two methyl substituents in the position ortho to the carboxyl group.

TABLE V

EFFECT OF METHYL SUBSTITUENTS ON THE RATE OF ESTERIFICATION OF BENZOIC ACID IN METHANOL

Acid	$k_{25} \times 10_5$, liters moles^{-1} sec.$^{-1}$	E, cal. mole^{-1}
Benzoic	21.7	14,600
Benzoic[a]	19.2	15,500
p-Toluic[a]	19.7	13,800
m-Toluic[a]	21.7	14,200
3,5-Dimethylbenzoic	21.0	14,900
3,4-Dimethylbenzoic	17.4	15,000
o-Toluic[a]	6.41	14,400
2,4-Dimethylbenzoic	5.87	15,500
2,5-Dimethylbenzoic	5.69	15,400
2,6-Dimethylbenzoic	No reaction	....

[a] Data of Hartman and Borders, ref. 2.

It is quite obvious that the acids fall into three groups, depending on the number of substituents in the ortho position, and that the rate of reaction is decreased with increasing number of such substituents. The results for benzoic acid reported here give an activation energy for the esterification of benzoic acid which is 900 calories lower than that reported by Hartman and Borders. With this revision, there seems to be little evidence for lowering of the activation energy by methyl substituents. On the contrary, there seems to be a slight increase when a methyl group is substituted in the ortho position. One would estimate that the activation energy for the 2,6-substituted acid is much greater than any value recorded in Table V.

It seems probable that the retarding influence of the 2-methyl groups is primarily steric in nature, and is much the same as that of β-methyl substituents in aliphatic acids.

Summary

The kinetics of the acid-catalyzed esterification in methanol of benzoic acid and of the dimethyl-substituted benzoic acids have been studied. Velocity constants and activation energies for these reactions have been compared with similar values for the toluic acids. It has been shown that the relative rates of esterification are influenced by substitution in the ortho, but not in the meta and para position.

KNOXVILLE, TENNESSEE RECEIVED OCTOBER 10, 1949

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE JOHNS HOPKINS UNIVERSITY]

The Electrolytic Reduction of *p*-Aminoacetophenone[1]

BY MILTON J. ALLEN[2a,b] AND ALSOPH H. CORWIN*

Numerous studies have been undertaken in the past to determine the effects of electrolytic reduction on ketones. Usually the reduction proceeds to a pinacol, an alcohol, a hydrocarbon or a mixture of both pinacol and alcohol. Of these reactions, the formation of a hydrocarbon is not usually a continuation of the secondary alcohol formation, as secondary alcohols are not easily reduced by electrolytic methods.[3] There is no doubt that the reaction which takes place depends upon the electrode material and the type of electrolyte used. Elbs and Brand[4] found that in alkaline solution, using a lead cathode, the aliphatic and aromatic ketones are reduced to the corresponding secondary alcohol, whereas in acid solution, a mixture of pinacol and alcohol is obtained.

Escherich and Moest[5] found that Michler ketone yields the pinacol with a copper cathode, while both pinacol and alcohol are formed in almost equal amounts at a nickel cathode.

The prime purpose of this investigation was to study the change in products resulting from a change in experimental conditions, using a single type of cathode material, in an attempt to find the conditions which would give a maximum yield of 2,3-bis-(*p*-aminophenyl)-2,3-butanediol.

Experimental

The apparatus used in this work was similar to that described by Lingane,[6] with the exception that cathode potentials as high as six volts and currents as high as 20 amperes were provided for. Essentially, this apparatus will give automatically controlled impressed voltage to secure constant cathode potential. Two cells were developed for both small (25–50-ml.) and larger (400–800-ml.) quantities of material (Fig. 1a and 1b).

In the experiments to be discussed, the *p*-aminoacetophenone was dissolved in the desired solution and placed in the cathode chamber. A blank solution which excluded the ketone was placed in the anode compartment. The two compartments were separated by a cellophane membrane.[7] Table I gives some experimental results using a carbon anode and a mercury cathode.[8] A smooth platinum anode and a mercury cathode were used in the experiments listed in Table II. Most of the experiments were performed with diluted hydrochloric acid as the electrolyte, as the pinacol dihydrochloride was the desired product.

The alcohol was isolated from the mother liquor after filtering off the pinacol. The solvent was removed, the

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* Harvard University Ph.D. 1932.

[1] This investigation was supported, in part, by a research grant awarded M. J. A., by the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service.

[2] (a) Research Fellow, National Cancer Institute, 1947-1949; (b) from the Ph.D. dissertation of Milton J. Allen, The Johns Hopkins University, June, 1949.

