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A new method for the reduction of nitronyl nitroxides

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Abstract—Reduction of nitronyl nitroxides using hexamethylenetetramine is a very convenient method for preparing the corresponding imino nitroxides and 2-imidazoline *N*-oxides.

The reaction of nitronyl nitroxide **1a** with $Cu(NO_3)_2{\cdot}3H_2O$ gave $[Cu(\mathbf{1a})_2](NO_3)_2(H_2O)_2$, in which Cu^{2+} is square planar (Fig. 1).[1,2]

Taking $[Cu(\mathbf{1a})_2]^{2+}$ as a building block we attempted the preparation of a highly dimensional heterospin structure using hexamethylenetetramine (HMTA) as a bridge capable of forming two-dimensional $(5,3_4)$-nets by reaction with Cu^{2+} square matrices.[3] However, unexpectedly, the reaction of **1a** with HMTA produced $[Cu(\mathbf{3a})_2](NO_3)_2$, whose coordination sites are occupied by two 2-imidazoline *N*-oxide molecules **3a** (Fig. 2).[1,2]

Significantly, in the absence of HMTA, the reaction of **1a** with $Cu(NO_3)_2{\cdot}3H_2O$ did not lead to reduction of **1a**. Therefore, the presence of HMTA in the reaction mixture is essential for the reduction of **1a**. Methods of transforming nitronyl nitroxides into imino nitroxides or further reduction products, 2-imidazoline *N*-oxides, are scarce,[4] which prompted us to investigate the possibility of reducing nitronyl nitroxides using HMTA.

Indeed, when reacting with HMTA in CH_3OH, **1a** is gradually reduced to **2a**, as indicated by the color change of the solution (from dark blue to red). After a day, the solution contained a significant amount of **3a** along with **2a**. No other products of transformation of **1a** by HMTA were observed. The ratio of **2a** to **3a** in the reaction mixture depends on the reaction time; the longer the reaction time, the larger the amount of **3a** accumulated in the reaction mixture. Thus, treatment of **1a** with a HMTA proved to be a convenient method for the preparation of both **2a** and **3a** (Scheme 1).[1,2]

Figure 1. Structure of $[Cu(\mathbf{1a})_2]^{2+}$. Selected metrical parameters: Cu–O 1.990(2), Cu–N 1.959(3), Cu–ONO$_2$ 2.539(3), N–OCu 1.305(3), N–O 1.272(3) Å; OCuN 91.03(9), NOCu 122.8(2)°.

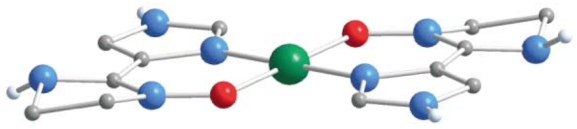
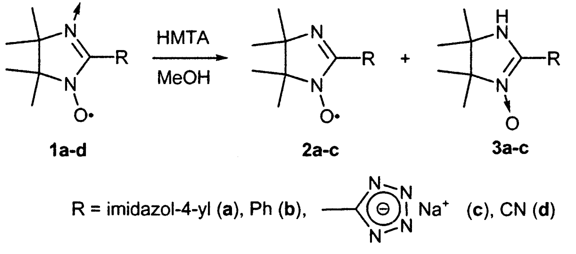


Figure 2. Structure of $[Cu(\mathbf{3a})_2]^{2+}$. Selected metrical parameters: Cu–O 1.931(2), Cu–N 1.933(3), N–O–Cu 1.349(4) Å; OCuN 92.9(1), NOCu 125.2(2)°.



Scheme 1. The reduction of nitronyl nitroxides to imino nitroxides and 2-imidazoline *N*-oxides.

Keywords: imino nitroxide; nitronyl nitroxide; reduction.

