Chemistry of Heterocyclic Compounds, Vol. 38, No. 4, 2002

SILYL MODIFICATION OF BIOLOGICALLY ACTIVE COMPOUNDS. 7*. SYNTHESIS, STRUCTURE, PHYSICOCHEMICAL AND BIOLOGICAL PROPERTIES OF SOME SILICON-CONTAINING "3+1" OXORHENIUM(V) COMPLEXES

A. Zablotskaya[1], I. Segal[1], A. Kemme[1], S. Germane[1], J. Popelis[1], E. Lukevics[1], R. Berger[2], and H. Spies[2]

With the aim of studying the structure–physicochemical properties–biological activity relation, we have synthesized a series of organosilicon neutral oxorhenium(V) complexes with mixed ligands and we have determined their lipophilicity. X-ray diffraction has been used to establish the molecular structure of (3-triphenylsiloxypropanethiolato)(3-thiapentane-1,5-dithiolato)oxorhenium(V), (2-trimethylsiloxy- and 2-hydroxyethanethiolato)[3-(N-methyl)azapentane-1,5-dithiolato]oxorhenium(V). We have studied the neurotropic properties and acute toxicity of the synthesized complexes in vivo and their dependence on the nature of the monodentate and tridentate ligands. We have established that all the studied compounds have pronounced sedative action (they prolong the life of mice under hypoxia conditions, they are phenamine antagonists, they exhibit anticonvulsive action and prevent retrograde amnesia).

Keywords: rhenium(V) complexes, trialkylsilyl ethers, psychotropic activity, X-ray diffraction.

Previously, with the aim of improving the lypophilicity of coordination compounds of rhenium as model diagnostic tools for tumor diseases of the central nervous system (CNS), we synthesized silicon-containing oxorhenium(V) complexes with mixed ligands, in which the oxorhenium core ReO^{3+} is coordinated with tridentate 3-thiapentane-1,5-dithiolate and monodentate thiolate, containing a silylated hydroxyl functional group with heavy organosilicon substituents ($SiMe_2Bu$-*t*, $SiPh_3$).

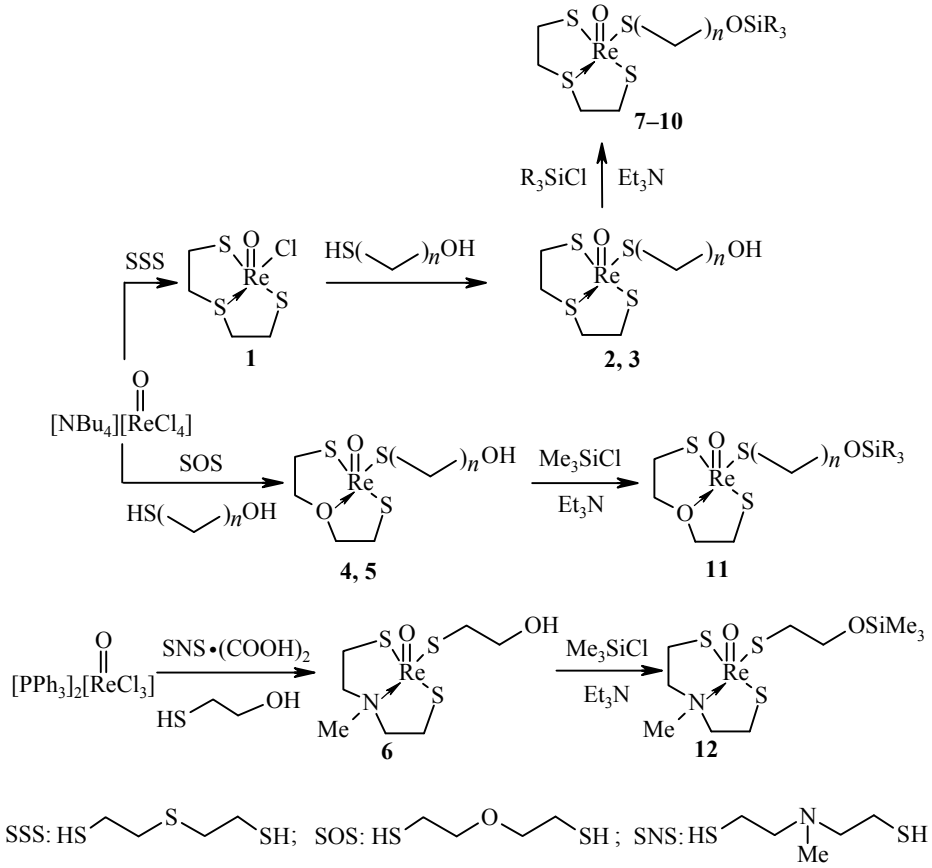
We naturally expected, in potential diagnostic tools of this type, the presence of psychotropic properties, which probably could serve as an indirect criterion for selection of these compounds. As we know, the efficacy of psychotropic drugs is intimately connected with their ability to pass through the blood–brain barrier, which is due not only to structural parameters but also, to a significant extent, to the lipophilicity of these compounds. Study of the neurotropic properties of (2-triphenylsiloxyethanethiolato)(3-thiapentane-1,5-dithiolate)-oxorhenium(V) (**9**) has shown that this compound exhibits anticonvulsive activity, having protective properties relative to corazole [1].

* For Communication 6, see [1].

[1] Latvian Institute of Organic Synthesis, Riga LV-1006; e-mail: aez@osi.lv. [2] Forschungszentrum Rossendorf [Rossendorf Research Center], PO Box 51 01 19, Dresden D-01314, Germany. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 543-555, April, 2002. Original article submitted October 18, 2000.

0009-3122/02/3804-0477$27.00

In this work, we have continued our study of the structure–physicochemical properties–biological activity relation for rhenium complexes. With the aim of a comparative description of their physicochemical and biological properties, we synthesized a series of neutral oxorhenium complexes with mixed ligands, where the oxorhenium(V) core ReO^{3+} is coordinated by tridentate 3-thia-, 3-oxa-, and 3-(N-methylazapentane-1,5-dithiolate, and also hydroxyl/triorganylsiloxyalkyl-containing monodentate thiolates.



7, 8, 11 R = Me; **9, 10** R = Ph; **2, 4, 7, 9** *n* = 2; **3, 5**, **8, 10, 11** *n* = 3

(2-Hydroxyethanethiolato)- and (3-hydroxypropanethiolato)(3-thiapentane-1,5-dithiolato)oxorhenium(V) (**2**), (**3**) were obtained by substitution of the chlorine atom in [ReO(SSS)Cl] (**1**) by the corresponding monodentate ligand [1].

(2-Hydroxyethanethiolato)-, (3-hydroxypropanethiolato)(3-oxapentane-1,5-dithiolato)- (**4**), (**5**), and also (2-hydroxyethanethiolato)[3-(N-methyl)azapentane-1,5-dithiolato]oxorhenium(V) (**6**) were obtained by simultaneous reaction of 3-oxa- or 3-methylaza-1,5-dithiol and mercaptoalkanol with the corresponding oxorhenium precursor. The silylated oxorhenium complexes **7-12** were obtained by reaction of presynthesized hydroxyalkyl-containing complexes with the corresponding triorganylchlorosilanes. For synthesis of the 2-triphenylsiloxyethane-containing 3-thiapentane complex **9**, we also tested the method of "3+1" complexation with participation of the presynthesized organosilicon ligand bis(triphenylsilyl)mercaptoethanol (**13**). The overall yields of compound **9** after all the steps were practically identical in both cases: 77%.

