Use of Heterocyclic Compounds as Photosensitisers for the Decarboxylation of Carboxylic Acids

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Irradiation of solutions of substituted acetic acids $ArX{\cdot}CH_2{\cdot}CO_2H$ (X = O, S, or NH) in the presence of acridine, phenazine, benzophenazines, and dyes such as Methylene Blue and eosin, leads to decarboxylation of the acids. Reaction occurs in the presence of oxygen and products derived from the substituted methyl radicals $ArX{\cdot}\dot{C}H_2$ are isolated. Under these conditions the heterocyclic compounds are recovered unchanged at the end of the reaction. Possible reaction mechanisms are discussed and the proposal is made that reaction occurs *via* electron transfer from the acid to an excited state of the sensitiser.

MANY examples are to be found of heterocyclic compounds acting as photosensitisers for the decarboxylation of carboxylic acids. Thus riboflavin [1] and closely related compounds [2] are known to act as sensitisers for the decarboxylation of indole-3-acetic acid and α-amino-acids. Evidence [1b,2b] points to participation of the triplet state of the flavin in these reactions although their exact course does not seem to have been rigorously established. Thus in some cases it appears that the presence of *N*-arylglycines leads to bleaching of the dye, but the concomitant formation of carbon dioxide was not noted.[8]

RESULTS AND DISCUSSION

We report that acids of the type $RX{\cdot}CH_2{\cdot}CO_2H$ (X = O, S, or NH) undergo decarboxylation on irradiation in the presence of the following compounds: acridine, phenazine, benzophenazines, Methylene Blue, and Rose Bengal. Reaction occurs both in the presence and in the absence of oxygen. The products, and their yields from reactions run in the presence of oxygen, are shown in the Table. Under these reaction conditions the heterocyclic compounds were recovered unchanged. Whilst reaction occurred readily under anaerobic conditions the isolation of characterisable products was much more difficult. Acridine was found to sensitise the decarboxylation of phenylacetic acid, 4-chlorophenylacetic acid, 4-methoxyphenylacetic acid, benzilic acid, phenoxyacetic acid, and *N*-methyl-*N*-phenylglycine. Product studies

Products and their yields (%) obtained by irradiating oxygenated solutions of carboxylic acids containing heterocyclic compounds

	N-Phenylglycine [a]			*N*-(*o*-Chlorophenyl)glycine [a]			*N*-Methyl-*N*-Phenylglycine [a]		
Heterocycle	CO_2	Aniline [b]	Formanilide [b]	CO_2	*o*-Chloroaniline [b]	*o*-Chloroformanilide [b]	CO_2	*N*-Methylaniline [b]	*N*-Methylformanilide [b]
Acridine	61	55	30	35	48	32	72	50	30
Phenazine	45	55	29	35	45	25	40	52	32
2,3-Diphenylquinoxaline	95	*d*	38	66	48	50	91	30	36
Acenaphtho[1,2-*b*]quinoxaline	90	*d*	53	82	28	50	90	21	39
Methylene Blue	100	49	46	67	33	35	52	37	
Rose Bengal	44	21	65	16		73	38	42	

	Phenylthioacetic acid [c]			Phenoxyacetic acid [c]		
	CO_2	Benzenethiol [b]	Methyl phenyl sulphide [b]	CO_2	Phenol [b]	Anisole [b]
Acenaphtho[1,2-*b*]quinoxaline	77	35	15	77	80	8
Phenanthro[9,10-*b*]quinoxaline	85	39	11	60	85	Trace

[a] Acetonitrile as solvent. [b] Yield based on amount of acid decarboxylated. [c] Benzene as solvent. [d] This product was present during the early stages of the reaction but became consumed as reaction proceeded.

reactions involve α-keto-acids as intermediates [2a] whereas in other cases (*e.g.* with *NN*-dialkyl α-amino-acids) the intermediacy of these acids is unlikely. Other heterocyclic sensitisers which have been studied include Methylene Blue,[3] purines,[4] pyrimidines,[5] pyridines,[6] and acridine.[7] This last compound was found to sensitise decarboxylation of alkanoic acids and also to scavenge alkyl radicals produced in the reaction. It has also been reported that irradiation of Methylene Blue in the

