

Metal-catalysed Organic Photoreactions. Photoreactions of 3,5-Dimethylisoxazole with and without Catalytic Assistance by Copper(II) Salts¹

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Although 3,5-disubstituted isoxazoles afforded products of reactions involving solvent participation when irradiated in alcohols, they gave products of reductive ring-cleavage when irradiated in acetonitrile in the presence of triethylamine. A similar reductive ring cleavage was the main reaction path when these isoxazoles were irradiated in alcohols in the presence of copper(II) salts. A reaction scheme involving exciplex formation is proposed for the reduction.

IN the preceding paper we reported that dypnone, *para*-substituted dypnones, and mesityl oxide undergo photo-oxidation only with catalytic assistance by copper(II) sulphate or other metal salts.² In search of other systems where metal compounds affect photochemical reactions, 3,5-disubstituted isoxazoles were irradiated under various conditions.

RESULTS AND DISCUSSION

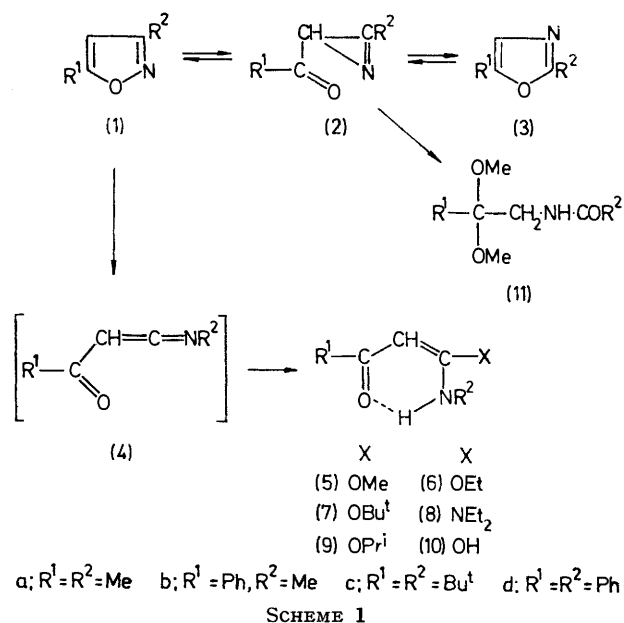
Photolyses without Additives.¹—When a methanolic solution of 3,5-dimethylisoxazole (1a) was irradiated in a quartz vessel, the enone (5a) and the amide (11a) were isolated as main products. Although transpositions are the most commonly observed type of photoreaction of five-membered heterocyclic compounds, the oxazole (3a) was a minor product in the present case.³ From the rates of formations of these products, we propose the illustrated reaction scheme (Scheme 1).^{1a}

Irradiation of (1a) in ethanol afforded an ethoxy-derivative (6a), but the diethoxy-amide corresponding to (11a) was not isolated.

When the irradiation was carried out in acetonitrile or tetrahydrofuran, the azirine (2a) was isolated (10–20% yield) together with the amide (10a), which might be produced from (4a) *via* addition of water present in the solvent. Irradiation of (1a) or (2a) in acetonitrile–water gave the amide (10a) as the main product, accompanied by a small amount of the amide (12).

The photoreaction of (1a) in ether was very slow, and

was accompanied by polymer formation. G.l.c. analysis of the volatile fraction indicated that only a small amount of photo-product was present, the rest being starting



material. The products have not yet been identified. Starting material unchanged after 15 h irradiation amounted to *ca.* 50%.

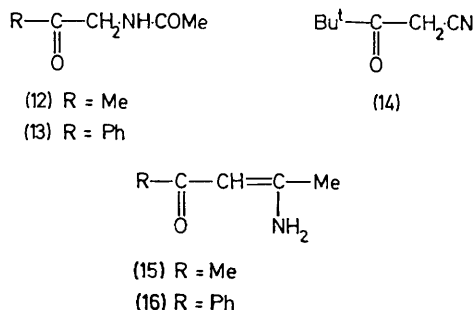
A similar product (5b) of solvent participation was obtained as well as the usual transposition product (3b)

¹ Preliminary reports, (a) T. Sato, K. Yamamoto, and K. Fukui, *Chem. Letters*, 1973, 111; (b) T. Sato and K. Saito, *J.C.S. Chem. Comm.*, 1974, 781; (c) T. Sato, S. Yoshiie, and K. Hayakawa, Abstract of 32nd Annual Meeting, Chemical Society of Japan, April 1975, Tokyo, vol. III, p. 1202.

