SYNTHESIS, AND CRYSTAL AND MOLECULAR STRUCTURES OF ANABASINIUM O,O-DIALKYL PHOSPHOROTHIOATES

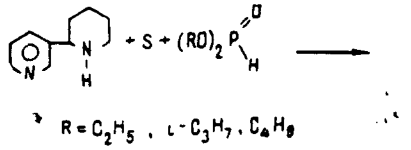
A. M. Gazaliev, M. Zh. Zhurunov, S. A. Dyusambaev,
K. M. Turdybekov, S. V. Lindeman, A. V. Maleev,
and Yu. T. Struchkov

UDC 548.73

The synthesis has been effected of anabasinium O,O-dialkyl phosphorothioates. The crystal and molecular structures of the complex compounds obtained have been determined by the method of x-ray structural analysis. It has been established that the cations and anions of the anabasinium O,O-dialkyl phosphorothioates are combined into cyclic associates each including two anions and two cations with different conformations.

As is known, complex phosphorus-containing salts of amines possess a broad spectrum of biological action, including analgesic [1], antiseptic [2], antiarrhythmic [3], and fungicidal [4] activities.

In order to find biologically active compounds we have performed the synthesis of new phosphorus-containing derivatives of the alkaloid anabasine by the scheme shown below.



It was established that the reaction of anabasine with dialkyl phosphites in the presence of sulfur has a general nature and readily takes place in benzene with gentle heating. The salts obtained consist of colorless acicular crystals readily soluble in water, alcohol, and other solvents. The yields and physicochemical constants of the anabasinium O,O-dialkyl phosphorothioates are given in Table 1.

The structures of the compounds synthesized were also confirmed by their IR spectra – by the presence of absorption bands in the 2400 and 2700 cm^{-1} regions due to the vibration of the N–H bond of the anabasinium cation. Absorption bands were also observed in the regions of 2820-2960 cm^{-1} (CH_{ar}) and 950-1040 cm^{-1} (P–O–C).

To confirm the structures of the complex compounds synthesized, we made an x-ray structural investigation of anabasinium diethyl phosphorothioate $C_{10}H_{15}N_2^+(EtO)_2PO^-$ (I) and of anabasinium diisopropyl phosphorothioate $C_{10}H_{15}N_2^+(iso\text{-}PrO)_2PO^-$ (II).

The structures of the cation and anion in compound (I) are shown in Fig. 1. The piperidinium ring in each of the two symmetrical independent cations (IA and IB) has the chair

TABLE 1. Physicochemical Constants and Elementary Analyses of Anabasinium O,O-Dialkyl Phosphorothioates

R	Empirical formula	Yield, %	mp, °C	Elementary analysis, %	
				N, calc	N, found
C_2H_5	$C_{14}H_{25}N_2PO_3S$	90	143-144	8,10	8,38
i-C_3H_7	$C_{16}H_{29}N_2PO_3S$	95	146–147	7,77	7,59
C_4H_9	$C_{18}H_{33}N_2PO_3S$	85	113–114	7,21	7,21

Institute of Organic Synthesis and Coal Chemistry, Academy of Sciences of the Kazakh SSR. A. N. Nesmayanov Institute of Organometallic Compounds, Academy of Sciences of the USSR, Moscow. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 500-505, July-August, 1990. Original article submitted July 20, 1989.

