Studies of reactions of dimethylphosphoramidic difluoride with *trans*-2-(*N*,*N*-dialkylamino)cycloalkanols in the presence of various sulfur-containing nucleophiles

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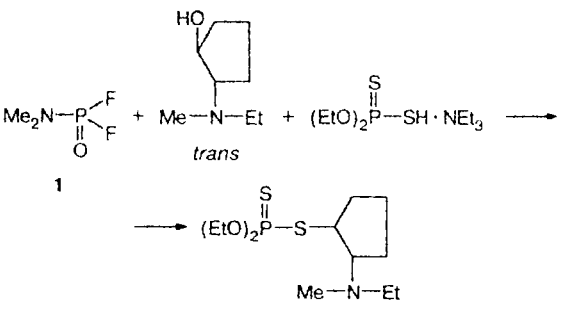
The reactions of dimethylphosphoramidic difluoride (**1**) with *trans*-2-(*N*,*N*-dialkylamino)cycloalkanols were studied in the presence of various sulfur-containing nucleophiles and Et_3N. When *O*,*O*-diisopropyl thiophosphoric acid was used as a nucleophile, the corresponding *O*,*O*-diisopropyl *S*-[2-(*N*,*N*-dialkylamino)cycloalkyl] thiophosphates were obtained in satisfactory yields. The direction of this reaction in the presence of *O*-isopropyl toluenephosphonothioic acid depends on the pK_a of aminoalcohol, namely, the amount of *O*-isopropyl tolylphosphonofluoridate that was formed along with *O*-isopropyl *S*-[2-(*N*,*N*-dialkylamino)cycloalkyl] tolylphosphonothioates was increased as the pK_a increased. The reactions of compound **1** with *trans*-2-(*N*,*N*-dialkylamino)cycloalkanols and thioacetic acid afforded 2-(*N*,*N*-dialkylamino)cycloalkanethiols, certain of which were readily oxidized to the corresponding disulfides. In the case of potassium ethyl xanthate, the composition of the reaction products depends on the nature of aminoalcohol. X-ray diffraction analysis of *S*-(2-piperidinocyclohexyl) *N*,*N*-dimethyldithiocarbamate demonstrated that this compound exists as the *trans* isomer. This fact supports the reaction mechanism, which we have suggested previously and which involves the formation of aziridinium cations followed by their opening under the action of nucleophilic agents.

Key words: dimethylphosphoramidic difluoride, reactions with *trans*-2-(*N*,*N*-dialkylamino)cycloalkanols; *O*,*O*-diisopropyl *S*-[2-(*N*,*N*-dialkylamino)cycloalkyl] thiophosphates, *O*-isopropyl *S*-[2-(*N*,*N*-dialkylamino)cycloalkyl] tolylphosphonothioates, *O*-isopropyl tolylphosphonofluoridate, 2-(*N*,*N*-dialkylamino)cycloalkanethiols, bis[*trans*-2-(*N*,*N*-dialkylamino)cycloalkyl] disulfides, bis[*trans*-2-(*N*,*N*-dimethylamino)cyclohexyl] disulfide, *S*-(*trans*-2-piperidinocyclohexyl) *N*,*N*-dimethyldithiocarbamate, synthesis; X-ray diffraction analysis.

Previously, we have demonstrated that the reactions of dimethylphosphoramidic difluoride (**1**) with *trans*-2-substituted cycloalkanols can be used for the synthesis of various organic and organometallic compounds.[1,2] In particular, the reaction of compound **1** with *trans*-2-(*N*-methyl-*N*-ethylamino)cyclopentanol in the presence of *O*,*O*-diethyl dithiophosphoric acid and Et_3N (Scheme 1) afforded *O*,*O*-diethyl *S*-[2-(*N*-methyl-*N*-ethylamino)cyclopentyl] phosphorodithioate in quantitative yield.[2]

With the aim of studying the mechanism of this reaction and extending the possibilities of its use for the synthesis of organometallic compounds, we studied the reactions of compound **1** with *trans*-2-(*N*,*N*-dialkylamino)cycloalkanols in the presence of different sulfur-containing nucleophiles. We used *O*,*O*-diisopropyl thiophosphoric acid (**2**), *O*-isopropyl toluenephosphonothioic acid (**3**), thioacetic acid (**4**), and potassium *O*-ethyl xanthate (**5**) as nucleophiles.

Scheme 1



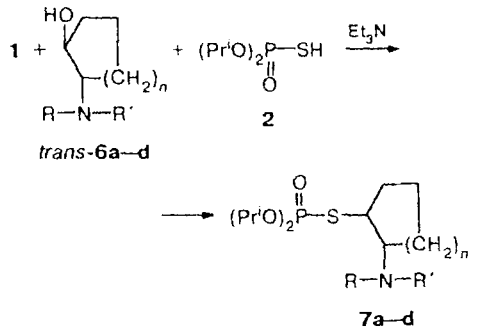
Results and Discussion

As in the case of *O*,*O*-diethyl dithiophosphoric acid, the reactions of *trans*-2-(*N*,*N*-dialkylamino)cycloalkanols **6a—d** with compound **1** in the presence of acid **2** and

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 9, pp. 1802—1809, September, 1998.

Et_3N afforded the corresponding *O,O*-diisopropyl thiophosphates **7a—d** in 55—70% yields (Scheme 2). An analogous result was obtained when the reaction of compound **1** with **6b** was carried out in the absence of Et_3N. However, in the last-mentioned case the yield of product **7b** was only ~40%.