We used X-ray diffraction to establish the molecular structure of (2-triphenylsiloxyethanethiolato)- [1] **9**, (3-triphenylsiloxypropanethiolato)(3-thiapentane-1,5-dithiolato)oxorhenium(V) (**10**) (Fig. 1), (2-trimethylsiloxyethanethiolato)[3-(N-methyl)azapentane-1,5-dithiolato]oxorhenium(V) (**12**) (Fig. 2), and the hydroxyl-containing complex **6** (Fig. 3).

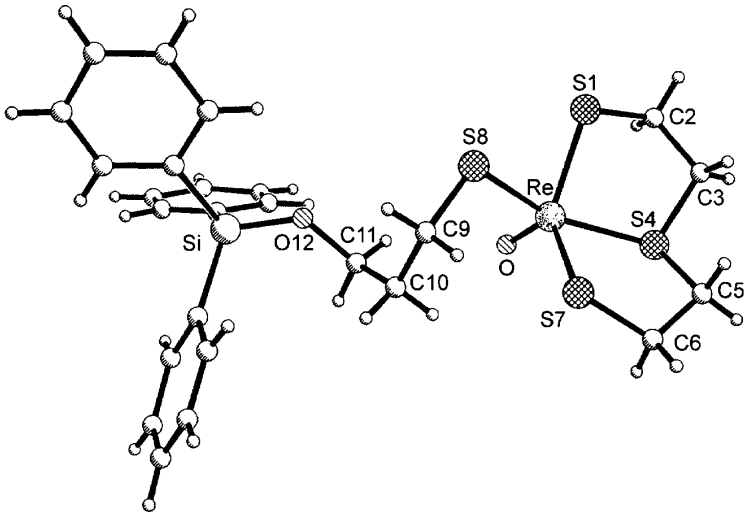


Fig. 1. Molecular structure of compound **10**.

According to the X-ray data, the silicon atom in compounds **9**, **10**, **12** has a tetrahedral configuration and the ligands are coordinated around the core ReO^{3+}, forming a distorted tetragonal pyramid with the rhenium atom in the center.

When the side chain was lengthened in the triphenylsiloxyalkanethiolate complexes (compare **9** and **10**) and when the hydrogen atom was replaced by a trimethylsilyl group in [3-(N-methyl)azapentane-1,5-dithiolato]oxorhenium complexes (compare **6** and **12**), we did not find any substantial changes in the molecular geometry.

We observe an increase in the Re=O bond length in the series 3-triphenylsiloxypropane-containing (1.624 Å), 2-triphenylsiloxyethane-containing (1.678 Å) thiapentane compounds **10**, **9** and then in the (2-trimethylsiloxyethanethiolato)(3-methylazapentane) complex **12** (1.693 Å).

In contrast to the unsilylated complex **6**, the atoms of the hydroxyethanethiolate substituent in compound **12** are located practically in the same plane, evidence for which comes from the value of the torsion angle $S_{(8)}–S_{(9)}–C_{(10)}–O_{(11)}$ (175.7°).

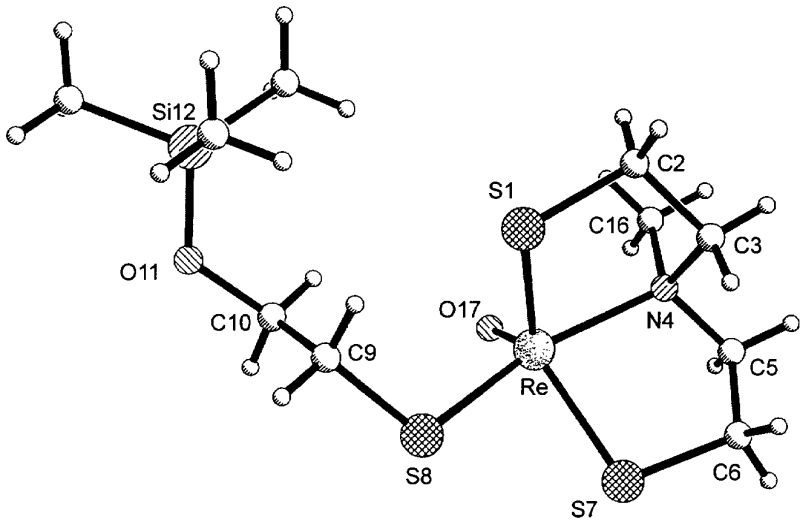


Fig. 2. Molecular structure of compound **12**.

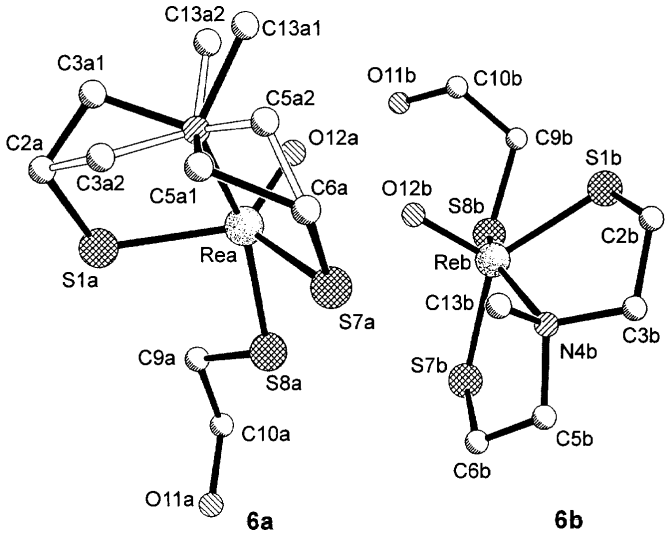


Fig. 3. Molecular structure of the two conformers **a** and **b** of compound **6**.

For compound **6**, we have established the presence of two independent conformers **a** and **b** in the crystallographic cell (Fig. 3). In conformer **6a**, we observe disordering of the carbon atoms in the α position relative to the $N_{(4)}$ atom of the tridentate ligand, with occupancy factor *g* 63:37 (**6a**1 and **6a**2 respectively). Furthermore, in the packing diagram for compound **6**, there are two independent tetramers located about the crystallographic center of symmetry and connected by hydrogen bonds (Fig. 4).

We used HPLC to study the lipophilicity of the synthesized complexes. The data obtained (Table 1) allow us to adequately assess the effects: introduction of an organosilicon substituent into the molecule; replacement of the central atom of a tridentate ligand; change in chain length for a monodentate ligand.

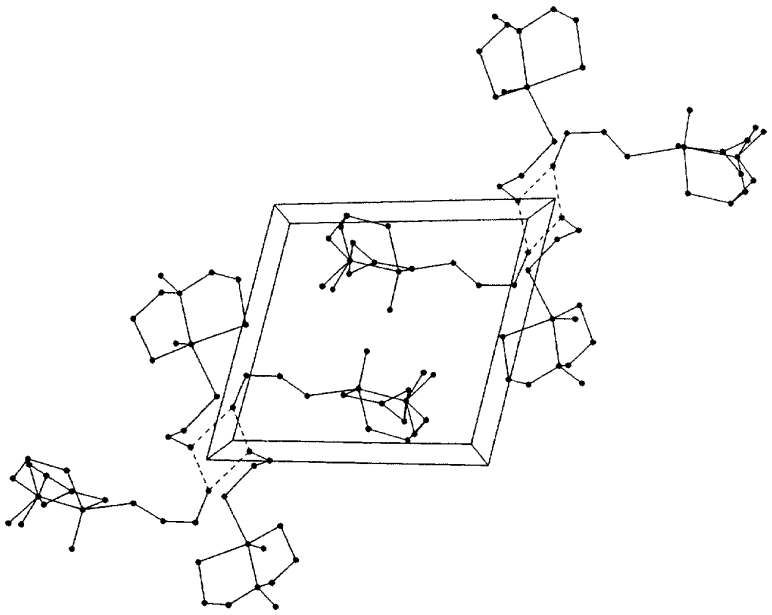


Fig. 4. Projection of the unit cell for compound **6**.