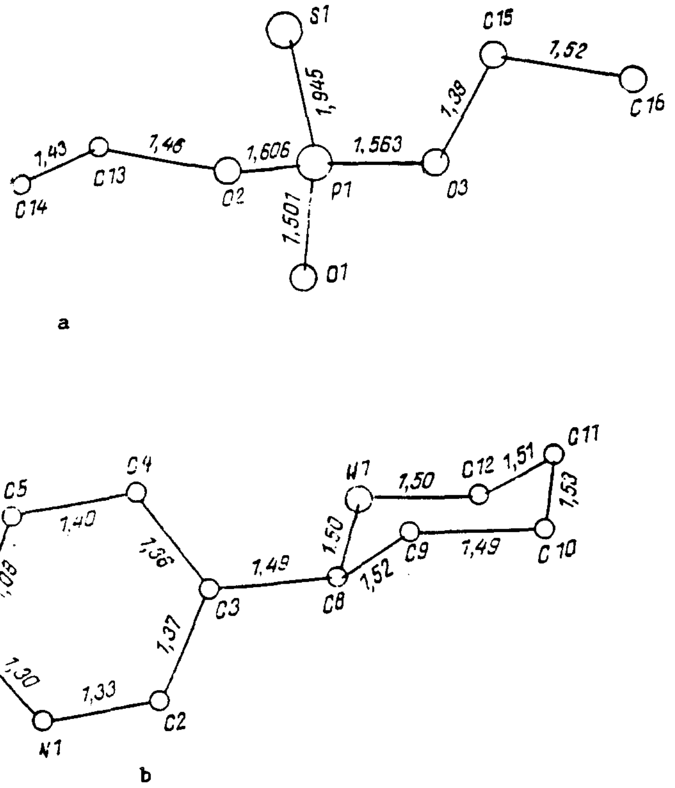


Fig. 1. Structure of anabasinium O,O-Diethyl phosphorothioate (a — anion; b — cation). The averaged bond lengths for the two independent molecules are given (σ not greater than 0.02 Å).

conformation [the maximum values of the asymmetry parameters $\Delta C_2^{9,10} = 5.8°$ in (IA) and 1.8° in (IB)]. The pyridine substituent is present in the equatorial position. The phosphorus atom in each of the symmetrically independent anions has distorted tetrahedral coordination.

The structures of the cation and anion in compound (II) are shown in Fig. 2. The conformation of the piperidinium rings in the four symmetrically independent anabasinium cations (IIA)-(IID) coincide with those found in [5]. The maximum values of the asymmetry parameters of these rings in cations (IIA)-(IID) are: $\Delta C_2^{10,11} = 6.5°$, $\Delta D_2^{8,9} = 10.0°$, $\Delta C_2^{8,4} = 6.1°$, and $\Delta C_2^{9,10} = 3.5°$, respectively. It is interesting to note that the symmetrically independent anabasinium cations in (I) and (II) differ by the rotation of the pyridine ring relative to the piperidinium ring: In the cations (IA), (IIA), and (IIC) the C2C3C8H8 torsion angle is 2.8(7), 29(1), and 31.4(9)° (cisoid arrangement of the C2 and H8 atoms), while in the cations (IB), (IIB), and (IID) this angle amounts to 168(1), −178(1), and −173(1)° (transoid arrangement of the C2 and H8 atoms).

The realization of the two conformers shown of the cations in both crystal structures indicates their approximately equal energetic advantageousness.

The absolute configuration of the anabasinium cation in (I) and (II) could not be determined objectively (from anomalous scattering) because of the inadequate accuracy of the experiment. The bond lengths (see Figs. 1 and 2) and valence angles* in structures (I) and (II) are the usual ones.

In the crystals of (I) and (II) the cations and anions are linked into cyclic associates each including two anions and two cations (with different conformations) through the formation of the H bonds N7—H···O1 [N···O 2.62-2.90 Å in (I) and 2.72-2.96 Å in (II)]. Here the O1 atoms of the anions are the acceptors of the two protons from two different cations

---

*The values of the valence angles can be attained from the authors.

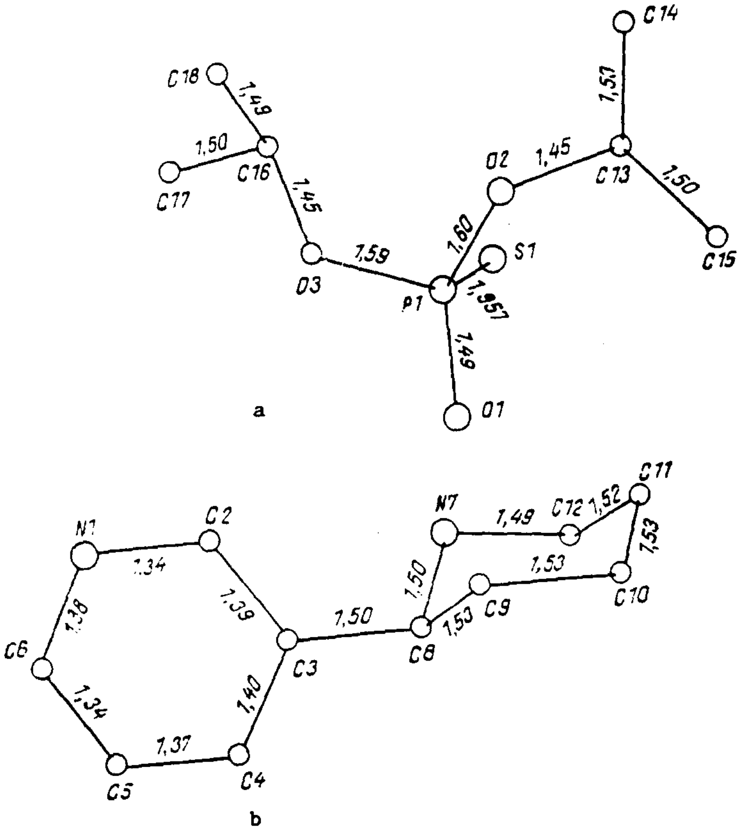


Fig. 2. Structure of anabasinium O,O-diisopropyl phosphorothioate (a – anion; b – cation). The averaged bond lengths for four independent molecules are given (σ not greater than 0.02 Å).