[1] (*a*) A. W. Galston, *Proc. Nat. Acad. Sci. U.S.A.*, 1949, **35**, 10; B. Nathanson, M. Brody, S. Brody, and S. B. Broyde, *Photochem. Photobiol.*, 1967, **6**, 177; J. Meyer, *Z. Botan.*, 1958, **46**, 124; W. R. Frisell, C. W. Chung, and C. G. Mackenzie, *J. Biol. Chem.*, 1959, **234**, 1297; W. J. Nickerson and G. Strauss. *J. Amer. Chem. Soc.*, 1960, **82**, 5007; K. Enno and W. H, Burgess, *ibid.*, 1965, **87**, 5766; S. Patton, *J. Dairy Sci.*, 1954, **37**, 446; (*b*) G. Oster and A. H. Adelman, *J. Amer. Chem. Soc.*, 1956, **78**, 913.

[2] (*a*) P. Byrom and J. H. Turnbull, *Photochem. Photobiol.*, 1967, **6**, 125; (*b*) L. R. Tether and J. H. Turnbull, *Biochem. J.*, 1962, **85**, 517; (*c*) P. Byrom and J. H. Turnbull, *Photochem. Photobiol.*, 1968, **8**, 243; G. R. Penzer and G. K. Radda, *Biochem. J.*, 1968, **109**, 259.

[3] J. C. Goodspeed, B. L. Scott, and J. G. Burr, *J. Phys. Chem.*, 1965, **69**, 1149.

[4] D. Elad and I. Rosenthal, *Chem. Comm.*, 1969, 905; R. Santus, C. Hélène, and M. Ptak, *Compt. rend.*, 1966, **262D**, 2077.

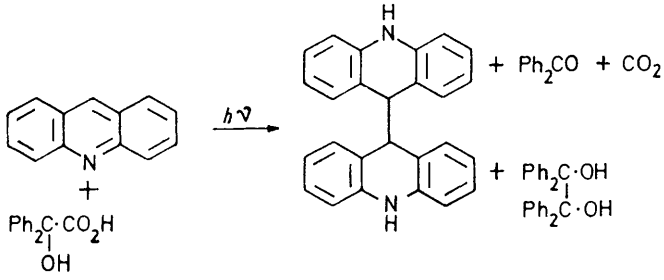
[5] S. Y. Wang, J. C. Nnadi, and D. Greenfield, *Chem. Comm.*, 1968, 1162; *Tetrahedron*, 1970, **26**, 5913.

[6] F. R. Stermitz and W. H. Huang, *J. Amer. Chem. Soc.*, 1970, **92**, 1446.

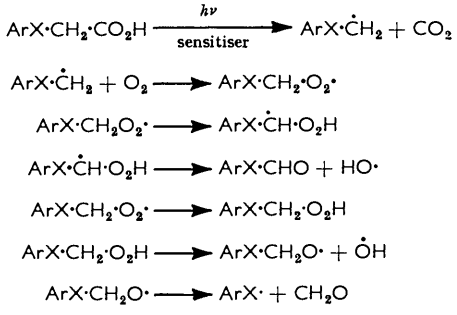
[7] R. Nogori, M. Kato, M. Kawanisi, and H. Nozaki, *Tetrahedron*, 1969, **25**, 1125.

[8] S. Matsumoto, *Bull. Chem. Soc. Japan*, 1962, **35**, 1860.

were made for reactions with benzilic acid and phenoxyacetic acid but the other reactions were not investigated. Benzilic acid was decarboxylated to give 9,9′-biacridan, 1,1,2,2-tetraphenylethylene glycol, and benzophenone.