TABLE 1. Lipophilicity of Oxorhenium Complexes [2]

Compound	P_{HPLC}	log P_{HPLC}	Compound	P_{HPLC}	log P_{HPLC}
2	2.66±0.06	0.4249	**10**	237360±23000	5.3754
4	2.06±0.12	0.3139	**11**	760	2.8808
5	2.73±0.04	0.4362	**6**	1.66±0.02	0.2201
7	577±14	2.7612	**12**	275±8	2.4393
8	982±48	2.9921			

For the unsilylated complexes, we found values of log P < 1 (0.2201-0.4362); for the silylated complexes, they vary from 2.4 to 5.4 and depend on the change in the steric environment about the silicon atom. The maximum value (log P 5.4) corresponds to compound **10**. The value of log P for (3-trimethylsiloxypropanethiolato)(3-thiapentane-1,5-dithiolato)oxorhenium(V) (**8**) is half that value. Both for silylated and for unsilylated complexes, the tendency toward an increase in log P in the series 3-(N-methyl)aza-, 3-oxa-, 3-thia is consistent with the electronic effect of the sulfur, oxygen, and nitrogen atoms of the tridentate ligands. For both types of complexes, an increase in lipophilicity as the chain of the monodentate ligand lengthens is characteristic.

We have studied the neurotropic properties and acute toxicity of the synthesized complexes (Table 2). The action of the compounds on the CNS was assessed from the indices of tests for hypoxic hypoxia, hexenal and ethanol narcosis, phenamine-induced hyperactivity, corazole-induced convulsions, electroshock, passive avoidance conditioned reflex, and retrograde amnesia.

All the studied compounds exhibit antihypoxic action to some degree, prolonging the life of mice under hypoxia conditions by 13% to 50%. In all the synthesized compounds, the pharmacological effect of interaction with phenamine is pronounced. Almost all of them are phenamine antagonists. The most active is compound **6**, which completely suppresses the antidepressant action. The only compound that definitely enhanced the action of phenamine, by almost a factor of two (83%), is compound **9**. We observe a consistent tendency toward weakening of the antiphenamine action as the heteroatom of the tridentate ligand changes (as we go from aza- to oxa- and then to thia-) in the series of both unsilylated and silylated hydroxyalkylthiolate complexes:

TABLE 2. Neurotropic Activity of Oxorhenium Complexes

Compound	*M*, % compared with control (100%)*					
	Test					
	Hypoxic hypoxia	Hexenal narcosis	Ethanol narcosis	Phenamine hyperactivity	Corazole convulsions, clonic/tonic	Retrograde amnesia
2	113*[2]	97	113	77*[2]	134*[2]/178*[2]	80*[2]
3	134*[2]	118*[2]	91	80	119*[2]/157*[2]	40
4	132*[2]	103	60*[2]	72*[2]	135*[2]/216*[2]	60
5	146*[2]	76*[2]	62*[2]	22*[2]	134*[2]/173*[2]	80*[2]
6	150*[2]	89	96	2*[2]	120/318*[2]	80*[2]
7	95	92	73	111	125*[2]/165*[2]	60
9 [1]	95	148*[2]	84	183*[2]	133*[2]/178*[2]	17
10	150*[2]	89	60*[2]	48*[2]	138*[2]/213*[2]	20
12	126*[2]	81*[2]	104	22*[2]	131*[2]/301*[2]	60

* *M* is the arithmetical-mean value of the neurotropic activity of the oxorhenium complexes.

*[2] Differences relative to the control are statistically significant with $P \leq 0.05$.

6 (98%) >> **4** (28%) > **2** (23%), **5** (78%) >> **3** (20%), **12** (78%) >> **7** (enhances the action of phenamine by 11%), and also when the complexes are silylated with the hydroxyethanethiolate monodentate ligand: **6** (98%) > **12** (78%), **2** (23%) > **7** > **9** (compounds **7** and **9** enhance the action of phenamine by 11% and 83% respectively).

For complexes with the hydroxypropanethiolate monodentate ligand, **3** and **10**, we observe the inverse effect: phenamine-induced hyperactivity is reduced upon triphenylsilylation.

In contrast to the action of the studied compounds in maximal electroshock, where no protective properties were observed, all the synthesized compounds exhibit anticonvulsive action in corazole-induced convulsions. As in the case of interaction with phenamine, the deciding role is played by the heteroatom of the tridentate ligand. The threshold for corazole-induced convulsions increases as the sulfur atom is replaced by an oxygen atom and then by a nitrogen atom in the series of both hydroxyalkylthiolato- and trimethylsiloxyethanethiolato-containing complexes:

2 (134/178) << **4** (135/216) << **6** (120/318);
3 (119/157) < **5** (134/173); **7** (125/165) << **12** (131/301).

The strongest anticonvulsive properties are exhibited by (3-methylazapentane-1,5-dithiolato) complexes **6** and **12**, which raise the threshold for corazole-induced convulsions by a factor of three (tonic phase). Introducing an organosilicon substituent has slight effect on the anticonvulsive properties of the complexes, except for compound **10**, the anticonvulsive action of which is 20% higher in the clonic phase and 60% higher in the tonic phase than for the unsilylated precursor.

The effect of the studied compounds on the duration of hexenal and ethanol narcosis in a dose of 5 mg/kg is weak. However, introducing a triphenylsiloxy substituent into the (2-hydroxyethanethiolato)-3-thiapentane complex **2** increases the duration of hexenal narcosis by 48%, while introducing it into compound **3** shortens the ethanol narcosis time by 40%. For 3-oxapentane-1,5-dithiolate complexes **4** and **5**, antagonistic activity with respect to ethanol is characteristic.

Almost all the studied complexes prevent retrograde amnesia by 60%-80%.

We did not observe a direct relationship between neurotropic activity and lipophilicity in these studies; more likely a role is played by structural factors.

Although introducing a trimethylsilyl group has little effect on the indices for hypoxia, duration of hexenal and ethanol narcosis, and anticonvulsive action, introducing a triphenylsilyl group (and increasing the lipophilicity up to 5.37) even more considerably changes the properties of the starting hydroxyl-containing

