

E- β -STYRYLGERMATRANE

L. Ignatovich, S. Belyakov, Yu. Popelis, and E. Lukevics

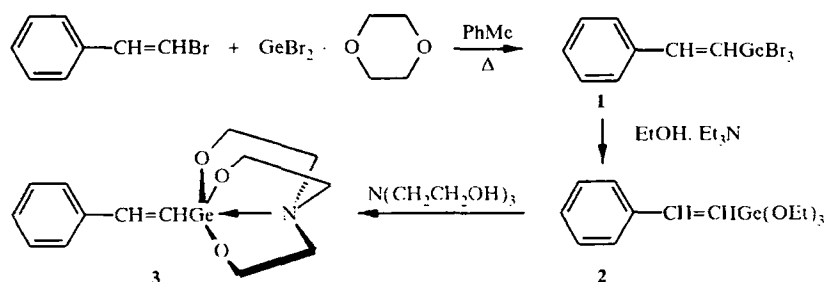
E- β -1-(2-Phenylethenyl)-2,8,9-trioxa-5-aza-1-germatricyclo[3.3.3.0^{1,3}]undecane (β -styrylgermatrane) was obtained as the result of sequential reactions: the introduction of germanium dibromide at the C-Br bond of β -bromostyrene and the alcoholysis of tribromogermane to the triethoxy derivative with subsequent transesterification by triethanolamine. The structure of β -styrylgermatrane and 2.215 Å length of the transannular N→Ge bond were established by the method of NMR and X-ray diffraction analysis. It was found that the introduction of the CH=CH portion between the aromatic ring and the atrane grouping lowers the toxicity of the compound by the factor of 40.

Keywords: germatrane, molecular structure, toxicity.

Practically all the germatranes show biological activity, depending to a significant extent on the substituent at the germanium atom [1-4]. We established that the presence of an aromatic or heteroaromatic ring directly connected to the germatrane grouping favors an increase in the toxicity of the compound [3]. Thus, phenylgermatrane is a toxic substance with the mean lethal dose for white mice, LD₅₀ 35.5 mg/kg [5]. Substitution of the benzene ring by the vinyl group lowers the toxicity of the germatrane by more than a factor of 150 (LD₅₀ 5600 mg/kg). In this connection, there was interest in combining both of these portions in one molecule and studying the structure and biological activity of the new germatrane.

On the other hand, compounds of germanium with expanded coordination – the germatranes – attract the attention of investigators as models for theoretical organic chemistry. Analysis of data of the Cambridge crystallographic bank showed that more than 30 structures of the germatranes have been studied and registered up to the present [5-32]. The structure of germatrane is a distorted trigonal bipyramid in which the substituent R and the nitrogen atom are disposed in the axial plane, and three oxygen atoms are disposed in the equatorial plane. Displacement of the Ge atom from the equatorial plane to the side of the substituent R (Δ Ge) in the structures studied occurs in the limits 0.095-0.37 Å. The length of the N→Ge bond is also determined by the nature of the substituent R, and varies from 2.011 to 2.290 Å. Thus, the N→Ge bond lengths for 1-fluoro-, 1-isothiocyanato-, and 1-*tert*-butylgermatrane are 2.011 Å [29], 2.081 Å [22], and 2.238 Å [10] respectively. Such a trend was also observed for silatranes (N→Si 1.965-2.24 Å) [33-38]. It was found [39] in the series of silatranes that the introduction of the CH=CH portion between the aromatic ring and the atrane group significantly lowers the length of the transannular bond (2.127 Å) in comparison with the N→Si bond determined for the α -modification of phenylsilatrane (2.193 Å) [40]. However, the value of the N→Si bond length in β -styrylsilatrane is comparable with the value of the transannular bond determined for the γ -modification of phenylsilatrane (2.132 Å) [41, 42].

β -Styrylgermatrane **3** was obtained with the yield of 51% by the boiling of the 1:7 mixture of *cis,trans*- β -bromostyrene with germanium dioxanedibromide in toluene for 10 h with subsequent treatment of β -styryltribromogermane **1** with ethyl alcohol in the presence of triethylamine and the transesterification of the triethoxy derivative **2** by triethanolamine.



The structure of *E*- β -1-(2-phenylethenyl)-2,8,9-trioxa-5-aza-1-germatricyclo[3.3.3.0]^{1,5}undecane (**3**) was studied by the method of X-ray diffraction analysis. The general shape of the molecule is presented in Fig. 1.

In the crystalline state, the length of the N $\rightarrow$ Ge bond in β -styrylgermatrane (2.215 Å) is comparable with the length of the transannular bond in phenylgermatrane (2.212 Å) [5]. The C–Ge bond in β -styrylgermatrane is 0.024 Å shorter than the C–Ge bond in phenylgermatrane. A similar change in bond length (C–Si) was also observed for β -styrylsilatrane by comparison with the α -modification of phenylsilatrane [39].

Study of the biological activity of β -styrylgermatrane showed that the removal of the atranyl grouping from the aromatic ring lowers the toxicity of the compound by a factor of ~ 40 (LD₅₀ 1410 mg/kg for β -styrylgermatrane, and LD₅₀ 35.5 mg/kg for phenylgermatrane). On the other hand, the introduction of the phenyl substituent at the β -position of the vinyl group increases the toxicity of the germatrane by fourfold.

