Observation of a single-pot aromatic reductive denitration

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Abstract: 4,*N*,*N*-Trimethyl-3-nitrobenzenamine gave reductive denitration products (ca. 28%) upon treatment with *n*-butyl nitrite in the presence of catalytic amounts of ammonium chloride and water in an unprecedented one-reagent single-pot process. The three isomeric *N*,*N*-dimethylnitrobenzenamines showed the same behaviour to a much lesser extent; the *ortho* isomer was partially (7%) transformed into 1-methylbenzotriazole.

Key words: aromatic protolytic denitration, nitroaromatics, *n*-butyl nitrite, *E*- and *Z*-nitrosamine.

Résumé : Au cours d'un processus unipot sans précédent, la 4,*N*,*N*-triméthyl-3-benzèneamine fournit des produits de dénitration réductrice (environ 28%) lorsqu'on la soumet à l'action du nitrite de butyle, en présence de quantités catalytiques de chlorure d'ammonium et d'eau. Le trois *N*,*N*-diméthylnitrobenzènamines isomères ont le même comportement, même si le degré est moindre; l'isomère *ortho* se transforme partiellement (7%) en 1-méthylbenzotriazole.

Mots clés : dénitration aromatique protolytique, nitroaromatiques, nitrite de butyle, *E*- et *Z*-nitrosamine.

[Traduit par la rédaction]

One-batch-one reagent aromatic reductive denitration, which could in principle be the reversal of classical nitration by the nitronium ion, is such a rare event that there is no such entry for it in Chemical Abstracts. As a matter of fact, the only way to perform this process appears that of reducing the nitro group to amino, which is subsequently diazotized and reduced by a suitable reagent.

Indeed, a few coherent observations of this one-batch process have been reported (1) as a side reaction in the treatment of a number of tertiary aromatic amines bearing a nitro group in the *ortho* position, with strong acid or photochemically, to yield benzimidazoles and benzimidazole oxides. The envisaged mechanism in the ground state experiment assumed the migration of the nitro group to the amino nitrogen to yield an oximonium nitroso ester, eventually bound for the formation of a Wheland-type intermediate by amino group assisted protonation of the carbon bearing the nitro group, as a final step (route A, Scheme 1), or a more straightforward variation that we would rather like to advance (route B, Scheme 1): both pathways would amount to the reversal of the *ortho*-nitration of an aromatic amine.

Interestingly, this behaviour attributed to the *ortho*-effect (1*a*) was reported only for tertiary amines, inferring that enough steric hindrance is there to cause the phenomenology observed. We now wish to report the observation that stirring 4,*N*,*N*-trimethyl-3-nitrobenzenamine (**1**) at room temperature with *n*-butyl nitrite (BN, 3 mol-equiv.), water (10 mol-equiv.), and ammonium chloride (AC, 0.1 mol-equiv.) during 2 days caused the complete disappearance of **1** and produced two reductive denitration compounds, namely, *N*,4-dimethylbenzenamine (**2**, identified on the basis of its retention properties and mass spectrum) and *N*,4-dimethyl-*N*-nitrosobenzenamine (**3**, in the ratio ca. 5:1), the latter being the GC precursor of the former by pyrolysis in the injector port. The material balance of the volatile fraction was completed by *N*,4-dimethyl-3-nitrobenzenamine (**4**), analogously derived by the thermal decomposition in the GC injector of the corresponding *N*-nitrosamine **5**, as shown in an independent experiment, and two distinct dinitro derivatives of *N*,*N*,4-trimethylbenzenamine (Scheme 2). A suitable work-up of the reaction mixture led to the isolation of **3** and its full identification. In the absence of BN no reaction was observed. The same reaction under the conditions described (2) for the oxidative *N*-demethylation-*N*-nitrosation reaction gave some 81% **5** and 5% **3**.

