Chemistry of Heterocyclic Compounds, Vol. 32, No. 6, 1996

SILYL MODIFICATION OF BIOLOGICALLY ACTIVE COMPOUNDS. 3.* ORGANOSILICON DERIVATIVES OF AMINOALCOHOLS IN THE SERIES OF TETRAHYDROQUINOLINE, TETRAHYDRO-ISOQUINOLINE, AND TETRAHYDROSILAISOQUINOLINE

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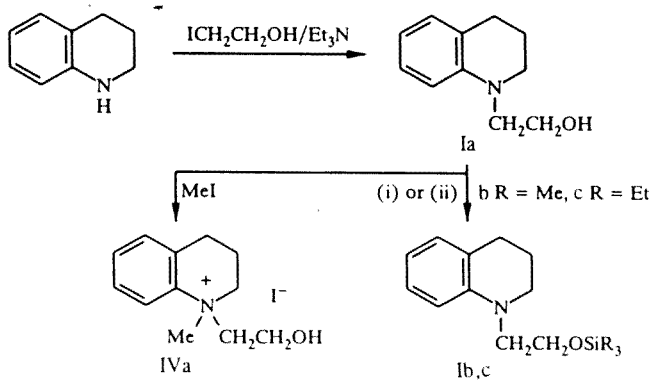
The N-(2'-hydroxyethyl)-1,2,3,4-tetrahydroquinoline, -isoquinoline, and -silaisoquinoline, and their trimethyl- and triethylsilyl derivatives and the corresponding methiodides were synthesized. The acute toxicity and psychotropic activity of the compounds synthesized were studied.

We showed previously [1, 2] that the silylation of aminoalcohols and their salts, which are potential agonists or antagonists of choline, leads to an increase in psychotropic activity. Their mechanism of action may be determined by the passage of the silyl derivatives through the lipophilic membrane [3]. With the purpose of checking the principles found in the series of heterocyclic aminoalcohols, new structural analogs of choline and colamine were synthesized, and their neurotropic activity was studied.

The N-(2'-hydroxyethyl)-1,2,3,4-tetrahydroquinoline (Ia) and the corresponding isoquinoline (IIa) were synthesized by heating 1,2,3,4-tetrahydroquinoline or 1,2,3,4-tetrahydroisoquinoline with ethylene iodohydrin in the presence of triethylamine. The 2-(2'-hydroxyethyl)-4,4-dimethyl-4-sila-1,2,3,4-tetrahydroisoquinoline (IIIa) was synthesized from 2-aminoethanol and dimethylchloromethyl(2-bromomethylphenyl)silane [4]. The trimethylsilyl ethers (Ib) and (IIb) were synthesized by boiling the (hydroxyethyl)tetrahydroquinoline (Ia) or the corresponding isoquinoline (IIa) with hexamethyldisilazane. The trimethylsilyl ether of the (hydroxyethyl)silatetrahydroisoquinoline (IIIb) and the triethylsilyl ethers (Ic)-(IIIc) were synthesized by the reaction of the aminoethanol (Ia), (IIa), or (IIIa) correspondingly with trimethyl- or triethylchlorosilane in the presence of triethylamine in ether. Treatment of compounds (Ia), (IIa,c), and (IIIa) with methyl iodide gave their methiodides (IVa-d).



(i) $(Me_3Si)_2NH$, (ii) Et_3SiCl/Et_3N

*For Communication 2, see [2].

Latvian Institute of Organic Synthesis, Riga LV-1006. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 793-799, June, 1996. Original article submitted April 25, 1996.

