3-Acyl-4,6-dinitro-5-hydroxybenzofurans (VIa-c). A) A solution of 0.03 mole of nitric acid was added gradually with stirring at room temperature to a suspension of 0.01 mole of benzofuran Ia-c in 20 ml of glacial acetic acid, and the mixture was stirred for 5 h. The precipitate was removed by filtration, washed on the filter with water, and recrystallized from ethyl acetate (Table 1).

B) A cooled (to 0-5°C) nitration mixture, prepared from 1 ml of concentrated nitric acid and 1.4 ml of concentrated sulfuric acid, was added dropwise at 10-15°C to a solution of 0.01 mole of Ila-c in 20 ml of glacial acetic acid, and the mixture was stirred at room temperature for 5 h. The resulting precipitate was removed by filtration, washed on the filter with water, dried, and recrystallized from ethyl acetate (Table 1).

No melting-point depression was observed for a mixture of samples obtained by methods A and B.

LITERATURE CITED


SYNTHESIS OF NEW UNCONDENSED BIHETEROCYCLIC COMPOUNDS —

2,2-DIMETHYLTETRAHYDROPYRAN DERIVATIVES

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A method for the synthesis of α-ethoxymethylene-β-(2,2-dimethyltetrahydro-4-pyranyl)-β-oxopropionate is proposed. New uncondensed biheterocyclic compounds were obtained on the basis of the latter. A fundamental difference in the behavior of this system with 1,2-, 1,3-, and 1,4-binucleophiles is demonstrated.

The synthesis of ethoxymethylene derivatives in order to use them in heterocyclization reactions to give uncondensed biheterocycles was a continuation of research on β-keto esters of the tetrahydropyran series.

An ethoxymethylene derivative of a β-keto ester was obtained by the method in [1] on the basis of ethyl β-(2,2-dimethyltetrahydro-4-pyranyl)-β-oxopropionate [2].

Compound II is capable of undergoing ambiguous cyclization, inasmuch as it contains three functions that compete for reaction with binucleophile. In fact, as one should have expected, cyclization products III–VI were obtained by reaction of the ethoxymethylene derivative with hydrazine, phenylhydrazine, o-phenylenediamine, and 2-amino-4-nitroaniline, as indicated in the following scheme:

III R₁=H; IV R₁=C₆H₅; V R²=H; VI R²=NO₂; VII X=O; VIII X=S; IX X=NH

At the same time, the products of the reaction of the ethoxymethylene derivative of the β-keto ester with urea, thiourea, and guanidine were exclusively ketones VII–IX. Numerous attempts to obtain 2-amino(mercapto, hydroxy)-4-(2,2-dimethyltetrahydro-4-pyranyl)-5-carbethoxypyrimidines were unsuccessful.

Thus the fundamental difference in the behavior of ethyl α-ethoxymethylene-β-(2,2-dimethyltetrahydro-4-pyranyl)-8-oxopropionate with 1,2-, 1,3-, and 1,4-binucleophiles is apparent. It is difficult to surmise whether the initial step is cyclization with the 1,3-binucleophile to give 5-carbethoxypyrimidines with subsequent rearrangement to 5-ketopyrimidines or whether the reaction products are formed as a result of direct cyclization at the ethoxy and carboxethoxy groups as a consequence of the steric hindrance due to the heterocyclic ring. There is no doubt that the fact of the different behaviors of 1,2-, 1,3-, and 1,4-binucleophiles with ethoxymethylene derivatives of β-keto esters that contain a bulky substituent requires further study of analogous systems in heterocyclization reactions.

A study of the tranquilizing antineurotic activity of the synthesized compounds was conducted in the laboratory of convulsive states of the Institute of Fine Organic Chemistry. It was established that almost all of the synthesized compounds to some degree prevent clonic spasms and consequently have not only antispasmodic but also tranquilizing activity. The antispasmodic activity with respect to Corazole increases with the introduction of a benzodiazepine grouping into the molecule, reaching a maximum in the case of VI, which contains a nitro group in the 8 position.

**EXPERIMENTAL**

Thin-layer chromatography (TLC) was carried out on KSK silica gel, prepared by the method in [3], in an ether–petroleum ether system (3:1). Analysis by gas–liquid chromatography (GLC) was performed with a Khrom-4 chromatograph with packed glass columns with 5% XE-60 silicone on Chromaton N-AW, silanized with hexamethylene disilane, as the liquid phase. The IR spectra were recorded with a UR-20 spectrometer, the PMR spectra were recorded with a Varian T-60 spectrometer with tetramethylsilane as the internal standard, and the mass spectra were obtained with an MKh-1320 mass spectrometer.

Ethyl α-Ethoxymethylene-β-(2,2-dimethyltetrahydro-4-pyranyl)-8-oxopropionate (II). A mixture of 4 g (18 mmole) of I, 4 g (40 mmole) of acetic anhydride, and 3 g (20 mmole) of ethyl orthoformate was heated slowly during which the temperature of the reaction mixture rose sharply to 140°C, after which it fell to 110°C. Stirring was continued at this temperature for another 2 h, after which the unchanged substances were removed by distillation. The reaction product was distilled in vacuo to give 4.0 g (80%) of II with bp 180-181°C (4.5 mm), μdp 1.6890, and d₄ 1.1086. IR spectrum (thin layer): 1630 (C=O), 1690 (keto C=O),