All of the three isomeric *N*,*N*-dimethylnitrobenzenamines (**6***a–c*), which were found unreactive at room temperature, gave some, but smaller, amounts of reduced denitrated product (**7**) under similar conditions at reflux temperatures and short contact times. The *meta* isomer **6***b* underwent mainly *N*-nitrosation-*N*-demethylation (78%) to *N*-methyl-*N*-nitroso-3-nitrobenzenamine (**8***b*), but some 9% *N*-methyl-*N*-nitrosobenzenamine (**7**) was also present. A similar yield of **6***b* was obtained from the *ortho* isomer **6***a*, which gave only 7% 1-methylbenzotriazole (**9**) but some 58% *N*-methyl-*N*-nitroso-2-nitrobenzenamine (**8***a*). The latter product represented the main course of the process also with the *para* isomer **6***c*, which produced only traces of the reduction product **7**.

The identification of **8***a* was arrived at by elemental analysis, mass spectrometry (the parent ion at *m/z* 181 lost NO to

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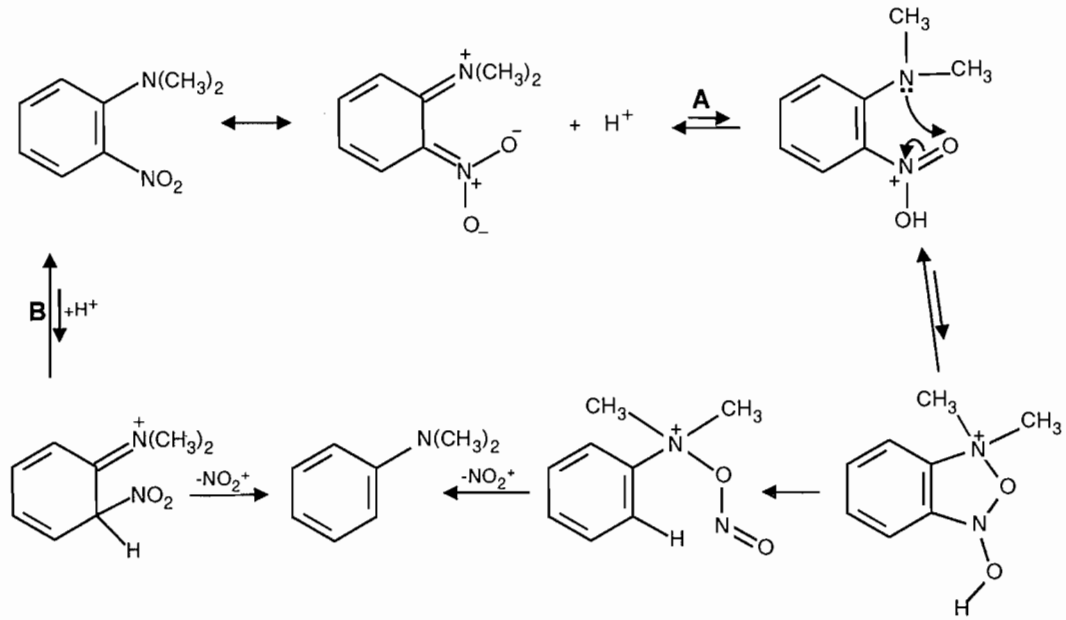
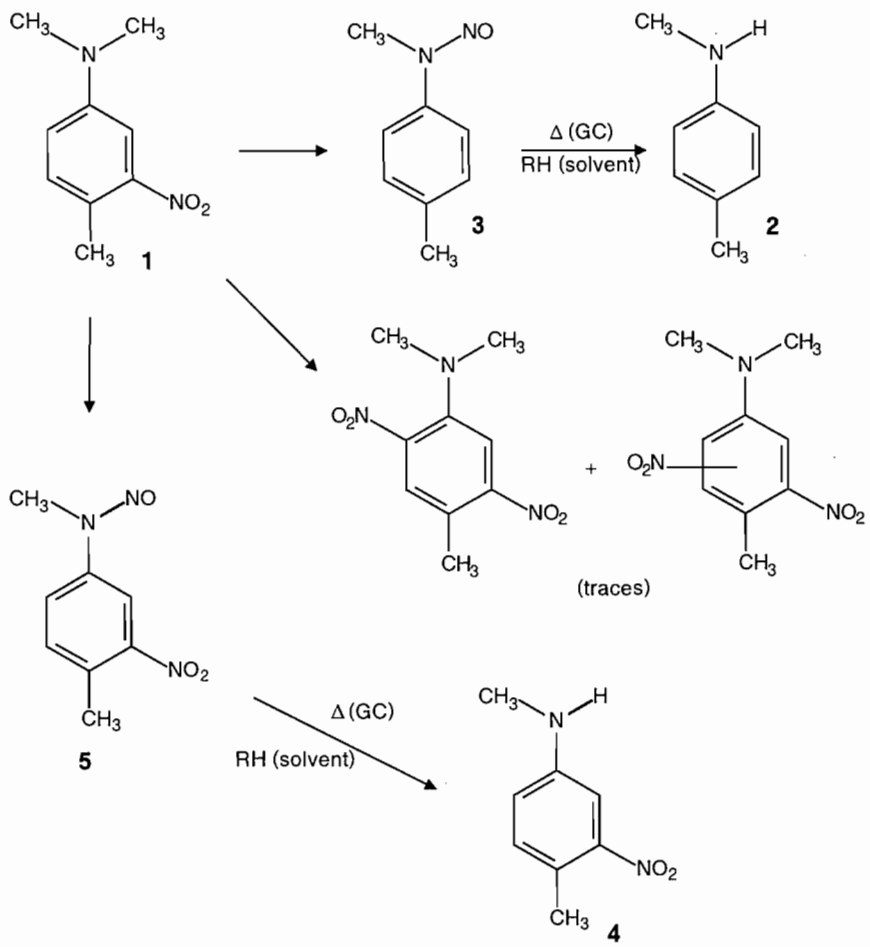
Scheme 1.

