SYNTHESIS AND INVESTIGATION OF SOME IMIDAZOLE DERIVATIVES.

VI. AN IMPROVED METHOD OF PREPARING ESTERS OF 4(5)-NITROIMIDAZOLE-5(4)-CARBOXYLIC ACID

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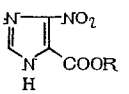
Esters of 4(5)-nitromidazole-5(4)-carboxylic acid are of interest as starting products for the synthesis of physiologically active substances. Literature data are available on the description of a number of esters of this acid which were obtained by the ordinary esterification method, i.e., by the action of alcohol on nitro acid in the presence of mineral acid or sulfonic acid [1-3], as well as by the action of acid chloride on alcoholate or phenolate (dimethylaminoethyl and p-diphenyl esters) [3] and, finally, by the action of silver salt of nitro acid on alkyl halide (imidazolylmethyl ester) [2].

The simplest method of preparing esters of nitroimidazolecarboxylic acid by the action of an excess of the corresponding alcohol on nitro acid in the presence of an acid catalyst yielded 48-60% of esters. In the application, in synthesizing esters of simplest alcohols – methyl and ethyl – this method gave products which are sufficiently pure; however, in the transition to higher molecular weight alcohols the yield and especially the quality of esters were effected. The esters were contaminated with unreacted nitro acid impurity which impeded purification to a great extent and also impeded subsequent reduction to esters of aminoimidazolecarboxylic acids. By far better results both with respect to the ester yields and their purity were pointed out in the study of the reaction of acid chloride of nitroimidazolecarboxylic acid with a 4-5 fold amount of the appropriate alcohol. The dilution of the reaction mixture with benzene or ether yielded a crystalline product from which one recrystallization from ethanol was adequate. The yield of esters, when using this method, reached 85-99% with the exception of cyclohexyl, benzyl, and allyl esters, which were obtained in

TABLE 1. Esters of 4(5)-Nitroimidazole-5(4)-carboxylic acid



Compound	R	Yield, %	Melting point, deg	Found (in %) C	Found (in %) H	Found (in %) N	Empirical formula	Calculated (in %) C	Calculated (in %) H	Calculated (in %) N
I	n-C_3H_7	92,6	179—80	—	—	—	—	—	—	—
II	n-C_4H_9	85,8	182	—	—	—	—	—	—	—
III	iso-C_4H_9	93,1	211—2	45,08	5,25	19,77	$C_8H_{11}N_3O_4$	45,07	5,16	19,76
IV	n-C_6H_{13}	99,5	172—3	47,39	5,71	18,74	$C_9H_{13}N_3O_4$	47,57	5,73	18,5
V	iso-C_5H_{11}	96,3	203—4	—	—	—	—	—	—	—
VI	n-C_6H_{13}	93,6	173—4	—	—	—	—	—	—	—
VII	Cyclohexyl	63,6	233—4	49,74	5,45	17,72	$C_{10}H_{13}N_3O_4$	50,21	5,49	17,56
VIII	$C_6H_5CH_2$	71,4	200—1	—	—	—	—	—	—	—
IX	CH_2CHCH_2	82,2	163—4	42,78	3,74	21,53	$C_7H_7N_3O_4$	42,64	3,55	21,32

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lower yields (64-82%). The melting point of the synthesized esters showed agreement with the literature data [2]. Elementary analysis data are given for esters III, IV, VII, and IX which were not reported the literature (Table 1).

EXPERIMENTAL

Esters of 4(5)-Nitroimidazole-5(4)-carboxylic Acid (I-IX). Acid chloride* of nitro acid was boiled on an oil bath with a 4-5-fold amount of the appropriate alcohol for 15-30 min to a complete disappearance of the yellow coloring of acid chloride. Benzene or ether was then added to the cooled, crystallized reaction mass. The product was filtered and the precipitate washed on the filler with benzene or ether. The product was crystallized from alcohol.

LITERATURE CITED

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*Prepared by the action of thionyl chloride or phosphorus pentachloride on acid [3].