[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE POLYTECHNIC INSTITUTE OF BROOKLYN]

The Addition of Bases to Polar Hydrocarbons. I. Reversal of the Mannich Reaction[1]

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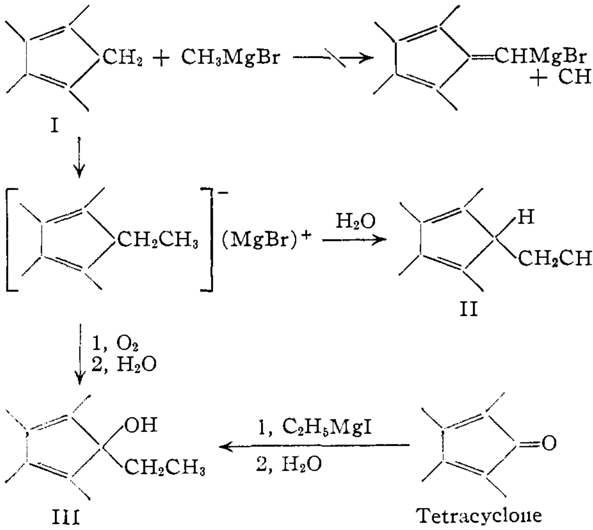
Methylmagnesium bromide adds to the exo-double bond of 1,2,3,4-tetraphenylfulvene (I) to give 1-ethyl-2,3,4,5-tetraphenylcyclopentadiene (II). The structure of the product was shown by oxidizing the intermediate Grignard reagent to the known 1-ethyltetraphenylcyclopentadien-1-ol (III). With refluxing piperidine I gives 2,3,4,5-tetraphenylcyclopentadiene (IV), proceeding *via* the somewhat unstable 1:1-adduct V, which is isolable at 0°. When heated alone V reverts to I, but when heated with piperidine it gives IV. Extension of this reaction to 1,4-diphenyl-2,3-bis-(4′-methoxyphenyl)-fulvene (VI) gave the corresponding dimethoxydiene VII. This reversal of the Mannich reaction was further demonstrated by the following example: β-(N-piperidyl)-α-phenylpropiophenone (VIII) is converted to α-phenylacetophenone (IX) by means of refluxing piperidine or aniline and 1-(N-piperidylmethyl)-2-naphthol (X) is converted to 2-naphthol by means of refluxing piperidine or morpholine.

In connection with studies toward the synthesis of a fulvene aldehyde it was desirable to prepare the fulvenyl Grignard reagent from 1,2,3,4-tetraphenylfulvene (I) by treatment of I with methylmagnesium bromide in analogy with the preparation of acetylenic Grignard reagents. This thought was prompted by the report of Dilthey and Huchtemann[4] that I condenses with *p*-nitrosodimethylaniline in the presence of piperidine to give a keteneimine XI, indicating the acidic character of the methylene hydrogen atoms. In addition, the theoretical considerations of Hückel,[5] Pullman and coworkers,[6,7] Coulson,[8] and Wheland[9,10] and the dipole moment measurements of Wheland[9] and Bergmann[11] all point to a dipole in the fulvene nucleus toward the C_5-ring.

However, when the reaction was carried out at 80° in anisole, the orange color was discharged and hydrolysis gave a colorless hydrocarbon analyzing for $C_{31}H_{26}$. Proof of the structure was obtained by direct comparison with 1-ethyl-2,3,4,5-tetraphenylcyclopentadiene (II) obtained by the alkylation of 2,3,4,5-tetraphenylcyclopentadiene (IV) with ethanol in the presence of alkali.[12,13] Additional proof was elicited by oxidizing the intermediate Grignard reagent to give the known[4] 1-ethyl-2,3,4,5-tetraphenylcyclopentadien-1-ol (III) (see Chart I).