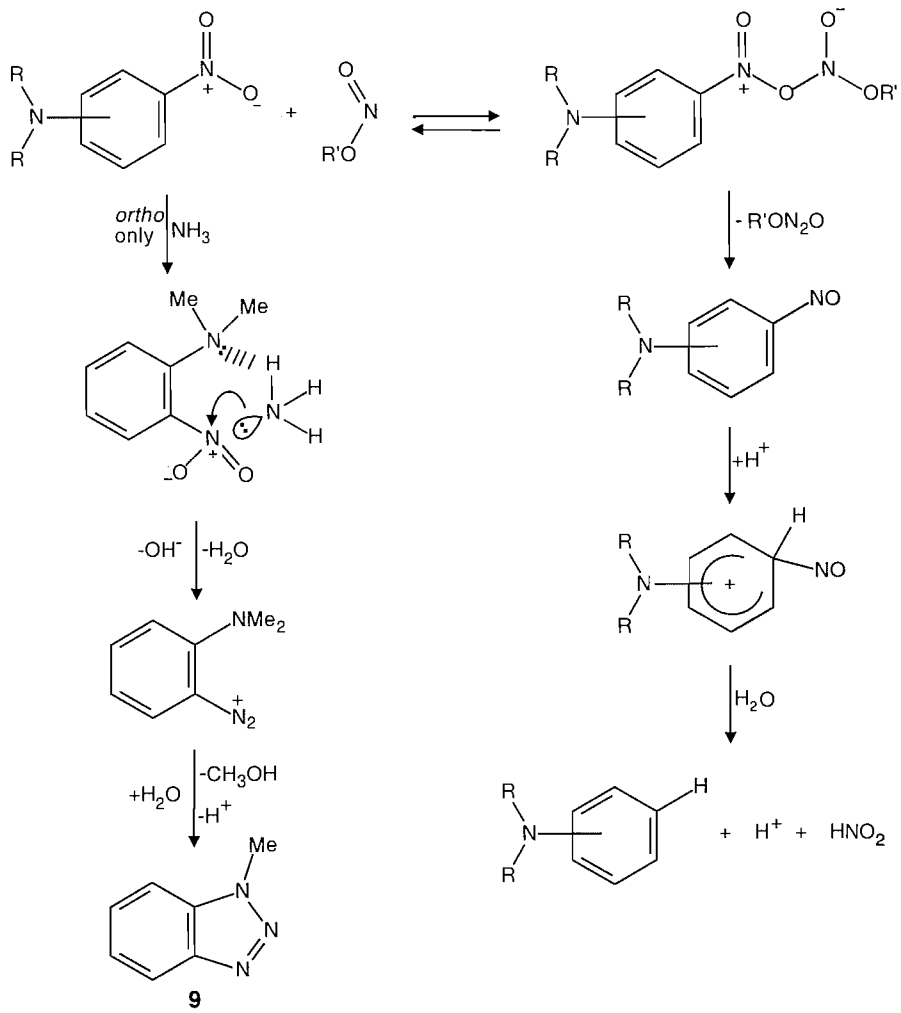


Scheme 2.



