

benzenes were obtained by a similar distillation of "Alkazene 21."

The physical constants and oxidation products of the aryl halides are given in Table I and the physical constants, yields and analyses of the diethylbenzenes are shown in Table II. The physical properties were determined by methods previously described.¹ The time-temperature freezing curves for *o*- and *p*-diethylbenzenes are shown in Fig. 1.

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The Hydrogenolysis of Ethyl β -Benzylaminopropionate¹

BY ALBERT M. MATTOCKS² AND WALTER H. HARTUNG

During the course of investigations under way in these Laboratories, we had occasion to prepare ethyl β -benzylaminopropionate, a compound previously reported by Thayer and McElvain.³ The prospect of converting it into ethyl β -aminopropionate by hydrogenolytic debenzoylation offered another route to the synthesis of β -alanine. It was observed that if the *N*-benzyl intermediate is treated at 13 atm. of hydrogen with a catalyst made from charcoal on which has been deposited the palladium from 0.3 g. of palladium chloride and the platinum from 0.15 g. of platinum chloride, the benzyl group is removed as toluene, and the ester of β -alanine may be isolated in excellent yields.

Experimental

Ethyl β -bromopropionate was synthesized from acrylonitrile according to the method of Kendall and McKenzie.⁴ This, on reaction with two equivalents of benzylamine in absolute ethanol, readily precipitated almost quantitatively benzylamine hydrobromide; removal of the crystals and addition of hydrogen chloride to the filtrate, led to the crystallization of the hydrochloride of ethyl β -benzylaminopropionate, melting 146–147°, the previously recorded value.¹

Hydrogenation was carried out as already indicated, in ethanolic solution. Removal of the catalyst, concentration of the filtrate and addition of ether caused the precipitation in yields approaching quantitative of the hydrochloride of the amino ester. The melting point of the salt was 67°, which agrees with the previously reported value³ for the hydrochloride of ethyl β -aminopropionate. *Anal.* Found: N (Kjeldahl), 9.29 and 9.35; calculated N for $C_8H_{11}O_2N \cdot HCl$, 9.12.

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(1) Paper no. 5 on synthesis of amino acids; for no. 4 see Mattocks and Hartung, *J. Biol. Chem.*, **165**, 501 (1946).

(2) Present address: Southern Research Institute, Birmingham, Ala.

(3) Thayer and McElvain, *THIS JOURNAL*, **49**, 2862 (1927).

(4) Kendall and McKenzie, "Organic Syntheses," Coll. Vol. I, p. 246.

(5) Hale and Hodan, *THIS JOURNAL*, **41**, 770 (1919).

The Preparation of Phenylsuccinonitrile

BY DAVID T. MOWRY

The preparation of phenylsuccinonitrile reported by Cobb¹ and improved by Gitsels and Wibaut² involves the action of an aqueous alcoholic solution of potassium cyanide on ethyl phenylpropionate. Attempts to improve the reported 20% yield have not been successful. Attempts made to cause hydrogen cyanide or sodium cyanide to react with cinnamonitrile to give the desired product were also unsuccessful. Its preparation by the action of potassium cyanide in an alcoholic solution on ethyl α -cyanocinnamate has now been worked out as follows.

Procedure.—A solution of 50 g. (0.25 mole) of ethyl α -cyanocinnamate and 29 g. (0.45 mole) potassium cyanide in 900 cc. of 90% ethanol was refluxed for two hours in the hood (some hydrogen cyanide is evolved along with the carbon dioxide). The alcohol was evaporated whereupon 30 g. of crude product (77% yield) crystallized from the residue. Two recrystallizations from dilute ethanol gave 25 g. (64% yield) of product, m. p. 68°. The melting point was not depressed by admixture with a sample prepared by the method of Gitsels and Wibaut.²

If the crude product did not crystallize readily from the reaction mixture after evaporation of the ethanol, the oil was dissolved in ether solution, washed with a little water and distilled. The colorless distillate boiled at 168–170° (3 mm.) and solidified in the receiver, m.p. 66–67°.

Ethyl α -cyanocinnamate is readily available in nearly quantitative yield from benzaldehyde and ethyl cyanoacetate. This new two-step synthesis, therefore, represents a decided improvement over the laborious four-step method, giving a 12% yield from the ethyl cinnamate through the intermediates ethyl α, β -dibromo- β -phenylpropionate,³ phenylpropionic acid⁴ and ethyl phenylpropionate.

(1) Cobb, *Am. Chem. J.*, **45**, 604 (1911).

(2) Gitsels and Wibaut, *Rec. trav. chim.*, **59**, 1093–1103 (1940).

(3) Abbott and Althausen, "Organic Syntheses," Coll. Vol. II, 270 (1943).

(4) Abbott, *ibid.*, p. 515.

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The Purification of Hesperidin with Formamide

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The purification of hesperidin has been difficult because of its inadequate solubility in methanol and pyridine, the solvents most frequently selected for this purpose. This difficulty is reflected in the 15° range in the melting points which have been recorded.^{3,4,5} It has now been found that the following procedure can be success-

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(3) H. Scarborough, *Biochem. J.*, **39**, 271–278 (1945).

(4) A. Hilger, *Ber.*, **9**, 26 (1876).

(5) F. Tiemann and W. Will, *ibid.*, **14**, 946 (1881).

fully used for the purification of hesperidin obtained from citrus fruit:

A 10% solution of hesperidin in formamide prepared by warming to about 60° is treated for thirty minutes with activated charcoal previously boiled with dilute hydrochloric acid. The formamide when tested in a 50% aqueous solution should be slightly acid. If it is not, a little glacial acetic acid or formic acid should be added. The solution is then filtered through diatomaceous earth, diluted with an equal volume of water and allowed to stand a few hours for crystallization of the precipitated hesperidin. The crystals are then filtered off, washed with hot water and then with isopropanol. Two such crystallizations give a white crystalline product melting at 261–263° with some decomposition which compares favorably with the highest melting point previously recorded,⁵ namely, 261–262°.

