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Silicon-, Germanium-, and Tin-containing Derivatives of Barbital and Methyluracil

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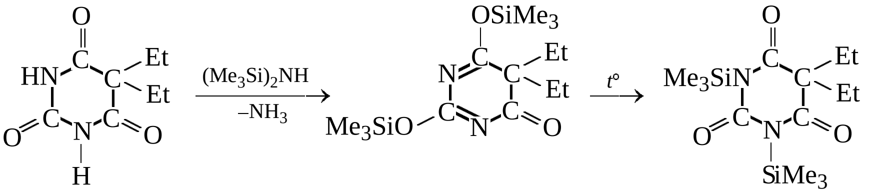
Abstract — 1,3-Bis(trimethylsilyl)- and 1,3-bis(tributylstannyl)-5,5-diethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-triones were synthesized in high yields by the reactions of 5,5-diethyl-2,4,6(1*H*, 3*H*,5*H*)-trione (barbital) with hexamethyldisilazane and bis(tributylstannyl) oxide, respectively. The products were reacted with acetyl, benzoyl, and 3-(triethylgermyl)propionyl halides to obtain the corresponding bisacylated pyrimidine derivatives. The reaction of 1-methyluracil with $(Bu_3Sn)_2O$ gave 1-methyl-3-(tributylstannyl)pyrimidine-2,4(1*H*,3*H*)-dione.

Aiming at extending the range of biologically active nitrogen-containing compounds we turned to the reactions of 5,5-diethyl-2,4,6(1*H*,3*H*,5*H*)-trione (barbital), one of the most active opiates, with HMDS and bis(tributylstannyl) oxide. Organosilicon derivatives of pyrimidine and *sym*-triazine have received sufficient study [1, 2], but 1,3-bis(trimethylsilyl)-5,5-diethyl(1*H*, 3*H*,5*H*)-trione (**Ib**) has only been mentioned in [3], where it, along with other nitrogen-containing compounds, has been characterized by GLC parameters. No physicochemical or spectral characteristics, elemental analysis, or synthesis of this compound have so far been reported.

We found that barbital reacts with HMDS in the presence of catalytic amounts of ammonium sulfate (no solvent, heating from 124 to 164°C, 2–3 h) to give compound **Ia** as an amorphous Paraffin-like colorless material formed upon cooling to room temperature of the yellowish thick transparent oil remaining after evacuation of the reaction mixture (3–4 mm Hg, 160°C, 1 h). Subsequent vacuum distillation of this material gave a colorless transparent glycerol-like liquid that no longer solidified (compound **Ib**). By NMR and IR spectroscopy we showed that compounds **Ia** and **Ib** are the O–Si and N–Si isomers of the organosilicon barbital derivatives that exist in different aggregative states at room temperature.



Ia **Ib**

(1)

Thus, undistilled compound **Ia** (solid) has the following ^1H NMR spectrum (200 MHz; DMF), δ, ppm: 0.09 s, 0.12 s ($OSiMe_3$), 0.86 t (6H, CH_3, *J* 7.0 Hz), 1.93 q (4H, CH_2CH_3). Compound **Ib** (liquid) formed during vacuum distillation has another ^1H NMR spectrum, δ, ppm: 0.42 s ($NSiMe_3$), 0.77 t (6H, CH_3, *J* 7.2 Hz), 1.88 q (4H, CH_2CH_3). The same method was used to show that compound **Ib** contains an admixture of isomer **Ia**, whereas compound **Ia** obtained under more rigid conditions (heating above 164°C longer than 3 h) contains an admixture of compound **Ib**. As seen from the table, the IR spectrum of compound **Ia**, unlike that of compound **Ib**, contains a Si–N absorption band (950 cm^{-1}). The IR spectrum of compound **Ib**, as would be expected [3], has a Si–O–C absorption band (1110 cm^{-1}). Expected changes in the

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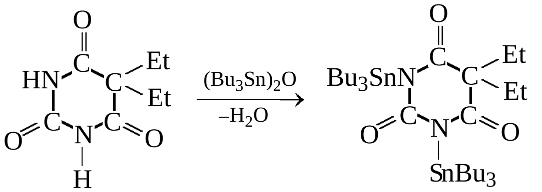
Absorption bands, ν, cm^{-1}, in the IR spectra of pyrimidine derivatives

