Some Observations on the Reaction Route of the Clemmensen Reduction in Fluorenone Derivatives

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The reduction of fluorenone (I) has been found in a few examples for the preparation of fluorenes in the presence of dilute alcohol or hydrocarbons[1].

But I has been best reduced to fluorene (II) by the Wolff-Kischner method with or without an alkaline catalyst, as has been observed by Weisburgers and Grantham[2], except fluorenone-1-carboxylic acid. This acid is unsatisfactory because of the formation of phthalazine derivatives[3].

In connection with this studies on the reaction of II and 2-bromofluorene (IV) from their corresponding fluorenones by the modification of the Clemmensen-Martin reduction we had occasion to investigate the substitution effect in 2-bromofluorenone (III).

A great part of I does not normally proceed by way of fluorenol (V) in the Clemmensen reduction and also many related products were obtained by an abnormal reaction. Moreover, some of them do not appear to have been previously reported as direct products from I in this reduction.

The present authors carried out the reduction by the procedure of 'Organic Reactions'[4]: I was dissolved in solvents such as toluene, benzene and xylene, which were mixed with the aqueous hydrochloric acid. The mixture was heated under reflux for a period of twenty-four hours, concentrated hydrochloric acid being added at intervals of about six hours.

In this study, V, II and dimeric reaction products, namely, 9,9'-dihydroxy-9,9'-bifluorenyl (fluorenopinacol) (VI), 10,10-diphenylene-9-phenanthrone (VII), 10,10-diphenylene-9,10-dihydro-9-phenanthrol (VIII), 9,10-diphenylenephenanthrene or tetrabenzonaphthalene (IX), 9-hydroxy-9,9'-bifluorenyl (X), 9,9'-bifluorenyl (XI) and mixed crystals of dibiphenylene-ethylene (XII) and IX were isolated by means of a combination of recrystallization and column chromatography.

I was converted to II and the other intermediates, V, VI, VII, VIII, X and XII, after a short reduction time (2 hr.) in toluene. Furthermore, XII, X and XI were increased, but VI was decreased and VI remained almost constant when the reaction was continued for twenty-four hours (red colored toluene). Three kinds of end-products, IX (10%), XI (55.6%) and (II, 8.7%) were obtained by extending the refluxing periods for seventy-two hours (almost colorless). IX and XI were then obtained in approximately a ratio of 1 : 5.6.

It may, therefore, be assumed that VII and X were also formed from VI through the positively charged ion VI' by the action of the acidic medium in the Clemmensen reduction.

From these results, the mechanism of the formation of IX via VIII from VII by the retropinacolone rearrangement involves the intramolecular transfer of the electron pair by formation of a carbonium ion. Thus, the reaction sequences can be written as in Chart 1.

On the other hand, there is only one reference in the literature to the Clemmensen-
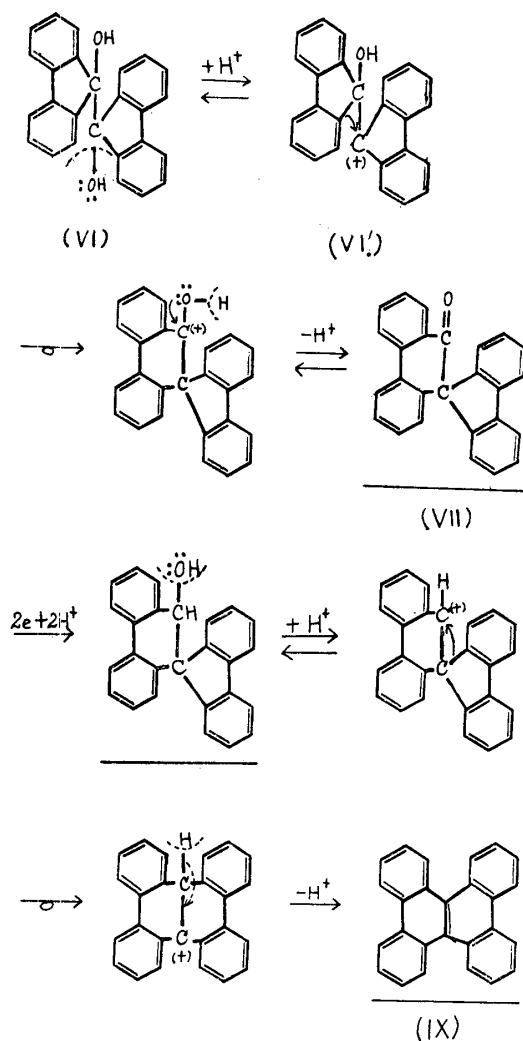
(Underscored compounds were isolated)

Chart 1.

