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PHOTO-INDUCED FRIEDEL-CRAFTS REACTION[1]

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In an extension of previous studies on the photochemistry of N-chloroacetyl derivatives of aromatic amino acids and pharmacodynamic amines, in which various intra-molecular cyclization reactions on aromatic nucleus have been reported,[2] inter-molecular reactions of phenol (Ia) or anisole (Ib) with chloroacetamide (II) are now reported.

An aqueous solution of Ib (10 mmole/l) and II (30 mmole/l) was irradiated by 2537 Å light (10 watts low pressure lamp) in nitrogen atmosphere at room temperature for 2 hr to give the mixture of o-, m- and p-methoxyphenylacetamides (IVb, Vb, VIb), which were separated by chromatography on silica-gel column and analyzed quantitatively by gas chromatography (Table I.)

Table I. Photolysis of Anisole and Chloroacetamide for 2 hr.

Solvent	% IVb	% Vb	% VIb
water	20.8 (21.0)	4.34 (3.6)	6.08 (1.8)
acetonitrile	0.6	0.09	0.03
dioxane	0.2	0.04	0.03
acetone	0.03	trace	trace

( ); isolation yields in preparative scale experiments

Recently, reactions of alkyl and aryl radicals on aromatic nucleus have been investigated and from the orientation and relative reactivity data resulting from reaction of alkyl radicals on a variety of monosubstituted benzenes, mechanisms of homolytic aromatic alkyations have been discussed.[3] More recently, Ogata et al. reported on the photochemical ethoxycarbonylation of benzene with ethyl chloroacetate in the presence and absence of aluminium chloride.[4]

The product distribution in Table I. suggests a mechanism involving an alkyl radical ($\cdot CH_2CONH_2$) produced by photolysis of II, and the above data provides another example of photo-induced Friedel-Crafts reaction.

Phenol (Ia) was also irradiated in the same condition to give a small amount of phenoxyacetamide (III) besides the mixture of hydroxyphenylacetamides (IVa, Va, VIa). Since the photochemical rearrangement of aryl ethers, in which phenoxyacetic acid[5] and its ester[6] are included, are known, it is reasonable to assume that simultaneous formation of phenoxyacetamide (III) from Ia with II and successive rearrangement to hydroxyphenylacetamides proceeded as one of the routes of this reaction. In fact on photolysis of III in aqueous solution, o- and p-hydroxyphenylacetamides (IVa, VIa) were obtained in 90 % yield. The existence of III (Table II.) as well as the fact that the relative rates of formation of IVa and VIa in both case (Table II. and III.) are almost same, may also support the above assumption.

Table II. Photolysis of Phenol and Chloroacetamide for 2 hr.

Solvent	%			
	III	IVa	Va	VIa
water	0.63	39.7 (41.3)	0.3	11.3 (14.2)
acetonitrile	3.2	1.07		0.34
dioxane	2.64	2.6		0.89

Table III. Photolysis of Phenoxyacetamide for 2 hr.

Solvent	%		
	III	IVa	VIa
water	3.8*	71.0*(66.2)	18.1*(19.0)
acetonitrile	26.2	15.2	9.2
dioxane	36.1	18.8	4.0

* ; reaction time, 70 min.

In photolysis of phenoxyacetamide (III), the addition of anisole (Ib) gave no trace of crossed reaction products, and moreover, the presence of added oxygen did not change the yields of the rearrangement products. These results indicate that this rearrangement involves a very tightly bound intermediate like the photo-Fries reaction.[7] Finally, both of photo-induced Friedel-Crafts reaction and the rearrangement were strikingly depressed by change in solvent from water to organic solvents.

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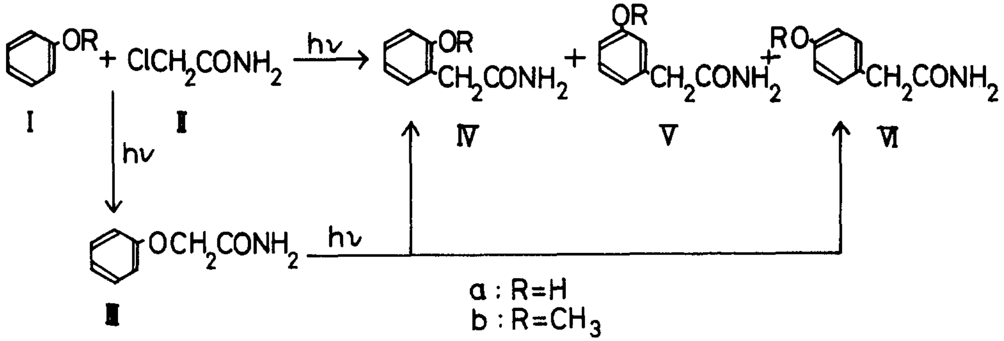

REFERENCES

1. Presented in part at the Annual Meeting of the Pharmaceutical Society of Japan, Nagoya, April 1969.

2. O.Yonemitsu, T.Tokuyama, M.Chykovsky and B.Witkop, *J. Am. Chem. Soc.*, **90**, 776 (1968); O.Yonemitsu, Y.Okuno, Y.Kanaoka, I.L.Karle and B.Witkop, *ibid.*, **90**, 6522 (1968).

3. R.Ito, T.Migita, N.Morikawa and O.Shimamura, *Tetrahedron*, **21**, 955 (1965); J.R.Shelton and C.W.Uzelmeier, *J. Am. Chem. Soc.*, **88**, 5222 (1966); G.E.Corbett and G.H.Williams, *J. Chem. Soc. (B)*, 877 (1966).

4. Y.Ogata, T.Itoh and Y.Izawa, *Bull. Chem. Soc. (Japan)*, **42**, 794 (1969).

5. D.P.Kelly and J.T.Pinhey, *Tetrahedron Letters*, 3427 (1964).

6. H.Chaimovich, R.J.Vaughan and F.H.Westheimer, *J. Am. Chem. Soc.*, **90**, 4088 (1968).

7. D.Bellus and P.Hrdlovic, *Chem. Rev.*, **67**, 599 (1967); M.R.Sandner and D.J.Trecker, *J. Am. Chem. Soc.*, **89**, 5725 (1967).