TABLE 3. Bond Lengths in Structures **6a** and **6b** of Compound **6**

Bond	*l*, Å	Bond	*l*, Å	Bond	*l*, Å
$Re_a–O_{(12a)}$	1.699(11)	$N_{(4a)}–C_{(5a2)}$	1.58(4)	$Re_b–S_{(7b)}$	2.292(4)
$Re_a–N_{(4a)}$	2.202(11)	$N_{(4a)}–C_{(13a1)}$	1.66(6)	$Re_b–S_{(8b)}$	2.309(4)
$Re_a–S_{(1a)}$	2.276(4)	$C_{(5a1)}–C_{(6a)}$	1.60(4)	$S_{(1b)}–C_{(2b)}$	1.83(2)
$Re_a–S_{(7a)}$	2.280(4)	$C_{(5a2)}–C_{(6a)}$	1.36(5)	$C_{(2b)}–C_{(3b)}$	1.48(3)
$Re_a–S_{(8a)}$	2.300(4)	$C_{(6a)}–S_{(7a)}$	1.80(2)	$C_{(3b)}–N_{(4b)}$	1.477(18)
$S_{(1a)}–C_{(2a)}$	1.814(18)	$S_{(8a)}–C_{(9a)}$	1.825(14)	$N_{(4b)}–C_{(13b)}$	1.45(2)
$C_{(2a)}–C_{(3a1)}$	1.35(4)	$C_{(9a)}–C_{(10a)}$	1.52(2)	$N_{(4b)}–C_{(5b)}$	1.53(2)
$C_{(2a)}–C_{(3a2)}$	1.53(3)	$C_{(10a)}–O_{(11a)}$	1.430(19)	$C_{(5b)}–C_{(6b)}$	1.38(3)
$C_{(3a1)}–N_{(4a)}$	1.65(4)			$C_{(6b)}–S_{(7b)}$	1.826(16)
$C_{(3a2)}–N_{(4a)}$	1.48(3)	$Re_b–O_{(12b)}$	1.685(10)	$S_{(8b)}–C_{(9b)}$	1.865(16)
$N_{(4a)}–C_{(13a2)}$	1.38(4)	$Re_b–N_{(4b)}$	2.205(13)	$C_{(9b)}–C_{(10b)}$	1.49(2)
$N_{(4a)}–C_{(5a1)}$	1.42(4)	$Re_b–S_{(1b)}$	2.289(4)	$C_{(10b)}–O_{(11b)}$	1.37(2)

TABLE 4. Bond Angles in Structures **6a** and **6b**

Angle	ω, deg.	Angle	ω, deg.
$O_{(12a)}$–Re_a–$N_{(4a)}$	98.0(6)	$C_{(13a1)}$–$N_{(4a)}$–Re_a	112(3)
$O_{(12a)}$–Re_a–$S_{(1a)}$	118.2(4)	$N_{(4a)}$–$C_{(5a1)}$–$C_{(6a)}$	107(2)
$N_{(4a)}$–Re_a–$S_{(1a)}$	82.9(3)	$C_{(6a)}$–$C_{(5a2)}$–$N_{(4a)}$	111(4)
$O_{(12a)}$–Re_a–$S_{(7a)}$	115.9(4)	$C_{(5a2)}$–$C_{(6a)}$–$C_{(5a1)}$	43(3)
$N_{(4a)}$–Re_a–$S_{(7a)}$	83.6(4)	$C_{(5a2)}$–$C_{(6a)}$–$S_{(7a)}$	121(3)
$S_{(1a)}$–Re_a–$S_{(7a)}$	125.40(18)	$C_{(5a1)}$–$C_{(6a)}$–$S_{(7a)}$	110.9(15)
$O_{(12a)}$–Re_a–$S_{(8a)}$	103.6(4)	$C_{(6a)}$–$S_{(7a)}$–Re_a	101.3(7)
$N_{(4a)}$–Re_a–$S_{(8a)}$	158.4(4)	$C_{(9a)}$–$S_{(8a)}$–Re_a	110.4(4)
$S_{(1a)}$–Re_a–$S_{(8a)}$	88.51(14)	$C_{(10a)}$–$C_{(9a)}$–$S_{(8a)}$	110.8(9)
$S_{(7a)}$–Re_a–$S_{(8a)}$	85.33(15)	$O_{(11a)}$–$C_{(10a)}$–$C_{(9a)}$	111.3(13)
$C_{(2a)}$–$S_{(1a)}$–Re_a	102.6(6)	$O_{(12b)}$–Re_b–$N_{(4b)}$	103.8(5)
$C_{(3a1)}$–$C_{(2a)}$–$C_{(3a2)}$	54(2)	$O_{(12b)}$–Re_b–$S_{(1b)}$	113.9(4)
$C_{(3a1)}$–$C_{(2a)}$–$S_{(1a)}$	115(2)	$N_{(4b)}$–Re_b–$S_{(1b)}$	81.7(3)
$C_{(3a2)}$–$C_{(2a)}$–$S_{(1a)}$	108.5(13)	$O_{(12b)}$–Re_b–$S_{(7b)}$	111.9(4)
$C_{(2a)}$–$C_{(3a1)}$–$N_{(4a)}$	108(2)	$N_{(4b)}$–Re_b–$S_{(7b)}$	83.0(3)
$N_{(4a)}$–$C_{(3a2)}$–$C_{(2a)}$	108(2)	$S_{(1b)}$–Re_b–$S_{(7b)}$	133.95(18)
$C_{(13a2)}$–$N_{(4a)}$–$C_{(5a1)}$	133(3)	$O_{(12b)}$–Re_b–$S_{(8b)}$	105.2(4)
$C_{(13a2)}$–$N_{(4a)}$–$C_{(3a2)}$	119(3)	$N_{(4b)}$–Re_b–$S_{(8b)}$	150.8(3)
$C_{(5a1)}$–$N_{(4a)}$–$C_{(3a2)}$	67.6(19)	$S_{(1b)}$–Re_b–$S_{(8b)}$	89.68(17)
$C_{(13a2)}$–$N_{(4a)}$–$C_{(5a2)}$	100(3)	$S_{(7b)}$–Re_b–$S_{(8b)}$	83.12(16)
$C_{(5a1)}$–$N_{(4a)}$–$C_{(5a2)}$	43(3)	$C_{(2b)}$–$S_{(1b)}$–Re_b	102.6(6)
$C_{(3a2)}$–$N_{(4a)}$–$C_{(5a2)}$	107(3)	$C_{(3b)}$–$C_{(2b)}$–$S_{(1b)}$	107.5(16)
$C_{(13a2)}$–$N_{(4a)}$–$C_{(3a1)}$	74(3)	$N_{(4b)}$–$C_{(3b)}$–$C_{(2b)}$	110.6(14)
$C_{(5a1)}$–$N_{(4a)}$–$C_{(3a1)}$	113(2)	$C_{(13b)}$–$N_{(4b)}$–$C_{(3b)}$	111.7(15)
$C_{(3a2)}$–$N_{(4a)}$–$C_{(3a1)}$	49.7(19)	$C_{(13b)}$–$N_{(4b)}$–$C_{(5b)}$	108.4(16)
$C_{(5a2)}$–$N_{(4a)}$–$C_{(3a1)}$	138(3)	$C_{(3b)}$–$N_{(4b)}$–$C_{(5b)}$	102.8(13)
$C_{(13a2)}$–$N_{(4a)}$–$C_{(13a1)}$	24(4)	$C_{(13b)}$–$N_{(4b)}$–Re_b	108.0(10)
$C_{(5a1)}$–$N_{(4a)}$–$C_{(13a1)}$	113(3)	$C_{(3b)}$–$N_{(4b)}$–Re_b	113.9(9)
$C_{(3a2)}$–$N_{(4a)}$–$C_{(13a1)}$	131(4)	$C_{(5b)}$–$N_{(4b)}$–Re_b	111.9(11)
$C_{(5a2)}$–$N_{(4a)}$–$C_{(13a1)}$	76(3)	$C_{(6b)}$–$C_{(5b)}$–$N_{(4b)}$	114.6(16)
$C_{(3a1)}$–$N_{(4a)}$–$C_{(13a1)}$	95(4)	$C_{(5b)}$–$C_{(6b)}$–$S_{(7b)}$	110.1(14)
$C_{(13a2)}$–$N_{(4a)}$–Re_a	107.4(18)	$C_{(6b)}$–$S_{(7b)}$–Re_b	100.4 (5)
$C_{(5a1)}$–$N_{(4a)}$–Re_a	113.3(18)	$C_{(9b)}$–$S_{(8b)}$–Re_b	109.4 (6)
$C_{(3a2)}$–$N_{(4a)}$–Re_a	110.9(11)	$C_{(10b)}$–$C_{(9b)}$–$S_{(8b)}$	111.1 (10)
$C_{(5a2)}$–$N_{(4a)}$–Re_a	113(2)	$O_{(11b)}$–$C_{(10b)}$–$C_{(9b)}$	111.8 (16)
$C_{(3a1)}$–$N_{(4a)}$–Re_a	108.3(15)		

complex. Thus compound **9** definitely prolongs the effect of hexenal (by a factor of 1.5), with the highest effect among all the synthesized compounds, while compound **10** has higher antihypoxic and anticonvulsive action compared with its unsilylated precursor **3** and also shortens the duration of ethanol narcosis.

