Photochemical Reactions. Part 23.[1] The Photo-Fries Rearrangement of Bis-(2-acetylaminophenyl) Disulphides [2]

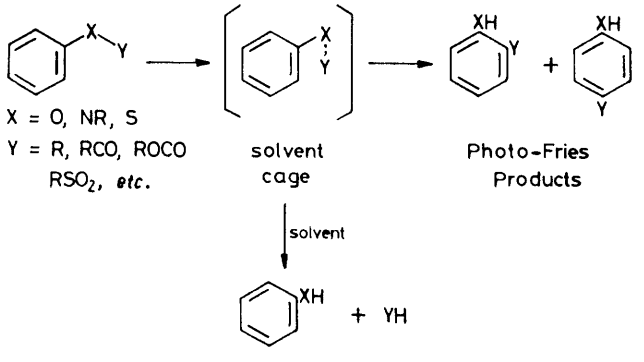
By **Yoshifumi Maki** * and **Magoichi Sako**, Gifu College of Pharmacy, 6–1, Higashi-5-Chome, Mitahora, Gifu, 502, Japan

Ultraviolet irradiation of the bis-(2-acetylaminophenyl) disulphides (1a and b) results in the preferential formation of 7-(2-acetylaminophenylthio)benzothiazoles (2a and b) accompanied by minor amounts of 2-methylbenzothiazoles (3a and b), respectively. A crossover experiment with (1a and b) clearly indicates that the formation of (2a and b) involves an intermolecular photo-Fries rearrangement.

THE photo-Fries rearrangement is fairly general for aromatic systems (Scheme 1).[3] The generally accepted mechanism of the rearrangement involves initial light-induced homolytic cleavage of the X–Y bond followed by rearrangement of the resulting biradical to the observed *ortho*- and *para*-products in a solvent cage. In addition, cleavage products resulting from hydrogen abstraction by the intermediate radicals, which escape from the solvent cage, usually accompany the rearrangement products.[3,4] The absence of crossover products has led to the suggestion that the rearrangements proceed by an intramolecular sigmatropic-shift, but this interpretation has been questioned.[5]

Although the photolysis of aromatic disulphides might be expected to cause an analogous Fries-type rearrangement (X = S, Y = SR in Scheme 1), details of their photorearrangement remain equivocal because of the occurrence of further photoreactions of the primary products leading to polymers.[6,7]

We overcame this difficulty by use of the bis-(2-acetylaminophenyl) disulphides (1a and b), in which the *ortho*-acetylamino-group can efficiently trap the initially formed thiol *via* rearrangement to prevent

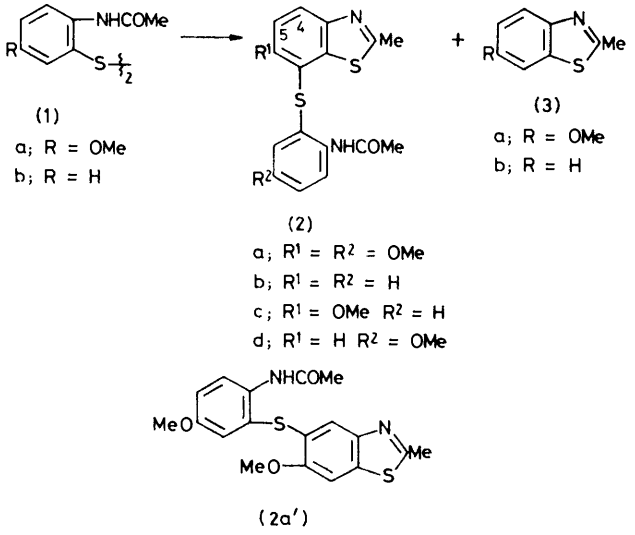


SCHEME 1

further reactions.[8] We now describe our observations which demonstrate the photo-Fries rearrangement of aromatic disulphides in an intermolecular fashion.

RESULTS AND DISCUSSION

Irradiation of bis-(2-acetylamino-4-methoxyphenyl) disulphide (1a) in acetonitrile (1×10^{-2} M) was carried out using a 400-W high-pressure mercury arc lamp through a Pyrex filter under nitrogen until disappearance of (1a) was complete (monitored by t.l.c.; *ca.* 1 h). Chromatography of the mixture of products allowed



SCHEME 2

isolation of the benzothiazoles (2a), m.p. 83—85 °C, and (3a) (an oil), in 62 and 10% yields, respectively. The expected 5-phenylthio-derivative (2a') and analogous compounds were not detected.