[3] Tafel, *Z. Elektrochem.*, **17**, 972 (1911).

[4] Elbs and Brand, *ibid.*, **8**, 783 (1902).

[5] Escherich and Moest, *ibid.*, **8**, 849 (1902).

[6] Lingane, *Ind. Eng. Chem., Anal. Ed.*, **17**, 332 (1945).

[7] Purchased from the Visking Corp., Chicago, Ill.

[8] Mercury was found more desirable as higher overvoltages were obtainable, and also because mercury is readily purified.

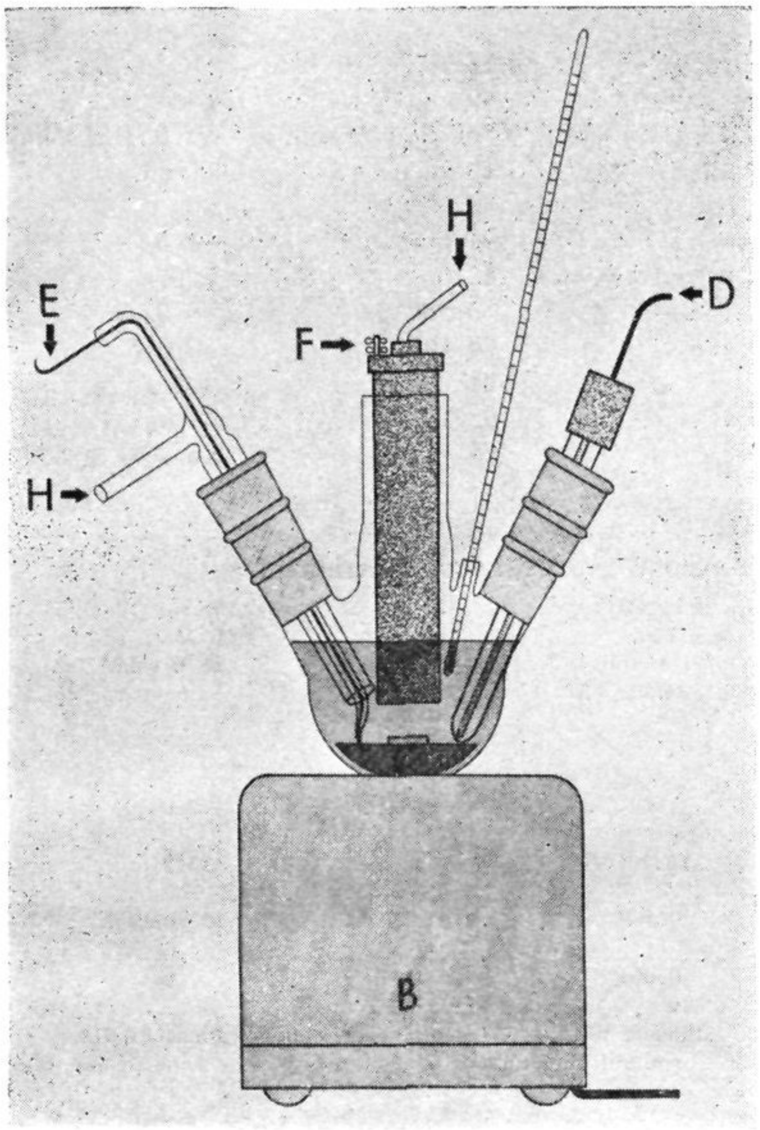

Fig. 1a.—Micro-cell: A. paddle type stirrer; B. magnetic stirrer; C. mercury cathode; D. electrode to controlling galvanometer; E. cathode contacts; F. anode contacts; G. carbon anode; H. nitrogen inlets (outlets not shown); I. cooling coil (temperature of small unit controlled with a cooling bath).

