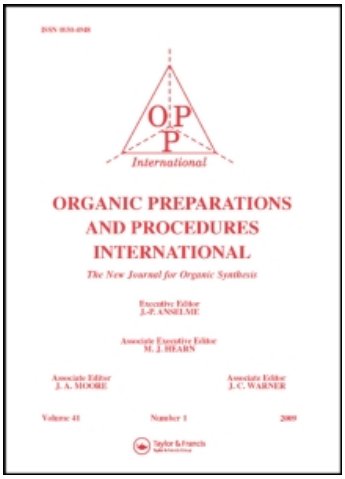

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SIMPLE AND CONVENIENT PROCEDURE FOR THE PREPARATION OF 1-METHYL-4-NITROBENZIMIDAZOLE

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SIMPLE AND CONVENIENT PROCEDURE FOR THE PREPARATION OF 1-METHYL-4-NITROBENZIMIDAZOLE

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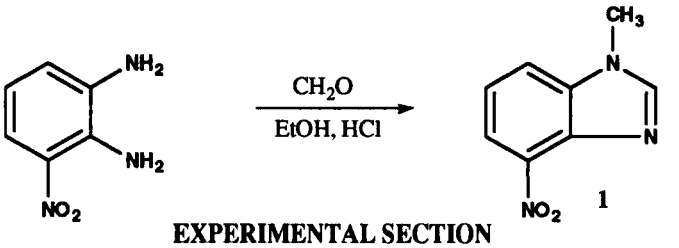
The application of the Gould-Jacobs reaction[1] for the preparation of 4-, 5-, 6-, and 7-substituted-1-methylbenzimidazoles[2,3] has been hampered by the unavailability of the starting 1-methyl-4-nitrobenzimidazole. The title compound 1-methyl-4-nitrobenzimidazole (**1**) has been obtained by alkaline methylation of 4(7)-nitrobenzimidazole,[4,5] a method which produces also the corresponding 7-nitro-substituted isomer. Another approach to **1** starts from 1-methyl-5-nitrobenzimidazole, which is first reduced to the amino derivative, then protected by tosylation to allow subsequent nitration at the desired 4-position. The final product is obtained after deprotection and deamination.[6] Another low-yield method employs 2,3-dinitroaniline as a starting material.[5] We now describe a simple and convenient synthesis of the latter.

In analogy to the reaction of 4-nitro-1,2-phenylenediamine with formaldehyde in methanolic hydrogen chloride to give 1-methyl-6-nitrobenzimidazole,[7] a reaction starting from 3-nitro-1,2-phenylenediamine would be expected to give the desired 1-methyl-4-nitrobenzimidazole. Thus, a

one-step reaction of 3-nitro-1,2-phenylenediamine with formaldehyde in ethanolic hydrogen chloride represents a simple and convenient approach, applicable to bulk synthesis. The proce-dure furnished pure 1-methyl-4-nitrobenzimidazole, without formation of the undesired 1-methyl-7-nitro isomer (GC). Its spectral properties (UV, ^1H and ^{13}C NMR) were in full accord with the published data.[4,8,9]



1

EXPERIMENTAL SECTION

1-Methyl-4-nitrobenzimidazole (1).- 3-Nitro-1,2-phenylenediamine (153 g, 1 mol) was dissolved in a mixture of 3 L of ethanol and 1 L of conc. hydrochloric acid. After addition of 140 ml (2 mol) of 40% aqueous formaldehyde, the mixture was refluxed for 2 hrs and allowed to cool to RT before being neutralized with 20% aqueous sodium hydroxide. The precipitated product was collected, washed with water and dried. Recrystallization from 2:1 toluene-*n*-heptane, gave 138 g (77%) of **1**, mp. 168°, lit.[4] mp. 168°, as a yellow crystalline solid.

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