[Contribution from the Endocrinology Section, National Cancer Institute, National Institutes of Health]

THE PREPARATION OF SOME SUBSTITUTED GLYCOLS BY ELECTROLYTIC REDUCTION

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In the course of our biological work it was necessary to prepare the glycols of *p*-hydroxyacetophenone, β-acetylpyridine, and *p*-dimethylaminobenzaldehyde. The first glycol had previously been prepared by Tutin, *et al.*, (6) using sodium amalgam as the reducing agent. However, an oil was obtained from which the pinacol was isolated and no yields were reported. The preparation of this compound has now been successfully carried out by the use of electrolytic reduction at controlled cathode potential.

Klingel (4) described the preparation of *p*-hydroxyacetophenone by hydrolysis of the diazonium salt of *p*-aminoacetophenone. Unfortunately the details of the procedure were not given and these had to be developed and are reported here.

As 3,3-*bis*-(*p*-hydroxyphenyl)-2-butanone was needed for other purposes it was prepared from the pinacol by a pinacol-pinacolone type rearrangement using acetic anhydride as the reagent.

The preparation of the pinacol of β-acetylpyridine was also accomplished by electrolytic reduction with resulting satisfactory yields of the pinacol.

Rousset (5) reduced *p*-dimethylaminobenzaldehyde with sodium amalgam and obtained a solid, m.p. 155° which was a mixture of the two isomeric glycols. Clemo and Smith (3) repeated this work under modified conditions and were able to isolate the two forms of the glycol. One form had m.p. 178° and the other form which predominated had m.p. 113°. Their attempts to prepare the glycol by electrolytic reduction resulted in a 5% yield of the high-melting glycol.

By using an aqueous-alcoholic potassium hydroxide solution of the aldehyde and performing the reduction at a constant cathode potential, an over-all yield of 97% of both forms of the glycol was obtained; the ratio was approximately 1:1.5.

EXPERIMENTAL[1]

p.-Hydroxyacetophenone. One hundred fifty grams of *p*-aminoacetophenone was dissolved in 2 l. of water containing 282 ml. of concentrated hydrochloric acid. The mixture was cooled to 0° and a solution of 79 g. of sodium nitrite in 240 ml. of water was slowly added. The temperature was not permitted to rise above 5°. The solution was boiled for one-half hour and then refrigerated overnight. The yellow crystals were purified from water using a small quantity of Norit. Yield 98.9 g. (65.5%), m.p. 106–107° (4).

2,3-Bis-(p-hydroxyphenyl)-2,3-butanediol. The apparatus used for the preparation of this compound by electrolytic reduction was recently described (2). Essentially, this apparatus will give automatically controlled impressed potential to secure constant cathode potential.

The cathode chamber consisted of a 150-ml. beaker, with a mercury cathode at the bottom. An alundum crucible 8 cm. high by 3 cm. in diameter served as an anode chamber. A

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[1] All melting points reported are uncorrected.

smooth sheet of platinum bent to encircle the inner surface of the crucible was the anode. A standard calomel reference electrode was placed against the cathode. A glass-enclosed magnet in conjunction with a magnetic stirrer was used to agitate the solution during reduction.

The catholyte consisted of 6 g. of *p*-hydroxyacetophenone in 50 ml. of 2 *N* sodium hydroxide. The anolyte was a 2 *N* sodium hydroxide solution. At a cathode potential of −2.2 volts, the initial current was 3.5 amperes. The electrolysis was allowed to proceed for twenty minutes at a temperature of 35° under a nitrogen atmosphere. The catholyte was chilled and made acid with dilute hydrochloric acid, the precipitate was washed with water, then lightly with 50% ethanol, ether, and dried; yield 4.6 g. (77%), m.p. 206–207°. Crystallization from ethanol gave colorless prisms, m.p. 209–210° (6).

The *tetraacetate* was prepared by dissolving 0.2 g. of the pinacol in 10 ml. of pyridine containing 1 ml. of acetic anhydride. After standing in the refrigerator for one week the contents were diluted with three volumes of water and allowed to crystallize. The collected crystals were washed with water and dried, m.p. 189–190° (6).

3,3-Bis-(p-hydroxyphenyl)-2-butanone. To a suspension of 2.6 g. of the above pinacol in 30 ml. of acetic anhydride was added a few drops of concentrated sulfuric acid. The mixture was shaken until all the pinacol was in solution and then poured on ice. The semi-solid ketone diacetate was washed a number of times with water by decantation. Fifty milliliters of 20% potassium hydroxide and 50 ml. of ethanol was added to the diacetate and the mixture heated on a steam-bath until all the alcohol had evaporated. The solution was chilled, made slightly acid and refrigerated overnight. The product was recrystallized from water to yield colorless platelets which turned white on drying, yield 1.95 g. (80%), m.p. 128–129° (1).

2,3-Bis-(β-pyridyl)-2,3-butanediol. The catholyte consisted of 6 g. of β-acetylpyridine in 1 ml. of concentrated hydrochloric acid and 49 ml. of distilled water. The anolyte was 0.5 ml. of concentrated hydrochloric acid and 24.5 ml. of water. The reduction was performed at a cathode potential of −1.8 volts against a standard calomel electrode. The initial current was 1.7 amperes for a cathode area of 22.9 cm.^{2}. The reduction was kept at 25°. The reaction was completed in about 50 minutes as indicated by the evolution of hydrogen at the cathode and a plateau of 0.69 amperes. The catholyte was distilled to dryness under reduced pressure at 25°, the residue triturated with a solution of 15 ml. of absolute ethanol and 10 ml. of ethyl acetate, and refrigerated. The filtered crystals were washed with a 50% solution of ethanol in ethyl acetate, yield 5.8 g. (73.4%). The *dihydrochloride* decomposes at about 244°.

The free *base* was prepared in almost quantitative yield by dissolving the dihydrochloride in water and making the solution slightly alkaline. The platelets which formed were recrystallized from water, m.p. 244–245° (dec).

Anal. Calc'd for $C_{14}H_{16}N_2O$: C, 68.83; H, 6.60.
Found C, 68.73; H, 6.81.

4,4-Bis-dimethylaminohydrobenzoin. A solution of 5 g. of *p*-dimethylaminobenzaldehyde, 38 ml. of ethanol, and 10% aqueous potassium hydroxide to make up a total volume of 75 ml. was placed in the cathode chamber. The anolyte consisted of equal parts of ethanol and aqueous potassium hydroxide.

At a cathode potential of −1.9 volts and a temperature of 35° the initial current was 3.3 amperes. Eight minutes after initiation of the reduction crystals appeared and at the end of 21 minutes a current plateau of 0.5 amperes had been reached which indicated completion of the reaction. The crystals were filtered and recrystallized from ethanol to give colorless prisms, yield 1.95 g. (39%), m.p. 178–179°.

The aqueous-alcoholic alkaline mother liquor was diluted with approximately an equal volume of water added portionwise with agitation. The crystals were collected, washed with water, and recrystallized from ethanol-petroleum ether (b.p. 65–85°) (1:9). A yield of 2.9 g. (58%) of colorless needles was obtained, m.p. 112–113°.

SUMMARY

The preparation of 2,3-bis-(*p*-hydroxyphenyl)-2,3-butanediol, 2,3-bis-(β-pyridyl)-2,3-butanediol, and 4,4-bis-dimethylaminohydrobenzoin in satisfactory yields by electrolytic reduction at constant cathode potential is described.

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