The structure of (3a) was confirmed by i.r. and n.m.r. spectral comparison with an authentic sample.[9a]

Spectral data and microanalytical results fully supported the structure of (2a). Its n.m.r. spectrum showed a well resolved AB-type signal (δ 7.13 and 7.94, *ca.* *J* 9 Hz), which was distinguishable from the NH signal, δ 8.46br (1 H), and other aromatic proton signals, δ 6.87 (1 H, q, *J* 3 and 9 Hz, 4'-H), 7.15 (1 H, d, *J* 3 Hz, 6'-H), and 8.18 (1 H, d, *J* 9 Hz, 3'-H). Thus, the AB signal can be assigned unequivocally to the vicinal benzene ring protons (4-H and 5-H) of the benzothiazole unit. On the basis of these data, the alternative structure (2a') can be eliminated.

When methanol was used as solvent, analogous irradiation of (1a) gave (2a) and (3a) in 66 and 22% yields, respectively.

Irradiation of bis-(2-acetylaminophenyl) disulphide (1b) in methanol under similar conditions led to the

formation of the benzothiazoles (2b), m.p. 153—159 °C, and (3b) in 40 and 30% yields, respectively. The structure of (2b) was tentatively assigned by analogy with the formation of (2a), and the (3b) was identical with a sample prepared by an unambiguous route.[9a]

A mixture of (1a) and (1b) (1 : 1) in methanol was irradiated under the same conditions. Careful chromatography of the resulting mixture led to the isolation of the crossover product (2c), m.p. 160—163 °C (20%), together with (2a) (15%), (2b) (13%), (3a) (10%), and (3b) (10%).

The structure of the crossover product (2c) was established on the basis of spectral data, in particular the fragmentation pattern in its mass spectrum and n.m.r. comparison with (2a). The mass spectrum showed a fragment peak at *m/e* 134 ($M^+ - 210$), attributed to loss of the acetylaminophenyl unit, as well as the molecular ion (*m/e* 344). The n.m.r. spectrum showed an AB system (δ 7.13 and 7.92, *J* 9 Hz) due to 4- and 5-H of the 6-methoxybenzothiazole ring.

The n.m.r. spectrum of the residual reaction mixture also showed signals at δ 2.02 (3 H, s, NHCO*Me*), 2.86 (3 H, s, =CMe), and 3.77 (3 H, s, OMe), suggesting the formation of another crossover product (2d).

Thus, we conclude that the formation of (2) from (1) involves an intermolecular rearrangement as depicted in Scheme 3.

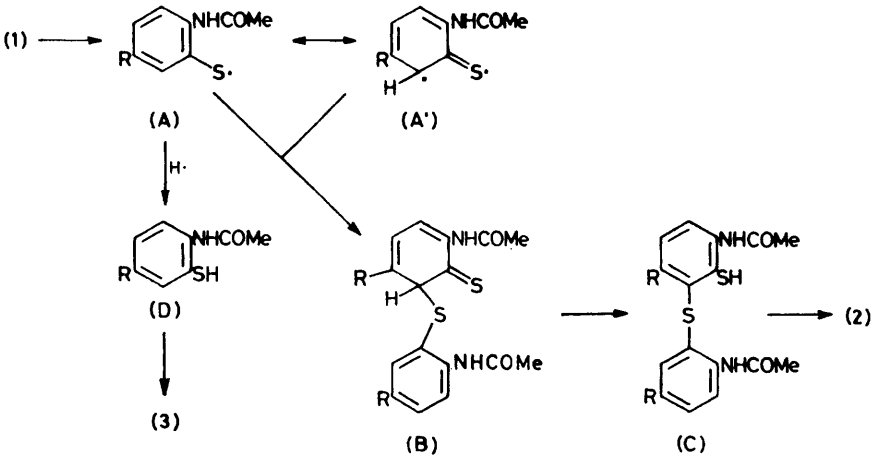
It has been proposed that photochemical rearrangement in cyclic divinyl disulphide systems could proceed *via* a concerted suprafacial 1,3-sigmatropic shift allowed in an excited state.[9b] Alternative intramolecular rearrangement in a solvent cage has been claimed in the photolysis of open-chain alkenyl disulphide systems.[10] A concerted process or an intramolecular process, however, is not a major pathway, at least in the case of aromatic disulphides as just demonstrated.

We propose that homolytic cleavage of the S–S bond of (1) in an excited state gives the arythiyl radical (A), which could combine intermolecularly with the resonance hybrid (A') to give the *ortho*-coupling intermediate (B). The intermediate (B) could be aromatized *via* a 1,3-hydrogen shift to the thiol intermediate (C), which would cyclize to give (2).