Scheme 2

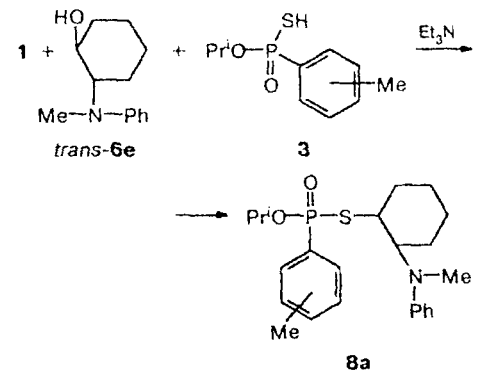


a: R + R′ = $(CH_2)_5$, n = 1
b: R = R′ = Me, n = 2
c: R + R′ = $(CH_2)_4$, n = 2
d: R + R′ = $(CH_2)_5$, n = 2

Therefore, the reaction under study is common to thiophosphoric and dithiophosphoric acids.

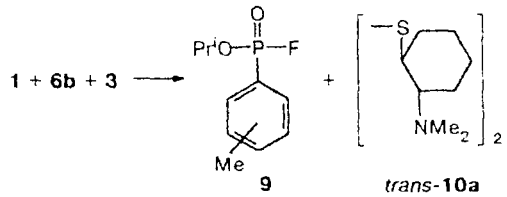
A somewhat different situation was observed in the case of phosphonothioic acid **3**. The selective formation of *O*-isopropyl *S*-[2-(*N*-methyl-*N*-phenylcyclohexyl)] tolylphosphonothioate (**8a**) in satisfactory yield was observed only in the reaction of compound **1** with *trans*-2-(*N*-methyl-*N*-phenylamino)cyclohexanol (**6e**) in the presence of Et_3N (Scheme 3).

Scheme 3



When the reaction was carried out with the use of *trans*-2-(*N,N*-dimethylamino)cyclopentanol (**6f**: R = R′ = Me, n = 1), *O*-isopropyl tolylphosphonofluoridate (**9**) was detected along with the product of formal nucleophilic replacement of the hydroxyl group, namely, *O*-isopropyl *S*-[2-(*N,N*-dimethylamino)cyclopentyl)] tolylphosphonothioate (**8b**). Compound **9** was the major target product of the reaction of compound **1** with **6b** in the presence of Et_3N. According to the data of NMR spectroscopy, the content of *O*-isopropyl *S*-[2-(*N,N*-dimethylamino)cyclohexyl] tolylphosphonothioate (**8c**) in the reaction mixture was no more than 10% with respect to the content of phosphonofluoridate **9**, and only compound **9** and bis[*trans*-2-(*N,N*-dimethylamino)cyclohexyl] disulfide (**10a**) were isolated in the pure form (Scheme 4).

Scheme 4



Conceivably, the difference in the behavior of aminocycloalkanols in the reaction under study (see Schemes 3 and 4) is associated with their basicity because the amount of phosphonofluoridate **9** formed increases as the value of pK_a increases in the series **6e**, **6f**, and **6b** (pK_a are <7, 9.03, and 10.16, respectively).

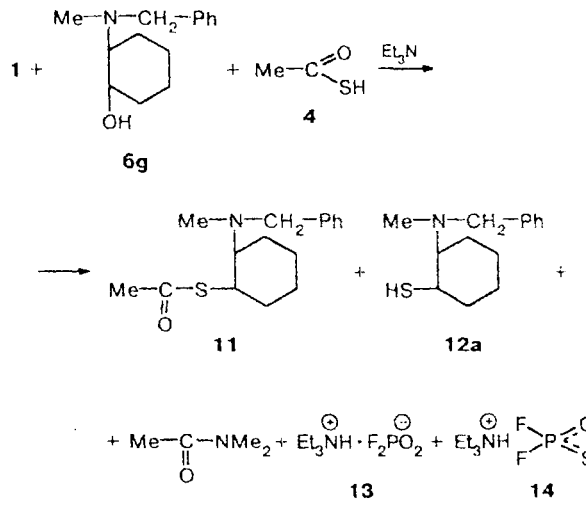
In most cases, the reactions of compound **1** with *trans*-2-(*N,N*-dialkylamino)cycloalkanols in the presence of sulfur-containing nucleophiles **4** and **5** that do not contain the P atom also proceed ambiguously, which is attributed to high reactivity of the products.

Thus, the reaction of compound **1**, *trans*-2-(*N*-benzyl-*N*-methylamino)cyclohexanol (**6g**: R = Me, R′ = CH_2Ph, n = 2), and acid **4** in the presence of Et_3N afforded a reaction mixture that contained (according to the data of NMR spectroscopy and GLC-MS) *S*-[2-(*N*-benzyl-*N*-methylamino)cyclohexyl] thioacetate (**11**), 2-(*N*-benzyl-*N*-methylamino)cyclohexanethiol (**12a**), Me_2NAc, the salt of difluorophosphoric acid **13**, and the salt of difluorothiophosphoric acid **14** (Scheme 5).

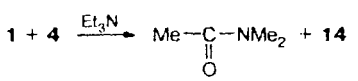
It can be suggested that thiol **12** and Me_2NAc were formed as a result of interaction of product **11** with the Me_2NH that appeared in the mixture. It should be noted that acid **4** slowly reacted with compound **1** in the presence of Et_3N to form salt **14** (Scheme 6), which is, apparently, the cause of the presence of salt **14** among the reaction products.

In some cases, the reactions of *trans*-2-(*N,N*-dialkylamino)cycloalkanols with compound **1** in the presence of acid **4** and Et_3N (see Scheme 5) can be used for the synthesis of 2-(*N,N*-dialkylamino)cycloalkanethiols. In particular, we prepared thiol **12a** by this procedure (the yield was 61%). According to the data of GLC-MS, the purity of compound **12a** was >98%. A compound which is apparently a product of intramolecular cycliza-

Scheme 5



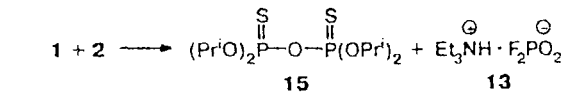
Scheme 6



tion of thiol **12a** (2-benzyl-3-methylperhydrobenzothiazole) was detected as an admixture (<1.5%; MS (EI, 70 eV), *m/z*: 233 $[M]^+$). It should be noted that some 2-(*N*,*N*-dialkylamino)cycloalkanethiols readily undergo oxidation. Thus, in the case of cycloalkanol **6f**, we succeeded in isolating only bis[2-(*N*,*N*-dimethylamino)cyclopentyl] disulfide (**10b**).