² T. Sato, K. Tamura, K. Maruyama, O. Ogawa, and T. Imamura, preceding paper.

³ H. Goeth and H. Schmidt, *Chimia (Switz.)*, 1966, 20, 148.

from the photoreaction of 3-methyl-5-phenylisoxazole (1b) in methanol. Photoinduced solvent attack was also observed with *t*-butyl alcohol in the case of (1b), which afforded the butoxy-enone (7b), as indicated by the



n.m.r. spectrum of the crude oil. This oil, when passed through a silica gel column, decomposed to the amide (10b).

When compound (1b) was irradiated in acetonitrile, an azirine (2b) was isolated. The azirine (2b) afforded compounds (1b), (3b), and (5b) on irradiation in methanol. In contrast with the photolytic hydrolysis of (2a), which afforded an amide (10a) as main product (see above), the azirine (2b) underwent hydrolysis on an alumina column to afford the amide (13).

When the isoxazole ring was substituted with a *t*-butyl group, fragmentation took place rather than attack by the solvent. Thus, the irradiation of 3,5-di-*t*-butylisoxazole (1c) in methanol gave a small amount of the nitrile (14), but no signal assignable to a methoxy-group was detected in the n.m.r. spectrum of the crude mixture.

Solvent participation as described above was not observed with 3,5-diphenylisoxazole (1d). Monitoring the reaction by u.v. and t.l.c. indicated that (1d) behaved in a similar way both in methanol and in ether, although the reaction rate was greater in methanol. No signal assignable to a methoxy-group was observed in the n.m.r. spectrum of the crude reaction mixture from (1d) in methanol. In accord with the result of Singh and Ullman,⁴ 2,5-diphenyloxazole (3d) was the sole product.

Photolyses in Methanol in the Presence of Copper(II) Salts.^{1c}—When the reaction in methanol was carried out in the presence of copper(II) sulphate, the reaction pathways shown in Scheme 1 were inhibited, and reductive ring cleavage leading to the amino-enone (15) became the major reaction. The reduction proceeded more satisfactorily when the irradiation was carried out in ethanol with copper(II) chloride as catalyst. Under these conditions, compound (15) was isolated in 49% yield, and (3a) and (6a) were obtained as minor products (6.2 and 3.8% yield, respectively). In a similar way, the amino-enone (16) was obtained from (1b) in fair yield.

The reduction pathway was first observed at a catalyst concentration of 0.001M [at 0.1M-concentration with (1a)], and was favoured by increasing amounts of catalyst. No solvent-participation product (6a) was identified at 0.1M-catalyst concentration, and the yield of

(15) under these conditions amounted to 70%, as revealed by n.m.r. analysis with nitrobenzene as internal reference.

When the copper(II) chloride-catalysed photoreaction was carried out in methanol, 3,5-diacetyl-2,6-dimethylpyridine (17) was isolated together with the amino-enone (15). The ratio of (15) to (17) depended on the time interval between cessation of irradiation and work-up (alumina column). The Table indicates that longer

Product distribution as a function of time interval before work-up

Run	Time interval	Yield (%)			
		(15)	(17)	(1a)	(6a)
1	15 min	12.4	12.4	6.2	5.1
2	1 h	10.4	14.5	6.2	6.2
3	24 h	0	22.1	3.1	3.1

time intervals resulted in greater proportions of (17), which must therefore be a secondary product derived from (15) by a dark reaction. An introduction of a one-carbon unit (C-4 of the pyridine nucleus) is necessary during the process [$2 \times (15) \rightarrow (17)$], and we considered that this might be supplied by the solvent methanol in the form of formaldehyde. A mixture of (15) and formaldehyde in methanol, left in the dark, however, afforded only a trace (17), accompanied by several other products. We found that the presence of copper(II) chloride was effective in inducing the dark reaction [(15) \rightarrow (17)]. However, even under these conditions, the reaction was not as clean as the photoreaction followed by the dark reaction as described above.

