215. The Preparation of Mixed Pinacols by Cathodic Reduction, and a Study of Some of Their Chemical Reactivities.

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Reductive coupling of 4-methoxyacetophenone with 4-amino- and 4-dimethylamino-acetophenone to yield the mixed pinacols is achieved by electrolysis at a mercury cathode. In dilute acid these pinacols rearrange to the unconjugated pinacones, which on reduction and treatment with acid yield styrenes. The pinacols, when treated with concentrated acid, undergo dehydration and ring closure to give indenes.

The mixed pinacol obtained by reductive coupling of 4-dimethylaminoacetophenone and 4-methoxyacetophenone was earlier[1] isolated by fractional crystallization of the basic fraction from isopropyl ether. Recently we found a more practical separation of the mixed pinacol from its symmetrical associates in chromatography on alumina. As a result we were able to investigate some of the reactivities of pinacols prepared by cathodic reductive coupling of 4-methoxy- with 4-amino- and 4-dimethylamino-acetophenone. The methoxyl content of the basic fractions indicated the amounts of mixed pinacol formed, which could be checked by means of the nitrogen contents, the results (see Table) showing satisfactory agreement. The presence of small amounts of basic products other than pinacols[2] is, however, not excluded, though these would not greatly affect the calculated end values.

As shown in the chart the mixed pinacols (I), on treatment with boiling N-hydrochloric acid, yielded the pinacones (II), whose infrared spectra showed a carbonyl band in the

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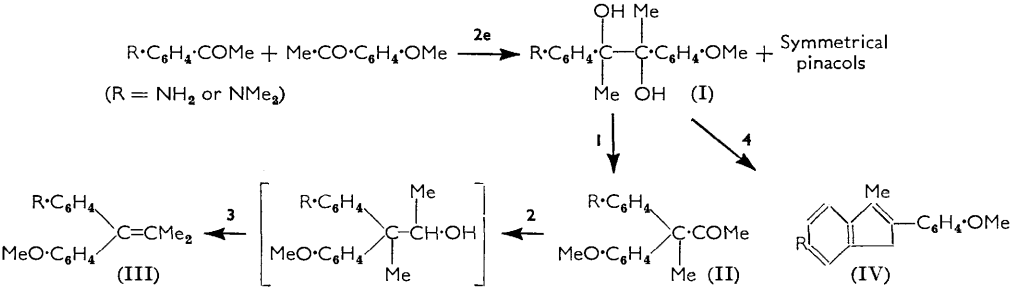
[1] Levine and Allen, *J.*, 1952, 254.

[2] Allen and Corwin, *J. Amer Chem. Soc.*, 1950, **72**, 114.

1700 cm.$^{-1}$ region indicative of an unconjugated ketone. The pinacones were further identified by conversion into their oximes. Reduction of the pinacones with sodium and propyl alcohol followed by reaction with boiling hydrochloric acid gave compounds whose absorption in the region of 255—270 mμ is indicative of a styrene (III) rather than a stilbene (which would have an absorption in the 235—240 mμ region).



Reagents: 1, N-HCl, b. p. 2, Na–PrOH. 3, H$^+$. 4, Conc. HCl, room temp.

The pinacols, upon reaction at room temperature for 70 hr. with concentrated hydrochloric acid, gave the corresponding indenes (IV). By utilizing the mechanism previously described for the formation of indene from pinacol[3] the positions of the methoxy- and amino-substituents are assigned on the basis of the fact that it has been found quite difficult to cause the pinacol of 4-methoxyacetophenone to undergo dehydration,[4] whereas the pinacols of 4-amino- and 4-dimethylamino-acetophenone are readily dehydrated to the corresponding indenes.[5]

EXPERIMENTAL

The electrolysis cells were similar to those previously described for reactions performed at the b. p.[6] A porous membrane separated the mercury cathode from the nickel anode. The Redoxotrol used for the controlled-potential reductions has also been described.[7] The reference potentials at which the electrolyses were performed were obtained from a voltammetric curve under conditions identical with those used preparatively.

Cathodic Reductions.—Equimolar quantities of each ketone were used. The anolyte was 40% aqueous potassium carbonate, and the reactions were performed at the b. p. (82—83°). The results are outlined in the Table.

Catholyte	*p*-MeO·C_6H_4·COMe (71·27 g.) *p*-NH_2·C_6H_4·COMe (63·72 g.) EtOH (590 ml.) H_2O (402 ml.) KOAc (354 g.)	*p*-MeO·C_6H_4·COMe (12 g.) *p*-NMe_2·C_6H_4·COMe (13·04 g.) EtOH (100 ml.) H_2O (68 ml.) KOAc (60 g.)
Reference potential *vs* S.C.E.	−1·8	−1·95 v
Cathode area (cm.^{2})	112·2	52·0
Initial amperage	5·0	6·95
Final amperage	0·7	0·5
Initial applied voltage	5·3	11·0
Final applied voltage	3·0	3·95
Electrolysis time (min.) to current plateau	571	75
Coulombs passed	85,005 (93·2%)	14,452 (93·7%)
Wt. of basic fraction (g.)	62·5	16·25
OMe in basic fraction (%)	5·39	5·82
Mixed pinacol in basic fraction (%)	49·9	59·2
Yield of mixed pinacol (%)	23·09	38·17
N, calc. in basic fraction (%)	6·10	7·58
N, found (%)	6·19	7·62

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[3] Allen and Corwin, *J. Amer. Chem. Soc.*, 1950, **72**, 117.

