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RESEARCH ARTICLE

N-Silylmethyl-2-(1-Naphthyl)Acetamides: Synthesis, Structure and Computational Screening

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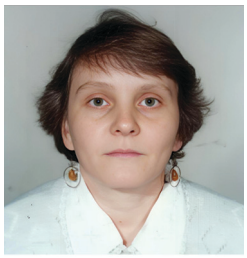
Abstract: Synthesis of new hybrid organosilicon compounds based on the amides 1-naphthylacetic acid was described. N-Organyl-2-(1-naphthyl)-N-[(triethoxysilyl)methyl]-acetamides were obtained by the reaction of 1-naphthylacetyl chloride with α-silylamines $RNHCH_2Si(OEt)_3$ (R = Me, i-Pr and Ph). Their subsequent interaction with $N(CH_2CH_2OH)_3$ led to the formation of N-organyl-2-(1-naphthyl)-N-(silatranylmethyl)acetamides. The structure of these hybrid compounds was characterized by ^1H, ^{13}C, and ^{29}Si NMR spectroscopy. The structure of N-methyl- and N-isopropyl-2-(1-naphthyl)-N-(silatranylmethy)acetamides was confirmed by X-ray diffraction analysis. Results of computational screening showed that these silatranes are bioavailable and have drug-likeness.



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Keywords: N-organyl-2-(1-naphthyl)-N-(silylmethyl)acetamides, NMR spectroscopy, X-ray diffraction analysis, computational screening, PASS, ADME.

1. INTRODUCTION

Aryl- and hetarylacetic acids and their derivatives have wide applications in synthetic organic chemistry [1-3], medicinal chemistry, agrochemistry, and pharmacy [4-7]. Of particular interest is their use as plant hormones. In recent years, considerable attention has been devoted to the study of chemistry, biochemistry, and agrochemistry of plant hormones. These compounds regulate an extremely *wide range* of basic biochemical and physiological processes in the plants throughout their life cycle and may, directly or indirectly, affect the yield of crops [8]. Indole-3-acetic acid is one of the most famous natural plant hormones [9], which is rapidly decomposed by the plant enzymes [10-12]. Synthetic plant hormones are not susceptible to enzymatic destruction, and therefore, their small doses can have a noticeable and long-lasting effect. The relevance of the search for the synthetic analogues of plant hormones with high efficiency and selectivity remains high [13-19]. Organosilicon compounds have become a novel, powerful source of chemical diversity in drug design [20-23] or agrochemicals [24-26].

One more point is important to note in this context: the investigations demonstrate the very important role of silicon in the life of plants. Silicon accelerates the growth and development of plants and, under conditions of abiotic stress, has a positive effect on plants [27-29]. In the second half of the last century, the first attempts at the synthesis of silicon-containing plant hormones were made [30-33]. 1-Naphthylacetic acid and its derivatives are the most important synthetic plant hormones used in agrochemistry and biotechnology [34-39]. Among the organosilicon derivatives of 1-naphthylacetic acid, only (triorganylsilyl)methyl esters $C_{10}H_7CH_2C(O)OCH_2SiR_3$ (R = Alk, Ar) are known to increase the growth rate of rice root by 15% compared to parent compound [40, 41].

Silatranes $XSi(OCHRCH_2)_3N$ belong to a widely known class of pentacoordinated silicon compounds with intramolecular dative bond Si←N. Their unique structure, in combination with properties of the X substituent provides high and diverse physiological and pharmacological activities: immunomodulatory, antitumor, growth-stimulating, antimicrobial and other [42-44]. Recently, several papers have been published on the study of growth-regulating activity of silatranes [45-49]. However, there are no systematic studies of plant hormones containing the silicon group in the molecule. Therefore, the development of methods of synthesis and analysis of the dependence of «structure-property» of new polyfunctional hybrid compounds containing penta- or tetracoordinate silicon atoms and structural fragments of plant hormone is an important task, the solution of which can lead to the creation of new agrochemicals. The aim of this work was to synthesize and analyze new hybrid compounds - N-organyl-2-(1-naphthyl)-N-(silylmethyl)acetamides.

2. RESULTS AND DISCUSSION

2.1. Synthesis

The first task was to create an amide bond between the 1-naphthyl acetyl group and silyl group. Three α-silylamines served as starting material: *N*-(triethoxysilyl)methyl-*N*-methyl-, *N*-(triethoxysilyl)methyl-*N*-isopropyl- and *N*-(triethoxysilyl)methyl-*N*-phenylamines. Their reactions with 1-naphthylacetyl chloride were performed in benzene in the presence of triethylamine (Scheme **1**). Si-Containing amides of 1-naphthyl acetic acid are obtained in the yields of 78%, 83%, and 50% for compounds **1**, **2,** and **3**, respectively.

