

method A resulted in less than 10% conversion to the acetylenic ketone, about 90% of the starting material being recovered.

C. **Silver Oxide.**—A solution of 5 g. of the  $\alpha$ -bromo compound in 50 cc. of anhydrous ether was refluxed with 5 g. of silver oxide for five hours. The starting material was recovered.

D. **Other Solvents than Acetone.**—When a solution of  $\alpha$ -bromo-*o*-chlorobenzalacetophenone in carbon tetrachloride, chloroform, or alcohol-free ether was refluxed for three hours with an equivalent quantity of potassium

hydroxide in water solution, the starting material was recovered.

### Summary

The preparation of acetylenic ketones from  $\alpha$ -bromobenzalacetophenones has been extended to include benzoylphenylacetylene, anisoylphenylacetylene, *p*-methoxyphenylbenzoylacetylene and phenyl-*p*-bromobenzoylacetylene.

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## Synthesis of Tetrahydro-5-substituted-2(1)-*s*-Triazones

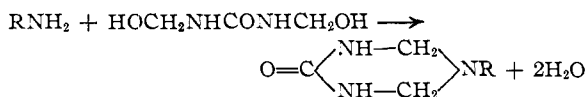
BY WM. JAMES BURKE<sup>1</sup>

Considerable attention has been given to the reaction of secondary amines with methylol compounds resulting from the condensation of formaldehyde with urea,<sup>2</sup> thiourea,<sup>3</sup> amides<sup>4</sup> and other compounds having hydrogen attached directly to nitrogen. The resulting formation of substituted aminomethyl derivatives is illustrated with dimethylolurea in the equation



Feldman and Wagner<sup>5</sup> have recently described the formation of heterocyclic derivatives by condensations involving formaldehyde and compounds containing both amino and amido groups. In a related type of reaction, acetaldehyde and ammonia have been found to react with thiourea<sup>6</sup> and urea<sup>6b</sup> to form the corresponding tetrahydro-4,6-dimethyl-2(1)-*s*-triazones, while use of an isocyanate<sup>6c</sup> in place of urea yields a tetrahydro-1,4,6-trisubstituted-2(1)-*s*-triazone.

The object of the present work was to study the reaction of dimethylolurea with primary amines. As a result, it was found that a series of new urea derivatives, the tetrahydro-5-substituted-2(1)-*s*-triazones, can be conveniently prepared as indicated in the following reaction.<sup>7</sup> The structure



assigned to these products is analogous to that given the related compounds prepared from

(1) Present address: Department of Chemistry, University of Utah, Salt Lake City, Utah.

(2) (a) Einhorn and Spröngerts, *Ann.*, **361**, 139 (1908); (b) Weaver, Simons and Baldwin, *This Journal*, **66**, 222 (1944); (c) Burke, British Patent 559,771 (1944).

(3) Bögemann and Zaucher, German Patent 575,114 (1933).

(4) (a) Einhorn, Bischkopf and Szelinski, *Ann.*, **343**, 223 (1905); (b) Einhorn and Feibelmann, *ibid.*, **361**, 140 (1908).

(5) Feldman and Wagner, *J. Org. Chem.*, **7**, 31 (1942).

(6) (a) Nencki, *Ber.*, **7**, 158 (1874); (b) Steindorff and Pacquin, U. S. Patent 2,016,521 (1935); (c) Dixon, *J. Chem. Soc.*, **61**, 509 (1892).

(7) Burke, U. S. Patent 2,304,624 (1942).

secondary amines and dimethylolurea,<sup>2</sup> which is a symmetrical derivative of urea. The reaction was also found to be applicable to substituted primary amines, such as 2-aminoethanol and 2-dimethylaminoethylamine. Identical products were formed when dimethylolurea was replaced with urea and formaldehyde in a molar ratio of 1:2, respectively.

In a study of the scope of the reaction, thiourea, formaldehyde, and primary aliphatic amines were also found to react readily in a 1:2:1 molar ratio with the formation of crystalline condensates and elimination of two moles of water. Similar results were obtained when 1,3-diphenylthiourea was used in place of thiourea and when formaldehyde was replaced with acetaldehyde. A tetrahydro-5-alkyl-2-thio-2(1)-*s*-triazone structure is proposed for these products in view of the fact that urea and thiourea have been reported<sup>5</sup> to behave in an analogous fashion in the reaction with acetaldehyde and ammonia.

