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Method for the synthesis of a stable heteroatom analog of trimethylenemethane*

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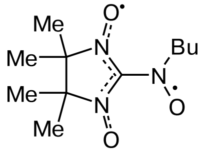
A procedure was developed for the synthesis of the kinetically stable nitroxide 2-(*N-tert*-butyl-*N*-hydroxyamino)-4,4,5,5-tetramethyl-4,5-dihydro-1*H*-imidazole-3-oxide-1-oxyl containing the sterically hindered hydroxylamino group. The crystal and molecular structure of this compound was determined. The isolation of this nitroxide hydroxylamine in the individual state enabled a new procedure for the preparation of its oxidation product, *viz.*, the corresponding nitroxide biradical. The results of quantum chemical calculations of the electron exchange in the biradical molecule are in good agreement with the experimental data on the triplet ground state of the molecule in the crystal obtained earlier.

Key words: nitroxide radicals, sterically hindered hydroxylamines, X-ray diffraction study, quantum chemical calculations.

Kinetically stable organic paramagnetic compounds attract considerable interest because of their use in catalytic processes, as well as their possible application in the design of molecular magnets, spintronic devices, magnetically active sensors, contrast agents for magnetic resonance tomography, and rechargeable electric batteries.[1—6] An ever-increasing attention is given to the development of methods for the synthesis and physicochemical investigation of bi- and polyradicals with specific structures.[1,7] The binding of the 1-oxyl-3-oxide-2-imidazolin-2-yl group to the radical moiety of another type can give rise to biradicals with a topology of trimethylenemethane and, as a consequence, with the triplet ground state.[7—10] This approach allows one to prepare rather "compact"[4] biradicals with a high singlet-triplet splitting energy. A recent example[4] comes from the synthesis of heteroatom analogs of trimethylenemethane, *viz.*, 2-(*N-tert*-butyl-*N*-oxylamino)-4,4,5,5-tetramethyl-4,5-dihydro-1*H*-imidazole-3-oxide-1-oxyl (**1**) and 2-(*N-tert*-butyl-*N*-oxylamino)-4,4,5,5-tetramethyl-4,5-dihydro-1*H*-imidazole-1-oxyl (**2**).[4]



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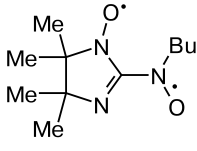

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In the present study, we describe a procedure for the synthesis of biradical **1**, the synthesis and structure of its hydroxyamine precursor **3**, which was isolated in the individual state, and the results of quantum chemical calculations. It was found that the reaction of lithium derivative **4** with 2-methyl-2-nitrosopropane affords 2-(*N-tert*-butyl-*N*-hydroxyamino)-4,4,5,5-tetramethyl-4,5-dihydro-1*H*-imidazole-3-oxide-1-oxyl (**3**), whose reaction with $K_3[Fe(CN)_6]$ and $NaHCO_3$ in a mixture of water with CH_2Cl_2 or MnO_2 in CH_2Cl_2 gives biradical **1** in high yield (Scheme 1).

The structures of **1** and **3** were confirmed by X-ray diffraction study. The structure of **3** (CCDC-809544) consists of chains formed through intermolecular O(1)—H(1)...O(3) hydrogen bonds between the N—OH group and one of the O atoms of the nitronyl nitroxide moiety ($d_{\mathrm{O-H}}$ = 0.94(4) Å, $d_{\mathrm{H...O}}$ = 2.12(4) Å, $d_{\mathrm{O...O}}$ = 2.874(3) Å, ∠OHO = 136(3)°). In addition, the H(1) atom is involved in the intramolecular O(1)—H(1)...O(2) hydrogen bond ($d_{\mathrm{H...O}}$ = 2.24(4) Å, $d_{\mathrm{O...O}}$ = 2.818(3) Å, ∠OHO = 119(3)°). The dihedral angles between the {C(2)N(1)O(1)}, {N(2)C(2)N(3)} planes and the {C(1)N(1)C(2)}, {C(2)N(1)O(1)} planes are 48.0(3)° and 45.9(3)°, respectively. The N—O bond lengths in the nitronyl nitroxide moiety are equal within experimental error (1.283(3) and 1.278(3) Å); the O(1)—N(1)

