and more reliable method for obtaining dioxopiperazines.

The reaction of α-chloroacetamides with sodium has not hitherto been studied. The work carried out in this direction has shown that in anhydrous media in the presence of sodium the chloroacetanilides form 2,5-dioxopiperazines (see table).

At temperatures of about 20° C no appreciable reaction takes place in 2 hr, but at only 40° C the reaction is complete in 1 hr.

To elucidate the influence of the solvents on the field of dioxopiperazines we carried out a series of experiments using various solvents (benzene, toluene, anisole, chlorobenzene). The results showed that the solvents have no substantial influence on the yield of dioxopiperazines.

To confirm the structure of the compounds obtained we recorded their IR spectra (see table). The spectra were taken on a UR-10 spectrophotometer. The substances were studied in the form of tablets with KBr.

EXPERIMENTAL

Synthesis of 1,4-diaryl-2,5-dioxopiperazines. With heating, in a flask fitted with a stirrer, reflux condenser, and thermometer, 0.023 mole of chloroacetanilide was dissolved in 70 ml of anhydrous benzene or toluene. The contents of the flask were brought to 60° C and 0.023 g-at of comminuted metallic sodium was added, after which the evolution of hydrogen, identified chromatographically, was observed. During the whole of the experiment, the solution was stirred vigorously and was thermostatted at 60 ± 2° C. After 1 hr, the flask was rapidly cooled, the mixture was filtered, and the precipitate was washed with hot ethanol to eliminate α-chloroacetamide and sodium. Then the crystals were treated with water until the reaction was neutral and the test for chloride ion was negative, and they were crystallized from acetic acid.

The constants of the diphenyl- and di-p-tolyldioxopiperazines obtained correspond to those given in the literature [4].

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5 June 1967

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INDOLE DERIVATIVES

XXXVIII. Synthesis of 2-O-(Indol-3'-ylalkyl)Glycerols*

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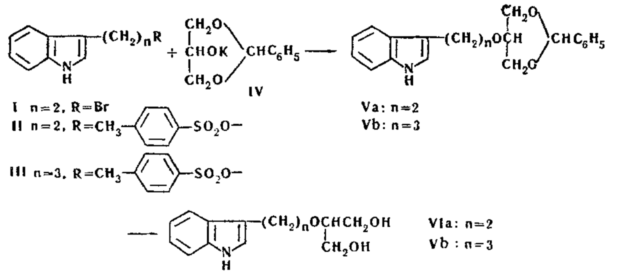
Khimiya Geterotsiklicheskikh Soedinenii, Vol. 5, No. 5, pp. 937–939, 1969

UDC 547.755.07:543.544.542.941

1,3-O-Benzylidene derivatives of 2-O-(indol-3'-ylalkyl)glycerols have been obtained by the reaction of ω-(indol-3-yl)alkyl tosylates with potassium 1,3-O-benzylideneglyceroxide. The removal of the benzylidene group by reduction with sodium in liquid ammonia has led to 2-O-(indol-3'-ylalkyl)glycerols. The tuberculostatic activity of the latter has been studied.

We have previously obtained 1-O-(indol-3'-ylalkyl) glycerols [1]. In the present work we have performed the synthesis of the 2-O-(indol-3'-ylalkyl)glycerols VI isomeric with them by the following route:



Potassium benzylideneglyceroxide (IV) was alkylated with tryptophyl tosylate (II) and with homotryptophyl tosylate (III), and also with indol-3-ylethyl bromide (I), with the formation of the 1,3-O-benzylidene-2-O-

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*For part XXXVII, see [1].

Tuberculostatic Activity of the Compounds Obtained*

Compound	With blood serum	Without blood serum
2-O-(Indol-3'-ylethyl)glycerol (VIa)	1 : 1000	1 : 1000
2-O-(Indol-3'-ylpropyl)glycerol (VIb)	1 : 1000	1 : 2000

*The work was carried out by T. N. Zykova of the laboratory of Chemotherapy of the All-Union Chemical and Pharmaceutical Scientific Research Institute under the direction of Prof. G. N. Persin, for which the authors express their deep gratitude to them.

(indol-3'-ylalkyl)glycerols (V). For the successful performance of the reaction the 1,3-O-benzylideneglycerol was used in considerable excess. On alkylation with tryptophyl tosylate the yield of Va was lower than on alkylation with the bromide I. The reductive debenzylidenation of compounds V with sodium in liquid ammonia gave the 2-O-(indol-3'-ylalkyl)glycerols (VI).

Compounds VIa and VIb possess weak tuberculostatic activity in relation to mycobacteria of tuberculosis of the human type (strain RV-30) (see table).

EXPERIMENTAL

All the IR spectra were taken in paraffin oil with a UR-10 instrument.

