

STUDIES IN THE FORMATION OF HETEROCYCLIC RINGS CONTAINING NITROGEN

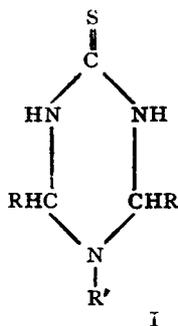
Part IX. Condensation of Thiourea with Aromatic Aldehydes and Ammonium Acetate

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Received September 29, 1961

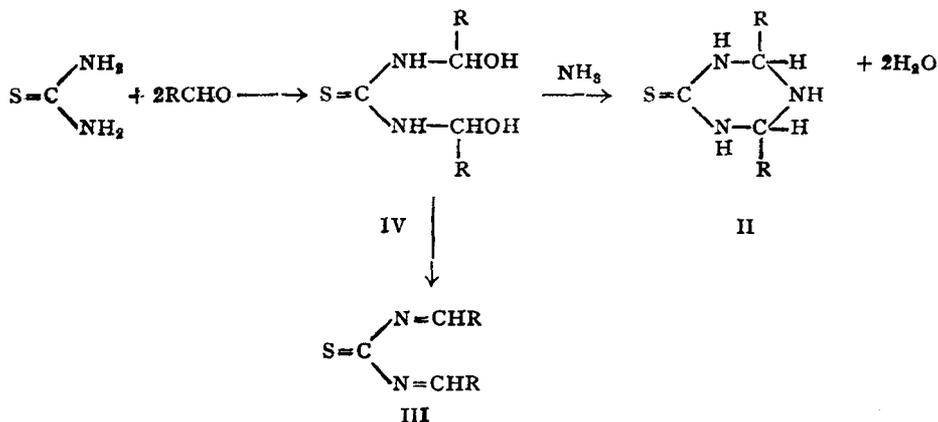
THE reaction between thiourea and aliphatic aldehyde-ammonias or the aldehyde and ammonia has been studied by a number of workers¹⁻⁴ who reported the formation of *s*-triazine derivatives (I). Paquin⁵ used primary amines in place of ammonia and obtained alkyl derivatives. Formaldehyde did not yield the normal product when ammonia was used but behaved normally with primary amines.⁶



According to Paquin⁵ the reaction between thiourea, aliphatic aldehydes and ammonia or aldehyde-ammonias followed a step-wise course through an intermediate sym-di-(aminoalkyl) thiourea.

In the preceding paper,⁷ the condensation between urea (one mole), aromatic aldehydes (two moles) and ammonium acetate (one mole) was described by us and the optimum conditions have been reported for the synthesis of 2-keto-4, 6-diaryl hexahydro-*s*-triazines. In the present work the reaction has been extended to thiourea leading to the synthesis of 2-thio-keto-4, 6-diaryl hexahydro-*s*-triazines and to a comparative study of the reaction with urea and thiourea. As in the case of urea, the reaction may be represented by a similar step-wise mechanism to explain the formation of 2-thio-keto-4, 6-diaryl hexahydro-*s*-triazine (II) and 1, 3-bis-(arylidene) thioureas (III). Compounds of the type (IV) may be considered to be more stable than the corresponding

urea compounds on the basis of the observation by Pollak,⁸ that thiourea under weakly acidic conditions condensed with formaldehyde producing dimethylol thiourea, whereas urea was reported to produce methylene type of compounds under similar conditions. Hence under weakly acidic conditions employed in the present work, the chances should be better for the intermediate (IV) to react with ammonia resulting in better yields of the thioketo-*s*-triazines.



Two moles of eight aromatic aldehydes have been condensed with thiourea (one mole) and ammonium acetate (one mole) under the conditions worked out for the urea condensation. The nature and the relative yields of the products are presented in Table I.

In almost all the cases, the thioketo triazines have been obtained in better yields compared to those of the corresponding keto triazines with the exception of *o*-chlorobenzaldehyde condensation. The benzylidene thioureas have been obtained in the case of *o*-nitro, *o*-chloro and 2,4-dichlorobenzaldehydes. The latter did not exhibit any tendency for polymerisation as in the case of some arylidene ureas. These results support the assumption that 1,3-bis-(α -hydroxybenzyl) thioureas are more stable compared to 1,3-bis-(α -hydroxybenzyl) ureas providing greater chance for the reaction with ammonia to take place resulting in better yields of thioketo triazines. 2-Thioketo-4,6-diphenylhexahydro-*s*-triazine has been found to exhibit a high intensity band at 249 $m\mu$ (log. $\epsilon_{\text{max.}} = 4.29$) in 95% ethanol and 2-thioketo-4,6-di-(*p*-methoxyphenyl) hexahydro-*s*-triazine between 274–285 $m\mu$ (log. $\epsilon_{\text{max.}} = 4.41$) in the ultraviolet region. In the infra-red region, 2-thio-keto-4,6-diphenyl hexahydro-*s*-triazine gave three bands at 1180 cm.^{-1} (8.46 μ), 1170 cm.^{-1} (8.55 μ) and 1149 cm.^{-1} (8.7 μ) which may be assigned to $> \text{C} = \text{S}$ stretching frequency.

