413. *Substituted Aromatic Glycols prepared by Electrolytic Reduction.*

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The pinacols from *p*-acetamidobenzaldehyde, *p*-acetamido-ω-dimethylaminopropiophenone, and ω-dimethylaminopropiophenone were prepared by electrolytic reduction at a constant reference potential. Attempted rearrangement of 4 : 4′-bis-*p*-acetamidohydrobenzoin and 3 : 4-bis-*p*-acetamidophenyl-1 : 6-bisdimethylaminohexane-3 : 4-diol to their respective pinacones was unsuccessful. The pinacol 1 : 6-bisdimethylamino-3 : 4-diphenylhexane-3 : 4-diol, on treatment with 80% sulphuric acid, was rearranged to 1 : 6-bisdimethylamino-4 : 4-diphenylhexan-3-one.

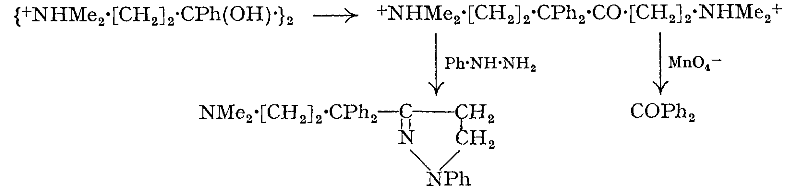
Continuing our work on the preparation of substituted glycols by electrolytic reduction at controlled reference potential (Allen and Corwin, *J. Amer. Chem. Soc.*, 1950, **72**, 114, 117; Allen, *ibid.*, p. 3797; 1951, **73**, 3503; *J. Org. Chem.*, 1950, **15**, 435; *J.*, 1951, 1598; Levine and Allen, *J.*, 1952, 254) we set out to prepare the pinacols of *p*-acetamidobenzaldehyde, *p*-acetamido-ω-dimethylaminopropiophenone, and ω-dimethylaminopropiophenone. We also attempted rearrangements of the pinacols to their respective pinacones.

The pinacol of *p*-acetamidobenzaldehyde was prepared in 79% yield in boiling aqueous-alcoholic potassium acetate, at a constant reference potential of —1·55 v (*versus* a standard calomel electrode with an instrument previously described; Allen, *Analyt. Chem.*, 1950, **22**, 804; *Trans. Electrochem. Soc.*, in the press). Use of aqueous-alcoholic potassium hydroxide as the catholyte medium gave only a 34% yield of the pinacol. An acidic medium was not used for fear that the aldehyde or its hydrobenzoin might be deacetylated at the elevated temperatures used. The yield of pinacol was negligible when the reaction was carried out at room temperature. Treatment of the 4 : 4′-bisacetamidohydrobenzoin with varying concentrations of aqueous hydrochloric acid or sulphuric acid resulted in the formation of unidentifiable tars. This pinacol is not affected by acetic anhydride containing catalytic amounts of sulphuric acid. Since 4 : 4′-bisdimethylaminohydrobenzoin is rearranged to the deoxybenzoin by aqueous hydrochloric acid (Allen, *J. Amer. Chem. Soc.*, 1951, **73**, 1841), it is possible that the acetamidohydrobenzoin is rearranged and that, owing to the nature of the reagents used, the product formed is deacetylated to a very unstable compound.

The Mannich base, *p*-acetamido-ω-dimethylaminopropiophenone hydrochloride whose preparation was unsuccessful in Mannich's laboratories (Mannich and Lammering, *Ber.*, 1922, **55**, 3510), was successfully prepared in excellent yield. The pinacol, 3 : 4-bis-*p*-acetamidophenyl-1 : 6-bisdimethylaminohexane-3 : 4-diol, was prepared by reduction at a reference potential of —1·7 v in 50% acetic acid; the yield of pinacol (37·5%) is satisfactory in view of the instability of the starting ketone. Reductions performed in mineral acid or basic media resulted in a negligible yield of the desired pinacol in addition to a large amount of unidentifiable decomposition products. Treatment of the pinacol with equal volumes of concentrated hydrochloric acid and water merely caused deacetylation. This is probably to be expected as the substituents on the hydroxylated carbon atoms in acidic medium both have electron attraction of about the same order of magnitude, thus holding the hydroxyl group securely in place. Dilute sulphuric acid also caused deacetylation.