Comp. no.	C–H	C=O	CN ring	CH in C_2H_5	Other vibrations
Ia	2980, 2920	1700, 1670	1400, 800	1280, 890	1245, 845 ($CHMe_3Si$), 1110 (SiOC)
Ib	2980, 2920	1730, 1690, 1680	1410, 780	1270, 870	1240, 840 ($CHMe_3Si$), 950 (SiN)
II	2960, 2910, 2870, 2845	1690, 1640, 1610	1450, 1425, 760	1240, 860	
III	1745, 1690	1460, 755	1220, 830	3100, 805 (Ph)	
IV	1740, 1690, 1650	1420, 740	1220, 850		
V	2960, 2920, 2860	1750, 1705, 1670	1430, 755	1230, 860	605, 505 (GeC)
VI	2980, 2940, 2870, 2840	1770, 1700	1460, 1450, 1415, 760	1240, 870	

carbonyl absorption region are also observed. Thus, unlike related *sym*-triazine derivatives [3], organosilicon derivatives of barbital prefer the oxo form.

The reaction of barbital with bis(tributylstannyl) oxide (no solvent, gradual heating from 100 to 208°C, slow evacuation from 760 to 3 mm Hg, 2 h) gave 92% of 1,3-bis(tributylstannyl)-5,5-diethylpyrimidine-2,4,62,4,6(1*H*,3*H*,5*H*)-trione (**II**) as a yellowish transparent glycerol-like liquid.

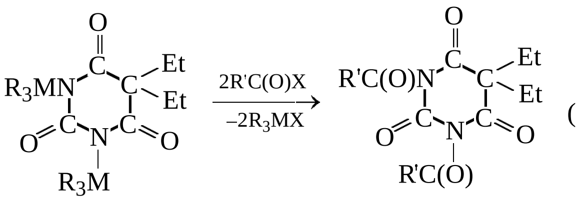


(2)

II

In the IR spectra of compound **II** (see table), like in those of organotin *sym*-triazines, the carbonyl absorption frequencies are decreased, probably, because of weakening of the C=O bonds due to metal coordination with neighboring ring nitrogen atoms [3].

Compounds **I** and **II**, like *sym*-triazines, can give acyl derivatives with carboxylic acid chlorides. Thus, compound **I** reacts with benzoyl chloride (gradual heating to 120°C with simultaneous distillation of chlorotrimethylsilane, 2 h) to give 88% of 1,3-dibenzoyl-5,5-diethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (**III**) as fine colorless crystals.



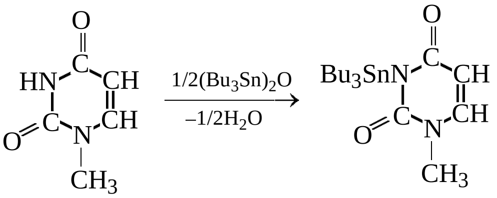
(3)

III–**IV**

R_3M = Me_3Si, Bu_3Sn; R' = Ph (**III**), Me (**IV**), $Et_3Ge\cdot(CH_2)_2$ (**V**); X = Cl, Br.

In a similar way, from compounds **I** and **II** we prepared 1,3-diacetyl-5,5-diethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (**IV**) and 1,3-bis[3-(triethylgermyl)propionyl]-5,5-diethyldiethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (**V**) in yields of up to 71 and 60%, respectively. The IR spectra show that acylated barbital derivatives **III**–**V**, as would be expected, prefer the lactam form. The same isomeric form of compounds **I** and **II** also follows from the calculated molecular refractions (MR_D).

Unlike barbital, 1-methyluracil, another pyrimidine derivative, is much less reactive toward HMDS. Upon prolonged heating of the reagents under reflux in the presence of catalytic amounts of ammonium sulfate (48 h, 124°C), slight ammonia evolution was observed, and the starting compounds were isolated almost unchanged. At the same time, when the same pyrimidine derivative was heated with bis(tributylstannyl) oxide under conditions of synthesis of compounds **II** [reaction (2)], 1-methyl-3-(tributylstannyl)pyrimidine-2,4(1*H*,3*H*)-dione (**VI**) was formed in a yield of up 90%.



(4)

VI

The IR spectrum gave evidence in favor of the lactam structure of compound **VI**.

Compounds **I** and **II** are readily hydrolyzed with atmospheric moisture, whereas compounds **III**–**VI** are fairly stable and fast react with water on heating only. The major hydrolysis product is the corresponding starting pyrimidine, which implies preservation of the ring structure in the course of all the above interconversions.