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As in the case of **1a**, the reaction of nitronyl nitroxide **1b** with HMTA gave, depending on the reaction time, imino nitroxide **2b** or 2-imidazoline *N*-oxide **3b** (Scheme 1), whose physicochemical characteristics were identical to those of the authentic samples described elsewhere.[5]

Note that the reduction of nitronyl nitroxides to imino nitroxides using HMTA may also be used in those cases where known procedures are inapplicable. Thus, for some time we were unable to obtain nitroxide **2c**. However, heating 2-(1*H*-tetrazol-5-yl)-4,4,5,5-tetramethyl-4,5-dihydro-1*H*-imidazol-3-oxide-1-oxyl sodium salt[6] (**1c**) with $NaNO_2$ in water in the presence of AcOH or in DMF[5] led to a change of color from deep-blue to orange, indicating that compound **2c** had been formed. However, we were unable to isolate **2c**. Boiling **1c** with PPh_3 in MeOH[5] for two days did not give **2c** according to TLC data. Previously, **1c** had been synthesized by the reaction of NaN_3 with **1d**. Attempts to apply the same approach to the synthesis of **2c** failed because on heating with NaN_3, compound **2d** decomposed before **2c** started to form. Compound **2c** could only be synthesized when HMTA was employed as a reducing agent.[1,2]

Also note the following peculiarities of the structures of **2c** and **3a**. In solid **2c**, each sodium atom is bonded to three imino nitroxide molecules, forming polymer layers (Fig. 3).

The presence of two N–H groups and two groups capable of forming stable H-bonds in molecule **3a** proved to be favorable for framework construction (Fig. 4).

Crystallographic data (excluding structure factors) for the structures in this paper, have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 209718-209723. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

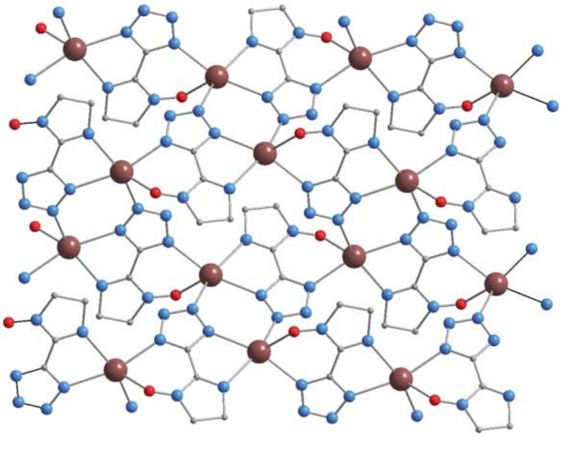

Figure 3. Structure of a layer in **2c**. Selected metrical parameters: Na–O 2.346(5), Na–N 2.439(5)–2.522(5), O–N 1.278(5) Å, NONa 126.6(3)°.

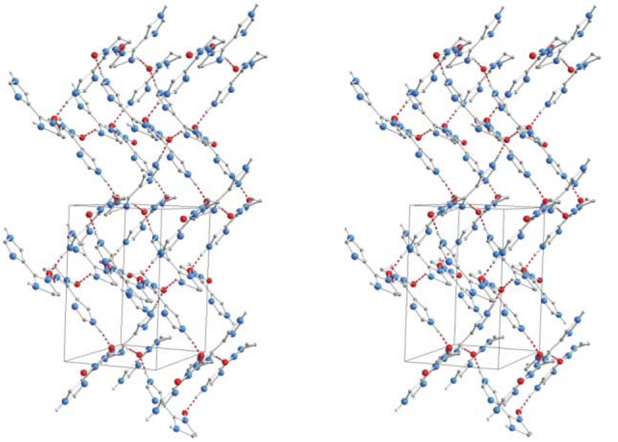

Figure 4. Stereoview of the frame structure of **3a**. Selected metrical parameters: O–N 1.346(2) Å, N–H···O′ 0.89(3), 2.21(3), 2.966(2) Å, 142(2), N–H···O″ 0.93(2), 1.69(3), 2.614(2) Å, 174(2).

Acknowledgements

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References

1. 2-(Imidazol-4-yl)-4,4,5,5-tetramethyl-4,5-dihydro-1*H*-imidazol 3-oxide 1-oxyl (**1a**) was synthesized according to the standard procedure,[7] by the reaction of 2,3-bis(hydroxylamino)-2,3-dimethylbutane[8] with 4(5)-imidazole carbaldehyde with further oxidation by PbO_2. Summary yield 85%; mp 184–185°C; $\mu_{\text{eff}}/\beta = 1.73$ (295 K); $a_N = 7.70$ G. Anal. found: C, 54.0; H, 6.9; N, 24.8. Calcd for $C_{10}H_{15}N_4O_2$: C, 53.8; H, 6.8; N, 25.0%.