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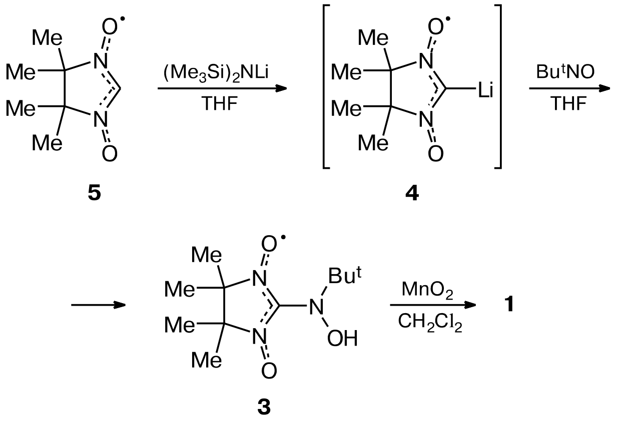
Scheme 1



bond length is typical of sterically hindered hydroxyamines (1.424(3) Å) (Fig. 1, *a*). The intermolecular exchange interactions between the paramagnetic centers are weak in spite of the hydrogen bonds that are present in the crystal structure of **3** (Fig. 2, Table 1), which are formed with the participation of the N—O group. This is evidenced by the fact that the effective magnetic moment $\mu_{eff} = 1.73\pm0.01\ \mu_B$ is virtually unchanged in a wide temperature range (35—300 K) and corresponds to the theoretical value for a particle with $S = 1/2$ and $g = 2$.

Table 1. Parameters of intermolecular (InterHB) and intramolecular (IntraHB) hydrogen bonds

Parameter	InterHB	IntraHB
Bond	*d*/Å	
O—H	0.82	0.82
H...O	2.42	2.17
O...O	2.880(3)	2.832(3)
Angle	ω/deg	
O—H—O	116.1	137.9

In biradical **1** (CCDC-809543), the N(1) atom (Fig. 1, *b*) lies in the {C(1)C(2)O(1)} plane. In the N—O groups, the bond lengths are 1.278±0.002 Å. The dihedral angle between the {C(2)N(1)O(1)} and {N(2)C(2)N(3)} planes is 69.4(1)°. (The latter value substantially differs from that reported in the study.[4] Apparently, this is associated with the fact that we studied the structure of **1** in the form of a heptane solvate, whereas the Japanese researchers analyzed solvates of **1** with other solvents.) In the temperature

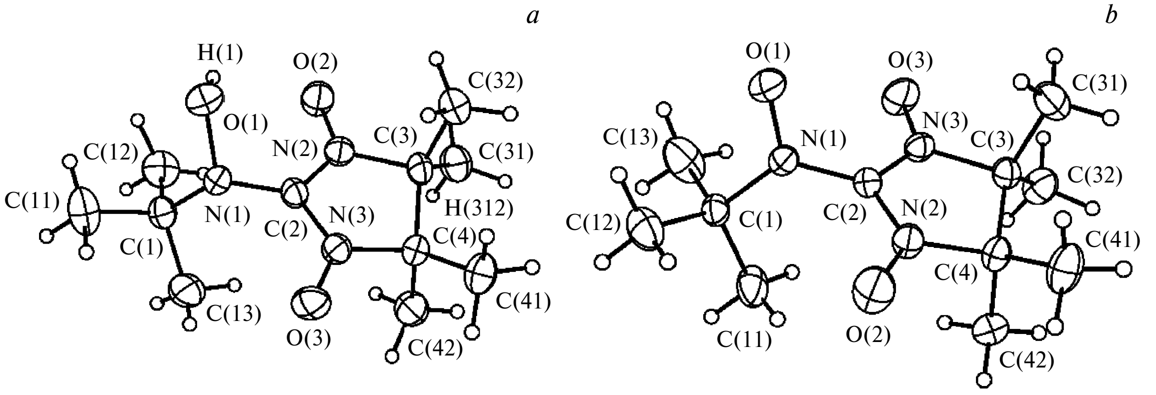


Fig. 1. Molecular structures of nitroxides **3** (*a*) and **1** (*b*) with atoms represented as probability displacement ellipsoids ($p = 35\%$).

