Study of alkaloids of Siberian and Altai flora

8.* Crystal and molecular structure of elatidal methylimine hydrate

N. V. Anferova,[a] *I. Yu. Bagryanskaya,*[a] *Yu. V. Gatilov,*[a] *J. Ganbaatar,*[b]
S. A. Osadchii,[a★] *E. E. Shults,*[a] *and G. A. Tolstikov*[a]

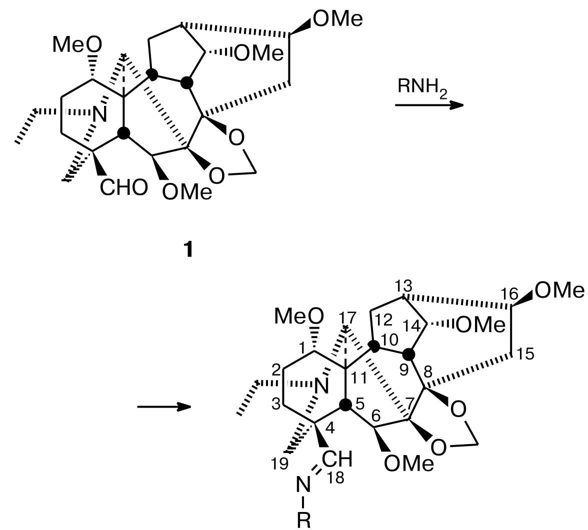
[a]*N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences,*
9 prosp. Akad. Lavrent´eva, 630090 Novosibirsk, Russian Federation.
Fax: +7 (383 2) 34 4752. E-mail: schultz@nioch.nsc.ru
[b]*Institute of Chemistry and Chemical Technology of the Mongolian Academy of Sciences,*
54-56 ul. Zhukova, 211051 Ulan-Bator, Mongolia.
Fax: (1097611) 32 1993. E-mail: inst_chemistry@arvis.ac.mn

The crystal and molecular structure of elatidal methylimine hydrate was established by X-ray diffraction analysis and a previous assumption of the *E* configuration of the methylimino group was confirmed.

Key words: diterpene alkaloids, methylimine, elatidal, X-ray diffraction analysis.

As part of our continuing studies on the synthesis of derivatives of diterpene alkaloids, which are promising as neurotropic and cardioactive agents, we synthesized 18-imino derivatives of elatidal (**1**), in particular, imines **2a**—**g** (Scheme 1).[1,2] According to the ^{1}H NMR spectroscopic data, the complete conversion of the starting elatidal (**1**) gave each of imines **2a**—**g** as the only geometric isomer with, presumably, the *E* configuration of the alkylimino group due to lower steric hindrances upon the formation of the imine bond. The present study was aimed at establishing the configuration of the methylimino group of elatidal methylimine (20-ethyl-1α,6β,14α,16β-tetramethoxy-7,8-methylenedioxy-18-methyliminoaconitane) (**2a**) based on the data on the molecular structure of hydrate of this compound. Attempts to grow single crystals of imine **2a** suitable for X-ray diffraction study failed. Unforced evaporation of the solvent from a saturated solution of this compound in 90% methanol afforded crystals of imine hydrate **2a** with m.p. 140—142 °C (with decomp.) with composition $C_{27}H_{42}N_2O_6 \cdot 0.5H_2O$, which was established by X-ray diffraction analysis. The imine hydrate lost water upon azeotropic distillation with chloroform followed by drying at 50 °C (3 Torr) to give anhydrous imine **2a** with m.p. 143—144 °C.

