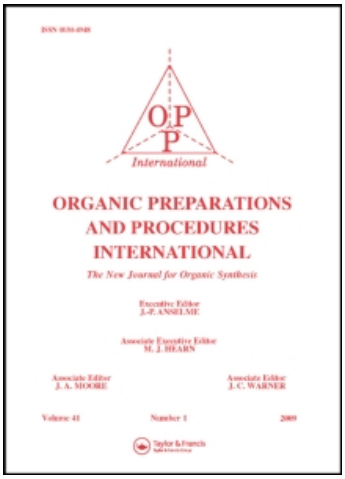

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OPPI BRIEFS

A SIMPLE PROCEDURE FOR THE PREPARATION OF 6-CHLORO-3-ACETOXY-1-ACETYLINDOLE

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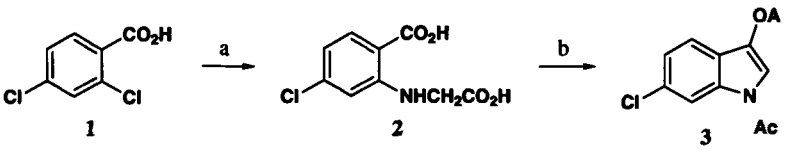
The 6-chloro-3-acetoxy-1-acetylindole (**3**) moiety is present either as aglycon or as a part of different chromogenic compounds which are very useful for the quality control of water and food.[1,2] The literature procedure[3] for the preparation of the title compound starts from the commercially available 5-chloro-2-methylaniline and involves five steps. A long reaction time is required for the aminoalkylation and the overall yield of the product is only 12%. In order to simplify the process, we have developed a two-step procedure using Ullman's method,[4] thus shortening the reaction time and improving the overall yield to about 38% Each step of the procedure was carried out with reproducible results and in excellent purity of the intermediate and of the final product.



1 **2** **3**

a) Cu, DMF, K_2CO_3, H_2NCH_2COOH, reflux, 6 h, 84%;
b) Ac_2O, NaOAc, reflux for 1 h and after T = 0°C, 24 h, 45%.

EXPERIMENTAL SECTION

Thin layer chromatography (TLC) were performed on pre-coated plates of silica gel GF-254 (Merck) with $CHCl_3$:AcOEt:AcOH (8:6:1) as the solvent system. The tlc plates were visualized by means of a CAMAG UV-Vis lamp with a wavelenght of 254 nm. The ^1H and ^{13}C NMR spectra were recorded on a Bruker AC 250F spectrometer in deuterated dimethyl- sulfoxide as solvent and TMS as an internal standard. Mps were determined on a Gallen-kamp capillary apparatus with a system of measurement and temperature control and are uncorrected.

***N*-(2-Carboxy-5-chlorophenyl)glycine (2).**- To a suspension of 10 g (52 mmol) of 2,4-dichlorobenzoic acid, 9.95 g (133 mmol) of glycine and 0.40 g (6.3 mmol) of copper powder in 70 mL of dimethylformamide, was slowly added 21.7 g (157 mmol) of potassium carbonate. The mixture was heated at reflux with a good stirring for 6 h. When all the 2,4-dichlorobenzoic acid had been consumed, the mixture was poured over 70 mL of cold 6M hydrochloric acid and stirred for 30 min. The precipitate obtained was collected and washed with cold water until neutral pH. The solid was dried at 50°C to constant weight affording 10.1 g, (84%) of product as colorless crystals, mp. 225°C (dec.), *lit.*[5] 228°C; mp[5] of monosodium salt 278-280°C.

^{1}H NMR: δ 7.88 (d, 1H, H6, $J_{6,4}$ = 8.5 Hz), 6.62 (dd, 1H, H4 $J_{4,6}$ = 8.5 Hz, $J_{4,3}$ = 1.9 Hz), 6.53 (d, 1H, H3 $J_{1,3}$ = 1.9 Hz), 3.97 (s, 2H, CH_2).

^{13}C NMR: δ (171.6 (CO), 169.6 (CO), 150.3 (C), 140.3 (C), 133.3 (CH), 115.3 (CH), 110.5 (CH), 109.2 (C).

6-Chloro-3-acetoxy-1-acetylindole (3).- A mixture of 10.5 g (45.7 mmol) of *N*-(2-carboxy-5-chlorophenyl)glycine, 70 mL of acetic anhydride and 14.4 g (175 mmol) of dry sodium acetate were heated at reflux. When the gas evolution had ceased, the mixture while still hot was poured into a beaker and left to cool overnight at 0°C. The precipitate was collected and poured into 70 mL of ice water and stirred for 1 h, collected again and recrystallized from ethyl acetate to yield 4.8 g (45%) of the product as a yellow solid, mp 111-113°C, *lit.*[6] 112-113°C.

^{1}H NMR: δ 8.34 (d, 1H, H7, $J_{7,5}$ = 1.9 Hz); 7.90 (s, 1H, H2), 7.52 (d, 1H, H4, $J_{4,5}$ = 8.5 Hz), 7.34 (dd, 1H, H5, $J_{5,7}$ = 1.9 Hz, $J_{5,4}$ = 8.5 Hz), 2.61 (s, 3H, CH_3, AcN); 2.28 (s, 3H, CH_3, AcO).

^{13}C NMR: δ 169.36 (C=O, Ac), 167.95 (C=O, AcO), 133.02 (C9), 132.57 (C6), 130.08 (C5), 123.56 (C8), 122.27 (C4), 119.06 (C7), 116.33 (C2), 115.59 (CH), 23.36 (C, CH_3, AcN), 20.25 (C, CH_3, AcO).

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