1,3-O-Benzylidene-2-O-(indol-3'-ylethyl)glycerol (Va). A) With gentle stirring, a hot solution of 9 g (0.05 mole) of 1,3-O-benzylideneglycerol, mp 81–82° C [2] in 40 ml of dry benzene was added dropwise to 0.49 g (0.0125 g-at) of freshly-cut potassium in 15 ml of boiling dry benzene, and the mixture was heated until all the potassium had reacted (1 hr). Then a solution of 3.95 g (0.0125 mole) of the tosylate II [3] in 20 ml of benzene was added dropwise over 40 min with the simultaneous removal of 40 ml of benzene by distillation. The mixture was heated for 3 hr. After cooling, the p-toluenesulfonic acid salt was filtered off and washed with benzene, and the filtrate was evaporated. The residue was dissolved in a mixture of ether and hexane (1 : 1) and deposited on a column of alumina. Elution was carried out with ether–hexane (1 : 1), the fraction with R_f 0.5 (alumina of activity grade II, ether) being collected. The solvent was evaporated off and the residue was dissolved in methanol, the solution was treated with carbon and filtered, and the methanol was evaporated off. This gave 0.5 g (12.2%) of compound Va in the form of a colorless porous mass. IR spectrum: 3500 cm^{-1} (N–H), group of bands at 1030–1200 cm^{-1} (C–O–C–O–C) [12]. Found, %: C 74.10; H 6.76; N 4.50. Calculated for $C_{20}H_{21}NO_3$, %: C 74.30; H 6.50; N 4.34.

B) A solution of 4.1 g (0.0183 mole) of the bromide I [5] was added dropwise to the potassium benzylideneglyceroxide prepared as described above from 1 g (0.0255 g-at) of potassium and 9 g (0.05 mole) of benzylideneglycerol. The mixture was boiled with stirring for 9 hr. Then it was treated as in method (A). Yield 1.8 g (22%). The IR spectrum was identical with that of substance Va obtained by method (A).

1,3-O-Benzylidene-2-O-(indol-3'-ylpropyl)glycerol (Vb). A benzene solution of 3.29 g (0.01 mole) of the tosylate III [6] was added dropwise to the potassium benzylideneglyceroxide prepared from 0.39 g (0.01 g-at) of potassium and 7.2 g (0.04 mole) of benzylideneglycerol, and the mixture was stirred with heating for 4 hr and was then treated as in (A). (R_f 0.75; alumina of activity grade II, ether). Yield 1.8 g (53.5%), mp 79–81° C (benzene–hexane, 1 : 1). IR spectrum: 3420 cm^{-1} (N–H), group of bands at 1030–1200 cm^{-1} (C–O–C–O–C). Found, %: C 74.51; H 6.74; N 4.00. Calculated for $C_{21}H_{23}NO_3$, %: C 74.77; H 6.83; N 4.15.

2-O-(Indol-3'-ylethyl)glycerol (VIa). With stirring, metallic sodium was slowly added to a solution of 1.8 g (0.0056 mole) of compound Va in 70 ml of liquid ammonia until a blue coloration appeared and persisted for 5 min. Then the excess of sodium was destroyed by the addition of ammonium chloride. After the spontaneous evaporation of the ammonia, the reaction mixture was dissolved in a small amount of water and the product was extracted with ethyl acetate, the extract was dried over anhydrous Na_2SO_4, the solvent was evaporated off, and the residue was transferred to a column of silica (pore size 100 Å [7]). Elution was carried out with ether, the fraction with R_f 0.36 (silica, ether) being collected. The ether was evaporated off, the residue was dissolved in methanol, the solution was treated with carbon and filtered, and the methanol was distilled off. After prolonged standing, crystallization set in. Yield 0.7 g (53%), mp 81–82° C (from chloroform). IR spectrum: 3300–3430 cm^{-1} (O–H, N–H), group of bands at 930–1075 cm^{-1} (C–O of primary hydroxyl groups [8]). Found, %: C 66.80; H 7.40; N 5.70. Calculated for $C_{13}H_{17}NO_3$, %: C 66.37; H 7.23; N 5.95.

2-O-(Indol-3'-ylpropyl)glycerol (VIb). This was obtained by the method given above. R_f 0.30 (silica, ether). Yield 89%, mp 55–57° C (from chloroform). IR spectrum: 3350–3420 cm^{-1} (OH and N–H), group of bands at 930–1075 cm^{-1} (C–O of primary hydroxyl groups [8]). Found, %: C 67.75; H 7.89; N 5.44. Calculated for $C_{14}H_{19}NO_3$, %: C 67.46; H 7.68; N 5.62.

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1 August 1967

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