parallels the previously reported[2,3] behavior of other adducts of I.

Experimental[5]

Reaction of 1,3-Diphenylisobenzofuran with Acetylenedicarboxylic Acid.—A solution of 0.61 g. of I[6,7] and 0.30 g. of II in 5 cc. of benzene and 5 cc. of ether was heated at reflux for 5 minutes. The ether was allowed to distil out of the reaction mixture and the residual solution was boiled an additional 55 minutes. After this time, the characteristic blue-green fluorescence of the isobenzofuran was no longer visible, even in ultraviolet light. The solution was concentrated by distillation and treated with a little carbon tetrachloride. The bis-adduct (III) crystallized as tiny, white prisms, m.p. 195.5–198.5°. The yield was 0.74 g. (quantitative). The analytical sample, recrystallized from benzene–carbon tetrachloride, had m.p. 203.5–204°.

Anal. Calcd. for $C_{24}H_{16}O_5$ (1:1 adduct): C, 74.99; H, 4.20. Calcd. for $C_{44}H_{30}O_6$ (bis-adduct): C, 80.72; H, 4.62. Found: C, 80.82, 80.54; H, 4.88, 5.00.

When the reaction was carried out under similar conditions using a 9:1 ratio of II to I, only III was isolated. The yield was 50%.

Reaction of 1,3-Diphenylisobenzofuran with Ethyl Acetylenedicarboxylate.—A solution of 0.54 g. of I and 0.34 g. of ethyl acetylenedicarboxylate in 4 cc. of benzene was heated at reflux for 105 minutes. The solvent was evaporated and the residue crystallized from benzene–ethanol to yield 0.74 g. (84%) of IVa, m.p. 139–140°. Recrystallization from benzene–ethanol raised the melting point to 143.0–143.5°. The substance instantaneously decolorized potassium permanganate in acetone at room temperature.

Anal. Calcd. for $C_{28}H_{24}O_5$: C, 76.35; H, 5.49. Found: C, 75.98; H, 5.18.

Catalytic Reduction of IVa.—A solution of 0.60 g. of IVa in 20.cc. of ethyl acetate was added to a suspension of Adams catalyst (previously generated from 0.05 g. of platinic oxide) in 10 cc. of ethyl acetate. The reaction mixture was stirred in hydrogen at one atmosphere pressure. The theoretical quantity of gas was absorbed in 38 minutes, whereupon the catalyst was filtered off and the filtrate evaporated to a thick oil which exhibited an intense blue-green fluorescence. The oil crystallized readily upon trituration and the product was recrystallized from ethanol to yield 0.40 g. of the dihydroester as white, rhombohedral tablets, m.p. 131.5–133°. After several recrystallizations from ethanol, the m.p. remained constant at 137.5–138°. A mixed m.p. with IVa was depressed to 106–120°. The dihydroester apparently suffers retrograde diene addition upon fusion, for the melt of the pure substance shows the characteristic blue-green fluorescence of I.

Anal. Calcd. for $C_{28}H_{26}O_5$: C, 76.00; H, 5.92. Found: C, 76.26; H, 6.07.

Saponification of IVa.—A mixture of 0.64 g. of IVa and 0.64 g. of potassium hydroxide in 10 cc. of ethanol was heated at reflux. The reaction mixture immediately turned bright-yellow and became strongly fluorescent. After 2.5 hours, the mixture was diluted with water and extracted with several portions of chloroform until the chloroform layer was no longer fluorescent. The chloroform solution was washed with water, dried over sodium sulfate and evaporated. The residue was recrystallized from benzene–Skellysolve B to give 0.03 g. of crude *o*-dibenzoylbenzene, m.p. 140–147° alone or mixed with an authentic sample.[8]

The original alkaline solution was acidified with concentrated hydrochloric acid and extracted with ether. The ether extract, after having been washed with water and dried over sodium sulfate, was evaporated to a thick, pale-yellow oil which crystallized readily from benzene–Skellysolve B as 0.30 g. (54%) of IVb, m.p. 134.5–135° with decomposition. Recrystallization from a mixture of ethyl acetate, benzene and Skellysolve B afforded pure-white rosettes of sharply-defined, transparent staves. The acid decomposed sharply at 139° with violent frothing when heated slowly from room temperature. When the substance was inserted into a bath preheated to 140.5° and the temperature was raised very slowly (1° per minute), decomposition occurred at 144.5–145°.