TABLE 2. Coordinates of the Nonhydrogen Atoms in the Structure of (I) ($\times 10^4$)

Atom	IA			IB		
	x	*y*	*z*	*x*	*y*	*z*
S1	3847 (4)	7375	7221 (2)	5724 (3)	10924 (1)	274 (2)
P1	4237 (3)	7754 (1)	5640 (2)	5364 (3)	10447 (1)	−1460 (2)
O1	4304 (6)	7294 (2)	4517 (4)	5482 (8)	10859 (3)	−2652 (5)
O2	5885 (8)	8152 (3)	6047 (6)	3728 (8)	10076 (3)	−1957 (7)
O3	3148 (7)	8301 (3)	4860 (5)	6494 (9)	9869 (3)	−1353 (8)
C13	7299 (16)	7942 (8)	7041 (11)	2231 (14)	10442 (8)	−2044 (11)
C14	8631 (13)	8322 (8)	7076 (15)	1352 (18)	10077 (8)	−1438 (13)
C15	2595 (15)	8801 (5)	5545 (13)	6711 (27)	9421 (8)	−359 (18)
C16	1220 (15)	9122 (6)	4500 (16)	8434 (17)	9276 (10)	498 (16)
N1	9103 (9)	7172 (5)	1713 (10)	905 (8)	973 (5)	3918 (7)
C2	7589 (9)	7290 (5)	1173 (9)	2388 (9)	842 (5)	4186 (7)
C3	6736 (9)	7466 (4)	1990 (7)	3161 (8)	897 (3)	3258 (6)
C4	7440 (9)	7499 (6)	3405 (8)	2312 (11)	1116 (5)	1941 (8)
C5	9047 (11)	7352 (6)	3988 (11)	757 (12)	1249 (7)	1632 (9)
C6	9423 (10)	7199 (5)	3046 (12)	123 (10)	1187 (6)	2637 (10)
N7	4051 (6)	7192 (3)	1753 (5)	5849 (6)	992 (3)	4906 (5)
C8	5065 (8)	7624 (4)	1272 (6)	4805 (9)	691 (3)	3563 (6)
C9	4621 (11)	8319 (4)	1466 (9)	5040 (10)	−24 (4)	3674 (9)
C10	2067 (12)	8465 (4)	639 (9)	6686 (11)	−219 (5)	3947 (10)
C11	1938 (10)	7989 (4)	1060 (9)	7743 (10)	103 (4)	5302 (8)
C12	2378 (8)	7302 (4)	942 (8)	7534 (8)	823 (4)	5217 (8)

TABLE 3. Coordinates of the Nonhydrogen Atoms in the Structure of (II) ($\times 10^4$)

