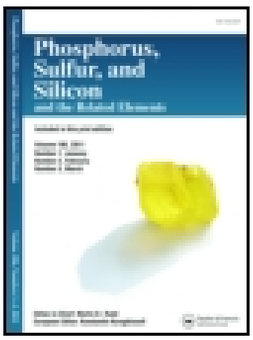

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ORGANOELEMENT JUVENILE HORMONE MIMETICS

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The synthesis of new organophosphorus and organosilicon compounds possessing insect juvenile hormone activity is described. The structure of the prepared compounds is confirmed by NMR spectra.

Keywords: Arylsilanes; amidophosphates; tertiary phosphine oxides; phenols phosphorylated; phosphinites; organoelement insect juvenile hormone mimetics; NMR spectra; biological activity

INTRODUCTION

Analogues of insect juvenile hormones, represent a relatively new category of insect control agents aimed mainly of covering the need for safer compounds and overcoming the development of resistance to classical insecticides.[1-5] Therefore search for such compounds with high activity, high field stability and safety can be considered as a promising approach to insect control.

In this communication, as part of our ongoing program aiming at the synthesis of new bioactive organoelement compounds, we describe new JH mimetics bearing organophosphorus and organosilicon substituents. We have prepared new organophosphorus compounds: N-substituted

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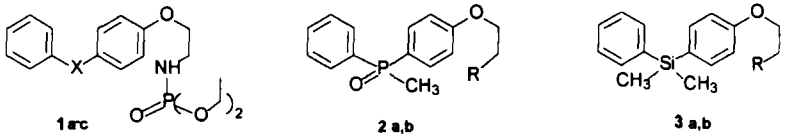
phosphamides **1a-c**, and tertiary phosphine oxides **2**. To compare the effect of phosphorus and silicon for the biological activity, we have also prepared organosilicon compounds **3**.



X =O (1a), C=O (1b), C=NOCH$_3$ (1c), R=NHCO$_2$CH(CH$_3$)$_2$(2a,3a); ON=CHCH$_2$CH$_3$ (2b,3b)

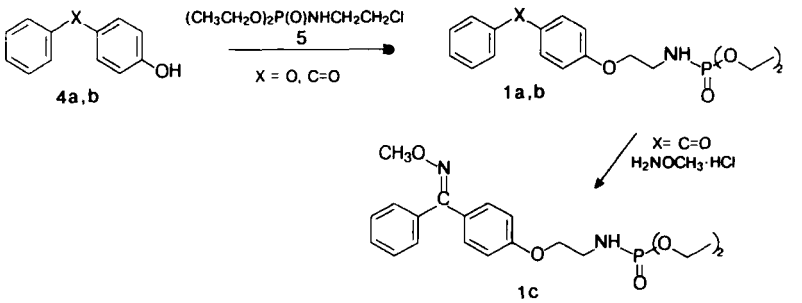
We found that N-substituted phosphamides **1a-c**, and tertiary phosphine oxides **2** possess insect juvenile hormone activity.[4] These compounds are the first organoelement mimetics of insect juvenile hormones, in spite of their structural differences from the naturally occurring JHs. At the same time the organosilicon compounds **3** show low JH activity, they are less active, than the organophosphorus compounds **1,2**.

RESULTS AND DISCUSSION

On the first step of studies we carried out the molecular modeling and the structure-activity analysis of desired JH's, containing the phosphorus atom in the chain to compare them with natural JH-III and some synthetic JH's (phenoxycarb, methoprene). The total length (~21A), the steric dimensions and other structural characteristics were varied so as to conform QSAR results.[6–8] Based on these results, we selected two types of the most interesting structures: the tertiary phosphine oxides **2**, bearing the phosphorus in the bridge between two aromatic rings and the N-substituted phosphamides 1, bearing a terminal phosphorus atom (Figure 1).

The synthesis of compounds **1a-c** bearing phosphorus atom in the side chain is shown in Scheme 1.

