

Ketone-photoinitiated Reactions of Formamide with Benzene and Alkylbenzenes

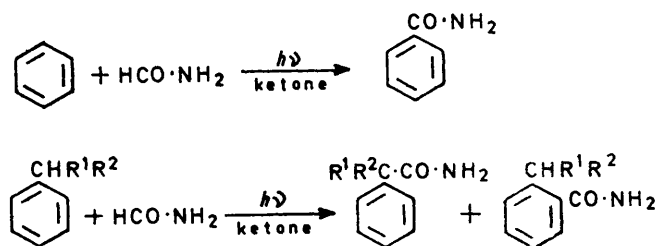
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Photoreactions of formamide with benzene and alkylbenzenes, photoinitiated by ketones are described. Nuclear and side-chain amidation took place. A free-radical mechanism is proposed.

PHOTOCHEMICAL amidations of various olefinic and acetylenic systems have been described extensively.¹ The reactions involve photoaddition of formamide to the unsaturated compound leading to homologous amide derivatives, and could be directly induced by u.v. irradiation, or, better, performed with the aid of ketonic photoinitiators, such as acetone or benzophenone. These processes have been shown to proceed *via* a free-radical mechanism involving carbamoyl ($\cdot\text{CONH}_2$) radicals. Application of the photoamidation reaction to aromatic systems offers a simple method of amidation of the aromatic ring and the active benzylic position under mild conditions.

The photochemical reactions of formamide with benzene and several alkylbenzene systems² are now reported in detail. Irradiation of benzene and formamide in the presence of acetone, benzophenone, or acetophenone gave the substitution product, benzamide. Exposure of alkylbenzenes and formamide to u.v. light under similar conditions led mainly to amidation at the benzylic position; nuclear substitution was also observed

in several cases (see Scheme). The reactions have been performed in mixtures in which both reactants were present in high concentrations together with acetone,



which served as photoinitiator as well as solvent. Irradiations were interrupted at moderate conversions. In this way, toluene gave mainly phenylacetamide and *o*-toluamide, ethylbenzene yielded α -phenylpropionamide,

¹ (a) D. Elad, 'Organic Chemistry,' vol. 2, ed. O. L. Chapman, Marcel Dekker, New York, 1969, p. 168; (b) D. Elad and G. Friedman, *J. Chem. Soc. (C)*, 1970, 893.

² D. Elad, *Tetrahedron Letters*, 1963, 77.

xylene gave tolylacetamides accompanied by dimethylbenzamides, and indane was converted into indane-1-carboxamide (see Table). A similar process took place

Photochemical reactions of formamide with aromatic hydrocarbons (with acetone)

Hydrocarbon	Photoproducts	Yield ^a (%)
Benzene ^b	Benzamide	15
Toluene ^c	Phenylacetamide	24
	<i>o</i> -Toluamide	9
Ethylbenzene ^c	α -Phenylpropionamide	31
<i>p</i> -Xylene ^c	<i>p</i> -Tolylacetamide	12
	2,5-Dimethylbenzamide	6
<i>m</i> -Xylene ^c	<i>m</i> -Tolylacetamide	25
	2,4-Dimethylbenzamide	9
Indane ^c	Indane-1-carboxamide	26

^a Based on hydrocarbon consumed. ^b Pyrex glass vessel. ^c Quartz vessel.

when acetophenone or benzophenone was used instead of acetone. Products were isolated by column chromatography on silica gel, and were identified by comparison with authentic samples.

By-products were also isolated and identified in order to confirm the proposed free-radical mechanism. Propan-2-ol, the photoreduction product of acetone was identified (g.l.c.) in the volatile fractions from all experiments. Oxamide, arising from the dimerization of two carbamoyl radicals,³ precipitated from irradiated mixtures. Products of dimerization of the aromatic hydrocarbons linked through the benzylic carbon atoms were isolated from experiments with toluene (1,2-diphenylethane), ethylbenzene (*meso*-2,3-diphenylbutane) and *p*-xylene (1,2-di-*p*-tolylethane). *p* $\alpha\alpha$ -Trimethylphenethyl alcohol⁴ was isolated from the reaction of *p*-xylene. This last product arises from the combination of the benzylic radical with an isopropyl (ketyl) radical.

From the reactions with benzophenone or acetophenone as initiator, the corresponding photoreduction products (benzpinacol and 2,3-diphenylbutane-2,3-diol) were isolated.