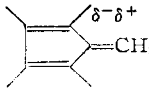
These data establish beyond doubt that the Grignard reagent adds as R^-MgX^+ to the exo-double bond of the fulvene system. This is chemical evidence confirming the theoretical prediction of the dipole in I. Further, this result is in accord with those of Fuson and York[14] who added benzylmagnesium chloride and *t*-butylmagnesium chloride to I.

CHART I



An unusual dependence of the course of the reaction on the grade of the magnesium was observed. When ordinary "Grignard Grade" magnesium was employed, the results were variable and a second product was obtained. Although the structure of the product was not determined in this study, its analysis indicated that it was isomeric with II. When sublimed magnesium was used, only II was obtained. In the light of this difference in the course of the reaction, it is pertinent that Fuson and York assigned structures without synthetic or degradative proof.

This finding that the Grignard reagent adds to the fulvene nucleus in a manner directed by the polarized structure A led to the prediction that other bases might be able to add across the exo-



A

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[2] The material reported here is taken from part of the Dissertation for the degree of Doctor of Philosophy presented by David Taber to the Graduate Faculty of the Polytechnic Institute of Brooklyn, June, 1953.

[3] To whom inquiries concerning this manuscript should be sent.

[4] W. Dilthey and P. Huchtemann, *J. prakt. Chem.*, **154**, 238 (1940).

[5] E. Hückel, "Grundzüge der Theorie ungesättigter and aromatischer Verbindungen," Verlag Chemie, Berlin, 1938, pp. 71–75.

[6] A. Pullman, B. Pullman and R. Rumpf, *Bull. soc. chim. France*, **280**, 757 (1948).

[7] G. Berthier and B. Pullman, *ibid.*, D457 (1949).

[8] C. A. Coulson, D. P. Craig and A. Maccoll, *Proc. Phys. Soc.*, **61**, 22 (1948).

[9] G. W. Wheland and D. E. Mann, *J. Chem. Phys.*, **17**, 264 (1949).

[10] J. I. F. Alonso, *Compt. rend.*, **223**, 56 (1951).

[11] E. D. Bergmann and E. Fischer, *Bull. soc. chim. France*, 1084 (1950).

[12] N. O. V. Sonntag, S. Linder, E. I. Becker and P. E. Spoerri, THIS JOURNAL, **75**, 2283 (1953).

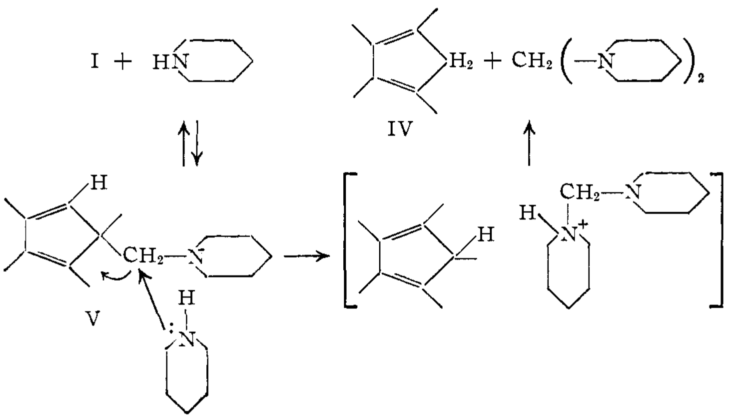
[13] S. M. Linder, E. I. Becker and P. E. Spoerri, *ibid.*, **75**, 5972 (1953).

[14] R. C. Fuson and O. York, Jr., *J. Org. Chem.*, **18**, 570 (1953). This work was first disclosed by Professor Fuson in his Medal Award Address at the Nichol's Medal Dinner in New York, March 13, 1953.