Atom	IIA			IIB		
	x	*y*	*z*	*x*	*y*	*z*
S1	10335 (4)	9554 (3)	10969 (2)	5586 (4)	6055 (3)	6970 (2)
P1	10000	10000	10000	6333 (4)	5422 (3)	7815 (2)
O1	9062 (8)	9004 (6)	9440 (4)	6629 (10)	6127 (7)	8502 (4)
O2	9143 (9)	10886 (7)	9934 (4)	5259 (11)	4062 (8)	7826 (5)
O3	11576 (8)	10756 (6)	9758 (4)	7888 (9)	5245 (7)	7761 (4)
C13	9838 (14)	12042 (10)	10351 (7)	3627 (16)	3561 (13)	7627 (8)
C14	10227 (19)	12935 (11)	9818 (9)	3321 (24)	2229 (15)	7533 (10)
C15	8652 (17)	12135 (12)	10778 (9)	2799 (23)	3877 (21)	8147 (13)
C16	13064 (13)	10741 (11)	10052 (8)	8058 (18)	4636 (15)	7134 (8)
C17	4215 (21)	1678 (21)	9697 (15)	9485 (23)	5482 (20)	6874 (10)
C18	13269 (20)	9716 (20)	9765 (9)	8329 (26)	3582 (16)	7359 (11)
N1	13097 (14)	6707 (14)	10159 (6)	11950 (12)	9177 (11)	7774 (5)
C2	11850 (15)	6659 (14)	10394 (6)	10653 (14)	9287 (12)	7916 (6)
C3	10443 (13)	6482 (11)	9963 (6)	9395 (12)	9218 (9)	7402 (5)
C4	10398 (16)	6419 (18)	9230 (6)	9525 (14)	9039 (11)	6695 (6)
C5	11627 (19)	6391 (23)	8968 (8)	10859 (16)	8944 (12)	6542 (6)
C6	12930 (21)	6499 (24)	9411 (9)	12018 (14)	9009 (13)	7076 (7)
N7	8013 (9)	8006 (7)	9897 (4)	7282 (10)	8533 (8)	8095 (5)
C8	9070 (12)	6318 (9)	10307 (5)	8003 (12)	9392 (9)	7583 (5)
C9	8172 (15)	5011 (10)	10396 (7)	8362 (14)	10532 (9)	7914 (6)
C10	6778 (15)	4844 (12)	10735 (8)	6857 (15)	10755 (11)	8039 (6)
C11	5750 (14)	5369 (12)	10311 (7)	6012 (14)	9790 (14)	8511 (7)
C12	6678 (13)	6672 (10)	10268 (6)	5814 (14)	8629 (13)	8205 (7)
S1	15435 (3)	9990 (3)	16020 (1)	9771 (4)	6917 (3)	12287 (2)
P1	15636 (3)	10586 (3)	15084 (1)	11187 (3)	6238 (3)	12747 (1)
O1	14873 (8)	9678 (6)	14460 (4)	12513 (8)	7042 (6)	13206 (4)
O2	14955 (8)	11558 (6)	14953 ([illegible])	10359 (10)	5125 (7)	13160 (4)
O3	17379 (8)	11299 (6)	15029 (4)	11781 ([illegible])	5701 (7)	12128 (4)
C13	15440 (14)	12512 ([illegible])	15450 (6)	8958 (15)	4166 (10)	12792 (8)
C14	16382 (16)	13663 (11)	15089 (8)	9254 (23)	3076 (13)	13009 (11)
C15	14018 (15)	12706 (11)	15651 (7)	7585 (18)	4284 (15)	13037 (11)
C16	18590 (12)	10883 (11)	15280 (6)	13039 (14)	5346 (10)	12268 (6)
C17	19383 (19)	10776 (16)	14710 ([illegible])	12690 (18)	4232 (11)	11798 (7)
C18	19715 (18)	11736 (16)	15888 (9)	14498 (14)	6326 (11)	12115 (6)
N1	8568 (11)	7082 (10)	4906 (5)	17374 (13)	9665 (10)	12732 (6)
C2	7276 (13)	7009 (11)	5148 (6)	16126 (14)	9851 (11)	12886 (6)
C3	5964 (11)	7021 (9)	4741 (5)	14809 (14)	9693 (9)	12385 (6)
C4	6005 (13)	7188 (12)	4022 (6)	14826 (16)	9331 (10)	11674 (6)
C5	7326 (13)	7299 (13)	3762 (6)	16111 (18)	9162 (12)	11524 (7)
C6	8533 (13)	7226 (12)	4206 (7)	17278 (17)	9283 (12)	12022 (8)
N7	3563 (9)	7388 (7)	4751 (4)	12917 (10)	9435 (7)	13208 (4)
C8	4539 (12)	6773 (10)	5038 (5)	13498 (13)	10005 (9)	12555 (5)
C9	3566 (13)	5459 (10)	3999 (7)	13938 (16)	11321 (10)	12700 (7)
C10	2152 (16)	5182 (12)	5352 (7)	12590 (17)	11627 (11)	12844 (7)
C11	1203 (13)	5904 (11)	5045 (6)	11969 (14)	11024 (11)	13478 (6)
C12	2222 (12)	7212 (10)	5119 (6)	11559 (13)	9692 (11)	13349 (7)

(the two H atoms on each N7 atom of the cations takes part in binding with the O1 atoms of two different anions).

EXPERIMENTAL

Synthesis of Anabasinium O,O-Dialkyl Phosphorothioates. A mixture of anabasine, sulfur, and a dialkyl phosphite in a ratio of 1:1:1 in absolute benzene was heated with stirring until the sulfur had dissolved completely. After the solution had cooled, the crystals that had deposited were filtered off and were crystallized from a mixture of benzene and petroleum ether.

