SUBSTITUTION IN THE BARBITURIC ACID MOLECULE

IV. Reactions with Hydrazines and Carboxylic Acid Hydrazides*

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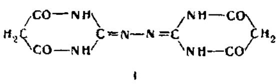
Condensation of barbituric acid with hydrazines with carboxylic acid hydrazides affords barbituric acid 2-hydrazones, as a result of the ketonic character of the 2-carbonyl group. Similarly, condensation with hydrazine hydrate gives the corresponding azine.

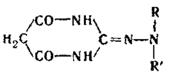
We have shown [1, 2] that the 2-carbonyl group of barbituric acid exhibits ketonic character, with the result that barbituric acid readily forms a 2-semicarbazone and a 2-thiosemicarbazone. In order to demonstrate further the ketonic character of the 2-carbonyl group, we set ourselves the aim of reacting barbituric acid with other reagents at the carbonyl group, in particular with hydrazines and carboxylic acid hydrazides.

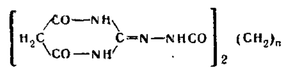
The Azine and Hydrazones of Barbituric Acid

Compound	R	R′	n	Mp, °C	Molecular formula	N, %		Yield, %	UV Spectrum	
						found	calculated		λmax, nm	lg ε
I	—	—	—	230	$C_8H_8N_6O_4$	33.24	33.32	79.4	279 200 327	4.21 4.50 3.33
II	C_6H_5	H	—	250	$C_{10}H_{10}N_4O_2$	25.83	25.67	45.9	245 320	3.84 3.46
II	C_6H_5	C_6H_5	—	257	$C_{16}H_{14}N_4O_2$	18.75	19.03	44.2	240 285	4.07 4.10
II	2.4-$(NO_2)_2C_6H_3$	H	—	205	$C_{10}H_8N_6O_6$	27.05	27.27	43.3	235 260 350	4.07 4.08 4.30
II	C_6H_5CO	H	—	248	$C_{11}H_{10}N_4O_3$	22.05	22.75	44.7	255 315	4.47 3.13
II	*m*-$NO_2C_6H_4CO$	H	—	260	$C_{11}H_9N_5O_5$	23.50	24.05	18.5	250	4.55
II	γ-NC_5H_4CO	H	—	250	$C_{10}H_9N_5O_3$	28.00	28.33	21.2	238 260 330	3.55 4.06 3.36
III	—	—	0	250	$C_{10}H_{10}N_8O_6$	33.55	33.13	74.0	250	4.03
III	—	—	4	274	$C_{14}H_{18}N_8O_6$	28.29	28.42	12.7	256 324	4.28 4.11

Our experiments showed that barbituric acid reacts with hydrazine hydrate to give the azine I, while phenylhydrazine, 1,1-diphenylhydrazine, 2,4-dinitrophenylhydrazine, and the hydrazides of benzoic, m-nitrobenzoic, and isonicotinic acids give the hydrazones II. With oxalic and adipic hydrazides, the hydrazones III are formed (see table):


I


II


III

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*For part III, see [1].

The hydrazones of barbituric acid retain their acidic properties with the result that all the compounds prepared, with the exception of the 2,4-dinitrophenylhydrazone, are readily soluble in solutions of strong alkalis.

The azine and hydrazones of barbituric acid resemble the acid itself [3] in possessing absorption maxima at 255–260 nm, except for the diphenylhydrazone, for which the absorption maximum is shifted to 285 nm. In addition, some of the hydrazones have less intense maxima at 229–245 and 324–350 nm.

EXPERIMENTAL

Barbituric acidazine (I). A mixture of a solution of 0.01 mole of barbituric acid in 25 ml of water, and 0.02 mole of hydrazine hydrate, was heated for 2 hr on the water bath, the condensation product beginning to separate after 3–5 min. After cooling, the product was filtered off, washed with water and recrystallized from dilute alcohol.

Barbituric acid hydrazones. A solution of 0.01 mole of barbituric acid and 0.01 mole of the hydrazine or hydrazide (in the cases of oxalic and adipic hydrazides, 0.005 mole of the compound was used) in a suitable solvent was heated on the water bath for 15 min–22 hr. The precipitate was filtered off after cooling and recrystallized from alcohol. The following solvents were used for the condensation: water (isoniazide), dilute acetic acid (phenylhydrazine, benzohydrazide, oxalohydrazide), dilute alcohol (diphenylhydrazine and adipic hydrazide), and dilute alcohol acidified with hydrochloric acid (2,4-dinitrophenylhydrazine, m-nitrobenzohydrazide).

UV spectra were taken on an SF-4 spectrophotometer (1–5 mg% solutions in twice-distilled alcohol).

REFERENCES

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