Martin reduction of III, that by Miller and Bachman[5], who reported a nearly quantitative yield of IV. However, the present study deals with the effect on this reduction of an electoron-attracting group such as bromine at the 2-position of I. This is of interest because the substituent influences may be transmitted to the carbonyl at the 9-position, both directly through the substituted ring and indirectly through the unsubstituted ring. III was submitted to same procedure as was I. From this reduction, II, 2-bromofluorenol (XIII) and several dimeric reaction products, namely 2, 2'-dibromo-9,9-dihydroxy-9,9'-bifluorenyl(XIV), 2,2'-dibromodibiphenylene-ehtylene(XV)[6],-ethane (XVI)[6] and a trace of spiro-(2-bromofluorene-9,9'-(10')-2'-bromophenanthrone) (XVII) were isolated by means of a combination of recrystallization and column chromatograpy. But the reduction of III is very slow; only 11% of it was recovered after 72 hr. And XIII was isolated after just a 24 hr.-period, while V has the short reduction period of 2 hr. of I.

2,2'-dibromophenanthreno-9',10' : 9,10-phenanthrene (XVIII) was, however, not isolated from this series, in contrast to the comparable reduction of I. The formation of XVIII is controlled by the formation of XVII from XIV. Actually, XVII was obtained only in trace amounts by this reduction, as is described in the experimental section.

First, the results can mean that the oxygen atom of the hydroxyl group attached to the carbon, C^1, is positively charged by the electron-attracting bromine in XIV. For this reason, the hydoxyl group is relatively more hindered for the elimination than it is in fluorenopinacol owing to the electron-repelling effect on the protonation. Under these conditions, carbonium ion formation is unlikely.

A second possible explanation is that, due to being stabilized by the formation of the transition carbonium ion, XIVa, by resonance, the hydroxyl group is dehydrated from the carbon, C^1 in XIV. However, state XIVa must cross a high energy barrier to reach stable state XVII. It seems that formation of III and XV from XIVa occurs preferentially to that of XVII. This fact is essential differnce from the case of VI. These sequences can be visualized, as Chart 2.
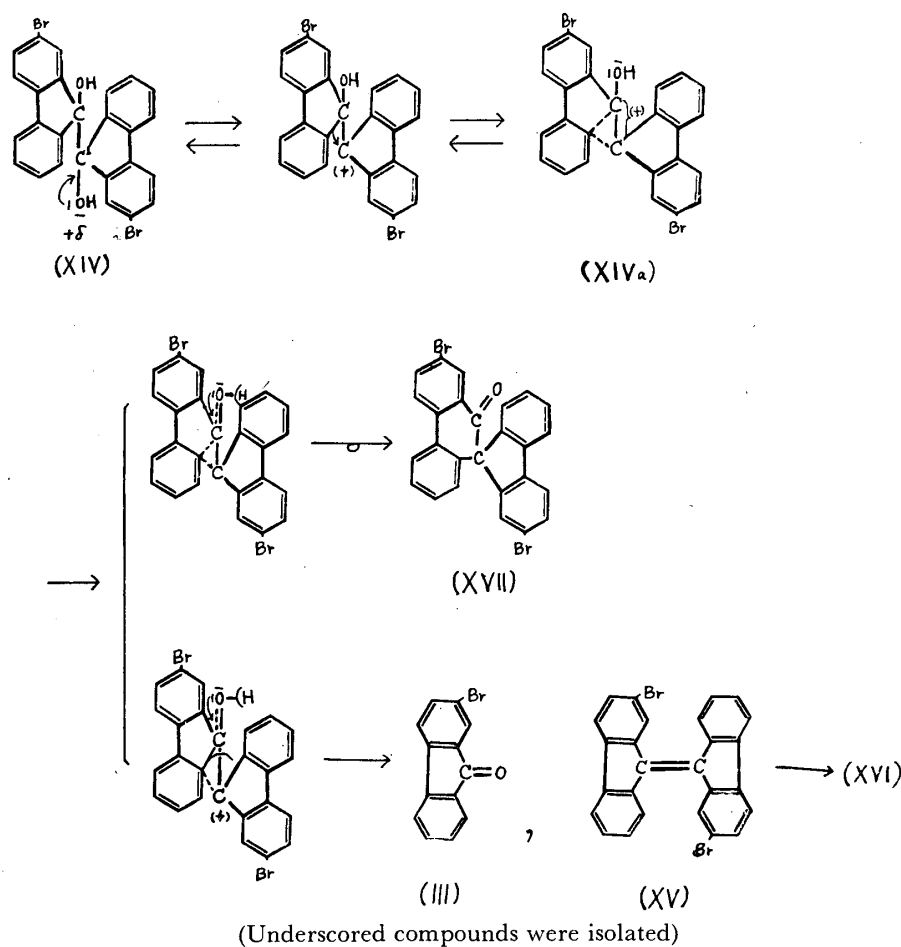