There remains the possibility that the reaction [(1a) \rightarrow (15)] was effected through the reducing function of copper(I), which should be formed from copper(II) during irradiation in methanol. This path was, however, ruled out because copper(I) chloride did not reduce the isoxazole (1a) in the dark.

Since the u.v. spectrum of the mixture of compound (1a) and copper(II) chloride or sulphate coincided exactly with the sum of the spectra of the two components, no interaction between these two compounds occurs in the ground state. A catalytic effect by copper(II) chloride was not observed in an aprotic solvent such as acetonitrile.

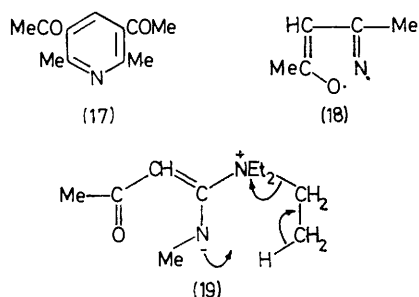
In elucidating the possible role of copper(II) salts, the photochemistry of the isoxazole (1a) in acetonitrile in the presence of triethylamine was informative.

Photolysis in Acetonitrile in the Presence of Triethylamine.^{1b}—Although the azirine (2a) was the main product of irradiation of the isoxazole (1a) in acetonitrile (see above), the reaction pattern changed when the irradiation was carried out in the presence of triethylamine. Under these conditions, no trace of the azirine (2a) was detected; instead compounds (15) and (8a) were obtained in yields of 50 and 8%, respectively. The n.m.r. spectrum showed that the crude reaction mixture prior

⁴ B. Singh and E. F. Ullman, *J. Amer. Chem. Soc.*, 1967, **89**, 6911.

to distillation contained compounds (1a), (15), and (8a) in the ratios 28 : 51 : 21.

Compound (15) could arise *via* (a) homolytic N-O fission in (1a) followed by hydrogen abstraction from solvent by the resulting diradical (18), (b) a secondary reaction induced by the photolysis products of triethylamine, or (c) exciplex formation between (1a) and triethylamine. In order to decide amongst these possibilities, irradiation was performed in propan-2-ol. The solvent-participation product (9a) was the only



product isolated (29.4%). The lack of reduction product in hydrogen-donating solvents such as propan-2-ol and tetrahydrofuran (see above) eliminates path (a). As compound (1a) and triethylamine have absorption maxima in nearly the same wavelength region, it is conceivable that triethylamine undergoes photolysis and that the photolysis products (or unstable intermediates) induce the reduction of (1a) [path (b)]. Therefore, we carried out the irradiation with various ratios of triethylamine to (1a). As the ratio was increased from 1 : 1 to 5 : 1 and then to 10 : 1 the yield of (15) in a specific reaction time decreased from 69 to 16 and then to 6%, as determined by g.l.c. and n.m.r. analyses. This indicates that the reaction is initiated by excitation of (1a) and thus path (b) is ruled out.

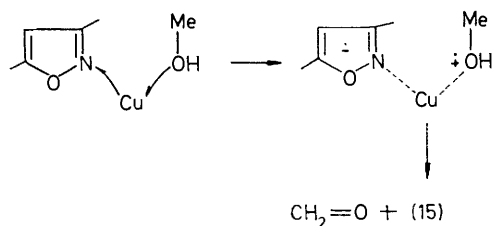
Birch-type photoreduction of aromatic hydrocarbons through exciplex formation is well known.⁵ Formation of a radical anion followed by proton transfer has been considered as the most probable mechanism. We consider that a similar path through exciplex formation [path (c)] operates in the present case, although reductive ring cleavage by this mechanism has no precedent.

