alanine were prepared in addition to the group already published.[1]

Ethyl (2,4-Dichlorobenzyl)-acetamidomalonate (I).—By the process previously reported,[1] 39.2 g. (0.2 mole) of 2,4-dichlorobenzyl chloride[2] and the sodium salt of 43.4 g. (0.2 mole) of ethyl acetamidomalonate, gave 60 g. of product (80%), m.p. 159–160°. Subsequent recrystallizations from aqueous alcohol did not significantly alter the melting point.

Anal.[3] Calcd. for $C_{16}H_{19}Cl_2NO_5$: C, 51.08; H, 5.09. Found: C, 51.40; H, 5.02.

β-(2,4-Dichlorophenyl)-alanine.—Hydrolysis of 37.6 g. (0.1 mole) of I by refluxing for 14 hours in 150 ml. of 48% hydrobromic acid, gave 24 g. (theoretical yield) of product, m.p. 237–239° dec. Two recrystallizations from water raised the melting point to 238–240° dec.

Anal. Calcd. for $C_9H_9Cl_2NO_2$: C, 46.18; H, 3.88. Found: C, 45.92; H, 4.22.

β-(3-Nitro-*p*-tolyl)-alanine.—3-Nitro-*p*-xylyl chloride was prepared by the method of Stephen, Short and Gladding.[4] By treatment of 25 g. (0.13 mole) of this material with 23 g. (0.13 mole) of ethyl acetamidocyanoacetate in the usual manner,[1] there was obtained a brown oil which could not be crystallized. The oil was hydrolyzed by heating at reflux temperature for four and a half hours in hydrochloric acid as described previously.[1] A solid formed in the neutralized solution after it had stood for several days; weight 17 g., m.p. 219° dec. (bath preheated to 210°). Recrystallization from aqueous alcohol gave 10 g. (34%) of product, m.p. 230° dec.

Anal. Calcd. for $C_{10}H_{12}N_2O_4$: C, 53.56; H, 5.40. Found: C, 53.77; H, 5.60.

(1) Burckhalter and Stephens, THIS JOURNAL, **73**, 56 (1951).
(2) Supplied by Heyden Chemical Corp., Garfield, N. J.
(3) Analyses by Mr. C. W. Beazley, Skokie, Illinois.
(4) Stephen, Short and Gladding, *J. Chem. Soc.*, **117**, 510 (1920).

DEPARTMENT OF PHARMACEUTICAL CHEMISTRY
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The Synthesis of 2,3-Bis-(*p*-carbethoxyphenyl)-2,3-butanediol by Electrolytic Reduction

BY MILTON J. ALLEN

It recently became necessary to prepare large quantities of 2,3-bis-(*p*-carbethoxyphenyl)-2,3-butanediol. A survey of the electrochemical literature[1] indicated that in acid medium an ester of an aromatic acid is readily reduced to an ether and aromatic acid reduced to an alcohol.

In view of the possibility of saponification of the *p*-carbethoxyacetophenone during reduction in alkaline medium, the free acid was reduced in alkaline medium at a constant reference potential with the resultant excellent yield of the pinacol. Treatment of the pinacol with ethanol and sulfuric acid yielded 2,3-bis-(*p*-carbethoxyphenyl)-2,3-butanediol.

Figure 1 illustrates the cell used in the electrolytic reduction. The instrument used for maintaining a constant reference potential has been previously described.[2]

Experimental[3]

2,3-Bis-(*p*-carbethoxyphenyl)-2,3-butanediol.—The catholyte consisted of 300 g. of *p*-carboxyacetophenone dissolved in 2500 ml. of distilled water containing 280.5 g. of potassium hydroxide (Baker reagent). The anolyte contained 56.1 g. of potassium hydroxide in 500 ml. of aqueous solution. At a reference potential of −2.0 volts the initial current was 4.2 amperes. After 937 minutes a current plateau of 0.9 ampere was reached. The catholyte was filtered, acidified with hydrochloric acid, refrigerated overnight and filtered. The residue was washed with water and dried in a vacuum oven; yield 290 g. (96.2%), m.p. 268–278°. Recrystallization from water gave platelets m.p. 272–273.5°. *Anal.* Calcd. for $C_{18}H_{18}O_6$: C, 65.45; H, 5.49. Found: C, 65.09; H, 5.85.