The acid was readily soluble in neutral ethanol. When this colorless solution was treated with a few drops of 10% sodium hydroxide, it immediately turned yellow and showed a blue-green fluorescence.

Freshly-purified samples of the acid were pure-white in the solid state. The crystals became yellow in about two hours when dried at 1 mm. at room temperature. The dried material showed essentially the same melting point characteristics as the freshly-recrystallized substance.

Anal. Calcd. for $C_{24}H_{16}O_5 \cdot H_2O$: C, 71.63; H, 4.51. Found (after drying at 56° and 1 mm. for 2 hours, then at room temperature for 48 hours over phosphorus pentoxide): C, 71.34; H, 4.10. Found (after drying at 56° and 1 mm. for 24 hours, then at room temperature for 1 week over phosphorus pentoxide): C, 71.47; H, 4.70.

Pyrolysis of IVb.—Eighteen-hundredths of a gram of finely-powdered IVb was carefully heated to its melting point in a slow current of nitrogen. The exit gases were passed into baryta. At 140° the solid frothed vigorously and a sudden surge of gas produced a voluminous precipitate in the baryta solution. The melt was kept at 140–143° for 15 minutes and then allowed to cool. The yellow-brown glassy residue was dissolved in ether and extracted with potassium carbonate solution. The aqueous layer was freed of a small quantity of insoluble material by filtration and then acidified with concentrated hydrochloric acid. The precipitated solid, after drying at the pump, weighed 0.12 g. Recrystallization from benzene–Skellysolve B afforded glittering, short needles or prisms, m.p. 204–205°, alone or mixed with a sample of III prepared by diene addition.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF SOUTHERN CALIFORNIA
LOS ANGELES 7, CALIFORNIA

(5) Melting points are corrected. The microanalyses are by Mr. Joseph Pirie of this Laboratory and by Dr. Adalbert Elek, Elek Microanalytical Laboratory.

(6) R. Adams and M. H. Gold, THIS JOURNAL, **62**, 56 (1940).

(7) The preparation of I by the procedure of reference 6 was found to be superior to that of A. Guyot and J. Catel, *Bull. soc. chim.*, **35**, 1124 (1906). Compare E. Bergmann, *J. Chem. Soc.*, 1147 (1938).

Preparation of *p*-Acetaminobenzaldehyde Thiosemicarbazone

BY A. DAS AND S. L. MUKHERJEE

RECEIVED AUGUST 13, 1952

Domagk, *et al.*,[1] reported the activity of thiosemicarbazones against tuberculosis. Of the two most effective thiosemicarbazones, *p*-acetaminobenzaldehyde thiosemicarbazone known commercially as TB/I and the *p*-ethylsulfonyl derivative known as TB/III, the former has found more popularity with the medical profession. This compound has been synthesized in a variety of ways[2,3,4] by using thiosemicarbazide in all cases. In still another method[5a] hydrazinium thiocyanate has reacted with aromatic aldehydes to give appropriate thiosemicarbazones. Almost simultaneously the preparation of acetone thiosemicarbazone by using hydrazinium thiocyanate with acetone has been reported by Sunner.[5b]

Following the well-known extension of Wöhler's synthesis as applied in the above two methods[5a,5b] as well as in the preparation of thiosemicarbazide[6]

(1) Domagk, *et al.*, *Naturwissenschaften*, **33**, 315 (1946).

(2) Domagk (to I. G. Farbenindustrie), *German Patent Appli.*, **176**, 219 (1943); *Ind. Eng. Chem.*, **42**,1868 (1950).

(3) "Manufacture of thiosemicarbazone derivative of acetylamino or amino substituted aromatic aldehyde," Indian Patent 43,527 dated 22nd July 1950.

(4) Wilheim, *Acta Univ. Szeged, Chem. Phys.*, **3**, 54 (1950); *C. A.*, **46**, 2521 (1952).

