Synthesis and study of organic nitrates of the heterofunctional series
3.* Synthesis and structure of tris(hydroxymethyl)aminomethane dinitrate benzoate hydronitrate

A. M. Korolev,[a] L. T. Eremenko,[a] L. V. Meshikhina,[a] S. E. Nefedov,[b] and I. L. Eremenko[b]*

[a] *Institute of Problems of Chemical Physics, Russian Academy of Sciences, 142432 Chernogolovka, Moscow Region, Russian Federation. Fax: +7 (096) 515 3588. E-mail: elt@icp.ac.ru*

[b] *N. S. Kurnakov Institute of General and Inorganic Chemistry, Russian Academy of Sciences, 31 Leninsky prosp., 117907 Moscow, Russian Federation. Fax: +7 (095) 952 1279. E-mail: ilerem@ionchran.msk.ru*

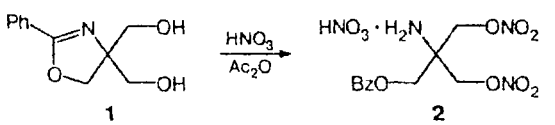
Tris(hydroxymethyl)aminomethane dinitrate benzoate hydronitrate, the first representative of mixed nitric and carboxylic esters of aminopolyatomic alcohols, was obtained by the reaction of a mixture of concentrated HNO_3 and Ac_2O with 4,4-bis(hydroxymethyl)-2-phenyl-2-oxazoline. X-ray structural analysis demonstrated that the title compound exists in the crystal as two independent molecules.

Key words: 4,4-bis(hydroxymethyl)-2-phenyl-2-oxazoline, *O*-nitration, opening of the 2-oxazoline ring, tris(hydroxymethyl)aminomethane dinitrate benzoate hydronitrate, X-ray analysis, independent molecules.

Previously,[1] we have synthesized 4,4-bis(hydroxymethyl)-2-(3-pyridyl)-2-oxazoline, the first representative of organic nitrates of the oxazoline series, under the action of an alcoholic solution of alkali on tris(hydroxymethyl)aminomethane trinitrate hydronitrate. The common procedure for the preparation of organic nitrates involves direct esterification of the corresponding alcohols.[2] In the case of *O*-nitration of alcohols of the heterofunctional series, the principal challenge is to retain other functional groups of a substrate in the final molecule.

Results and Discussion

As part of continuing studies of the possibility of the synthesis of organic nitrates of the oxazoline series by direct *O*-nitration of the corresponding alcohols, we investigated the reaction of the known 4,4-bis(hydroxymethyl)-2-phenyl-2-oxazoline (**1**)[3] with an equimolar mixture of concentrated HNO_3 and Ac_2O. It appeared that the reaction afforded tris(hydroxymethyl)aminomethane dinitrate benzoate hydronitrate (**2**) as the major product. The resulting compound is the previously unknown first member of the series of mixed nitric and carboxylic esters of aminopolyatomic alcohols.



1 **2**

The formation of compound **2** can be represented as a result of opening of the oxazoline ring at the azomethine bond in the product of *O*-nitration of glycol **1**. The composition and structure of mixed ester **2** was established by elemental analysis, spectral methods (IR and ^1H NMR), and X-ray diffraction analysis (Fig. 1, Table 1).

There are two independent organic cations and two NO_3 anions per asymmetric unit of **2**, the anions being arranged so that they are bonded to the NH_3^+ groups of both cations (N—H, 0.840(19) Å, 1.001(17) Å, and 1.019(21) Å (**A**) and 0.675(19) Å, 1.021(16) Å, and 1.032(17) Å (**B**)) through hydrogen bonds (Fig. 2) (N—H(**B**)...ONO_2(**B**), 1.810(21) Å and 1.992(19) Å; N—H(**A**)...ONO_2(**B**), 2.309(23) Å).