TABLE 5. Bond Lengths in the Structure of Compound **10**

Bond	*l*, Å	Bond	*l*, Å	Bond	*l*, Å
Re–O_{Re}	1.624(12)	$C_{(3)}$–$S_{(4)}$	1.76(2)	$C_{(11)}$–$O_{(12)}$	1.44(3)
Re–$S_{(7)}$	2.279(5)	$S_{(4)}$–$C_{(5)}$	1.85(2)	$O_{(12)}$–Si	1.619(14)
Re–$S_{(1)}$	2.290(6)	$C_{(5)}$–$C_{(6)}$	1.46(3)	$C_{(13)}$–Si	1.85(2)
Re–$S_{(8)}$	2.310(5)	$C_{(6)}$–$S_{(7)}$	1.817(18)	$C_{(19)}$–Si	1.86(2)
Re–$S_{(4)}$	2.382(5)	$S_{(8)}$–$C_{(9)}$	1.83(2)	Si–$C_{(25)}$	1.889(19)
$S_{(1)}$–$C_{(2)}$	1.82(3)	$C_{(9)}$–$C_{(10)}$	1.52(3)		
$C_{(2)}$–$C_{(3)}$	1.51(3)	$C_{(10)}$–$C_{(11)}$	1.48(3)		

TABLE 6. Bond Angles in the Structure of Compound **10**

Angle	ω, deg.	Angle	ω, deg.
O_{Re}–Re–$S_{(7)}$	116.7(7)	$S_{(7)}$–$C_{(6)}$–$H_{(6B)}$	109.2
O_{Re}–Re–$S_{(1)}$	114.6(7)	$H_{(6A)}$–$C_{(6)}$–$H_{(6B)}$	107.9
$S_{(7)}$–Re–$S_{(1)}$	128.5(2)	$C_{(6)}$–$S_{(7)}$–Re	107.0(8)
O_{Re}–Re–$S_{(8)}$	105.7(6)	$C_{(9)}$–$S_{(8)}$–Re	110.8(7)
$S_{(7)}$–Re–$S_{(8)}$	87.52(18)	$C_{(10)}$–$C_{(9)}$–$S_{(8)}$	113.7(13)
$S_{(1)}$–Re–$S_{(8)}$	83.2(2)	$C_{(10)}$–$C_{(9)}$–$H_{(9A)}$	108.8
O_{Re}–Re–$S_{(4)}$	98.1(6)	$S_{(8)}$–$C_{(9)}$–$H_{(9A)}$	108.8
$S_{(7)}$–Re–$S_{(4)}$	84.13(18)	$C_{(10)}$–$C_{(9)}$–$H_{(9B)}$	108.8
$S_{(1)}$–Re–$S_{(4)}$	84.6(2)	$S_{(8)}$–$C_{(9)}$–$H_{(9B)}$	108.8
$S_{(8)}$–Re–$S_{(4)}$	156.03(19)	$H_{(9A)}$–$C_{(9)}$–$H_{(9B)}$	107.7
$C_{(2)}$–$S_{(1)}$–Re	105.2(7)	$C_{(11)}$–$C_{(10)}$–$C_{(9)}$	117.6(18)
$C_{(3)}$–$C_{(2)}$–$S_{(1)}$	113.3(16)	$C_{(11)}$–$C_{(10)}$–$H_{(10A)}$	107.9
$C_{(3)}$–$C_{(2)}$–$H_{(2A)}$	108.9	$C_{(9)}$–$C_{(10)}$–$H_{(10A)}$	107.9
$S_{(1)}$–$C_{(2)}$–$H_{(2A)}$	108.9	$C_{(11)}$–$C_{(10)}$–$H_{(10B)}$	107.9
$C_{(3)}$–$C_{(2)}$–$H_{(2B)}$	108.9	$C_{(9)}$–$C_{(10)}$–$H_{(10B)}$	107.9
$S_{(1)}$–$C_{(2)}$–$H_{(2B)}$	108.9	$H_{(10A)}$–$C_{(10)}$–$H_{(10B)}$	107.2
$H_{(2A)}$–$C_{(2)}$–$H_{(2B)}$	107.7	$O_{(12)}$–$C_{(11)}$–$C_{(10)}$	112.5(19)
$C_{(2)}$–$C_{(3)}$–$S_{(4)}$	109.7(15)	$O_{(12)}$–$C_{(11)}$–$H_{(11A)}$	109.1
$C_{(2)}$–$C_{(3)}$–$H_{(3A)}$	109.7	$C_{(10)}$–$C_{(11)}$–$H_{(11A)}$	109.1
$S_{(4)}$–$C_{(3)}$–$H_{(3A)}$	109.7	$O_{(12)}$–$C_{(11)}$–$H_{(11B)}$	109.1
$C_{(2)}$–$C_{(3)}$–$H_{(3B)}$	109.7	$C_{(10)}$–$C_{(11)}$–$H_{(11B)}$	109.1
$S_{(4)}$–$C_{(3)}$–$H_{(3B)}$	109.7	$H_{(11A)}$–$C_{(11)}$–$H_{(11B)}$	107.8
$H_{(3A)}$–$C_{(3)}$–$H_{(3B)}$	108.2	$C_{(11)}$–$O_{(12)}$–Si	125.6(13)
$C_{(3)}$–$S_{(4)}$–$C_{(5)}$	105.3(11)	$C_{(18)}$–$C_{(13)}$–Si	122.7(19)
$C_{(3)}$–$S_{(4)}$–Re	108.1(7)	$C_{(14)}$–$C_{(13)}$–Si	122.0(16)
$C_{(5)}$–$S_{(4)}$–Re	105.8(8)	$C_{(24)}$–$C_{(19)}$–Si	126.0(18)
$C_{(6)}$–$C_{(5)}$–$S_{(4)}$	107.6(18)	$C_{(21)}$–$C_{(19)}$–Si	119.9(17)
$C_{(6)}$–$C_{(5)}$–$H_{(5A)}$	110.2	$O_{(12)}$–Si–$C_{(13)}$	111.2(9)
$S_{(4)}$–$C_{(5)}$–$H_{(5A)}$	110.2	$O_{(12)}$–Si–$C_{(19)}$	110.8(9)
$C_{(6)}$–$C_{(5)}$–$H_{(5B)}$	110.2	$C_{(13)}$–Si–$C_{(19)}$	108.7(10)
$S_{(4)}$–$C_{(5)}$–$H_{(5B)}$	110.2	$O_{(12)}$–Si–$C_{(25)}$	104.8(8)
$H_{(5A)}$–$C_{(5)}$–$H_{(5B)}$	108.5	$C_{(13)}$–Si–$C_{(25)}$	110.2(9)
$C_{(5)}$–$C_{(6)}$–$S_{(7)}$	112.2(15)	$C_{(19)}$–Si–$C_{(25)}$	111.2(9)
$C_{(5)}$–$C_{(6)}$–$H_{(6A)}$	109.2	$C_{(30)}$–$C_{(25)}$–Si	121.8(16)
$S_{(7)}$–$C_{(6)}$–$H_{(6A)}$	109.2	$C_{(26)}$–$C_{(25)}$–Si	118.5(17)
$C_{(5)}$–$C_{(6)}$–$H_{(6B)}$	109.2		

With regard to the phenamine test, in some cases probably we can talk about a tendency toward weakening of the antagonistic properties relative to phenamine, and the appearance of the opposite effect with introduction of a silyl group (compare **2, 7** and **9**; **6** and **12**).

