Selective reduction of the aromatic nitro group with retention of the nitrate group

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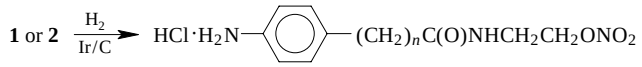
Selective reduction of a nitro group whilst retaining the ONO_2 group has been carried out for the first time in the hydrogenation of nitrates of *N*-ethanolamides, *p*-nitrobenzoic and nitrophenylacetic acids.

Selective reduction of organic compounds containing different nitro groups bonded to atoms of carbon, oxygen and nitrogen is a synthetic problem which is difficult to solve due to the high susceptibility of N–O bonds in those groups to reduction. Thus, for example, up to now there are no literature data on the selective reduction of aromatic nitro compounds with nitrate groupings in the side chain. Therefore, aromatic amines with nitrate groups in the side chain are not easily accessible. At the same time, the synthesis of previously unknown aromatic amines with nitrate groupings is of great practical interest for the development of new drugs with enhanced efficiency. The basis for this is the biological activity of aromatic amines,[1] on the one hand, and the ability of alcohol nitrates to generate nitric oxide[2–6] in the organism, which is known to play a principal role in the regulation of different physiological processes, on the other hand.[7–9]

In the present paper, using as an example nitrates of *N*-ethanolamides of *p*-nitrobenzoic **1** and *p*-nitrophenylacetic **2** acids, we have carried out for the first time a selective reduction of an aromatic nitro group whilst retaining the ONO_2 group.



3 $n = 0$
4 $n = 1$

Compounds **3** and **4**† were prepared in yields of 26% and 29%, respectively, in the hydrogenation of products **1** and **2** in a solution of acetic acid with addition of benzene on a Ir/C (5% Ir) heterogeneous catalyst at temperature 20–40 °C and atmospheric pressure using the method described earlier.[10] In the course of the reaction the reduction products passed into solution and precipitated out as hydrochlorides, after the distillation of organic solvents at lower pressure followed by the addition of HCl.

N-(2-Nitroxyethyl)amides of *p*-aminobenzoic **3** and *p*-aminophenylacetic **4** acids are not described.

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† *Spectral data*. **3**: mp 135–137 °C. Found (%): C, 41.40; H, 4.44; N, 16.03; Cl, 13.47. Calc. for $C_9H_{12}ClN_3O_4$ (%): C, 41.31; H, 4,62; N, 16.06; Cl, 13.55. IR (ν/cm^{-1}): 759 (NO_2); 795 (CH, Ph); 854 (O–NO_2); 1019 (C–O); 1276, 1631 (ONO_2); 1405, 1500, 1562, 1611 (C–C, Ph), 1657 (C=O); 1664, 2581, 2850 (NH_3^+); 3293 (NH). ^{1}H NMR ([$^2H_7$]DMF) δ: 3.78 (dt, 2H, $NHCH_2$, $^3J_{CH-CH} = {}^3J_{CH-NH}$ = 5.0 Hz); 4.79 (t, 2H, CH_2ONO_2, $^3J_{CH-CH}$ = 5.0 Hz); 6.6 (br. s, NH_2 + HCl + H_2O); 7.53 (d, 2H, CH); 8.02 (d, 2H, CH); 8.97 (br. t, 1H, CONH, $^3J_{NH-CH}$ = 5.0 Hz).

4: mp 123.5–125 °C. Found (%): C, 43.58; H, 5.04; N, 15.17; Cl, 12.85. Calc. for $C_{10}H_{14}ClN_3O_4$ (%): C, 43.56; H, 5.08; N, 15.24; Cl, 12.88. IR (ν/cm^{-1}): 758 (NO_2); 797 (CH, Ph); 857 (O–NO_2); 1024 (C–O); 1278, 1632 (ONO_2); 1414, 1510, 1618 (C–C, Ph); 1550, 3240 (NH); 1652 (C=O); 1660, 2604, 2867, 2943 (NH_3^+). ^{1}H NMR ([$^2H_6$]DMSO) δ: 3.42 (dt, 2H, $NHCH_2$, $^3J_{CH-CH} = {}^3J_{CH-NH}$ = 4.7 Hz); 3.49 (s, 2H, CH_2CO); 4.54 (t, 2H, CH_2ONO_2, $^3J_{CH-CH}$ = 4.7 Hz); 7.35 (m, 4H, CH, AB, $\Delta\nu_{AB}$ = 7.1; $|^2J_{AB}|$ = 8.8); 8.58 (br. t, 1H, CONH, $^3J_{CH-NH}$ = 4.7 Hz); 10.4 (br. s,$NH_3^+ \cdot$ HCl).

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