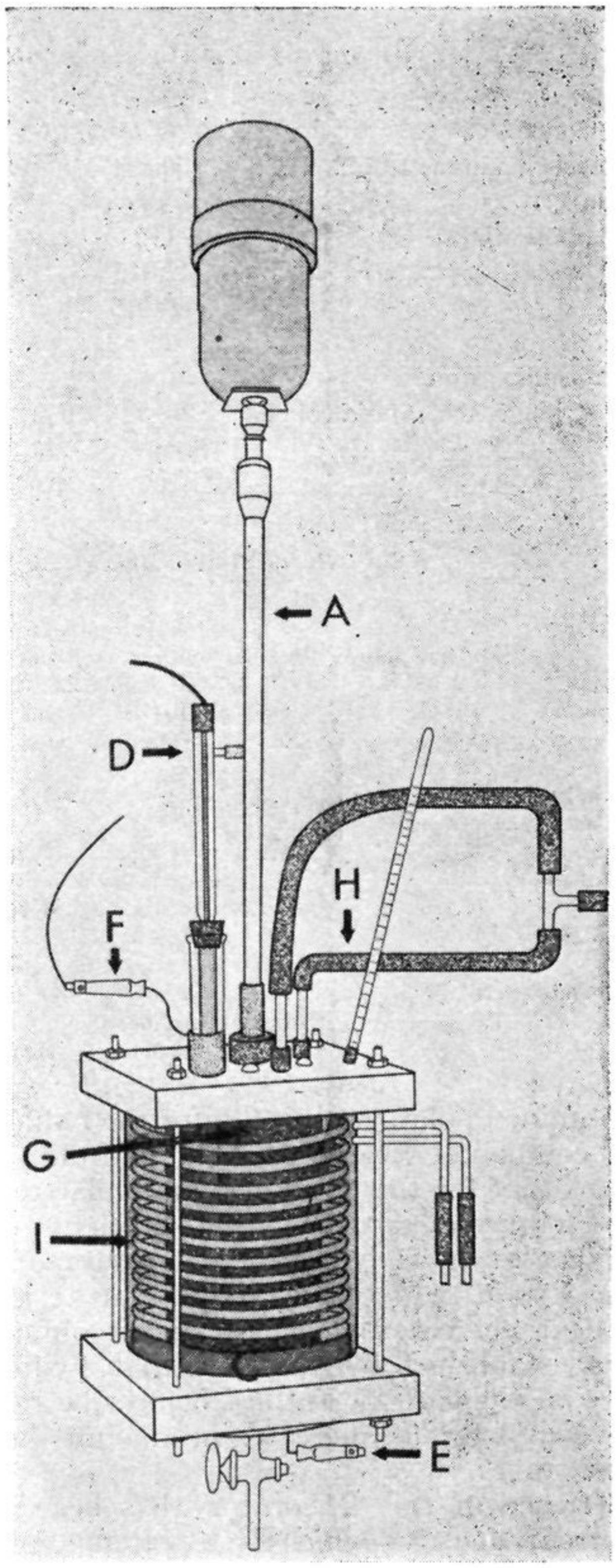

Fig. 1b.—Macro-cell

residue diluted with water, made slightly alkaline and extracted a number of times with ether. The ether extracts were combined and dried over anhydrous sodium sulfate. The ether was evaporated and the residue distilled at 18 mm. pressure. The fraction coming over at 185–192° was collected. The solid mass was recrystallized from water; m. p. 92–93°. This corresponds to the reported[9] value of 94° for the hydrol of *p*-aminoacetophenone.

A typical experiment in which 2,3-bis-(*p*-aminophenyl)-2,3-butanediol was obtained is as follows: Eighty-one grams of *p*-aminoacetophenone was dissolved in 600 ml. of distilled water containing 81 ml. of concentrated hydrochloric acid and placed in the cathode chamber of the large cell. In the anode chamber was placed 100 ml. of 13.5% by volume concentrated hydrochloric acid. At a cathode potential of −1.5 volts, the initial current was 3.2 amperes. According to the calculations for a one electron change per molecule of ketone, the reduction should take five hours assuming theoretical current efficiency. During the reduction, the temperature was kept between 25–30°. After five hours, the current dropped and gaseous hydrogen appeared in the catholyte, indicating the completion of the reaction. The solution was evaporated to dryness under reduced pressure at a temperature not higher than 25°. The residue was triturated with absolute ethanol on the steam-bath until a uniform suspension was obtained. Approximately an equal volume of ethyl acetate was then added and the mixture chilled overnight. Upon filtration and washing with a 1:1 ethyl acetate–absolute ethanol solution, a light yellow crystalline product was obtained in 62.6% yield. The 2,3-bis-(*p*-aminophenylmethyl)-2,3-butanediol dihydrochloride began to decompose at about 230°.

The free base was prepared and upon recrystallization from acetone or ethyl cellosolve, platelets were obtainable; m. p. 248–249° (dec.).

Anal. Calcd. for $C_{16}H_{20}N_2O_2$: C, 70.54; H, 7.4; N, 10.28. Found: C, 70.36; H, 7.4; N, 10.14.

Discussion

In Table I, the results of Experiments 48, 49 and 50 show that as the cathode potential is increased, within certain limits, the yield of pinacol increases at the expense of alcohol formation.