The formation of the minor product (8a) is considered to involve the species (19), which could be derived from (4a) and triethylamine. Triethylamine had no effect when methanol was used as solvent: compounds (5a), (11a), and (12) were the main products.

Exciplex formation between benzene and ether is known to proceed only under acidic conditions.⁶ Ohashi, Iio, and Yonezawa⁷ found that 3,5-diphenylisoxazole underwent photoreduction when the nitrogen atom was

quarternized (to give the hydrochloride or the methoxy-tetrachloroferrate). Although a mechanism involving exciplex formation could be considered for these systems also, we could not achieve reduction of (1a) by irradiation in the presence of hydrochloric acid.

Possible Role of Copper(II) Salts.—We are inclined to believe that the copper(II) salt-catalysed photoreduction proceeds through a similar exciplex formation. The formation of formaldehyde, evident from the isolation of the pyridine (17) as product, suggests removal of electron(s) from methanol. As the most probable pathway, we propose a photo- and metal-assisted electron transfer from alcohol to isoxazole as shown in Scheme 2.



SCHEME 2

Although exciplexes with alcohols are not widely known, definitive evidence for their existence has been presented.⁸

Similar assistance by a metal-containing compound in photo-induced electron transfer is proposed in the photo-reactions of $\alpha\beta$ -unsaturated ketones in the presence of titanium(IV) chloride.⁹

EXPERIMENTAL

General procedures are the same as reported previously.² All irradiations were carried out in a quartz vessel.

Photolysis of 3,5-Dimethylisoxazole (1a) in Methanol.—A solution of the isoxazole (1a) (1.3 g) in methanol (150 ml) was irradiated for 24 h. The solvent was removed *in vacuo* and the residual oil was distilled under reduced pressure. Two fractions were obtained: (i) b.p. 100–110° at 4 mmHg (0.3 g), and (ii) b.p. 130–140° at 4 mmHg (0.35 g). G.l.c. revealed that fraction (i) was mainly compound (5a), and fraction (ii) mainly (11a). Pure samples were collected by preparative g.l.c. 4-Methoxy-4-methylaminobut-3-en-2-one (5a) showed *m/e* 129 (*M*⁺) and 114, ν_{\max} 3 400–3 200, 1 633, 1 580, 1 520, and 1 125 cm^{-1} , δ (CCl_4) 1.95 (3 H, s), 2.90 (3 H, d, *J* 5 Hz), 3.82 (3 H, s), 4.70 (1 H, s), and 10.40br (1 H), λ_{\max} (MeOH) 286 nm (ϵ 20 300) (Found: C, 55.9; H, 8.6; N, 10.7. $\text{C}_8\text{H}_{11}\text{NO}_2$ requires C, 55.8; H, 8.5; N, 10.9%). N-(2,2-Dimethoxypropyl)acetamide (11a) showed *m/e* 129 (*M* - MeOH), 87, and 72, ν_{\max} (CCl_4) 3 300, 1 665, 1 180, and 1 050 cm^{-1} , δ (CCl_4) 1.18 (3 H, s), 2.00 (3 H, s), 3.18 (6 H, s), 3.30 (2 H, d, *J* 6 Hz), and 7.50br (1 H, t, *J* 6 Hz) (Found: C, 52.3; H, 9.3; N, 8.6. $\text{C}_7\text{H}_{15}\text{NO}_3$ requires C, 52.1; H, 9.3; N, 8.7%).

The presence of compound (3a) in the crude reaction mixture was indicated by g.l.c. and n.m.r. data, which were compared with those of an authentic sample.¹⁰

⁵ For a review see A. Lablache-Combier, *Bull. Soc. chim. France*, 1972, 915.

⁶ D. Bryth-Smith and G. B. Cox, *Chem. Comm.*, 1971, 915.

⁷ M. Ohashi, A. Iio, and T. Yonezawa, Abstract of 24th Annual Meeting, Chemical Society of Japan, April 1971, Osaka, vol. III, p. 1383.