At the dose of 50 mg/kg, β -styrylgermatrane shows marked antihypoxic activity, increasing the life period of animals in conditions of hypoxia by the factor of 2.5. The antihypoxic activity is weaker for phenylgermatrane whereby the life period only increases by a factor of 1.7.

EXPERIMENTAL

β -1-(2-Phenylethenyl)-2,8,9-trioxa-5-aza-1-germatricyclo[3.3.3.0]^{1,5}undecane (3). The mixture of *cis,trans*- β -bromostyrene (1:7, 1.46 g, 0.008 mol) and germanium dioxanedibromide (2.28 g, 0.007 mol) in toluene (20 ml) is boiled for 10 h. The formation of β -styryltribromogermene **1** is monitored by chromato-mass spectrometry. Mass spectrum of compound **1** (EI, 70 eV), *m/z* (%): 414 (*M*⁺, 25), 335 (*M*⁺ - Br, 50), 256 (*M*⁺ - 2Br, 46), 182 (91), 153 (GeBr, 40), 103 (C₆H₅CH=CH, 75), 77 (C₆H₅, 100), 51 (56). Tribromogermene **1** is not isolated from the reaction mixture, and is treated with ethyl alcohol (0.97 g, 0.021 mol) in the presence of triethylamine (2.13 g, 0.021 mol). Salt Et₃N·HBr is filtered off. The transesterification of the triethoxy derivative **2** with triethanolamine (1.04 g, 0.007 mol) affords 1.15 g (51%) of *E*- β -styrylgermatrane **3** as a white crystalline substance; mp 208–210°C. Recrystallization is performed from 1:1 chloroform–ethanol mixture. ¹H NMR spectrum, δ (CDCl₃): 2.91 (6H, t, N–CH₂); 3.86 (6H, t, O–CH₂); 6.38 (1H, d, CH=CH); 6.44 (1H, d, CH=CH,

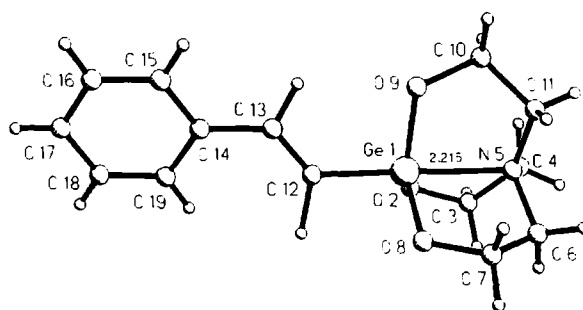


Fig. 1. Molecular structure of *E*- β -styrylgermatrane.

TABLE 1. Conditions of X-Ray Diffraction Analysis and Geometrical Parameters of the β -Styrylgermatrane Molecule

Empirical formula	$C_{14}H_{19}GeNO_3$
Molecular mass	321.89
Temperature of exposure	293(2) K
Wavelength ($\text{\AA}$)	0.71069
Crystal system	Rhombic
Space group	$Pbca$ (No. 61)
Cell parameters ($\text{\AA}$)	
<i>a</i>	10.759 (2)
<i>b</i>	13.571 (2)
<i>c</i>	19.493 (3)
Volume of the elementary cell ($\text{\AA}^3$)	2846.2 (8)
<i>Z</i>	8
Density (g/cm^3)	1.502 (1)
Absorption coefficient (mm^{-1})	2.156
<i>F</i> (000)	1328
$2\theta_{\text{max}}$ (deg)	45.0
No. of measured reflections	1870
No. of reflections with the $I > 2\sigma(I)$	1251
Method of interpretation and specification of structure	Method of heavy atom, full-matrix MLS [43]
No. of specified parameters	173
Final factor of divergence	0.0551
Extinction coefficient	0.0046
Ge–N, $\text{\AA}$	2.215 (6)
Ge–C, $\text{\AA}$	1.939 (7)
Ge–O, $\text{\AA}$	1.793 (5)
C=C, $\text{\AA}$	1.321 (10)
$\angle$ N–Ge–C, deg	178.6 (2)
$\angle$ C–Ge–O, deg	96.3 (2)
Δ Ge, $\text{\AA}$	0.239 (1)

$J = 18.3$ Hz); 7.18–7.45 ppm (5H, m, C_6H_5). ^{13}C NMR spectrum, δ (CDCl_3): 42.21 ($\text{CH}_2\text{--N}$); 61.88 ($\text{CH}_2\text{CH}_2\text{--N}$); 88.11 ($\text{CH}=\text{CH}\text{--Ge}$); 125.06 (*m*- C_6H_5); 128 (*p*- C_6H_5); 129.42 (*o*- C_6H_5); 135.66 (*i*- C_6H_5); 146.26 ppm ($\text{CH}=\text{CH}\text{--Ge}$). Mass spectrum (EI, 70 eV), m/z (%): 323 (M^+ , 23), 293 (13), 280 (6), 263 (8), 220 ($M^+ - C_6H_5\text{CH}=\text{CH}$, 10), 190 (9), 176 (15), 160 (57), 146 (100), 130 (18), 117 (8), 103 ($M^+ - \text{Ge}(\text{OCH}_2\text{CH}_2)_3\text{N}$, 15), 77 (32), 66 (45), 42 (39). Found, %: C 51.58; H 6.01; N 4.37. $C_{14}H_{19}NGeO_3$. Calculated, %: C 52.35; H 5.96; N 4.36.

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