The pinacol, 1 : 6-bisdimethylamino-3 : 4-diphenylhexane-3 : 4-diol was prepared by reduction at a reference potential of —0·85 v, in boiling 3N-hydrochloric acid. Lowering the acid concentration did not significantly decrease the amount of pinacol formed. Reduction at 30° gave a lower yield. In N-sulphuric acid as supporting electrolyte a slightly lower yield was obtained than in refluxing hydrochloric acid.

This pinacol was relatively resistant to rearrangement. Refluxing moderately strong acids, such as formic or dilute hydrochloric, had no effect. Partial conversion was effected by 64% sulphuric acid at 100°. Rearrangement proceeded smoothly when the pinacol was heated in 80% sulphuric acid or merely dissolved in the concentrated acid. The crude rearrangement product as free base was an oil which slowly lost dimethylamine and decomposed extensively when distilled. It was characterized as picrate and ditoluene-*p*-sulphonate. Oxidation to benzophenone and formation of a pyrazoline by reaction with phenylhydrazine proved that the compound was 1 : 6-bisdimethylamino-4 : 4-diphenylhexan-3-one. Apparently rearrangement was complete and went exclusively in one direction since no benzoic acid was found on oxidation. The migration of the phenyl group agrees with the observation that the strongest electron-donating group migrates preferentially when symmetrical pinacols are rearranged (Bachman and Sternberger, *J. Amer. Chem. Soc.*, 1934, **56**, 170; Price and Mueller, *ibid.*, 1944, **66**, 634; Allen and Corwin, *loc. cit.*; Allen, *ibid.*, 1951, **73**, 1841).



The crude β-form of the pinacol when treated with 80% sulphuric acid rearranged to give a product identical with that obtained from the α-form.

EXPERIMENTAL

M. p.s were taken on a Kofler hot stage and are corrected.

4 : 4′-*Bis*-p-*acetamidohydrobenzoin*.—The cell used was that previously described (Levine and Allen, *loc. cit.*). A mercury cathode with an area of 23·5 cm.^{2} was used. The anode was of platinum.

The catholyte consisted of a mixture of *p*-acetamidobenzaldehyde (5 g.) in ethanol (30 ml.), and potassium acetate (13·5 g.) in distilled water (11·2 ml.). The anolyte was aqueous potassium carbonate (40%). At a reference potential of $-1{\cdot}55$ v and at the b. p. (81°) the initial current density was 0·178 amp. per cm.^{2}. After 14 minutes the current reached a plateau of 0·002 amp. per cm.^{2}. The catholyte was filtered, diluted with water (200 ml.), and chilled overnight. The precipitate was washed with water and dried *in vacuo*. The *pinacol* (3·95 g.) melted at 258—260°. Recrystallization from 2-ethoxyethanol–ether (1 : 1) gave colourless crystals, m. p. 265—266° (Found: C, 66·1; H, 6·3; N, 8·3. $C_{18}H_{20}O_4N_2$ requires C, 65·8; H, 6·1; N, 8·5%).

Attempts to rearrange this product by mineral acids of various strengths gave unidentifiable tars. On treatment with acetic anhydride and a few drops of concentrated sulphuric acid, the pinacol was quantitatively recovered.

p-*Acetamido*-ω-*dimethylaminopropiophenone Hydrochloride*.—*p*-Acetamidoacetophenone (248 g.), dimethylamine hydrochloride (184·8 g.), paraformaldehyde (42 g.), *n*-propyl alcohol (280 ml.), and concentrated hydrochloric acid (14 drops) were heated under reflux for 30 minutes. An additional amount of paraformaldehyde (10·5 g.) was then added and refluxing continued for another 30 minutes. Acetone (280 ml.) was then added and the whole allowed to cool slowly to room temperature and then chilled overnight. The bright yellow *hydrochloride* was filtered off, washed with alcohol and then acetone, and dried (313 g.). Recrystallization from 83% ethanol gave light yellow crystals (266·7 g.), m. p. 203° (Found: C, 57·7; H, 7·2; N, 9·95. $C_{13}H_{19}O_2N_2Cl$ requires C, 57·7; H, 7·1; N, 10·35%).