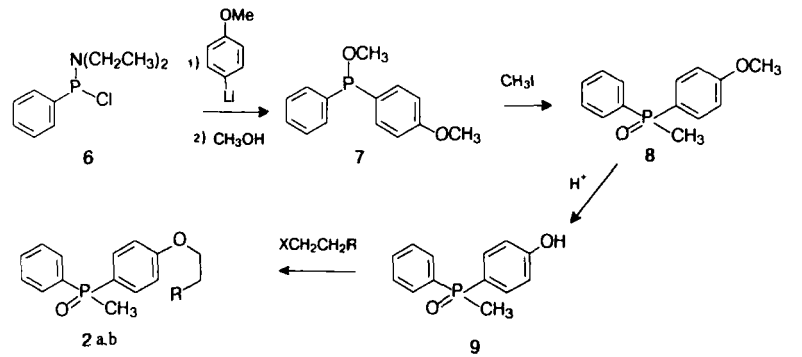
The appropriate phenol **4** has been treated with sodium methylate and then in the solution of dimethylformamide with N-2-chloroethylaminodiethylphosphate **5** to give the appropriate N-(2-aroxy)ethylaminodiethylphosphates **1a,b**. Treatment of the diarylketone **1b** with O-methylhydroxylamine hydrochloride leads to the formation of the oxime **1c**. The compounds **1a-c** are viscous liquids, non-distillable under



SCHEME 1

vacuum, which have been purified by column chromatography with silica gel. The compounds have been identified by elemental analysis, and NMR spectra. Their purity was confirmed by high performance liquid chromatography.

The tertiary phosphine oxides **2a,b** were prepared as shown in Scheme 2.



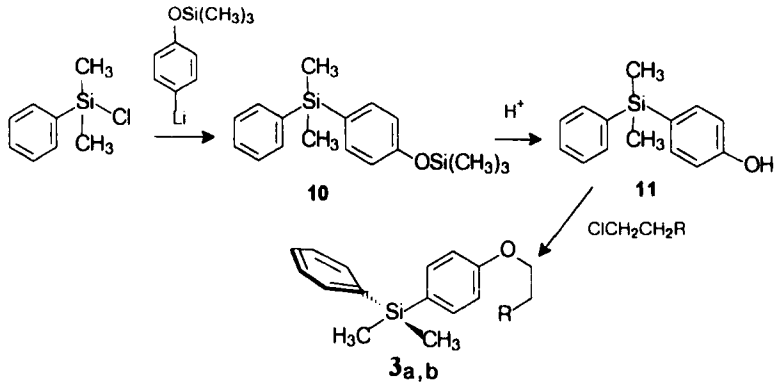
R = $NHCO_2CH(CH_3)_2$ (a); $ON{=}CHCH_2CH_3$ (b)

SCHEME 2

Chlorodiethylamino-phenylphosphine reacts with the anisyle lithium to give anisyldiethylamino-phenylphosphine which is treated with methanol to yield methyl anisylphenylphosphinite **7**. The latter reacts with

iodomethane to form anisyl-methylphenylphosphine oxide **8**, which through heating with pyridine hydrochloride in dimethylformamide is transformed into 4-hydroxyphenyl-methyl-phenylphosphine oxide **9**. The alkylation of the phenol **9** by the XCH_2CH_2R leads to the tertiary phosphine oxides **2**, which are purified by silica gel column chromatography.

To compare the effect of phosphorus and silicon atoms in the chain for the JH properties we have prepared silanes **3** of similar structure to tertiary phosphine oxides **2**. The synthesis of the silyl derivatives **3a-c** was carried out as shown in Scheme 3.



R = $NHCO_2CH(CH_3)_2$ (a); $ON{=}CHCH_2CH_3$ (b).

SCHEME 3

Dimethylphenylchlorosilane reacts with 4-trimethylsilyloxyphenyllithium to give an silane **10**, which was hydrolyzed with the formation of the phenol **11**. The latter reacts with N-chloroethylcarbamate to afford compound **3a**.

BIOLOGICAL ACTIVITY

All compounds were bioassayed for their hormonomimetic activity against three selected insect species (*Tenebrio molitor, Hyphantria cunea and Trialeurodes vaporariorum Wstw.*).