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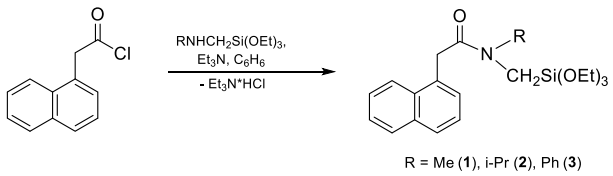
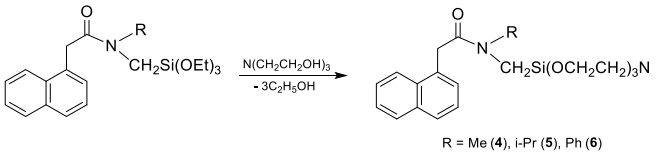


Scheme 1. Synthesis of Si-containing amides of 1-naphtylacetic acid **1-3**.

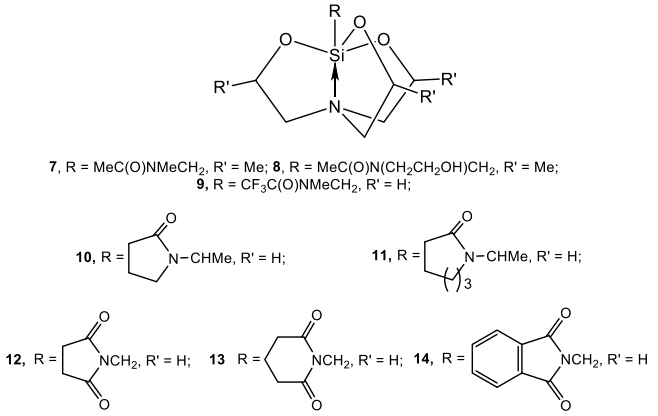
Unfortunately, the methods of purifying compounds **1-3** are limited. By-products can be completely removed by distillation at high temperature heating or using column chromatography. However, the use of these methods leads to the decomposition of the target compounds. Therefore, compounds **1-3** were used in the synthesis of silatranes **4-6** without purification.

The next purpose was to build the silatranyl groups on base compounds **1-3**. Transetherification of amides **1-3** by triethanolamine leads to the formation of corresponding N-(silatranyl)methyl-N-methyl-, N-(silatranyl)methyl-N-isopropyl- and N-(silatranyl) methyl]-N-phenylamides of 1-naphthylacetic acid **4-6** (Scheme **2**). Compounds **4** and **5** were obtained at room temperature without any catalyst, but catalytic amounts of KOH and heating of the reaction mixture to 110°C were used for the synthesis of silatrane **6**. N-(silatranyl)methylamides of 1-naphthyl acetic acid are obtained in yields of 98%, 94%, and 66% for compounds **4**, **5,** and **6**, respectively.



Scheme 2. Synthesis of N-silatranyl(methyl)amides of 1-naphtylacetic acid **1-3**.

Data of ^{1}H, ^{13}C, ^{29}Si NMR and IR Confirmed the Structure of Compounds **1-6** spectroscopy. Restricted rotation around the C(O)–N bond results in the appearance of two signal sets in the NMR spectra of the compounds **1**, **2**, **4**, and **5** [50, 51]. Previously, we have shown that N-silylmethylated carboxamides exist as a mixture of *E*- and *Z*-conformers; their ratio and stability depend on the stereoelectronic effects of the substituents in the amide group, the nature of the solvent, and the temperature [52]. To date, several N-(silatranyl)methylamides **7-9**, -lactams **10-11**, and imides **12-14** have been synthesized (Scheme **3**) [53-60]. The chemical shifts ^{29}Si of silatranes **4-6** lie within the range of the values that are typical for α-carbofunctional silatranes with pentacoordinate silicon atoms (Scheme **3**, Table **1**).



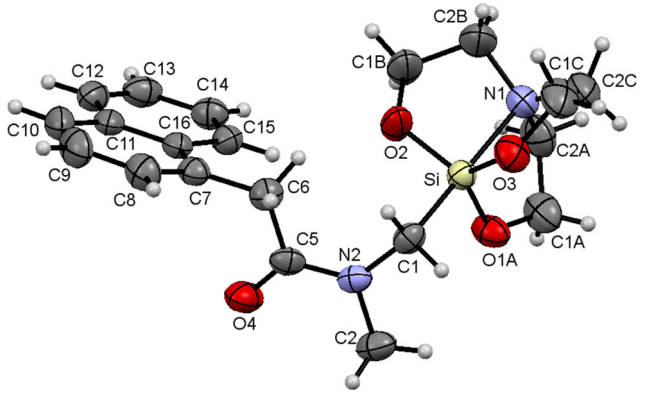
Scheme 3. N-(Silatranyl)methylamides **7-9**, -lactams **10-11** and imides **12-14**.

Table 1. The ^{29}Si chemical shifts of silatranes 4-6 and related compounds.

Compound	^{29}Si, ppm	References
4	-77.7 and -71.4	this work
5	-77.2	this work
6	-76.6	this work
7	-76.7 and -79.2	53
8	-77.8 and -80.2	53
9	-78.5 and -79.6	52
12	-78.7	54
13	-77.0	54
14	-78.4	54

2.2. X-ray Diffraction Analysis

The structure of silatranes **4** and **5** was studied by X-ray diffraction analysis; their molecular structures are shown in Fig. (**1**). The selected bond lengths and angles are presented in Table **2**. The asymmetric part of the unit cell of compound **4** contains one molecule, which is multiplied into four molecules in the total unit cell by symmetry elements. The asymmetric part of the unit cell of compound **5** contains one molecule, which is symmetrically copied to the second one, forming two molecules inside the whole unit cell (Fig. **S1**).