yield the base peak at *m/z* 151, this daughter ion subsequently lost OH, as expected from the location of the nitro group with respect to the methyl group), and infrared (2*a*, 3) ($\nu_{N=O}$ at 1459 cm^{-1}, ν_{N-N} at 961 cm^{-1}, and ν_{C-N} at 1198 cm^{-1}) spectroscopy. The ^1H NMR spectrum of **8***a* was in excellent agreement with what can be expected from a mixture of geometric isomers of a single nitrosamine, showing two sharp singlets for the methyl group. But, curiously, this is at variance with

Scheme 3.



the spectra of the strictly related nitrosamines **5** (vide infra) and *N*,4-dimethyl-*N*-nitroso-2-nitrobenzenamine **10** ($\delta_{N\text{-}Me}$ at 3.38, singlet, in $CDCl_3$) (*2a*), which exhibited under the same conditions a single peak for the *N*-methyl group, like all of the other *N*-nitroso aromatic nitrosamines investigated by us (*2a*), which are assumed to be in the *E* configuration. Like *N*-methyl-*N*-nitroso-2,6-diisopropylbenzenamine **11** ($\delta_{N\text{-}Me}$ at 3.36 ppm) (*2a*), the phenyl ring is expected to be almost perpendicular to the C-N-N=O plane also in **8***a*, but the ring in the latter case may be prone to some electron charge transfer from the oxygen of the nitro function, thus increasing the stability of the *Z* configuration, which would nonetheless be the lesser represented, showing the methyl resonance at δ 4.50 ppm. When a methyl group is in the *para* position, as is the case for **10**, its electron-releasing effect is allowed to restore a better planarity of the ring (not necessary of the NO_2 group!) and excludes the *Z* form from the equilibrium.

Nitronaphthalene, water, and AC did not yield any naphthalene after long reflux. The addition of BN to the mixture did not change matters. We have repeated the reported (*1b*) reaction between **6***a* and refluxing aqueous hydrochloric acid, but no substantial *N*-methylbenzimidazole-*N*-oxide was detected: denitration proceeded only to a very small extent. Moreover, 2-nitrobenzenamine did not undergo denitration at all under these conditions.

The mechanisms invoked for the reductive denitration of the *ortho*-nitrated tertiary amines cannot be valid here. By and large, the reaction conditions are far from being those for a necessary strong acid catalysis, although at the present time we have no well-grounded rationale for the behaviour of the system described. The formation of **9** indicated the involvement of ammonia (from AC) in the process. Speculations about mechanism are condensed in Scheme 3.

Experimental section

Materials

4,*N*,*N*-Trimethyl-3-nitrobenzenamine (**1**) (4) and 2-, 3-, and 4-nitro-*N*,*N*-dimethylbenzenamine (**6***a*, **6***b*, and **6***c*) (5) as well as *n*-butyl nitrite (BN) (6) were prepared according to described procedures. Compounds for which no references are given were available from previous work (*2a*). Alumina (active neutral Brockmann Grade I) was purchased from BDH (Milan, Italy). Solvents were used as received.

Equipment

GC–MS analyses were performed with a Fisons TRIO 2000 gas – chromatograph-mass spectrometer, working in the positive ion 70 eV electron impact mode. Injector temperature was kept at 250°C and column (Supelco® SE-54, 30 m long, 0.32 mm i.d., coated with a 0.25 μm phenyl methyl silicone rubber film) temperature was programmed from 80 to 300°C with a gradient of 10°C/min. Direct inlet mass spectra (DI-MS) were obtained on the same instrument: temperatures between 30 and 70°C were found suitable to volatilize all the compounds into the ion source. IR spectra were obtained with a Nicolet FT-IR Magna 550 spectrophotometer using the KBr technique for solids. ^{1}H NMR spectra were recorded in $CDCl_3$ at room temperature on a Bruker AC-F 200 spectrometer at 200 MHz. NMR peak locations are reported as δ-values from TMS. Some ^{1}H multiplets are characterized by the term *app* (apparent): this refers only to their appearance and may be an oversimplification. Elemental analyses were performed with a Carlo Erba model 1106 elemental analyzer and were in satisfactory agreement with calculated values. Melting points were determined with an automatic Mettler (model FP61) apparatus and are not corrected. Boiling points refer to the center cut of small distillations and are uncorrected.