EXPERIMENTAL

The IR spectra were obtained on Specord IR-75 and Specord M-80 spectrophotometers in thin films (neat or with mineral oil) between KBr or ZnSe plates. The 1H NMR spectra were measured on a Bruker DPX-200 spectrometer (200 MHz, DMF). The reactions were performed under dry argon or in a vacuum. The starting $Et_3Ge(CH_2)_2C(O)Cl$ was prepared by the procedure in [4].

Reaction of barbital with hexamethyldisilazane. A mixture of 10.0 g of barbital and 8.75 g of HMDS (reagent ratio 1 : 1) was refluxed in the presence of catalytic amounts of $(NH_4)_2SO_4$ until ammonia no longer evolved (3 h). The final temperature of the reaction mixture was 130°C. During reaction the starting pyrimidine dissolved completely. After cooling, 17.0 g (95%) of compound **Ia** was obtained as a Paraffin-like material, mp > 50°C. Vacuum distillation of the product gave 14.3 g (80%) of compound **Ib** as a colorless glycerol-like liquid, bp 137–138°C (5 mm Hg), d_4^{20} 1.0320, n_D^{20} 1.4720. MR_D 89.145, calc. 89.184 (ring increment –1.20 [5]). Found, %: C 51.28; H 8.61; Si 16.61. $C_{14}H_{28}N_2O_3Si_2$. Calculated, %: C 51.18; H 8.59; Si 17.10.

Reaction of barbital with bis(tributylstannyl) oxide. A mixture of 0.22 g of barbital and 0.71 g of bis(tributylstannyl) oxide (reagent ratio 1 : 1) was heated in a distillation flask for 1 h at atmospheric pressure and then for 1 h with gradual evacuation to 5 mm Hg. The maximal temperature was 208°C. Compound **II**, 0.84 g (92%), was obtained as a yellowish transparent glycerol-like liquid, d_4^{20} 1.2240, n_D^{20} 1.5081. MR_D 185.676, calc. 185,168. Found, %: C 50.30; H 8.82; Sn 31.55. $C_{32}H_{64}N_2O_3Sn_2$. Calculated, %: C 50.42; H 8.46; Sn 31.14. Water separation was observed during reaction.

Reaction of 1,3-bis(trimethylsilyl)-5,5-diethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (Ib) with benzoyl chloride. A mixture of 0.76 g of compound **Ib** and 0.66 g of benzoyl chloride (reagent ratio 1 : 2) was heated in a distillation flask until chlorotrimethylsilane no longer distilled, n_D^{20} 1.3880. After cooling to room temperature, a precipitate formed and was washed with absolute ether and dried in a vacuum to obtain 0.80 g (88%) of compound **III** as colorless fine crystals, mp 214°C. Found, %: C 67.00; H 5.54. $C_{22}H_{20}N_2O_5$. Calculated, %: C 67.34; H 5.14.

Compound **IV** was obtained in a similar way from compound **II** and acetyl bromide, yield 71%. Found, %: C 53.36; H 6.26. $C_{12}H_{16}N_2O_5$. Calculated, %: C 53.72; H 6.02.

Reaction of 1,3-bis(trimethylsilyl)-5,5-diethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)trione with 3-(triethylgermyl)propionyl chloride. A solution of 3.15 g of $Et_3Ge(CH_2)_2C(O)Cl$ in 10 ml of dry toluene was added dropwise with stirring to a solution of 1.97 g of compound **Ib** in 30 ml of the same solvent (reagent ratio 1 : 2). The mixture was stirred for 12 h, the solvent was removed, and the viscous residue was dissolved in chloroform. Compound **IV**, 2.22 g (60%), was precipitated as yellowish crystals from the chloroform solution with hexane, mp 184–189°C. Found, %: C 50.55; H 7.99; Ge 23.59. $C_{26}H_{48}Ge_2N_2O_5$. Calculated, %: C 50.87; H 7.88; Ge 23.65.

Reaction of 1-methyluracil with bis(tributylstannyl) oxide. A mixture of 0.28 g of 1-methyluracil and 0.67 g of bis(tributylstannyl)oxide (reagent ratio 2 : 1) was heated in a distillation flask for 1 h at atmospheric pressure and then for 1 h with gradual evacuation to 5 mm Hg [3]. The maximal temperature was 200°C. Compound **VI**, 0.84 g (90%), was obtained as a yellowish salvelike material. Found, %: C 49.00; H 7.71; Sn 28.89. $C_{17}H_{32}N_2O_2Sn$. Calculated, %: C 49.18; H 7.77; Sn 28.59. Water separation was observed during reaction.

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