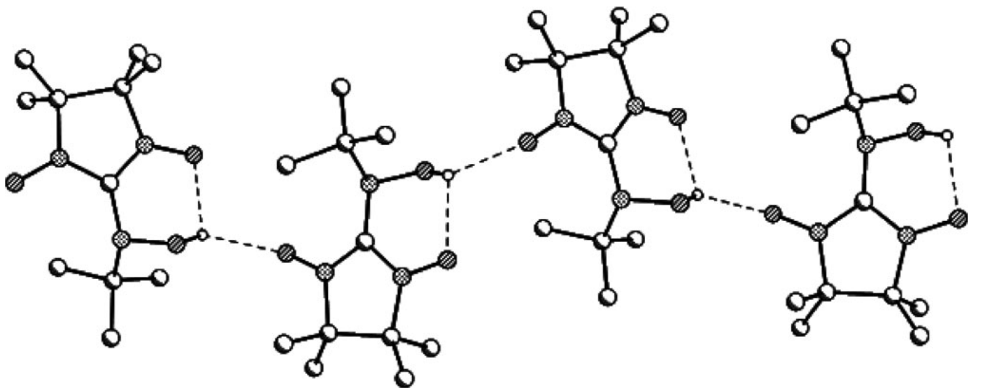


Fig. 2. Hydrogen bonds in the structure of **3**.

range of 100—300 K, the experimental value of μ_{eff} for **1** (the molecules of the solvent were removed by storing a sample *in vacuo*) remains unchanged and is equal to 2.87 μ_B, which is close to the theoretical value (2.83 μ_B) for the triplet biradical with $S = 1$ and $g = 2$. At $T < 40$ K, the magnetic moment μ_{eff} decreases, which is indicative of weak intermolecular antiferromagnetic exchange interactions. The dependence $\mu_{\text{eff}}(T)$ is well described by the modified Bleaney—Bowers model[11] ($H = -2JS_{1/2} \cdot S_{1/2}$) for the fixed value of the intramolecular exchange $J/k = 400$ K and the variable effective intermolecular exchange parameter $zJ'/k = -3.1 \pm 0.1$ K.

The calculations[12] of J by the equation

$$J = -(E^{HS} - E^{LS}{}_{BS})/(\langle S^2\rangle)/(\langle S^2\rangle - \langle S^2\rangle^{LS}{}_{BS}),$$

where E^{HS} is the energy of the triplet state and $E^{LS}{}_{BS}$ is the energy of the low-spin broken-symmetry state,[13] were performed in terms of the density functional theory with the use of two hybrid functionals B3LYP and PBE0.[14—16] The calculations of J for the geometry of the biradical determined from the X-ray diffraction data are in good agreement with the triplet ground state of **1** in the crystal. The UB3YP/TZV method gave $J/k = 439$ K, and the PBE0/TZV method estimated J/k at the same order of magnitude (474 K).

The ESR spectrum of compound **1** is typical of biradicals with $S = 1$. Thus, the spectrum shows a Pake doublet at 340 mT associated with the dipole interaction between two electron spins and a low-intensity line at half-field (Fig. 3, *a*). The doublet at $g = 2$ was adequately simulated in terms of the first-order perturbation theory[17] for the parameters D and E of the spin-Hamiltonian $\hat{H} = \hbar\omega_0\hat{S}_z + D[\hat{S}^2{}_Z - 2/3] + E[\hat{S}^2{}_X - \hat{S}^2{}_Y]$ equal to 27.3 and 2.0 mT, respectively, and the Gaussian linewidth of 1.7 mT (see Fig. 3, *b*). Since the ESR spectrum was recorded in a glassy matrix, the parameters D and E were calculated for the geometry optimized by the UB3LYP/TZV method. It should be noted that this geometry is substantially different (for example, the N(3)C(2)N(1)O(1) dihedral angle is 49.2°) from that of the biradical in the crystal. The parameter $D_{\text{calc}} = 33.1$ mT calculated[18—20] by the ROBP88/EPR-II method is in good agreement with the experimental data, whereas the parameter E is significantly overestimated ($E_{\text{calc}} = 10.2$ mT).

The asymmetry of two central lines in the ESR spectrum of biradical **1** is caused by the anisotropy of the g tensor. The components of the g tensor calculated by the UBP86/EPR-II method are $g_{xx} = 2.004023$, $g_{yy} = 2.006489$, $g_{zz} = 2.008089$ ($g_{\text{iso}} = 2.0062$). The linewidth of the ESR spectrum (1.7 mT) is consistent with the hyperfine coupling constants calculated at the UB3LYP/TZV level of theory. The isotropic and anisotropic (a_{zz}) hyperfine coupling constants for three N atoms are in the ranges of 0.31—0.35 and 1.11—1.38 mT, respectively.