IR spectra were recorded on a Specord IR-71 spectrometer in KBr tablets.

X-Ray Structural Investigation. Compound (I). The cell parameters and the intensities of the reflections were measured on a Hilger—Watts automatic four-circle diffractometer (20°C, λ MoK_α, graphite monochromator, $\theta/2\theta$ scanning, $2\theta \leq 60°$). The crystals were monoclinic, $a = 9.176(1)$, $b = 20.755(2)$, $c = 10.128(1)$ Å, $\beta = 110.214(8)°$, $V = 1811.9(3)$ Å^3, $d_{calc} = 1.22$ g/cm^3, $Z = 4$ [$C_{10}H_{15}N_2$ + $(EtO)_2PO^-$], group $P2_1$, two independent formula units (A and B).

In the calculations we used 2043 reflections with $I \geq 2\sigma$. The structure was interpreted by the direct method and was refined by block-diagonal MLS in the anisotropic approximation for the nonhydrogen atoms. The positions of the H atoms were calculated and not refined (the H atoms of the methyl groups were not taken into account). The final divergence factors were R = 0.056 and R_w = 0.065. The coordinates of the nonhydrogen atoms are given in Table 2.

Compound (II). The cell parameters and the intensities of the reflections were measured at a low temperature on a Syntex $P2_1$ automatic four-circle diffractometer (150 K, λMoK_α, graphite monochromator, $\theta/2\theta$ scanning, $2\theta \leq 50°$). The crystals were triclinic, a = 9.485(5), b = 12.327(4), c = 19.02(1) Å, α = 92.14(4), β = 98.69(4), γ = 111.66(4)°, V = 2033(2) Å^3, d_{calc} = 1.27 g/cm^3, Z = 4 [$C_{10}H_{15}N_2$ + (iso-$P_2O)_2PO^-$], space group P1, four independent formula units (A, B, C, and D).

In the calculation we used 5971 reflections with $I \geq 3\sigma$. The structure was interpreted by the heavy-atom method and was refined by block-diagonal MLS in the anisotropic approximation for the nonhydrogen atoms. The positions of the H atoms were calculated and were not refined (the H atoms of the methyl groups were not taken into account). The final divergence factors were R = 0.063 and R_w = 0.085. The coordinates of the nonhydrogen atoms are given in Table 3.

All the calculations were performed on Eclipse S/200 computer by means of the INEXTL program [5].

LITERATURE CITED

1. D. E. Corbridge, Phosphorus: An Outline of Its Chemistry, Biochemistry, and Technology, Elsevier Scientific Publications, Amsterdam (1978).
2. USSR Inventors' Certificate No. 3,322,833 (1969); Byull. Izobret., No. 6, 15 (1969).
3. D. Purdela and P. Vylchanu, The Chemistry of Organic Phosphorus Compounds [in Russian], Khimiya, Moscow (1972), p. 287.
4. US Patent No. 3,529,041 (1970), Chem. Abstr., 72, 32022 (1970).
5. R. G. Gerr, A. I. Yanovskii, and Yu. T. Struchkov, Kristallografiya, 28, 1029 (1983).

PREPARATION OF DEOXYPEGANINE HYDROCHLORIDE

K. D. Sargazakov, Kh. N. Arupov, L. V. Molchanov,
and V. N. Plugar'

UDC 547.856+661.12

Details are given of the technology of the synthesis and stagewise analysis of the alkaloids deoxyvasicinone and deoxypeganine hydrochlorides.

Deoxypeganine hydrochloride (1,2,3,9-tetrahydropyrrolo[2,1-b]quinazoline hydrochloride) is the hydrochloric acid salt of the alkaloid deoxypeganine, which has been isolated from Peganum harmala [1] and is a highly effective relatively nontoxic anticholinesterase drug which has been introduced into medical practice [2]. The process of its isolation from the plant has serious defects owing to the low yield of product (0.35% on the weight of the raw material), difficulties in the collection and drying of the raw materials, the multistage nature of the process and, as a consequence, its high cost [3].

Investigations of synthetic possibilities of obtaining the alkaloids deoxyvasicinone and deoxypeganine [4, 5] have predetermined the development of a convenient technological scheme for their synthesis which avoids the disadvantages of the technology from the plant raw material.

Institute of Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 506-507, July-August, 1990. Original article submitted November 13, 1989.

0009-3130/90/2604-0427$12.50