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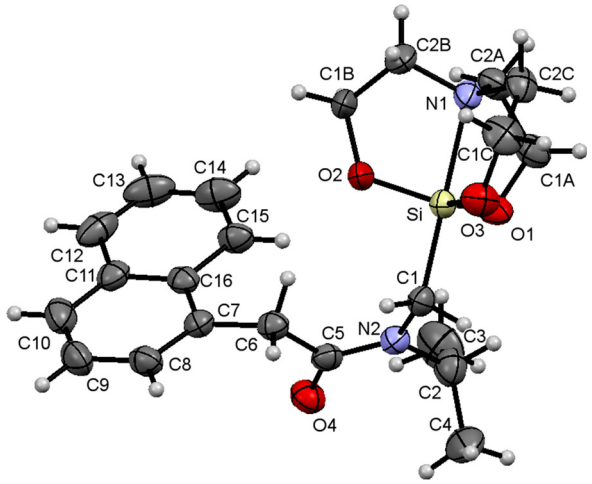

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Fig. (1). The molecular structures of compounds **4** and **5**. The thermal ellipsoids are drawn at the 50% probability level. *(A higher resolution / colour version of this figure is available in the electronic copy of the article).*

It should be noted that the geometric characteristics of the silicon atom in compounds **4** and **5** are typical for silatranes. The coordination polyhedron of the silicon atom in these compounds is a distorted trigonal bipyramid (TBP) with nitrogen and carbon atoms in axial positions and three oxygen atoms lying in equatorial positions. The N→Si dative bond length is 2.139(3) Å and 2.122(5) Å for compounds **4** and **5**, respectively. The angles of the N-Si-C axial fragment are almost linear in both compounds (176.50 ^{o} and 176.40^{o} for silatrane **4** and **5**, respectively). Characteristics η_e and $\eta_{ax,}$ in terms of the percentage TBP geometry are used as indicators of the pentacoordinate characters of the silicon atom . The degree of pentacoordination of the silicon atom was calculated using the formulas Tamao and Kano [55, 56]. These geometrical parameters of compounds **4** and **5** are in close agreement with those of structurally similar compounds (Table **2**).

The short intramolecular contacts C–H...O between atoms O of the silatrane skeleton and hydrogen atoms of $CH_2C(O)$ groups stabilize the conformation of molecules in compounds **4** and **5** (Fig. **S2**). Their lengths are 2.369 Å and 2.406 Å, respectively. There are four intermolecular short contacts in compound **4**. Three of them are of contacts between the aromatic system of the naphthyl group and hydrogen atoms of NCH_2 and OCH_2 group of silatranyl moieties of the neighboring molecule: $O_{atr.}$CH...C12 (2.781 Å); $N_{atr.}$CH...C11 (2.895 Å) and $N_{atr.}$CH...C16 (2.852 Å). These contacts provide the existence of dimer of molecule four by type "head to tail," which are linked together by the fourth contact between the oxygen of carbonyl group and hydrogen atom of naphthyl group of another molecule C13H13···O4 (2.598 Å) into long chains (Fig. **S3**). The existence of the crystal structure of compound **5**, just like compound **4**, is ensured by intermolecular noncovalent interactions. The long chains of molecule **5** located as "head to tail", were formed as a result of the intermolecular short contacts between hydrogen atoms of NCH_2 groups and aromatic system of naphthyl groups of neighboring molecules $N_{atr.}$CH...C10 (2.758 Å); $N_{atr.}$CH...C11(2.781 Å) and between hydrogen atoms of OCH_2 groups of neighboring molecules $O_{atr.}$CH...$HCO_{atr.}$ (2.202 Å). These chains are linked by the contacts between the oxygen of carbonyl groups and hydrogen atoms of OCH_2 groups of silatranyl moieties $O_{atr.}$CH...O (2.564 Å) (Fig. **S4**). The crystal structure of compounds **4** and **5** is shown in Figs. (**S5** and **S6**), respectively.

2.3. Prediction of Physic-chemical and Pharmacokinetic Properties and Pharmacological Activity of Compounds 4-6

The biological activity of silatranyl derivatives has been investigated by the use of computational screening *via* PASS and ADME. Their potential pharmacological activity profiles were calculated by using the silico PASS program. The *in silico* ADME assessment reveals that properties are similar to those of drugs that obeyed Lipinski's rule.