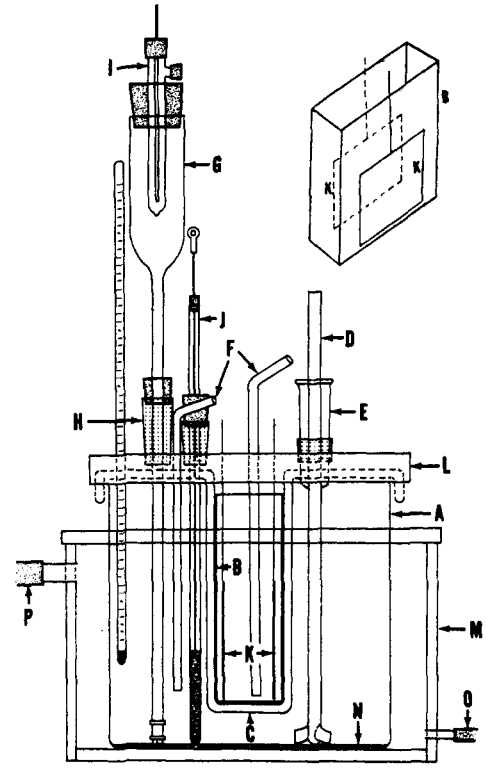

Fig. 1.—Electrolysis cell: A, glass electrolysis cell 8¼" i.d. × 8¾" high; B, alundum membrane 2" wide × 6" long × 6" deep, ⅛" wall mix RA 1143 (Norton Company); C, membrane support ¼" diameter rod; D, paddle stirrer 16" long × ⅜" diameter; E, mercury seal type bearing with 29/42 joint; F, nitrogen inlet tubes to cathode and anode chambers; G, salt bridge, top portion 2" diam. × 4" high narrowing to 7/16" × 12" long at end of which is sealed a 14/35 male joint, ⅜" up from the bottom on one side of joint is a 1/64" hole, over the male end of the joint is a female collar ⅝" in lengh; H, support for salt bridge 24/40 joint extended 1.5 inches; I, standard Beckman calomel electrode; J, contact to mercury cathode consisting of tube 1/16" o.d. × 14" long at bottom of which is sealed a piece of platinum wire. The tube is filled part way with mercury and copper wire inserted for connection to cathode lead. The entire tube passes through a rubber stoppered 24/40 joint; K, platinum anode 4" × 4" × 1/64"; L, Plexiglas cover; M, cooling chamber 11" × 11" × 7¼" high o.d. ¼" thick Plexiglas; N, mercury cathode; O, one water inlet to cooling chamber, ¼" i.d. P; two water outlet from cooling chamber, ¼" i.d.

2,3-Bis-(*p*-carbethoxyphenyl)-2,3-butanediol.—Fifty grams of the pinacol was mixed with 1000 ml. of absolute ethanol and 200 ml. of sulfuric acid. The solution was refluxed for eight hours and diluted with an equal volume of water. After neutralization with aqueous sodium carbonate, most of the alcohol was evaporated on a steam-bath. The cooled solution was extracted a number of times with ether. The combined ether extracts were evaporated to a small volume and refrigerated; yield 48 g. (82%), m.p. 167–168°. Recrystallization from 61.5% methanol gave a crystalline compound m.p. 169.5–170.5°.

(1) "Organische Elektrochemie," Fr. Fichter, Verlag von Theodor Steinkopf, Dresden, 1942, pp. 251-263.
(2) M. J. Allen, *Anal. Chem.*, **22**, 804 (1950).
(3) All melting points reported were done on a Kofler hot-stage and are corrected.

Anal. Calcd. for $C_{22}H_{26}O_6$: C, 68.38; H, 6.78. Found: C, 68.50; H, 6.87.

The compound was insoluble in dilute sodium carbonate which eliminated the possibility of it being a diether.

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Purification of 2,6-Lutidine

BY JOHN A. CATHCART AND DELBERT D. REYNOLDS

2,6-Lutidine is a very useful reagent in synthetic organic chemistry. It is a stronger base toward hydrogen chloride than is pyridine,[1] and it has less tendency to quaternize than does pyridine or the picolines.[2] The combination of these properties makes it especially useful in the chemistry of the sulfonates, in which quaternization is often an undesirable side reaction.

This note deals with the separation of 2,6-lutidine from the picolines. Commercial 2,6-lutidine contains β- and γ-picolines. Previous methods of separation have depended upon the fractional crystallization of derivatives such as hydrohalides, picrates, dimercurichlorides and oxalates, or upon azeotropic distillation.[3] The method described here is based upon the fact that 2,6-lutidine quaternizes with alkyl sulfonates much more slowly than do the picolines. Thus, when a mixture of 2,6-lutidine and the picolines reacts with an alkyl sulfonate, the picoline forms insoluble, undistillable quaternary salts which may be separated from the 2,6-lutidine by decantation or distillation. The effectiveness of this method is illustrated in the experimental section.

Experimental

The crude 2,6-lutidine was Eastman Kodak Co. Practical grade (m.p. −8.5°). The impurity is not water alone, since distillation over calcium hydride raised the melting point to only −7.6° instead of −5.9° which was the value found for pure 2,6-lutidine by repeated fractional crystallization.[3]

Any of the alkyl sulfonates may be used, but we prefer ethyl *p*-toluenesulfonate because of its availability and because of the rate with which it reacts with the picolines.

Removal of β- and γ-Picolines.—A. One kilogram of 2,6-lutidine (m.p. −8.5°) was mixed with 200 g. of ethyl *p*-toluenesulfonate and heated to reflux for one hour. The reaction mixture was cooled and the upper layer separated and distilled without fractionation. This product was refluxed over 100 g. of calcium hydride and distilled through a 20-inch column packed with glass helices; first fraction: b.p. < 144°, 25 g.; second fraction: b.p. 144°, 741 g., m.p. −6.15°.

