Photo-rearrangements of Methyl Indole-1-acetate, Indole-1-acetamide and Methyl Indoline-1-acetate

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Although the mechanism still unsettled, a number of studies on photo-Fries and related rearrangements of aromatic esters,²⁾ ethers,³⁾ carbonates,⁵⁾ amides⁶⁾ and amines⁷⁾ have been reported. So far there are few examples on the photorearrangement in pyrrole or indole series. According to the reports by Shizuka, *et al.* 1-acetylpyrrole (I) rearranged photochemically to 2-acetylpyrrole (II)^{6d)} and N-acetylcarbazole (III) gave a mixture of 1-acetylcarbazole (IV) and 3-acetylcarbazole (V) by the rearrangement to *ortho* and *para* positions. The mechanism was also discussed from the standpoint of the relation between the rate constants of the rearrangement and the odd electron densities calculated by simple Hückel MO method.^{6e)}

In the connection with our recent study on photo-Friedel-Crafts reaction of indole,⁸⁾ photo-rearrangements of methyl indole-1-acetate (VI), indole-1-acetamide (VII) and methyl indoline-1-acetate (X) have been examined here in analogy with the case of methyl phenoxyacetate or phenoxyacetamide.^{4f)}

When *ca.* 10 mM solution of methyl indole-1-acetate (VI) in aqueous ethanol was irradiated for 9 hr with 10 W low pressure mercury lamp, a mixture of methyl indoleacetates (VIII) and indole were produced. As shown in the separate paper,⁸⁾ the separation of methyl indoleacetates though difficult were carried out by repeated column chromatographies and their yields also determined by nuclear magnetic resonance (NMR) spectroscopy.

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Indole-1-acetamide (VII) was also irradiated in the same condition. The resulting mixture of indoleacetamides (IX) was hydrolyzed with sodium hydroxide, followed by esterification to yield methyl indoleacetates, whose separation and characterization were carried out in the same way. The yields of these photo-rearrangements are summarized in Table I.

TABLE I. Photo-rearrangements of Methyl Indole-1-acetate (VI) and Indole-1-acetamide (VII)

Position	Yield (%)			
	Me-ester		Amide	
	Indole	4.4		trace
	VI	8.4	VII	18.9
2	VIIIa	1.5	IXa	1.3
3	VIIIb	12.9	IXb	16.8
4	VIIIc	6.7	IXc	2.6
5	VIIId	—	IXd	—
6	VIIIe	16.3	IXe	11.5
7	VIIIf	1.2	IXf	1.1

As already mentioned above N-acetylcarbazole (III) in analogy with acetanilide^{6e)} and N-acetyldiphenylamine^{6e)} rearranged photochemically to *ortho* and *para* positions. However, strangely the photo-rearrangements of VI and VII mainly occurred to the 6- and 3-positions of the indole nucleus. These data suggest that the mechanism may be different with that of the cases of acetanilide, *etc.* In spite of some efforts, we have not yet any reliable calculation data, which can interpret the high reactivity of the 6-position.

Chart 2

Finally, methyl indoline-1-acetate (X) was irradiated similarly. The tarry product was chromatographed on a silica gel column to yield small amounts of indole and methyl indole-5-acetate (VIIId). The formation of VIIId may be interpreted that a photo-rearrangement to the *para* position occurred first, followed by dehydration to VIIId, because of instability of the indoline compound.

Experimental

All methyl indoleacetates (VIII) were identified as shown in the separate paper.⁹⁾

Photo-rearrangement of Methyl Indole-1-acetate (VI)—A solution of 122.5 mg (0.648 mmole) of methyl indole-1-acetate (VI) in 32 ml of methanol and 43 ml of water was irradiated with 10 W low pressure mercury lamp for 9 hr. Four batches totaling a volume of 300 ml were combined and concentrated *in vacuo* to remove the methanol. After salting-out by the addition of sodium chloride, the red cloudy solution was extracted with ethyl acetate. The extract was dried over sodium sulfate and evaporated *in vacuo* to leave 500 mg of a deep brown oil, which was chromatographed on a column of 25 g of silica gel. Elution with methylene chloride-*n*-hexane (1:1) gave 13.2 mg (4.4%) of indole and 25 mg of a pale yellow oil. The oil was rechromatographed on a short alumina column eluting with methylene chloride-*n*-hexane (1:3) to give 7.1 mg (1.47%) of methyl indole-2-acetate (VIIIa) and 5.6 mg (1.15%) of methyl indole-7-acetate (VIIIf). Further elution with methylene chloride from the silica gel column gave 176 mg of a mixture of methyl indole-3-acetate (VIIIb), methyl indole-4-acetate (VIIIc) and methyl indole-6-acetate (VIIIe).