The reaction occurred readily in an aqueous system except in syntheses involving such water-insoluble reactants as 1,3-diphenylthiourea or dodecylamine. In such instances it was found desirable to employ a water-miscible, inert solvent such as dioxane, which permitted the reaction to occur in a single phase. Although thiourea reacted readily with formaldehyde and primary amines in all instances at room temperature to give a high yield of condensation product, it was found advantageous with urea to heat the reaction mixture at 70–100°.

### Experimental

**Tetrahydro-5-(2-hydroxyethyl)-2(1)-*s*-triazone.**—2-Aminoethanol (122 g., 2 moles) was added with cooling to 240 g. of dimethylolurea (2 moles) in 340 cc. of water. The resulting solution was heated under reflux at 90–100° for two hours and kept at room temperature overnight. The reaction mixture was concentrated under reduced pressure and the resulting 166 g. of crude product recrystallized from 95% ethanol, m. p. 158°, yield 57%.

*Anal.* Calcd. for C<sub>6</sub>H<sub>11</sub>N<sub>3</sub>O<sub>2</sub>: C, 41.37; H, 7.64; N, 28.95. Found: C, 41.44; H, 7.62; N, 28.76.

Comparable yields of the same product were obtained

TABLE I  
TETRAHYDRO-5-SUBSTITUTED-2(1)-S-TRIAZONES FROM DIMETHYLOUREA AND PRIMARY AMINES

Primary amine	Yield, % <sup>a</sup>	M. p., °C. <sup>b</sup>	Empirical formula	Analyses, %					
				Carbon		Hydrogen		Nitrogen	
				Calcd.	Found	Calcd.	Found	Calcd.	Found
Methyl	62	210	C <sub>4</sub> H <sub>9</sub> N <sub>3</sub> O <sup>c</sup>	41.72	41.77	7.88	8.07	36.50	36.63
Isobutyl	34	200	C <sub>7</sub> H <sub>16</sub> N <sub>3</sub> O					26.73	26.63
2-Hydroxyethyl	57	158	C <sub>6</sub> H <sub>11</sub> N <sub>3</sub> O	41.37	41.44	7.64	7.62	28.95	28.76
2-Dimethylaminoethyl	36	114	C <sub>7</sub> H <sub>16</sub> N <sub>4</sub> O					32.53	32.71

<sup>a</sup> Based on crude product. <sup>b</sup> Uncorrected; all products were recrystallized from 95% ethanol except the isobutyl derivative, which was recrystallized from ethyl acetate. <sup>c</sup> *Anal.* Calcd.: mol. wt., 115. Found: 114. The product was readily soluble in water and hot methanol and practically insoluble in ether and hydrocarbons.

when dimethylolurea was replaced with urea and formaldehyde (37% aqueous solution) in a molar ratio of 1:2. Formaldehyde was evolved when the triazone was heated above 160° and a light brown, brittle resinous product resulted. The triazone was readily hydrolyzed by warming in dilute aqueous solutions of sodium hydroxide or hydrogen chloride or in 85% phosphoric acid, but no decomposition was observed when a 5% aqueous solution of the triazone was boiled for several minutes.

A summary of data on products from dimethylolurea and primary amines is given in Table I.

**Tetrahydro-5-cyclohexyl-2-thio-2(1)-s-triazone.**—Dioxane (100 cc.) and 49.5 g. of cyclohexylamine (0.5 mole) were added with cooling to a solution of 38 g. of thiourea (0.5 mole) in 81 g. of 37% aqueous formaldehyde (1 mole). After eighteen hours at room temperature, the reaction mixture was concentrated and cooled. The crude product (85 g.) was removed by filtration, washed with cold ethanol, and recrystallized from 95% ethanol; m. p. 172°, yield 85%. The product was moderately soluble in dioxane and hot ethanol but only slightly soluble in water.