Scheme 1



R = Me (**a**), CH_2=CH—CH_2 (**b**), Ph (**c**), $(CH_2)_2C_6H_4OH$-*p* (**d**), CH_2CH_2OH (**e**), $CH(CH_3)CH_2OH$ (**f**), CH_2CO_2Me (**g**)

Experimental

The X-ray diffraction data were collected on a Bruker P4 diffractometer (Mo-Kα radiation, graphite monochromator, 2θ/θ scan technique in the region 2θ < 50°) from a crystal of imine hydrate **2a** of dimensions 0.70×0.38×0.26 mm. The intensities of 4691 independent reflections were measured. Absorption was ignored. The structure was solved by direct methods using the SHELXS-97 program package. The positions of the H atoms of the water molecule were not located. The structure was refined anisotropically by the full-matrix least-squares method with the use of the SHELXL-97 program package. The hydrogen atoms were not icluded in the refinement, and the parameters of the H atoms were calculated in each cycle of the refinement from the coordinates of the corresponding carbon atoms.

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* For Part 7, see Ref. 1.

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The structure was finally refined based on all F^2 to $wR_2 = 0.1252$, $S = 1.024$, 641 refinable parameters ($R = 0.0448$ for 3907 $F > 4\sigma$). The crystallographic parameters of the imine hydrate are as follows: monoclinic system, $a = 8.6432(7)$, $b = 29.268(2)$, $c = 10.667(1)$ Å, $\beta = 104.690(7)°$, $V = 2610.2(4)$ Å^3, space group $P2_1$, $Z = 4$, $C_{27}H_{42}N_2O_6 \cdot 0.5H_2O$, $d_{calc} = 1.271$ g cm^{-3}, $\mu = 0.090$ mm^{-1}.

Results and Discussion

In the crystal of imine hydrate **2a**, there are two crystallographically independent molecules per asymmetric unit. The three-dimensional structure of one of these molecules is shown in Fig. 1. Selected bond lengths and torsion angles of compound **2a** are given in Table 1. The bond lengths and bond angles in two molecules have standard values[3] (to within 3σ). The exceptions are the bonds with the peripheral atoms, which is attributable to their high thermal motions. The results of our study provide evidence for the aconitane skeleton of the molecule and the *E* configuration of the methylimino groups. Apparently, the imino groups in compounds **2b—g** also have the *E* configuration.

Table 1. Selected bond lengths (*d*) and torsion angles (φ) for two crystallographically independent molecules of imine hydrate **2a**

Parameter	Molecule 1	Molecule 2
Bond	*d*/Å	
C(4)—C(18)	1.503(6)	1.516(7)
C(18)=N(23)	1.231(6)	1.235(7)
C(17)—N(20)	1.460(5)	1.462(5)
C(19)—N(20)	1.468(5)	1.474(5)
C(21)—N(20)	1.458(5)	1.463(6)
C(7)—O(5)	1.433(4)	1.437(5)
O(5)—C(29)	1.421(5)	1.427(5)
C(8)—O(6)	1.453(5)	1.458(5)
O(6)—C(29)	1.398(5)	1.401(5)
C—OMe*	1.427	1.428
O—Me*	1.411	1.399
Torsion angle	φ/deg	
C(4)—C(18)—N(23)—C(24)	177.6(5)	−178.2(5)
C(7)—C(6)—C(5)—C(11)	−13.5(4)	−13.0(4)
C(7)—O(5)—C(29)—O(6)	−5.6(5)	−4.0(5)
C(14)—C(9)—C(8)—C(15)	−30.3(4)	−30.3(5)
C(14)—C(13)—C(16)—C(15)	16.4(5)	22.4(5)
C(17)—C(7)—C(6)—C(5)	−21.7(4)	−22.3(4)
C(9)—C(10)—C(12)—C(13)	12.7(4)	8.7(5)
C(14)—C(9)—C(10)—C(12)	18.8(4)	20.9(4)

* Average bond length.