   $[Cu(\mathbf{1a})_2](NO_3)_2$. A solution of $Cu(NO_3)_2$ (27 mg, 0.112 mmol) in water (1.5 ml) was added to a solution of **1a** (50 mg, 0.195 mmol) in water (4 ml). The dark blue crystals that precipitated 6 h later were filtered off and washed with acetone (2–3 ml). Yield 65%; temp. of decomp. >203°C. Anal. found: C, 38.0; H, 4.9; N, 22.1. Calcd for $CuC_{20}H_{30}N_{10}O_{10}$: C, 37.9; H, 4.8; N, 22.1.

   $[Cu(\mathbf{3a})_2](NO_3)_2$. A solution of $Cu(NO_3)_2$ (27 mg, 0.112 mmol) in water (1.5 ml) was added to a solution of **1a** (50 mg, 0.195 mmol) in water (4 ml), then a solution of HMTA (7 mg, 0.05 mmol) in water (1 ml) was added. After a day, brown crystals were filtered off and washed with cold water. Yield 55%; temp. of decop. >270°C. Anal. found: C, 40.0; H, 5.4; N, 23.5. Calcd for $C_{20}H_{32}CuN_{10}O_8$: C, 39.8; H, 5.3; N, 23.2.

   2-(1*H*-Tetrazol-5-yl)-4,4,5,5-tetramethyl-4,5-dihydro-1*H*-imidazol-1-oxyl sodium salt (**2c**). Typical procedure. A solution of **1c** (1.12 g, 3.96 mmol) and HMTA (137 mg, 0.98 mmol) in MeOH (10 ml) was stirred for 10 h at room temperature. Then, PbO_2 (2.0 g, 8.4 mmol) was added and the reaction mixture was stirred for 1 h. The precipitate was filtered off and washed with EtOH. The solvent was distilled from the filtrate in vacuo, and the residue was quenched with acetone (5 ml) and filtered off. The product was crystallized from a mixture of MeOH with AcOEt. The initial colorless crystalline precipitate was removed by filtration and the filtrate was kept in a refrigerator for a few days. The resulting orange crystals were filtered off. Yield 520 mg (57%); temp. of decomp. 285°C. Anal. found: C, 41.4; H, 5.2. Calcd for $C_8H_{12}N_6NaO$: C, 41.6; H, 5.2%. $\mu_{\mathrm{eff}}/\beta = 1.73$ (295 K), $a_{\mathrm{N1}} = 9.39$ G, $a_{\mathrm{N2}} = 4.54$ G.

2-(Imidazol-4-yl)-4,4,5,5-tetramethyl-4,5-dihydro-1*H*-imidazol 1-oxyl (**2a**). Yield 57%; mp 174–175°C; $\mu_{\mathrm{eff}}/\beta = 1.74$ (295 K), $a_{\mathrm{N1}} = 9.35$ G, $a_{\mathrm{N2}} = 4.30$ G. Anal. found: C, 57.7; H, 7.5. Calcd for $C_{10}H_{15}N_4O$: C, 57.9; H, 7.3.

4,4,5,5-Tetramethyl-4,5-dihydro-1*H*,3′*H*-[2,4′]biimidazolyl 3-oxide (**3a**). The reaction time was 3 days. Yield 55%; mp 216–220°C. Anal. found: C, 57.5; H, 8.0; N, 26.9. Calcd for $C_{10}H_{16}N_4O$: C, 57.6; H, 7.7; N, 26.9.