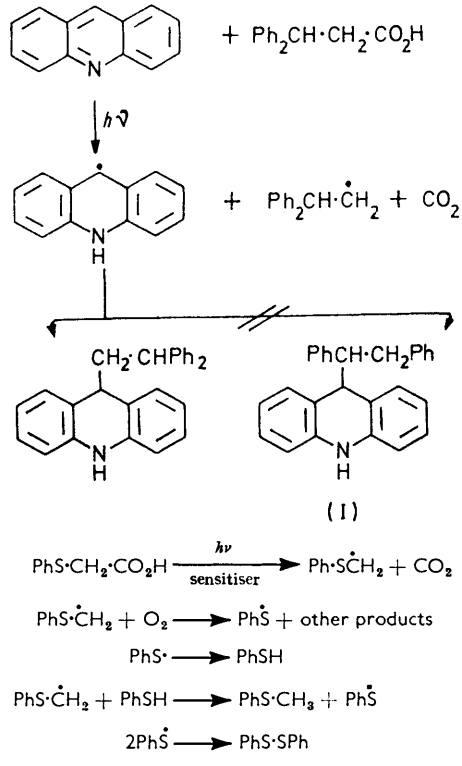
In the decarboxylation reactions run in the presence of oxygen, dealkylation also occurs ($ArX{\cdot}CH_2{\cdot}CO_2H \longrightarrow ArXH$). From previous studies on the decarboxylation of carboxylic acids [9] and of the sensitised oxidation of amines,[10] we conclude that these dealkylation products arise from intermediate substituted methyl radicals $ArX{\cdot}\dot{C}H_2$. The products derived from the amino-acids are those known to be produced from amino-methyl radicals. With phenylthioacetic acid, less dealkylation



occurred than with phenoxyacetic acid. We attribute this as being due to the benzenethiol formed in the reaction acting as a source of hydrogen atoms for the phenylthiomethyl radicals. This reaction has been previously observed.[8b]

The observation that 1,1,2,2-tetraphenylethylene glycol is formed in the reaction between benzilic acid and acridine is a further indication that these decarboxylations are free-radical in character. It has been previously pointed out [7] that the reactions may be ionic, the evidence being that decarboxylation of 2,2-diphenylpropionic acid did not give any products of phenyl migration. However, the lack of any of the product (I) may be due to the extremely efficient radical recombination reaction.

The question as to the nature of the primary photochemical process is particularly intriguing. In the case of acridine, there is the possibility that reaction occurs *via* the acid protonating the highly basic and fluorescent $^1\pi\pi^*$ state.[11] However for the solvent systems used in these reactions, no fluorescence from the acridine in the absence or the presence of the acid was observed, and for this reason the $^1\pi\pi^*$ state is discounted as being the reactive species. Since oxygen has little effect on the rate of the reactions we must conclude that either an excited singlet state or a highly reactive triplet state is involved. Recent results support the conclusion that the $^1n\pi^*$ state is the reactive species in the photoreduction of acridine [12] and phenazine [13] and the $^3n\pi^*$ state as being the reactive state in the photoreduction of the benzophenazines.[14] With the evidence available we cannot, at present, decide whether either the $^1n\pi^*$ or the $^3n\pi^*$ state (or both) is involved in the decarboxylation reactions. In the case of Methylene Blue and Rose Bengal it is almost certainly a triplet state which is responsible.



The sensitisers used in these decarboxylation reactions are all easily reducible (*e.g.* as judged by their $E_{\frac{1}{2}}$ values). This, together with the fact that all the acids have relatively low ionisation potentials, leads us to propose that the decarboxylations occur *via* electron-transfer from the acid to the excited sensitiser; the resulting exciplex can then react with the production of carbon dioxide. It has been shown previously that the triplet

[9] (*a*) R. S. Davidson and P. R. Steiner, *Chem. Comm.*, 1971, 1115; *J.C.S. Perkin II*, 1972, 1357; R. S. Davidson, K. Harrison, and P. R. Steiner, *J. Chem. Soc.* (*C*), 1971, 3480; R. S. Davidson, S. Korkut, and P. R. Steiner, *Chem. Comm.*, 1971, 1052; D. R. G. Brimage and R. S. Davidson, *J.C.S. Perkin I*, in the press; (*b*) R. S. Davidson and P. R. Steiner, *J. Chem. Soc.* (*C*), 1971, 1682.

[10] R. F. Bartholomew and R. S. Davidson, *Chem. Comm.*, 1970, 1174; *J. Chem. Soc.* (*C*), 1971, 2342.

