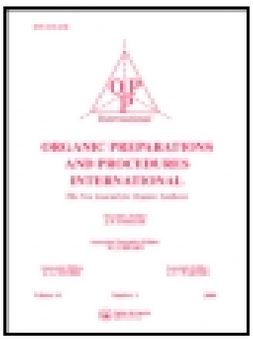

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SYNTHESIS OF 4,6-DINITROINDOLE

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7. V. V. Dhekne, B. D. Kulkarni and A. S. Rao, *Indian J. Chem.*, **15B**, 755 (1977).

8. S. Sethna and R.Phadke, *Org. React.*, **7**, 1 (1953).

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SYNTHESIS OF 4,6-DINITROINDOLE

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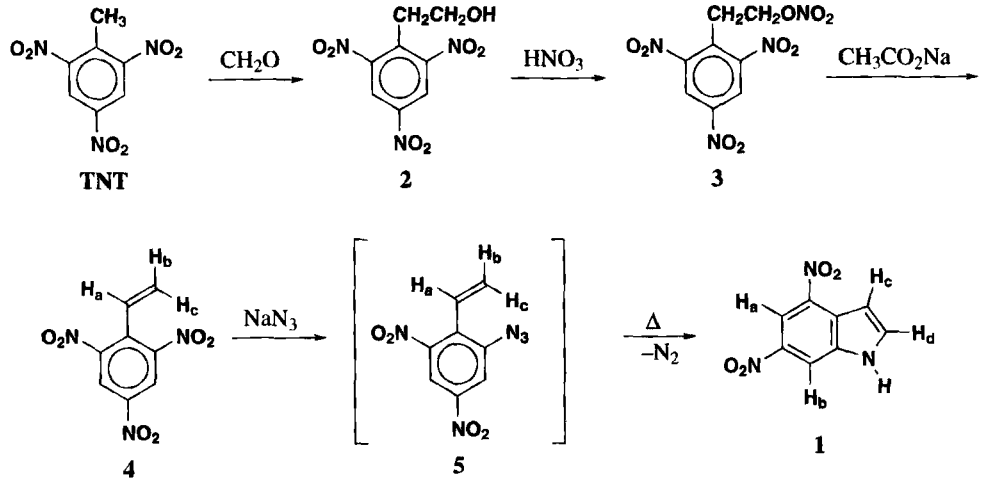
Nitroindoles represent an attractive synthetic target for the preparation of physiologically active compounds.[1,2] To our surprise, 4,6-dinitroindole is not a known compound. The present paper describes the synthesis of **1** from 2,4,6-trinitrotoluene (TNT) according to the following scheme.



Although compounds **2**, **3** and **4** have been described previously,[6,7] they were not characterized by NMR spectroscopy. The assignment of protons H_a, H_b and H_c in 2,4,6-trinitrostyrene (**4**) has been made on the basis of the following NMR criteria: ${}^3J_{trans} > {}^3J_{cis} >> {}^2J_{gem}$.[8] The *ortho*-nitro group is substituted selectively upon interaction of styrene **4** with sodium azide in DMF at 20°. 2-Azido-4,6-dinitrostyrene (**5**) is a labile compound which is converted to **1** even during crystallization from Pr^iOH. The structure of **1** was unambiguously determined by IR, ^1H and ^{13}C NMR spectroscopy, mass spectrometry and microanalysis.

EXPERIMENTAL

Mps were measured using a Boetius melting point apparatus and are uncorrected. IR spectra were recorded with a Perkin-Elmer spectrometer. Mass spectra were recorded on a MS-30 (Kratos) spectrometer using electron ionization technique. All reactions were monitored by TLC using Silufol precoated aluminiun plates which were visualized with ultraviolet light. ^1H and ^{13}C NMR spectra were measured on a Brüker WM-400 spectrometer. Chemical shifts are reported in ppm downfield from TMS using the δ scale. Organic solvents and reagents were purified by accepted literature procedures.

CAUTION! **2,4,6-Trinitrotoluene (TNT) as well as all the intermediate compounds are explosive. It is strongly recommended that they be handled with great care and proper precautions.**

2-(2',4',6'-Trinitrophenyl)ethan-1-ol (2),[6] brown plates, mp. 110-112°, *lit.*[6] mp. 110-112°. ^1H NMR (acetone-d_6): δ 3.38 (t, 2 H, CH_2Ar, ^3J = 8.0), 3.85 (q, 2 H, $C\underline{H}_2OH$, $^3J_{HH} = {}^3J_{HOH}$ = 5.8), 4.04 (t, 1 H, OH, $^3J_{HOH}$ = 5.8), 8.93 (s, 2 H, H-Ar); ^{13}C NMR (acetone-d_6): δ 28.64, 61.69, 123.19, 135.14, 147.26, 152.92.

2-(2',4',6'-Trinitrophenyl)-1-nitroxyethane (3),[7] viscous oil. ^1H NMR (DMSO-d_6): δ 3.48 (t, 2 H, CH_2Ar, $^3J_{HH}$ = 6.0), 4.85 (t, 2 H, CH_2ONO_2, $^3J_{HH}$ = 6.0), 9.08 (s, 2 2 H, H-Ar); ^{13}H NMR (acetone-d_6): δ 26.78, 72.08, 124.24, 132.98, 147.83, 152.58.

