Crystal and Molecular Structure of 3-(*N*-Methoxy-*N*-methylcarbamoyl)-2,2,5,5-tetramethyl-1-oxy-pyrroline

Guido D. Frey and Eberhardt Herdtweck

Department für Chemie, Lehrstuhl für Anorganische Chemie, Technische Universität München,
Lichtenbergstraße 4, 85747 Garching, Germany

Reprint requests to Dr. Guido D. Frey. Fax: +49(0)89 289 13473. E-mail: guido.frey@ch.tum.de or
Dr. Eberhardt Herdtweck. E-mail: eberhardt.herdtweck@ch.tum.de

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The crystal structure of the stable nitroxide radical 3-(*N*-methoxy-*N*-methylcarbamoyl)-2,2,5,5-tetramethyl-1-oxy-pyrroline was determined from single-crystal X-ray data: orthorhombic, space group *Pbca* (no. 61), a = 9.0213(1), b = 12.8625(1), c = 21.2406(2) Å, V = 2464.68(4) Å^3 and Z = 8. The adjacent molecules assemble to a supramolecular layer structure in the solid state, linked by two intermolecular C–H$\cdots$O hydrogen bonds.

Key words: Crystal Structure, Nitroxide, Radical

Introduction

The current interest in free nitroxide radicals stems from their utility in electron spin resonance (EPR) spectroscopy as spin labels in normally diamagnetic spin systems [1 – 9] and ferromagnetic materials [10, 11]. They are used frequently in biochemical, biophysical and medical studies [12 – 14], for example as daunomycin spin-labeled derivatives, and are used as antitumor agents [15, 16]. The fine structure of the ESR spectra provides information about the environment of the radical moiety and allows a description of the dynamic, structural, and redox properties of its surroundings [17 – 21]. The sensitivity of these labels to the local environment of the diamagnetic molecule is related to the geometry of the label itself. The most widely used spin-labels are the stable nitroxide radicals derived either from oxazolidines, 2,2,5,5-tetramethylpyrrolines [22, 23], 2,2,5,5-tetramethylpyrrolidines or 2,2,6,6-tetramethylpiperidines [17, 24, 25]. The two earliest structure reports in the literature for di-*p*-anisyl nitroxide [26] and di-*tert*-butyl nitroxide [27] were consistent with a planar configuration at the nitrogen atom but could not be regarded as completely conclusive with respect to this point. Therefore, a report by Lajzérowicz-Bonneteau that a nonplanar nitroxide configuration exists in 2,2,6,6-tetramethyl-4-piperidinol-1-oxyl arose considerable interest [28]. At the same time, the existence of a planar form of the nitroxide free radical was definitively established by the remeasurement of potassium-2,2,5,5-tetramethyl-3-carboxy-pyrrolin-1-oxyl [29].

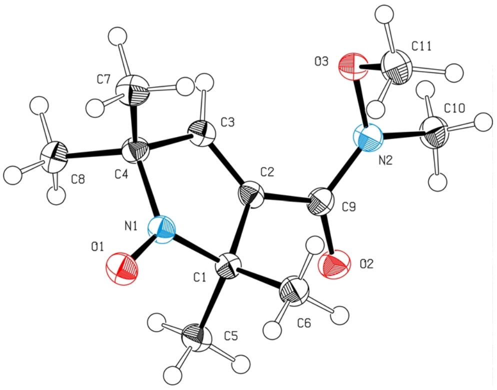

Fig. 1. ORTEP-style [37] plot of compound **1** in the solid state, showing displacement ellipsoids at the 50 % probability level and the crystallographic numbering scheme.

Results and Discussion

We report here the crystal structure of a closely related compound, 3-(*N*-methoxy-*N*-methylcarbamoyl)-2,2,5,5-tetramethyl-1-oxy-pyrroline (**1**). A view of the molecular structure of compound **1** is given in Fig. 1. Selected structural parameters are listed in Tables 1 and 2.