[11] G. Jackson and G. Porter, *Proc. Roy. Soc.*, 1961, **A260**, 13.

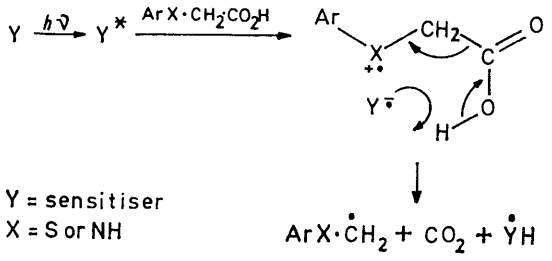
[12] D. G. Whitten and G. J. Lee, *J. Amer. Chem. Soc.*, 1971, **93**, 961.

[13] G. A. Davis, J. D. Gresser, and P. A. Carapellucci, *J. Amer. Chem. Soc.*, 1971, **93**, 2179.

[14] G. A. Davis, *Tetrahedron Letters*, 1971, 3045.

states of flavins [15] and the thionine dyes [16] undergo electron-transfer reactions with amines of low ionisation potential. Similarly, other heterocyclic compounds such as 9,10-diazaphenanthrene [17] undergo photo-redox reactions with amines.

The decarboxylation process may be envisaged as



SCHEME

occurring as shown (Scheme). A similar scheme has been written to describe decarboxylation reactions sensitised by carbonyl compounds, nitro-compounds,[9a,b] and aromatic hydrocarbons.[9c]

EXPERIMENTAL

Materials.—Acridine (R. Emanuel) was used as received. Phenazine (Koch–Light) was recrystallised from ethanol–water to give material of m.p. 176—177°. Quinoxalines were prepared by condensation of the appropriate quinones with *o*-phenylenediamine.[18] Phenanthro[9,10-*b*]quinoxaline had m.p. 225—226° (lit.,[18] 217°) (from aqueous ethanol), and acenaphtho[1,2-*b*]quinoxaline had m.p. 239—241° (lit.,[19] 241°) (from aqueous ethanol). Light petroleum refers to the fraction of b.p. 40—60°.

Spectra and G.l.c. Analyses.—These details are the same as previously reported.[8c] Anisole, phenol, thioanisole, and benzenethiol were detected in a glass column (5 ft × ¼ in) packed with 10% E30 on 100—120 mesh acid-washed and silanised Celite at 100, 100, 120, and 120°, respectively. Naphthalene was used as an internal standard for quantitative estimations.

Irradiation Procedure for Studying Decarboxylation of Amino-Acids.—A solution of the sensitiser (10^{-3}M) in benzene (25 ml) in a 1 cm diam. quartz tube was flushed with a stream of carbon dioxide-free oxygen. The exit gases were passed through two wash bottles in series containing saturated aqueous barium hydroxide. After flushing for 15 min the solutions were irradiated. When acridine, phenazine, and the quinoxalines were employed as sensitisers a Rayonet reactor, fitted with fluorescent lamps having maximum emission at 350 nm, was used. For reactions which used Methylene Blue and Rose Bengal as sensitisers, the irradiations were carried out with eight (25 W) fluorescent 'daylight' lamps which were arranged in a circle around the vessel. After the irradiation was complete (6 h) the solution was flushed for a further 15 min before the barium carbonate was filtered off and weighed. The reaction mixture was subjected to g.l.c. analysis.

Irradiation of a Benzene Solution of Acenaphtho[1,2-b]*quinoxaline containing (Phenylthio)acetic Acid in the Presence of Air.*—A benzene solution (40 ml) of acenaphtho[1,2-*b*]quinoxaline (0·635 g) containing (phenylthio)acetic acid (0·42 g) was irradiated in a Pyrex vessel with the Rayonet reactor. Throughout the irradiation (3 h) a stream of carbon dioxide-free air was passed through the mixture. The exit gases were passed through a solution of barium hydroxide. From the amount of barium carbonate precipitated it was estimated that an 87% yield of carbon dioxide was obtained. G.l.c. analysis showed that benzenethiol (0·09 g) and methyl phenyl sulphide (0·04 g) had been produced. Removal of the solvent from the reaction mixture left an oil which was chromatographed on alumina (50 g). Elution with light petroleum–ether (20 : 1 v/v) gave diphenyl disulphide (0·07 g), m.p. and mixed m.p. 60—61° (from ethanol). Elution with light petroleum–ether (7 : 2 v/v) gave acenaphtho[1,2-*b*]quinoxaline (0·55 g), m.p. and mixed m.p. 240—241° (from aqueous ethanol).