The primary steps for substitution both of the aromatic nucleus and at the benzylic position seem to resemble those of the photoamidation of olefins and acetylenes.¹ The ketone is excited by irradiation and (in the lowest triplet state) abstracts a hydrogen atom from a formamide molecule, giving a carbamoyl radical⁵ which subsequently reacts with the aromatic system. Interaction with benzene results in the substitution of a carbamoyl group for a hydrogen atom.⁶ Amidation of the side chain seems, however, to require a benzylic radical to combine with the carbamoyl radical. Such a process, unlike the nuclear amidation or the chain process taking place with olefins and acetylenes, is dependent on the presence of a sufficiently high concentration of both radicals to enable combination to take place to an observable extent, and to compete with the homodimerization of formamide to oxamide. The re-

quired benzylic radicals can be formed either *via* hydrogen atom abstraction from the alkylbenzene by an excited ketone molecule, or by direct photolysis of the alkylbenzene,⁷ although the photoexcited alkylbenzene may also be transferring energy to the acetone to produce a high concentration of triplet acetone. We have observed that irradiation of formamide, toluene, and acetone with filtered light of $\lambda > 290$ nm (Pyrex filter), which is absorbed only by the acetone, yields very small amounts of phenylacetamide. Similarly, poor yields of phenylacetamide were obtained in an experiment where no acetone was present and unfiltered light ($\lambda > 200$ nm) was employed.⁸ Considerable yields of products could only be achieved when the acetone-containing reaction mixture was irradiated with light of short wavelength ($\lambda > 200$ nm), which is absorbed by both toluene and acetone.

Ring-substitution of alkylated benzenes took place mainly at the *ortho*-position, following the common trend in homolytic aromatic substitution.⁹

EXPERIMENTAL

For general experimental details see refs. 1b and 8. U.v. sources used were (a) Hanau-Q81 high-pressure mercury vapour lamp, (b) Hanovia 200 W high-pressure mercury vapour lamp, (c) Hanovia 450 W high-pressure mercury vapour lamp. Crystalline products were compared with authentic samples (prepared by standard methods) by t.l.c. and mixed m.p. determinations.

Benzene, Formamide, and Acetone.—A mixture of benzene (15 g), formamide (60 g), and acetone (43 ml) was irradiated [lamp (a), Pyrex filter] for 48 h. A precipitate, which started to form after *ca.* 20 h, was filtered off and washed with acetone to yield oxamide (1.03 g). The filtrate was distilled from a steam-bath; g.l.c. analysis of the distillate indicated the presence of benzene (13.4 g), acetone, and propan-2-ol. The residue was treated with *ca.* 3 vol. of saturated aqueous sodium chloride and extracted several times with chloroform. The organic extract was washed with water, dried (Na₂SO₄), and evaporated, leaving a residue (1.25 g) which was chromatographed (silica gel; 60 g). Acetone–light petroleum (3 : 7) eluted benzamide (0.37 g).

Benzene, Formamide, and Benzophenone.—A mixture of benzene (90 g), formamide (20 g), benzophenone (2 g), and *t*-butyl alcohol (70 ml) was irradiated [lamp (c), Pyrex filter] for 72 h. Benzophenone (14 g) was added in seven equal portions as the u.v. spectrum of the mixture indicated its consumption. Unchanged reagents were removed in the usual way. Photoproducts of benzophenone (mainly benzpinacol) were separated by column chromatography, and benzamide (1.85 g), m.p. 98–103°, was isolated after repeated chromatography.

Benzene, Formamide, and Acetophenone.—A mixture of benzene (15 g), formamide (59 g), acetophenone (3.2 g), and *t*-butyl alcohol (20 ml) was irradiated [lamp (a), quartz filter]. The usual work-up led to benzamide (0.45 g) and 2,3-diphenylbutane-2,3-diol.

⁷ C. J. Calvert and J. N. Pitts, 'Photochemistry,' Wiley, New York, 1966, p. 515.

⁸ Cf. D. Elad and J. Sperling, *J. Chem. Soc. (C)*, 1969, 1579.

⁹ Cf. D. Hey, 'Homolytic Aromatic Substitution,' in 'Vistas in Free Radical Chemistry,' ed. W. A. Waters, Pergamon, London, 1959.

³ H. Grossmann, *Z. Naturforsch.* 1965, **20b**, 209.