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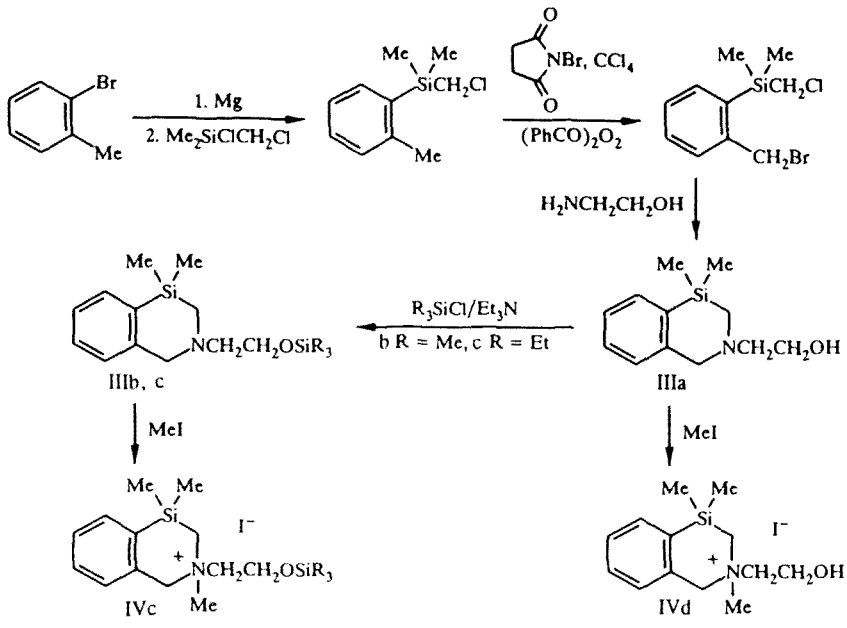

The results of the study of neurotropic properties and acute toxicity of the compounds synthesized are presented in Table 1.

The influence of the compounds on the tone of skeletal musculature and coordination of movements depends on the substituent in the 2-hydroxyethyl side chain. Thus, in the series of 1-(2′-hydroxyethyl)tetrahydroquinoline, the activity decreases in the transition from the unsubstituted compound (Ia) to the 2′-trimethylsiloxyethyl derivative (Ib), and further to the 2′-triethylsiloxyethyl derivative (Ic). Approximately the same principle also appears in the investigation of derivatives of tetrahydroisoquinoline (IIa-c).

In the series of derivatives of tetrahydroisoquinoline, where the dimethylsilyl group is present in the piperidine ring (IIIa-c), the greatest depriming activity was established in the tests referred to above. However, the parameters of influence on the tone of skeletal musculature and coordination of movements for these compounds did not have significant difference, i.e. the introduction of the trimethylsilyl group in (IIIb) or the triethylsilyl group in (IIIc) into the side chain does not alter their activity significantly. Among the methiodides investigated, the highest depriming activity is shown by the methiodide of the triethylsilyl ether of 2-(2′-hydroxyethyl)-1,2,3,4-tetrahydroisoquinoline (IVc).

Hypothermic action was expressed very weakly in the derivatives of N-(2′-hydroxyethyl)tetrahydroquinoline (Ia-c) and the isoquinolines (IIa-c).

For the derivatives of silatetrahydroisoquinoline (IIIa-c), the hypothermic effect appears at approximately the same doses at which was noted activity in the "rotating rod" and the "tube" tests. No marked difference is thereby observed between the separate compounds according to the given parameter. In the group of investigated methiodides (IVa-d), the hypothermic action also appears at doses comparable with the doses for the manifestation of depriming activity in other tests.

In the test of "pulling on a cross-beam," the action of all the investigated compounds was expressed weakly, only appearing at subtoxic doses.

Investigation of analgesic activity showed that the analgesic effect only appears in the derivatives of tetrahydroquinoline (Ia-c) and tetrahydroisoquinoline (IIa-c) at doses close to that at which is noted the manifestation of depriming action. The silatetrahydroisoquinolines (IIIa-c) and the investigated methiodides do not possess the analgesic property, with the exception of compound (IVc).

All the investigated compounds show antihypoxic action to one or the other degree (by 30-55%).