(Underscored compounds were isolated)

Chart 2.

And, this is indicated in view of the following experimental evidence.

Traces of XVII, XV and XVI were also obtained by the Clemmensen reduction of III. III, XV and XVI were isolated from XIV by the same reduction procedure.

Therefore, XIV was treated with hydrochloric acid in toluene under the same conditions but without amalgamated zinc; a small amount of III and XV was isolated.

Subsequently the quantity of the reduced form of XV and XVI was gradually increased after 72 hr.

On the other hand, the fairly large amount of XVII accompanying III and XV was obtained directly from XIV by pinacol rearrangement with sulfuric acid in acetic acid.

In Fig. 1 below, the infrared spectra of compounds VI, XIV, VII and XVII are compared with one other.
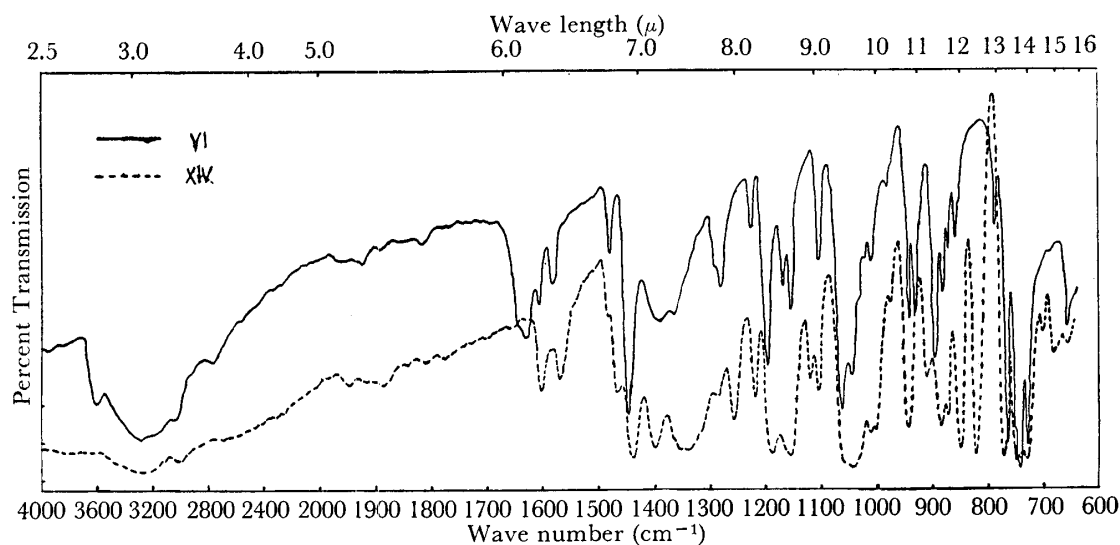
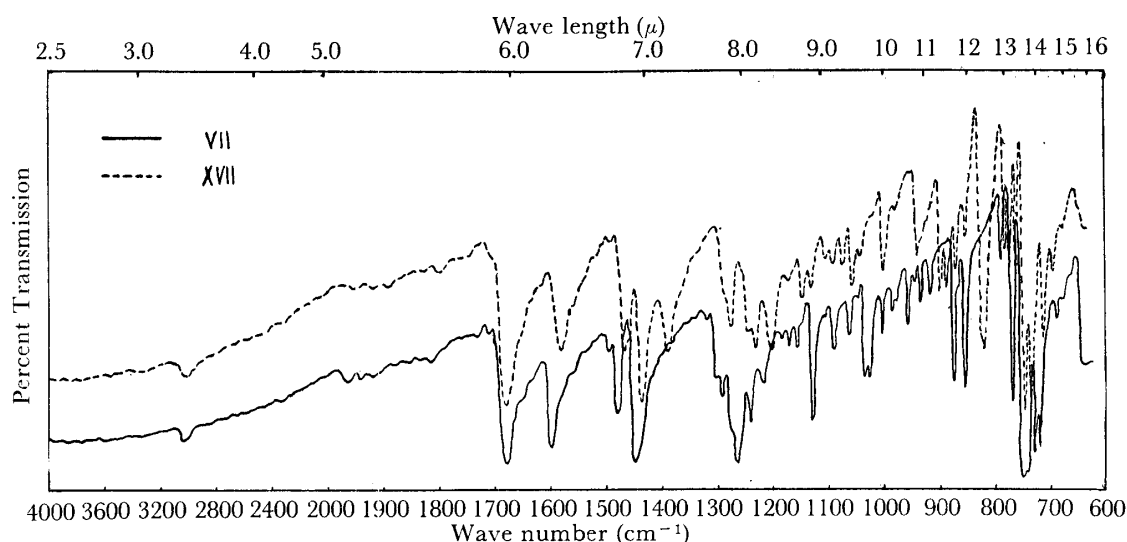The infrared spectra of compounds VI and XIV.