Physical and spectroscopic properties of materials of common occurrence and (or) commercial origin are not reported.

4,*N*,*N*-Trimethyl-3-nitrobenzenamine (1), BN, AC, and water

Procedure A

The amine **1** (8.1 mmol), BN (24.5 mmol), AC (0.81 mmol), and water (81 mmol) were stirred during 2 days at room temperature. TLC analysis (alumina, hexane–CH_2Cl_2, 70:30 vol/vol) showed the total disappearance of starting material with the formation of two products. GC–MS analysis of the intact mixture from which volatile material was evaporated under vacuum showed the following: *N*,4-dimethylbenzenamine (**2**, 36%); *N*,4-dimethyl-*N*-nitrosobenzenamine (**3**, 8%), showing up as a peak tail of the former, of which it is a thermal decomposition product; *N*,4-dimethyl-3-nitrobenzenamine (**4**, 51%), analogously derived by thermal decomposition of the corresponding *N*-nitrosamine **5** in the injector; and two distinct dinitro derivatives (**12***a*, 1% and **12***b* 4%) of *N*,*N*,4-trimethylbenzenamines, identified on the basis of their mass spectra (**12***a*; MS *m/z*: 225(M^+, 46), 208(36), 180(24), 178(25), 162(48), 161(21), 150(100), 133(46), 132(57), 118(48), 117(28), 91(30), 77(24), 65(25), 51(17), and 42(24); **12***b*, MS *m/z*: 225(M^+, 70), 208(30), 180(5), 178(11), 162(17), 161(27), 150(64), 133(53), 132(100), 118(93), 117(43), 91(32), 77(19), 65(25), 51(10), and 42(24)]. Absorption chromatography, performed on alumina using hexane with increasing concentration of CH_2Cl_2 as eluant, of the total reaction mixture, after evaporation under vacuum of volatile material, yielded only *N*,4-dimethyl-*N*-nitrosobenzenamine (**3**, 28%; mp 56°C (lit. (7) mp 52°C); IR (KBr): 3020w, 2905w, 1510s, 1430vs, 1386vs, 1311s, 1287m, 1218vs, 1205vs, 1098vs, 1017s, 970s, 958s, 818vs, and 533s cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 2.39 (3H, s, ar-CH_3), 3.43 (3H, s, N-CH_3), 7.15–7.55 (4H, *app* m, ar-H); DI-MS *m/z*: 150(M^+, 34), 120(100), 92(51), 91(76), 77(54), 65(53), and 51(25). Anal. calcd. for $C_8H_{10}N_2O$: C 49.23, H 4.65, N 21.53; found: C 49.20, H 4.61, N 21.56) and *N*,4-dimethyl-*N*-nitroso-3-nitrobenzenamine (**5**, 75%; mp 58°C; IR (KBr): 3060w, 3020w, 1525vs, 1500s, 1460vs, 1400s, 1343vs, 1188vs, 1110s, 975s, 881m, 834s, 790m, 760m, and 708m cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 2.65 (3H, s, ar-CH_3), 3.46 (3H, s, N-CH_3), 7.22–8.19 (3H, m, ar-H); DI-MS *m/z*: 195(M^+, 19), 165(100), 148(13), 119(49), 118(29), 117(17), and 91(43). Anal. calcd. for $C_8H_9N_3O_3$: C 63.98, H 6.71, N 18.65; found: C 63.91, H 6.71, N 18.63).

