J* 7 Hz, CH), and 7.2—8.8 (7 H, m, phenanthrene ring protons); *m/e* 309 (M^+) (Found: C, 70.1; H, 5.05; N, 4.5. $C_{18}H_{15}NO_2S$ requires C, 69.89; H, 4.89; N, 4.53%).

(*b*) The thiazole (10) (2.453 g) was similarly irradiated in refluxing benzene (600 ml) for 97 h. Work-up as above led to the isothiazole (9) (471 mg), unchanged (10) (253 mg), and the phenanthrothiazole (11) (637 mg).

(*c*) A solution of the thiazole (10) (246 mg) in refluxing ethanol (600 ml), open to air, was irradiated through a Pyrex filter for 10 h. Work-up as above and chromatography (benzene) led to the phenanthrothiazole (11) (83 mg), m.p. 153 °C.

Photolysis of 5-(p-*Methoxyphenyl*)-2-*phenylthiazole* (12).—A solution of the thiazole (12) (2.999 g) in refluxing benzene (600 ml) was irradiated through a Pyrex filter for 100 h. Work-up as above gave only the unchanged thiazole (12) (2.768 g).

Photolysis of 2-(p-*Methoxyphenyl*)-4-*phenylthiazole* (13).—A solution of the thiazole (13) (3.005 g) in refluxing benzene (600 ml) was irradiated through a Pyrex filter for 63 h. The solvent was removed and the residue was chromatographed on silica gel (benzene) to give two fractions. The first was rechromatographed [benzene–light petroleum (1 : 1)] and recrystallised twice from ethanol to give 4-(*p*-methoxyphenyl)-2-phenylthiazole (15) (1.388 g) as a powder, m.p. 134.5—135 °C, identical with an authentic sample.[26] The second fraction, after rechromatography [benzene–light petroleum (1 : 1)] and recrystallisation from ethanol, gave 3-(*p*-methoxyphenyl)-5-phenylisothiazole (14) (175 mg) as leaflets, m.p. 124—125 °C; $\lambda_{max.}$(EtOH) 264 (log ε 4.50) and 278 nm (4.46); $\nu_{max.}$(KBr) 1 608, 1 250, 866, 760, and 686 cm^{-1}; δ($CDCl_3$) 3.87 (3 H, s, OCH_3), 7.3—7.8 (8 H, A_2B_2 m, Ar), and 7.67 (2 H, s, isothiazole ring and aromatic protons); *m/e* 267 ($C_{16}H_{13}NOS$, M^+), 165 (C_8H_7NOS), 134 (C_8H_6S), 133 (C_8H_7NO), 121 (C_7H_5S), and 77 (C_6H_5) [24] (Found: C, 72.2; H, 5.05; N, 5.0. $C_{16}H_{13}NOS$ requires C, 71.91; H, 4.93; N, 5.24%).

Photolysis of 4-(p-*Methoxyphenyl*)-2-*phenylthiazole* (15).—A solution of the thiazole (15) (2.410 g) in refluxing benzene (480 ml) was irradiated through a Pyrex filter. After 50 h, the residue obtained after removal of the solvent was chromatographed on silica gel (benzene) to give two fractions. The first fraction gave unchanged (15) (1.670 g) after recrystallisation from ethanol. The second, after recrystallisation and sublimation (120 °C and 5 mmHg), gave the isothiazole (14) (39 mg), m.p. 124—125 °C.

2-*Phenylthiazole* (17).[27]—A mixture of thiobenzamide (7.2 g) and dichloroethyl acetate (8.1 g) was heated in a sealed tube at 60—70 °C for 6 h. After cooling, the mixture was refluxed with 2N-HCl for 5 min, made alkaline

[26] J. Okamiya, *Nippon Kagaku Zasshi*, 1965, **86**, 315.
[27] K. Hubacher, *Annalen*, 1890, **259**, 228.

(2N-NaOH) and extracted with ether. After drying (Na_2SO_4) and removal of the ether, chromatography on silica gel (benzene) gave a yellow oil. Distillation afforded the thiazole (17) (3.4 g, 40%) as an oil, b.p. 127—128 °C at 12 mmHg [lit.,[28] 135—138 °C at 18 mmHg]; $\lambda_{max.}$(cyclohexane) 287 nm (log ε 4.14); δ($CDCl_3$) 7.28 (1 H, d, *J* 6 Hz), 7.85 (1 H, d, *J* 6 Hz), and 7.3—8.0 (5 H, m, Ar); *m/e* 161 (M^+) (Found: C, 66.95; H, 4.35; N, 8.7. C_9H_7NS requires C, 67.05; H, 4.37; N, 8.68%).