⁴ A. Landis and C. A. VanderWerf, *J. Amer. Chem. Soc.*, 1958, **80**, 5277.

⁵ J. Ollivier and C. Leibovici, *Tetrahedron*, 1971, **27**, 5515.

⁶ Cf. C. Walling and M. J. Gibian, *J. Amer. Chem. Soc.*, 1965, **87**, 3361.

Toluene, Formamide, and Acetone.—A mixture of toluene (32 g), formamide (24 g), and acetone (65 ml) was irradiated [lamp (a), quartz filter] for 36 h. The precipitate was filtered off (oxamide; 0.4 g) and the volatile reagents were distilled. Unchanged toluene was identified in the distillate (29.5 g). The residue was treated with saturated sodium chloride solution and extracted with chloroform; the extract was dried (Na_2SO_4) and evaporated and the residue (3.8 g) was chromatographed on silica gel. Light petroleum eluted 1,2-diphenylethane (traces, identified by t.l.c. and i.r.). Acetone–light petroleum (3 : 7) eluted *o*-toluamide (0.33 g). The same solvents in 3 : 2 ratio eluted phenylacetamide (0.9 g).

Ethylbenzene, Formamide, and Acetone.—Ethylbenzene (20 g), formamide (65 g), and acetone (10 ml) were irradiated [lamp (a), quartz filter] for 48 h. The precipitated oxamide (1.5 g) was filtered off, and unchanged reagents were removed by distillation; the distillate contained ethylbenzene (16 g; g.l.c.). The residue was treated in the usual manner. Chromatography afforded 2,3-diphenylbutane (0.030 g), eluted with light petroleum, and (\pm)- α -phenylpropionamide (1.8 g), eluted with acetone–light petroleum (2 : 3).

p-Xylene, Formamide, and Acetone.—A mixture of *p*-xylene (20 g), formamide (60 g), and acetone (100 ml) was irradiated [lamp (b), quartz filter] for 48 h. Propan-2-ol and unchanged *p*-xylene (16.8 g) were identified in the volatile fraction. Treatment with saturated sodium chloride solution and extraction with chloroform afforded a mixture (3.52 g) which was crystallised to yield *p*-tolyl-

¹⁰ G. S. Hammond, W. P. Baker, and W. M. Moore, *J. Amer. Chem. Soc.*, 1961, **83**, 2795.

acetamide (0.22 g), m.p. 177–181°, hydrolysed to *p*-tolylacetic acid, m.p. 92–93°. The residue from the mother liquor was chromatographed to yield (a) (eluant light petroleum) 1,2-di-*p*-tolylethane (0.15 g), m.p. 77–78°, mixed m.p. (with an authentic sample prepared by irradiation of *p*-xylene and benzophenone¹⁰) 77–78°, τ 2.9 (8H, s, aromatic), 8.1 (4H, s, methylenic), and 7.7 (6H, s, methyls); (b) [acetone–light petroleum (1 : 4)] *p* $\alpha\alpha$ -trimethylphenethyl alcohol (0.72 g), τ 2.95 (4H, s, aromatic), 7.32 (2H, s, $\text{C}_6\text{H}_4\text{-CH}_2$), 7.45 (1H, s, OH), 7.71 (3H, s, $\text{C}_6\text{H}_4\text{-CH}_3$), and 8.85 (6H, s, CMe_2); (c) [acetone–light petroleum (2 : 3)] 2,5-dimethylbenzamide (0.3 g); (d) [acetone–light petroleum (9 : 11)] *p*-tolylacetamide (0.29 g); (e) [ethanol–acetone (3 : 7)] a polar fraction (0.72 g).

Indane, Formamide, and Acetone.—A mixture of indane (15 g), formamide (70 g), and acetone (85 ml) was irradiated [lamp (b), quartz filter] for 48 h. Unchanged indane (20.5 g) was identified in the volatile fraction. After treatment with saturated salt solution, extraction with chloroform and evaporation of solvent left a residue (11 g). Chromatography afforded indane-1-carboxamide (1.8 g) [eluted with acetone–light petroleum (3 : 7)], m.p. 140–147°. A sample crystallised from acetone–light petroleum had m.p. 158° (lit.,¹¹ 162°) and was identical with an authentic sample.

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¹¹ W. S. Knowles, J. A. Kuck, and R. C. Elderfield, *J. Org. Chem.*, 1942, **7**, 374.