Fig. 1. The infrared spectra of compounds VII and XVII.

In another analogous case in this series, 1-bromofluorenone were attached slowly under the same conditions whereby 1-bromofluorene and small amount of 9-hydroxy-1,1'-bifluorenyl were produced[7], this may be owing to the steric hindrance to dimerization.

II and IV were obtained in a poor yield by means of steam distillation from the reaction mixture, V and XIII were isolated as an intermediate to fluorenes in the case of short reduction period.

In general, it has often been stated heretofore that the carbonyl compound is not reduced to hydrocarbon by way of the crresponding alcohol. However, II and IV were obtained as a normal products from the corresponding fluorenols in a process independent of fluorenopinacols formation by the Clemmensen reduction.

VI and XIV were obtained in a case of a short reduction time as main products, and that both yields were increased by the use of a more concentrated hydrochloric acid,

former exhibits an interesting behavior in the course of the reaction since it reacts further (see Chart 1 and 3).

Dibiphenylene-ethylene (XII) and -ethane (XI) reported by Harpe and Dorp[8] previously. In this reaction, a major part of VI through the VI' carbonium ion was converted into X and then to XII, which on further reduction afforded the end-product XI (56%). X was isolated as an intermediate product by short reduction of I (2 hr.) or VI (3 hr.) in the toluene solution.

X was readily converted to XII[9] by hydrochloric acid in acetic acid. Therefore, XII could be obtained in a better yield by treating X under the same conditions as in the Clemmensen reduction but without the amalgamated zinc. The formation mechanism of XI and XII can be visualized, as Chart 3.
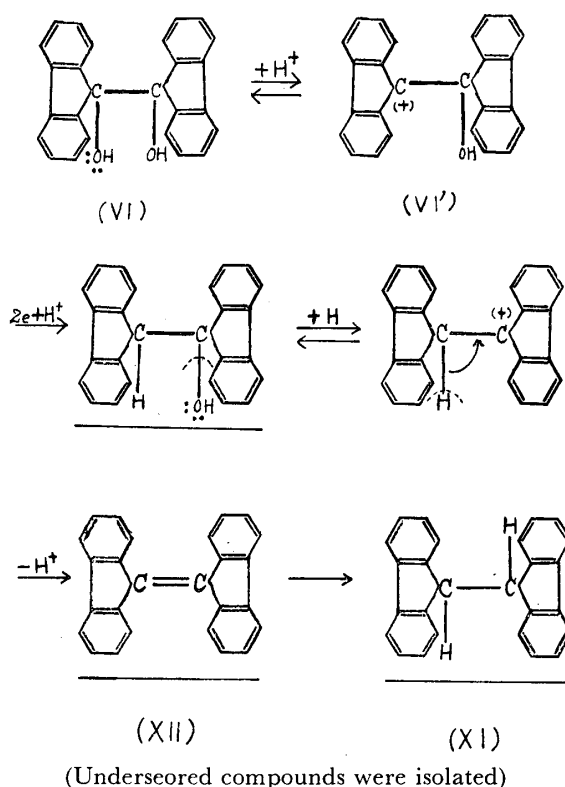

(VI)   (VI')

(XII)   (XI)

(Underseored compounds were isolated)

Chart 3.