The C—NH_3^+ bond is substantially elongated (1.514(8) and 1.497(8) Å in cations **A** and **B**, respectively) compared to the standard bond between the carbon and nitrogen atoms (C—NH_3^+, 1.488 Å) with the sp^3 configuration.[4] This bond elongation can also be caused by considerable steric hindrances due to the presence of the bulky substituents at the central C(2) atom. In two of these substituents, namely, in the CH_2ONO_2 groups, the C—C and C—O bonds have close values (C—C, 1.519(9) and 1.506(9) Å (**A**) and 1.546(9) and 1.536(9) Å (**B**); C—O, 1.440(7), 1.450(8) Å (**A**) and 1.436(7) and 1.470(9) Å (**B**)), and the third group, CH_2OOCPh (O(11)—C(5), 1.342(7) (**A**) and

* For Part 2, see Ref. 1.

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 3, pp. 505—509, March, 1999.

1066-5285/99/4803-0501 $22.00

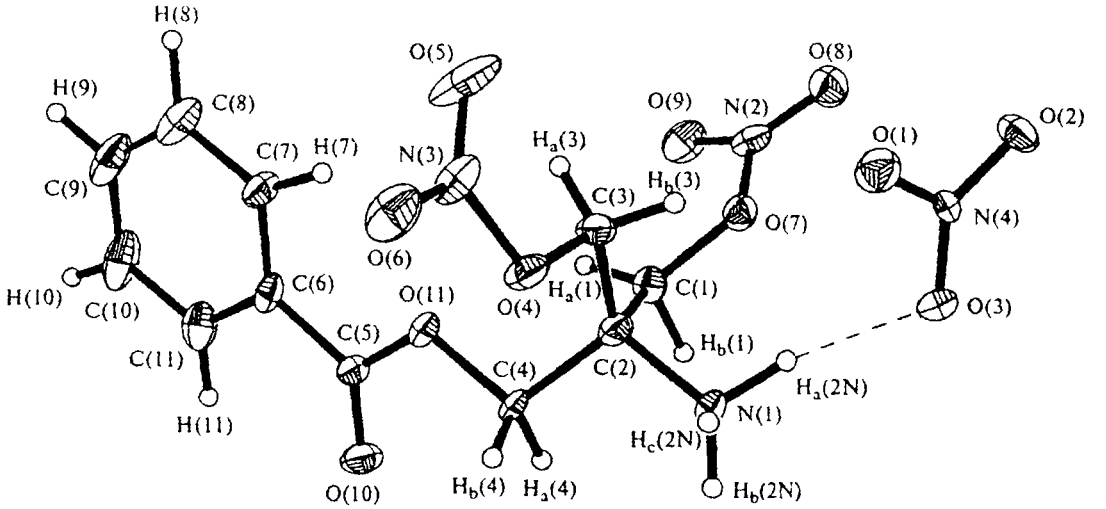


Fig. 1. Structure of the organic cation in molecule **2** (one of the two independent cations is shown).

Table 1. Principal geometric parameters of compound **2**

Bond	*d*/Å		Bond	*d*/Å		Bond	*d*/Å	
	Molecule **A**	Molecule **B**		Molecule **A**	Molecule **B**		Molecule **A**	Molecule **B**
O(1)—N(4)	1.236(8)	1.240(7)	O(8)—N(2)	1.168(7)	1.189(8)	C(2)—C(4)	1.525(8)	1.514(7)
O(2)—N(4)	1.268(6)	1.225(8)	O(9)—N(2)	1.230(8)	1.181(7)	C(5)—C(6)	1.477(9)	1.509(10)
O(3)—N(4)	1.242(6)	1.236(7)	O(10)—C(5)	1.207(7)	1.178(7)	C(6)—C(7)	1.399(9)	1.384(9)
O(4)—N(3)	1.398(7)	1.391(8)	O(11)—C(4)	1.465(7)	1.429(8)	C(6)—C(11)	1.369(9)	1.391(10)
O(4)—C(3)	1.450(8)	1.470(9)	O(11)—C(5)	1.342(7)	1.361(7)	C(7)—C(8)	1.404(12)	1.364(11)
O(5)—N(3)	1.187(9)	1.195(8)	N(1)—C(2)	1.514(8)	1.497(8)	C(8)—C(9)	1.376(11)	1.366(11)
O(6)—N(3)	1.184(8)	1.176(8)	C(1)—C(2)	1.519(9)	1.546(9)	C(9)—C(10)	1.394(11)	1.354(11)
O(7)—N(2)	1.401(7)	1.426(7)	C(2)—C(3)	1.506(9)	1.536(9)	C(10)—C(11)	1.400(12)	1.376(12)
O(7)—C(1)	1.440(7)	1.436(7)						