The configuration at the nitrogen atom is again found to be almost planar [mean deviation from the best plane = 0.04(1) Å]. The O1 atom is found in

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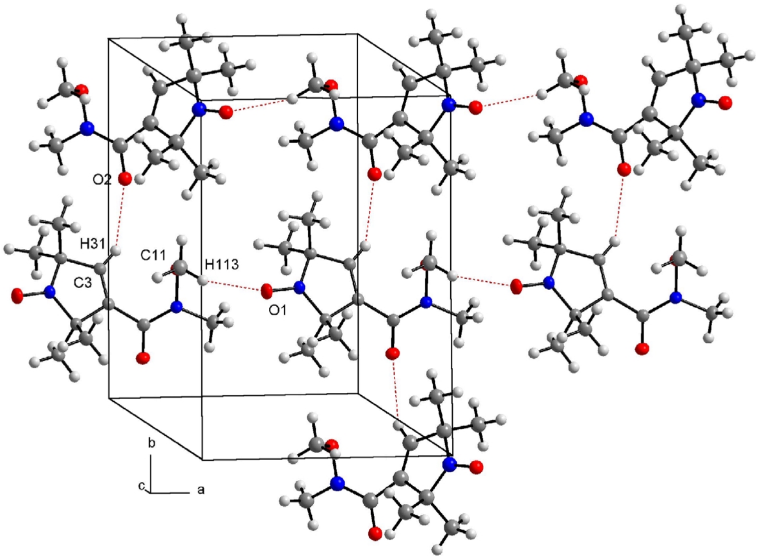


Fig. 2. DIAMOND [38] plot of the molecular packing of compound **1**, as viewed perpendicular to the crystallographic *c* axis. C–H···O interactions are shown as dashed lines.

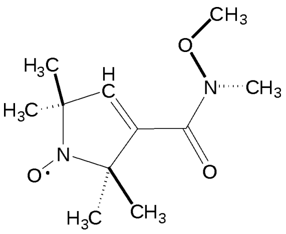
Table 1. Selected bond lengths (Å) and bond angles (deg) for **1**.

O1–N1	1.272(1)	N2–O3–C11	109.85(9)
O2–C9	1.228(1)	O1–N1–C1	122.0(1)
O3–N2	1.396(1)	O1–N1–C4	122.3(1)
O3–C11	1.434(2)	C1–N1–C4	114.70(9)
N1–C1	1.480(2)	O3–N2–C9	120.55(9)
N1–C4	1.477(2)	O3–N2–C10	114.20(9)
N2–C9	1.346(2)	C9–N2–C10	125.1(1)
N2–C10	1.444(2)	N1–C1–C2	99.23(9)
C1–C2	1.514(2)	C1–C2–C3	112.3(1)
C2–C3	1.326(2)	C2–C3–C4	113.2(1)
C3–C4	1.496(2)	N1–C4–C3	99.56(9)
		C5–C1–C6	110.9(1)
		C7–C4–C8	111.0(1)

Table 2. Hydrogen bond geometry (Å, deg) for **1**^{a}.

D–H···*A*	*D*–H	H···*A*	*D*···*A*	*D*–H···*A*
C11–H113...O1^{i}	0.98(2)	2.41(2)	3.355(2)	160.7(14)
C3–H31...O2^{ii}	0.94(1)	2.67(1)	3.494(1)	146.8(10)

^{a} Symmetry code: (i) $1+x, y, z$; (ii) $1.5-x, 0.5+y, z$.



1

the plane of the five-membered ring with a deviation of 0.04(2) Å. All bond lengths and bond angles are in excellent agreement with the values found by Turley and Boer [30].

With respect to the radical group, the N1–O1 distance of 1.272(1) Å is intermediate between a normal O–N single bond and a O=N double bond [31]. It agrees well with N–O radical bonds in comparable molecules measuring 1.267(3) Å [11], 1.277(8) Å [29], 1.267(5) Å [30], 1.269(4) Å [32], 1.270(2) Å [33], and 1.2752(14) Å [34], and is consistent with an electronic structure in which the bonding σ and π orbitals are filled by electron pairs, and the antibonding π^* orbital contains the lone electron. Therefore the N–O bond in nitroxides has been described as a three-electron bond [35]. The C1/4–N1 distances of 1.477(2) and 1.480(2) Å, and the C2=C3 distance of 1.326(2) Å of the heterocycle are in the normal range and indicate the absence of electron delocalization in the double bond [36].