Interestingly, unlike other amides of phosphorus acids, dimethylphosphoramidic difluoride **1** is rather stable in acidic media. For example, compound **1** reacted with acid **2** at an appreciate rate only upon heating to form salt **13** and *P*,*P*′-oxybis(*O*,*O*-diisopropyl thiophosphate) (**15**) (Scheme 7).

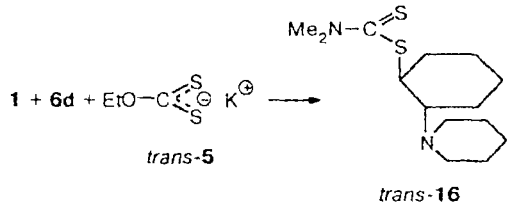
Scheme 7



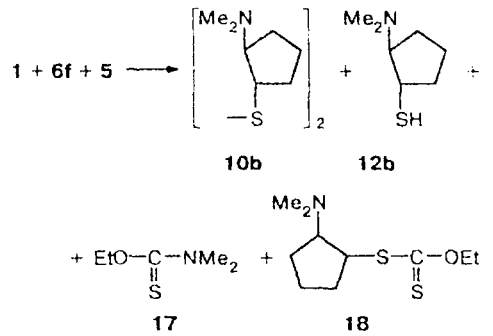
The reaction of compound **1** with **6d** in the presence of salt **5** afforded *S*-(*trans*-2-piperidinocyclohexyl) dimethyldithiocarbamate (**16**) as the major product (Scheme 8).

However, when this reaction was carried out with the use of cycloalkanol **6f**, 2-(*N*,*N*-dimethylamino)cyclopentanethiol (**12b**), the product of its transformation **10b**, and ethyl thiocarbamate (**17**) were obtained as the major products. In addition, the reaction mixture contained a small amount of *S*-[2-(*N*,*N*-dimethylamino)cyclopentyl] *O*-ethyl xanthate (**18**) (Scheme 9).

Scheme 8



Scheme 9



The results obtained in this work demonstrate that when salt **5** is used as a nucleophilic agent, the composition of the reaction products depends on the nature of the aminoalcohol. We believe that in both cases, the corresponding *S*,*S*-di(aminocycloalkyl) dithiocarbonates were formed. However, these thioesters reacted differently with Me_2NH. In the molecule of cyclohexyl thioester, the cleavage of the ester C—O bond predominated, while in the molecule of cyclopentyl thioester, the cleavage of the C—S bond predominated.

The physicochemical constants of the compounds synthesized by us and the data of elemental analysis are given in Table 1. The parameters of the NMR spectra are listed in Table 2.

The structures of bis[*trans*-2-(*N*,*N*-dimethylamino)cyclohexyl] disulfide **10a** and *S*-(*trans*-2-piperidinocyclohexyl) *N*,*N*-dimethyldithiocarbamate **16** were unambiguously established by X-ray diffraction analysis.

The structure of molecule **10a** is shown in Fig. 1. In the crystal, molecule **10a** is located on the crystallographic twofold axis passing through the midpoint of the S—S bond. The cyclohexane rings of the molecule adopt a chair conformation. The S and N atoms are in *trans* positions (the N(1)—C(1)—C(6)—S(1) torsion angle is −46.8°). The C(5)—C(6)—S(1)—S(1a) and C(6)—S(1)—S(1a)—C(6a) torsion angles, which characterize the molecular conformation, are −53.9° and −82.5°, respectively. All bond lengths and bond angles in the molecule are close to the standard values. The intermolecular

distances are close to the standard values of the corresponding van der Waals contacts.

The structure of molecule **16** is shown in Fig 2. The molecule contains the cyclohexane and piperidine rings

Table 1. Physicochemical constants and the data of elemental analysis of the synthesized compounds

Compound	B.p./°C (*p*/Torr) / M.p./°C (solvent)	n_D^{25}	Found / Calculated (%) C	H	N	P	S	Molecular formula
7a	125—126 (10^{-2}) / —	1.4899	55.09 / 54.99	9.24 / 9.23	4.03 / 4.01	8.92 / 8.86	9.23 / 9.17	$C_{16}H_{32}NO_3PS$
7b	115—116 (10^{-2}) / —	1.4835	52.20 / 51.99	9.41 / 9.35	4.39 / 4.33	9.71 / 9.58	9.99 / 9.91	$C_{14}H_{30}NO_3PS$
7c	120—121 (10^{-2}) / —	1.4940	55.03 / 54.99	9.26 / 9.23	4.02 / 4.01	8.91 / 8.86	9.29 / 9.17	$C_{16}H_{32}NO_3PS$
7d	140—143 (10^{-2}) / —	1.5090	56.33 / 56.17	9.48 / 9.43	3.87 / 3.85	8.60 / 8.52	8.89 / 8.82	$C_{17}H_{34}NO_3PS$
8a	* / —	—	65.36 / 65.19	7.97 / 7.90	3.49 / 3.46	7.71 / 7.65	7.95 / 7.90	$C_{22}H_{32}NO_2PS$
9	90—91 (1) / —	—	55.59 / 55.56	6.51 / 6.48	—	14.43 / 14.35	—	$C_{10}H_{14}FO_2P$
10a	153—155 (1) / 85 (hexane—Pr^{i}OH, 1 : 5)	—	60.79 / 60.76	10.15 / 10.13	8.87 / 8.86	—	20.28 / 20.25	$C_{16}H_{32}N_2S_2$
10b	137—138 (10^{-3}) / —	—	58.40 / 58.33	9.80 / 9.72	9.79 / 9.72	—	22.34 / 22.22	$C_{14}H_{28}N_2S_2$
12a	102—105 ($3 \cdot 10^{-3}$) / —	—	71.72 / 71.49	9.08 / 8.94	6.07 / 5.96	—	13.81 / 13.62	$C_{14}H_{21}NS$
16	— / 78 (acetone—Pr^{i}OH, 1 : 5)	—	58.75 / 58.69	9.18 / 9.15	10.16 / 9.78	—	21.05 / 22.38	$C_{14}H_{26}N_2S$

* Oil.