Study of the acute toxicity of the compounds confirms the previously indicated presence of a tendency toward a decrease in toxicity when a trialkylsilyl group is introduced.

TABLE 7. Bond Lengths in the Structure of Compound **12**

Bond	*l*, Å	Bond	*l*, Å	Bond	*l*, Å
Re–$O_{(17)}$	1.693(14)	$C_{(3)}$–$N_{(4)}$	1.51(3)	$C_{(10)}$–$O_{(11)}$	1.46(3)
Re–$N_{(4)}$	2.157(19)	$N_{(4)}$–$C_{(5)}$	1.46(3)	$O_{(11)}$–$Si_{(12)}$	1.646(17)
Re–$S_{(1)}$	2.280(6)	$N_{(4)}$–$C_{(16)}$	1.48(3)	$Si_{(12)}$–$C_{(15)}$	1.83(3)
Re–$S_{(7)}$	2.280(7)	$C_{(5)}$–$C_{(6)}$	1.42(4)	$Si_{(12)}$–$C_{(14)}$	1.84(3)
Re–$S_{(8)}$	2.302(6)	$C_{(6)}$–$S_{(7)}$	1.85(3)	$Si_{(12)}$–$C_{(13)}$	1.86(3)
$S_{(1)}$–$C_{(2)}$	1.81(2)	$S_{(8)}$–$C_{(9)}$	1.85(2)		
$C_{(2)}$–$C_{(3)}$	1.58(3)	$C_{(9)}$–$C_{(10)}$	1.47(3)		

TABLE 8. Bond Angles in the Structure of Compound **12**

Angle	ω, deg.	Angle	ω, deg.	Angle	ω, deg.
$O_{(17)}$–Re–$N_{(4)}$	95.8(7)	$C_{(3)}$–$C_{(2)}$–$S_{(1)}$	107.7(14)	$C_{(9)}$–$S_{(8)}$–Re	112.6(9)
$O_{(17)}$–Re–$S_{(1)}$	116.3(6)	$N_{(4)}$–$C_{(3)}$–$C_{(2)}$	107(2)	$C_{(10)}$–$C_{(9)}$–$S_{(8)}$	109.8(18)
$N_{(4)}$–Re–$S_{(1)}$	83.5(5)	$C_{(5)}$–$N_{(4)}$–$C_{(16)}$	108(2)	$O_{(11)}$–$C_{(10)}$–$C_{(9)}$	112(2)
$O_{(17)}$–Re–$S_{(7)}$	118.9(6)	$C_{(5)}$–$N_{(4)}$–$C_{(3)}$	106.4(19)	$C_{(10)}$–$O_{(11)}$–$Si_{(12)}$	126.4(15)
$N_{(4)}$–Re–$S_{(7)}$	82.8(5)	$C_{(16)}$–$N_{(4)}$–$C_{(3)}$	105.3(19)	$O_{(11)}$–$Si_{(12)}$–$C_{(15)}$	111.7(13)
$S_{(1)}$–Re–$S_{(7)}$	124.1(3)	$C_{(5)}$–$N_{(4)}$–Re	114.4(15)	$O_{(11)}$–$Si_{(12)}$–$C_{(14)}$	104.9(12)
$O_{(17)}$–Re–$S_{(8)}$	106.5(6)	$C_{(16)}$–$N_{(4)}$–Re	110.3(16)	$C_{(15)}$–$Si_{(12)}$–$C_{(14)}$	110.2(16)
$N_{(4)}$–Re–$S_{(8)}$	157.5(5)	$C_{(3)}$–$N_{(4)}$–Re	111.5(14)	$O_{(11)}$–$Si_{(12)}$–$C_{(13)}$	110.0(12)
$S_{(1)}$–Re–$S_{(8)}$	89.2(2)	$C_{(6)}$–$C_{(5)}$–$N_{(4)}$	112(2)	$C_{(15)}$–$Si_{(12)}$–$C_{(13)}$	109.3(15)
$S_{(7)}$–Re–$S_{(8)}$	83.7(3)	$C_{(5)}$–$C_{(6)}$–$S_{(7)}$	113(2)	$C_{(14)}$–$Si_{(12)}$–$C_{(13)}$	110.7(13)
$C_{(2)}$–$S_{(1)}$–Re	103.5(6)	$C_{(6)}$–$S_{(7)}$–Re	101.4(10)		

EXPERIMENTAL

The ^{1}H and ^{29}Si NMR spectra were recorded on a Varian Mercury 200 spectrometer (200 MHz) in $CDCl_3$, internal standard HMDS. The reaction and purity of the compounds were monitored on Polygram R Sil G/UV-254 plates in a chloroform–methanol 19:1 (by volume) system. The compounds were separated by column chromatography on Kieselgel 60 (Merck) silica gel.

Chloro(3-thiapentane-1,5-dithiolato)oxorhenium(V) (1) was obtained according to the procedure in [3].

(2-Hydroxyethane- (2), (3-Hydroxypropane- (3), (2-Triphenylsiloxyethane- (9) and (3-Triphenylsiloxypropanethiolato)(3-thiapentane-1,5-dithiolato)oxorhenium(V) (10) were synthesized according to the procedure in [1].

(2-Hydroxyethanethiolato)(3-oxapentane-1,5-dithiolato)oxorhenium(V) (4). A solution of 3-oxapentane-1,5-dithiol (31.8 mg, 0.3 mmol) and 2-mercaptoethanol (31.2 mg, 1.33 mmol) in chloroform (4 ml) was added dropwise with stirring to a suspension (cooled down to 0°C) of (tetrabutylammonium)-tetrachlorooxorhenate(V) (175.8 mg, 0.3 mmol) in chloroform (10 ml). As the solution was added, a dark cherry red color developed gradually. The mixture was stirred for 30 min, bringing the temperature up to room temperature. The solvent was evaporated under vacuum, the residue was dissolved in a chloroform–methanol mixture (ratio 19:1 by volume) and the latter was purified by column chromatography, using the same solvent mixture as the eluent. After evaporation of the solvent, compound **4** was isolated as a light pink powder in yield 45.8 mg (37%); mp 95-97°C. R_f 0.26. ^{1}H NMR spectrum, δ, ppm: 1.93 (2H, br. s, SCH_2); 3.37, 3.52, 3.71, 4.69 (2H, m; 2H, m; 2H, m; 2H, t, $SCH_2CH_2OCH_2CH_2S$); 4.09 (2H, br. s, OCH_2). Found, %: C 17.52; H 3.10; S 23.10. $C_6H_{13}O_3ReS_3$. Calculated, %: C 17.35; H 3.13; S 23.13.