The crystal packing is dominated by two weak intermolecular C–H···O hydrogen bond interactions (Table 2). As expected, the partly negatively charged nitroxide group is involved in a hydrogen bond to a methyl group of an adjacent molecule [H113...O1] with 2.41(2) Å. The acidic hydrogen atom H31 from the five-membered ring is involved in a hydrogen bond to the oxygen O2 from the carbonyl functionality of a second adjacent molecule [H31...O2] with 2.67(1) Å. As shown in Fig. 2, these hydrogen bonds give a two-dimensional infinite network perpendicular to the crystallographic *c* axis. In addition very weak C–H...O interactions H...O with > 2.7 Å connect the layers to build up the three-dimensional overall structure.

Experimental Section

Compound **1** was prepared analogously to the procedure reported by Stork and Makinen [39].

*Single-crystal X-ray structure determination of compound **1***

Crystal data and details of the structure determination are presented in Table 3. Suitable single crystals for the X-ray diffraction study were grown from a mixture of diethyl ether/ethyl acetate and transferred into a Lindemann capillary, fixed and sealed. Preliminary examination and data collection were carried out on an area detector system (Nonius, Mach3, κ-CCD) equipped with a rotating anode (Nonius; FR591) with graphite-monochromatized MoK_α radiation (λ = 0.71073 Å). The unit cell parameters were obtained from the refinement on 2594 reflections. Data collection [40] was performed at 123 K. Eight data sets were measured in rotation scan modus with $\Delta\varphi/\Delta\Omega$ = 1.0°. The raw data were corrected for Lorentz, polarization, decay, and absorption effects [41]. The structure was solved by Direct Methods using SIR92 [42]. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were found in the final difference Fourier maps and allowed to refine freely with isotropic displacement parameters. Full-matrix least-squares refinement was carried out with SHELXL-97 [43]. Small extinction effects were corrected for with the procedure implemented in the program. Neutral atom scattering factors for all atoms and anomalous dispersion corrections for the non-hydrogen atoms were taken from International Tables for Crystallography [44].

CCDC 767908 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

Table 3. Summary of the crystallographic data of **1**.

Chemical formula	$C_{11}H_{19}N_2O_3$
Molecular weight	227.28
Crystal color / shape	yellow / prism
Crystal size, mm^3	$0.25 \times 0.38 \times 0.38$
Crystal system	orthorhombic
Space group	*Pbca* (no. 61)
a, Å	9.0213(1)
b, Å	12.8625(1)
c, Å	21.2406(2)
V, Å^3	2464.68(4)
Z	8
$\rho_{\text{calcd.}}$, g cm^{-3}	1.23
μ, mm^{-1}	0.1
Wave length; λ, Å	MoK_α; 0.71073
T, K	123
θ range, deg	1.92 – 25.36
Reflections integrated	54381
Independent reflections (all data) / R_{int}	2254 / 0.043
Observed reflections [$I \geq 2\sigma(I)$]	1943
Parameters refined	222
$R1$ (observed / all data)[a]	0.0317 / 0.0386
$wR2$ (observed / all data)[b]	0.0792 / 0.0831
Weighting scheme: A / B[b]	0.0422/0.7754
GOF[c]	1.050
Final shift/error	< 0.001
Extinction coefficient ε	0.0026(7)
Largest diff. peak / hole, e Å^{-3}	0.24 / −0.18

[a] $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$; [b] $wR2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$, $w = [\sigma^2(F_o^2) + (AP)^2 + BP]^{-1}$, where $P = (\text{Max}(F_o^2, 0) + 2F_c^2)/3$ and A and B are constants adjusted by the program; [c] $\text{GoF} = S = [\Sigma w(F_o^2 - F_c^2)^2/(n_{\text{obs}} - n_{\text{param}})]^{1/2}$, where n_{obs} is the number of data and n_{param} the number of refined parameters.

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