2. Cystal data for **1a**·CH_3OH: $C_{11}H_{19}N_4O_3$, $M_w = 255.30$, monoclinic, space group $P2_1/n$, $a = 10.081(1)$, $b = 12.260(2)$, $c = 11.614(2)$ Å, $\beta = 110.884(2)°$, $V = 1341.0(3)$ Å^3, $Z = 4$, $D_{\mathrm{calcd}} = 1.265$ g cm^{-3}, $\mu = 0.094$ mm^{-1}, reflections collected/unique = 5700/1929 ($R_{\mathrm{int}} = 0.2027$), 231 parameters, Goof = 0.932, $R_1 = 0.0640$, $wR_2 = 0.1393$ ($I > 2\sigma(I)$), $R_1 = 0.0909$, $wR_2 = 0.1525$ for all data. CCDC reference number 209723. For **2a**: $C_{10}H_{15}N_4O$, $M_w = 255.30$, triclinic, space group $P\bar{1}$, $a = 13.972(3)$, $b = 14.044(3)$, $c = 14.484(3)$ Å, $\alpha = 111.036(5)$, $\beta = 95.644(5)$, $\gamma = 113.217(5)°$, $V = 2340.7(9)$ Å^3, $Z = 8$, $D_{\mathrm{calcd}} = 1.176$ g cm^{-3}, $\mu = 0.080$ mm^{-1}, reflections collected/unique = 9993/6626 ($R_{\mathrm{int}} = 0.0851$), 752 parameters, Goof = 0.763, $R_1 = 0.0642$, $wR_2 = 0.1039$ ($I > 2\sigma(I)$), $R_1 = 0.2088$, $wR_2 = 0.1447$ for all data. CCDC reference number 209719. For [Cu(**1a**)$_2$]$(NO_3)_2$·$3H_2O$: $C_{20}H_{36}CuN_{10}O_{13}$, $M_w = 688.13$, orthorhombic, space group $Pccn$, $a = 13.353(3)$, $b = 25.864(6)$, $c = 8.675(2)$ Å, $V = 2996.3(12)$ Å^3, $Z = 4$, $D_{\mathrm{calcd}} = 1.525$ g cm^{-3}, $\mu = 0.808$ mm^{-1}, reflections collected/unique = 11733/2149 ($R_{\mathrm{int}} = 0.0758$), 274 parameters, Goof = 0.761, $R_1 = 0.0394$, $wR_2 = 0.1048$ ($I > 2\sigma(I)$), $R_1 = 0.0514$, $wR_2 = 0.1141$ for all data. CCDC reference number 209722. For [Cu(**3a**)$_2$]$(NO_3)_2$: $C_{20}H_{32}CuN_{10}O_8$, $M_w = 604.10$, monoclinic, space group $P2_1/n$, (No. 14), $a = 7.301(1)$, $b = 23.701(4)$, $c = 8.002(1)$ Å, $\beta = 105.295(3)°$, $V = 1335.7(3)$ Å^3, $Z = 2$, $D_{\mathrm{calcd}} = 1.502$ g cm^{-3}, $\mu = 0.881$ mm^{-1}, 5676 reflections measured, 1920 unique ($R_{\mathrm{int}} = 0.1116$), 1920 observed ($I > 2\sigma(I)$), 243 parameters, Goof = 0.827, $R_1 = 0.0462$, $wR_2 = 0.1167$ ($I > 2\sigma(I)$), $R_1 = 0.0636$, $wR_2 = 0.1324$ for all data. CCDC reference number 209718. For **2c**: $C_8H_{12}N_6NaO$, $M_w = 231.23$, monoclinic, space group $P2_1/c$, $a = 10.354(2)$, $b = 8.962(1)$, $c = 12.915(2)$ Å, $\beta = 113.630(1)°$, $V = 1097.9(3)$ Å^3, $Z = 4$, $D_{\mathrm{calcd}} = 1.399$ g cm^{-3}, $\mu = 0.133$ mm^{-1}, reflections collected/unique = 3059/1564 ($R_{\mathrm{int}} = 0.1199$), 194 parameters, Goof = 0.870, $R_1 = 0.0619$, $wR_2 = 0.1114$ ($I > 2\sigma(I)$), $R_1 = 0.1155$, $wR_2 = 0.1287$ for all data. CCDC reference number 209720. For **3a**: $C_{10}H_{16}N_4O$, $M_w = 208.27$, orthorhombic, space group $P2_12_12_1$, $a = 7.5254(9)$, $b = 12.096(2)$, $c = 12.488(2)$ Å, $V = 1136.7(2)$ Å^3, $Z = 4$, $D_{\mathrm{calcd}} = 1.217$ g cm^{-3}, $\mu = 0.083$ mm^{-1}, reflections collected/unique = 4924/1638 ($R_{\mathrm{int}} = 0.1301$), 201 parameters, Goof = 1.009, $R_1 = 0.0391$, $wR_2 = 0.0989$ ($I > 2\sigma(I)$), $R_1 = 0.0404$, $wR_2 = 0.1002$ for all data. CCDC reference number 209721. The reflection data were collected on a Smart Apex Bruker AXS, Mo-Kα radiation ($\lambda = 0.71073$ Å), all structures were solved using standard direct method techniques, and refined using full-matrix least-squares based on F^2. Hydrogen atoms were localized in $\Delta\rho$ synthesis and refined isotropically with anisotropic non-hydrogen atoms.

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