[4] Price and Mueller, *J. Amer. Chem. Soc.*, 1944, **66**, 634.

[5] Allen and Corwin, *J. Amer. Chem. Soc.*, 1950, **72**, 117; Allen, *J.*, 1951, 1598.

[6] Allen and Cohen, *J. Amer. Electrochem. Soc.*, 1959, **106**, 451.

[7] Allen, *Canad. J. Chem.*, 1959, **37**, 257.

Isolation of Pinacols.—(a) 2-p-*Aminophenyl*-3-p-*methoxyphenylbutane*-2,3-*diol* (I; R = NH_2). The catholyte obtained from the electrolysis was evaporated to an oil under reduced pressure. This was washed with water, dissolved in methylene chloride (1500 ml.), and extracted with N-hydrochloric acid (3 × 480 ml.). The symmetrical pinacol of 4-methoxyacetophenone remained in the methylene chloride. The acid extracts were combined, made basic, and extracted with methylene chloride (3 × 300 ml.). The combined extracts, when kept, yielded a crystalline precipitate, as 2,3-di-(*p*-aminophenyl)butane-2,3-diol,[2] m. p. 247—248°. The methylene chloride filtrate was dried (Na_2SO_4) and evaporated to a viscous amber oil (62·5 g.). This was chromatographed in benzene (3 l.) on neutral alumina (Woelm; activity No. 3; 3 kg.). The column was eluted with benzene (2 × 3 l.) and then with 3 : 1 benzene–ether (11 × 3 l.) The benzene–ether fractions gave oily solids (28·07 g.) which on repeated extraction with hot cyclohexane and decolorization with norite gave pale yellow crystals (13·4 g.) of 2-p-*aminophenyl*-3-p-*methoxyphenylbutane*-2,3-*diol*, m. p. 137—138° (Found: C, 70·95; H, 7·2. $C_{17}H_{21}O_3N$ requires C, 71·1; H, 7·4%).

Additional quantities of this mixed pinacol could be obtained from the cyclohexane filtrate by evaporation and distillation of the residue. The fraction distilling at 160—190°/0·01 mm. was collected and crystallized from cyclohexane. In this manner it was possible to obtain 2·01 g. of mixed pinacol, m. p. 137—138°, from 7·35 g. of residue.

(b) 2-p-*Dimethylaminophenyl*-3-p-*methoxyphenylbutane*-2,3-*diol* (I; R = NMe_2). The catholyte, treated as described above, gave a neutral fraction containing the pinacol of 4-methoxyacetophenone and a basic fraction (16·25 g.). The basic fraction was dissolved in ether (50 ml.) and left at room temperature for 2 days, during which a white precipitate formed and was collected. This was identified as the pinacol,[8] m. p. 163—164°, of 4-dimethylaminoacetophenone. The filtrate was evaporated and the residue (13·55 g.) dissolved in 1 : 1 pentane–benzene and chromatographed as described above. The column was eluted with 1 : 1 pentane–benzene (11 × 500 ml.), benzene (15 × 500 ml.), and finally 3 : 1 benzene–ether (6 × 500 ml.). The residue (8·07 g.) obtained from the benzene elutions was a mixture of the mixed pinacol and the pinacol of 4-dimethylaminoacetophenone. The latter compound, since it was insoluble in ether, could be separated by trituration of the residue with ether and filtration. The filtrate was then evaporated and the residue (3·69 g.) combined with that (3·70 g.) obtained from evaporation of the 3 : 1 benzene–ether eluate. Recrystallization from ether–pentane gave white needles (5·3 g.), m. p. 124—125°, identified as 2-*p*-dimethylaminophenyl-3-*p*-methoxphenylbutane 2,3-diol.[1]

3-p-*Aminophenyl*-3-p-*methoxyphenylbutan*-2-*one* (II; R = NH_2).—A solution of 2-*p*-aminophenyl-3-methoxyphenyl-2,3-butanediol (4·0 g.) in N-hydrochloric acid (120 ml.) was refluxed for 5½ hr., chilled, and then made basic with aqueous potassium hydroxide. This was extracted with methylene chloride (3 × 75 ml.), and the extracts were dried (Na_2SO_4), filtered, and evaporated. The residue was distilled and the fraction distilling at 140—170°/0·01 mm. collected (2·92 g.) (Found: C, 76·65; H, 7·0; N, 5·3. $C_{17}H_{19}O_2N$ requires C, 75·8; H, 7·1; N, 5·2%). The infrared spectrum of this *ketone* shows a carbonyl band at 1706 $cm.^{-1}$. Attempts to crystallize it failed.

