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SYNTHESIS OF β-CARBOLINE WITH THE GERMATRANE PORTION

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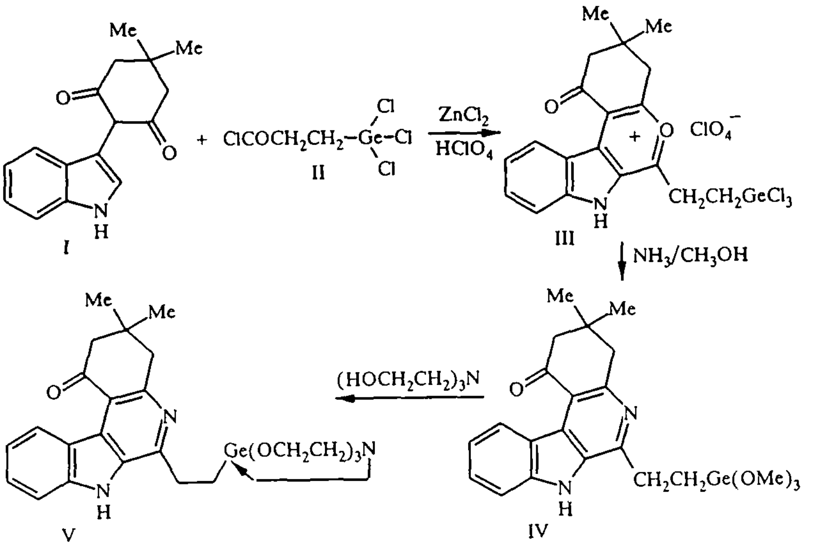
The 1-oxo-3,3-dimethyl-6-(β-trichlorogermyl)ethyl-1,2,3,4-tetrahydroindolo[2,3-c]pyrylium salt, obtained by the acid-catalyzed acylation of 2-(indol-3-yl)dimedone with β-trichlorogermylpropionyl chloride and the subsequent reaction with ammonia and triethanolamine, was converted to the corresponding β-carboline with the germatrane portion.

The distribution in nature and the variety of pharmacological properties of β-carbolines have drawn the attention of chemists and biologists to them for many decades [1]. Hetarylgermatranes also have a wide spectrum of biological action and are actively studied [2, 3]. It can be assumed that the production of an organic molecule with the β-carboline and germatrane portions will significantly improve known forms of activity or reveal new forms of activity.



In order to accomplish this task, the approach to the synthesis of pyridine bases from the corresponding pyrylium salts, developed in our laboratory, was utilized. The method consists of the acid-catalyzed acylation of 2-(indol-3-yl)dimedone (I) by β-trichlorogermylpropionyl chloride (II) in the presence of anhydrous zinc chloride. The resulting chlorozincate was converted to the perchlorate by perchloric acid. The IR spectrum of the perchlorate (III) contains absorption bands characteristic of the pyrylium ring at 1635 cm^{-1} and the carbonyl group at 1680 cm^{-1}. The ^1H NMR spectrum of the salt (III) contains characteristic triplets of the protons of the α-CH_2 group at 4.17 ppm and the β-CH_2 group at 2.83 ppm, pertaining to the $CH_2CH_2GeCl_3$ portion. The boiling of the perchlorate (III) with the methanolic solution of ammonia leads to the formation of the corresponding pyridine base and the simultaneous methanolysis of the trichlorogermanium group. Transetherification of the trimethoxygermane (IV) with triethanolamine affords the germatrane (V).

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EXPERIMENTAL

The ^1H NMR spectrum of compound (III) was registered on the Tesla BS-467 instrument (60 MHz) in trifluoroacetic acid. The ^1H NMR spectra of the compounds (IV) and (V) were registered on the Gemini-200 instrument in pyridine-D_5; the internal standard was TMS. The IR spectra of the compounds obtained were registered on the UR-20 spectrometer in mineral oil.

