

The Reaction between Thioamides and Primary Amines

BY MAURICE J. SCHLATTER¹

The older literature² implies that the reaction between thioamides and primary amines proceeds solely with elimination of hydrogen sulfide and resultant formation of amidine. The present studies show that under certain conditions ammonia may be split out between the reacting molecules giving an N-substituted thioamide.³ The interaction may also result in the simultaneous elimination⁴ of hydrogen sulfide and ammonia.

Experimental

Thioacetamide and *n*-Butylamine.—Five grams of thioacetamide (0.077 mole) was mixed with 16.8 g. of *n*-butylamine (0.23 mole) and heated under reflux until the initially brisk gas evolution had almost ceased (about three hours). Fractionation of the product *in vacuo* gave 5.3 g. of light yellow oil,⁵ the major portion of which boiled at 131.5° (5 mm.) and gave analytical figures for *N*-butylthioacetamide.

Anal. Calcd. for C₆H₁₃NS: C, 54.91; H, 9.99; N, 10.67. Found: C, 54.91; H, 10.06; N, 10.73.

Thioacetamide and Benzylamine.—Benzylamine (2.14 g. = 0.020 mole) was mixed with thioacetamide (1.43 g. = 0.022 mole) and heated in a bath at 80° for one and one-quarter hours. The initially vigorous gas evolution almost stopped after forty-five minutes. On fractionation, the reaction mixture distilled almost completely at 158–162° at 2 mm. The distillate (2.28 g.) solidified on cooling and on recrystallization from anhydrous ether gave colorless needles, insoluble in water, soluble in alcohol, m. p. 65.1–65.3°⁶ (cor.).

Anal. Calcd. for C₉H₁₁NS: C, 65.41; H, 6.71; N, 8.48. Found: C, 65.60; H, 6.68; N, 8.27.

Thioacetamide and Ethanolamine.—Ethanolamine (15.3 g. = 0.25 mole) and thioacetamide (18.0 g. = 0.276 mole) were mixed in a flask equipped with stirrer and immersed in a bath. On heating at 60–75° an active gas evolution took place which lasted about one-half hour. The stirrer was then replaced by a distilling head and the temperature of the bath raised slowly to 215° while volatile material was removed *in vacuo* (30 mm.). The residue (17.9 g.) solidified on cooling and was recrystallized from absolute alcohol; colorless rectangular prisms, m. p. 101.0–101.5° (cor.). The analysis indicates that two molecules of each of the reactants have combined with loss of two molecules of ammonia and one of hydrogen sulfide; a possible formula is [HOCH₂CH₂N=C(CH₃)–]₂S.

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(2) Berntsen, *Ann.*, **184**, 290 (1877).

(3) Compare Westphal and Andersag, *Chem. Abstr.*, **35**, 1413 (1941); **36**, 1950 (1942); see also Gatewood and Johnson, *THIS JOURNAL*, **50**, 1423 (1928).

(4) Compare Buchman, Reims, Skei and Schlatter, *ibid.*, **64**, 2696 (1942).

(5) Compare Sakurada, *Chem. Zentr.*, **99**, I, 683 (1928).

(6) Worrall, *THIS JOURNAL*, **50**, 1459 (1928), gives m. p. 62–63° for *N*-benzylthioacetamide.

Anal. Calcd. for C₈H₁₆N₂O₂S: C, 47.03; H, 7.90; N, 13.71; S, 15.69. Found: C, 47.09; H, 7.79; N, 13.64; S, 15.82.

A derivative crystallized from the reaction mixture when equal volumes of saturated solutions of the substance and of picric acid in ethyl acetate were mixed, heated to boiling and then cooled to 0°. The crystals were washed with ether and dried, m. p. 95.0–95.5° (cor.).

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Preparation of *d*-Fructose-1,6-diphosphate by Means of Baker's Yeasts

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The preparation of the phosphoric esters of carbohydrates has not been achieved up to now with fresh baker's yeast, as phosphorylation with top yeast was only possible by addition of co-ferment to acetone yeast or alcohol-ether dried yeast (phosphorylation to 100%), or, with the same type of yeast, if dried before in the usual manner (phosphorylation to 20%).¹ By means of the procedure described below, *d*-fructose-1,6-diphosphate is readily obtained by the use of commercial bakers' yeasts without the necessity of treating brewers' yeast by washing, pressing, etc. Nearly equally satisfactory results have been obtained with various brands of fresh bakers' yeast (Atlantic, Federal, Blue Ribbon and National Grain), but not with fresh Fleischmann's yeast.

Procedure

To a solution of 200 g. of sucrose, 42 g. of monosodium phosphate (NaH₂PO₄·2H₂O) and 11 g. of sodium bicarbonate in 1000 cc. of tap water contained in a 5-l. bottle add 450 g. of fresh bakers' yeast (Atlantic) and 150 cc. of ether.² Shake the mixture until homogeneous, stopper the bottle in a manner which will allow the escape of gases, and place in an incubator at 37° until phosphorylation is complete³ (four and one half hours). The completeness of this process may be judged by adding 3 cc. of 2.5% ammonia and 1 cc. of 10% ammonium chloride to 2 cc. of the filtered fermentation mixture and then adding magnesia mixture. An immediate precipitation does not occur when phosphorylation is complete.

When phosphorylation is complete, add a few cc. of a

(1) C. Neuberger and A. Gottschalk, *Biochem. Z.*, **154**, 492 (1924).

(2) Carbon tetrachloride is an equally satisfactory plasmolytic agent, also for the phosphorylation with brewers' yeast, as our experiments with yeasts obtained from the Piel and Schaefer breweries (bottom yeasts) demonstrate.

(3) The time required for complete phosphorylation varies with different brands of yeast and with the temperature. Similar experiments made with Atlantic and Federal yeasts at room temperature (20–24°) required twenty and seventy-two hours, respectively.