No action was found for the investigated substances in the prolongation of hexenal-induced narcosis at the dose of 5 mg/kg among the derivatives of N-(2′-hydroxyethyl)tetrahydroquinoline (Ia-c) and the corresponding isoquinolines (IIa-c). For the derivatives of N-(2′-hydroxyethyl)-4,4-dimethyl-4-silatetrahydroisoquinoline (IIIa-c), the triethylsilyl ether (IIIc) prolongs the hexenal-induced narcosis to a greater degree (by 61.1%) than the corresponding aminoalcohol (IIIa) (by 20%). The trimethylsilyl ether (IIIb) is inactive in this test. At the same time, all the investigated methiodides (IVa-d) prolong the hexenal-

TABLE 1. Neurotropic Activity of Derivatives of N-(2-Hydroxyethyl)tetrahydroquinoline and the Corresponding Isoquinolines

Compound	LD_{50}, mg/kg	ED_{50}, mg/kg				M ± m, % to the control (100%)						
		Test										
		of the rotating rod	of the tube	of rectal temperature	of analgesia	of hypoxic hypoxia	of hexenal-induced narcosis	of ethanol-induced narcosis	of phenamine-induced hyperactivity	of Corazol-induced convulsions, clonic/tonic	of retrograde amnesia†	training, sec‡
Ia	346 (120...664)	163 (109...227)	141 (68...209)	224 (144...285)	141 (92...209)	155,4*	125,0	57,1*	112,6	163,8*/150,0*	83,3*	114,1*
Ib	755 (348...1215)	178 (112...253)	178 (112...253)	>250	258 (145...404)	121,7*	110,0	41,9*	108,8	323,5*/195,4*	83,3*	120,0*
Ic	>2000	258 (145...404)	224 (120...332)	>400	>400	129,9*	110,0	40,2*	101,5	140,7*/119,2	50,0	84,1
IIa	282 (159...419)	129 (61...202)	89 (63...120)	>200	112 (79...147)	135,2*	107,0	59,8*	67,5*	206,1*/212,6*	66,4	104,2
IIb	325 (219...455)	178 (112...253)	141 (92...209)	>250	109 (41...206)	114,0	100,0	53,5*	77,0*	148,4*/131,8*	66,7*	105,0
IIc	708 (501...925)	224 (120...332)	216 (61...461)	>250	282 (183...372)	131,0*	96,7	51,8*	91,4	166,7*/145,5*	33,3	50,0
IIIa	112 (79...147)	56 (39...74)	65 (44...89)	71 (43...102)	82 (57...111)	132,0*	120,0	35,7*	127,6	171,8*/246,7*	100*	148,3*
IIIb	224 (144...285)	65 (37...100)	71 (43...102)	71 (43...102)	>100	118	106,6	58,0*	128,9*	149,8*/239,3*	66,7*	100,8*
IIIc	178 (126...230)	56 (39...74)	71 (50...92)	65 (37...100)	>100	116,1	161,1*	33,0*	79,3*	160,3*/168,5*	83,3*	126,6*
IVa	69 (24...130)	>50	41 (21...62)	>50	>50	131,0*	158,0*	84,4	108,4	122,5/133,2*	83,3*	145,8*
IVb	71 (50...93)	45 (26...64)	45 (31...60)	56 (39...74)	>50	134,8*	127,7*	128,0	105,0	188,3*/167,5*	83,3*	135,8*
IVc	45 (31...60)	9 (6...12)	14 (9...12)	10 (7...14)	22 (14...28)	136,7*	172,2*	280,5*	117,4	164,5*/224,8*	83,3*	136,7*
IVd	36 (20...51)	22 (12...33)	18 (11...25)	>25	>25	111	139*	100	113	–/128	83,3*	121,6*

*Differences in relation to the control are statistically significant at $P < 0.05$.

†The control is 16.6%.

‡The control is 62.5 ± 15.3 sec.

induced narcosis by 27.7-72.2%. However, here also, the triethylsilyl ether (IVc) prolongs the duration of hexenal-induced narcosis more (by 72.2%) than the corresponding aminoalcohol (IVb) (by 27.7%).

