THE CONDENSATION OF CAFFEINE-, ISOCAFFEINE-, AND THEOBROMINE-8-ALDEHYDES WITH RHODANINES

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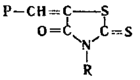
The crotonic condensation of caffeine-, isocaffeine-, and theobromine-8-aldehydes with 3-methyl-, 3-ethyl-, 3-allyl-, and 3-phenylrhodanines in the presence of piperidine with brief heating in methanolic and methanolic–acetic acid solutions has been studied. Purine derivatives of the rhodanines have been synthesized.

Continuing earlier investigations on the reaction of purine-8-aldehydes [1–3] with alkyl iodide derivatives of heterocyclic bases containing active methyl groups, we have studied the condensation of caffeine-, isocaffeine-, and theobromine-8-aldehydes with 3-methyl-, 3-ethyl-, 3-allyl-, and 3-phenylrhodanines in the presence of piperidine by heating the components for one minute in methanolic and methanolic–acetic acid solutions. We have used this catalyst in the synthesis of 3-alkyl-5-(quinol-6-ylidene)rhodanines [4] and 5-alkyl-2-(pyridin-3-ylidene)rhodanines [5].

In this way we have synthesized in high yields purine derivatives of the rhodanines with the general formula:



where P is a purine residue—a caffeine residue in compounds I–IV, an isocaffeine residue in V–VIII, and a theobromine residue in IX–XII—and R is alkyl or phenyl (see table).

Because of the poor solubility of theobromine-8-aldehyde in methanol, the reaction was carried out not only in methanolic solution but also in glacial acetic acid. However, under these conditions the yields of compounds IX, X, and XI fell. The purine rhodanines I–XII synthesized are yellow or orange (3-methyl-rhodanines) crystalline compounds stable on storage and very sparingly soluble in organic solvents and insoluble in water.

The IR spectra of the purine 3-ethylrhodanines II, VI, and X have high-intensity bands in the 1700–1715 cm^{-1} (C=O) and 1670 cm^{-1} (C=N) region and in addition there are intense bands at 1592–1598, 1552, and 1240 cm^{-1}. The spectrum of the rhodanine X has a very diffuse absorption band superposed on the (N—H) and (C—H) bands. The spectra of the purine 3-ethylrhodanines studied are similar to that of 1, 9-dimethylisoxanthine [6].

EXPERIMENTAL

Synthesis of the initial aldehydes*. Caffeine-8-aldehyde [7] (mp 166–167° C) was obtained by the oxidation of 8-hydroxymethylcaffeine [8] with selenium dioxide [9]. Isocaffeine-8-aldehyde [10] (mp 203–204° C) and theobromine-8-aldehyde (XI) (mp 289–290° C) were obtained by the chlorination of 8-methylisocaffeine and 8-methyltheobromine with subsequent hydrolysis of the dichloro derivatives.

Synthesis of the purine rhodanines. An alkyl- or arylrhodanine was dissolved in a heated methanolic or methanolic–acetic acid solution of the purine aldehyde, and then 0.2–0.3 ml of freshly distilled piperidine was added. A colored precipitate rapidly deposited; to complete the reaction the mixture was boiled for 1 min. After cooling, the precipitate was filtered off and washed with methanol. The melting point did not change when the rhodanines were washed twice with hot glacial acetic acid. The melting points of all the substances (in sealed

Characteristics and Conditions for the Synthesis of the Purine Rhodanines

Compound	R	Amounts of reactants, g		Amount of solvent (methanol), ml	Mp, °C	Empirical formula	Found, %		Calculated, %		Yield, %
		purine aldehyde	alkyl- or phenylrhodanine				N	S	N	S	
I	CH_3	0.50	0.34	10	326—327	$C_{13}H_{13}N_5O_3S_2$	19.61	18.57	19.93	18.25	95.0
II	C_2H_5	0.50	0.36	10	316—317	$C_{14}H_{15}N_5O_3S_2$	19.11	17.76	19.17	17.56	94.0
III	C_3H_5	0.50	0.39	10	286—287	$C_{15}H_{15}N_5O_3S_2$	18.81	16.99	18.65	17.00	94.0
IV	C_6H_5	0.25	0.24	15*	364—365	$C_{18}H_{15}N_5O_3S_2$	16.58	15.88	16.94	15.51	96.0
V	CH_3	0.50	0.34	10	375—377	$C_{13}H_{13}N_5O_3S_2$	19.50	18.60	19.93	18.25	98.7
VI	C_2H_5	0.50	0.36	10	367—368	$C_{14}H_{15}N_5O_3S_2$	18.80	17.92	19.17	17.56	92.7
VII	C_3H_5	0.50	0.39	10	336—338	$C_{15}H_{15}N_5O_3S_2$	18.21	17.36	18.65	17.00	90.0
VIII	C_6H_5	0.25	0.24	15*	409—410	$C_{18}H_{15}N_5O_3S_2$	17.24	15.80	16.94	15.51	96.0
IX	CH_3	0.24	0.14	40	402—404	$C_{12}H_{11}N_5O_3S_2$	20.70	19.11	20.76	19.01	73.8
X	C_2H_5	0.20	0.16	40	375—376	$C_{13}H_{13}N_5O_3S_2$	19.60	17.93	19.97	18.25	73.5
XI	C_3H_5	0.20	0.17	40	334—335	$C_{14}H_{13}N_5O_3S_2$	18.90	17.86	19.28	17.65	86.0
XII	C_6H_5	0.20	0.20	20**	389—390	$C_{17}H_{13}N_5O_3S_2$	17.14	15.70	17.54	16.06	73.7

*3 ml of glacial CH_3COOH was added.

**5 ml of glacial CH_3COOH was added.

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*I express my deep thanks to Prof. E. S. Golovchinskii for providing the methylxanthines.

capillaries) were determined in a cylindrical metal block previously heated to 300° C (for II and III the capillaries were heated from 250° C).

The IR spectra of the purine rhodanines II, VI, and X were taken on a UR-10 spectrophotometer in the form of mulls in paraffin oil in the Butlerov Kazan chemical institute by A. Zolova, to whom I express my thanks.

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