There is a hypothesis that dietary plant hormones impact human physiological processes such as glucose assimilation, inflammation, and cell division, but their mode of action remains unclear [61]. Therefore, at the initial stage of this investigation, we attempted to assess the potential biological activity of compounds **4**-**6**. The most important pharmacokinetic characteristics that present a behavior of compound in the live organism. Swiss ADME software [62, 63] was used for the virtual evaluation of the properties of silatranes **4**-**6,** and selected data of their physical–chemical and pharmacokinetic properties, drug-likeness, and bioavailability are presented in Tables **3** and **4**. These results demonstrate compliance of compounds **4**-**6** to Lipinski's rule. According to Lipinski's rule [64], for good bioavailability (drug-likeness (DrugL)) the compounds must have the following properties: M.W. < 500, lipophilicity (Log *P*) < 5, a number of H-bond acceptors (HBA) < 10 and a number of H-bond

Table 2. The geometrical parameters of silatranes 4, 5 and related compounds 7, 8, 10-14.

Compound	*l*, Å		Angle N-Si-CH_2, ^{o}	$\sum_{eq.\ angles}$	η_{es}, %*	η_{ax}, %*	References
	N→Si	Si-CH_2					
4	2.139(3)	1.910(3)	176.50(1)	356.68	89.46	68.77	this work
5	2.122(5)	1.903(6)	177.40(2)	356.70	89.52	68.92	this work
7	2.139(2)	1.907(2)	175.48(9)	356.46	88.76	66.10	[53]
8	2.137(2)	1.907(2)	176.00(3)	356.60	89.21	68.38	[53]
10	2.126(9)	1.939(1)	178.50(4)	356.99	90.44	70.34	[57]
11	2.122(2)	1.909(3)	177.30(1)	356.72	89.59	68.96	[58]
12	2,102(9)	1.910(1)	176.95(4)	357.51	92.10	72.92	[59]
13	2.093(1)	1.918(1)	178.05(5)	357.14	90.92	71.08	[59]
14	2.134(1)	1.901(2)	173.51(6)	356.89	90.13	69.59	[60]

Tables 3. Physical–chemical properties of compounds 4-6.

Compound	M.W.	Log P	Log S	TPSA, Å^2	HBA	HBD	RB	DrugL
4	386.52	1.70	-3.59	51.24	5	0	5	yes
5	414.57	2.27	-4.18	51.24	5	0	6	yes
6	448.59	2.84	-4.98	51.24	5	0	6	yes

Abbreviations: M.W. - Molecular weight, Log P - Octanol–water partition coefficient (P is the ratio of the concentration of the compound in n-octanol to the concentration in water), Log S (water solubility) is directly related to the water solubility of a drug and it is defined as a common solubility unit corresponding to the 10-based logarithm of the solubility of a molecule measured in mol/L, TPSA - topological polar surface area (TPSA of a molecule is defined as the surface sum over all polar atoms or molecules, primarily oxygen and nitrogen, also including their attached hydrogen atoms), HBA - Hydrogen bond acceptors (number of functional groups H-bond acceptors) HBD - Hydrogen bond donors (number of functional groups - H-bond donors), RB - Rotatable bonds (A rotatable bond is defined as any single non-ring bond, attached to a non-terminal, non-hydrogen atom), DrugL – Drug-likeness (bioavailability) (Lipinski rule).

donors (HBD) < 5, polar surface area (PSA) < 140 and the number of rotatable bonds (RB) < 15.

The compounds have low values of skin permeation can, and they overcome the blood-brain barrier. These silatranes possess high gastrointestinal absorption and bioavailability (Table **5**). Most often, drug interactions occur at the metabolic level with the participation of isoenzymes CYP2D6 and CYP3A4 [65, 66]. The compounds **4-6** are potentially able to inhibit CYP2D6 and may affect metabolism in live organisms.

The potential pharmacological activity of compounds **4-6** was studied *in silico* using the PASS software [67, 68]. The values P_a and P_i vary, indicating the probability of the compound being active or inactive. Selected results for compounds **4-6** are given in Table **5**. The produced hybrid silatranes are expected to have a strong likelihood of acting as antineoplastics, platelet aggregation stimulants, respiratory analeptics, histamine release stimulants, neurotransmitter uptake inhibitors, and treatments for phobic disorders.

3. MATERIALS AND METHODS

1-Naphthylacetic acid, triethylamine, triethanolamine, and organic solvents are commercially available products (Sigma-Aldrich, Alfa Aesar). 1-Naphthylacetyl chloride [69], *N*-methyl- and *N*-isopropyl-*N*-(triethoxysilyl)methylamine were prepared *via* the reported protocols [70, 71]. The organic solvents used were dried and purified according to the standard procedure [72]. All reactions were carried out in the atmosphere of argon.

IR spectra were registered on a Varian 3100 FTIR spectrometer in the 4000–400 cm^{-1} range with the sample as a thin film. ^{1}H, ^{13}C, and ^{29}Si spectra were run in $CDCl_3$ at room temperature on Bruker DPX-400 and AV-400 spectrometers (400.13, 100.61, and 79.46, respectively). Chemical shifts were referred to internal standard GMDS ($(Me_3Si)_2O$). Elemental analysis was performed on a CHNS Thermo Scientific Flash 2000 Elemental analyzer. Melting points were measured with the Boetius Block device.