Photolysis of 2-Phenylthiazole (17).—(*a*) A solution of the thiazole (17) (3.001 g) in refluxing ethanol (700 ml) was irradiated through a quartz filter for 14 h. The ethanol was removed and the residue was chromatographed on silica gel [benzene–light petroleum (2 : 1)] to give two fractions. The first, after rechromatography on silica gel [benzene–light petroleum (2 : 1)] and alumina (300 mesh; Ishizu Pharm. Co., Ltd.) with benzene, gave 3-phenylisothiazole (18) (356 mg) as an oil; δ($CDCl_3$) 7.58 (1 H, d, *J* 4.8 Hz, 4-H), 8.67 (1 H, d, *J* 4.8 Hz, 5-H), and 7.3—8.2 (5 H, m, Ar) (Found: C, 67.3; H, 4.4; N, 8.6. C_9H_7NS requires C, 67.05; H, 4.37; N, 8.69%). The u.v., mass, and i.r. spectral data agreed with those reported.[16,24,29] The second fraction, after purification by chromatography on silica gel [benzene–light petroleum (2 : 1)] and alumina with benzene, gave 4-phenylthiazole (19) (621 mg) as needles, m.p. 50—51 °C, identical with an authentic sample.[30]

(*b*) A solution of the thiazole (17) (1.986 g) in refluxing benzene (500 ml) was similarly irradiated for 15 h. Work-up as above and chromatography on silica gel (benzene) led to the isothiazole (18) (191 mg) and a final fraction, after the separation by preparative g.l.c. (3/8 in × 20 ft, 30% SE-30, 200 °C) gave the thiazole (19) (99 mg) and unchanged (17) (762 mg).

Photolysis of 4-Phenylthiazole (19).—(*a*) A solution of the thiazole (19) (3.006 g) in refluxing ethanol (700 ml) was irradiated through a quartz filter for 38.5 h. The solvent was removed and the residue was chromatographed on silica gel [benzene–light petroleum (2 : 1)] to give two fractions. The first, after purification by rechromatography (benzene), gave 3-phenylisothiazole (18) (40 mg) as an oil. The second fraction gave the unchanged thiazole (19) (2.320 g).

(*b*) The thiazole (19) (2.878 g) was similarly irradiated in refluxing benzene (700 ml) for 48 h. Work-up as above led to the isothiazole (18) (18 mg) and the starting material (19) (2.538 g).

Photolysis of 5-Phenylthiazole (20).—(*a*) A solution of the thiazole (20) (2.829 g) in refluxing ethanol (700 ml) was irradiated through a quartz filter. After 26 h, the solvent was removed and the residue was chromatographed on silica gel [benzene–light petroleum (2 : 1)] to give two fractions. The first fraction, after purification by rechromatography on alumina (benzene), gave 4-phenylisothiazole (21) (339 mg) as a solid, m.p. 30—31 °C (Found: C, 67.25; H, 4.25; N, 8.55. C_9H_7NS requires C, 67.05; H, 4.37; N, 8.68%), which showed u.v. and n.m.r. spectral data as reported.[16] The second fraction gave unchanged (20) (718 mg).

(*b*) The thiazole (20) (2.725 g) was similarly irradiated in benzene (600 ml) for 33 h. Work-up as above and chromatography on silica gel [benzene–light petroleum (2 : 1)] led to the isothiazole (21) (82 mg) and the starting material (20) (1.407 g).

Quantum Yield Determinations.—All quantitative measurements were made on a concave monochromator at room temperature. Samples were purged initially with nitrogen for at least 30 min and the quartz sample cells (4 ml) were sealed during irradiation. Light intensity and absorption were measured by ferrioxalate actiometry.[31] After irradiation, the degree of reaction was determined by g.l.c. (5 wt % Carbowax 20M Chromosorb WAW, 60—80 mesh, 150 °C). The conversions were run to 30—40% or less. Benzophenone was used as internal standard.

Quenching and Sensitization Studies.—Solutions of 2-phenylthiazole (17) containing freshly distilled penta-1,3-diene as a standard triplet quencher were irradiated under conditions where more than 98% of the light was absorbed by the thiazole (17) (311 nm irradiation). The reaction was monitored by g.l.c. and in no case was the amount of the rearrangement products formed affected by the penta-1,3-diene. Sensitization experiments utilized benzophenone or acetophenone as a standard triplet sensitizer. The reaction was monitored by g.l.c. analysis as described above and in no case were rearrangement products detected.

5-Deuterio-2-phenylthiazole (22).—To a solution of 2-phenylthiazole (17) (6.7 g) in glacial acetic acid (34 ml), boiling under reflux for 3 h, was added a solution of bromine (6.7 g) in glacial acetic (34 ml). The mixture was cooled and poured onto ice, extracted with ether, and the extracts washed with water, Na_2CO_3, and then dried (Na_2SO_4). After removal of the ether, the residue was chromatographed on silica gel [benzene–light petroleum (2 : 1)] to give 5-bromo-2-phenylthiazole (4.4 g, 44%), m.p. 82—83 °C; $\lambda_{max.}$(EtOH) 298 nm (log ε 4.23) (Found: C, 45.0; H, 2.4; N, 5.9. C_9H_6BrNS requires C, 45.01; H, 2.51; N, 5.83%). The thiazole (22) was prepared by treatment of 5-bromo-2-phenylthiazole (4.483 g) in n-propyl bromide (20.1 g) with fresh magnesium (1.04 g) in ether (70 ml) followed by reaction with 99.75% deuterium oxide (10 ml). Extraction of the reaction mixture with chloroform and chromatography of the product on silica gel [benzene–light petroleum (2 : 1)] gave the thiazole (22) (2.923 g, 96%) as an oil; $\lambda_{max.}$(EtOH) 288 nm (log ε 4.15); *m/e* 162 (M^+). The n.m.r. spectrum completely lacked the characteristic doublet signal at 7.28.