2,4,6-Trinitrostyrene (4),[7] yellow needles, mp. 65-66°, *lit.*[7] mp. 65-66°. ^1H NMR (acetone-d_6): δ 5.54 (dd, 1 H, H_c, $^3J_{ca}$ = 17.8, $^2J_{cb}$ = 0.7), 5.69 (dd, 1 H, H_b, $^3J_{ba}$ = 11.7, $^3J_{bc}$ = 0.7), 7.12 (dd, 1 H, H_a, $^3J_{ac}$ = 17.8, $^3J_{ab}$ = 11.7). ^{13}C NMR (acetone-d_6): δ 123.19, 123.45, 123.75, 123.84, 128.38, 134.28.

4,6-Dinitroindole (1).- To a solution 1g (4.2 mmol) of **4** in 15 mL of anhydrous DMF was added 0.3g (4.6mmol) of sodium azide and the mixture was stirred at ~20° for 6 h (TLC). The reaction mixture was then poured into 75 ml of water and the precipitated solid was collected and dried on air. The black solid was dissolved in hot Pr^iOH and refluxed with a small amount of charcoal for 1 h and then the hot solution was filtered. The charcoal was washed with hot Pr^iOH (2×3 mL) and the combined filtrates were cooled to −5° to give 0.53g (54%) of yellow needles, mp. 268-270° (Pr^iOH).

IR (KBr): 3440 (NH), 1500, 1480 (NO_2) cm^{-1}; ^1H NMR (DMSO-d_6): δ 7.18 (dd, 1 H, H_c, $^3J_{cd}$ = 3.0, $^5J_{ca}$ = 0.7), 8.16 (d, 1 H, H_d, $^3J_{cd}$ = 3.0), 8.72 (dd, 1 H, H_a, $^4J_{ab}$ = 2.2, $^5J_{ac}$ = 0.7), 8.75 (d, 1 H, H_b, $^3J_{ba}$ = 2.2), 9.17 (br, 2 H, NH_2); ^{13}C NMR (DMSO-d_6): δ 102.48, 111.85, 114.11, 124.99, 136.92, 137.26, 137.95, 140.22. EIMS *m/z*, % 207 (M^+, 100), 177(22), 161(15), 131(20), 103 (22), 115 (68), 55 (55).

Anal. Calcd for $C_8H_5N_3O_4$: C, 46.53; H, 2.58; N. 40.61. Found: C, 46.39; H, 2.42; N, 40.58

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REFERENCES

1. M. Somei and M. Tsuchiya, *Chem. Pharm. Bull.*, **29,** 3145 (1981).

2. M. Murase, T. Koike, Y. Moriya and S. Tobinaga, *ibid.*, **35,** 2657 (1987).

3. L. Lee Melhado and J. L. Brodsky, *J. Org. Chem.*, **53.** 3852 (1988).

4. A. R. Katritzky, S. Rachwal and S. Bayyuk, *Org. Prep. Proced. Int.*, **23**, 357 (1991).

5. M. Somei, F. Yamada, H. Hamada and T. Kawasaki, *Heterocycles,* **29,** 643 (1989).

6. E. E. Gilbert, *J. Energetic Mater.*, **2**, 215 (1984).

7. N. A. Barba and M. S. Nedelko, *Zhur. Org. Khim.*, **19,** 2220 (1983).

8. A. J. Gordon and R. A. Ford, *"The Chemist's Companion"*, Wiley-Interscience, New York-London-Sydney-Toronto, 1972.

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A CONVENIENT SYNTHESIS OF N-Boc-4-FORMYLPIPERIDINE

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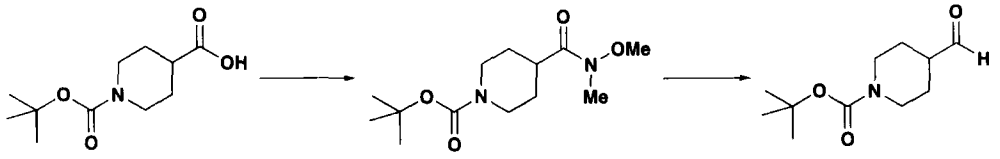
The title compound, N-Boc-4-formylpiperidine (**3**), has been reported several times in recent years as a useful synthetic intermediate, particularly in the pharmaceutical industry. In the various methods that have been used for its preparation, at least one significant shortcoming exists which makes the reported syntheses unattractive for larger scale preparations. The drawbacks include the need for extremely expensive reagents,[1-2] toxic/environmentally unfriendly reagents,[3] extremely low temperatures,[4] chromatographic purifications,[5] and/or malodorous by-products.[6-8] In addition, some of these reported syntheses proceeded in only moderate overall yields. We report here a convenient, high yielding, cost-effective procedure which does not have the drawbacks of the previously reported procedures.



1 **2** **3**

The starting material, N-Boc-piperidine-4-carboxylic acid (**1**), which is commercially available,[9] can be readily prepared from the inexpensive piperidine-4-carboxylic acid.[1] This carboxylic acid was converted into Weinreb amide[10] **2** on a 50 gram scale by using standard, cost-efficient