Other features were found in regard to ethanol-induced narcosis. Thus, on the other hand, all the investigated derivatives of N-(2′-hydroxyethyl)tetrahydroquinoline (Ia-c) and the corresponding isoquinolines (IIa-c), (IIIa-c), reduce the duration of ethanol-induced narcosis. The triethylsilyl ethers (Ic-IIIc) thereby show the greatest antagonistic activity in all the subgroups. The investigated methiodides (IVb) and (IVc) increase the duration of ethanol-induced narcosis, whereby the triethylsilyl ether (IVc) is more active (prolonging the narcosis by 180%) than the corresponding aminoalcohol (IVb) (prolonging the narcosis by 28%).

A weak effect is shown when the substances synthesized interact with phenamine.

Almost all the compounds of N-(2′-hydroxyethyl)tetrahydroquinoline and tetrahydroisoquinoline show anticonvulsive action on Corazol-induced convulsions — clonic and tonic. The greatest activity on Corazol-induced convulsions in the tetrahydroquinoline series is shown by the trimethylsilyl ether (Ib), and the greatest activity in the tetrahydroisoquinoline series is shown by the unsubstituted derivative (IIa). In the series of N-(2′-hydroxyethyl)-4,4-dimethyl-4-silatetrahydroisoquinoline, all the compounds (IIIa-c) are active. In the series of methiodides, the most marked anticonvulsive properties are shown by the triethylsilyl ether (IVc).

In regard to the action of the investigated substances in maximal electroshock, no protective properties were found.

Study of the influence of the investigated substances on processes of memory showed that the greatest activity is exhibited by compounds with the dimethylsilyl group in the tetrahydroisoquinoline structure (IIIa-c). Thus, N-(2′-hydroxyethyl)-4,4-dimethyl-4-sila-1,2,3,4-tetrahydroisoquinoline (IIIa) completely (100%) prevents retrograde amnesia, and the latent period of training increases by the factor of 2.4. All the investigated methiodides, at the dose of 5 mg/kg, decrease the level of retrograde amnesia and prolong the latent period of training.

Results of the study of acute toxicity show that the acute toxicity decreases with the lengthening of the side chain of derivatives of N-(2′-hydroxyethyl)tetrahydroquinoline and the corresponding isoquinolines as follows: $-OH > -SiMe_3 > -SiEt_3$. It should be noted that the tetrahydroisoquinoline derivatives (IIa-c) are twofold to threefold more toxic than the corresponding tetrahydroquinoline derivatives (Ia-c). The introduction of the dimethylsilyl group at the position 4 of the tetrahydroisoquinoline structure increases the acute toxicity by a factor of 1.5-4. However, also in this series, compounds containing the trimethyl group (IIIb) or the triethylsilyl group (IIIc) in the side chain are less toxic ($-OH > -SiR_3$) than the unsubstituted derivative (IIIa). The investigated methiodides of tetrahydroquinoline (IVa) and tetrahydroisoquinoline (IVb), (IVc) are significantly (by a factor of 5-10.5) more toxic than the corresponding aminoalcohols (Ia), (IIa). The methiodide of the triethylsilyl ether of N-(2′-hydroxyethyl)tetrahydroisoquinoline (IVc), which contains the triethylsilyl group in the side chain, is more toxic by a factor of 1.6 than the methiodide of the initial aminoalcohol (IVb).

It was established as a result of the investigations performed that the greatest activity of the depriming type is shown by the methiodides and derivatives of silatetrahydroisoquinoline. All the investigated aminoalcohols and their trialkylsilyl derivatives are antagonists of ethanol. All the investigated compounds show antihypoxic action and clearly marked anticonvulsive action after induction by Corazol. A decrease in the acute toxicity was found in the transition from the unsubstituted hydroxyethyl derivatives of tetrahydroquinoline, -isoquinoline, and -silaisoquinoline to the trialkylsiloxyethyl derivatives.

EXPERIMENTAL

The PMR spectra were taken on the Bruker WH-90/DS instrument in $CDCl_3$ or DMSO-D_6 using TMS as the internal standard. The error in measurement was ±0.05 ppm. The GLC analysis was performed on the Khrom-4 chromatograph (Czechoslovakia) with a flame ionization detector. A glass column of 1.2 m by 3 mm, filled with 5% OV-17 on the carrier of Chromosorb W-HP (80-100 mesh), was utilized.