2-Deuterio-4-phenylthiazole (25).—The thiazole was prepared by refluxing 2-chloro-4-phenylthiazole[32] (4.472 g) with a mixture of acetic anhydride (20 ml) and 99.75% deuterium oxide (20 ml) to which Zn (9.752 g) had been added. The reaction was carried out for 2 h. The resulting mixture was diluted with water, filtered, and extracted three times with ether; the ether extract was washed with aqueous $NaHCO_3$ until neutral and once with water. After drying (Na_2SO_4), removal of the ether gave colourless crystals on cooling. Further chromatographic purification [benzene–light petroleum (2 : 1)] gave the thiazole (25) (2.652 g, 72%), m.p. 50 °C; $\lambda_{max.}$(EtOH) 253 nm (log ε 4.18); *m/e* 162 (M^+). The n.m.r. spectrum showed the complete disappearance of hydrogen at the 2-position.

Photolysis of 5-Deuterio-2-phenylthiazole (22).—A solution of the thiazole (22) (2.023 g) in refluxing benzene (500 ml)

[28] H. Erlenmeyer, C. Becker, E. Sorkin, H. Bloch, and E. Suter, *Helv. Chim. Acta*, 1947, **30**, 2058.
[29] M. Beringer, B. Prijs, and H. Erlenmeyer, *Helv. Chim. Acta*, 1966, **49**, 2468.
[30] G. Popp, *Annalen*, 1889, **250**, 273.
[31] C. A. Parker, *Proc. Roy. Soc.*, 1953, **A220**, 104.
[32] H. Beyer and G. Ruhlig, *Chem. Ber.*, 1956, **89**, 107.

was irradiated for 23 h under the same conditions as described in the photolysis of (17). After a similar work-up of the photolysate, the isothiazole [(24) and (18)] (139 mg), unchanged (22) (901 mg), and (23) (60 mg) were obtained. The n.m.r. spectrum of the isothiazole [singlet at 8.67 (5-H), doublet at 8.67 (5-H, *J* 4.8 Hz), and doublet at 7.58 (4-H, *J* 4.8 Hz)] consisted of (24) and (18) in the ratio of 69 : 31. A signal at 8.86 corresponding to 2-H was observed as a singlet (1 H) in the n.m.r. spectrum of (23).

Photolysis of 2-*Deuterio*-4-*phenylthiazole* (25).—A solution of the thiazole (25) (2.216 g) in refluxing benzene (500 ml) was irradiated for 67.5 h under the same conditions as described in the photolysis of (19). After similar work-up of the photolysate, the isothiazole (26) (30 mg) and unchanged (25) (1.190 g) were obtained. The n.m.r. spectrum of the isothiazole (26) showed complete disappearance of a doublet signal (δ 8.67, *J* 4.8 Hz).

Photolysis of 2-*Phenylthiazole* (17) *in the Presence of Deuterium Oxide.*—A solution of the thiazole (17) (786 mg) in a mixture of dry benzene (250 ml) and deuterium oxide (5 ml) was irradiated for 30 h under conditions similar to those used for the other isomers. After similar work-up of the photolysate, the isothiazole [(24) and (18)] (124 mg), unchanged (22) (51 mg), and the thiazole (19) (30 mg) were obtained. The n.m.r. spectrum of the isothiazole [singlet at 8.67 (5-H), doublet at 8.67 (5-H, *J* 4.8 Hz), and doublet at 7.58 (4-H, *J* 4.8 Hz)] consisted of (24) and (18) in the ratio of 22 : 78.

Photolysis of 4-*Phenylthiazole* (19) *in the Presence of Deuterium Oxide.*—A solution of the thiazole (19) (2.430 g) in a mixture of dry benzene (400 ml) and deuterium oxide (5 ml) was irradiated for 60 h. After similar work-up of the photolysate, the isothiazole [(24) and (18)] (23 mg) and unchanged (19) (2.285 g) were obtained. The n.m.r. spectrum of the isothiazole [singlet at 8.67 (5-H), doublet at 8.67 (5-H, *J* 4.8 Hz), and doublet at 7.58 (4-H, *J* 4.8 Hz)] showed it consisted of (24) and (18) in the ratio of 33 : 67.

Photolysis of 5-*Phenylthiazole* (20) *in the Presence of Deuterium Oxide.*—A solution of the thiazole (20) (2.676 g) in a mixture of dry benzene (600 ml) and deuterium oxide (5 ml) was irradiated for 33 h. Chromatography of the residue, after work-up as above, gave the isothiazole (21) (25 mg) and unchanged (20) (1.499 g); the n.m.r. spectrum of neither indicated incorporation of deuterium.

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