*Anal.* Calcd. for C<sub>9</sub>H<sub>17</sub>N<sub>3</sub>S: C, 54.23; H, 8.60; S, 16.09. Found: C, 54.39; H, 8.60; S, 16.03.

Data concerning products of this type, prepared by reaction of thiourea with formaldehyde and primary amines in a 1:2:1 molar ratio, are summarized in Table II.

TABLE II

TETRAHYDRO-5-SUBSTITUTED-2-THIO-2(1)-S-TRIAZONES FROM THIOUREA, FORMALDEHYDE, AND PRIMARY AMINES

Primary amine	Yield, % <sup>a</sup>	M. p., °C. <sup>b</sup>	Empirical formula	S analyses, %	
				Calcd.	Found
Methyl	69	180	C <sub>4</sub> H <sub>9</sub> N <sub>3</sub> S <sup>c</sup>	24.44	24.45
Isobutyl	72	139	C <sub>7</sub> H <sub>15</sub> N <sub>3</sub> S	18.50	18.65
Cyclohexyl	85	172	C <sub>9</sub> H <sub>17</sub> N <sub>3</sub> S <sup>d</sup>	16.09	16.03
Dodecyl	95	153	C <sub>16</sub> H <sub>31</sub> N <sub>3</sub> S	11.23	10.82
2-Hydroxyethyl	50	162	C <sub>6</sub> H <sub>11</sub> N <sub>3</sub> OS	19.89	19.73

<sup>a</sup> Based on crude product. <sup>b</sup> Uncorrected; all products were recrystallized from 95% ethanol except the isobutyl derivative, which was recrystallized from trichloroethylene. <sup>c</sup> *Anal.* Calcd. for: C, 36.62; H, 6.92; N, 32.03. Found: C, 37.05; H, 7.15; N, 32.01. <sup>d</sup> *Anal.* Calcd. for: C, 54.23; H, 8.60. Found: C, 54.39; H, 8.60.

**Tetrahydro-1,3-diphenyl-5-(2-hydroxyethyl)-2-thio-2(1)-s-triazone.**—2-Aminoethanol (61 g., 1 mole) was added with cooling to 162 g. of 37% aqueous formaldehyde (2 moles). A solution of 228 g. of 1,3-diphenylthiourea (1 mole) in 400 cc. of dioxane was added to the above reactants and the resulting mixture was warmed until a clear solution was obtained. The solution was cooled in ice and water after twenty hours at room temperature and 100 g. of crystalline material was obtained by filtration. An additional 125 g. was obtained by concentration of the filtrate. The product melted at 178° after recrystallization from ethanol; yield 72%.

*Anal.* Calcd. for C<sub>17</sub>H<sub>19</sub>N<sub>3</sub>OS: N, 13.41; Found: N, 13.30, 13.35.

**Tetrahydro-4,6-dimethyl-5-(2-hydroxyethyl)-2-thio-2(1)-s-triazone.**—Acetaldehyde (35.2 g., 0.8 mole) was added portionwise with cooling to 24.4 g. of 2-aminoethanol (0.4 mole) and 30.4 g. of thiourea (0.4 mole) dissolved in 150 cc. of water. The reaction mixture turned dark red after twenty hours at room temperature. The crystalline product (10 g.) which separated out upon cooling was removed by filtration and recrystallized from ethanol, m. p. 168°, yield 13%.

*Anal.* Calcd. for C<sub>7</sub>H<sub>15</sub>N<sub>3</sub>OS: N, 22.20; S, 16.94. Found: N, 22.58; S, 16.93.

The product was readily soluble in water and liberated acetaldehyde when warmed in 85% phosphoric acid.

### Summary

1. The reaction of dimethylolurea with primary aliphatic amines resulted in the formation of crystalline tetrahydro-5-substituted-2(1)-s-triazones, a new type of heterocyclic urea derivative.

2. Thiourea and 1,3-diphenylthiourea were also found to give new cyclic derivatives by reaction with formaldehyde and a primary amine in a molar ratio of 1:2:1. A tetrahydro-5-substituted-2-thio-2(1)-s-triazone structure was proposed for these products.

3. Replacement of formaldehyde with acetaldehyde in the reaction of thiourea with a primary amine gave an analogous product, but in lower yield.