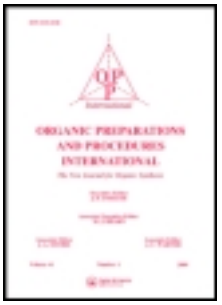

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IMPROVED PREPARATION OF SOME NITROINDOLINES

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REFERENCES

1. R. J. Gedye. F. Smith, K. Westaway, H. Ali, L. Baldisera, L. Laberge and J. Rousell, *Tetrahedron Lett.*, **27**, 279 (1986).
2. R. J. Giguere, T. L. Bray, S. M. Duncan and G. Majetich, *ibid.*, **27**, 4945 (1986).
3. R. A. Abramovitch, *Org. Prep. Proced. Int.*, **23**, 683 (1991).
4. R. S. Zhu. P. J. Hong and S. S. Dai, *Synth. Commun.*, **24**, 2417 (1994).
5. A. Krishna and S. Naggraju, *J. Chem. Soc. Perkin Trans. I*, **3**, 311 (1992).
6. R. J. Giguere, *"Organic Synthesis: Theory and Application"*, Vol. 1, p 103, JAI Press Inc., Greenwich, CT, 1989.
7. C. Xu, G. Chen and X. Huang, *Org. Prep. Proced. Int.*, **27**, 459 (1995).
8. X. Huang and Z. Z. Huang, *Huaxue Shigi (China)*, **9**, 193 (1987); *Chem. Abst.*. **108**, 221649u (1987).
9. X. Huang and C. C. Chen, *Synthesis*, 851 (**1984**).
10. H. H. Freedman and A. E. Frost, *J. Org. Chem.*, **23**, 1292 (1958).
11. M. Jacques, V. Micheal and P. Delaunay, *Chem. Ther.*, **4**, 80 (1969);*Chem. Abst.*, **71**, 112872 (1969).
12. F. S. Babichev, *Zh. Obshch. Khim.*, **20**, 1904 (1950).
13. P. Janina and B. D. Halina, *Acta Pol. Pharm.*, **24**, 245 (1967); *Chem. Abst.*, **69**, 19098 (1968).

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IMPROVED PREPARATION OF SOME NITROINDOLINES

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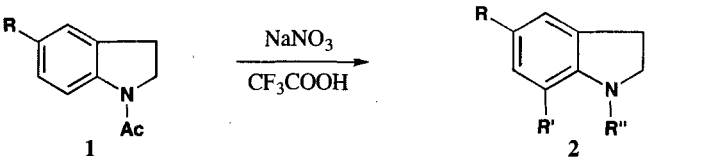
Amides of 5,7-dinitroindoline and of 5-bromo-7-nitroindoline have been used as photolabile protective groups for carboxylic acids[1,2] as well as photochemically activatable coupling reagents in peptide synthesis[3,4] and for the derivatization of polymer surfaces.[5] 5-Bromo-7-nitroindoline has been

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 effective[7] and recycling of the spent acid is possible. We now report nitration of N-acetylindoline[8] (**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 $NaNO_3$ 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**).



1

a) R = H
b) R = Br

2

a) R = NO_2, R' = H, R" = Ac
b) R = R' = NO_2, R" = Ac
c) R = Br, R' = NO_2, R" = Ac
d) R = R' = NO_2, R" = H

EXPERIMENTAL SECTION

Sodium nitrate and trifluoroacetic acid were used as recieved 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-acetylindoline[8]. 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 $C_{10}H_{10}N_2O_3$: C, 58.25; H, 4.89; N, 13.59. Found: C, 58.16; H, 4.90; N, 13.75

^{1}H NMR ($CDCl_3$): δ 8.28 (br. d, J = 9 Hz, 1 H); 8.11 (dd, J_1 = 2 Hz, J_2 = 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 a 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
^{1}H 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-acetylindoline (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-acetylindoline[6] at RT for 4 hrs to give 11.2 g (94%) of a pale yellow powder, mp. 199-201, lit.[6] 197-198°. ^{1}H 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-acetylindoline, 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. ^{1}H 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).

REFERENCES

1. B. Amit, D. A. Ben-Efraim and A. Patchornik, *J. Am. Chem. Soc.*, **98**, 843 (1976).

2. Yeda Research and Development Company Ltd., *Israeli IL* 48421 791031 (30 october 1975), Chem. Abs. **92**, 181004 (1975).

3. Sh. Pass, B. Amit and A. Patchornik, *J. Am. Chem. Soc.*, **103**, 7674 (1981).

4. G. Goissis, B. W. Erickson and R. B. Merrifield, *Pept., Proc. Am. Pept. Symp., 5th*, 559 (M. Goodman and J. Meienhofer eds. Wiley, N. Y. 1977).

5. S. K. Chadda, B. E. McCarry, R. F. Childs, C. V. Rogerson, I. O. Tse-Sheepy and J. M. Dickson, *J. Appl. Polym. Sci.*, **34**, 2713 (1987).

6. W. G. Gall, B. D. Astill and V. Boekelheide, *J. Org. Chem.*, **20**, 1538 (1955).

7. U. A. Spitzer and R. Stewart, *ibid.*, **39**, 3936 (1974).

8. L. G. S. Brooker, D. W. Heseltine (Eastman Kodak Co.), *US* 2,646,430 (21 july 1953), Chem. Abs. **48**, 1186h (1954).