A test devised by C. W. Wilson and Laverra Hill (as yet unpublished) based on the color reaction of boric acid with flavone derivatives⁷ gives only very slightly positive results with hesperidin thus purified. Its color density, by this test, as determined with a Beckman spectrophotometer was only 0.008 at 402 millimicrons as compared with a color density of 0.088 and 0.072 for samples purified by means of methanol and pyridine, respectively. Crude hesperidin gives a color density of 0.8 or more at this same wave length.

The formamide may be recovered by fractional distillation under vacuum, although slight decomposition into ammonia and carbon monoxide occurs during this step. According to literature⁸ formamide may be stabilized by the addition of small amounts (0.001–1.0%) of a purine ring compound such as caffeine, xanthine, theobromine, uric acid, guanine, etc. However, formamide recovered without a stabilizer has been found to be still acceptable as a solvent for hesperidin.

(6) Kwang Fong Tseng and Ren Dzin Yu, *J. Chinese Pharm. Assoc.*, **1**, 14–23 (English) (1936).

(7) Clarence W. Wilson, Leroy S. Weatherby and William Z. Bock, *Ind. Eng. Chem.*, **14**, 425 (1942).

(8) Edward C. Kirkpatrick (to E. I. du Pont de Nemours and Co.), U. S. Patent 2,346,425, April 11, 1944; C. A., **38**, 4962 (1944).

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Retention of the Carbon Skeleton in the Kindler-Willgerodt Reaction

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It was assumed by Willgerodt² that the course of the reaction bearing his name involved no rearrangement of the alkyl chain when aralkyl ketones were converted to carboxylic acids or amides by heating with ammonium polysulfide, and it seems reasonable to assume that the Kindler³ modification, employing anhydrous amines in place of ammonia, follows the same mechanism. However, substantial proof of this has been lack-

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(2) Willgerodt, *Ber.*, **20**, 2467 (1887); **21**, 534 (1888).

(3) Kindler, *Ann.*, **431**, 187 (1923).

ing until the appearance of recent papers by Cavalieri, *et al.*,⁴ and King and McMillan.^{5,6} At the time of the appearance of this latter paper, which demonstrates by the use of branched chain ketones that the carbon skeleton is unchanged, we had just completed an experiment which offers further direct evidence of non-rearrangement of the carbon chain during the course of the reaction.

Acetophenone containing C¹³ in the carbonyl group was transformed to phenylacetic acid by a modified Willgerodt reaction. The carbon dioxide obtained upon decarboxylation of this phenylacetic acid was analyzed and no excess of C¹³ over normal could be detected. Subsequent oxidation of the residual dibenzyl ketone from the above experiment gave benzoic acid which was found to contain the isotopic carbon in the carboxyl group. It is thus evident that the carbon atom originally attached to the benzene ring in the acetophenone has remained there throughout the above series of reactions.

Experimental

Barium carbonate (4.8 g.) containing an 0.34% excess of C¹³ was acidified and the carbon dioxide evolved was passed into an ethereal solution of methyl magnesium iodide at –30°. After acidification the resulting acetic acid was distilled with water and isolated from the distillate as the silver salt (yield, 3.7 g.). This was converted to sodium acetate, which was dried and heated with 4.25 g. of *p*-toluenesulfonyl chloride. The resulting acetic anhydride (0.95 ml.) was refluxed for half an hour with 15 ml. of dry benzene and 6 g. of anhydrous aluminum chloride, yielding 1.14 g. of crude acetophenone.

A modified Willgerodt reaction was performed according to Schwenk and Bloch⁷ by refluxing the acetophenone for three hours with 0.84 g. of morpholine and 0.30 g. of sulfur. The thiomorpholide thus obtained was refluxed for eight hours with 10 ml. of 10% aqueous potassium hydroxide, yielding 0.62 g. of crude phenylacetic acid. Distillation at 15 mm. pressure gave 0.40 g. of a pale yellow solid which was recrystallized twice from 5-ml. portions of hot water. The product was dried, yielding 167 mg. of phenylacetic acid melting at 74–75°.

The phenylacetic acid was mixed thoroughly with 2 g. of 40-mesh iron filings and decarboxylated by heating to 250°. The carbon dioxide evolved was examined in a mass spectrometer. No excess C¹³ over normal could be detected, showing definitely that no rearrangement had occurred.

The residue from the decarboxylation of the phenylacetic acid (probably mostly dibenzyl ketone) was oxidized to benzoic acid by refluxing for twelve hours with 6 *N* sulfuric acid containing 20% sodium dichromate. The benzoic acid obtained was converted to the silver salt and this was decarboxylated by heating. The carbon dioxide evolved, when examined in the mass spectrometer, was found to contain 0.27% excess isotopic carbon. The 20% lowering of the excess isotopic carbon content found here is far outside the limits of error of the mass spectrometer and must be attributed mainly to introduction of extraneous carbon dioxide during the various reactions and is partly due to the use of normal phenylacetic and benzoic acids used for seeding in the crystallization steps. However, this in no way invalidates the results, since absolutely

(4) Cavalieri, Pattison and Carmack, *THIS JOURNAL*, **67**, 1783 (1945).

(5) King and McMillan, *ibid.*, **68**, 525 (1946).

(6) King and McMillan, *ibid.*, **68**, 632 (1946).

(7) Schwenk and Bloch, *ibid.*, **64**, 3051 (1942).