## Preparation and Properties of S-Acetyl-N-benzoylcysteamine[1]

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The acetylation of aromatic amines in a physiological system is known to proceed through the intermediate acetyl coenzyme A,[2] a molecule in which the acetyl group is attached to coenzyme A through a thioester linkage.[3] The known susceptibility of thioesters to nucleophilic agents in general,[4] and particularly to aminolysis, has led Tarbell *et al.* to study the kinetics of the acetylation of the aliphatic amine, *n*-butylamine, by model thioesters related to acetyl coenzyme A.[5,6] However, the *enzymatic* acetylation of aromatic amines in a system in which the acetyl group is transferred to the acceptor amine from a model acetyl thioester instead of from acetyl coenzyme A has not been studied. We became interested in this problem in the course of experiments concerned with the effect of structure of the aromatic amine on the rate of *in vitro* acetylation. It was hoped that a simple, stable acetyl thioester could be synthesized which might replace the rather complex and relatively unstable acetyl coenzyme A as the acetylating agent. *S*-Acetyl-*N*-benzoylcysteamine was selected because it was thought that this compound, unlike most of the model thioesters employed by Tarbell *et al.*[5,6] would be a solid. This expectation was fully realized and the compound proved to be a stable solid melting at 91.5–92°.

Ethyleneimine was benzoylated and the intermediate, benzoylethyleneimide,[7] prepared *in situ*, was converted to the thioester by reaction with thioacetic acid. *S*-Acetyl-*N*-benzoylcysteamine was found to exhibit only feeble acetylating activity in the standard enzymatic test.[2] As these rate studies are no longer being pursued, we wish to report the preparation and properties of this new thioester.

### EXPERIMENTAL

A solution of 42.2 g. (0.30 mole) of benzoyl chloride in 35 ml. of benzene was added dropwise to an ice cold, stirred mixture of 12.9 g. (0.30 mole) of ethyleneimine, prepared by the modifications[8,9] of the procedure of Wenker,[10] and 30.4 g. (0.30 mole) of triethylamine in 250 ml. of anhydrous benzene. After stirring for 1 hr., the precipitate of triethylamine hydrochloride was removed by filtration. The benzene filtrate was then added rapidly to a cooled (ice bath), stirred solution of 22.8 g. (0.30 mole) of thioacetic acid in 100 ml. of benzene. After 1 hr., the benzene was removed by distillation *in vacuo* at room temperature to incipient precipitation of the product. The product was collected after stirring the mixture with 500 ml. of ligroin, and the crude material was dissolved in approximately 750 ml. of a mixture of benzene and ethyl acetate (4:1). The solution was washed three times with 50 ml. portions of distilled water and dried over anhydrous sodium sulfate. The solution was then concentrated *in vacuo* to 400 ml., warmed slightly, and diluted to 800 ml. with ligroin. On standing at room temperature, the product precipitated as fine, flocculent clusters (needles). There was obtained 52.1 g. of material melting at 90–91° (corr.); 78% yield. An analytical sample was recrystallized from ethyl acetate:ligroin, m.p. 91.5–92.0° (corr.).

*Anal.* Calcd. for $C_{11}H_{13}O_2NS$: C, 59.2; H, 5.87; S, 14.4. Found: C, 59.4; H, 5.89; S, 14.2.

The ultraviolet absorption spectrum of the compound in ethanol showed an absorption maximum at 230 mμ ($\epsilon$ = 15,100). The infrared spectrum showed the characteristic thioester band at 5.90 μ.[11] Hydrolysis of the thioester was accomplished with 0.5*N* sodium hydroxide. The hydrolysis was followed spectrophotometrically by the decrease in absorption at 230 mμ and was essentially complete in 30 min., but was allowed to proceed for 4 hr. Calculation of the molar extinction coefficient of the thioester bond based on the difference spectrum gave a value of $4.54 \times 10^3$. This is in excellent agreement with the values for ethyl thioacetate and β-acetaminoethyl thioacetate ($4.57 \times 10^3$ and $4.51 \times 10^3$ respectively) reported by Hawkins and Tarbell.[5]

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## p,p′-Nitro and Amino Derivatives of 1,3-Diphenylpropane

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Nitration of 1,3-diphenylpropane by fuming nitric acid has been reported to yield a dinitro derivative of m.p. 139°.[1] Investigation of a variety of nitrating conditions has shown that the *p,p′*-dinitro derivative, m.p. 140–141°, may be obtained in 22% yield by use of acetic anhydride, nitric, and sulfuric acids. The proof of structure lies in the oxidation to *p*-nitrobenzoic acid in substantially greater than 50% yield. Reduction of the

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dinitro compound by hydrazine, catalyzed by Raney nickel, afforded the *p,p'*-diamino compound. From the partial reduction of the dinitro compound by sodium polysulfide, the *p*-amino-*p'*-nitro compound was obtained in 38% yield. Although the aminonitro compound is bright yellow in the solid state in contrast to the dinitro and the diamino compounds both of which are colorless, the ultraviolet absorption spectrum of the aminonitro compound in 95% ethanol is virtually identical with a calculated spectrum derived from the dinitro and the diamino compounds, indicative of a lack of intramolecular complexing in the former compound in solution.[2]