The source of hydrogen for the formation of the benzothiazoles (3), which is a minor process in every case, appears to be undetermined side reactions rather than the solvent.

Photolysis of phenylthioacetates[7] and benzenesulphenanilides[11] leads to a Fries-type rearrangement to give both *ortho*- and *para*-coupling products. In contrast to these observations, it is notable that the present rearrangement leads to the exclusive formation of the *ortho*-coupling product (2). At present, however, we have no evidence as to why only the *ortho*-product is formed.

Several examples of the addition of thiyl radicals to aromatic systems are now known,[12] and an alternative pathway which proceeds *via* addition of the arythiyl radical (A) to the initially formed benzothiazole (3) may be considered for the formation of (2). The absence of formation of (2c) upon irradiation of a mixture of (1b) and (3a) clearly eliminates this alternative pathway.



SCHEME 3

EXPERIMENTAL

M.p.s were determined on a Yanagimoto micro-hot-stage apparatus. I.r. spectra were recorded on a Hitachi 215 spectrometer for neat films or potassium bromide discs. ^{1}H N.m.r. spectra were obtained on a Hitachi R 20-B (60 MHz) spectrometer using $CDCl_3$ as solvent and tetramethylsilane as internal standard. U.v. spectra were obtained for dilute methanolic solution on a Hitachi 323 spectrophotometer. All irradiations were conducted in an immersion reaction vessel equipped with a water-cooling jacket (Rikosha model UVL 400P) using a 400-W high-pressure mercury arc lamp through a Pyrex filter. Prior to irradiation, solutions were flushed with nitrogen and nitrogen was bubbled through the solutions during the irradiation. Column chromatography was carried out on silica gel (Mallincrodt; 100 mesh) using chloroform–acetone (15 : 1) as eluant.

Photolysis of Bis-(2-acetylamino-5-methoxyphenyl) Disulphide (1a) *in Acetonitrile or Methanol.*—A solution of (1a) (100 mg) in acetonitrile (30 ml) was irradiated until (1a) had disappeared (monitored by t.l.c.; *ca.* 1 h). After

removal of solvent under reduced pressure, silica gel column chromatography of the residue led to the isolation of 6-methoxy-2-methylbenzothiazole (3a) as an oil (9.1 mg, 10%), and 7-(2-*acetylamino*-5-*methoxyphenylthio*)-6-*methoxy*-2-*methylbenzothiazole* (2a). The expected 5-(2-acetylamino-5-methoxyphenylthio)-isomer (2a') and analogous products were not detected. The structure of (3a) was confirmed by i.r. and n.m.r. comparison with an authentic sample.[9a] Recrystallization of (2a) from ether afforded crystals, m.p. 83—85 °C (Found: C, 57.7; H, 4.8; N, 7.5. $C_{18}H_{18}N_2O_3S_2$ requires C, 57.75; H, 4.85; N, 7.5%); $\nu_{max.}$ 3 300 (NH) and 1 680 cm^{-1} (CONH); δ 2.17 (3 H, s, NHCO*Me*), 2.78 (3 H, s, =CMe), 3.76 (3 H, s, OMe), 3.97 (3 H, s, OMe), 7.13 and 7.92 (each 1 H, AB system, *J* 9 Hz, 4- and 5-H), 8.46br (1 H, NH), 6.87 (1 H, q, J_1 3, J_2 9 Hz, 4'-H), 7.15 (1 H, d, *J* 3 Hz, 6'-H), and 8.18 (1 H, d, *J* 9 Hz, 3'-H); $\lambda_{max.}$ (ε) 308 (5 × 10^3), 297 (6 × 10^3), and 246 nm (2 × 10^4); *m/e* 374 (M^+), 332 (M^+ − 42), and 164 (M^+ − 210).

Analogously, a solution of (1a) (100 mg) in methanol (30 ml) was irradiated for 1 h. After removal of solvent under reduced pressure, silica gel column chromatography of the residual oil led to isolation of (3a) (20.0 mg, 22%) and (2a) (63.0 mg, 66%), respectively.