3 : 4-*Bis*-p-*acetamidophenyl*-1 : 6-*bisdimethylaminohexane*-3 : 4-*diol*.—The electrolysis cell used in this preparation consisted of a 1500-ml. beaker, with a mercury cathode of 103·8 cm.^{2} area. An alundum crucible, 16·5 cm. high by 5 cm. in diameter, served as the anode chamber in which was placed a sheet of platinum 10 × 10 cm. bent to encircle the inner surface.

The catholyte consisted of *p*-acetamido-ω-dimethylaminopropiophenone hydrochloride (135 g.) in 50% aqueous acetic acid (500 ml.). The anolyte was 50% aqueous acetic acid. At a reference potential of $-1{\cdot}7$ v and 52° the initial current was 0·047 amp. per cm.^{2}. After 360 minutes the current gave a plateau at 0·014 amp./cm.^{2}. The catholyte was distilled at a reduced pressure to a small volume, basified with dilute sodium hydroxide, and chilled overnight. The aqueous fraction was decanted off and the residue washed with water. The residue was then triturated with hot ethanol (75 ml.), chilled, filtered, and washed lightly with cold ethanol and then ether (yield, 32·4 g.; m. p. 285—286°). Recrystallized from ethanol the colourless *diol* had

m. p. 286—287° (Found: C, 66·2; H, 8·0; N, 11·8. $C_{26}H_{38}O_4N_4$ requires C, 66·4; H, 8·1; N, 11·9%).

3 : 4-*Bis*-p-*aminophenyl*-1 : 6-*bisdimethylaminohexane*-3 : 4-*diol*.—The above pinacol (1 g.) was dissolved in concentrated hydrochloric acid (5 ml.) and water (5 ml.), and the whole refluxed for 20 hours. The cooled solution was made basic and extracted a number of times with ether. The ethereal solution was evaporated to a small volume and chilled. The crystals of *amine* (0·65 g.) had m. p. 214·5—215·5° and, on recrystallization from ethanol, m. p. 215—216° (Found: C, 68·3; H, 8·7. $C_{22}H_{34}O_2N_4$ requires C, 68·4; H, 8·9%).

1 : 6-*Bisdimethylamino*-3 : 4-*diphenylhexane*-3 : 4-*diol*.—A solution of ω-dimethylaminopropiophenone (21·3 g.) in concentrated hydrochloric acid (12·5 ml.) and distilled water (27·5 ml.) was placed in the cathode chamber. The anolyte was 3N-hydrochloric acid. A mercury cathode and a platinum anode were employed. The contents were heated to the b. p. (106°) and at a reference potential of −0·85 v the current density was 0·221 amp. per cm.^{2}. After 30 minutes the current had decreased and there was a plateau at 0·055 amp./cm.^{2}. The cooled catholyte was made basic with a slight excess of 30% sodium hydroxide solution and extracted with ether, the ethereal extracts were dried and on evaporation gave a yellow semi-solid oil (8·71 g.). Crystallization from cold ethanol gave the α-form of the pinacol, m. p. 146·9—148·4 (1·25 g.) (Mannich and Heilner, *Ber.*, 1922, **55**, 356, reported m. p. 146°). Evaporation of the mother-liquor followed by recrystallization from acetone (10 ml.)–water (7·5 ml.) gave the colourless β-form, m. p. 86—90° (2·34 g.), contaminated with a small amount of the α-form. Repeated fractional crystallization from ethanol–water gave a small amount of the pure β-form as large trapezoid-faced cubic crystals, m. p. 107·4—108·9° (lit., sinter 100°, melt 107°).