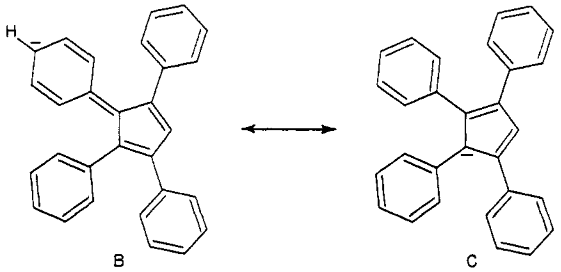
double bond and this was first tried with piperidine, which was selected in order to avoid steric complications.

When I was dissolved in excess cold piperidine, the orange-red color of I was discharged almost completely to give a solution which fluoresced blue-white under ultraviolet light. After refluxing the solution, a colorless solid was obtained which was presumed to be 1-(N-piperidylmethyl)-2,3,4,5-tetraphenylcyclopentadiene (V). However, melting point, mixture melting point and analysis for the elements showed that the product was tetraphenylcyclopentadiene (IV) and not V.

This transformation, which appears to be a reversal of the formation of a Mannich base of a hydrocarbon—a new class of compounds—may be formulated as



The first step would be the expected addition of piperidine to the exomethylene group. A bimolecular reaction involving V and a second molecule of piperidine could then produce the tetraphenylcyclopentadienyl carbanion and the salt of N,N′-dipiperidylmethane. Interaction of these ions would give IV and N,N′-dipiperidylmethane. The ease with which the displacement takes place may be ascribed to the formation of the resonance-stabilized anion for which a total of seventeen structures can be written—twelve such as B and five such as C.



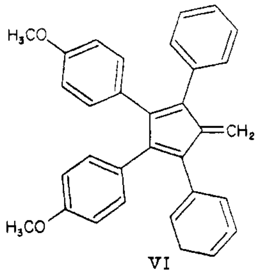
B C

N,N′-Dipiperidylmethane is a well-characterized compound,[15] which, since it is a nitrogen analog of an acetal of formaldehyde, gives formaldehyde upon hydrolysis. When the reaction mixture, obtained after I and excess piperidine were refluxed together for one hour, was acidified and distilled with steam, formaldehyde was obtained and characterized as the bis-methone derivative[16] in 64.2% yield, which compares favorably with the crude yield of IV, 61.9%, obtained in a separate experiment omitting the hydrolysis.

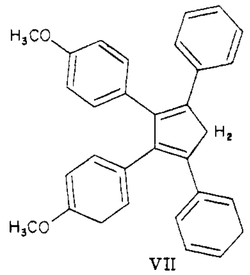
Although these results point to the mechanism presented above, it seemed desirable to emphasize its probability by isolating the postulated intermediate V. This was accomplished by employing a brief contact time between I and excess piperidine at about 0°. V was found to be unstable to heat, melting at 48.5–57.5° dec. and reverting to its components even at room temperature. Heating at 100° at reduced pressure over phosphorus pentoxide converted V to I essentially quantitatively.

The reaction was extended to include 1,4-diphenyl-2,3-bis-(4′-methoxyphenyl)-fulvene (VI). Despite the seemingly unfavorable electronic effect of the two methoxy groups, the diene VII[17] was obtained from it in 71.8% yield upon refluxing VI with excess piperidine for two hours.

These results redirected our attention to the report of Dilthey and Huchtemann[4] that I gave a ketene-imine upon treatment with *p*-nitrosodimethylaniline in the presence of an unstated amount of piperidine. Inasmuch as Stevens and French[18] have shown that ketene-imines are readily hydrated, the report that the product was "very stable"[4] was regarded as worthy of reinvestigation. When the reaction was repeated in this Laboratory and the presumed ketene-imine was hydrolyzed with hydrochloric acid, tetracyclone was obtained. This can only mean that the product is the *p*-dimethylamino anil (XII) of tetracyclone, and that the interpretation of Dilthey and Huchtemann is incorrect (see Chart II). It is germane that the calculated percentage of nitrogen for the keten-eimine XI, 5.46%, does not differ significantly from that for XII, 5.58%. Only a nitrogen analysis was reported by the prior authors.