Irradiation of a Benzene Solution of Phenanthro[9,10-b]*quinoxaline containing (Phenylthio)acetic Acid in the Presence of Air.*—A benzene solution (45 ml) of phenanthro[9,10-*b*]quinoxaline (0·70 g) containing (phenylthio)acetic acid (0·42 g) was irradiated under similar conditions to those employed in the previous experiment for 2 h. Carbon dioxide (85%), benzenethiol (0·09 g), and methyl phenyl sulphide (0·03 g) were formed. After removal of the solvent, the mixture was chromatographed on alumina (50 g). Elution with light petroleum–ether (25 : 1 v/v) gave diphenyl disulphide (0·065 g), m.p. and mixed m.p. 61° (from ethanol). Elution with light petroleum–ether (9 : 1 v/v) gave phenanthro[9,10-*b*]quinoxaline (0·63 g), m.p. and mixed m.p. 225—226° (from aqueous ethanol).

Decarboxylation of Phenoxyacetic Acid Sensitised by Acenaphtho[1,2-b]*quinoxaline and Phenanthro*[9,10-b]*quinoxaline.*—A benzene solution (45 ml) of the sensitiser {acenphtho[1,2-*b*]quinoxaline (0·635 g) or phenanthro[9,10-*b*]quinoxaline (0·70 g)} containing phenoxyacetic acid (0·38 g) was irradiated in the Rayonet reactor for 4·5 h. Throughout the irradiation a stream of carbon dioxide-free air was passed through the mixture. The products and their yields are shown in the Table. By chromatography on alumina (see previous experiments for details) the unchanged quinoxalines were recovered: acenaphtho[1,2-*b*]quinoxaline (0·59 g), m.p. and mixed m.p. 240—241° (from aqueous ethanol) and phenanthro[9,10-*b*]quinoxaline (0·60 g), m.p. and mixed m.p. 225—226° (from aqueous ethanol).

Decarboxylation of Benzilic Acid Sensitised by Acridine.—A solution of benzilic acid (0·57 g) in benzene (150 ml), containing acridine (0·45 g) was irradiated with a 100 W medium-pressure mercury vapour lamp (Hanovia) contained in a water-cooled Pyrex well. Throughout the irradiation the solution was flushed with a stream of carbon dioxide-free nitrogen. The exit gases were passed through aqueous barium hydroxide. Irradiation for 5 h gave a 95% yield of carbon dioxide. During the irradiation a white precipitate of 9,9′,10,10′-tetrahydro-9,9′-biacridine (0·47 g), m.p. and mixed m.p. 237—239° (from pyridine), was formed. Removal of the solvent from the reaction mixture left a residue which was chromatographed on silica (100 g). Elution with light petroleum–ether (9 : 1 v/v) gave benzo-

[15] A. Terenin, V. Tachin, and P. Shakhuerdov, *Photochem. Photobiol.*, 1965, **4**, 505; O. D. Dmitrievskii and A. N. Terenin, *Optics and Spectroscopy*, 1968, **24**, 557.

[16] R. S. Davidson and R. F. Bartholomew, *J. Chem. Soc.* (*C*), 1971, 2347.

[17] G. A. Davis and S. G. Cohen, *Chem. Comm.*, 1971, 675.

[18] A. I. Vogel, 'Practical Organic Chemistry,' 3rd edn., Longmans, London, 1956, p. 749.

[19] W. Bradley and F. W. Pexton, *J. Chem. Soc.*, 1954, 4436.

phenone (0·38 g), identified by i.r. spectroscopy. Elution with light petroleum–ether (9 : 2 v/v) gave 1,1,2,2-tetraphenylethylene glycol, m.p. and mixed m.p. 203—204° (from benzene).

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