Procedure B

A mixture of **1** (18.0 mmol), AC (2.0 mmol), and water (90.0 mmol) was refluxed during 60 min. Absorption chromatography, performed on alumina using hexane with increasing concentration of CH_2Cl_2 as eluant, of the total reaction mixture, after evaporation under vacuum of volatile material, yielded only **3** (5%) and **5** (81%).

N,*N*-Dimethyl-2-nitrobenzenamine (6*a*), BN, AC, and water

A mixture of **6***a* (18.0 mmol), BN (72.3 mmol), AC (2.0 mmol), and water (90.0 mmol) was refluxed during 120 min. Absorption chromatography, performed on alumina using hexane with increasing concentration of CH_2Cl_2 as eluant, of the total reaction mixture, after evaporation under vacuum of volatile material, yielded nitrobenzene (**13**, 1%), unreacted **6***a* (1%), *N*-methyl-2-nitrobenzenamine (**14***a*, 5%), *N*-methyl-*N*-nitrosobenzenamine (**7**, 9%; bp 83°C at 17 Torr (lit. (7) bp 86–87°C at 17 Torr; 1 Torr = 133.3 Pa) IR (neat): 3030w, 2910w, 1618m, 1595m, 1492m, 1467s, 1438vs, 1390m, 1350m, 1330m, 1312m, 1291m, 1263m, 1200s, 1090s, 1028m, 952m, 756s, and 690m cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 3.44 (3H, s, N-CH_3) and 7.29–7.66 (5H, m, ar-H); DI-MS *m/z*: 136(M^+, 40), 106(100), 105(38), 104(31), 79(73), and 77(92). Anal. calcd. for $C_7H_8N_2O$: C 61.75, H 5.92, N 20.57; found: C 61.72, H 5.92, N 20.58), *N*-methyl-*N*-nitroso-2-nitrobenzenamine (**8***a*, 58%; mp 39°C (lit. (8) mp 36°C); IR (KBr): 3100w, 3077w, 3049w, 1607m, 1528vs, 1459vs, 1441vs, 1358vs, 1277s, 1198s, 1070s, 1016s, 961s, 855m, 820m, 780vs, 748s, 704s, and 647m cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 3.42 and 4.23 (3H, two s, N-CH_3 in different conformations, % ratio 6.5/1) and 7.17–8.15 (4H, m, ar-H); DI-MS *m/z*: 181(M^+, 29), 151(100), 134(61), 120(8), 106(14), 105(28), 104(32), 93(34), 92(19), 91(22), 79(22), 78(47), 77(61), 76(23), 66(26), 65(31), 63(26), and 51(27). Anal. calcd. for $C_7H_7N_2O_2$: C 55.63, H 4.67, N 18.53; found: C 55.61, H 4.69, N 18.50), and 1–methylbenzotriazole (**9**, 7%; mp 66°C (lit. (9) mp 64–65°C); IR (KBr): 3050w, 2950w, 1498m, 1452m, 1299m, 1268m, 1198s, 1161m, 1024s, 780m, 739vs, and 662m cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 4.30 (3H, s, N-CH_3), 7.33–7.43 (1H, m, ar-H), 7.48–7.55 (2H, m, ar-H), and 8.06 (1H, *app* dt, J_o = 8.3 Hz, J_m = J_p = 1.1 Hz, ar-H); DI-MS *m/z*: 133(M^+, 100), 105(78), 104(42), 90(55), 78(27), 77(44), 64(27), 63(39), 51(21), and 50(16). Anal. calcd. for $C_7H_7N_3$: C 63.10, H 5.30, N 31.56; found: C 63.13, H 5.28, N 31.59).

N,*N*-Dimethyl-3-nitrobenzenamine (6*b*), BN, AC, and water

A mixture of **6***b* (18.0 mmol), BN (72.3 mmol), AC (2.0 mmol), and water (90.0 mmol) was refluxed during 120 min. Absorption chromatography, performed on alumina using hexane with increasing concentration of CH_2Cl_2 as eluant, of