Refluxing the ketone (0·4 g.) with hydroxylamine hydrochloride (0·4 g.) and potassium hydroxide (2·0 g.) in 95% ethanol (20 ml.) for 2 hr. gave the *oxime* (0·4 g.), m. p. 156—157° (from 60% ethanol) (Found: C, 72·1; H, 7·3; N, 9·8. $C_{17}H_{20}O_2N_2$ requires C, 71·8; H, 7·1; N, 9·85%).

p-(1-p-*Methoxyphenyl*-2-*methylpropenyl*)*aniline* (III; R = NH_2).—To the ketone described above (2·92 g.) in boiling anhydrous n-propyl alcohol (60 ml.) sodium (3·6 g.) was added portionwise during 1 hr., and the solution then refluxed for an additional 1½ hr. Water (100 ml.) was added and most of the alcohol removed by distillation. The oily layer which was formed was extracted with ether (3 × 30 ml.), the ether extracts were dried (Na_2SO_4) and evaporated, and the residue (2·35 g.) was refluxed with concentrated hydrochloric acid (25 ml.) and water (25 ml.) for 3 hr. Immediately upon onset of reflux a precipitate began to be formed. The chilled solution was filtered, and the white solid collected [2·01 g.; m. p. 223—232° (decomp.)]. Recrystallization from water gave the *hydrochloride*, m. p. 234—238° (decomp.) (Found: C, 70·3; 7·2; N, 4·9; Cl, 12·6. $C_{17}H_{20}ONCl$ requires C, 70·45; H, 7·0; N, 4·8; Cl, 12·2%). The derived free *base* had m. p. 84—85° (Found: C, 80·7; H, 7·5; N, 5·6. $C_{17}H_{19}ON$ requires C, 80·6; H, 7·6; N, 5·6%); $\lambda_{max.}$ 256 mμ.

[8] Allen, *J.*, 1951, 1598.

6-*Amino*-2-p-*methoxyphenyl*-3-*methylindene* (IV; R = NH_2).—The pinacol (I; R = NH_2) (1·0 g.) was dissolved in concentrated hydrochloric acid (40 ml.). The solution rapidly became bright yellow and semisolid material was precipitated. After 70 hr. at room temperature the mixture was chilled and kept at $<10°$ while aqueous potassium hydroxide was added until a pH of 9—10 had been achieved. Extraction with methylene chloride yielded an amber residue (0·97 g.). This was distilled and the fraction of b. p. 153—165°/0·001 mm. collected (0·52 g.). Trituration with ether followed by recrystallization from ether gave the *indene* (0·51 g.), m. p. 136° (Found: C, 81·0; H, 6·9; N, 5·6. $C_{17}H_{17}ON$ requires C, 81·2; H, 6·8; N, 5·6%), $\nu_{max.}$ 820 (s) and 850 (w) cm.$^{-1}$ (1,2,4-trisubstituted benzene).

3-p-*Dimethylaminophenyl*-3-*methoxyphenylbutan*-2-*one*.—The crossed pinacol (2·0 g.) of 4-dimethylamino- and 4-methoxy-acetophenones was refluxed in N-hydrochloric acid for 5 hr. Working up as above gave a crude ketone (1·97 g.), b. p. 148—160°/0·001 mm. (1·80 g.), $\nu_{max.}$ 1705 cm.$^{-1}$ (C=O). This free base discoloured rather rapidly and attempts to prepare the usual salts failed. The *oxime*, obtained as above, had m. p. 177—178° after recrystallization (from 60% ethanol) (Found: C, 72·8; H, 8·9. $C_{19}H_{24}O_2N_2$ requires C, 73·1; H, 7·7; N, 9·0%).

p-(1-p-*Methoxyphenyl*-2-*methylpropenyl*)-NN-*dimethylaniline*.—The freshly distilled crude ketone (0·94 g.) was heated in n-propyl alcohol while sodium (1·04 g.) was added during 1 hr. After refluxing for an additional 1½ hr. the mixture was treated as previously described. The crude alcohol (0·90 g.) was refluxed for 3 hr. in concentrated hydrochloric acid (15 ml.) and water (15 ml.). From this was obtained an oil (0·797 g.) which, when dissolved in a minimum amount of hot ethanol and chilled overnight, gave crystals (0·24 g.) of the *ethylene*, m. p. 93—94° (Found: C, 80·9; H, 8·4; N, 5·15. $C_{19}H_{23}ON$ requires C, 81·1; H, 8·2; N, 5·0%), $\lambda_{max.}$ 268—270 mμ. Chromatography of the mother-liquor on neutral alumina (activity No. 1) yielded an additional 0·12 g. of the compound.

6-*Dimethylamino*-2-p-*methoxyphenyl*-3-*methylindene*.—The pinacol (I; R = NMe_2) (1·0 g.) was dissolved in concentrated hydrochloric acid and left at room temperature for 70 hr. From this was obtained, as described previously, an amber oil (0·908 g.). Distillation and crystallization from anhydrous ethanol gave the *indene* (0·32 g.), m. p. 136—137° (Found: C, 81·5; H, 7·6; N, 5·1. $C_{17}H_{21}ON$ requires C, 81·7; H, 7·6; N, 5·0%).

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[*Received, September 17th*, 1959.]