Angle	ω/deg		Angle	ω/deg		Angle	ω/deg	
	Molecule **A**	Molecule **B**		Molecule **A**	Molecule **B**		Molecule **A**	Molecule **B**
N(3)—O(4)—C(3)	113.2(5)	113.4(5)	O(2)—N(4)—O(3)	120.9(5)	121.5(5)	O(10)—C(5)—C(6)	123.4(6)	126.4(6)
N(2)—O(7)—C(1)	114.9(5)	114.7(5)	O(7)—C(1)—C(2)	107.2(5)	107.8(5)	O(11)—C(5)—C(6)	113.3(5)	110.8(5)
C(4)—O(11)—C(5)	116.9(4)	116.9(5)	N(1)—C(2)—C(1)	107.9(5)	110.5(5)	C(5)—C(6)—C(7)	120.8(6)	122.6(6)
O(7)—N(2)—O(8)	113.4(6)	116.0(5)	N(1)—C(2)—C(3)	110.9(5)	110.6(5)	C(5)—C(6)—C(11)	117.2(6)	117.5(6)
O(7)—N(2)—O(9)	117.0(5)	113.1(5)	C(1)—C(2)—C(3)	109.7(5)	106.1(5)	C(7)—C(6)—C(11)	122.0(7)	119.9(7)
O(8)—N(2)—O(9)	129.6(6)	130.8(6)	N(1)—C(2)—C(4)	104.8(4)	108.2(4)	C(6)—C(7)—C(8)	118.9(6)	119.4(7)
O(4)—N(3)—O(5)	117.3(6)	113.6(5)	C(1)—C(2)—C(4)	108.7(5)	108.3(5)	C(7)—C(8)—C(9)	119.5(7)	120.7(7)
O(4)—N(3)—O(6)	114.2(5)	116.3(6)	C(3)—C(2)—C(4)	114.7(5)	113.1(5)	C(8)—C(9)—C(10)	120.7(8)	120.5(8)
O(5)—N(3)—O(6)	128.5(7)	130.0(7)	O(4)—C(3)—C(2)	107.3(4)	105.6(5)	C(9)—C(10)—C(11)	120.3(7)	120.4(7)
O(1)—N(4)—O(2)	116.9(5)	122.6(5)	O(11)—C(4)—C(2)	105.1(4)	107.6(4)	C(6)—C(11)—C(10)	118.6(6)	119.1(7)
O(1)—N(4)—O(3)	122.2(5)	115.9(5)	O(10)—C(5)—O(11)	123.3(6)	122.8(6)			

1.361(7) Å (**B**); C(5)=O(10), 1.207(7) (**A**) and 1.178(7) Å (**B**); and OC(5)—C(Ph), 1.477(9) (**A**) and 1.509(10) Å (**B**)) is bonded to the central C(2) atom *via* a single C(2)—C(4) bond (1.525(8) and 1.514(7) Å in **A** and **B**, respectively). The Ph—C(O)O dihedral angles in cations **A** and **B** are 1.2 and 2.8°, respectively. In both molecules, the O=C groups lie in the planes of the rings.

The central fragment of compound **2** is formally analogous to the corresponding fragment of *N*-nicotinoyltris(hydroxymethyl)aminomethane trinitrate (**3**), which we have studied previously.[5] In the latter compound, the bonds with the participation of the central carbon atom (C—C, 1.521(11)—1.522(12) Å; and C—N, 1.486(9) Å) are virtually equivalent and their values are close to the corresponding bond lengths in ester **2**.