Although the separation could be carried out as shown in the separate paper,⁸⁾ the yield of each compound was determined by comparing intensities of respective signals in the NMR spectrum of the mixture as 12.9 and 16.3%.

Photo-rearrangement of Indole-1-acetamide (VII)—A solution of 148 mg (0.85 mmole) of indole-1-acetamide (VII) in 85 ml of 20% aqueous ethanol was irradiated with 10 W low pressure mercury lamp for 12 hr. Three batches totaling a volume of 255 ml were combined and concentrated *in vacuo* to a volume of ca. 30 ml, to which 2 g of sodium hydroxide in 10 ml of ethanol was added and heated at 100° for 1.5 hr. After evaporation of the ethanol, the solution was acidified by the addition of 10% hydrochloric acid under ice-cooling to precipitate a pale red solid, which was extracted with ether. The ether extract was washed with water, dried over sodium sulfate and concentrated to leave a pale red crystalline powder, which was esterified by the treatment with diazomethane in ether. Evaporation of the ether left 303 mg of a pale brown oil. The yield of each compound was determined in the same manner to the preceding experiment.

Photo-rearrangement of Methyl Indoline-1-acetate (X)—A solution of 164 mg (0.86 mmole) of methyl indoline-1-acetate (X) in 85 ml of ethanol was irradiated with 10 W low pressure mercury lamp under nitrogen for 17 hr. Two batches were combined and the solvent was evaporated *in vacuo* to leave a deep brown tarry oil, which was dissolved in methylene chloride and passed over a short column of 4 g of silica gel. Evaporation of the methylene chloride left 262 mg of a deep brown oil, which was chromatographed on a column of 20 g of silica gel. Elution with methylene chloride gave 20 mg (10%) of indole, 16.5 mg (5%) of the starting material and 10.6 mg (3.26%) of methyl indole-5-acetate (VIIIId). Their structures were confirmed by comparing with the authentic sample in IR, NMR and TLC.

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Isolation of a New Type of Pyrazine Metabolite from *Aspergillus ochraceus* WILH.¹⁾

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We now would like to report briefly that a new type of pyrazine metabolite (I) which is hydroxylated on β -position of an isobutyl side chain has first been isolated as a fungal product from a strain of *A. ochraceus*³⁾ together with flavacol⁴⁾ and neoaspergillic acid.⁵⁾

Colorless needles of I, mp 122.5—123° were afforded by crystallization from ethyl acetate of an eluate with CHCl_3 in silica gel chromatography and its molecular formula, $\text{C}_{12}\text{H}_{20}\text{O}_2\text{N}_2$ was given by mass spectrometry ($M^+ m/e$ 224) and elementary analysis (found: C, 64.49%; H, 9.35%; N, 12.50%). Pale purple fluorescence was observed under ultraviolet light but negative with FeCl_3 solution. Ultraviolet absorption spectrum of I in ethanol showed a close resemblance to that of flavacol in which the absorption maxima at 230 (ϵ 5016) and 326.5 (ϵ 5528) nm were observed. The presence of hydroxyl and amide groups was suggested by infrared absorption spectrum: IR_{KBr} cm^{-1} 3290, 2945, 1907, 1634, 1520, 1464, 1364, 1174. It was thus indicated from above spectral data that 2-hydroxypyrazine ring would be contained in its structure. Furthermore, in nuclear magnetic resonance (NMR) spectrum, signals at 0.99 (6H, doublet, $J=6.5$ Hz), 2.47 (1H, multiplet) and 2.89 ppm (2H,

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