(3-Hydroxypropanethiolato)(3-oxapentane-1,5-dithiolato)oxorhenium(V) (5). A solution of 3-oxapentane-1,5-dithiol (53 μl, 0.5 mmol) and 3-mercaptopropanol (50.6 mg, 47.4 μl, 0.55 mmol) in chloroform (5 ml) was added dropwise to a solution of (tetrabutylammonium)tetrachlorooxorhenate(V) (293 mg, 0.5 mmol) in ethanol (10 ml) at 0°C.

The mixture was stirred for 30 min at room temperature, then the solvent was evaporated, the residue was dissolved in chloroform, and the reaction product was isolated by column chromatography. The eluent was chloroform–methanol, 19:1. After removal of the solvent, compound **5** was obtained as a cherry-red oil in a yield of 68.7 mg (32%). R_f 0.27. ^{1}H NMR spectrum, δ, ppm: 2.16 (2H, m, C–CH_2–C); 3.31-3.85 (10H, m, $SCH_2CH_2OCH_2CH_2S$, SCH_2, OCH_2); 4.66 (2H, br. s, $SCH_2CH_2OCH_2CH_2S$). Found, %: C 20.01; H 3.50; S 22.24. $C_7H_{15}O_3ReS_3$. Calculated, %: C 19.68; H 3.50; S 22.38.

(2-Hydroxyethanethiolato)[3-(N-methyl)azapentane-1,5-dithiolato]oxorhenium (V) (6). A mixture of 3-(N-methylaza)-1,5-dithiol oxalate (72.3 mg, 0.3 mmol) and mercaptoethanol (25.7 mg, 23 μl, 0.33 mmol) in methanol (3 ml) was added with stirring to a suspension of *trans*-monooxotrichloro-bis(triphenylphosphine)rhenium(V) (250 mg, 0.3 mmol) in methanol (30 ml). The reaction mixture was alkalinized using a 0.1 M solution of sodium methoxide in methanol, and then boiled for 3 h. The yellow suspension then was converted to a dark green solution. After the suspension was cooled down to room temperature, methylene chloride (25 ml) was added to the reaction mixture and it was acidified to pH 4 with dilute hydrochloric acid. The organic phase was removed, and the aqueous phase was re-extracted with chloroform. The organic extracts were combined and dried over Na_2SO_4. Then the solvent was removed and the reaction product was isolated by column chromatography in the system chloroform–methanol, 19:1 as the mobile phase. When the solvent was slowly evaporated, compound **6** crystallized as dark-green crystals in a yield of 101.4 mg (79%); mp 127-129°C. R_f 0.24. ^{1}H NMR spectrum, δ, ppm: 2.66 (2H, m, SCH_2); 3.17, 3.56 (4H, m; 2H, m, $SCH_2CH_2NMeCH_2CH_2S$); 3.37 (3H, s, CH_3N); 4.00 (4H, m, OCH_2, $SCH_2CH_2NMeCH_2CH_2S$). Found, %: C 19.82; H 3.78; S 22.44; N 3.17. $C_7H_{16}NO_2ReS_3$. Calculated, %: C 19.63; H 3.74; S 22.43; N 3.27.

(2-Trimethylsiloxyethanethiolato)(3-thiapentane-1,5-dithiolato)oxorhenium(V) (7). Triethylamine (50 μl, 0.360 mmol) and then with cooling trimethylchlorosilane (17.2 mg, 20 μl, 0.158 mmol) were added to complex **2** (60.0 mg, 0.139 mmol) in chloroform (4 ml). The reaction mixture was stirred at room temperature for 1 h. The course of the reaction was monitored by TLC. After removal of the solvent, the reaction product was isolated by column chromatography. Eluent chloroform–methanol, 19:1. The fractions with R_f 0.67 were combined, evaporated down, and lyophilized. Compound **7** was obtained as a light-beige powder in a yield of 42.0 mg (64%); mp 101-102°C. ^{1}H NMR spectrum, δ, ppm: 0.15 (9H, s, $SiMe_3$); 1.96, 3.12, 4.30 (2H, m; 2H, td; 2H, dd, $SCH_2CH_2NMeCH_2CH_2S$); 3.93 (4H, m, SCH_2, $SCH_2CH_2NMeCH_2CH_2S$); 4.06 (2H, t, OCH_2). Found, %: C 21.47; H 4.20;S 25.65. $C_9H_{21}O_2ReS_4Si$. Calculated, %: C 21.47; H 4.18; S 25.45.

(3-Trimethylsiloxypropanethiolato)(3-thiapentane-1,5-dithiolato)oxorhenium(V) (8) was obtained from of complex **2** (66.5 mg, 0.149 mmol), trimethylchlorosilane (25.8 mg, 30 μl, 0.238 mmol), and triethylamine (30.2 mg, 42 μl, 0.298 mmol) according to the procedure described for synthesis of compound **7** in a yield of 63.2 mg (82%); mp 48-49°C. R_f 0.69. ^{1}H NMR spectrum, δ, ppm: 0.12 (9H, s, $SiMe_3$); 1.96, 3.10, 4.28 (2H, m; 2H, m; 2H, dd, $SCH_2CH_2SCH_2CH_2S$); 2.12 (2H, m, C–CH_2–C); 3.74-3.99 (6H, m, $SCH_2CH_2SCH_2CH_2S$, SCH_2, OCH_2). Found, %; C 23.28; H 4.42; S 24.61. $C_{10}H_{23}O_2ReS_4Si$. Calculated, %: C 23.21; H 4.45; S 24.76.

(2-Triphenylsiloxyethanethiolato)(3-thiapentane-1,5-dithiolato)oxorhenium(V) (9) [1]. 1,2-Bis-(triphenylsilyl)mercaptoethanol (**13**) (122.0 mg, 0.2054 mmol) and triethylamine (10 mg, 14.3 μl, 0.1027 mmol) were added to a boiling solution of complex **1** (40 mg, 0.1023 mmol) in acetonitrile (5 ml). The reaction mixture was boiled for 20 min. After cooling, the solvent was evaporated, the residue was dissolved in chloroform. The reaction product was isolated by column chromatography. Eluent chloroform–methanol, 19:1. Yield 64.4 mg (91%).

(3-Triphenylsiloxypropanethiolato)(3-thiapentane-1,5-dithiolato)oxorhenium(V) (10) [1]. ^{29}Si NMR spectrum, δ, ppm: -75.46.

(3-Trimethylsiloxypropanethiolato)(3-oxapentane-1,5-dithiolato)oxorhenium(V) (11) was obtained from complex **5** (92.5 mg, 0.216 mmol), trimethylchlorosilane (35.15 mg, 41 μl, 0.324 mmol), and triethylamine (43.63 mg, 60 μl, 0.432 mmol) according to the procedure described for compound **7**. The reaction product was isolated as a dark cherry-red oil. R_f 0.78. ^{1}H NMR spectrum, δ, ppm: 0.11 (9H, s, $SiMe_3$); 2.18 (2H, m, C–CH_2–C); 3.30-3.81 (10H, m, $SCH_2CH_2OCH_2CH_2S$, SCH_2, OCH_2); 4.64 (2H, br. s, $SCH_2CH_2OCH_2CH_2S$). Found, %: C 23.81; H 4.51; S 19.18. $C_{10}H_{23}O_3ReS_3Si$. Calculated, %: C 23.95; H 4.59; S 19.16.