The studies of the juvenile-hormonal activity of compounds were performed according to the Gar methodology with a synchronized fourth-larval instars of insects as described previously.[6,7] The juvenile-hormonal activity of compounds was estimated by violations of the insect metamorphosis. Phenoxycarb and methoprene were used as standard compounds. Every test was repeated three times. The JH activity of compounds was estimated by violations of the insect metamophosis.[9,10] The compounds **1a,c** inhibit the development of the first generation of insects at a concentration of 0.0001–0.001%. They show a preventive juvenile hormone-like effect and therefore can be used for the control of insects. The activity of the most active mimetic, diethyl N-[2-(4-phenoxyphenoxyethyl]aminophosphate **1a**, is comparable to that of methoprene [isopropyl *(2E,4E)*-11-methoxy-3,7,11-tridecadienoate], one of the most active JH-mimetic compounds.[11] The tertiary phosphine oxides **2a,b** are less active than aminophosphate **1a** (Table I).

Unlike the organophosphorus compounds **1,2**, the diarylsilanes **3a,b** show low JH activity.

TABLE I JH activity of compounds **1–3**

Compound	*Concentration, (%)*	*JH activity*[a]		
		Tenebrio molitor	*Trialeurodes vaporariorum Wstw.*	*Hyphantrea cunea*
(1a)	0.01	95	55	60
	0.001	85	45	50
	0.0001	73	42	40
(1b)	0.01	62	65	65
	0.001	30	60	55
(1c)	0.01	70	60	60
	0.001	62	45	50
(2a)	0.01	70	65	–
(2b)	0.01	70	60	
(3a)	0.01	20	40	0
(3b)	0.01	20	35	0

a. Percent of insects with abnormalities.

We have also compared the effect of the substituent × in diarylderivatives **1a-c**, where × = O, C =O, C=NOMe, for the hormonomimetic activity: the diaryl ether **1a** (X=O) is the most active, the activity of the diarylketone imine **1c** (X = C=NOCH$_3$) is slightly lower, and the diarylketone **1b** (X = C=O) is the less active.

Some selected data of biological tests are presented in Table I, detailed data will be described in a separate publication[12].

DESIGN AND STRUCTURE-ACTIVITY RELATIONSHIPS

In order to clarify the role of the structures of the organoelement compounds **1–3** on the JH receptor we have studies their active conformations by means of semi-empirical molecular mechanic calculations.[6,7] The molecular orbital calculations were performed using the modified MOPAC-97 and HYPERCHEM program with PM1 parametrization, which were considered to be superior to other semi-empirical methods for the study of steric properties.[8]

In order to find out the global and local minimum energy conformation of the structure, more detailed conformation energy studies were carried out by means of the MM+ molecular mechanics calculations at first for 4-phenoxyanisole, dimethyl(4-anisyl)phenylsilane and 4-anisylphenylmethylphosphine oxide derivatives and then for the compounds **1–3**. The analysis showed that the rotation of the phenyl groups in diarylether derivatives **1** along the ether bonds and in phosphine oxides **2** is restricted within the low energy valleys in which two phenyl rings are perpendicular to each other (Fig. 1). The lowest energy conformation of the alkoxy side chain is shown to be twisted ~120° from the plane of attached phenyl ring.

The positional effect of these functions was made clear through this study. The heteroatom-receptor interaction is most favorable at the δ-position of phenoxyphenoxy oxygen, when a molecule is constructed optimum in its length (about 21 A). The compounds **1** are more active, when a P=O group rather than an C=O group is at the δ-position of the side chain.

The twisted phenyl ring **B** is evidently corresponding to the 7-branched terpenoid structure at the receptor site and the position of phenyl ring **A** may also replace the terminal structure of methoprene. On the other hand conformational analyses of the diarylketone derivative **1b**, which is less

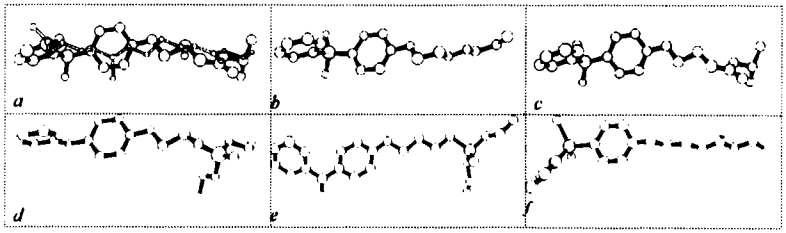


FIGURE 1 Molecular modeling of JH mimetics: *a*- the superimposed model of JH-III and compound **2a**; *b*-compound **2b**; *c* – compound **2a**; *d* - compound **1a**; *e* – compound **1b**; *f* – compound **3a**

active than **1a**, revealed, that the aryl groups lies in the same plane of the attached phenyl ring in the most stable conformation and that it is difficult to adopt the twisted active conformation (fig. 1*d*). The heteroatom-receptor interaction is most favorable at the d-position of phenoxyphenoxy oxygen or at the 4-position of the side chain terminal when a molecule is constructed optimum in its length (about 21 A). The compounds **1** show the highest activity when a P=O group rather than an C=O group is at this position.