The data of the elemental analysis for C, H, and N correspond with the calculated data.

N-(2′-Hydroxyethyl)-1,2,3,4-tetrahydroquinoline (Ia). To the mixture of 16.1 g (0.12 mole) of 1,2,3,4-tetrahydroquinoline and 17 ml (12.2 g, 0.12 mole) of triethylamine are added, dropwise with stirring, 21.0 g (0.12 mole) of ethylene iodohydrin. Spontaneous warming up is observed. The mixture is then heated for 10 h at 60°C. The reaction mixture is treated with 100 ml of 10% NaOH and extracted with ether; the extract is dried over $MgSO_4$. The residue remaining after the distillation of the solvent is distilled *in vacuo* at 123-126°C (3 gPa). The literature data [1] are as follows: bp 160-164°C

(4 mm of Hg stem). The yield of compound (Ia) is 5.5 g (26%). The PMR spectrum ($CDCl_3$) is as follows: 6.42-7.17 ppm (4H, m, 5,6,7,8-H), 3.73 ppm (2H, t, OCH_2), 3.16-3.53 ppm (4H, m, NCH_2 ring + NCH_2), 2.75 ppm (2H, t, 4-H), and 1.60-2.11 ppm (3H, m, 3-H + OH).

N-(2′-Trimethylsiloxyethyl)-1,2,3,4-tetrahydroquinoline (Ib). ($C_{14}H_{23}NOSi$). The mixture of 3.24 g (18 mmole) of the aminoalcohol (Ia) and 20 ml of hexamethyldisilazane is boiled for 1 h. The course of the reaction is followed by the method of GLC. At the end of the reaction, the excess of the hexamethyldisilazane is removed *in vacuo* using a rotary evaporator. The residue is distilled *in vacuo* at 124-128°C (4 gPa). The yield of compound (Ib) is 2.48 g (55%); the n_D^{21} = 1.5221. The PMR spectrum ($CDCl_3$) is as follows: 6.37-7.08 ppm (4H, m, 5,6,7,8-H), 3.71 ppm (2H, t, OCH_2), 3.22-3.50 ppm (4H, m, NCH_2 ring + NCH_2), 2.71 ppm (2H, t, 4-H), 1.92 ppm (2H, m, 3-H), and 0.10 ppm (9H, s, $SiMe_3$).

N-(2′-Triethylsiloxyethyl)-1,2,3,4-tetrahydroquinoline (Ic). ($C_{17}H_{29}NOSi$). To the solution of 1.31 g (7.4 mmole) of the aminoalcohol (Ia) and 1.2 ml (0.86 g, 8.5 mmole) of triethylamine in 10 ml of ether are added, dropwise with stirring, 1.38 ml (1.24 g, 8.2 mmole) of triethylchlorosilane in 1.5 ml of ether. The reaction mixture is heated for 2 h, cooled, and left at room temperature for 18 h. The residue is filtered off, and the filtrate is concentrated on a rotary evaporator; the residue is distilled *in vacuo* at 162-164°C (4 gPa). The yield of compound (Ic) is 1.18 g (54%), and the n_D^{21} = 1.5230. The PMR spectrum ($CDCl_3$) is as follows: 6.39-7.09 ppm (4H, m, 5,6,7,8-H), 3.73 ppm (2H, t, OCH_2), 3.22-3.49 ppm (4H, m, NCH_2 ring + $N(CH_2)_2$), 2.72 ppm (2H, t, 4-H), 1.92 ppm (2H, m, 3-H), 0.80-1.09 ppm (9H, m, CH_3), and 0.41-0.76 ppm (6H, m, $SiCH_2$).

