Chemistry of Heterocyclic Compounds, Vol. 36, No. 1, 2000

REDUCTIVE ELIMINATION OF THE AMINO GROUP IN 5-DIALKYLAMINO-4-NITROIMIDAZOLE

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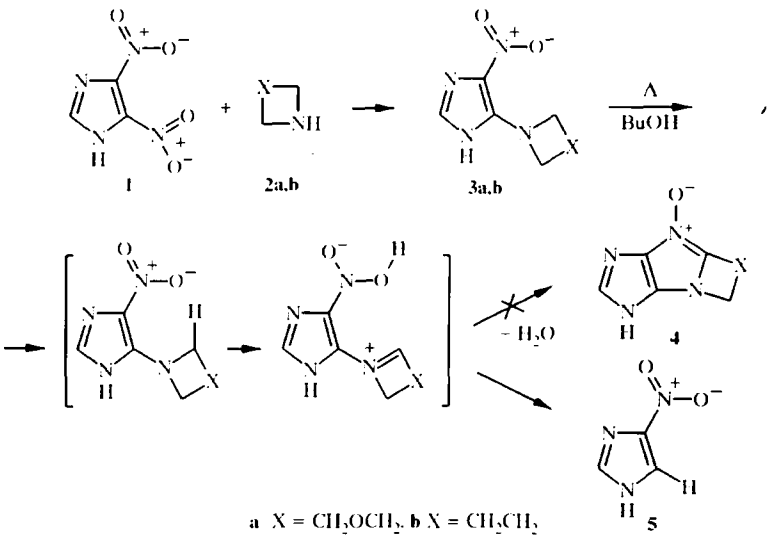
Keywords: nitroimidazole, *tert*-amino effect.

ortho-Nitro substituted N,N-dialkylanilines are cyclized thermally into N-oxides of benzimidazoles by a *tert*-amino effect mechanism [1,2], including transfer of hydride ion from an α-methylene atom in the N,N-dialkylamino group to an oxygen atom of the nitro group (1,6-hydride shift) [3] with subsequent cyclization.

We have synthesized 5-morpholino- and 5-pyrrolidino-4-nitroimidazoles **3a,b** by the reaction of 4,5-dinitroimidazole (**1**) with dialkylamines **2a,b**. On extended heating (10 days) of compounds **3a,b** in dry butanol, instead of the expected imidazoimidazole **4**, the nitroimidazole **5** was isolated in 65% yield and was identical (R_f, mp, ^{1}H NMR and mass spectrum) to a sample synthesized by the method in [4].



Probably, analogously to the reaction described for nitroanilines [1,2], a so-called 1,6-hydride shift occurs initially with the formation of structure **6**. However, under the action of butanol, cyclization to the condensed imidazole does not take place but fission of the C–N bond occurs.

Compound **3a** was boiled in butanol for 5 days and the reaction mixture was examined by chromato-mass spectrometry. The initial compound **3a** was detected [R_T = 9.250 min, (M^++1) 199], and also imidazole **4** [8.349 min, (M^++1) 114]; dibutoxybutane (5.491 min, M^+ 202), and morpholine [4.880 min, (M^+-1) 86]. We have therefore shown that this reaction occurs with the formation of nitroimidazole **5** and butyraldehyde, which exists in butanol solution as the acetal.

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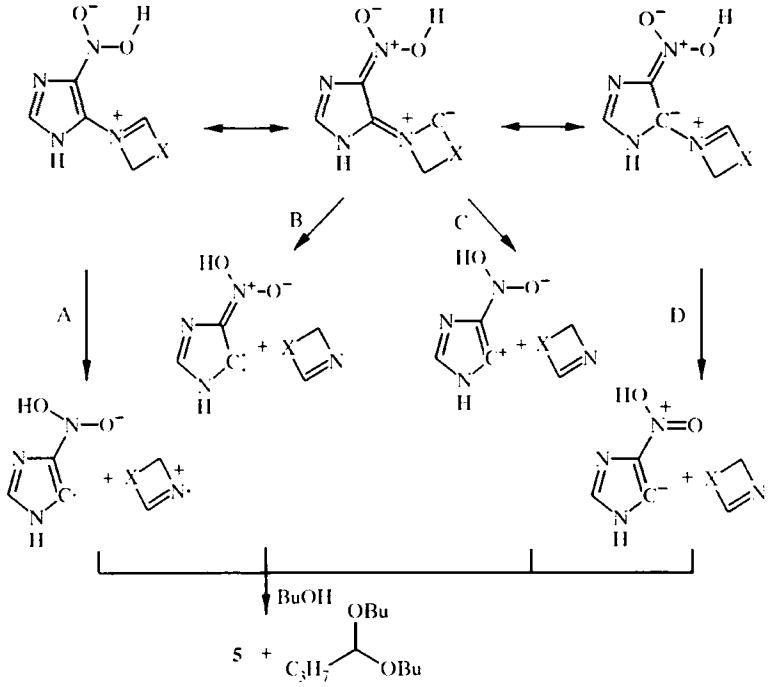

It may be suggested from the data of chromato-mass spectrometry that the reaction proceeds by a mechanism of homolytic fission of the C–N' bond (route A), with the formation of a carbene (route B), or by a heterogeneous fission mechanism (routes C and D). Since we failed to isolate any morpholine fission products the problem of the mechanism remains open.

EXPERIMENTAL

5-Morpholino-4-nitroimidazole (3a). mp 140°C. IR spectrum (KBr): 3440, 3000, 2850, 2730, 2450, 1610, 1530, 1500 cm^{-1}. ^1H NMR spectrum (DMSO-d_6): 12.1 (1H, br. s, NH); 6.93 (1H, s, CH_{imid}); 3.75 (4H, t, J = 4.9 Hz, CH_2); 3.10 (4H, t, J = 4.9 Hz, CH_2). Found, %: N 31.60. $C_7H_{10}N_4O_3$. Calculated, %: N 31.45.

4-Nitro-5-pyrrolidinoimidazole (3b). mp 200°C (alcohol). ^1H NMR spectrum (DMSO-d_6): 12.5 (1H, br. s, NH); 7.47 (1H, s, CH_{imid}); 3.52 (4H, t, J = 6.9 Hz, CH_2); 1.90 (4H, t, J = 6.9 Hz, CH_2). Found, %: N 31.50. $C_7H_{10}N_4O_2$. Calculated, %: N 31.22.

4-Nitroimidazole (5). mp 302-303°C (decomp.). Literature [4], mp 303°C (decomp.). ^1H NMR spectrum (DMSO-d_6): 12.5 (1H, br. s, NH); 8.29 (1H, s, CH_{imid}); 7.83 (1H, s, CH_{imid}). Mass spectrum, m/z (I_{rel}, %): 114 (4.5), 113 (100), 97 (5.9), 83 (1.7), 70 (3.7), 69 (3.7), 67 (21), 66, (4.2), 55 (18).

The work was carried out with the financial support of the Russian Fund for Fundamental Investigations, grant No. 98-03-33045a.

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