EXPERIMENTAL

Melting points were uncorrected. The NMR spectra are recorded on a "Varian VXR-300" spectrometer at 300 (^{1}H) and 126.16 MHz (^{31}P). All chemical shifts are expressed in δ (ppm). ^{1}H chemical shifts are expressed relative to Me_4Si as internal standard. ^{31}P NMR spectra are referenced to external 85% H_3PO_4. All manipulations were carried out under inert atmosphere (N_2 or Ar), solvents were distilled under inert atmosphere from the following drying agents: diethyl ether, hexane (P_2O_5), methanol (sodium), ethyl acetate ($CaCl_2$). HPLC analyses were performed on a "Milichrom-4A" instrument (UV detector 270 nm, Silasorb SPH-C_{18} column, 120 mm length and 2 mm diameter, acetonitrile-water 9:1) thin layer chromatography on Silufol UV 254 plates using various solvents as eluent. TLC was carried out on Silufol UV 254, using chloroform-methanol (9:1) as eluent.

Diethyl N-[2-(4-phenoxyphenoxy)ethyl]aminophosphate 1a

A solution of 4-phenoxyphenol **4a** (1.86 g, 0.01 mol) in 3 ml of ethanol was treated with sodium methylate, prepared from 0.13 g of the sodium and 3 ml of methanol. The solution of the sodium phenolate was evaporated in vacuo, the residue was dissolved in 5 ml of dimethylformamide, and N-2-chloroethylaminodiethylphosphate **5** (2.2 g, 0.0105 mol), and potassium iodide (0.1–0.2 g) were added. Then the mixture was stirred for 7h at 80°C. The mixture was cooled, poured into 50 ml of water, and extracted with ethyl acetate. The extracts were washed with a 5% aqueous solution of potassium hydroxide and with a saturated solution of sodium chloride and dried with sodium sulfate. The solvent was evaporated, the residue was chromatographed with ethyl acetate-hexane mixture (10:1) as an eluent. R_f0.75. Yield 1.82 g (50%).

Calcd for the $C_{18}H_{24}NO_5P$: N 3.83; P 8.48 Found N 3.92; P 8.50

NMR spectra (δ, ppm; J, Hz; $CDCl_3$): δ_H: 1.25 t, (J_{HH} 8, 6H, CH_3); 3.28 m (2H, CH_2N); 3.93 m (2H, CH_2O); 4.02 dq (J_{HP} 8, 4H, P-OCH_2); 5.28 br (1H, NH); 6.75–7.25 m (9H, $C_6H_5 + C_6H_4$). δp: 9.62.

Diethyl N-[2-(4-benzoylphenoxy)ethyl]aminophosphate 1b

A solution of 4-hydroxybenzophenone **4b** (2.95 g, 0.015 mol) in 3 ml of ethanol was treated with sodium methylate, prepared from 0.36 g of sodium and 3 ml of methanol. The solution of sodium phenolate was evaporated in vacuo, the residue was dissolved in 10 ml of dimethylformamide, and N-2-chloroethylaminodiethylphosphate (3.2 g, 0.015 mol) and 0.1–0.2 g of potassium iodide were added. The mixture was refluxed for 3 h. Then the mixture was cooled, poured into 50 ml of water, and extracted with ethyl acetate. The extracts were washed with 10% aqueous solution of potassium hydroxide, with a saturated solution of sodium chloride and dried with sodium sulphate. Ethylacetate was evaporated, the residue was purified by column chromatography (Silicagel L 100/160m) with ethyl acetate as a eluent, R_f= 0.68. Yield of 2.8 g (50%).

Calcd for the $C_{19}H_{24}NO_5P$: N 3.72; P 8.21. Found: N 3.83; P 8.42

NMR spectra (δ, ppm; J, Hz; $CDCl_3$): δ_H: 1.25 t (J_{HH} 8, 6H, CH_3); 3.29 m (2H, CH_2N); 3.95 m (2H, CH_2O); 4.02 m J 8, (4H, P-OCH_2); 5.55 br (1H, NH); 6.88–7.76 m (9H, C_6H_5+ C_6H_4). δp 9.80.

