

CYTISINE DERIVATIVES CONTAINING A TRIPLE BOND

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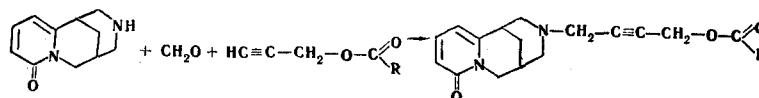
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N-(δ -Acyloxy-2-butynyl)cytisines are obtained by the condensation of cytosine, via the Mannich reaction, with propargyl esters of monobasic carboxylic acids.

The union of the natural alkaloid cytosine with acetylene derivatives may lead to substances which are of interest in both a chemical and pharmacological respect.

A method for the preparation of aminoacetylenic esters of piperidine and morpholine is described in [1]. In this study we have accomplished the synthesis of cytosine derivatives via the Mannich reaction with propargyl esters of monobasic aliphatic carboxylic acids.

The reaction was carried out by heating a mixture of cytosine, the propargyl ester of an aliphatic acid, and paraformaldehyde in alcohol:



The synthesized aminoacetylenic esters of cytosine are white, crystalline substances or undistillable liquids which are soluble in organic solvents and insoluble in water. Their IR spectra indicate the presence of a pyridone ring (1640, 1545, and 800 cm⁻¹), an N-alkyl group (2700-2800 cm⁻¹), an ester group (1740 cm⁻¹), and an acetylenic grouping (2200 cm⁻¹, weak band).

TABLE 1.

R	mp	[α] _D (in ethanol)	Empirical formula	N, %			mp of the salts
				found	calc.	Yield, %	
CH ₃	62-63	-164,5	C ₁₇ H ₁₈ N ₂ O ₃	9,4	9,3	26	156-157 [†]
CH ₃ (CH ₂) ₄		-151,3	C ₂₁ H ₂₈ N ₂ O ₃	7,8	7,8	85	184-185*
CH ₃ (CH ₂) ₆		-139,2	C ₂₃ H ₃₂ N ₂ O ₃	7,4	7,3	85	192-193*
CH ₃ (CH ₂) ₈		-130,0	C ₂₅ H ₃₆ N ₂ O ₃	6,8	6,8	88	156-157*
CH ₃ (CH ₂) ₁₀	40-41	-125,4	C ₂₇ H ₄₀ N ₂ O ₃	6,3	6,4	84	96-97*
CH ₃ (CH ₂) ₁₂	51-52	-111,1	C ₂₉ H ₄₄ N ₂ O ₃	6,1	6,0	79	99-100*
CH ₃ (CH ₂) ₁₄	60-61	-110,8	C ₃₁ H ₄₈ N ₂ O ₃	5,5	5,6	75	153-154 [‡]
CH ₃ (CH ₂) ₁₅	72-73	-102,5	C ₃₂ H ₅₀ N ₂ O ₃	5,3	5,5	79	165-166 [‡]
CH ₃ (CH ₂) ₁₆	66-67	-100,9	C ₃₃ H ₅₂ N ₂ O ₃	5,3	5,3	96	161-162 [‡]
CH ₃ (CH ₂) ₇ CH=CH(CH ₂) ₇		-104,8	C ₃₃ H ₅₀ N ₂ O ₃	5,5	5,4	57	171-172 [‡]

* Hydrochloride.

[†] Hydrobromide.

[‡] Hydriodide.

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EXPERIMENTAL

N-(δ -Acyloxy-2-butynyl)cytisines. A mixture of 1 g (0.005 mole) of cytosine, 0.23 g (0.0075 mole) of paraformaldehyde, and 5 ml of absolute ethanol was refluxed for 1 h in a three-necked flask equipped with a reflux condenser with a calcium chloride tube, a dropping funnel, and a stirrer. Anhydrous copper acetate (0.1 g) was then introduced, 0.005 mole of the propargyl ester of an acid dissolved in 20 ml of dioxane was added dropwise, and the mixture was heated at 101-103° for 6 h. The reaction mixture was then treated with 100 ml of 5% hydrochloric acid, and the unchanged propargyl ester was extracted with ether. The aqueous layer was made alkaline with 25% ammonium hydroxide and extracted with ether. The ether extract was dried with anhydrous sodium sulfate. The solvent was removed, and the residue was recrystallized from ether or purified by passing an ether solution of it through a column filled with activity II Al_2O_3 .

The purities of all of the compounds were confirmed by paper chromatography [n-butanol-concentrated HCl-water (100:15:27)] and by chromatography on a thin layer of aluminum oxide [ether-acetone (4:1)].

The IR spectra were obtained from carbon disulfide solutions with a UR-10 spectrometer.

LITERATURE CITED

1. A. G. Makhsumov, A. S. Safaev, A. M. Sladkov, and U. A. Abidov, Zh. Organ. Khim., 5, 716 (1969).