⁸ A. Castellano, J.-P. Catteau, and A. Lablache-Combier, *J.C.S. Chem. Comm.*, 1972, 1207.

⁹ T. Sato, G. Izumi, and T. Imamura, following paper.

¹⁰ A. Treibs and W. Sutter, *Chem. Ber.*, 1951, 84, 96.

Photolysis of 3,5-Dimethylisoxazole (1a) in Ethanol.—Irradiation was carried out in the same way as in methanol. Vacuum distillation afforded an oil, b.p. 100–130° at 3 mmHg (0.2 g). Preparative g.l.c. gave 4-ethoxy-4-methylaminobut-3-en-2-one (6a), *m/e* 143 (M^+), 128, 115, 100, and 85, ν_{\max} (CCl₄) 3 400–3 200, 1 630, 1 580, 1 520, and 1 115 cm⁻¹, δ (CCl₄) 1.33 (3 H, t, *J* 7 Hz), 1.94 (3 H, s), 2.91br (3 H, s), 4.09 (2 H, q, *J* 7 Hz), 4.74 (1 H, s), and 10.50br (1 H).

Photolysis of 3-Methyl-5-phenylisoxazole (1b) in Methanol.—A solution of the isoxazole (1b) (1 g) in methanol (100 ml) was irradiated for 4 h and the solvent was removed *in vacuo*. The crude mixture was chromatographed on an alumina column, and two compounds, (3b) and (5b), were obtained. The former (3b) was identical with an authentic sample (m.p., mixed m.p., i.r. and n.m.r. spectra).¹¹ The latter (5b) showed i.r. and u.v. spectra, elemental analysis, and m.p. identical with reported data,¹² and δ (CCl₄) 2.83 (3 H, d, *J* 5 Hz), 3.83 (3 H, s), 5.18 (1 H, s), 7.1–7.7 (5 H, m), and 10.72br (1 H).

Photolysis of 3,5-Dimethylisoxazole (1a) in Propan-2-ol.—A solution of the isoxazole (1a) (1.54 g) in propan-2-ol (150 ml) was irradiated for 23 h. The solvent was removed and the residual oil was distilled under reduced pressure. A fraction, b.p. 52° at 3.5 mmHg (0.45 g) was almost pure 4-isopropoxy-4-methylaminobut-3-en-2-one (9a) (g.l.c. analysis), ν_{\max} (CCl₄) 3 400–3 200, 1 620, and 1 110 cm⁻¹, δ (CCl₄) 1.36 (6 H, d, *J* 7 Hz), 1.95 (3 H, s), 2.95 (3 H, d, *J* 4 Hz), 4.62 (1 H, sept, *J* 7 Hz), 4.68 (1 H, s), and 10.67br (1 H).

Photolysis of 3-Methyl-5-phenylisoxazole (1b) in t-Butyl Alcohol.—A solution of the isoxazole (1b) (1 g) in *t*-butyl alcohol (100 ml) was irradiated for 5 h, and the solvent was evaporated off *in vacuo*. The residual light yellow oil showed δ 1.62 (9 H, s), 2.93 (3 H, d, *J* 5 Hz), 5.60 (1 H, s), 7.0–7.5 (5 H, m), and 11.22br (1 H), assignable to compound (7b). Chromatography on a silica gel column (CHCl₃-MeOH) gave crystals of the amide (10b; keto-form). Recrystallization from tetrahydrofuran-*n*-hexane afforded *N*-methyl-3-oxo-3-phenylpropionamide (10b), m.p. 101–102° (lit.,¹³ 101–102°), ν_{\max} (KBr) 3 320, 3 120, 1 680, 1 635, and 1 340 cm⁻¹, δ (CDCl₃) 2.90 (3 H, d, *J* 5 Hz), 4.01 (2 H, s), 6.5–7.0br (1 H), and 7.5–8.2 (5 H, m).

