

SYNTHESIS OF 1-(2-PYRIDYL)INDOLES BY THE PHOTOREACTION OF
2-FLUOROPYRIDINE WITH INDOLES¹

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Abstract — Photoreaction of 2-fluoropyridine with indoles gave 1-(2-pyridyl)indoles regioselectively. The yields of the coupling products improved significantly by using the indole anion derivatives instead of the indoles.

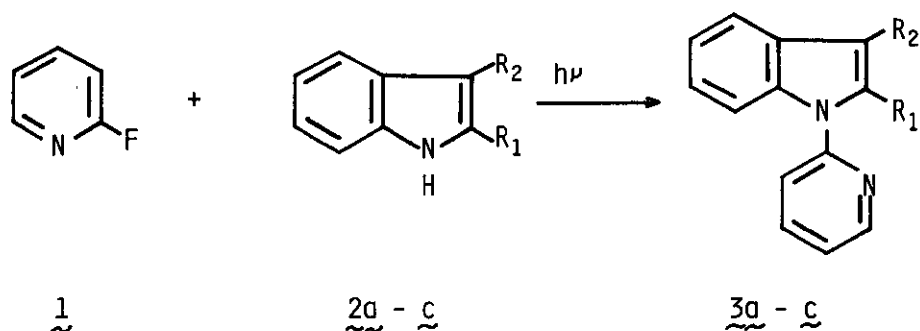
In our continuing studies on the photoreaction of halopyridines with aromatic compounds, we have recently reported that the photoreaction of 2-iodopyridine and indole afforded substituted (2-pyridyl)indoles as a mixture of possible regioisomers, reflecting the calculated frontier electron densities of the indole 1-radical,² and that the isomer distribution was altered by the choice of solvents.³ In view to explore the synthetic utility of the present photoreaction, we have further investigated the photolyses of 2-fluoropyridine in the presence of indole derivatives. In this paper, we describe the facile synthesis of 1-(2-pyridyl)indoles by the photoreaction of 2-fluoropyridine with indole anions.

A solution of 2-fluoropyridine (**1**) (0.11 mmol) and indole (**2a**) (0.1 mmol) in acetonitrile (10 ml) was irradiated under argon (1 atm) with a 60 W low-pressure mercury lamp for 10 h. The reaction mixture was submitted to silica gel column chromatography to afford 1-(2-pyridyl)indole (**3a**)⁴ in 14% yield (based on **2a** consumed), as a sole product, together with the recovery of **2a** (86%) (Table 1).

Under the similar conditions, no coupling product was detected in the reaction with 1-methylindole.

Since the reaction of $2a$ with 1 was found to afford $3a$ in better yield in ether than in acetonitrile solution (Table 1), the further photoreaction of 1 with other indoles, i.e., skatole ($2b$) and carbazole ($2c$) was carried out in the former solvent. Thus, $2b$ furnished 1-(2-pyridyl)skatole ($3b$)⁵ in 32% yield, but no product was obtained from $2c$ (Table 1).

Table 1. Photoreaction of 2-Fluoropyridine (1) with Indoles (2)



a ; $R_1, R_2 = H$

b ; $R_1 = H, R_2 = CH_3$

c ; $R_1, R_2 = -CH=CH-CH=CH-$

2	Solvent	Yield of 3 (%) ^{a), b)}	Conv. of 2 (%) ^{a)}
a	CH ₃ CN	14	14
a	Ether	19.5	52
b	Ether	32	28
c	Ether	0	5

a) Determined by GLC. b) Based on 2 consumed.

It has been reported that fluoride and chloride are the most satisfactory leaving group in the photonucleophilic substitutions of haloarenes bearing some activating substituent with nucleophiles such as alkoxide or hydroxide anion.⁶ We then examined the photoreaction of **1** with an indole anion instead of a neutral indole. A mixture of **1** (0.17 mmol) and the sodium salt of **2a** (0.1 mmol), prepared from **2a** and the equimolar amounts of sodium hydride, in situ, in various solvents (10 ml) was irradiated under the similar reaction conditions described above (5 h). The reaction in dimethylformamide (DMF) gave the best result, affording **3a** in 85% yield (Table 2). Under the similar conditions, the photoreaction of **1** was carried out with sodium salts of **2b** and **2c** to give corresponding **3b** and 1-(2-pyridyl)-carbazole (**3c**)⁷ in 93% and 83% yields, respectively (Table 2).

Table 2. Photoreaction of 2-Fluoropyridine (**1**) with Sodium Salts of Indoles

2	Yield of 3 (%) ^{a),b)}	Conv. of 2 (%) ^{a)}
a	85	59
b	93	40
c	83	44

a) Determined by GLC. b) Based on **2** consumed.

No significant effect on the quenching of the reaction was observed by the addition of piperylene. Taking into consideration that the photo-induced substitution of 2-fluoropyridine by aliphatic amines has been reported to proceed by the photonucleophilic substitution,⁸ it might be assumed that the present reaction proceeded by the same type of substitution via a singlet excited state. Because of the simple procedure and appreciable yields, the present reaction provides a facile synthetic method for 1-(2-pyridyl)indole derivatives and is complementary to the reported procedures.^{4,7}

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