The addition of an alcoholic solution of the α-form to a saturated solution of picric acid gave a picrate as plates, m. p. 253—254° (decomp.). The β-form gave a picrate, m. p. 212—213° (decomp.).

The diacetate of the α-form was prepared by use of boiling acetic anhydride (4 parts). Crystallization of the washed product from dioxan–water gave crystals which melted at 104·5—107·5° with evolution of water, solidified, and remelted at 124—128°. Crystals obtained from methanol showed similar behaviour. Recrystallization from *n*-butyl ether gave colourless rhombic crystals of the *diacetate*, m. p. 137—138° (Found: C, 70·8; H, 8·2; N, 6·4. $C_{26}H_{36}O_4N_2$ requires C, 70·9; H, 8·2; N, 6·4%).

1 : 6-*Bisdimethylamino*-4 : 4-*diphenylhexan*-3-*one*.—A mixture of crude pinacols (32 g.) and 80% sulphuric acid (80 ml.) was stirred until complete solution had occurred, then heated to 100° and kept at that temperature for 15 minutes. The resulting brown solution was diluted with three volumes of water, chilled in an ice-bath, and cautiously basified with an excess of concentrated ammonia solution. The aqueous layer was decanted and extracted with ether, and the ethereal extracts were washed with water and then dried (Na_2SO_4). Evaporation under reduced pressure gave a clear pale yellow oil (29·6 g.). A crystalline picrate, m. p. 177—179°, was prepared by adding an alcoholic solution of the product to saturated alcoholic picric acid.

The *ditoluene*-p-*sulphonate* was prepared by mixing cool alcoholic solutions of the rearrangement product (1·69 g.) and toluene-*p*-sulphonic acid monohydrate (1·9 g.). *iso*Propyl ether was added until the solution became turbid and the whole was refrigerated. The white crystalline material (3·1 g.), m. p. 166·5—168°, recrystallized from cold methanol (25 ml.) by addition of *iso*propyl ether (60 ml.), gave the pure compound, m. p. 167·5—168° (Found: C, 63·5; H, 6·6; N, 4·1. $C_{36}H_{46}O_7N_2S_2$ requires C, 63·3; H, 6·8; N, 4·1%).

Oxidation of 1 : 6-*Bisdimethylamino*-4 : 4-*diphenylhexan*-3-*one*.—A solution of freshly prepared rearrangement product (5 g.) in 2N-hydrochloric acid (50 ml.) was slowly added to a boiling mixture of potassium permanganate (56 g.), sodium hydroxide (3 g.), and water (150 ml.). The mixture was then steam-distilled. The distillate was extracted with ether and the extracts were evaporated, to give an amber-coloured oil (1·33 g.). The oil was purified by boiling alkaline permanganate solution followed by steam-distillation. The almost colourless oil obtained distilled at 307—308° (benzophenone, b. p. 306°) and completely solidified to give a solid, m.p. 47—48° on seeding with a crystal of the stable form of benzophenone. It was finally identified as benzophenone by preparation of the phenylhydrazone and the oxime. Benzoic acid could not be found in the oxidation mother-liquors.

Reaction of Phenylhydrazine with the Foregoing Pinacone.—A mixture of the crude rearrangement product (2·03 g.), phenylhydrazine (1·3 g.), sodium acetate (1 g.), and 50% acetic acid (10 ml.) was heated at reflux for 12 hours, then diluted with water, basified with 30% sodium hydroxide solution, chilled to solidfy the precipitated oil, and filtered. Recrystallization of the crude yellow solid obtained, from ethanol (10 ml.), gave a colourless microcrystalline material

(0·87 g.), m. p. 115—116·5°. By analogy with the work of Jacob and Machinaveita (*J.*, 1937, 1929) the compound is a pyrazoline obtained by cyclization of the phenylhydrazone of the Mannich base ketone. It is probably 3-(3-*dimethylamino*-1 : 1-*diphenylpropyl*)-1-*phenylpyrazoline* (Found : C, 81·6; H, 7·6; N, 10·8. $C_{26}H_{29}N_3$ requires C, 81·4; H, 7·6; N, 11·0%).

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