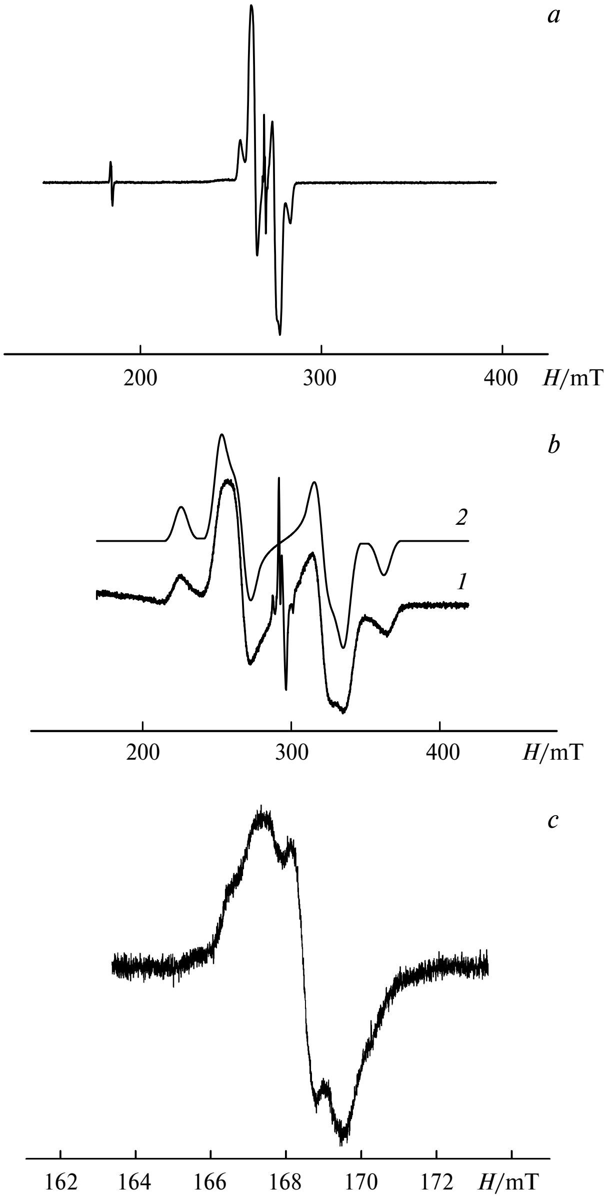


Fig. 3. ESR spectrum of a 0.01% solid solution of **1** in glassy *o*-terphenyl (*a*); the ESR signal at $g = 2$ (*1*) and the result of its simulation (*2*) (*b*); the ESR signal at $g = 4$ (*c*).

Therefore, in the present study we developed a new method for the synthesis of biradical **1**, which is a stable heteroatom analog of trimethylenemethane. Nitronyl nitroxide **3**, which is a hydroxyamine precursor of **1**, was isolated in the individual state, and its structure was studied. The calculated magnetic parameters for biradical **1** are in good agreement with the experimental values.

Experimental

2-(*N-tert*-Butyl-*N*-hydroxyamino)-4,4,5,5-tetramethyl-4,5-dihydro-1*H*-imidazole-3-oxide-1-oxyl (3). A 1.0 *M* $LiN(SiMe_3)_2$

solution in THF (2.8 mL, 2.8 mmol) was added to a solution of **5** (400 mg, 2.54 mmol) in dry THF (30 mL) vigorously stirred at –90 °C under argon. The reaction mixture was stirred at –90 °C for 0.5 h. Then a solution of 2-methyl-2-nitrosopropane (221 mg, 2.54 mmol) in THF (10 mL) was added. The cooling was terminated. After the reaction mixture warmed to room temperature, a concentrated aqueous NH_4Cl solution (5 mL), water (20 mL), and CH_2Cl_2 (50 mL) were successively added. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3×20 mL). The combined organic extracts were dried with Na_2SO_4 and concentrated. The residue was chromatographed on a column with SiO_2 using ethyl acetate as the eluent. The fraction containing compounds **1** and **3** was concentrated. The residue was chromatorgaphed on a column with neutral Al_2O_3 (CH_2Cl_2 as the eluent). Then product **3** was purified by several crystallizations from a mixture of heptane and ethyl acetate in a MBRAUN glove box. The yield was 105 mg (17%), blue-violet crystals, m.p. 115—118 °C; $R_f = 0.52$ with ethyl acetate on Silica gel 60 F_{254} plates (Merck), $R_f = 0.26$ with CH_2Cl_2 on Alumina N/UV_{254} plates (Macherey—Nagel). IR, ν/cm^{-1}: 3304, 2979, 2934, 1515, 1452, 1417, 1391, 1350, 1331, 1210, 1171, 1139, 1025, 1008, 959, 871, 832, 738, 638, 620, 582, 541, 462. ESR: $g_{iso} = 2.0065$, a_N (1 N) = 0.742 mT, a_N (1 N) = 0.736 mT, $a_{H(OH)}$ (1 H) = 0.037 mT, $a_{H(Me)}$ (12 H) = 0.024 mT. Found (%): C, 63.8; H, 8.8; N, 17.1. $C_{11}H_{22}N_3O_3$. Calculated (%): C, 54.1; H, 9.1; N, 17.2. (The yields of compound **3** were low due to difficulties of its separation from **1** that formed upon exposure of solutions of **3** to air. Hence, if the aim is to prepare compound **1**, it is recommended to combine the synthesis of compound **3** and the oxidation of the latter to compound **1** described below; in this case, the biradical was obtained in a total yield of 40—50%).

