A Simple Synthesis of *N*-Acyl- and *N*-Sulfonylindoles

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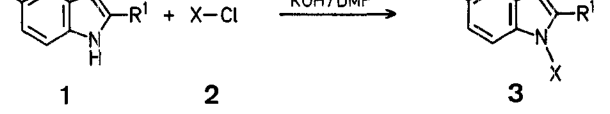
Acylation of metalloindole derivatives has been carried out under anhydrous conditions to give 1-, 3-, or a mixture of 1- and 3-acyl derivatives depending on the metal, the solvent, and the indole derivative used[1]. The most general method for the *N*-acylation of indole derivatives involves the acylation of the sodium salt of the indole derivative in anhydrous dimethylformamide[2]. Recently, the *N*-acylation[3] and *N*-sulfonylation[4] of indole derivatives have been reported in the presence of the phase transfer catalyst, tetrabutylammonium hydrogen sulfate.

I now report a convenient, alternative method for the synthesis of 1-acyl- and 1-(*p*-toluenesulfonyl)-indole derivatives (**3**), involving the formation of the potassium salts of indole derivatives (**1**) by reaction with powdered potassium hydroxide in dimethoxyethane at room temperature. The *N*-acylation or *N*-sulfonylation is achieved without the isolation of the potassium salts of the indole derivatives by addition of acyl chloride or *p*-toluenesulfonyl chloride (**2**).



1 **2** **3**

X = acyl, sulfonyl

Table. *N*-Acylation and *N*-Sulfonylation of Indoles **1**[a]

Product No.	R¹	R²	R³	X	Reaction time [min]	Yield [%]	m.p. [°C] or b.p. [°C]/torr found	reported	M.S. m/e (M⁺)
3a	H	H	H	C_6H_5—CO	20	83	69–71° (CH_3OH)	67–68°[6]	221
3b	H	H	H	H_3C—CO	20	77[b]	138–140°/12	123–125°/8[3]	159
3c	H	H	H	4-H_3C—C_6H_4—SO_2	30	89	85–86° (hexane)	86°[4]	271
3d	H	CH_3	H	4-H_3C—C_6H_4—SO_2	30	84	104–106° (hexane)	—[c]	285
3e	CH_3	$CH_2COOC_2H_5$	H_3CO	4-Cl—C_6H_4—CO	60 40[e]	35 (45)[d] 48 (35)[d]	97–99° (H_2O/C_2H_5OH)	97–99°[7]	387, 385

[a] Reaction conditions, molar ratio **2**:**1** = 1.1, KOH:**1** = 5; solvent: dimethoxyethane.

[b] Using acetic anhydride instead of acetyl chloride and 90 min reaction time, the yield is 49%.

[c] $C_{16}H_{15}NO_2S$ (285.3)

		C	H	N
$C_{16}H_{15}NO_2S$ (285.3)	calc.	67.36	5.30	4.91
	found	67.16	5.41	5.09

[d] Amount of starting material recovered [%].

[e] Anhydrous tetrahydrofuran as solvent.

0039-7881/81/0632-0460 $ 03.00

Anhydrous tetrahydrofuran can also be used as the solvent, whereas in acetone the reaction mixture became turbid and colored and undesirable results were achieved. The procedure is very simple and the reaction conditions are mild. After the reaction, excess insoluble potassium hydroxide was removed by filtration before work-up with water as described in the experimental section, the alkali-labile 1-(*p*-chlorobenzoyl)-indole derivative, which was reported[5] to be completely hydrolyzed by aqueous 5% sodium hydroxide at 60 °C within 3 min, was not hydrolyzed under the present reaction conditions.

1-Benzoylindole (3; R^1, R^2, $R^3 = H$, $X = C_6H_5CO$); Typical Procedure:
To a dimethoxyethane solution (9 ml) of indole (**1**; R^1, R^2, $R^3 = H$; 255 mg, 2.18 mmol) is added powdered potassium hydroxide (610 mg, 10.9 mmol) with cooling. After few min, benzoyl chloride (**2**; $X = C_6H_5—CO$; 336.8 mg, 2.4 mmol) is added to the solution with vigorous stirring and the reaction mixture is stirred for 20 min at room temperature. Benzene (70 ml) is added to the reaction mixture and insoluble materials are removed by filtration. The benzene solution is washed with saturated sodium chloride solution (20 ml) and dried with sodium sulfate. Benzene is evaporated and the residue is purified by chromatography on a short silica gel column using benzene for elution to give 1-benzoylindole; yield: 398 mg (83%); m.p. 69–71 °C (from methanol); Ref.[6], m.p. 67–68 °C.

Received: January 2, 1981

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