1-Oxo-3,3-dimethyl-6-(β-trichlorogermyl)ethyl-1,2,3,4-tetrahydroindolo[2,3-c]pyrylium Perchlorate (III). The mixture of 2.37 g (0.01 mole) of 2-(indol-3-yl)dimedone (I), 5.4 g (0.02 mole) of β-trichlorogermylpropionyl chloride (II), and 2.7 g (0.02 mole) of anhydrous zinc chloride in 25 ml of dry CH_2Cl_2 is stirred for 24 h at room temperature. The methylene chloride is evaporated, and to the residue is added the solution of 2 ml of 70% perchloric acid in 10 ml of glacial acetic acid. The residue is filtered off, washed with dry ether, and dried. The yield of 2.4 g (56%) of compound (III) is obtained; it has the T_{decomp} 200°C. Purification is performed by reprecipitation with ether from nitromethane. The ^1H NMR spectrum (CF_3COOH) is as follows: 1.40 ppm (6H, s, 3,3-CH_3), 2.83 ppm (2H, t, $CH_2\underline{CH_2}GeCl_3$), 3.06 ppm (2H, s, 2-$CH_2$), 3.57 ppm (2H, s, 4-$CH_2$), 4.17 ppm (2H, t, $\underline{CH_2}CH_2$-$GeCl_3$), 7.81 ppm (3H, m, 8,9,10-H arom.), and 9.33 ppm (1H, d, 11-H). Found, %: C 53.4, H 4.1, N 3.1, and Cl 33.4. $C_{19}H_{19}NCl_4O_6Ge$. Calculated, %: C 53.1, H 4.1, N 3.3, and Cl 33.1.

1-Oxo-3,3-dimethyl-6-(β-trimethoxygermyl)ethyl-1,2,3,4-tetrahydroindolo[2,3-c]quinoline (IV). The perchlorate (III) (2 g, 4.7 mmole) is treated with 30 ml of the methanolic solution of ammonia. The mixture is boiled for 15 min and cooled. The crystalline substance is filtered off. The yield of 1 g (47%) of compound (IV) is obtained; it has the mp >350°C. Purification is performed by reprecipitation with ether from acetone. The ^1H NMR spectrum (pyridine-D_5) is as follows: 1.16 ppm (6H, s, 3,3-CH_3), 2.13 ppm (2H, t, $CH_2\underline{CH_2}Ge(CH_3)_3$), 2.62 ppm (2H, s, 2-$CH_2$), 2.93 ppm (2H, s, 4-$CH_2$), 3.20 ppm (2H, t, $\underline{CH_2}CH_2Ge(OCH_3)_3$), 3.50 ppm (9H, s, $Ge(OCH_3)_3$), 7.25 ppm (1H, t, 10-H), 7.45 ppm (1H, t, 9-H), 7.53 ppm (1H, d, J = 8 Hz, 8-H), 9.35 ppm (1H, d, J = 8 Hz, 11-H), and 11.09 ppm (1H, s, 7-NH). Found, %: C 57.5, H 6.4, and N 6.3. $C_{22}H_{24}N_2O_4Ge$. Calculated, %: C 57.8, H 6.1, and N 6.1.

1-Oxo-3,3-dimethyl-1,2,3,4-tetrahydroindolo[2,3-c]quinolyl-6-(β-ethylgermatrane) (V). The mixture of 1 g (2.2 mmole) of the trimethoxygermane (IV) and 0.37 g (2.5 mmole) of triethanolamine in 50 ml of $CHCl_3$ is boiled for 10 h. The solvent is removed, and the residue is crystallized from alcohol. The yield of 0.7 g (63%) of compound (V) is obtained; it has the mp 244-246°C. The 1H NMR spectrum (pyridine-D_5) is as follows: 1.16 ppm (6H, s, 3,3-CH_3), 1.45 ppm (2H, t, $CH_2\underline{CH_2}Ge$), 2.68 ppm (2H, s, 2-CH_2), 2.83 ppm (6H, t, N−CH_2), 3.19 ppm (2H, s, 4-CH_2), 3.38 ppm (2H, t, $\underline{CH_2}CH_2Ge$), 3.79 ppm (6H, t, O−CH_2), 7.25 ppm (1H, t, 10-H), 7.45 ppm (1H, t, 9-H), 7.53 ppm (1H, d, J = 8 Hz, 8-H), 9.35 ppm (1H, d, J = 8 Hz, 11-H), and 11.09 ppm (1H, s, 7-NH). Found, %: C 58.6, H 6.3, and N 8.4. $C_{25}H_{31}N_3O_4Ge$. Calculated, %: C 58.9, H 6.1, and N 8.2.

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