TABLE I

Products of condensation of thiourea with aromatic aldehydes and ammonium acetate: Time of reaction: six hours

No.	Name of aldehyde	Percentage yield of	
		2-thioketo- 4, 6-diaryl hexahydro- s-triazine	1, 3-bis- arylidene thiourea
1	Benzaldehyde	82.2	..
2	Salicylaldehyde	38.0	..
3	Anisaldehyde	10.7	..
4	<i>o</i> -Nitrobenzaldehyde	50.0	7.3
5	<i>m</i> -Nitrobenzaldehyde	66.6	..
6	<i>p</i> -Nitrobenzaldehyde	47.5	..
7	<i>o</i> -Chlorobenzaldehyde	56.8	18.7
8	2, 4-Dichlorobenzaldehyde	29.4	11.1

EXPERIMENTAL

All m.p.'s are uncorrected.

General procedure for the Condensation of Thiourea with Aromatic Aldehydes and Ammonium Acetate

Thiourea (one mole), aromatic aldehydes (two moles) and ammonium acetate (one mole) were heated with excess of ethyl alcohol (95%), first to dissolve the solids and then under reflux conditions in general, for a period of six hours. The reaction mixture was worked out, either by cooling it to room temperature and leaving overnight or by removing the solvent under reduced pressure if the solids did not separate on standing overnight. The crude product was fractionated by using suitable solvents. The substances isolated in this manner were purified and characterised.

2-Thioketo-4, 6-diphenyl hexahydro-s-triazine.—Thiourea, benzaldehyde, ammonium acetate and 95% ethanol were refluxed on a steam-bath. The orange yellow solution was left overnight, resulting in a yellow granular

solid which was filtered, washed with hot water and dried. Two recrystallisations from ethanol yielded pale yellow needles, *m.p.* 175° (Found: C, 67·1; H, 5·9; N, 15·9; $C_{15}H_{15}N_3S$ requires C, 66·9; H, 5·5; N, 15·6%).

2-Thioketo-4,6-di-(o-hydroxyphenyl) hexahydro-s-triazine.—Thiourea, salicylaldehyde and ammonium acetate were condensed in ethanol and the reaction mixture was subjected to steam distillation to remove the unreacted salicylaldehyde. The orange yellow residue left in the flask could be purified by dissolving in ethyl alcohol and precipitation with water. Further purification from ethyl acetate gave yellow plates which did not melt sharply but decomposed at 250° (Found: C, 60·1; H, 4·9; N, 13·8; $C_{15}H_{15}N_3O_2S$ requires C, 59·8; H, 4·9; N, 13·9%).

2-Thioketo-4, 6-di-(p-methoxyphenyl) hexahydro-s-triazine.—Thiourea, anisaldehyde and ammonium acetate were condensed in ethanol and the solvent was removed under reduced pressure. The pale brown solid left in the flask was washed with hot water and a little ether resulting in a colourless solid. Four recrystallisations from ethanol gave colourless plates, *m.p.* 148–49° (Found: C, 62·0; H, 5·8; N, 12·4; $C_{17}H_{19}N_3O_2S$ requires C, 62·0; H, 5·7; N, 12·4%).

2-Thioketo-4, 6-di-(o-nitrophenyl) hexahydro-s-triazine.—Thiourea, *o*-nitrobenzaldehyde and ammonium acetate were condensed in ethanol. The reaction mixture was cooled and the solid that separated was filtered and washed with hot water. The solid was extracted with excess of cold acetone. The acetone insoluble part was repeatedly recrystallised from ethyl acetate, giving yellow needles, *m.p.* 195° (Found: C, 50·5; H, 3·3; N, 19·4; $C_{15}H_{13}N_5O_4S$ requires C, 50·1; H, 3·6; N, 19·5%).

1, 3-*Bis-(o-nitrobenzylidene) thiourea.*—The acetone-soluble portion from the above experiment was recrystallised twice from dilute acetone giving light brown rods, *m.p.* 175° (Found: C, 53·0; H, 3·0; N, 16·6; $C_{15}H_{10}N_4O_4S$ requires C, 52·6; H, 2·9; N, 16·3%).

2-Thioketo-4,6-di-(m-nitrophenyl) hexahydro-s-triazine.—Thiourea, *m*-nitrobenzaldehyde and ammonium acetate were condensed in ethanol. The solid that separated was dissolved in pyridine, cooled and kept overnight. Pale yellow square plates, *m.p.* 208–9°, were deposited. (Found: C, 50·6; H, 3·9; N, 19·4; $C_{15}H_{13}N_5O_4S$ requires C, 50·1; H, 3·6; N, 19·5%).