B. This example omits the steps in which the quaternized product is separated and the distillation over calcium hydride.

One kilogram of 2,6-lutidine (m.p. −8.5°) was refluxed for one hour with 200 g. of ethyl *p*-toluenesulfonate. The 2,6-lutidine was distilled from the reaction mixture through a 20-inch packed column; first fraction: 24 g., b.p. 64–144°; second fraction: 780 g., b.p. 141°, m.p. −6.4°.

Removal of β-Picoline.—Four hundred and seventy-five grams of 2,6-lutidine (m.p. −6.3°) was mixed with 25 g. (5%) β-picoline. This mixture melted at −9.1°. One hundred grams of ethyl *p*-toluenesulfonate was added, the solution refluxed for one hour and then distilled as above; first fraction: 26 g., b.p. < 144°; second fraction: 350 g., b.p. 144°, m.p. −6.3°.

Redistillation of the second fraction over calcium hydride raised the melting point to −6.2°.

Removal of γ-Picoline.—Four hundred and seventy-five grams of 2,6-lutidine (m.p. −6.5°) was mixed with 25 g. of γ-picoline. The mixture (m.p. −9.1°) was refluxed for 1.5 hours with 100 g. of ethyl *p*-toluenesulfonate. The upper layer was separated and fractionally distilled; first fraction: b.p. < 144°, 18 g.; second fraction: 338 g. b.p. 144°, m.p. −6.3°.

Removal of α-Picoline.—Four hundred and seventy-five grams of 2,6-lutidine (m.p. −6.5°) was mixed with 25 g. of α-picoline. This mixture (m.p. −9.1°) was refluxed one hour with 100 g. of ethyl *p*-toluenesulfonate. The lutidine layer was separated and distilled; first fraction: b.p. < 144°, 42 g., second fraction: b.p. 144, 325 g., m.p. −6.4°.

RESEARCH LABORATORY
EASTMAN KODAK COMPANY
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Pyrido[3,2-d]thiazoles

BY SCOTT J. CHILDRESS[1] AND R. L. MCKEE

At the time of this work, previous reports of pyridothiazoles had been confined to the [2,3-d][2] and the [2,1-b][3] series. As a background for future research, the formation of the pyrido[3,2-d]thiazole system has been briefly investigated. During the course of this work, other examples of this system have appeared[4] and certain intermediates have been reported.[5]

The preparation of 5-methylpyrido[3,2-d]thiazole was accomplished by simultaneous reduction and cyclization of 5-methyl-3-nitro-2-pyridinethiol by means of iron filings and formic acid. The 2,5-dimethyl analog, similarly prepared, was not obtained in a pure condition.

Experimental

5-Methyl-2-nitraminopyridine was prepared from 1.0 g. of 2-amino-5-methylpyridine, 4.6 ml. of concentrated sulfuric acid and 0.7 ml. of concentrated nitric acid maintained below 10°. One gram of light yellow needles melting with decomposition at 181° was obtained.

Anal. Calcd. for $C_6H_7N_3O_2$: N, 27.4. Found: N, 27.3, 27.5.

2-Amino-5-methyl-3-nitropyridine was prepared as recently described.[5] The present authors were unable to obtain a yield greater than 36% of a dark yellow powder melting at 192–194°.

Anal. Calcd. for $C_6H_7N_3O_2$: N, 27.4. Found: N, 27.5.

5-Methyl-3-nitro-2-pyridol.—A. Following the procedure of Lapin and Slezak,[5] a crude yield of 55% was obtained. The purified product melted at 251–253.5°. B. The procedure of Hawkins and Roe[6] when applied to 2-amino-5-methylpyridine produced a crude yield of 40% of the desired compound melting at 250–252°.

Anal. Calcd. for $C_6H_6N_2O_3$: N, 18.2. Found: N, 18.2.

2-Chloro-5-methyl-3-nitropyridine.—The action of 50 ml. of phosphorus oxychloride under reflux for six hours upon 9.5 g. of 5-methyl-3-nitro-2-pyridol followed by treatment with crushed ice resulted in a crude yield of 94% of the desired compound melting at 49–51°. For analysis, a portion

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(2) D. D. Reynolds and W. O. Kenyon, *ibid.*, **72**, 1596 (1950).

(3) E. A. Coulson and J. I. Jones, *J. Soc. Chem. Ind.*, **65**, 169 (1946).

(1) Tennessee Eastman Corporation, Kingsport, Tennessee.

(2) J. Bernstein, B. Stearns, E. Shaw and W. A. Lott, THIS JOURNAL, **69**, 1151 (1947).

(3) L. Panizzi, *Gazz. chim. ital.*, **78**, 207 (1948).

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(6) G. F. Hawkins and A. Roe, *J. Org. Chem.*, **14**, 328 (1949).