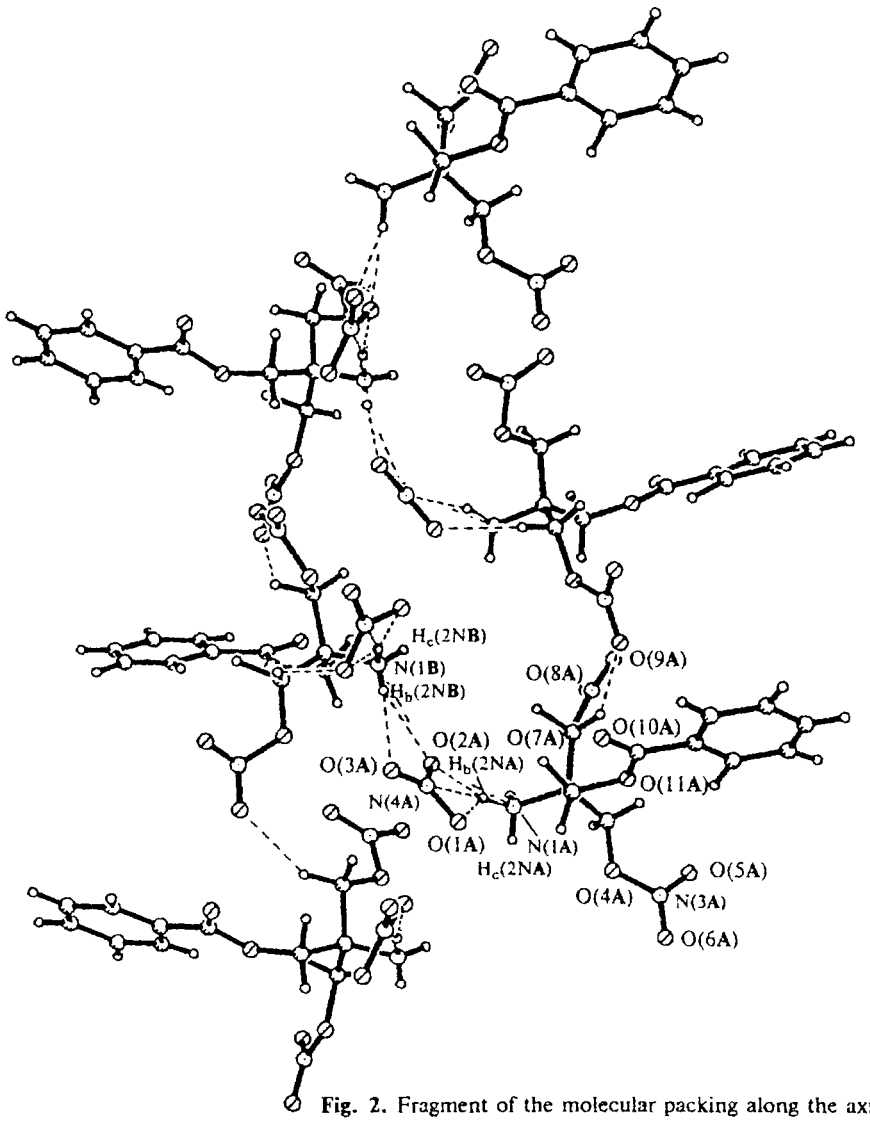
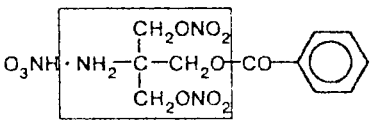
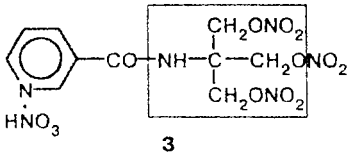


Fig. 2. Fragment of the molecular packing along the axis *y*.



2



3

Experimental

The IR spectrum was recorded on a Specord M 82 spectrometer. The ^{1}H NMR spectrum was obtained on a cryogenic NMR spectrometer operating at 294 MHz for protons (the instrument was designed and built at the Institute of Problems of Chemical Physics of the Russian Academy of Sciences). The melting temperature was determined on a Boetius RNMK-05 instrument.