Table 2. Parameters of the ^1H and ^{31}P NMR spectra of the synthesized compounds

Compound[a]	δ ^{31}P (*J*/Hz)	δ ^1H (*J*/Hz)
7a	25.6	1.3 (d, 12 H, $(CMe_2)_2$, J = 7); 1.55 (m, 12 H, $(CH_2)_4$, $(CH_2)_2$); 2.5 (m, 4 H, $N(CH_2)_2$); 2.7 (m, 1 H, NCH); 3.35 (m, 1 H, SCH); 4.6 (m, 2 H, OCH)
7b	25.0	1.2 (d, 12 H, $(CMe_2)_2$, J = 7); 1.9 (m, 8 H, $(CH_2)_4$); 2.6 (s, 6 H, NMe_2); 2.7 (m, 1 H, NCH); 3.2 (m, 1 H, SCH); 4.5 (m, 2 H, $(OCH)_2$)
7c	24.2	1.1 (d, 12 H, $(CMe_2)_2$, J = 7); 1.5 (m, 4 H, $(CH_2)_2$); 1.6 (m, 8 H, $(CH_2)_4$); 2.2 (m, 1 H, NCH); 2.4 (m, 4 H, $N(CH_2)_2$); 3.3 (m, 1 H, SCH); 4.4 (m, 2 H, $(OCH)_2$)
7d	25.6	1.1 (d, 12 H, $(CMe_2)_2$, J = 7); 1.3 (m, 14 H, $(CH_2)_2$, $(CH_2)_3$); 2.1 (m, 4 H, $N(CH_2)_2$); 2.3 (m, 1 H, NCH); 3.1 (m, 1 H, SCH); 4.3 (m, 2 H, $(OCH)_2$)
8a	42.8	1.3 (d, 6 H, CMe_2, J = 7); 1.5 (m, 4 H, $(CH_2)_2$); 1.7 (m, 4 H, $(CH_2)_2$); 2.1 (m, 3 H, CH_3); 2.3 (s, 3 H, NCH_3); 2.5 (m, 1 H, NCH); 3.1 (m, 1 H, SCH); 4.3 (m, 1 H, OCH); 7.5 (m, 5 H, Ph); 8.0 (m, 4 H, H arom.)
9[b]	16.6 (br.d, J = 1055)	1.0 (d, 6 H, CMe_2, J = 7); 2.1 (m, 3 H, CH_3); 4.6 (m, 1 H, OCH); 7.2 (m, 4 H, H arom.)
10a	—	1.4 (m, 16 H, 2 $(CH_2)_4$); 1.9 (s, 12 H, 2 NMe_2); 2.1 (m, 2 H, 2 NCH); 2.5 (m, 2 H, 2 SCH)
10b	—	1.5 (m, 12 H, 2 $(CH_2)_3$); 2.1 (s, 12 H, 2 NMe_2); 2.2 (m, 2 H, 2 NCH); 2.5 (m, 2 H, 2 SCH)
12a	—	1.5 (m, 4 H, $(CH_2)_2$); 1.8 (m, 4 H, $(CH_2)_2$); 2.2 (s, 3 H, NMe); 2.6 (m, 1 H, NCH); 3.5 (m, 1 H, SCH); 3.8 (m, 1 H, SH); 7.1 (m, 5 H, Ph)
16	—	1.0—2.2 (m, 14 H, $(CH_2)_4$, $(CH_2)_3$); 1.5 (m, 5 H, $CHN(CH_2)_2$); 2.6 (m, 1 H, NCH); 3.5 (s, 6 H, NMe_2); 3.95 (m, 1 H, SCH)

[a] The spectra were recorded in $CDCl_3$ (**7a—d**, **8a**, and **12a**) and in CD_3OD (**10a,b** and **16**).

[b] Without a solvent. ^{19}F NMR for **9**: δ −61.0 (br.d, J = 1055 Hz).

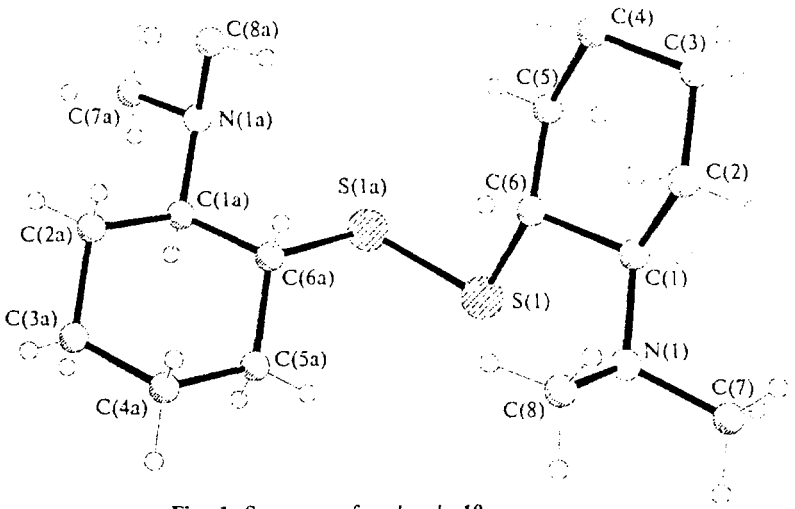
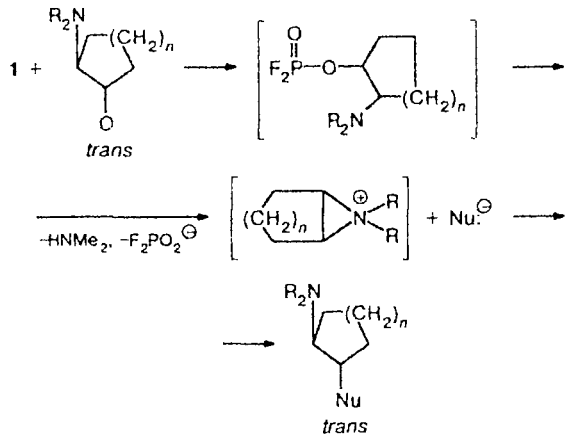


Fig. 1. Structure of molecule **10a**.