Photolysis of Bis-(2-acetylaminophenyl) Disulphide (1b) *in Methanol.*—A solution of (1b) (100 mg) in methanol (30 ml) was irradiated for 1 h. After removal of solvent under reduced pressure, silica gel column chromatography of the residual oil led to the isolation of 2-methylbenzothiazole (3b) (26.9 mg, 30%) and of 7-(2-*acetylaminophenylthio*)-2-*methylbenzothiazole* (2b) (37.8 mg, 40%), respectively. The structure of (3b) was confirmed by i.r. and n.m.r. comparison with an authentic sample.[9a] Recrystallization of (2b) from ether afforded crystals, m.p. 153—155 °C (Found: C, 61.0; H, 4.55; N, 8.9. $C_{16}H_{14}N_2OS_2$ requires C, 61.1; H, 4.5; N, 8.9%); $\nu_{max.}$ 3 200 (NH) and 1 680 cm^{-1} (NHCO); δ 2.06 (3 H, s, NHCO*Me*), 2.85 (3 H, s, =CMe), and 7.0—9.0 (8 H, m, NH and ArH); $\lambda_{max.}$ (ε) 278 (5 × 10^3) and 246 (1.7 × 10^4); *m/e* 314 (M^+) and 149 (M^+ − 165).

Photolysis of a Mixture of (1a) *and* (1b) *in Methanol.*—A solution of (1a) (50 mg) and (1b) (50 mg) in methanol (30 ml) was irradiated for 1 h. After removal of solvent under reduced pressure, silica gel column chromatography of the residual oil led to the isolation of (3a) (4.6 mg, 10%), (3b) (4.5 mg, 10%), (2a) (7.2 mg, 15%), (2b) (6.1 mg, 13%), and the crossover product, 7-(2-*acetylaminophenylthio*)-6-*methoxy*-2-*methylbenzothiazole* (2c). Recrystallization of (2c) from ether afforded crystals, m.p. 160—163 °C (Found: C, 59.25; H, 4.65; N, 8.1. $C_{17}H_{16}N_2O_2S_2$ requires C, 59.3; H, 4.7; N, 8.1%); $\nu_{max.}$ 3 360 (NH) and 1 690 cm^{-1} (NHCO); δ 2.18 (3 H, s, NHCO*Me*), 2.77 (3 H, s, =CMe), 3.97 (3 H, s, OMe), and 7.0—9.0 (7 H, m, NH and ArH); the signals include an AB system centred at δ 7.13 and 7.92, *J* 9 Hz); $\lambda_{max.}$ 308 (ε 5 × 10^3), 297 (6 × 10^3), and 242 nm (2 × 10^4); *m/e* 344 (M^+) and 134 (M^+ − 210).

The n.m.r. spectrum of the residue showed signals at δ 2.02 (3 H, s, NHCO*Me*), 2.86 (3 H, s, =CMe), and 3.77 (3 H, s, OMe), suggesting the formation of another crossover product (2d).

[8/1211 *Received*, 30*th June*, 1978]

REFERENCES

[1] Part 22, Y. Maki and T. Furuta, *Synthesis*, 1978, 382.

[2] A part of this work has appeared in preliminary form: Y. Maki and M. Sako, *Tetrahedron Letters*, 1976, 851

[3] For reviews, see D. Bellus, *Adv. Photochem.*, 1978, **8**, 109; V. I. Stenberg, *Org. Photochem.*, 1967, **1**, 127.

[4] For a leading reference, see D. Masilami, R. O. Hutchins, and J. Ohr, *J. Org. Chem.*, 1976, **41**, 3687.

[5] C. E. Kalmus and D. M. Hercules, *J. Amer. Chem. Soc.*, 1974, **96**, 449, and references therein.

[6] Y. Schaafsma, A. F. Bickel, and E. C. Kooyman, *Tetrahedron*. 1960, 76.

[7] E. L. Lovoridge, B. R. Beck, and J. S. Bradohaw, *J. Org. Chem.*, 1971, **36**, 221.

[8] For example, see Y. Maki and M. Sako, *J. Amer. Chem. Soc.*, 1977, **99**, 5021; *Tetrahedron Letters*, 1976, 375.

[9] (*a*) A. Hoffmann, *Ber.*, 1880, **13**, 21, 1236, 1238; (*b*) L. Dalgaard and S. O. Lawesson, *Tetrahedron Letters*, 1973, 4319.

[10] H. Morita and S. Oae, *Tetrahedron Letters*, 1976, 35.

[11] T. Ando, M. Nojima, and N. Tokura, *J.C.S. Perkin I*, 1977, 2227.

[12] L. Benati, C. M. Camaggi, and G. Zanardi, *J.C.S. Perkin I*, 1972, 2817; G. Buchholz, J. Martens, and K. Praefcke, *Tetrahedron Letters*, 1975, 3213; W. Ando, T. Oikawa, K. Kishi, T. Saiki, and T. Migita, *J.C.S. Chem. Comm.*, 1975, 704.