(5) (a) Puetzer, *et al.*, THIS JOURNAL, **73**, 2958 (1951); (b) Sunner, *C. A.*, **45**, 5486 (1951).

(6) Freund and Wischewiansky, *Ber.*, **26**, 2877 (1893).

the present investigation was undertaken to see whether a thiosemicarbazone can be successfully developed from a hydrazone which can be prepared from an excess of hydrazine hydrate and an aldehyde. *p*-Acetaminobenzaldehyde thiosemicarbazone has thus been prepared by allowing *p*-acetaminobenzaldehyde hydrazone to react with ammonium thiocyanate.

Further attempts to prepare it *in situ* from a mixture of *p*-acetaminobenzaldehyde, excess hydrazine sulfate and ammonium thiocyanate in water also resulted in the formation of thiosemicarbazone in excellent yield. The reaction in this case proceeds through the formation of azine which is converted into its hydrazone in the presence of excess of hydrazine. This with thiocyanate gives the thiosemicarbazone after subsequent rearrangement of the thiocyanate derivative as

$$\underset{\text{aldehyde}}{RCHO} + \underset{\text{hydrazine}}{NH_2NH_2} \longrightarrow \underset{\text{azine}}{RCH{=}NN{=}CHR} \longrightarrow$$

$$\underset{\text{hydrazone}}{RCH{=}H{-}NH_2} \longrightarrow \underset{\text{thiocyanate}}{RCH{=}N{-}NH_2HSCN} \longrightarrow$$

$$R = CH_3CONHC_6H_4- \qquad \underset{\text{thiosemicarbazone}}{RCH{=}N{-}NH{-}\overset{\overset{S}{\|}}{C}{-}NH_2}$$

Experimental

p-**Acetaminobenzaldehyde.**—The *p*-aminobenzaldehyde (Beard and Hodgson[7]) was acetylated in chloroform with acetic anhydride. It recrystallized from hot water in pale yellow needles, m.p. 158°.[8]

p-**Acetaminobenzaldehyde Hydrazone.**—*p*-Acetaminobenzaldehyde (7 g.) was refluxed with 75% hydrazine hydrate (20 cc.) in alcohol (40 cc.) for one hour. The clear solution was allowed to cool when colorless crystalline needles of hydrazone separated, m.p. 165–166°.

Anal. Calcd. for $C_9H_{11}N_3O$: N, 23.7. Found: N, 23.6.

It is of interest to note that when *p*-acetaminobenzalazine is heated with hydrazine hydrate in alcohol *p*-acetaminobenzaldehyde hydrazone is formed which when heated with water changes itself to *p*-acetaminobenzalazine, m.p. 315–316° as confirmed by a mixed m.p. with an authentic sample prepared by the method of Bernstein, *et al.*[9]

p-**Acetaminobenzaldehyde Thiosemicarbazone.**—(i) The hydrazone was suspended in water and acidified to congo red with concd. hydrochloric acid. Ammonium thiocyanate (15 g.) was then added and the mixture concentrated on a water-bath. Water was added and concentrated as before. This process was repeated until the residue was crystalline. It was then filtered and washed with hot water. Yellow crystals were obtained having m.p. 225–226° (dec.). There was no depression of m.p. when mixed with a sample prepared from the aldehyde and thiosemicarbazide; Bernstein, *et al.*,[9] reported a m.p. 223–224° (dec.).

Anal. Calcd. for $C_{10}H_{12}N_4OS$: N, 23.7. Found: N, 23.5.

This identification was confirmed by deacetylating when *p*-aminobenzaldehyde thiosemicarbazone was obtained m.p. 196° with no depression of m.p. with an authentic sample (Berstein, *et al.*).

(ii) To *p*-acetaminobenzaldehyde (8 g.) in alcohol (50 cc.) was added a 300-cc. solution of a mixture of hydrazine sulfate (20 g.) and sodium carbonate (8 g.) when an instantaneous precipitate[10] was formed. To this mixture was added ammonium thiocyanate (16 g.) in water (100 cc.) and the mixture heated under a reflux for 11 hours until the frothing completely subsided. The large flat crystals of *p*-acetaminobenzaldehyde thiosemicarbazone were collected; yield (8 g.) m.p. 226–227° (dec.) confirmed by a mixed m.p. with the above specimen.