The cathode potential of approximately −1.1

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[9] Rousset, *Bull. soc. chim.*, [3] **11**, 321 (1894).

TABLE I

REDUCTIONS PERFORMED WITH A CARBON ANODE AND A MERCURY CATHODE

Expt. no.	48	50	49	64
Ketone concn., g.	6.75 (1 *M* soln.)	6.75 (1 *M* soln.)	6.75 (1 *M* soln.)	81.0 (1 *M* soln.)
Electrolysis medium, 1.67 *M* HCl	50 ml.	50 ml.	50 ml.	600 ml.
Av. temp., °C.	30	30	30	30
Cathode potential	−1.2	−1.4	−1.5	−1.5
Cathode area, sq. cm.	12.6	12.6	12.6	129
Initial c. d./sq. cm.	0.127	0.238	0.262	0.024
Final c. d./sq. cm.	0.083	0.158	0.194	0.017
Reduction time, min.	51	27	24	302
Products, pinacol, % and alcohol	26.3	46.4	62.1	62.6
	Some	Some	No	No

TABLE II

REDUCTIONS PERFORMED WITH A PLATINUM ANODE AND A MERCURY CATHODE

Expt.	93	94	95	96	97	98
Ketone concn., g.	3 (0.41 *M* soln.)	3 (0.41 *M* soln.)	6.75 (1 *M* soln.)	6.75 (1 *M* soln.)	6.75 (1 *M* soln.)	6.75 (1 *M* soln.)
Electrolysis medium, ml.	53, 2.98 *M* H_2SO_4	23.6, 6.73 *M* H_2SO_4 29.5 ml. EtOH	25, 3.34 *M* HCl, 25 ml. EtOH	Same as 95	Same as 95	Same as 95
Av. temp., °C.	25	25	60	27	45	30
Cathode potential, v.	−1.5	−1.5	−1.5	−1.5	−2.6	−2.6
Cathode area sq. cm.	15.2	15.2	15.2	15.2	15.2	15.2
Initial c. d./sq. cm.	0.270	0.158	0.164	0.138	0.270	0.202
Final c. d./sq. cm.	0.164	0.092	0.063	0.064	0.197	0.131
Red. time, min.	10	17	36	40	25	38
Products	Tar	No pinacol, some alcohol, much tar	No pinacol, some alcohol, much tar	Pinacol 36.1%, some alcohol, tars	No pinacol, some alcohol, tars	Pinacol 0.01%, some alcohol, tars

volts obtained polarographically for the reduction of this compound yielded only the hydrol. This indicates that for this type of bimolecular reduction polarographic data are not a sufficient guide. This is due to the fact that the potential required for the desired reduction is above that at which theoretical current efficiency can be obtained. This is established by the fact that hydrogen appears on the cathode surface before the reduction is complete and increases in amount during the last stages.

Experience in this Laboratory has been that the current density, which is so often a major experimental point in literature, is of little significance in reproducing this synthesis unless all other conditions are also reproduced. Many other experimenters also mention the applied voltage, but this is also unsatisfactory as it cannot be used as a focal point for reproduction, the voltage varying with the volume of solution and cathode area. The important factor, as certain other investigators have concluded,[10] is the cathode potential which will give the necessary conditions for obtaining desirable results over a large range of volumes of solutions and cathode areas. This interesting fact is shown by experiments 49 and 64 in which the cathode potential is kept constant. The total current delivered to the smaller area is approximately the same as that to the larger area and upon calculation, the current density of the smaller area is found to be about ten times as great as that of the larger area. This would indicate that within the limits of these experiments the total initial current delivered to the cell is independent of the mercury cathode area.

It is obvious from the nature of the end-product that a prolonged period at an elevated temperature is not desirable because of the possibility of a pinacol–pinacolone type rearrangement. It has also been found that a one molar concentration of the ketone gives the maximum yield of pinacol. If less than one molar concentration is used, the yield of alcohol increases and the yield of pinacol decreases. When the ketone concentration is 1.4 molar the yield of pinacol is approximately 30% with the remainder consisting of unidentifiable tars.

The concentration of hydrochloric acid was also found to influence the reduction results. It was found that a 1.67 *M* hydrochloric acid concentration resulted in the highest yield of pinacol. A lower acidity resulted in the formation of larger quantities of alcohol and lower quantities of pinacol. However, it must be remembered that one of the functions of the acid is to serve as an electrolyte, and there is the possibility that increased cathode potentials might have resulted in better yields of pinacol. A higher acid concentration resulted in the formation of tars with lower yields of pinacol.

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(10) Lingane, Gardner and Fields, THIS JOURNAL, **65**, 1348 (1943).