N-(2′-Hydroxyethyl)-1,2,3,4-tetrahydroisoquinoline (IIa). This compound was synthesized by analogy with compound (Ia) from 16.2 g (0.12 mole) of 1,2,3,4-tetrahydroisoquinoline and 21.4 g (0.12 mole) of ethylene iodohydrin in the presence of 17 ml (12.2 g, 0.12 mole) of triethylamine. The bp is 123-125°C (3 gPa). The literature data [1] are as follows: bp 120-123°C (2 mm of Hg stem). The yield of compound (IIa) is 7.9 g (37%), and the n_D^{20} = 1.5594, the d_4^{20} = 1.0886, and the MR_D = 52.59 (found), 52.90 (calculated). The PMR spectrum ($CDCl_3$) is as follows: 7.00 ppm (4H, m, 5,6,7,8-H), 3.67 ppm (4H, m, OCH_2 + $ArCH_2N$), and 2.55-3.02 ppm (7H, m, NCH_2 + 3,4-CH_2 + OH).

N-(2′-Trimethylsiloxyethyl)-1,2,3,4-tetrahydroisoquinoline (IIb). ($C_{14}H_{23}NOSi$). This compound was synthesized by analogy with compound (Ib) from 7.0 g (40 mmole) of the aminoalcohol (IIa) and 30 ml of hexamethyldisilazane. The bp is 124-128°C (4 gPa), and the n_D^{21} = 1.5055. The yield is 3.3 g (32%). The PMR spectrum ($CDCl_3$) is as follows: 7.04 ppm (4H, m, 5,6,7,8-H), 3.80 ppm (2H, t, OCH_2), 3.67 ppm (2H, s, $ArCH_2N$), 2.84 ppm (4H, m, 3,4-CH_2), 2.70 ppm (2H, t, NCH_2), and 0.16 ppm (9H, s, $SiMe_3$).

N-(2′-Triethylsiloxyethyl)-1,2,3,4-tetrahydroisoquinoline (IIc). ($C_{17}H_{29}NOSi$). This compound was synthesized by analogy with compound (Ic) from 2.72 g (15 mmole) of (IIa) and 2.60 ml (2.33 g, 15 mmole) of triethylchlorosilane in the presence of 2.4 ml (1.72 g, 17 mmole). The bp is 164°C (5 gPa), and the n_D^{21} = 1.5072. The yield is 2.62 g (60%). The PMR spectrum ($CDCl_3$) is as follows: 7.00 ppm (4H, m, 5,6,7,8-H), 3.78 ppm (2H, t, OCH_2), 3.67 ppm (2H, s, $ArCH_2N$), 2.84 ppm (4H, m, 3,4-CH_2), 2.69 ppm (2H, t, NCH_2), 0.80-1.13 ppm (9H, m, $SiCH_2\underline{CH_3}$), and 0.42-0.80 ppm (6H, m, $OSiCH_2$).

N-(2′-Hydroxyethyl)-4,4-dimethyl-4-sila-1,2,3,4-tetrahydroisoquinoline (IIIa). This compound was synthesized according to the method of [4]. The PMR spectrum ($CDCl_3$) is as follows: 6.98-7.57 ppm (4H, m, 5,6,7,8-H), 3.67 ppm (4H, m, OCH_2 + $ArCH_2N$), 2.73 ppm (3H, t, NCH_2 + OH), 2.22 ppm (2H, s, $SiCH_2$), and 0.28 ppm (6H, s, $SiMe_2$).

N-(2′-Trimethylsiloxyethyl)-4,4-dimethyl-4-sila-1,2,3,4-tetrahydroisoquinoline (IIIb). ($C_{15}H_{27}NOSi_2$). To the solution of 3.02 g (14 mmole) of the β-ethanolamine (IIIa) and 2.2 ml (1.6 g, 16 mmole) of triethylamine in 10 ml of ether are added, dropwise with stirring, 1.73 ml (1.48 g, 14 mmole) of trimethylchlorosilane in 1.5 ml of ether. The reaction mixture is heated for 4 h, cooled, and left to stand at room temperature for 18 h. The residue is filtered off, and the filtrate is evaporated; the residue is distilled *in vacuo* at 130°C (4 gPa). The yield of compound (IIIb) is 1.97 g (48%). The PMR spectrum ($CDCl_3$) is as follows: 6.92-7.52 ppm (4H, m, 5,6,7,8-H), 3.53-3.87 ppm (4H, m, OCH_2 + $ArCH_2N$), 2.69 ppm (2H, t, NCH_2), 2.19 ppm (2H, s, $SiCH_2$), 0.27 ppm (6H, d, $SiMe_2$), and 0.11 ppm (9H, s, $SiMe_3$).