3.1. Synthesis

3.1.1. N-(Triethoxysilyl)methyl-N-methyl-2-(1-naphthyl)acetamide 1

The solution of 1-naphthylacetyl chloride 1.852 g (9.05 mmol) in benzene (10 ml) was added to the mixture of *N*-methyl-*N*-(triethoxysilyl)methylamine 1.877 g (9.05 mmol), triethylamine 0.916 g (9.05 mmol) and benzene (40 ml) and the reaction mixture stirred at the room temperature for 8 h. The precipitate was filtered off and washed with dry benzene. The solvent from the pooled filtrate was removed under reduced pressure. The residue dried under vacuum at room temperature until constant weight. The rest is viscous oil, yielding 78% (2.645 g, 7.04 mmol). Compound **1** is a mixture of E- and Z- conformers. NMR ^{1}H (δ, ppm): 1.14 and 1.18 (2t, 9H, -$CH_2\underline{CH_3}$); 3.00 (s, 2H, NCH_2); 3.03 and 3.09 (s, 3H, NMe); 3.82 (q, 6H, -$\underline{CH_2}CH_3$); 4.09 and 4.17 (s, 2H, -$CH_2C(O)$); 7.21-7.99 (m, 7H, $C_{10}H_7$). NMR ^{13}C (δ, ppm.): 18.20 and 18.02 (-$CH_2\underline{CH_3}$); 35.50 and 36.33 (NCH_2); 37.65 (NMe); 38.32 and 38.18 (-$\underline{CH_2}C(O)$); 58.65 and 58.96 ($\underline{CH_2}CH_3$); 123.61 (C_{Ar}), 123.83 (C_{Ar}), 125.45 (C_{Ar}), 125.54 (C_{Ar}), 125.61 (C_{Ar}), 126.02 (C_{Ar}), 126.09 (C_{Ar}), 126.28 (C_{Ar}), 126.54 (C_{Ar}), 127.43 (C_{Ar}), 128.27 (C_{Ar}), 128.60 (C_{Ar}), 128.65 (C_{Ar}), 131.60 (C_{Ar}), 132.04 (C_{Ar}), 132.07 (C_{Ar}), 132.32 (C_{Ar}), 133.28 (C_{Ar}), 133.78 (C_{Ar}); 169.91 and 170.73 (C=O). NMR ^{29}Si (δ, ppm): -54.82 and -56.37. IR (film, cm^{-1}): 419, 454, 535, 570, 601, 645, 681, 732, 790, 860, 962, 1083, 1104, 1165, 1258, 1295, 1394, 1443, 1483, 1509, 1598, 1636, 1648, 1731, 1811, 1921, 2327, 2484, 2632, 2737, 2768, 2891, 2925, 2974, 3046, 3257.

3.1.2. N-(Triethoxysilyl)methyl-N-isopropyl-2-(1-naphthyl)acetamide 2

The solution of 1-naphthylacetyl chloride 1.653 g (8.08 mmol) in benzene (10 ml) was added to the mixture of *N*-methyl-*N*-(triethoxysilyl)isopropylamine 1.902 g (8.08 mmol), triethylamine 0.818 g (8.08 mmol) and benzene (40 ml). This mixture was stirred at room temperature for 10 h. The precipitate was filtered off, and washed with dry benzene. The solvent from the pooled filtrate was removed under reduced pressure. The residue dried under vacuum

Tables 4. Pharmacokinetic properties of compounds 4-6.

Compound	GI	BBB	Log Kp	BA	CYP2D6 Inhibitor	CYP3A4 Inhibitor
4	high	yes	-7.07	0.55	Yes	No
5	high	yes	-6.68	0.55	Yes	No
6	high	yes	-6.35	0.55	yes	yes

Abbreviations: GI - Gastrointestinal absorption, BBB - Blood-brain barrier permeant, Log Kp - Skin permeation, BA - Bioavailability.

Table 5. The predicted pharmacological activity of silatranes 4-6 evaluated by PASS.

Prediction Activity	P_a/P_i*		
	4	**5**	**6**
Neurotransmitter uptake inhibitor	0.607/0.028	0.340/0.164	0.387/0.123
Phobic disorders treatment	0.648/0.100	0.494/0.177	0.528/0.159
CYP2D16 substrate	0.551/0.024	0.538/0/026	0.393/0.077
Antihypoxic	0.548/0.026	0.618/0.016	0.437/0.060
CYP2H substrate	0.591/0.072	0.609/0.064	-
Platelet aggregation stimulant	0.550/0.040	0.483/0.080	0.545/0.046
Respiratory analeptic	0.448/0.040	0.405/0.066	0.430/0.057
Histamine release stimulant	0.460/0.048	0.433/0.064	-
Antineoplastic	0.387/0.109	-	0.483/0.077

Note: * P_a – Probability of pharmacological active, P_i - Probability of pharmacological inactive.

