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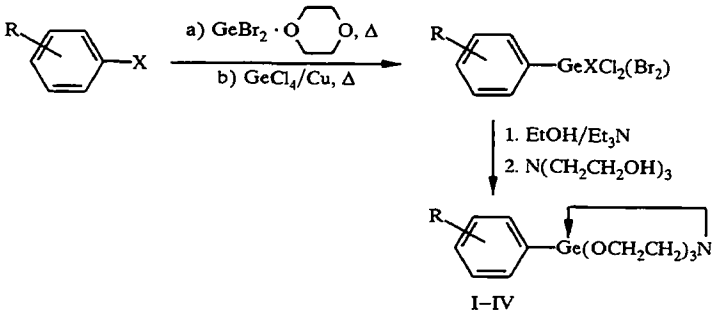
SYNTHESIS, STRUCTURE, AND TOXICITY OF ARYLGERMATRANES

E. Lukevics, L. Ignatovich, L. Khokhlova, and S. Belyakov

A series of tolylgermatranes were synthesized. Their structures and the length of the transannular N→Ge bond were determined. It was shown that arylgermatranes are less toxic than the corresponding silatranes.

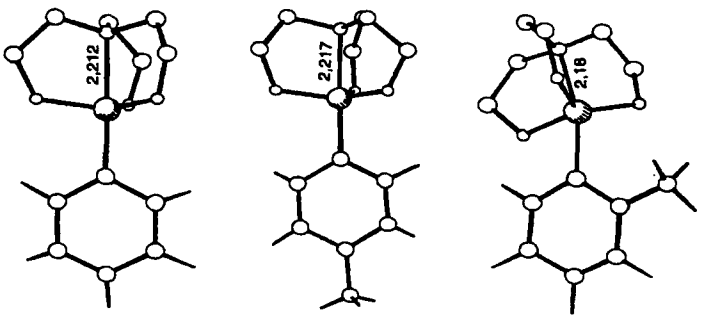
Heteroarylgermatranes and heteroarylsilatranes have a wide range of biological activity [1-4]. In order to study the effect of an aromatic substituent on the structure and biological characteristics of germatranes we synthesized a series of new phenyl- and tolylgermatranes. For their preparation we used the insertion of germanium dibromide dioxanate at the C—halogen bond (a) [5] or the reaction of aryl halides with germanium tetrachloride in the presence of copper powder (b) [6] followed by alcoholysis and transesterification of the obtained trihalogen derivatives:



I–IV

I R = H, X = I; II R = 4-CH_3, X = Br; III R = 3-CH_3, X = Br; IV R = 2-CH_3, X = Br

The yields of the compounds (I-IV), the elemental analyses, and the ^1H NMR spectra are given in Table I. The structure of the germatranes (I, II, IV) was studied by x-ray crystallographic analysis. The general appearance of the



I II IV

Fig. 1. Stereochemical models of the germatranes (I, II, IV).

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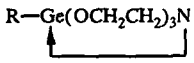
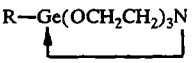
TABLE 1. Physicochemical Characteristics of the Arylgermatranes



R	mp, °C	Molecular formula	Found %/ Calculated %			^{1}H NMR, δ, ppm	Yield, %
			C	H	N		
C_6H_5	233...235	$C12H_{17}NO_3Ge$	48,69 48,72	5,72 5,79	4,64 4,73	2,91 (6H, t, N—CH_2); 3,89 (6H, t, O—CH_2); 7,31...7,71 (5H, m, C_6H_5)	67
4-$CH_3C_6H_4$	211...213	$C13H_{19}NO_3Ge$	50,04 50,39	6,30 6,18	4,55 4,52	2,30 (3H, s, CH_3); 2,90 (6H, t, N—CH_2); 3,88 (6H, t, O—CH_2); 7,09...7,18 (2H, d, C_6H_4); 7,57...7,66 (2H, d, C_6H_4)	15
3-$CH_3C_6H_4$	217...218	$C13H_{19}NO_3Ge$	50,07 50,39	6,17 6,18	4,54 4,52	2,31 (3H, s, CH_3); 2,89 (6H, t, N—CH_2); 3,89 (6H, t, O—CH_2); 7,11...7,56 (4H, m, C_6H_4)	28
2-$CH_3C_6H_4$	192...194	$C13H_{19}NO_3Ge$	50,16 50,39	6,20 6,18	4,49 4,52	2,56 (3H, s, CH_3); 2,89 (6H, t, N—CH_2); 3,84 (6H, t, O—CH_2); 7,15 (3H, m, C_6H_4); 7,85 (1H, m, C_6H_4)	14

TABLE 2. Geometric Parameters of the Molecules of the Germatranes



Parameters	C_6H_5	4-$CH_3C_6H_4$	2-$CH_3C_6H_4$
Crystal system	Orthorhombic	Monoclinic	Orthorhombic
a, Å	15,910(2)	13,608(3)	9,759(2)
b, Å	6,661(1)	14,012(3)	12,719(2)
c, Å	11,719(2)	14,330(2)	11,011(2)
β,°	90,0	99,13(1)	90,0
V Å^3	1242,0(3)	2697,8(9)	1366,7(5)
Space group	P $na2_1$	P $2_1/c$	P $na2_1$
Z	4	8	4
D_x, g·cm^{-3}	1,582(1)	1,526(1)	1,506(1)
Number of reflections	1083	2872	915
R factor	0,0323	0,0458	0,1083
Ge—N, Å	2,212(5)	2,217(4)	2,18(1)
Ge—C, Å	1,947(6)	1,946(5)	1,94(1)
Gr—O, Å	1,797(4)	1,791(3)	1,79(1)
< N—Ge—C, deg	177,5(2)	178,9(2)	145(2)

molecules is shown in Fig. 1, and the principal geometric parameters are given in Table 2. The crystal structures of the germatranes (I, II) are isomorphous with the corresponding silatranes [7, 8]. In compounds (II, IV) disordering of the molecules in the crystal is observed. Change in the position of the substituent in the aromatic ring has a substantial effect on the N—Ge—C angle and hardly changes the length of the transannular N→Ge bond at all (Table 2).

In the crystalline state the N→Ge bonds in the arylgermatranes are rather longer than in the corresponding furyl- and thienylgermatranes [9]. The introduction of a methyl substituent at the *o* position of the benzene ring reduces the N—Ge—C angle from 177.5° to 145° (Table 2).

It is known that phenylsilatrane and to an even greater degree *p*-tolylsilatrane are unusually toxic for warm-blooded animals; the lethal dose (LD_{50}) of 1-phenylsilatrane for white mice amounts to 0.33 mg/kg, while that of *p*-tolylsilatrane is 0.20 mg/kg [1]. Study of the biological activity of the germatranes (I, II) showed that 1-phenylgermatrane (LD_{50} 35.5 mg/kg) is 100 times less toxic than its silicon analog. The introduction of a methyl group at the *p* position of the aromatic ring reduces the toxicity of compound (II) even more (LD_{50} 70.5 mg/kg).

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