Tris(hydroxymethyl)aminomethane dinitrate benzoate hydronitrate (2). Concentrated HNO_3 (d_4^{20} 1.51) (1.0 mL, 24 mmol) was added with stirring and cooling to a solution of Ac_2O (2.3 mL, 24 mmol) in CH_2Cl_2 (4 mL). Then compound **1** (0.83 g, 4 mmol) was added at approximately −10 °C. After 1 h, a crystalline product that precipitated was filtered off and washed with CH_2Cl_2. Compound **2** was obtained in a yield of 1.12 g (74%), m.p. 141—142 °C (from PrⁱOH). Found (%): C, 34.80; H, 3.63; N, 14.95. $C_{11}H_{13}N_3O_8 \cdot HNO_3$. Calculated (%): C, 34.93; H, 3.73; N, 14.81. IR (KBr), ν/cm^{-1}: 1646, 1289, 848 (ONO_2); 2914, 2600, 1658 (NH_3^+); 1730, 1265, 1113 (COO); 1385 (NO_3^-); 1601, 1568, 704 (Ph). ^{1}H NMR (DMSO-d_6), δ: 4.55 (s, 2 H, OCH_2); 4.95 (s, 4 H, 2 CH_2ONO_2); 7.55 (2 H, C(3)H, C(5)H, $^3J_{CH-CH}$ = 7.5 Hz); 7.69 (t, 1 H, C(4)H,

Table 2. Crystallographic parameters in compound **2**

Parameter	Value	Parameter	Value
Formula	$C_{11}H_{14}N_4O_{11}$	θ-2θ scanning range/deg	3—56
Space group	$Pca2_1$	Number of measured reflections	4002
a/Å	14.768(5)	Number of reflections with $I > 4\sigma$	1738
b/Å	6.639(2)	Weighting scheme	$w^{-1} = \sigma^2(F) + 0.0023F^2$
c/Å	33.050(12)	R	0.059
V/Å^3	3240(2)	R_w	0.070
Z	8*		
ρ_{calc}/g cm^{-3}	1.551		

* There are two independent molecules per asymmetric unit.

Table 3. Atomic coordinates (×10^4) and equivalent isotropic temperature factors ($B_{eq} \cdot 10^2$/Å^2) in compound **2**

Atom	Molecule A				Molecule B			
	x	y	z	B_{eq}	x	y	z	B_{eq}
O(1)	1403(4)	10348(7)	4363(2)	65(1)	4999(4)	−3348(7)	−452	59(1)
O(2)	2495(3)	11794(6)	4670(2)	56(1)	6154(3)	−5003(7)	−227(2)	55(1)
O(3)	2296(4)	8553(6)	4740(2)	59(1)	5124(3)	−6424(6)	−586(2)	54(1)
O(4)	546(3)	6180(6)	3552(1)	53(1)	6913(3)	1159(6)	633(2)	51(1)
O(5)	471(4)	8452(9)	3065(2)	118(1)	8130(3)	1630(8)	987(2)	77(1)
O(6)	−660(4)	6537(8)	3184(2)	79(1)	7016(4)	3682(8)	1055(2)	108(1)
O(7)	3118(3)	7865(6)	3937(2)	48(1)	4340(3)	2677(6)	219(1)	48(1)
O(8)	3993(4)	10455(7)	3944(2)	73(1)	3124(4)	2768(7)	614(2)	76(1)
O(9)	4348(4)	8006(8)	3539(2)	75(1)	3452(4)	5298(7)	233(2)	68(1)
O(10)	2572(4)	343(6)	3176(2)	65(1)	4897(4)	−4758(7)	974(2)	57(1)
O(11)	1998(3)	3471(6)	3203(1)	49(1)	5509(3)	−1685(6)	956(1)	49(1)
N(1)	1774(3)	5144(7)	4259(2)	36(1)	5791(4)	102(7)	−90(2)	46(1)
N(2)	3889(4)	8874(8)	3796(2)	53(1)	3558(4)	3679(7)	373(2)	50(1)
N(3)	83(4)	7146(9)	3238(2)	60(1)	7386(5)	2259(8)	923(2)	60(1)
N(4)	2058(4)	10195(6)	4594(2)	35(1)	5440(4)	−4925(8)	−415(2)	49(1)
C(1)	3001(4)	5856(8)	3780(2)	47(1)	4473(5)	671(8)	371(2)	48(1)
C(2)	2001(5)	5347(8)	3814(2)	47(1)	5494(4)	184(7)	343(2)	32(1)
C(3)	1446(4)	6988(8)	3620(2)	44(1)	5985(5)	1887(8)	568(2)	57(1)
C(4)	1847(5)	3250(8)	3638(2)	49(1)	5652(5)	−1868(8)	529(2)	47(1)
C(5)	2352(4)	1882(8)	3008(2)	41(1)	5123(4)	−3287(8)	1146(2)	42(1)
C(6)	2438(4)	2197(8)	2567(2)	47(1)	5033(4)	−2890(8)	1594(2)	50(1)
C(7)	2167(5)	4013(9)	2389(2)	61(1)	5284(5)	−1082(9)	1770(2)	65(1)
C(8)	2260(6)	4248(10)	1969(3)	85(1)	5192(6)	−840(10)	2177(3)	88(1)
C(9)	2595(6)	2682(11)	1741(3)	103(1)	4842(6)	−2347(11)	2411(3)	121(1)
C(10)	2862(5)	885(10)	1924(3)	85(1)	4601(6)	−4130(10)	2244(3)	92(1)
C(11)	2783(5)	641(10)	2343(3)	66(1)	4691(6)	−4437(10)	1834(3)	76(1)
H_a(2N)	2011(12)	6428(12)	4377(11)	51(1)	6242(12)	−29(12)	−110(11)	50(1)
H_b(2N)	1917(12)	3882(12)	4422(11)	50(1)	5505(12)	−1211(12)	−188(11)	51(1)
H_c(2N)	1212(12)	5244(12)	4293(11)	51(1)	5625(12)	1492(12)	−209(11)	50(1)