at room temperature until constant weight. The rest is viscous oil, yielding 83% (2.700 g, 6.69 mmol). Compound **2** is a mixture of E- and Z- conformers. NMR ^{1}H (δ, ppm): 1.04 and 0.91 (s, 6H, Me-CH); 1.21 (t, 9H, $CH_2\underline{CH_3}$); 2.60 and 2.70 (s, 2H, NCH_2); 3.87 and 3.82 (q, 6H, -$\underline{CH_2}CH_3$); 3.96 and 4.10 (quint 1H, CH-Me); 4.16 and 4.16 (s, 2H, $CH_2C(O)$); 7.22-7.98 (m, 7H, $C_{10}H_7$). NMR ^{13}C (δ, ppm): 18.32 and 18.20 ($CH_2\underline{CH_3}$); 20.37 and 19.64 (CH-Me); 26.40 and 29.67 (NCH_2); 37.99 and 37.35 ($\underline{CH_2}C(O)$); 49.16 and 46.89 (CH-Me); 58.70 ($\underline{CH_2}CH_3$); 123.38 (C_{Ar}), 123.95 (C_{Ar}), 125.43 (C_{Ar}), 125.49 (C_{Ar}), 125.67 (C_{Ar}), 125.85 (C_{Ar}), 126.16 (C_{Ar}), 127.28 (C_{Ar}), 127.48 (C_{Ar}), 127.96 (C_{Ar}), 128.28 (C_{Ar}), 128.57 (C_{Ar}), 128.67 (C_{Ar}), 128.72 (C_{Ar}), 131.61 (C_{Ar}), 131.85 (C_{Ar}), 132.35 (C_{Ar}), 132.45 (C_{Ar}), 133.59 (C_{Ar}), 133.76 (C_{Ar}); 169.62 and 170.55 (C=O). NMR ^{29}Si (δ, ppm): -58.52 and -56.09. IR (film, cm^{-1}): 418, 444, 476, 498, 536, 572, 596, 651, 676, 721, 733, 751, 789, 858, 879, 960, 1018, 1081, 1105, 1166, 1257, 1295, 1352, 1366, 1395, 1442, 1456, 1510, 1542, 1558, 1599, 1632, 1699, 1718, 1736, 1827, 1870, 1921, 2767, 2892, 2925, 2972, 3047.

3.1.3. N-(Triethoxysilyl)methyl-N-phenyl-2-(1-naphthyl)acetamide 3

The solution of 1-naphthylacetyl chloride 2.893 g (14.14 mmol) in benzene (10 ml) was added to the mixture of N-(triethoxysilyl) methylaniline 3.808 g (14.14 mmol) (its synthesis see in Supplementary Information), triethylamine 1.430 g (14.14 mmol) and benzene (60 ml). This mixture was stirred at room temperature for 3 h and refluxed for 16 h. The precipitate was filtered off, and the solvent was removed under reduced pressure. The unreacted N-(triethoxysilyl)methylaniline was removed using standard methods under reduced pressure. The rest was extracted by Et_2O after it was removed. Compound **3** is viscous oil, yielding 50% (3.100 g, 7.08 mmol). NMR ^{1}H (δ, ppm): 1.10 (t, 9H, $CH_2\underline{CH_3}$); 3.26 (s, NCH_2); 3.72 (q, 6H, $\underline{CH_2}CH_3$); 3.87 (s, $CH_2C(O)$); 7.08-7.75 (m, 12H, Ph +$C_{10}H_7$). NMR ^{13}C (δ, ppm): 17.99 ($CH_2\underline{CH_3}$); 29.64 (NCH_2); 38.76 ($\underline{CH_2}C(O)$); 58.51 ($\underline{CH_2}CH_3$); 123.80 (C_{Ar}), 125.26 (C_{Ar}), 125.73 (C_{Ar}), 125.93 (C_{Ar}), 127.37 (C_{Ar}), 127.85 (C_{Ar}), 128.07 (C_{Ar}), 128.42 (C_{Ar}), 128.52 (C_{Ar}), 129.41 (C_{Ar}), 129.75 (C_{Ar}), 132.12 (C_{Ar}), 133.72 (C_{Ar}), 144.01 (C_{Ar}); 170.87 (C=O). NMR ^{29}Si (δ, ppm): -55.28. IR (film, cm^{-1}):

