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BRIEF COMMUNICATIONS

SOME HYDRAZIDES AND HYDRAZONES BASED ON N-AMINOMORPHOLINE AND N-AMINOPIPERIDINE

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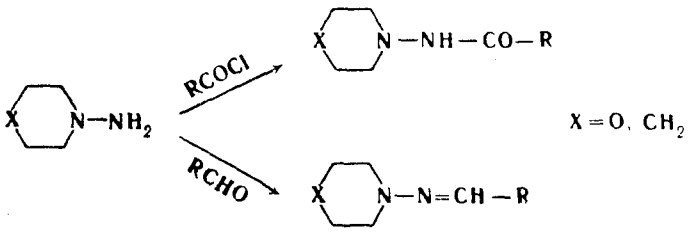
Some new hydrazides and hydrazones based on N-aminomorpholine and N-aminopiperidine have been synthesized and their antibacterial properties studied.

N-Aminomorpholine and N-aminopiperidine are structurally disubstituted hydrazines. They form hydrazides with derivatives of organic acids and hydrazones on condensation with aldehydes and ketones:



It has been noted in the literature [1] that among compounds of these types there are biologically active materials, in particular those which decrease the growth of malignant tumors.

Hydrazides and Hydrazones Based on N-Aminomorpholine and N-Aminopiperidine

Compound no.	Mp, °C	Empirical formula	Found, %			Calculated, %			Yield, %
			C	H	N	C	H	N	
III	198	$C_9H_{11}N_3O_5$	44.40	4.52	17.28	44.81	4.60	17.42	70.7
IV	239	$C_{11}H_{12}N_4O_6$	44.33	4.14	18.62	44.60	4.08	18.91	53.8
V	117	$C_9H_{11}N_3O_4$	47.75	5.11	18.73	48.00	4.92	18.66	93.7
VI	76	$C_9H_{11}BrN_2O_2$*	41.62	4.62	11.29	41.70	4.28	10.89	90
VII	140	$C_9H_{13}N_3O$	60.10	7.51	23.08	60.31	7.31	23.45	74.5
VIII	86—87	$C_{13}H_{16}N_2O$	71.79	7.29	12.95	72.19	7.46	12.95	90
IX	84—85	$C_{10}H_{13}N_3O_3$	53.66	6.33	18.73	53.80	5.87	18.83	81
X	178	$C_{10}H_{13}N_3O_4$	50.59	5.55	17.50	50.20	5.48	17.57	23
XI	283	$C_{14}H_9N_3O_5$	56.01	3.10	13.90	56.19	3.03	14.04	95

* Found: Br 30.70%; calculated Br 30.84%

In continuing our studies in the field of synthesis of chemotherapeutic substances we have prepared some new derivatives of N-aminomorpholine (I) and N-aminopiperidine (II).

Condensation of (I) with 5-nitrofuroyl chloride gave 5-nitrofuroylaminomorpholine (III), with 3,5-dinitrobenzoyl chloride it gave 3,5-dinitrobenzoylaminomorpholine (IV), with 5-nitrofurfural it gave 5-nitrofurfurylidenaminomorpholine (V), with 5-bromofurfural it gave 5-bromofurfurylidenaminomorpholine (VI), with α-pyrrolaldehyde it gave azomethine (VII), and with cinnamaldehyde it gave cinnamylidenaminomorpholine (VIII).

5-Nitrofurfurylidenaminopiperidine (IX) and 5-nitrofuroylaminopiperidine (X) were prepared in a similar way from N-aminopiperidine. Some information on the properties of those compounds prepared for the first time are presented in the Table.

Preliminary studies of the antibacterial activity of these compounds have shown that many of them stop the growth of Escherichia coli and pyogenic bacteria.

For example, the bacteriostatic activity of V against B. coli (strain M17) appeared at a dilution of 11.2 μg/ml, and against Staphylococcus aureus (strain 209P) at a dilution of 5.5 μg/ml; substance IX had activity at 11.2 and

11.5 μg/ml respectively. The bacteriostatic activity of substances III and IV against B. coli appeared at 100 μg/ml, and of substances X and VI at 10 μg/ml. It has already been reported [2] that the hydrazide of coumarillic acid has antitubercular activity. We have prepared the hydrazide of coumarillic acid in 90% yield from ethyl coumarilate by normal methods, and then we have converted it to its 5-nitrofurfurylidenehydrazone (XI). This hydrazone showed activity against B. coli and B. proteus at a dilution of 1:22 000, but in preliminary tests its antitubercular activity was negligible.

Experimental *

N-Aminomorpholine (I) was prepared by the reduction of nitrosomorpholine [3] with zinc powder in acetic acid by Knorr's method [4]. It was a colorless oil, bp 167°–168° $n_D^{21.5}$ 1.4755; lit. gives [4]; bp 168°, n_D^{20} 1.4770.

N-Aminopiperidine (II) was prepared as its hydrochloride by an analogous method from nitrosopiperidine [4]. It consists of slightly yellow platelets with mp 160°, lit. gives [4], mp 162°.

Typical synthetic methods are cited below.

N-(5-Nitrofuroyl) aminomorpholine (III). 0.3 g (1.7 mmole) of 5-nitrofuroylchloride was dissolved in the minimum amount of dry benzene. To this solution 0.3 g (3 mmole) of aminomorpholine was added; yellow crystals deposited. They were filtered off and recrystallized from ethanol. Yield 70.7%, mp 198°. It dissolved well in hot ethanol, but was insoluble in benzene, acetone, ether, and dioxane. Its solubility in water was 1:200 (21°).

5-Nitrofurfurylidenaminomorpholine (V). Ethanolic solutions of 0.5 g (3.5 mmole) of aminomorpholine hydrochloride and 0.6 g (4.3 mmole) of 5-nitrofurfural were mixed. After 2–3 min orange-red crystals precipitated. These were filtered off and recrystallized from ethanol. Yield 93.7%, mp 117°. The hydrazone dissolved poorly in cold ethanol and carbon tetrachloride, and was insoluble in ether and ligroin. It dissolved well in hot ethanol, benzene, acetone, dichloroethane, and dioxane. Its solubility in water was 1:1800 (18°).

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