Diethyl N-{2-[4-phenyl(methoxymethylimino)phenoxy]ethylamino} phosphate 1c

The O-methylhydroxylamine chlorohydrate (1.05g, 0.015 mol) and 0.80 ml of pyridine were added to a solution of N-[2-(4-benzoylphenoxy)ethyl]aminodiethylphosphate **1b** (2.8 g, 0.015 mol) in 8 ml of methanol and the mixture was refluxed during 3 h. Then the mixture was cooled, and the methanol was evaporated in vacuo. The residue was diluted with water and acidified with hydrochloric acid till pH 1–2. The product was extracted with ethyl acetate, the extract was washed with a saturated solution of sodium chloride and dried with sodium sulfate. Ethyl acetate was evaporated, the residue was purified by column chromatography, (Silicagel L 100/160m) with ethyl acetate as a eluent. R_f 0.72. Yield of 2.5 g (63%).

Calcd. for the $C_{20}H_{27}N_2O_5P$: N 6.89; P 7.62. Found: N 7.20; P 8.23

NMR spectra (δ, ppm; J, Hz; $CDCl_3$): δ_H: 1.25 t (J_{HH} 8, 6H, CH_3); 3,20 m (2H, CH_2N); 3.93 m (2H, CH_2O): 3.99 dq (J_{HP} 7, 2H, P-OCH_2); 5.73 br (1H, NH); 3.90 s (3H, $NOCH_3$) 6.75–7.40 m (9H, $C_6H_5 + C_6H_4$). δp 9.75.

Anisyl-methyl-phenylphosphine oxide 8

12.0 g of diethylamino- p-methoxyphenyl-phenyl-phosphine in 25 ml of methanol was refluxed for 4 hours. The yield of methyl anisyl-phenylphosphinite **7** determined by P-NMR spectra was 96%. NMR spectra (δ, ppm; $CDCl_3$): δ_P: 111.8. The solution of methyl anisylphenylphosphinite **7** was added with stirring to 25 ml of methyl iodide at 40–45 C. The mixture was stirred 0.5 hour at refluxing temperature and then was concentrated under reduced pressure to dryness. The residue was purified by crystallization from ether-hexane.Yield 10.0 g (91.5%), mp. 120°C. NMR spectra (δ, ppm; J, Hz; $CDCl_3$): δ_H: 1.92 d (J_{HP} 13, 3H, CH_3P); 3.77 s (3H, CH_3O); 6.90–7.60 (9H, C_6H_5+C_6H_4). δ_P: 31.5.

Methyl(4-hydroxyphenyl)(phenyl)phosphine oxide 9

A mixture of 6.0 g of anisyl-methyl-phenylphosphine oxide **8**, 8.4 g pyridine hydrochloride and 1.2 ml of acetic acid was heated for 2 hours at 190°C. After being cooled to room temperature, the mixture was poured into water and dilute hydrochloric acid was added to pH 1–2. The mixture was extracted with ethyl acetate. The ethyl acetate solution was treated

with 10% KOH and the aqueous layer was separated. The aqueous layer was made acidic with dilute hydrochloric acid to pH 1–2 and extracted with ethyl acetate. The ethyl acetate layer was washed with a saturated solution of NaCl, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was distilled in vacuum. Yield of **9** 2.5 g (44%), b.p. 260°C (0.01 mm Hg), mp. 67–68°C.

Calcd for the $C_{13}H_{13}O_2P$: C 67.03, H 5.62, P 13.35. Found C 67.24, H 5.64, P 13.33. NMR spectra (δ, ppm; J, Hz; $CDCl_3$): δ_H: 1.89 d (J 13, 3H, CH_3P); 6.90–7.60 (9H, $C_6H_5 + C_6H_4$); 9.8 br (1H, OH). δ_P: 34.0.