*Photolysis of 3,5-Di-*t*-butylisoxazole (1c) in Methanol.*—The isoxazole (1c) was prepared from dipivaloylmethane and hydroxylamine hydrochloride in aqueous methanol; m.p. 92° (lit.,¹⁴ 98°). A solution of the product (1c) (0.5 g) in methanol (200 ml) was irradiated for 1.5 h, and evaporated *in vacuo*. The residual oil was chromatographed on a silica gel column (ether-*n*-hexane, 1 : 3) to afford 4,4-dimethyl-3-oxopentanitrile (14), m.p. 66–67° (lit.,¹⁵ 68–68.5°), *m/e* 125 (M^+), 110, 97, 82, 68, and 57, ν_{\max} (KBr) 2 220, 1 730, 1 480, 1 390, 1 370, and 1 300 cm⁻¹, δ (CDCl₃) 1.24 (9 H, s) and 3.70 (2 H, s).

Photolysis of 3,5-Dimethylisoxazole (1a) in Methanol-Triethylamine.—A solution of the isoxazole (1a) (1.56 g) and triethylamine (1.54 g) in methanol (150 ml) was irradiated for 25 h. The solvent was removed *in vacuo* and the residual oil was distilled under reduced pressure to give two

fractions. N.m.r. and g.l.c. analyses revealed that fraction (i), b.p. 50–70° at 4 mmHg (0.44 g), was a mixture of compounds (5a) (80%), (11a) (7%), and (12) (13%), and fraction (ii), b.p. 70–100° at 4 mmHg (0.48 g), was a mixture of compounds (5a) (17%), (11a) (34%), and (12) (49%). A pure sample of (12) collected by preparative g.l.c. was identical with an authentic sample¹⁶ (m.p., mixed m.p., and i.r. and n.m.r. spectra).

Photolysis of 3,5-Dimethylisoxazole (1a) in Acetonitrile.—A solution of the isoxazole (1a) (2.3 g) in acetonitrile (120 ml) was irradiated for 23 h. Solvent and starting material were removed *in vacuo* and the residual oil was distilled under reduced pressure. Two fractions were obtained: fraction (i), b.p. 40–45° at 3 mmHg, was almost pure (2a), and fraction (ii), b.p. 60–90° at 3 mmHg, was a mixture of (2a) and (10a). From g.l.c. analysis of each fraction, the overall yields of (2a) and (10a) were 14.2 and 4.6%, respectively. 2-Acetyl-3-methyl-2H-azirine (2a) had *m/e* 97 (M^+) and 82 (base peak), ν_{\max} (CCl₄) 1 795, 1 705, and 1 360 cm⁻¹, δ (CCl₄) 1.92 (3 H, s), 2.60 (3 H, s), and 2.48 (1 H, s). The amide (10a; keto-form) (lit.,¹⁷ m.p. 47°) had ν_{\max} (CHCl₃) 1 710, 1 655, and 1 200 cm⁻¹, δ (CDCl₃) 2.35 (3 H, s), 2.90 (3 H, d, *J* 5 Hz), 3.54 (2 H, s), and 7.5br (1 H).

When the solvent contained water (0.5%) (10a) became the main product.

Photolysis of 3-Methyl-5-phenylisoxazole (1b) in Acetonitrile.—A solution of the isoxazole (1b) (2 g) in acetonitrile (120 ml) was irradiated for 4 h, and the solvent was removed *in vacuo*. The residual oil was chromatographed on a silica gel column (ether-*n*-hexane) to afford the azirine (2b). Although this sample showed i.r. and n.m.r. spectra identical with those reported,¹⁸ and was considered as pure, it did not solidify (lit.,¹⁸ m.p. 40–41°). When the sample was chromatographed on an alumina column, it gave the amide (13), m.p. 86–88° (lit.,¹⁹ 86°), ν_{\max} (KBr) 3 360, 1 680, 1 650, 1 370, and 1 240 cm⁻¹, δ (CDCl₃) 2.05 (3 H, s), 4.40 (2 H, d, *J* 5 Hz), 6.33br (1 H, s), and 6.8–7.7 (5 H, m).