3.1.4. N-Silatranylmethyl-N-methyl-2-(1-naphthyl)acetamide 4

Compound **1** (1.871 g, 4.98 mmol) was added to triethanolamine (0.743 g, 4.98 mmol), and this mixture is maintained at room temperature for 6 days. The ethanol released by the reaction was removed from the reaction vessel under vacuum. The solid residue was crystallized from chloroform. Yield 98% (1.887 g, 4.88 mmol), M. p. = 202-203°C. Compound **4** is mixture E and Z conformers. NMR ^{1}H (δ, ppm): 2.69 (s, 2H, NCH_2Si); 2.79 and 2.75 (t, 6H, C-CH_2-N); 3.03 and 2.97 (s, 3H, NMe); 3.76 and 3.73 (t, 6H, OCH_2C); 4.26 and 4.13 (s, 2H, $CH_2C(O)$); 7.24-8.06 (m, 7H, $C_{10}H_7$). NMR ^{13}C (δ, ppm): 35.51 and, 37.39 (NCH_2); 38.11 and 38.18 (NMe); 41.40 and 38.69 ($\underline{CH_2}C(O)$); 50.83 and 50.97 (C-CH_2-N); 57.10 and 57.23 (OCH_2C); 123.74 (C_{Ar}), 124.67 (C_{Ar}), 125.15 (C_{Ar}), 125.38 (C_{Ar}), 125.48 (C_{Ar}), 125.57 (C_{Ar}), 125.85 (C_{Ar}), 126.09 (C_{Ar}), 126.75 (C_{Ar}), 126.84 (C_{Ar}), 127.06 (C_{Ar}), 128.20 (C_{Ar}), 128.29 (C_{Ar}), 128.51 (C_{Ar}), 132.19 (C_{Ar}), 132.64 (C_{Ar}), 132.91 (C_{Ar}), 133.63 (C_{Ar}), 133.72 (C_{Ar}), 133.92 (C_{Ar}); 170.50 and 169.16 (C=O). NMR ^{29}Si (δ, ppm): -77.66 and -71.37. IR (film, cm^{-1}): 480, 505, 540, 576, 599, 628, 648, 696, 730, 789, 810, 877, 912, 938, 1018, 1049, 1089, 1122, 1170, 1191, 1253, 1270, 1311, 1353, 1398, 1453, 1482, 1509, 1627, 1718, 2706, 2878, 2926, 2969, 3009, 3044. Anal. Calcd for $C_{20}H_{26}N_2O_4Si$. C, 62.15; H, 6.78; N 7.25. Found, %: C, 61.88; H, 6.55; N 7.44.

3.1.5. N-Silatranylmethyl-N-isopropyl-2-(1-naphthyl)acetamide 5

Compound **2** (1.863 g, 4.62 mmol) was added to triethanolamine (0.688 g, 4.62 mmol), and this mixture was maintained at room temperature for 13 days. The ethanol released by the reaction was removed from the reaction vessel under vacuum. The solid residue was crystallized from benzene. Yield 94% (1.801 g, 4.34 mmol). M. p. = 182-183°C. NMR ^{1}H (δ, ppm): 1.23 (d, 6H, Me-CH, ^3J = 6.6 Hz); 2.63 (s, 2H, NCH_2); 2.74 (t, 6H, C-CH_2-N, ^3J = 5.5 Hz); 3.72 (t, 6H, OCH_2-C, ^3J = 5.5 Hz); 4.17 (s, 2H, $CH_2C(O)$); 4.40 (quint, 1H, CHMe, ^3J = 6.6 Hz); 7.24-8.06 (m, 7H, $C_{10}H_7$). NMR ^{13}C (δ, ppm): 19.55 (Me-CH); 36.26 (NCH_2); 39.48 ($\underline{CH_2}C(O)$); 48.54 (Me-CH); 50.90 (C-CH_2-N); 57.29 (OCH_2-C); 124.81 (C_{Ar}), 125.10 (C_{Ar}), 125.42 (C_{Ar}), 125.49 (C_{Ar}), 126.59 (C_{Ar}), 127.04 (C_{Ar}), 128.28 (C_{Ar}), 132.98 (C_{Ar}), 133.72 (C_{Ar}), 134.35 (C_{Ar}) 170.22 (C=O). NMR ^{29}Si (δ, ppm): -77.17. IR (film, cm^{-1}): 484, 539, 584, 625, 647, 730, 733, 788, 820, 849, 876, 911, 938, 1018, 1050, 1096, 1122, 1171, 1272, 1301, 1361, 1410, 1454, 1478, 1510, 1626, 1718, 2707, 2877, 2928, 2969, 3045. Anal. Calcd for $C_{22}H_{30}N_2O_4Si$, %: C, 63.74; H, 7.30. Found, %: C, 63.39; H, 7.25.

3.1.6. N-Silatranylmethyl-N-phenyl-2-(1-naphthyl)acetamide 6

Compound **3** (1.478 g, 3.38 mmol) was mixed with triethanolamine (0.504 g, 3.38 mmol) in toluene (10 ml) and added a few drops of ethanol solution of KOH. This mixture was stirred at 110°C for 25h. The solvent and ethanol released by the reaction were removed from the reaction vessel under vacuum. The solid residue was crystallized from benzene. Yield 66% (1.00 g, 2.23 mmol), M. p. = 184-185°C. NMR ^{1}H (δ, ppm): 2.59 (t, 6H, C-CH_2-N, ^3J = 4.7 Hz); 3.25 (s, NCH_2); 3.52 (t, 6H, OCH_2-C, ^3J = 4.7 Hz); 3.81 (s, 2H, $CH_2C(O)$); 7.17-7.75 (m, 12H Ph + $C_{10}H_7$). NMR ^{13}C (δ, ppm): 38.85 (NCH_2); 40.93 ($\underline{CH_2}C(O)$); 50.96 (C-CH_2-N); 57.14 (OCH_2-C); 124.18 (C_{Ar}), 125.13 (C_{Ar}), 125.34 (C_{Ar}), 125.51 (C_{Ar}), 126.68 (C_{Ar}), 126.87 (C_{Ar}), 127.18 (C_{Ar}), 128.25 (C_{Ar}), 128.38 (C_{Ar}), 128.53 (C_{Ar}), 132.27 (C_{Ar}), 133.48 (C_{Ar}), 133.53 (C_{Ar}), 145.16 (C_{Ar}); 169.02 (C=O). NMR ^{29}Si (δ, ppm): -76.61. Anal. Calcd for $C_{25}H_{28}N_2O_4Si$, %: C, 66.94; H, 6.29; N 6.24. Found, %: C, 66.80; H, 5.94; N 6.10.