$^3J_{CH-CH}$ = 7.5 Hz); 8.10 (d, 2 H, C(2)H, C(6)H, $^3J_{CH-CH}$ = 7.5 Hz); 9.00 (br.s, 3 H, NH_3^+).

X-ray diffraction study. Crystals of **2** suitable for X-ray diffraction study were prepared by keeping a solution of this compound in a THF—CH_2Cl_2 mixture at 5 °C for 7 days. The X-ray intensity data were collected on an automated Siemens R3/PC diffractometer at ~20 °C (λMo Kα radiation, λ = 0.71073 Å, T = 22 °C). The unit cell parameters were determined and refined using 24 equivalent reflections with 2θ < 24—26°. Three strong reflections with χ 1—65° were used as the standards for monitoring possible movements of the crystal and decomposition of the sample. The standard reflections revealed no significant intensity variation in the course of data collection, and therefore, no correction was applied. The structure of **2** was solved by direct methods and refined by the full-matrix least-squares method with anisotropic thermal parameters for all non-hydrogen atoms. The positions of the hydrogen atoms were located from the difference Fourier synthesis and refined using the riding model. The protons of the NH_3^+ groups were refined isotropically. No absorption correction was applied because of the low value of the coefficient. All calculations were carried out with the use of the SHELXTL PLUS program package (PC version).[6] The crystallographic parameters and details of the structure refinement are given in Table 2. The principal geometric parameters of the molecule are listed in Table 1. The atomic coordinates are given in Table 3.

This work was financially supported by the International Science and Technology Center (Project No. 123-94).

References

1. A. M. Korolev, L. T. Eremenko, L. V. Meshikhina, I. L. Eremenko, and S. E. Nefedov, *Izv. Akad. Nauk, Ser. Khim.*, 1998, 478 [*Russ. Chem. Bull.*, 1998, **47**, 462 (Engl. Transl.)].
2. R. Boschan, R. T. Merrow, and R. W. van Dolah, *Chem. Revs*, 1955, **55**, 485.
3. J. H. Bilman and E. E. Parker, *J. Am. Chem. Soc.*, 1945, **67**, 1069; US Pat. 2556791 (1951), *Chem. Abstrs.*, 1952, **46**, 525.
4. F. H. Allen, O. Kennard, D. G. Watson, L. Brammer, A. G. Orpen, and R. Taylor, *J. Chem. Soc., Perkin Trans. 2*, 1987, S1.
5. A. M. Korolev, L. T. Eremenko, L. V. Meshikhina, I. L. Eremenko, and S. E. Nefedov, *Izv. Akad. Nauk, Ser. Khim.*, 1997, 2224 [*Russ. Chem. Bull.*, 1997, **46**, 2110 (Engl. Transl.)].
6. G. M. Sheldrick, *Crystallographic Computing 3: Data Collection, Structure Determination, Proteins, and Databases*, Calderon, New York, 1985, 175.

Received June 18, 1998;
in revised form September 8, 1998