Scheme 10



linked through the N—C bond. The S(1) atom of the planar thiocarbamate fragment is in the *trans* orientation with respect to the N atom of the piperidine ring. The S(1)—C(1)—C(2)—N(1) torsion angle is 46.9°. The orientation of the thiocarbamate fragment with respect to the cyclohexane ring is described by the C(2)—C(1)—S(1)—C(12) and C(6)—C(1)—S(1)—C(12) torsion angles (−161.6° and 77.2°, respectively). The piperidine ring is rotated with respect to the cyclohexane ring by 66.1° (the C(1)—C(2)—N(1)—C(7) torsion angle). The intermolecular distances are close to the corresponding standard values of the van der Waals contacts. The atomic coordinates of compound **10a** are given in Table 3. The bond lengths and bond angles are listed in Table 4. The corresponding characteristics for compound **16** are given in Tables 5 and 6, respectively.

The mechanism of the reaction of dimethylphosphoramidic difluoride **1** with *trans*-2-(*N*,*N*-dialkylamino)cycloalkanols through the formation of aziridinium cations followed by their opening under the action of nucleophiles that are present in the reaction mixture (Scheme 10) is supported by the fact that compound **16** is the *trans* isomer.

Based on the above-mentioned facts, it can be suggested that compounds **7a—d**, **8a**, **12a**, and **10b** are also *trans* isomers.

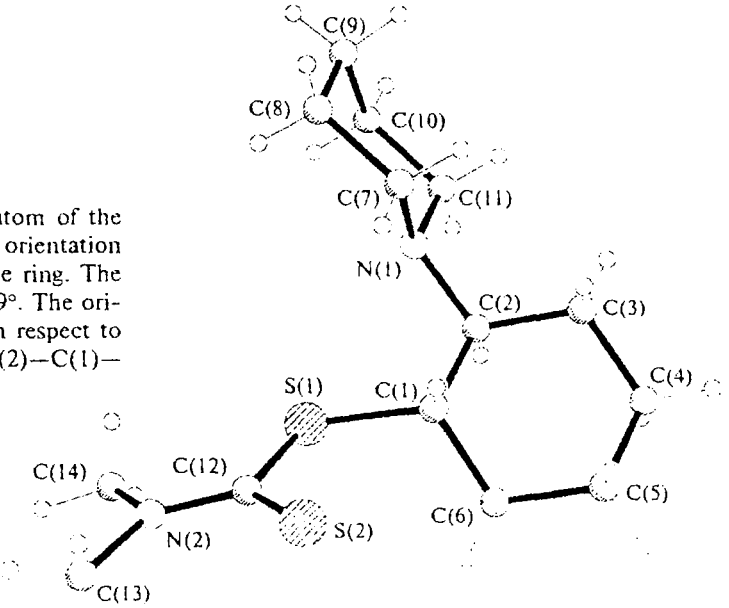


Fig. 2. Structure of molecule **16**.

Table 3. Bond lengths (d) and principal bond angles (ω) in molecule **10a**

Bond	d/Å	Bond	d/Å	Angle	ω/deg	Angle	ω/deg
S(1)—S(1a)	2.042(1)	C(4)—C(5)	1.526(6)	S(1a)—S(1)—C(6)	103.0(1)	C(3)—C(4)—C(5)	110.4(4)
S(1)—C(6)	1.832(4)	C(5)—C(6)	1.526(5)	S(1)—C(6)—C(1)	107.5(2)	C(4)—C(5)—C(6)	110.8(3)
C(1)—C(2)	1.524(5)	C(7)—N(1)	1.455(4)	S(1)—C(6)—C(5)	113.8(2)	C(2)—C(1)—N(1)	115.7(3)
C(1)—C(6)	1.529(4)	C(8)—N(1)	1.455(5)	C(1)—C(2)—C(3)	110.9(3)	C(6)—C(1)—N(1)	111.5(3)
C(2)—C(3)	1.520(5)	C(1)—N(1)	1.474(4)	C(1)—C(6)—C(5)	109.6(3)	C(1)—N(1)—C(7)	112.5(3)
C(3)—C(4)	1.510(6)			C(2)—C(3)—C(4)	112.0(4)	C(1)—N(1)—C(8)	114.7(3)
				C(2)—C(1)—C(6)	108.8(3)	C(7)—N(1)—C(8)	112.2(3)

Table 4. Fractional atomic coordinates ($\times 10^4$) and equivalent thermal parameters (B_{eq}) for compound **10a**

Atom	x	y	z	B_{eq}/Å^2
S(1)	274(1)	970(2)	2935(0)	4.26(2)
C(1)	−53(2)	−1544(6)	3879(1)	3.35(9)
C(2)	−509(2)	−3722(8)	4124(2)	4.6(1)
C(3)	−1543(3)	−353(1)	3958(2)	6.3(2)
C(4)	−1868(3)	−3360(9)	3307(2)	5.7(1)
C(5)	−1391(2)	−1230(8)	3058(2)	4.7(1)
C(6)	−356(2)	−1517(6)	3217(1)	3.44(9)
C(7)	1244(3)	−721(9)	4661(2)	5.8(1)
C(8)	1433(3)	−3588(8)	3902(2)	6.4(1)
N(1)	950(2)	−1417(6)	4054(1)	3.78(8)

Experimental

The NMR spectra were recorded on a Bruker-AC200 spectrometer (^{31}P NMR, 87.02 MHz, a 85% H_3PO_4 solution as the standard; ^{19}F NMR, 188.31 MHz, Freon-12 as the standard; ^{1}H NMR, 200.13 MHz, Me_4Si as the standard).