Photolysis of 3,5-Dimethylisoxazole (1a) in Tetrahydrofuran.—A solution of the isoxazole (1a) (1.3 g) in tetrahydrofuran (130 ml) was irradiated for 23 h. The solvent was removed *in vacuo* and the residual oil was distilled under reduced pressure to give two fractions. N.m.r. spectra revealed that fraction (i), b.p. 30–55° at 3.5 mmHg (0.18 g), was almost pure azirine (2a), contaminated with a small amount of (1a), and fraction (ii), b.p. 60–110° at 3.5 mmHg (0.44 g), was mainly the amide (10a), contaminated with a small amount of unidentified compound.

Photolysis of the Azirine (2a) in Acetonitrile-Water.—A solution of the azirine (2a) (0.1 g) in acetonitrile (25 ml) containing water (0.1 ml) was irradiated for 22 h. The solvent was evaporated off *in vacuo* and the remaining oil was shown to be a mixture of (10a) and (12) (10 : 1) by n.m.r. analysis.

Photolysis of 3,5-Dimethylisoxazole (1a) in Acetonitrile-Triethylamine.—A solution of the isoxazole (1a) (1.5 g) and triethylamine (1.5 g) in acetonitrile (150 ml) was irradiated for 24 h. The solvent was removed *in vacuo*, and the residual oil was found to be a mixture of compounds (1a) (28%),

¹¹ G. Caronna, *Gazzetta*, 1950, **80**, 217.

¹² R. B. Woodward and R. A. Olofson, *Tetrahedron*, Suppl. 7, 1966, 415.

¹³ O. Mumm and G. Münchmeyer, *Ber.*, 1910, **43**, 3344.

¹⁴ V. Bertini, A. DeMunno, D. Tafuri, and P. Pino, *Gazzetta*, 1964, **94**, 915.

¹⁵ O. Widman and E. Wahlberg, *Ber.*, 1911, **44**, 2065.

¹⁶ R. H. Wiley and O. H. Borum, *J. Amer. Chem. Soc.*, 1948, **70**, 2006.

¹⁷ Z. Bukac and J. Sebenda, *Czech. P.*, 126,471, 1968 (*Chem. Abs.*, 1969, **70**, 19609x).

¹⁸ B. Singh, A. Zweig, and J. B. Gallivan, *J. Amer. Chem. Soc.*, 1972, **94**, 1199.

¹⁹ A. Pictet and A. Gams, *Ber.*, 1910, **43**, 2384.

(15) (51%), and (8a) (21%) by n.m.r. analysis. Vacuum distillation afforded a fraction b.p. 65–98° at 4 mmHg (1.2 g), which was a mixture of compounds (15) (67.3%) and (8a) (16.5%) (g.l.c. analysis). Pure samples were collected by preparative g.l.c. The amino-enone (15), *m/e* 99 (M^+), and 84 (base peak), showed i.r. and n.m.r. spectra identical with those reported.²⁰ 4-Diethylamino-4-methylaminobut-3-en-2-one (8a) showed *m/e* 170 (M^+), 155, 153, 141, 127, and 98 (base peak), ν_{\max} (CCl_4) 3 400–3 200, 1 612, 1 590, and 1 520 cm^{-1} , δ (CDCl_3) 1.29 (6 H, t, J 7 Hz), 2.06 (3 H, s), 2.93 (3 H, d, J 5 Hz), 3.29 (4 H, q, J 7 Hz), 4.80 (1 H, s), and 10.30br (1 H) (Found: C, 63.3; H, 10.5; N, 16.6. $\text{C}_9\text{H}_{19}\text{N}_2\text{O}$ requires C, 63.5; H, 10.6; N, 16.5%).

Photolysis of 3,5-Dimethylisoxazole (1a) in Methanol-Copper(II) Sulphate.—A solution of the isoxazole (1a) (1 g) and copper(II) sulphate pentahydrate (0.5 g) in methanol (100 ml) was irradiated for 2 h. The solvent was evaporated off *in vacuo* and the residue was extracted with carbon tetrachloride. The extract was evaporated and the residue was recrystallized from acetonitrile. The solid was a mixture of complexes of copper(II) with acetylacetone and with the amino-enone (15) as revealed from i.r. spectrum and elemental analysis. Although the mixture (as chloroform solution) could be passed through a silica gel column without decomposition, it decomposed on an alumina column and compound (15) was isolated from the eluate.