In general, an ethylenic link, is reduced easily when it is conjugatetd with a carbonyl group. In contratst, the reduction of the ethylenic link in XII and XV were extremely slow upon treatment with hydrochloric acid and amalgamated zinc in the toluene sloution, and a red color remained even after twenty-four hours. XII was isolated from the reaction mixture as mixed crystals (red prisms) with IX. However, IX was not obtained by Harris et al.[1] from an alcoholic solution; hence, their product was simply XII.

Mixed crystals (IX · XII) gave 9,9'-dibromo-9,9'-bifluorenyl[10] and VII (no reaction) by bromination; with the Clemmensen reduction of zinc and ammonium hydroxide, they gave XI and IX, and with oxidation, I and tetrabenzocyclodecane-1, 6-dione. Therefore, the mixed crystals can be supposed to consist of IX and XII. Moreover, the ultraviolet spectrum showed maxima in the regions of 220~350 and 450 mμ. These maxima were almost identical with those of IX and XII respectively[11, 12].

The infrared spectrum also indicated a mixture, and the analytical results were identical with $C_{26}H_{16}$.

The same mixed crystals were produced in nearly a quantitative yield from the solution of IX : XII (0.2 : 1) in acetic ester.

So that, IX is slightly yellow, even when recrystallized several times from different solvents. It is best to purify it by reduction and then by recrystallization.

In case of IX[13~15] has been reported previously, but it has not been obtained heretofore by the Clemmensen reduction of I. IX would be formed through the intermediate VIII. VIII[13] was prepared from VII by the use of zinc and ammonium hydroxide in an alcoholic solution, and was then converted to IX[cf.16] by treating it under the same conditions as in the Clemmensen reduction but without zinc amalgam. Furthermore, IX (80%) and intermediate VIII (10%) could be isolated by the Clemmensen reduction of VII for fifteen hours in the xylene system.

In order to polarize the central double bond, IX was oxidized to tetrabenzocyclodecane-1,6-dione[13]; which was then converted to IX and VII by reduction.

In Fig. 2 the infrared spectra of compounds IX and XVIII are compared with one other.
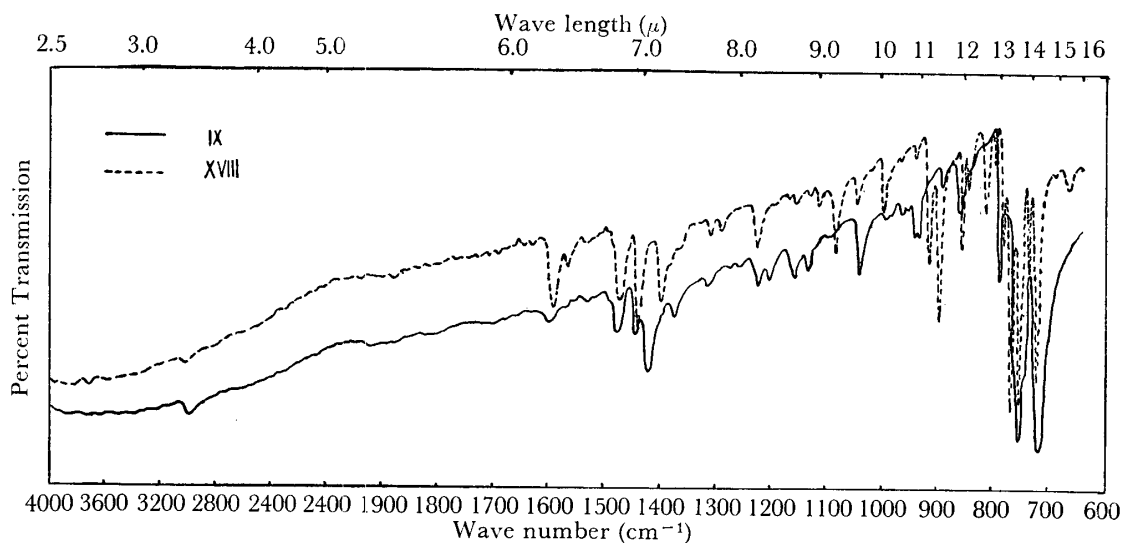

Fig. 2. The infrared spectra of compounds IX and XVIII.