Anal. Calcd. for $C_{10}H_{12}N_4OS$: N, 23.7. Found: N, 23.6.

RESEARCH SECTION
ALBERT DAVID LTD. (LABORATORIES)
CALCUTTA 13, INDIA

(7) Beard and Hodgson, *J. Chem. Soc.*, 4 (1944).

(8) Friedlander and Cohn, *Monatsh.*, **24**, 1, 87 (1903), reported a m.p. 161°.

(9) Bernstein, *et al.*, THIS JOURNAL, **73**, 906 (1951).

(10) Identified as the *p*-acetaminobenzalazine, m.p. 315–316° with no depression on mixed m.p. with an authentic sample. *Anal.* Calcd. for $C_{18}H_{18}N_4O_2$: N, 8.69. Found: N, 8.48.

Preparation and Properties of Pure Ammonium DL-Lactate[1]

BY E. J. COSTELLO AND E. M. FILACHIONE

RECEIVED OCTOBER 31, 1952

Ammonium lactate, which can readily be prepared by fermentation of carbohydrates in the presence of ammonia[2–4] is potentially an important primary fermentation product. Previous studies at this Laboratory have shown that ammonium lactate upon interaction with alcohols produces lactic ester and ammonia in high yields.[5–7] However, comparatively little information about the physical properties of ammonium lactate has been reported,[8–11] only the distillation of ammonium lactate in vacuum[10] and certain properties of aqueous ammonium lactate[11] having been recorded. Pure crystalline ammonium lactate, however, was not used in these investigations, and lactamide was most likely a contaminant.[12] This paper reports the preparation of pure crystalline ammonium lactate and the determination of various properties of this pure salt.

Experimental

Preparation of Ammonium Lactate.—The equivalence point of ammonium lactate was first determined as follows: An approximately 0.1 *N* lactic acid solution was prepared by diluting a high quality 20% lactic acid solution and refluxing for one day to completely remove any polylactic acid. A 25-cc. aliquot of this solution (0.098 *N*) was titrated potentiometrically with freshly standardized ammonium hydroxide (0.102 *N*). The change in *p*H in the vicinity of the equivalence point was pronounced, considerably more than in the titration of a weaker acid such as acetic acid. The equivalence point for ammonium lactate corresponded to a *p*H of 6.65.

The 80% edible grade DL-lactic acid of commerce (4 kg.) was diluted to approximately 20% concentration with water (12 kg.) and this diluted solution was heated under a reflux condenser for 24 hours at 85–90°. Thus the polylactic acid, present in concentrated lactic acid solutions, was almost completely hydrolyzed to lactic acid. The equilibrated 20% aqueous lactic acid solution was then neutralized with concentrated ammonium hydroxide to a *p*H of 7.0. The dilute ammonium lactate solution was concentrated

(1) Article not copyrighted.

(2) H. C. Jansen, Dutch Patent 57,848 (July 15, 1946).

(3) L. H. C. Perquin, Dutch Patent 58,545 (Nov. 15, 1946).

(4) L. L. Kempe, H. O. Halvorson and E. L. Piret, *Ind. Eng. Chem.*, **42**, 1852 (1950).

(5) E. M. Filachione, E. J. Costello and C. H. Fisher, THIS JOURNAL, **73**, 5265 (1951).

(6) E. M. Filachione and E. J. Costello, *Ind. Eng. Chem.*, **44**, 2189 (1952).

(7) E. M. Filachione and C. H. Fisher, U. S. Patent 2,565,487 (Aug. 28, 1951).

(8) B. E. Brown and F. R. Reid, *Am. Fertilizer*, **95**, No. 12, 12 (1941).

(9) F. Groebe and O. Spengler, German Patent 680,660 (Aug. 17, 1939).

(10) R. Escales and H. Koepke, *J. prakt. Chem.*, **87**, 258 (1913).

(11) A. A. Dietz, E. F. Degering and H. H. Schopmeyer, *Ind. Eng. Chem.*, **33**, 1444 (1941).

(12) J. Wislicenus, *Ann.*, **133**, 257 (1865).