2-(*N*-*tert*-Butyl-*N*-oxylamino)-4,4,5,5-tetramethyl-4,5-dihydro-1*H*-imidazole-3-oxide-1-oxyl (1). Manganese oxide MnO_2 (400 mg, 4.6 mmol) was added to a solution of compound **3** (160 mg, 0.66 mmol) in CH_2Cl_2 (15 mL) stirred at ~0 °C. The reaction mixture was stirred for 10 min, filtered, and concentrated *in vacuo*. The residue was chromatographed on a column with SiO_2 (ethyl acetate as the eluent). The red fraction was concentrated, and the residue was recrystallized from a mixture of hexane and CH_2Cl_2. The yield was 130 mg (82%), red needle-like crystals, m.p. 124—127 °C; $R_f = 0.62$ with ethyl acetate on Silica gel 60 F_{254} plates, $R_f = 0.50$ with CH_2Cl_2 on Alumina N/UV_{254} plates. IR, ν/cm^{-1}: 3440, 2979, 2934, 1697, 1532, 1455, 1419, 1374, 1334, 1200, 1174, 1137, 870, 748, 620, 576, 541, 465. Found (%): C, 54.0; H, 8.4; N, 17.1. $C_{11}H_{21}N_3O_3$. Calculated (%): C, 54.3; H, 8.7; N, 17.3.

X-ray diffraction study was performed on a SMART APEX II CCD diffractometer (Bruker AXS) (Mo-Kα, λ = 0.71073 Å, T = 240 K, the absorption correction was applied using the Bruker SADABS program, version 2.10). The structures were solved by direct methods and refined by the full-matrix least-squares method with anisotropic displacement parameters for all nonhydrogen atoms. Most of the H atoms were positioned geometrically. The H atoms of the methyl groups were refined isotropically using a riding model. All calculations were carried out with the use of the Bruker Shelxtl Version 6.14 software. In the structure of **1**, the molecules are packed so that they form channels along the crystallographic direction [001], which are filled by disordered heptane molecules. Since an attempt to fill the channels with occupancies of 1/6 C_7H_{16} molecule per molecule **1** was unsuccessful, the final refinement was performed without taking into account the solvent molecules (SQUEEZE, PLATON[21]). Principal crystallographic data for compound **1**: $C_{11}H_{21}N_3O_3$, FW = 243.31, trigonal crystals, space group *R-3*, a = 34.832(2) Å, b = 34.832(2) Å, c = 6.1146(5) Å, V = 6424.8(8) Å^3, Z = 18, D_{calc} = 1.132 g cm^{-3}, μ = 0.083 mm^{-1}, 19610 measured reflections (θ_{max} = 28.21°), 3499 independent reflections (R_{int} = 0.0521), 1980 reflections with $F > 4\sigma_F$, 155 refined parameters; GOOF = 0.937, R_1 = 0.0469, wR_2 = 0.1317 ($I > 2\sigma_I$); for compound **3**: $C_{11}H_{22}N_3O_3$, FW = 244.32, orthorhombic crystals, space groups $Pna2_1$, a = 11.9609(9) Å, b = 9.4098(7) Å, c = 11.9529(8) Å, V = 1345.30(17) Å^3, Z = 4, D_{calc} = 1.206 g cm^{-3}, μ = 0.088 mm^{-1}, 18180 measured reflections (θ_{max} = 28.31°), 1749 independent reflections (R_{int} = 0.1261), 784 reflections with $F > 4\sigma_F$, 155 refined parameters; GOOF = 0.870, R_1 = 0.0465, wR_2 = 0.0904 ($I > 2\sigma_I$).

The magnetochemical measurements were performed on a MPMS*XL* (Quantum Design) magnetometer in the 2—300 K temperature range. The effective magnetic moment was calculated by the equation $\mu_{eff}(T) = 2.84(\chi'_M T)^{1/2}$, where χ'_M is the molar paramagnetic component of the magnetic susceptibility calculated with the use of Pascal constants.[22]

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