4-Phenyl-methyl-(2-N-isopropoxycarbonylaminoethoxy) phenylphosphine oxide 2a

A solution of phenol **9** (1.0 g) in 5 ml of methanol was treated with sodium methylate (0.1 g sodium in 1 ml of methanol) and the solution of sodium phenolate was evaporated in the vacuum to dryness, the residue was dissolved in 5 ml of dimethylformamide and then was added to $ClCH_2CH_2NHCO_2Et$ (1.0 g). The mixture was refluxed for 0.5 hour, diluted with water, and extracted with benzene. The benzene layer was washed with 10% NaOH and water, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using methanol-chloroform as eluent to give the oily tertiary phosphine oxide. The purity of the compounds was confirmed by TLC and HPLC method R_f 0.27 ($CHCl_3$-CH_3OH 9:1). Yield of 58%.

NMR spectra (δ, ppm; J, Hz; $CDCl_3$): δ_H: 1.16 d (6H, J 7, CH_3); 1.93 d (J 13, 3H, CH_3P); 3.52 q (J 5, 2H, CH_2N); 4.00 t (J 5, 2H, CH_2O); 4.85 sp (J 6, 1H, CH); 5.11 s (1H, NH); 6.80–7.60 m (9H, $C_6H_5 + C_6H_4$). δ_P: 30.3. Calcd for the $C_{19}H_{24}NO_4P$: P 8.57. Found P 8.60.

4-Phenyl(2-O-propionaldoxime ethoxy) methylphenylphosphine oxide 2b

The compounds **2b** has been prepared analogously to **2a** from phenol **9** and $BrCH_2CH_2ON{=}CHCH_2CH_3$ R_f 0.42 ($CHCl_3$-CH_3OH 9:1). Yield of 45%.

Calcd for the $C_{19}H_{24}NO_3P$: N 4.06; P 8.97. Found N 4.05; P 9.73
NMR spectra (δ, ppm; J, Hz; $CDCl_3$): δ_H: 0.87 t (J 7, 3H, CH_3); 1.42 m (J 7, 2H, CH_2); 1.93 d (J 9, 3H, CH_3P); 2.11 m (2H, CH_2); 4.15 m (2H,

CH_2ON); 4.30 m (2H, CH_2O); 6.80–7.60 m (9H, C_6H_5 +C_6H_4); 7.28 t (J 8, 1H, CH=N). δ_P: 30.3.

4-Phenyl-dimethylsilylphenyloxytrimethylsilane 10

A solution of $LiC_6H_4OSiMe_3$ (0.02 mol) was added to an ether solution of phenyldimethylchlorosilane (3.3 g, 0.03 mol) and the reaction mixture was stirred for a 0.5 h. Mixture was refluxed at stirring for 2h. Ether was evaporated, the residue was distilled in vacuo.

Yield of 4.5 g, bp 142–143°C/0.04 mm Hg, n_D^{20}1.5544.

NMR spectra (δ, ppm; J, Hz; $CDCl_3$): δ_H: 0.131 s (9H, $SiMe_3$), 0.238 s (6H, $SiMe_2$); 6.3–7.4 m (9H, C_6H_4+C_6H_5).

4-Phenyldimethylsilylphenole 11

A solution of **10** (4 g) in 15 ml of methanol containing 1 ml of water and 0.1 ml of hydrochloric acid was stirred for 0.5 h at room temperature. Then the reaction mixture was poured into water, and extracted with ether, the extract was washed with water, dried with Na_2SO_4, evaporated under reduced pressure and the residue was distilled in vacuo. Yield of 2.0 g (75%), bp 130°C/0.01 mmHg. NMR spectra (δ, ppm; J, Hz; $CDCl_3$): δ: 0.205 s (6H, $SiMe_2$), 5.25 br (1H, OH), 6.5–7.7 (9H, C_6H_4+C_6H_5).

4-Phenyl-dimethylsilyl-(2-N-isopropoxycarbonylaminoethoxy) benzene 3a

The phenol **11** (2.58 g, 0.01 mol) in 3 ml of ethanol was treated with sodium methylate, prepared by dissolving of 0.25 g of the sodium in 3 ml of methanol. The sodium phenolate was evaporated in vacuo, the residue was dissolved in 8 ml of dimethylformamide, and 2.05 ml (0.012 mol) of $BrCH_2CH_2NHCO_2Pr$-i was added. The mixture was stirred for 1h at 80°C till pH 7. The solvent was evaporated and the residue poured into 50 ml of water, extracted with hexane, and the extracts were washed with a 5% solution of potassium hydroxide, and a saturated solution of sodium chloride and then dried with sodium sulfate. Then the solvent was evaporated, the residue was distilled in vacuo: bp 186–188°C/0.015 mm. Yield of 1.7 g (50%).