the total reaction mixture, after evaporation under vacuum of volatile material, yielded nitrobenzene (**13**, 9%), unreacted **6***b* (3%), *N*-methyl-*N*-nitrosobenzenamine (**7**, 10%), *N*-methyl-3-nitrobenzenamine (**14***b*, 4%; mp 67°C (lit. (10) mp 67.5°C); IR (KBr): 3412s, 3106w, 2896w, 2873w, 2858w, 1627s, 1539vs, 1498s, 1483s, 1345vs, 1278s, 1153m, 1093s, 1082m, 840m, 809s, 731s, and 668s cm^{-1}; ^1H NMR ($CDCl_3$) δ: 2.89 (3H, s, N-CH_3), 4.14 (1H, br s, N-H), 6.86 (1H, ddd, J_o = 8.1 Hz, J_m = 2.4 Hz, $J_{m'}$ = 0.9 Hz, ar-H), 7.27 (1H, *app* t, J = 8.1 Hz, ar-H), 7.37 (1H, *app* t, J = 2.4 Hz, ar-H), and 7.51 (1H, ddd, J_o = 8.1 Hz, J_m = 2.2 Hz, $J_{m'}$ = 1.0 Hz, ar-H); DI-MS *m/z*: 152(M^+, 100), 122(7), 106(41), 105(17), 104(15), 94(11), 91(8), 79(39), 78(23), 77(61), 76(14), and 65(23). Anal. calcd. for $C_7H_8N_2O_2$: C 55.26, H 5.30, N 18.41; found: C 55.24, H 5.30, N 18.39), and *N*-methyl-*N*-nitroso-3-nitrobenzenamine (**8***b*, 78%; mp 78°C (lit. (11) mp 76°C); IR (KBr): 3107m, 3088m, 2942w, 2878w, 1533vs, 1473vs, 1433s, 1405m, 1355vs, 1312s, 1288s, 1201s, 1120vs, 1090s, 1076s, 972vs, 882vs, 813s, 740vs, 728vs, and 672s cm^{-1}; ^1H NMR ($CDCl_3$) δ: 3.52 (3H, s, N-CH_3), 7.71 (1H, *app* t, J = 8.2 Hz, ar-H), 8.00 (1H, ddd, J_o = 8.2 Hz, J_m = 2.2 Hz, $J_{m'}$ = 1.0 Hz, ar-H), 8.21 (1H, ddd, J_o = 8.2 Hz, J_m = 2.1 Hz, $J_{m'}$ = 1.0 Hz, ar-H), and 8.40 (1H, *app* t, J = 2.1 Hz, ar-H); DI-MS *m/z*: 181(M^+, 29), 151(100), 105(73), 104(60), 79(10), 78(25), 77(25), 76(18), and 63(22). Anal. calcd. for $C_7H_7N_2O_2$: C 55.63, H 4.67, N 18.53; found: C 55.60, H 4.67, N 18.56).

N,N-Dimethyl-4-nitrobenzenamine (6*c*), BN, AC, and water

A mixture of **6***c* (18.0 mmol), BN (72.3 mmol), AC (2.0 mmol), and water (90.0 mmol) was refluxed during 120 min. Absorption chromatography, performed on alumina using hexane with increasing concentration of CH_2Cl_2 as eluant, of the total reaction mixture, after evaporation under vacuum of volatile material, yielded nitrobenzene (**13**, 1%), unreacted **6***c* (7%), *N*-methyl-*N*-nitrosobenzenamine (**7**, 2%), *N*-methyl-4-nitrobenzenamine (**14***c*, 4%), and *N*-methyl-*N*-nitroso-4-nitrobenzenamine (**8***c*, 80%; mp 105°C (lit. (12) mp 104°C); IR (KBr): 3095w, 1610m, 1595m, 1510m, 1463m, 1395m, 1338s, 1300s, 1203m, 1175m, 1073s, 943m, 847m, 810m, and 745m cm^{-1}; ^1H NMR ($CDCl_3$) δ: 3.48 (3H, s, N-CH_3), 7.76 (2H, *app* d, J = 9.2 Hz, ar-H), and 8.37 (2H, *app* d, J = 9.2 Hz, ar-H); DI-MS *m/z*: 181(M^+, 32), 151(96), 105(100), 104(30), 90(15), and 63(17). Anal. calcd. for $C_7H_7N_2O_2$: C 55.63, H 4.67, N 18.53; found: C 55.65, H 4.69, N 18.51).

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