The six-membered rings *A* and *E* adopt chair conformations. The seven-membered ring *B trans*-fused with the ring *A* also adopts a slightly distorted chair conformation (C(7)—C(6)—C(5)—C(11) torsion angles are −13.5° (4) and −13.0° (4) for two molecules), which is most stable for cycloheptanes. The 1,3-dioxolane ring *cis*-fused with the ring *B* has an envelope conformation with the C(8) atoms deviating from the plane pass-

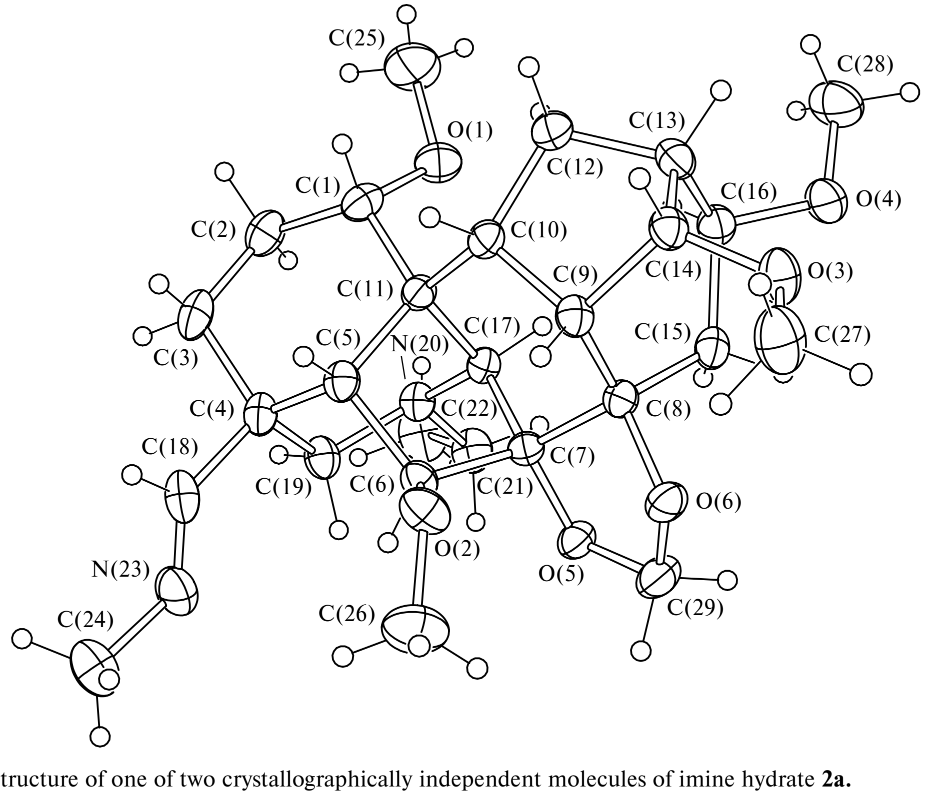

Fig. 1. Molecular structure of one of two crystallographically independent molecules of imine hydrate **2a.**

ing through the remaining four atoms by 0.661(5) and 0.676(6) Å (for two independent molecules). The six-membered ring *D* (C(8), C(9), C(13)—C(16)) adopts a distorted boat conformation with the C(14) and C(15) atoms deviating in the same direction by 0.845(6), 0.324(6) Å and 0.843(6), 0.247(6) Å, respectively, for two molecules. The five-membered rings *C* and *F* are substantially distorted. The bridgehead N(20) atoms are in the vertices of pyramids with the heights of 0.349(4) and 0.366(5) Å. The data on the diterpene alkaloid dictyocarpine (6β-acetoxy-20-ethyl-1α,16β-dimethoxy-4-methyl-7,8-methylenedioxyaconitane-10,14α-diol)[4] are available in the Cambridge Structural Database.[5] This compound is analogous to compound **2a** in the types of fusion and conformations of the corresponding rings. We did not compare the bond lengths in molecules **2a** with those in dictyocarpine because of the low accuracy (high *R* factor) of the determination of the dictyocarpine structure.

To summarize, we established the crystal and molecular structure of elatidal methylimine hydrate as 20-ethyl-1α,6β,14α,16β-tetramethoxy-7,8-methylenedioxy-18(*E*)-methyliminoaconitane and confirmed the previous assumption of the *E* configuration of the methylimino group in this compound. The results of our study provide also indirect evidence in favor of the *E* configuration of the alkylimino groups in compounds **2b—g** taking into account that the steric requirements of the iminoalkyl substituents in these compounds are higher than those of the methyl group in imine **2a**.

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