In view of these observations, the behavior of each intermediate in the course of the Clemmensen-Martin reduction of I and III can be explained. There have also been some other discussions reported recently of the mechanism of the Clemmensen reduction[17].

Experimental

All the melting points are uncorrected.

General procedure for the Clemmensen Reduction of Fluorenone Materials. —Amalgamated zinc filings were prepared according to Martin's method[4].

A mixture of amalgamated zinc (20 g.), water (15 ml.), xylene (20 ml.), concentrated hydrochloric acid (35 ml.) and fluorenone (10 g.) was refluxed briskly for twenty-four hours in a 500 ml. round-bottomed flask. A 10 ml. portion of concentrated hydrochloric acid was added every six hours during the heating period. The xylene layer turned

a bright red color after ten minutes.

The red reaction mixture was cooled to room temperature after 24 hr., and the deposited crystals in the xylene layer were collected and washed free of acid with a small amount of water and then recrystallized from benzene. Colorless crystalline needless of XI (1.6 g.) were obtained. (Part of XI coats the surface of the zinc; m.p. and mixed m.p. 224°C). The mother liquor was evaporated to half volume. The deposited crystals were filtered and recrystallized from acetic ester to yield VII (0.75 g.) as colorless prisms, m.p. 258°C (Found: C, 90.91; H, 4.86%). This was identical with those of specimen which was prepared from VI with sulfuric acid in acetic acid following the procedure of Gomberg and Bachmann[18]. Further evaporation of the mother liquor to half volume yielded IX (slightly yellow), which recrystallized several times from benzene as nearly colorless material, (1.3 g.), m.p. 214~215°C.

Found: C, 95.28: H, 5.20. Calcd. for $C_{26}H_{16}$; C, 95.09%; H, 4.91%: Picrate, Found: C, 69.21; H, 3.64; N, 7.60. Calcd. for $C_{32}H_{19}O_7N_3$: C, 68.94; H, 3.44; N, 7.54%.

IX, λ_{max}^{MeOH} mμ (logε): 265 (4.73), 286 (4.69), 299 (4.84), 335 (4.22), 350 (4.20).

The xylene was separated from the water layer and submitted to steam distillation for one hour to remove both the solvent and the fluorene which was recrystallized from alcohol (1.3 g.), m.p. 113~114°C. This was corfirmed by mixed melting point.

The red residue was filtered, dried, and recrystallized from benzene to yield additional XI (0.8g.) (total 2.4 g.), m.p. 243~244°C.

The last benzene mother liquor was evaporated to a small volume, and the deposited red crystals were recrystallized from acetic ester in a red prism to give mixed crystals (0.5 g.), m.p. 185°C.

Found: C, 95.10; H, 5.19. Calcd. for $C_{26}H_{16}$: C, 95.09; H, 4.91%.

λ_{max}^{MeOH} mμ (logε): 244 (4.62), 268 (4.71), 286 (4.63), 299 (4.76), 335 (4.15), 348 (4.13), 382 (3.23), 450 (3.60).

Then, VI was isolated from the mother liquor as colorless needles (1.0 g.), m.p. 192°C (Found: C, 86.24; H, 5.14%). The identity of this compound was confirmed by mixed melting point with an authentic sample.

The separation of the reaction products was much simpler when the reduction time was longer (72 hr.). In this reduction, the amalgamated zinc and hydrochloric acid were charged every 24 hr.

In the case of a short reduction period (2 hr.) the first deposited crystals were almost pure VI (m.p. 192°C). V (0.1g., m.p. 158°C) was extracted by 20% boiling alcohol from the residue of the steam distillation; furthermore, other compounds were separated by the method described above. The last residual benzene solution was chromatographed on alumina, and two products, X (0.65g., m.p. 192~193°C) and I (0.3g., m.p. 80°C), were isolated; their identity was confirmed by mixed melting point with authentic samples.