Table II gives a few typical experiments performed with a mercury cathode and a smooth platinum anode, of approximately the same area as the carbon anode used in the previous experiments. Apparently as shown by experiment 93, aqueous sulfuric acid in this concentration is not a desirable electrolyte for this reduction. However, there is a possibility that other cathode potentials and other sulfuric acid concentrations may yield the pinacol. An aqueous alcohol acid solution will, by some mechanism, yield larger quantities of *p*-aminoacetophenone hydrol than an aqueous acid solution. Another observation is that, under conditions of experiments 95 and 96, 97 and 98, relatively higher temperatures favor hydrol, rather than pinacol formation. Also from 97 and 98, it can be seen that -2.6 volts cathode potential is too high for the satisfactory formation of pinacol.

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Summary

An electrolytic reduction method has been developed for the preparation of 2,3-bis-(*p*-aminophenyl)-2,3-butanediol which gives satisfactory yields. It has been shown that the formation of this pinacol is dependent on the cathode potential, temperature, concentration of ketone and acid, and is somewhat independent of the current density and applied voltage. Therefore, more stress should be placed on cathode potential than on current density or applied voltages which are not constants in the electrolytic reduction process.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE JOHNS HOPKINS UNIVERSITY]

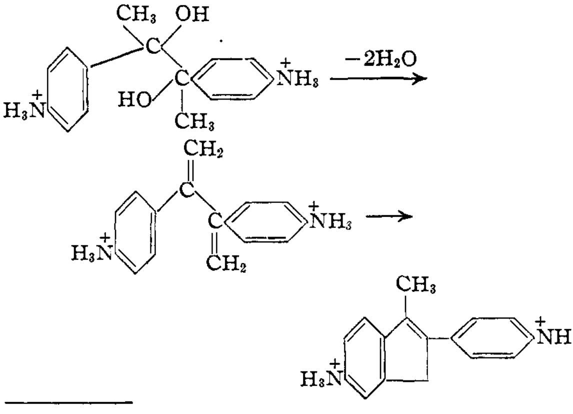
Chemical Studies on Pinacols Obtained from *p*-Aminoacetophenone and *p*-Aminopropiophenone[1]

BY MILTON J. ALLEN[2] AND ALSOPH H. CORWIN*

This study was undertaken primarily to develop a method for the synthesis of α,β-dialkyl-4,4′-stilbenediamines. A method has been reported[3] for the preparation of α,β-diethyl-4,4′-stilbenediamine by the conversion of α,β-diethyl-4,4′dibromostilbene to the desired diamine. However, the preparation of the intermediates appeared laborious, and, therefore, a simpler method was developed. Previous work has shown[4] that α,β-diethyl-4,4′-stilbenediol could be prepared by use of the pinacol–pinacolone and retro-pinacol rearrangements. This general scheme was followed with some very interesting side reactions.

The rearrangement of 2,3-bis-(*p*-aminophenyl)-2,3-butanediol dihydrochloride (I), which was accomplished by refluxing the compound with a 1:2 ratio by volume of concentrated hydrochloric acid to water, yielded two products, a ketone (III) and a compound which had a molecular formula of $C_{16}H_{18}N_2Cl_2$ (II). The last compound was presumed to be either a butadiene or an indene. If the compound possessed a butadiene structure and reduction with sodium and alcohol proceeded predominantly one-four, the resulting compound would be a substituted stilbene. This compound in turn would be readily reduced to the saturated compound under the conditions of the experiment because of the presence of a conjugated system. Therefore, the first possibility was eliminated, for as a result of reduction, a compound $C_{16}H_{18}N_2$ (IIA) was obtained.

A butadiene type structure may be intermediate in the formation of the indene. Recently Hausmann and Smith[5] demonstrated that treatment of dienestrol with 1N mineral acids gave 1-methyl-2-(*p*-hydroxyphenyl)-3-ethyl-6-hydroxyindene. On the basis of this experimental evidence we may propose the following mechanism for the formation of the aminoindene.



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* Harvard University Ph.D. 1932.

[1] This investigation was supported (in part) by a research grant awarded to M. J. A., by the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service.

[2] (a) Research Fellow, National Cancer Institute 1947–1949; (b) from the Ph.D. dissertation of Milton J. Allen, The Johns Hopkins University, June, 1949.

[3] Vargha and Kovacs, *Ber.*, **75**, 794 (1942).

[4] Wessely, *et al.*, *Monatsh.*, **73**, 127 (1940).

[5] Hausmann and Smith, *Nature*, **161**, 892 (1948).