Calcd for the $C_{20}H_{27}NO_3Si$: N 3.89. Found: N 3.92

NMR spectra (δ, ppm; J, Hz; $CDCl_3$): δ_H: 0.409 s (6H, $SiMe_2$); 1.11 d, J 6 (3H, $C\underline{H}_3CH$); 3.45 q (J_{HH} 5.5, 2H, CH_2N); 3.9 q (J_{HH} 4, 2H, OCH_2) 4.8 spt (1H, OCH); 5.0 br (1H, NH); 6.8–7.5 m (9H, C_6H_4+C_6H_5).

O-[4-Dimethyl(phenyl)silylphenoxyethyl]-propionaldoxime 3b

A solution of phenol **11** (1.29 g, 0.005 mol) in 3 ml of methanol was treated with sodium methylate, prepared by dissolving of 0.13 g of sodium in 3 ml of methanol. The prepared solution of sodium phenolate was evaporated in vacuo, the residue was dissolved in 5 ml of dimethylformamide and 1.4 ml (0.0068 mol) of $ClCH_2CH_2ON{=}CHCH_2CH_3$ was added. The mixture was stirred for 7 h at 80°C till pH 7. Then the mixture was cooled, poured into 50 ml of waters and extracted with hexane. The extracts were washed with 5% of a solution of potassium hydroxide, and with a saturated solution of sodium chloride, dried with sodium sulfate. The solvent was evaporated and the residue was distilled in vacuo, bp. 165°C/0.015 mm. Yield: 0.7 g (50%).

Calcd for the $C_{19}H_{25}NO_2Si$: N 4.28. Found: N 4.21

NMR spectra (δ, ppm; J, Hz; $CDCl_3$): δ_H: 0.517 s (6H, $SiMe_2$); 1.0 t (J_{HH} 7, 3H, CH_3); 1.5 m (2H, CH_2); 2.2 dt (J_{HH} 5.0, J_{HH} 8 2H, $C\underline{H}_2CH$); 3.9 m (2H, OCH_2); 4.2 m (2H, OCH_2); 6.6 t (J_{HH} 8, 1H, $C\underline{H}{=}N$); 6.8–7.3 m (9H, C_6H_4+C_6H_5).

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References

1. Z. Wimmer, M. Romanuk, *Collect. Czech. Chem. Commun.*, **54**, 2302 (1989).
2. F. Sehnal, in: *The Juvenile Hormones* (L.I. Gilbert, Ed.), Plenum Press, New York 1976, p. 301.
3. C.A Henrick, *Juvenile Hormone Analogs. In: Insecticidal Modes of Action* (J.R. Coats, Ed.), Academic Press, New York 1982, p. 315–402.
4. O.I. Kolodiazhnyi, V.N. Zemlianoy, L.I. Baranova, *Pat. USSR*, SU 1786037 A1.
5. P. Masner, M. Angst, S. Dorn, *Pestic. Sci*, **18**, 89 (1987).
6. H. Imamura, T. Fujita. *In Pesticide Science and Biotechnology*. R. Greenhalgh and T.R. Roberts Eds Blackwell Scientific Publications, 1987, P. 61–64.
7. T. Fujita. In *QSAR and Strategies in the Design of Biooactive Compounds* (J.R. Seidel, Ed,.). VCH, Weinheim, 1985, p. 207–218.

8. M.J.S. Dewar, E.G. Zoebisch, E.F. Healy, J.J.P. Stewart. *J. Am. Chem. Soc.* **107**, 3902 (1985).
9. O.I. Kolodiazhnyi, E.V. Grishkun, L.I. Baranova, O.V. Man'ko, *Doklady Akad. Nauk Ukrainy*, 102 (1991).
10. K.A. Gar. *Methods of tests of toxicity and effectiveness of insecticides*. Selhozizdat, Moscow. 1963, p. 1–200.
11. C.A. Henrick, W.E. Willy, G.B. Staal, *J. Agric. Food Chem.* **24**, 207 (1976).
12. O.I. Kolodiazhnyi, E.V. Grishkun, L.I. Baranova, *Physiologically Active Substances*, in press.