N-(2′-Triethylsiloxyethyl)-4,4-dimethyl-4-sila-1,2,3,4-tetrahydroisoquinoline (IIIc). ($C_{18}H_{33}NOSi_2$). This compound was synthesized by analogy with compound (IIIb) from 2.45 g (11 mmole) of compound (IIIa) and 1.82 ml (1.63 g, 11 mmole) of triethylchlorosilane in the presence of 1.75 ml (1.26 g, 12 mmole) of triethylamine. The bp is 156°C (3 gPa). The yield of compound (IIIc) is 0.80 g (24%). The PMR spectrum ($CDCl_3$) is as follows: 6.91-7.51 ppm (4H, m, 5,6,7,8-H), 3.54-3.89 ppm (4H, m, OCH_2 + $ArCH_2N$), 2.71 ppm (2H, t, NCH_2), 2.21 ppm (2H, s, $SiCH_2$), 0.80-1.13 ppm (9H, m, $SiCH_2\underline{CH_3}$), 0.50-0.77 ppm (6H, m, $SiCH_2$), and 0.28 ppm (6H, d, $SiMe_2$).

N-(2'-Hydroxyethyl)-1,2,3,4-tetrahydroquinoline Methiodide (IVa). ($C_{12}H_{18}INO$). The solution of 0.82 g (5 mmole) of the aminoalcohol (IIIa) and 1.5 ml (3.42 g, 24 mmole) of methyl iodide in 10 ml of acetone is heated for 4 h. The mixture is cooled and left at room temperature for 15 h. The precipitated residue is filtered off and recrystallized from the mixture of abs. alcohol and ether. The yield of compound (IVa) is 0.65 g (56%). The mp is 95°C. The PMR spectrum (DMSO-D_6) is as follows: 7.37-8.05 ppm (4H, m, 5,6,7,8-H), 5.2 ppm (1H, broad s, OH), 4.21 and 3.86 ppm (2H, d. t, NCH_2 ring), 4.04 ppm (2H, m, OCH_2), 3.71 ppm (2H, m, NCH_2), 3.61 ppm (3H, s, N^+CH_3), 2.95 ppm (2H, t, 4-CH_2), and 2.21 ppm (2H, m, 3-CH_2).

N-(2'-Hydroxyethyl)-1,2,3,4-tetrahydroisoquinoline Methiodide (IVb). ($C_{12}H_{18}INO$). This compound was synthesized by analogy with compound (IVa) from 2.02 g (11 mmole) of the aminoalcohol (IIa) and 1.0 ml (2.28 g, 16 mmole) of methyl iodide. The yield of compound (IVb) is 1.03 g (28%). The mp is 147-149°C. The PMR spectrum (DMSO-D_6) is as follows: 7.18-7.40 ppm (4H, m, 5,6,7,8-H), 4.72 ppm (2H, q, $ArCH_2N$), 3.94 ppm (2H, m, OCH_2), 3.79 ppm (2H, t, 3-CH_2), 3.50 ppm (2H, t, NCH_2), and 3.20 ppm (5H, m, 4-CH_2 + N^+CH_3).

N-(2'-Triethylsiloxyethyl)-1,2,3,4-tetrahydroisoquinoline Methiodide (IVc). ($C_{18}H_{32}INOSi$). This compound was synthesized by analogy with compound (IVa) from 1.40 g (5 mmole) of the ether (IIb) and 0.8 ml (1.82 g, 13 mmole) of methyl iodide in 7 ml of ether. The yield of compound (IVc) is 0.31 g (15%). The mp is 97-99°C. The PMR spectrum (DMSO-D_6) is as follows: 7.17-7.39 ppm (4H, m, 5,6,7,8-H), 4.72 ppm (2H, q, $ArCH_2N$), 4.12 ppm (2H, t, OCH_2), 3.18 ppm (2H, t, 3-CH_2), 3.55 ppm (2H, t, NCH_2), 3.20 ppm (5H, m, 4-CH_2 + N^+CH_3), 0.94 ppm (9H, t, CH_3), and 0.65 ppm (6H, q, $SiCH_2$).

