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IMPROVED PREPARATION OF SOME NITROINDOLINES

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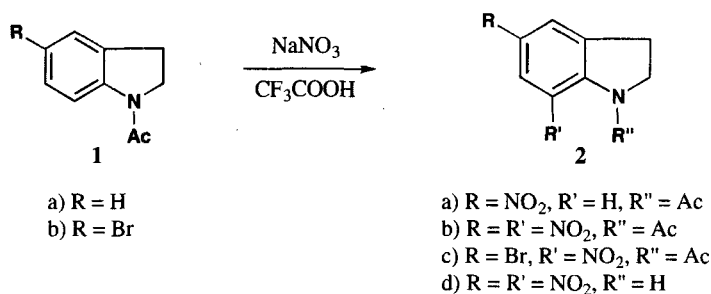
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Amides of 5,7-dinitroindoline and of 5-bromo-7-nitroindoline have been used as photolabile protective groups for carboxylic acids^{1,2} as well as photochemically activatable coupling reagents in peptide synthesis^{3,4} and for the derivatization of polymer surfaces.⁵ 5-Bromo-7-nitroindoline has been

prepared by nitration of the corresponding N-acetylindoline with fuming nitric acid in a mixture of acetic and sulfuric acid.⁶ However, since the published synthesis only gave modest yields in our hands, we decided to search for an alternative method. The synthesis of 5,7-dinitroindoline (**2d**) has not been reported.

Nitration of simple aromatic compounds with sodium nitrate in trifluoroacetic acid have been reported to be very effective⁷ and recycling of the spent acid is possible. We now report nitration of N-acetylindoline⁸ (**1a**) with sodium nitrate in trifluoroacetic acid gives 5-nitro-1-acetylindoline (**2a**) and 5,7-dinitro-1-acetylindoline (**2b**) in 93% and 87% yields, respectively, depending on the substrate to NaNO₃ ratio. 5-Bromo-1-acetylindoline (**1b**) affords 5-bromo-7-nitro-1-acetylindoline (**2c**) in 94% yield. These compounds were converted in ~85% yields to the corresponding indolines by hydrolysis as illustrated for the preparation of 5,7-dinitroindoline (**2d**).



EXPERIMENTAL SECTION

Sodium nitrate and trifluoroacetic acid were used as received from Aldrich.

5-Nitro-1-acetylindoline (2a). Representative Procedure.- To a stirred solution of 1.70 g (20 mmol) of sodium nitrate in 50 mL trifluoroacetic acid was added 3.22 g (20 mmol) of 1-acetylindoline⁸. The mixture was stirred at RT for 4 hrs and poured into 150 mL of cold water. The dark orange solid was collected, washed with 3 x 100 mL water and dried at 80 to yield 3.84 g (93%) of a yellow solid. An analytical sample was obtained by crystallization from ethanol (Norite) to give pale yellow needles, mp. 180-181, lit.⁶ 173.5-175.5.

Anal. calcd. for C₁₀H₁₀N₂O₃: C, 58.25; H, 4.89; N, 13.59. Found: C, 58.16; H, 4.90; N, 13.75

¹H NMR (CDCl₃): δ 8.28 (br. d, J = 9 Hz, 1 H); 8.11 (dd, J₁ = 2 Hz, J₂ = 9 Hz, 1 H); 8.03 (d, J = 1 Hz); 4.20 (t, J = 9 Hz, 2 H); 3.28 (t, J = 9 Hz, 2 H); 2.29 (s, 3 H).

5,7-Dinitro-1-acetylindoline (2b) was prepared according to the general procedure from 1.70 g (20 mmol) of sodium nitrate, 30 mL trifluoroacetic acid and 1.61 g (10 mmol) of 1-acetylindoline at RT

for 20 hrs to give 2.17 g (87%) of an orange-red solid, mp. 214-216. An analytical sample was obtained by crystallization from ethanol-benzene (1:1) (Norite) to give yellow-orange crystals, mp. 216-217.

Anal. calcd. for $C_{10}H_9N_3O_5$: C, 47.85; H, 3.61; N, 16.74. Found: C, 47.96; H, 3.69; N, 17.12

1H NMR ($CDCl_3$): δ 8.57 (d, J = 2 Hz, 1 H); 8.26 (m, 1 H); 4.37 (t, J = 8 Hz, 2 H); 3.37 (t, J = 9 Hz, 2 H); 2.32 (s, 3 H).

5-Bromo-7-nitro-1-acetyldoline (2c) was prepared according to the general procedure from 3.80 g (45 mmol) of sodium nitrate, 100 mL of trifluoroacetic acid and 10.0 g (44 mmol) of 5-bromo-1-acetyldoline⁶ at RT for 4 hrs to give 11.2 g (94%) of a pale yellow powder, mp. 199-201, lit.⁶ 197-198°. 1H NMR ($CDCl_3$): δ 7.77 (d, J = 7 Hz, 1 H); 7.53 (m, 1 H); 4.24 (t, J = 8 Hz, 2 H); 3.24 (t, J = 8 Hz, 2 H); 2.20 (s, 3 H).

5,7-Dinitroindoline (2d). A mixture of 1.05 g (4.2 mmol) 5,7-dinitro-1-acetyldoline, 10 mL ethanol and 15 mL 6 M HCl was refluxed for 1.5 hrs and poured into 150 mL cold water. The orange solid was collected, washed with water and dried at 80 to give 0.75g (86%) of an orange solid, mp. 250-252. An analytical sample was obtained as orange fluffy needles by crystallization from ethanol. 1H NMR ($CDCl_3$): δ 8.85 (d, J = 2 Hz, 1 H); 8.02 (d, J = 1 Hz, 1 H); 4.05 (t, J = 9 Hz, 2 H); 3.30 (t, 8 Hz, 2 H).

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