The GLC-mass spectrometric analysis was carried out on an HP 5890 GLC-mass spectrometer (EI, 70 eV) equipped with a MSD 5972 mass-selective detector (an HP-5MS quartz capillary column (30 m × 0.25 mm); methylphenylsiloxane as the stationary liquid phase; the evaporator temperature was 250 °C; the detector temperature was 175 °C; the rate of carrier gas (He) was 1 mL min^{-1}; and the volume of the sample was 1 mL).

The values of pK_a were determined according to a known procedure.[4]

A series of the initial compounds were synthesized according to known procedures: for **1**, see Ref. 3; for *trans*-2-(*N*,*N*-dialkylamino)cycloalkanols, see Ref. 5; and for acids **2** and **3**, see Refs. 6 and 7. The other starting compounds and solvents were commercial products and were purified before use. All procedures described below were carried out under an atmosphere of argon.

***O*,*O*-Diisopropyl *S*-[2-(*N*,*N*-dimethylamino)cyclohexyl] thiophosphate (7b).** *A.* Compound **1** (3.9 g, 0.03 mol) was added to a solution of acid **2** (5.4 g, 0.027 mol) and cycloalkanol **6a** (3.9 g, 0.027 mol) in benzene (10 mL). The reaction mixture was stirred at ~20 °C for 6 h and then at 70 °C for 1 h. Then the reaction mixture was washed successively with water and a solution of sodium carbonate and extracted with benzene (2×15 mL). The combined organic extracts were dried over $MgSO_4$. The solvent was evaporated, and the residue was distilled off. Compound **7b** was obtained in a yield of 3.5 g (40%).

B. Compound **1** (4.6 g, 0.036 mol) was added to a solution of acid **2** (6.0 g, 0.03 mol), Et_3N (3.1 g, 0.03 mol), and cycloalkanol **6a** (4.3 g, 0.03 mol) in benzene (15 mL). The reaction mixture was stirred at 80 °C for 6 h. Then the reaction mixture was washed successively with water and a solution of sodium carbonate and extracted with benzene (2×15 mL). The combined organic extracts were dried over $MgSO_4$. The solvent was evaporated, and the residue was distilled off. Compound **7b** was obtained in a yield of 5.3 g (55%).

Compounds **7a**, **7c**, and **7d** were prepared as described above. The IR spectra of compounds **7a—d** (in CCl_4) have the following characteristic absorption bands, ν/cm^{-1}: 2786—2801 (Boltzmann band); 1386 (Pr^i); 1244—1249 (P=O); 985—986 (P—O—C); 613—614 (P—S); 571—575 (P—S).

Table 5. Bond lengths (d) and bond angles (ω) in molecule **16**

Bond	d/Å	Bond	d/Å	Angle	ω/deg	Angle	ω/deg
S(1)—C(1)	1.821(3)	C(10)—C(11)	1.518(5)	C(1)—S(1)—C(12)	103.7(1)	N(1)—C(2)—C(1)	112.8(2)
S(2)—C(12)	1.667(3)	S(1)—C(12)	1.767(3)	C(2)—N(1)—C(11)	112.6(2)	C(2)—C(3)—C(4)	111.1(3)
N(1)—C(7)	1.461(4)	N(1)—C(2)	1.462(4)	C(12)—N(2)—C(13)	120.7(3)	C(3)—C(4)—C(5)	110.7(3)
N(2)—C(12)	1.341(4)	N(1)—C(11)	1.461(4)	C(13)—N(2)—C(14)	116.1(3)	C(4)—C(5)—C(6)	110.5(3)
N(2)—C(14)	1.442(5)	N(2)—C(13)	1.462(5)	S(1)—C(1)—C(6)	112.4(2)	C(1)—C(6)—C(5)	110.1(3)
C(1)—C(6)	1.536(4)	C(1)—C(2)	1.532(4)	C(2)—C(1)—C(6)	109.6(3)	N(1)—C(7)—C(8)	110.1(3)
C(2)—C(3)	1.537(4)	C(4)—C(5)	1.524(5)	N(1)—C(2)—C(3)	116.0(2)	C(7)—C(8)—C(9)	111.2(3)
C(3)—C(4)	1.522(5)	C(7)—C(8)	1.521(5)	C(1)—C(2)—C(3)	107.5(2)	C(8)—C(9)—C(10)	110.0(3)
C(5)—C(6)	1.523(5)	C(9)—C(10)	1.514(5)	S(1)—C(12)—C(2)	112.9(2)	C(9)—C(10)—C(11)	111.2(3)
C(8)—C(9)	1.511(5)			C(2)—N(1)—C(7)	115.3(2)	N(1)—C(11)—C(10)	110.1(3)
				C(7)—N(1)—C(11)	110.9(2)	S(1)—C(12)—S(2)	123.7(2)
				C(12)—N(2)—C(14)	123.2(3)	S(2)—C(12)—N(2)	123.4(2)
				S(1)—C(1)—C(2)	108.2(2)		

Table 6. Fractional atomic coordinates ($\times 10^4$) and equivalent thermal parameters (B_{eq}) for compound **16**