When the methanolic solution after the irradiation was directly passed through an alumina column, a mixture of compounds (15) and (5a) was obtained, in yields 9.6 and 3.2%, respectively, together with 9.4% of starting material. A trace of (17) was also detected (n.m.r. spectrum).

Photolysis of 3,5-Dimethylisoxazole (1a) in Methanol-Copper(II) Chloride.—A solution of the isoxazole (1a) (0.4 ml) and copper(II) chloride dihydrate (0.2 g) in methanol (50 ml) was irradiated for 2 h. It was then kept in the dark for a set period (Table), an equal volume of carbon tetrachloride was added, and the mixture was passed through an alumina column. All products were eluted with carbon tetrachloride. For quantitative analysis (Table), a known amount of nitrobenzene was added as an internal reference, the solvent was evaporated off, and the residue was analysed by n.m.r. spectroscopy. A pure sample of the pyridine (17) was obtained by recrystallizing the crude material obtained from run 3 (Table) from n-hexane; m.p. 68°, *m/e* 191 (M^+)

²⁰ G. O. Dudek and R. H. Holm, *J. Amer. Chem. Soc.*, **1961**, **83**, 2099.

and 176 (base peak). Spectroscopic data (i.r., n.m.r., and u.v.), m.p., and elemental analysis were identical with reported data.²¹

Photolysis of 3,5-Dimethylisoxazole (1a) in Ethanol-Copper(II) Chloride.—A solution of the isoxazole (1a) (0.5 g) and copper(II) chloride dihydrate (0.25 g) in ethanol (50 ml) was irradiated for 3.5 h. An equal volume of carbon tetrachloride was added and the mixture was passed through an alumina column. All products were eluted with carbon tetrachloride-ethanol (1:1). From n.m.r. analysis, the eluate contained compounds (15) (49%), (3a) (6.2%), and (6a) (3.8%), together with starting material (3.8%). Vacuum distillation afforded 0.2 g of (15) contaminated with a trace of (1a).

Photolysis of 3-Methyl-5-phenylisoxazole (1b) in Methanol-Copper(II) Chloride.—A solution of the isoxazole (1b) (0.2 g) and copper(II) chloride dihydrate (0.1 g) in methanol (50 ml) was irradiated for 3.5 h. The mixture was passed through an alumina column to remove copper compounds. The eluate was concentrated and chromatographed on an alumina column (CHCl_3). After a small amount of compounds (3b) and (5b), the reduction product (16) was eluted; m.p. 143°, identical with an authentic sample (mixed m.p., i.r., and n.m.r. spectra).²² No pyridine derivative corresponding to (17) was detected.

Conversion of the Amino-enone (15) into the Pyridine (17) in the Dark.—A solution of compound (15) (0.1 g), copper(II) chloride dihydrate (50 mg), 0.6N-hydrochloric acid (0.25 ml), and 37% formalin (0.25 ml) in methanol (20 ml) was kept in the dark for 2.5 h. The mixture was passed through an alumina column and the eluate was analysed by n.m.r. spectroscopy. Signals of compound (17) were observed together with unassigned signals at δ 3.22 (s), 3.32 (s), 4.24 (s), and 4.60 (s). The intensities of the unassigned signals were one-third to half of that of the methyl signal of (17). Although the absence of the hydrochloric acid in this reaction did not cause any appreciable difference in the reaction pattern, the absence of copper(II) chloride reduced the yield of (17) to a negligible amount, and several unidentified products were observed. The absence of formalin resulted in no reaction.

[5/1626 Received, 18th August, 1975]

²¹ U. Eisner, J. R. Williams, B. W. Metthews, and H. Ziffer, *Tetrahedron*, **1970**, **26**, 899.

²² E. Knoevenagel, *Ber.*, **1903**, **36**, 2187.