3.2. X-Ray Experiment

The intensities from single crystals of compound **4** (0.2×0.2×0.4 mm) and **5** (0.1×0.2×0.3 mm) dimensions were collected at 296(2) K using SMART APEX II single crystal diffractometer (Bruker AXS, analytical equipment of Krasnoyarsk Center of collective use of SB RAS) equipped with a CCD-detector, graphite monochromator and Mo Kα radiation source. The orientation matrix and cell parameters were defined and refined for the sets of 19549 reflections for compound **4** and 15037 reflections for compound **5**. The main crystallographic characteristics and experimental parameters are given in Table **6**.

The unit cell corresponds to monoclinic symmetry. The unit cell corresponds to monoclinic symmetry for these compounds. The space group ($P2_1/n$) for compound **4** and space group ($P2_1$) for compound **5** were determined from the statistical analysis of the intensities of all the reflections. The absorption corrections were applied using the SADABS program. The structure was solved by the direct methods using the package SHELXS and refined in the anisotropic approach for non-hydrogen atoms using the SHELXL program [73]. All the hydrogen atoms of these molecules were positioned geometrically as riding on their parent atoms with d(C-H) = 0.97 Å for the C-H bonds and d(N-H)=0.89 Å for all other N-H bonds and $U_{iso}(H) = 1.2U_{eq}(C,N)$. The structural tests for the presence of missing symmetry elements and possible voids were produced using the PLATON program [74].

Table 6. Crystallographic data, details of intensity measurements, and structure refinement of compounds 4 and 5.

Parameter	4	5
Chemical formula	$C_{20}H_{26}NO_4Si$	$C_{22}H_{30}N_2O_4Si$
Molecular weight	386.52	414.57
Temperature (K)	296(2)	296(2)
Space group, *Z*	$P2_1/n$, 4	$P2_1$, 2
a (Å)	12.719(4)	7.5852(6)
b (Å)	11.244(4)	13.3355(9)
c (Å)	14.416(5)	10.6063(8)
β (°)	111.234(8)	95.415(2)
V (Å^3)	1921.7(11)	1068.07(14)
ρ_{calc}(g/cm^3)	1.336	1.289
μ (mm^{-1})	0.151	0.141
Reflections measured	19549	15037
Reflections independent	3922	6464
Reflections with $F > 4\sigma(F)$	2784	3812
$2\theta_{max}$ (°)	52.888	61.378
h, *k*, *l* - limits	$-15 \le h \le 15$; $-13 \le k \le 14$; $-17 \le l \le 17$	$-10 \le h \le 10$; $-19 \le k \le 19$; $-15 \le l \le 15$
R_{int}	0.0653	0.0783
Refinement results	-	-
The weighed refinement of F^2	$w=1/[\sigma^2(F_o^2)+(0.0712P)^2+0.6900P]$ where $P=\max(F_o^2+2F_c^2)/3$	$w=1/[\sigma^2(F_o^2)+(0.1155P)^2]$ where $P=\max(F_o^2+2F_c^2)/3$
Number of refinement parameters	244	262
$R1[F_o > 4\sigma(F_o)]$	0.0535	0.0805
wR2	0.1340	0.1975
Goof	1.037	1.029
$\Delta\rho_{max}$(e/Å^3)	0.374	0.709
$\Delta\rho_{min}$(e/Å^3)	-0.363	-0.333
$(\Delta/\sigma)_{max}$	<0.001	<0.001
Extinction coefficient (SHELXL 2014/7)	none	none

The coordinates of atoms are shown in Tables **1S** and **2S**. The main crystal data are shown in Tables **S3-S6**. The MERCURY program is used for the crystal structure plotting (Fig. **1**) [75]. The crystallographic data are deposited in the Cambridge Crystallographic Data Centre (CCDC 2268388-2268389). The data can be downloaded from the site (www.ccdc.cam.ac.uk/data_request/cif).

CONCLUSION

In conclusion, we note that an approach has been found to synthesize new hybrid silicon-containing amides of 1-naphthyl acetic acid, which can potentially exhibit the properties of phytohormones. The structure of synthesized compounds was confirmed by NMR spectroscopy and X-ray diffraction analysis. The results confirmed the existence of the dative bond N→Si in N-(silatranyl)methylamides of 1-naphtylacetic acid. Results of computational screening have shown that these silatranes are bioavailable and have drug-likeness. Computational screening of silatranyl derivatives shows that they are bioavailable and drug-like. The potential pharmacological activity of all synthesized compounds was calculated. In addition, these compounds can be applications in material science and technology.

LIST OF ABBREVIATIONS

TBP = Trigonal Bipyramid

HBA = H-bond Acceptors

PSA = Polar Surface Area

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

The data and supportive information are available within the article.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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SUPPLEMENTARY MATERIAL

Supplementary material is available on the publisher's web site along with the published article.

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