Atom	x	y	z	$B_{eq}/Å^2$
S(1)	7916(1)	1174(1)	9627(1)	4.20(2)
S(2)	8615(1)	776(1)	12117(1)	4.97(3)
N(1)	5895(2)	2602(2)	8824(2)	2.98(6)
N(2)	8799(2)	−838(2)	10542(2)	4.30(8)
C(1)	7658(2)	2657(3)	10214(3)	3.42(8)
C(2)	6831(2)	3357(3)	9338(2)	3.20(8)
C(3)	6559(3)	4565(3)	9875(3)	4.17(9)
C(4)	7580(3)	5346(3)	10244(3)	5.4(1)
C(5)	8445(3)	4640(3)	11062(3)	5.5(1)
C(6)	8705(3)	3424(3)	10556(3)	4.6(1)
C(7)	5181(3)	2216(3)	9570(3)	3.87(9)
C(8)	4368(3)	1259(4)	8999(3)	5.1(1)
C(9)	3701(3)	1744(4)	7917(3)	5.2(1)
C(10)	4454(3)	2225(4)	7188(3)	4.6(1)
C(11)	5261(3)	3153(3)	7809(3)	3.97(9)
C(12)	8491(2)	286(3)	10808(3)	3.64(9)
C(13)	9295(3)	−1704(3)	11410(4)	5.7(1)
C(14)	8676(3)	−1265(3)	9409(3)	5.4(1)

***O*-Isopropyl *S*-[2-(*N*-methyl-*N*-phenylamino)cyclohexyl] tolylphosphonothioate (8a).** Compound **1** (4.64 g, 0.036 mol) was added to a solution of acid **3** (6.9 g, 0.03 mol), Et_3N (3.1 g, 0.03 mol), and cycloalkanol **6e** (6.15 g, 0.03 mol) in benzene (15 mL). The reaction mixture was stirred at 80 °C for 6 h. Then the reaction mixture was washed successively with water and a solution of sodium carbonate and extracted with benzene (2×15 mL). The combined organic extracts were dried over $MgSO_4$. The solvent was evaporated, and the residue was kept *in vacuo* with the use of an oil pump. Compound **8a** was obtained in a yield of 5.3 g (90%) as an yellow oil.

Reaction of dimethylphosphoramidic difluoride (1) with *trans*-2-(*N*,*N*-dimethylamino)cyclopentanol (6f) in the presence of *O*-isopropyl toluenephosphonothioic acid (3) and Et_3N. Compound **1** (4.64 g, 0.036 mol) was added to a solution of acid **3** (6.9 g, 0.03 mol), Et_3N (3.1 g, 0.03 mol), and cycloalkanol **6f** (3.9 g, 0.03 mol) in benzene (15 mL). The reaction mixture slightly warmed up. The reaction mixture was stirred at 80 °C for 2.5 h. Then the reaction mixture was washed successively with water and a solution of sodium carbonate and extracted with benzene (2×15 mL). The combined organic extracts were dried over $MgSO_4$. The solvent was evaporated, and the residue was kept *in vacuo* using an oil pump. According to the data of ^{31}P and ^{19}F NMR spectroscopy, the resulting product consisted of compound **8b** [80%; δ ^{31}P 40.9 (s)] and compound **9** [20%; δ ^{31}P 16.4 (br.d, J = 1030 Hz); δ ^{19}F −60.7 (br.d, J = 1030 Hz)]. We failed to separate these compounds by distillation under high vacuum.

The reaction of compound **1** with *trans*-2-(*N*,*N*-dimethylamino)cyclohexanol **6b** in the presence of acid **3** and Et_3N was carried out analogously. According to the data of ^{31}P and ^{19}F NMR spectroscopy, the resulting mixture contained compounds **7c** [δ ^{31}P 42.8 (s)] and **12** [δ ^{31}P 16.6 (br.d, J = 1030 Hz); δ ^{19}F −61.0 (br.d, J = 1030 Hz)] in a ratio of 1 : 9.

Reaction of compound 1 with *trans*-2-(*N*,*N*-dimethylamino)cyclohexanol (6b) in the presence of acid 3. Compound **1** (4.64 g, 0.036 mol) was added to a solution of acid **3** (6.9 g, 0.03 mol) and cycloalkanol **6b** (4.3 g, 0.03 mol) in benzene (10 mL). The reaction mixture was stirred at −20 °C for 1 h and then at 70 °C for 2.5 h. Then the reaction mixture was washed successively with water and a solution of sodium carbonate and extracted with benzene (2×15 mL). The combined organic extracts were dried over $MgSO_4$. The solvent was evaporated, and the residue was distilled off. Compounds **9** and **10a** were obtained in yields of 3.4 g (52%) and 1.3 g (27%, the yield after recrystallization), respectively. MS of **9**, m/z: 216 $[M]^+$. MS of **10a**, m/z: 191 $[M-Me_2NC_6H_9]^+$.

2-(*N*-Benzyl-*N*-methylamino)cyclohexanethiol (12a). Compound **1** (7 g, 0.054 mol) was added portionwise to a solution of acid **4** (3.4 g, 0.045 mol), Et_3N (4.6 g, 0.045 mol), and cycloalkanol **6g** (9.9 g, 0.045 mol) in benzene (50 mL). The reaction mixture was stirred at −20 °C for 2 h and then at 50 °C for 7 h. The solvent was evaporated. According to the data of GLC-MS, the mixture contained Me_2NAc and compounds **12a** and **11**. MS of **11** (EI, 70 eV), m/z: 277 $[M]^+$. According to the data of ^{31}P and ^{19}F NMR spectroscopy, the reaction mixture contained also salt **14**, which was not detected by GLC-MS [δ ^{31}P 48.0 (d, J = 1080 Hz); δ ^{19}F −34.5 (d, J = 1080 Hz)[1]]. Then the reaction mixture was hydrolyzed with an alkaline solution (pH 12) at 60–70 °C for 6 days. Product **12a** was extracted with ethyl ether (2×20 mL). The combined organic extracts were dried over $MgSO_4$. The solvent was evaporated, and then hexane (50 mL) was added. The precipitate that formed was filtered off, the solvent was evaporated, and the reside was distilled off. Compound **12a** was obtained in a yield of 6.5 g (61%). MS, m/z: 235 $[M]^+$.