The potentiometric titration curve for the diamine was markedly similar to that for *p*-toluidine. The lack of two breaks is suggestive of only a small difference in the first and second ionization constants, in accord with the results of Schwarzenbach on a series of straight chain aliphatic diamines.[3] The lack of appreciable interaction of the aryl amino group with the aryl ammonium group is also suggested by the close resemblance of the ultraviolet absorption spectrum of a 50% ethanol-water solution of the diamino compound 0.1*N* in sulfuric acid with that of 1,3-diphenylpropane. The correspondence in ultraviolet spectra of protonated aryl amines with the spectra of the parent hydrocarbons has been observed in other cases.[4]

## EXPERIMENTAL[5]

*p,p'-Dinitro-1,3-diphenylpropane.* A nitration medium was prepared by the slow addition of 4 ml. of concentrated sulfuric acid and 12 ml. of concentrated nitric acid to 20 ml. of acetic anhydride, keeping the temperature below 0°. To the medium was added a solution of 15 ml. of 1,3-diphenylpropane (b.p. 78–80° at 0.1 mm.; $n_D^{25}$ 1.5570) in 20 ml. of acetic anhydride over a 30-min. period. After the mixture was stirred at 0° for 30 min., 100 ml. of water was added and the mixture was stirred at room temperature for an additional 30 min. The crude product was collected by filtration and washed with water, 19 g., m.p. 85–100°. Four recrystallizations from ethanol afforded 4.5 g. (yield 22%) of colorless needles, m.p. 140–141° (reported for *x,x*-dinitro-1,3-diphenylpropane, white needles, m.p. 139°).[1] The ultraviolet absorption spectrum in 95% ethanol has a maximum at 216 mμ (ε 15,400) and 278 mμ (ε 21,000) and a minimum at 233 mμ (ε 4,250).

Oxidation of a 0.28-g. sample of the dinitro compound essentially by the procedure of Shriner, Fuson, and Curtin[6] afforded 0.24 g. (yield 74%) of *p*-nitrobenzoic acid after recrystallization from ethanol, m.p. 234–236°, mixed m.p. with an authentic sample, 238–240°.

*p,p'-Diamino-1,3-diphenylpropane* was prepared by a modification of the general procedure of Balcom and Furst.[7] To a warmed solution of 0.55 g. of the dinitro compound and 0.5 ml. of 95% hydrazine hydrate in 10 ml. of dioxane was added 0.5 g. of Raney nickel catalyst. After 1 hr. at 60°, during which time additional small amounts of catalyst were added, the solution was filtered, treated with Norite, filtered, and 30 ml. of water was added. White platelets separated on cooling, m.p. 99–101°. Recrystallization from 20 ml. of hexane afforded 0.2 g. (yield 50%) of lustrous white needles, m.p. 103–104°.

*Anal.* Calcd. for $C_{15}H_{18}N_2$: C, 79.60; H, 8.02; N, 12.38. Found: C, 79.54; H, 8.14; N, 12.29.

The ultraviolet absorption spectrum of the diamine in 95% ethanol has maxima at 238 mμ (ε 21,200) and 290 mμ (ε 2,960) and minima at 216 mμ (ε 7,810) and at 266 mμ (ε 1,280).

*p-Amino-p'-nitro-1,3-diphenylpropane.* To a solution of 2 g. of *p,p'*-dinitro-1,3-diphenylpropane in 150 ml. of ethanol was added 3.2 g. of sodium sulfide nonahydrate and 0.8 g. of sulfur in 12 ml. of water. The mixture was heated at reflux for 4 hr., cooled, diluted with 500 ml. of water, and extracted with 4–100 ml. portions of ether. The combined ether layers were extracted with 4–80 ml. portions of 5% hydrochloric acid. From the ether layer, 0.23 g. of impure starting material was recovered. The acidic aqueous phase was made basic and extracted with ether. Removal of ether after drying over magnesium sulfate yielded 1.34 g. of a red oil. The oil was dissolved in benzene and chromatographed on a 50-g. column of alumina in benzene. Elution with benzene afforded 776 mg. (yield 38%) of crystalline material. Two recrystallizations from cyclohexane afforded bright yellow needles m.p. 92–93°.

*Anal.* Calcd. for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.31; N, 10.93. Found: C, 70.34; H, 6.45; N, 10.61.

The ultraviolet absorption spectrum in 95% ethanol has maxima at 238 mμ (ε 4,080) and 278 mμ (ε 11,100) and minima at 225 mμ (ε 9,680) and at 256 mμ (ε 8,150).

Further elution of the column with benzene-ether yielded 180 mg. of impure diamine, established as such by m.p. and mixed m.p. of 103–104° for a recrystallized sample. Elution with ether and ether-methanol yielded two oily fractions which were not investigated further.

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(5) Melting points are corrected. We are indebted to Dr. S. M. Nagy and his associates for analyses and spectra.

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## Hydrogen Bromide–Acetic Acid Cleavage of Several Methoxyindanones and Methoxytetralones

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The cleavage of methoxyl groups *ortho* to the

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