(2-Trimethylsiloxyethanethiolato)[3-(N-methyl)azapentane-1,5-dithiolato]oxorhenium(V) (12) was obtained from complex **6** (80 mg, 0.187 mmol), trimethylchlorosilane (60.8 mg, 71 μl, 0.561 mmol), and triethylamine (75.6 mg, 104 μl, 0.748 mmol), similarly as for compound **7**. The reaction product was isolated by column chromatography. Eluent chloroform–methanol, 19:1. After crystallization from ether, compound **12** was obtained as dark-green crystals in a yield of 77.6 mg (83%); mp 112-113°C. R_f 0.72. ^{1}H NMR spectrum, δ, ppm: 0.14 (9H, s, $SiMe_3$); 2.63 (2H, t, SCH_2); 3.14, 3.55 (4H, m; 2H, t, $SCH_2CH_2NMeCH_2CH_2S$); 3.35 (3H, s, NCH_3); 3.89 (4H, br. s, $SCH_2CH_2NMeCH_2CH_2S$). ^{29}Si NMR spectrum, δ, ppm: +18.45. Found, %: C 24.12; H 4.77; S 19.32; N 2.79. $C_{10}H_{24}NO_2ReS_3Si$. Calculated, %: C 24.00; H 4.80; S 19.20; N 2.80.

1,2-Bis(triphenylsilyl)mercaptoethanol (13). A solution of triphenylchlorosilane (1.47 g, 5 mmol) in ether (3 ml) was added dropwise with cooling to a mixture of 2-mercaptoethanol (0.125 g, 0.18 ml, 2.5 mmol), triethylamine (0.505 g, 0.7 ml, 5 mmol), and ether (10 ml). The reaction mixture was stirred at room temperature for 2 h. The precipitate of ammonium salt formed was filtered out, the filtrate was evaporated down to dryness, the residue was extracted with hexane, and the extract was evaporated down. After removal of the hexane, the yield of compound **13** was 1.25 g (85%); mp 58°C. ^{1}H NMR spectrum, δ, ppm: 2.85 (2H, t, SCH_2); 4.11 (2H, t, OCH_2); 7.56-7.89 (30H, m, Ar). ^{13}C NMR spectrum, δ, ppm: 26.9 (SCH_2); 65.5 (OCH_2); 127.7, 127.8, 130.0, 133.7, 134.9, 135.2 (Ar). Found, %: C 77.00; H 5.76; S 5.41. $C_{38}H_{34}OSSi_2$. Calculated, %: C 76.77; H 5.72; S 5.39.

An X-ray Diffraction Study of single crystals of compounds **6**, **10**, and **12** was performed at 25°C on a Syntex P21 automatic 4-circle diffractometer (MoKα radiation, graphite monochromator, 2θmax = 50°), ω/2θ scanning (**6** and **12**) and ω/ω scanning (**10**). The basic crystallographic characteristics of the crystals of the studied compounds are given in Table 9.

TABLE 9. Crystallographic Data for Compounds **6**, **10**, and **12**

	Compound **6**	Compound **10**	Compound **12**
Empirical formula	$C_{14}H_{32}N_2O_4Re_2S_6$	$C_{25}H_{29}O_2ReS_4Si$	$C_{10}H_{24}NO_2ReS_3Si$
Molecular weight	857.18	704.01	500.77
Syngony	Triclinic	Monoclinic	Monoclinic
Space group	*P*-1	*P* 2_1/n	*P* 2_1/c
Lattice parameters			
a, Å	10.119(2)	7.597(2)	10.544(2)
b, Å	11.109(3)	39.554(8)	10.553(3)
c, Å	11.995(2)	9.453(2)	18.186(4)
α, degrees	105.49(2)	90	90
β, degrees	93.93(2)	107.66(3)	120.33(2)
γ, degrees	103.00(3)	90	90
Volume of cell, *V*, Å^3	1254.2(5)	2706.7(11)	1746.6(7)
Number of molecules per cell, *Z*	2	4	4
Density, *d*, g/cm^3	2.270	1.728	1.904
Number of reflections with $I > 2\sigma(I)$	3658	3346	2146
Number of refined parameters	281	298	163
R factor	0.0530	0.0753	0.0744

The structures were deciphered by the direct method and refined by full-matrix least-squares in the anisotropic approximation, taking into account the coordinates of the hydrogen atoms, calculated from geometric considerations. The calculations were performed by the software in [4, 5]. The spatial arrangement of the atoms with their labels is shown in Figs. 1-3. The interatomic distances and bond angles are given in Tables 3-8. The coordinates of the atoms with the crystallographic characteristics of compound **6**, **10**, and **12** have been deposited in the Cambridge Structural Data Bank (CSD) under the numbers 150661-150663 respectively.

BIOLOGICAL SECTION

The neurotropic activity was studied in mice of the BALB/c and JCR lines weighing 18-23 g in Autumn. The temperature in the laboratory and the vivarium was maintained at 21±2°C while conducting the experiments. The study compounds were dissolved in DMSO and injected intraperitoneally 1 h before setting up the test. The control animals were injected with the same volume of DMSO into the peritoneal cavity. We made a comparative assessment of the action of the study compound in a dose of 5 mg/kg on the indices of hypoxia, hexenal and ethanol narcosis, phenamine-induced hyperactivity, corazole-induced convulsions, training and the Porsolt test, in groups of animals each including 6 individuals.

The action of the compounds on the CNS was assessed by the tests:

1) anticonvulsive activity, studied by the maximal electroshock test (a.c. current 50 mA, frequency 50 pulses per second, stimulus duration 0.2 sec) and the corazole-induced convulsions test, induced by intravenous titration with a 1% solution of corazole at a rate of 0.01 ml/sec);
2) effect on the duration of hexenal narcosis (0.4% hexenal solution intravenously in a dose of 70 mg/kg); effect on duration of ethanol narcosis (4 g/kg intraperitoneally);
3) effect on survival time of animals under hypoxic hypoxia conditions, induced by placing the mice (one by one) into a hermetically sealed chamber of volume 220 cm^3 without absorption of carbon dioxide;
4) change in the degree of phenamine-induced hyperactivity (0.4% phenamine solution subcutaneously in a dose of 10 mg/kg);
5) effect on training processes and retrograde amnesia induced by electroshock.

We also determined the acute toxicity for intraperitoneal injection and established the median lethal doses (LD_{50}, mg/kg).

The experimental data were treated statistically, determining the median effective doses (ED_{50}) and median lethal doses (LD_{50}) by the rapid method in [6]; to assess the mean duration of the narcotic action of hexenal and ethanol, phenamine-induced hyperactivity, hypoxia, protective properties in corazole-induced convulsions, we calculated the arithmetic-mean values and their standard error ($M \pm m$) compared with the corresponding control data. We used the Student's t test to assess the significance of the difference between the means. The differences were considered significant for probability level $P \leq 0.05$.

The authors would like to thank the Latvian Taiho Foundation and the BMBF International Bureau (Germany) for supporting this research.

REFERENCES

1. H. Spies, Th. Fietz, A. Zablotskaya, S. Belyakov, and E. Lukevics, *Khim. Geterotsikl. Soedin.*, 116 (1999).
2. A. Zablotskaya, I. Segal, A. Kemme, E. Lukevics, R. Berger, and H. Spies, *Ann. Rep. FZR*, **270**, 156 (1999).
3. Th. Fietz, H. Spies, H.-J. Pietzsch, and P. Leibnitz, *Inorg. Chim. Acta*, **231**, 233 (1995).

4. G. M. Sheldrick, *SHELX97*. Program for the Solution of Crystal Structures, University of Göttingen, Germany.
5. G. M. Sheldrick, *SHELXL97*. Program for the Refinement of Crystal Structures, University of Göttingen, Germany.
6. B. B. Prozorovskii, M. P. Prozorovskaya, and V. M. Demchenko, *Farmakol. i Toksikol.*, 497 (1987).