Reaction of compound 1 with thioacetic acid (4) in the presence of Et_3N. A solution of acid **4** (0.76 g, 0.01 mol), Et_3N (1 g, 0.01 mol), and compound **1** (1.3 g, 0.01 mol) in benzene (5 mL) was kept for 1 day. According to the data of ^{31}P and ^{19}F NMR spectroscopy, the reaction mixture contained triethylammonium phosphorodifluoridate **14** [δ ^{31}P 47.7 (d, J = 1083 Hz); δ ^{19}F −34.5 (d, J = 1083 Hz)[1]] along with the initial compound **1**.

Reaction of compound 1 with *O*,*O*-diisopropyl thiophosphoric acid (2). Equimolar amounts of compounds **1** and **2** were heated at 70 °C for 2 days. The precipitate that formed was filtered off, washed with hexane, and dried *in vacuo*. According to the data of ^{31}P and ^{19}F NMR spectroscopy, the precipitate was phosphorodifluoridate **13** [δ ^{31}P −15.2 (t, J = 944 Hz); δ ^{19}F −82 (d, J = 944 Hz)[1]]. The residue was *P*,*P*′-oxybis(*O*,*O*′-diisopropyl thiophosphate) **15**.[8] ^{31}P NMR, δ: 41.6 (s). MS, m/z: 378 $[M]^+$.

Bis[2-(*N*,*N*-dimethylamino)cyclopentyl] disulfide (10b). Et_3N (23 mL, 0.163 mol) and a solution of cycloalkanol **6f** (14.2 g, 0.11 mol) in benzene (20 mL) were added successively with stirring and cooling to a solution of acid **4** (12.4 g, 0.163 mol) in benzene (50 mL). Compound **1** (17.5 mL, 0.163 mol) was added to the resulting mixture. The reaction mixture was stirred at 60 °C for 7 h. Then the solvent was evaporated. The residue was hydrolyzed with an alkaline solution at 60 °C for 20 h. The reaction mixture was extracted with ethyl ether (2×50 mL). The combined extracts were dried over $MgSO_4$, the solvent was evaporated, and the residue was distilled off. Compound **10b** was obtained in a yield of 8 g (51%). MS, m/z: 177 $[M-Me_2NC_5H_{17}]^+$.

***S*-(*trans*-2-Piperidinocyclohexyl) *N*,*N*-dimethyldithiocarbamate (16).** Compound **1** (25.8 g, 0.2 mol) was added dropwise to a solution of salt **5** (29.5 g, 0.184 mol) and cycloalkanol **6d** (20.5 g, 0.12 mol) in MeCN (200 mL). The reaction mixture warmed up to 80 °C. Then the reaction mixture was stirred at 70 °C for 9 h. The solvent was evaporated, and the residue was washed with an alkaline solution and extracted with ethyl ether (2×50 mL). The organic phase was dried over $MgSO_4$, and the solvent was evaporated. The residue was kept at 80 °C

in vacuo (10^{-2} Torr) until it crystallized out. Compound **16** was obtained in a yield of 9.9 g (30%) (the yield after recrystallization). IR (KBr), ν/cm^{-1}: 2801 (Boltzmann band); 1256 (C=S); 1489 (C—N); 1449 (C—N); 1142 (C=S). MS, *m/z*: 198 $[M-Me_2NC(S)]^+$.

Reaction of compound 1 with *trans*-2-(*N,N*-dimethylamino)cyclopentanol (6f) in the presence of potassium *O*-ethyl xanthate (5). Compound **1** (7.7 g, 0.06 mol) was added dropwise to a solution of salt **5** (9.9 g, 0.06 mol) and cycloalkanol **6f** (6.5 g, 0.05 mol) in MeCN (100 mL). The reaction mixture was stirred at 50 °C for 7 h, and the solvent was evaporated. According to the data of GLC-MS, the resulting mixture contained compounds **10b**, **12b**, **17**, and **18**. MS of **17**, *m/z*: 133 $[M]^+$. MS of **18**, *m/z*: 233 $[M]^+$.

The resulting product was heated with diethylamine at 50 °C for 8 h. After the removal of diethylamine, the residue was distilled off. According to the data of GLC-MS, the major fraction (b.p. 146 °C (10^{-2} Torr)) consisted of compounds **10b** (55.5%) and **12b** (45.5%). MS of **12b**, *m/z*: 144 $[M-H]^+$.

X-ray diffraction study of single crystals of 10a and 16. The X-ray intensity data sets were collected on an automated Enraf-Nonius CAD-4 diffractometer (Mo-Kα radiation, θ/2θ-scanning technique, $\theta_{max} = 25°$).

Crystals of **10a** (M = 316.6) are monoclinic, a = 14.921(7) Å, b = 5.394(9) Å, c = 23.417(6) Å, β = 101.15(3)°, V = 1849.2(3.5) Å^3, space group $C2/c$, Z = 4, d_{calc} = 1.137 g cm^{-3}. A total of 1448 independent reflections were measured of which 1048 reflections had $I_{hkl} \geq \sigma(I)$.

Crystals of **16** (M = 286.5) are monoclinic, a = 12.470(2) Å, b = 10.880 Å, c = 12.247 Å, β = 101.62(3)°, V = 1627.5(1.3) Å^3 space group $P2_1/c$, Z = 4, d_{calc} = 1.169 g cm^{-3}. A total of 2396 independent reflections were measured of which 2103 reflections had $I_{hkl} \geq \sigma(I)$.

The structures were solved and the geometric and thermal parameters of the molecules were refined using the SHELX-93 program package. All nonhydrogen atoms were refined anisotropically by the full-matrix least-squares methods. The positions of the H atoms were located from the difference Fourier synthesis and refined using the riding model. For both compounds, the final values of the R factor was 0.037, and R_w = 0.038.

This work was financially supported by the International Science and Engineering Center (Grant 125).

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