N-(2'-Hydroxyethyl)-4,4-dimethyl-4-sila-1,2,3,4-tetrahydroisoquinoline Methiodide (IVd). This compound was synthesized according to the method of [4]. The PMR spectrum ($CDCl_3$) is as follows: 7.26-7.70 ppm (4H, m, 5,6,7,8-H), 4.96 ppm (2H, s, $ArCH_2N$), 4.18 ppm (3H, broad s, OCH_2 + OH), 3.91 ppm (2H, broad s, NCH_2), 3.67 ppm (2H, d, $SiCH_2$), 3.45 ppm (3H, s, N^+CH_3), and 0.50 ppm (6H, s, $SiMe_2$).

BIOLOGICAL

Neurotropic activity was studied on mice of the BALB/c line with the mass of 18-23 g in the autumn-winter season. The temperature in the laboratory installation and the vivarium was maintained in the limits of 21 ± 2°C in the performance of the experiments. The investigated substances were dissolved in olive oil or the isotonic solution of sodium chloride (for the methiodides) and introduced ip at 1 h before the corresponding test. Control animals were injected ip with the same volume of olive oil or isotonic sodium chloride solution. Comparative evaluation of the action of the substances on indicators of hypoxia, hexenal- and ethanol-induced narcosis, phenamine-induced hyperactivity, Corazol-induced convulsions, training, and the test of Porsolt was performed on groups of animals consisting of six individuals. The investigated substances were introduced at the dose of 5 mg/kg.

The action of the substances on the central nervous system was evaluated by the following tests:

1) the influence on coordination of movements and muscle tone by methods of the "rotating rod" on apparatus of the firm Ugo Basile (Italy) at the rotational frequency of 80 rpm for 2 min, and the "tube" test using a glass tube of the size 30 by 2 cm for 30 sec.

2) the influence on body temperature which was measured in the rectum using an electrothermometer; the decrease in the rectal temperature of 3°C and greater served as the criterion for evaluation in the given case.

3) the analgesic effect, determined by the "hot plate" method using apparatus of the firm Ugo Basile (Italy).

4) the anticonvulsive activity, investigated by the test of maximal electroshock (the alternating current of 50 mA and the frequency of 50 impulses/sec with the 0.2 sec duration of the stimulation) and the test of Corazol-induced convulsions produced by the iv titration with the 1% solution of Corazol at the rate of 0.01 ml/sec.

5) the influence on the duration of hexenal-induced narcosis (the 0.4% solution of hexenal given iv at the dose of 70 mg/kg), and the influence on the duration of ethanol-induced narcosis (4 g/kg, ip).

6) the influence on the duration of the life of animals under conditions of hypoxic hypoxia produced by putting the mice, singly, into an hermetic compartment of the capacity 220 cm^3 without the absorption of carbon dioxide.

7) the change in the extent of phenamine-induced hyperactivity (the 0.4% solution of phenamine given sc at the dose of 10 mg/kg).

8) the influence on processes of training and retrograde amnesia produced by electroshock.

9) the determination, also, of the acute toxicity with ip introduction, and the establishment of mean lethal doses (LD_{50}, mg/kg).

The experimental data were treated statistically with the determination of the mean effective doses (ED_{50}) and mean lethal doses (LD_{50}) by the quick method [5]. The mean arithmetic values and their standard error ($M \pm m$) by comparison with the corresponding control were calculated for the evaluation of the mean duration of the narcotic action of hexenal and ethanol, the phenamine-induced hyperactivity, the hypoxia, and protective properties under conditions of Corazol-induced convulsions. Student's "t" criterion was utilized to evaluate the significance of the difference between the mean values. Differences were considered significant at the probability level of $P < 0.05$.

The authors express their thanks to the Council of Latvia for Science for the Grant N 96 443 to achieve the present investigation.

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