In the case of a short reduction period (3 hr.) of VI, each product was separated by a procedure almost identical to that employed for the reduction products of I.

General Procedure for the Clemmensen Reduction of 2-Bromofluorenone (III). —2-Bromofluorene was obtained by the bromination of fluorene in chloroform; it was then oxidized to III[19] in over 80% yields.

About 0.077 mol. (20 g.) of the ketone III was refluxed vigorously for 24 hr. with

40 g. of amalgamated zinc, 30 ml. of water, 70 ml. of concentrated hydrochloric acid and 40 ml. of xylene in a 1000 ml. flask.

Concentrated hydrochloric acid (20 ml.) was added every six hours, according to Martin's method. The xylene layer turned an orange-red color after 24 hr.

When the mixture had been left standing, the crystals in the xylene layer were recrystallized from benzene, m.p. 195~196°C (4.7 g.), identical with 2, 2′-dibromo-fluorenopinacol (XIV).

Found: C, 59.99; H, 3.13. Calcd. for $C_{26}H_{16}O_2Br_2$: C, 60.02; H, 3.10%. IR 3450 (OH) cm^{-1} (KBr-disk).

The products which coated the surface of the zinc were filtered, dried and dissolved in benzene by heating; upon cooling XVI (m.p. 274°C, 0.36 g.) was obtained and III (m.p. 140°C, 0.5 g.) was recovered from benzene mother solution. The identity of both compounds was confirmed by mixed melting point determination.

The original xylene mother liquor was evaporated, and XVI (m.p. 275°C, 0.05 g.), XVII (m.p. 253~254°C, 0.005 g.), and recovered III (m.p. 140°C, 0.35 g.) were isolated by fractional recrystallization. XVII was identical with the material which had been prepared by the pinacol rearrangement of XIV with sulfuric acid in acetic acid.

Found: C, 61.95; H, 2.70. Calcd. for $C_{26}H_{14}OBr_2$: C, 62.18; H, 2.81%.

The xylene mother solution was steam-distilled to remove the solvent, and IV (m.p. 112°C, 2.7 g.) was obtained: this was confirmed by mixed melting point determination.

The orange residue was filtered and dried, and XVI (m.p. 275°C, 0.38 g.), XV (m.p. 264°C, 0.01 g.) III (m.p. 140°C, 1.3 g.) and XIII (m.p. 130°C, 0.26 g.) were separated by a combination of fractional recrystallization and chromatography in benzene on an alumina column. Mixed melting points established the nature of the products.

Clemmensen Reduction of XIV. —A mixture of amalgamated zinc (11 g.), toluene (13.4 ml.) and XIV (4.2 g.) were refluxed for 24 hr. A 5 ml. portion of concentrated hydrochloric acid was added every six hours.

The toluene layer turned yellow after five minutes, and orange-yellow after 12 hr.

After the mixture had been left standing 24 hr., the deposited products were filtered and then recrystallized from benzene, whereupon (m.p. 195°C, 1.2 g.) was recovered. Then XV (m.p. 263°C, 0.2 g.) was isolated by evaporation and recrystallization from the mother liquor.

The last toluene mother liquor was subjected to steam distillation, and yellow residue was filtered and recrystallized from benzene to yield XVI (m.p. 273°C, 0.005 g.), then XIV (m.p. 195°C, 0.8 g.) and III (m.p. 140°C, 0.51 g.) from the benzene mother solution. These compounds were confirmed by mixed melting point determinations.

Reaction of XIV with Hydrochloric Acid. —XIV (0.5 g.), toluene (2 ml.), water (0.8 ml.) and concentrated hydrochloric acid (1.8 ml.) were refluxed for 24 hr. A 0.5 ml. portion of hydrochloric acid was added every six hours.

The toluene layer turned an orange-yellow color after 20 hr. When the mixture had been left standing, the precipitate was filtered and recrystallized from benzene, m.p. 193°C (0.21 g.), identical with the recovered XIV. The toluene mother liquor was steam-distilled to remove the solvent, yielding III (m.p. 140°C, 0.05 g.), which was recrystallized from alcohol.

The residual products were filtered; III (m.p. 142°C, 0.06 g.) and XV (m.p. 263°C,

0.002 g.), obtained by means of chromatography in benzene on alumina, were confirmed by mixed melting point determinations.

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