2-Thioketo-4, 6-di-(p-nitrophenyl) hexahydro-s-triazine.—Thiourea, *p*-nitrobenzaldehyde and ammonium acetate were condensed in ethanol. The dark brown solid that separated was filtered, washed with hot water and then with ether. Two recrystallisations from acetone and finally once from ethyl

acetate gave the pure thioketo-triazine, reddish-brown plates, m.p. 240° (Found: C, 50.0; H, 3.4; N, 19.4; C₁₅H₁₃N₅O₄S requires C, 50.1; H, 3.6; N, 19.5%).

2-Thioketo-4,6-di-(o-chlorophenyl) hexahydro-s-triazine.—Thiourea, *o*-chlorobenzaldehyde and ammonium acetate were condensed in ethanol. The pale yellow solid that separated on cooling was fractionated into (i) alcohol-soluble and (ii) alcohol-insoluble fractions. The alcohol-soluble fraction was purified by recrystallisation from ethyl acetate, colourless needles, m.p. 176° (Found: C, 53.1; H, 3.9; N, 12.3; C₁₅H₁₃Cl₂N₃S requires C, 53.2; H, 3.8; N, 12.4%).

1, *3-Bis-(o-chlorobenzylidene) thiourea.*—The alcohol-insoluble fraction could be purified from benzene. The compound on two recrystallisations from the solvent yielded colourless plates, m.p. 171°. (Found: C, 55.6; H, 3.6; N, 8.5; C₁₅H₁₂Cl₂N₂S requires C, 56.0; H, 3.1; N, 8.7%.)

2-Thioketo-4, 6-di-(2', 4'-dichlorophenyl) hexahydro-s-triazine.—Thiourea, 2, 4-dichlorobenzaldehyde and ammonium acetate were condensed in ethanol. To the reaction mixture excess of distilled water was added with slow agitation, when a white granular solid separated. The colourless solid was taken up in boiling ethanol and the solution cooled in ice, depositing a little unreacted thiourea. The solution was filtered, concentrated and left for eighteen hours at the room temperature. Pale yellow crystalline solid separated, which on further recrystallisation from ethyl acetate gave white rectangular plates, m.p. 190° (Found: C, 44.3; H, 2.9; N, 10.4; C₁₅H₁₁Cl₄N₃S requires C, 44.2; H, 2.7; N, 10.3%).

1, *3-Bis-(2', 4'-dichlorobenzylidene) thiourea.*—The mother liquor from the above experiment was treated with excess of water resulting in the precipitation of pale yellow needles. It was dissolved in benzene and kept for three days, when pale yellow fine needles, m.p. 65°, were obtained. (Found: C, 46.1; H, 2.2; N, 7.1; C₁₅H₈Cl₄N₂S requires C, 46.1; H, 2.1; N, 7.1%.)

SPECTROPHOTOMETRIC DETERMINATIONS

(a) *Ultraviolet absorption spectra.*—The compounds were thoroughly purified before taking the spectra. Ethanol (95%) was used as solvent. The readings were recorded on Unicam Spectrophotometer Model S.P. 500, in the ultraviolet region. Quartz cells of one cm. thickness and narrow slit-width (0.12 mm.) were used.

(i) *2-thioketo-4, 6-diphenyl hexahydro-s-triazine.*—

$$\lambda_m \ 249 \text{ m}\mu \ (\log. \ \epsilon_{\text{max.}} = 4.29)$$

(ii) 2-Thioketo-4, 6-di-(*p*-methoxyphenyl) hexahydro-*s*-triazine.—

λ_{\max} , 274—285 m μ (log. ϵ_{\max} . = 4.41).

(b) *Infra-red absorption spectrum*.—The absorption was recorded on a Perkin-Elmer Model 21, double beam infrared spectrophotometer using rock-salt prism. The characteristic absorptions in the wave numbers are given below with the intensity of the bands in brackets:

2-Thioketo-4, 6-diphenyl hexahydro-*s*-triazine.—2891 (*m*), 1515 (*m*), 1504 (*m*), 1414 (*m*), 1401 (*m*), 1377 (*m*), 1277 (*m*), 1180 (*m*), 1170 (*m*), 1149 (*w*), 1075 (*w*), 1027 (*w*), 984 (*w*), 957 (*w*), 917 (*w*), 907 (*w*), 856 (*w*), 850 (*w*), 827 (*m*), 818 (*m*), 808 (*m*), 756 (*m*), 723 (*m*), 701 (*w*), 693 (*w*), 668 (*w*).

SUMMARY

Under the optimum conditions worked out for the condensation of urea, aromatic aldehydes and ammonium acetate, the reaction has been extended to thiourea. 2-Thioketo-4, 6-diaryl hexahydro-*s*-triazines have been obtained in all the cases in better yields; 1, 3-bis-arylidene thioureas could be isolated only in a few cases. The ultraviolet and infrared absorption data for some of the thioketo-hexahydro-*s*-triazines are recorded and the $>C = S$ stretching frequency in these compounds has been assigned.

We thank Dr. K. Babu Rao for the microanalysis.

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