VI



VII

Inspection of formula V reveals that it is the Mannich base of the hydrocarbon IV, and the production of tetraphenylfulvene (I) from it by heating is entirely similar to the known decomposition of Mannich bases to form olefins.[19,20]

The formation of IV from V is the reversal of the formation of the Mannich base of a hydrocarbon.

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(15) E. Schmidt and P. Kohler, *Arch. Pharm.*, **240**, 230 (1902).

(16) W. Weinberger, *Ind. Eng. Chem., Anal. Ed.*, **3**, 365 (1931).

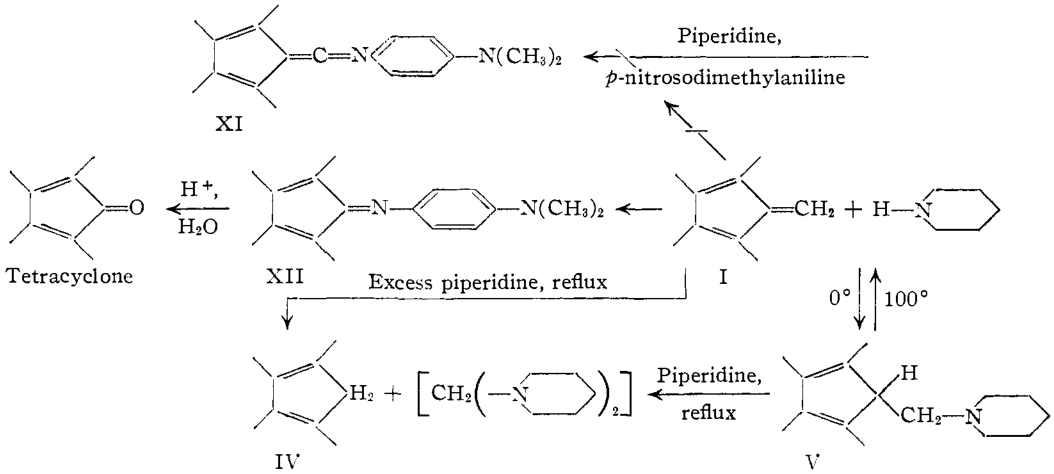
(17) L. Mehr, Dissertation, Polytechnic Institute of Brooklyn, June, 1953.

(18) C. L. Stevens and J. C. French, THIS JOURNAL, **75**, 657 (1953).

(19) F. F. Blicke, in "Organic Reactions," Vol. I, edited by R. Adams, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 303.

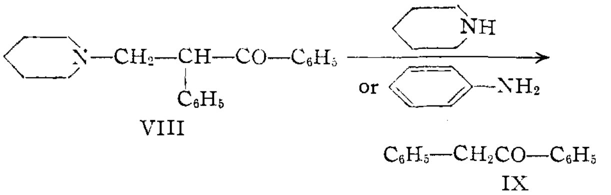
(20) J. H. Brewster and E. L. Eliel, *ibid.*, Vol. VII, 1953, p. 99.

CHART II



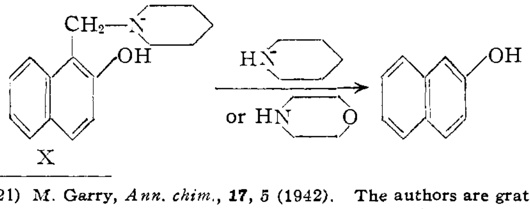
It was thus thought that other Mannich bases might give the reversal with excess piperidine.

When α-phenyl-β-(1-piperidyl)-propiophenone (VIII), the Mannich base of α-phenylacetophenone (IX), was refluxed in excess piperidine for 3.5 hr., IX was obtained in 4.4% yield. When the reaction was repeated for the same time using refluxing aniline, IX was obtained in 66% yield.



This result is interesting in view of the report[21] that when α-chloro-α-phenylpropiophenone is treated with one mole of aniline, α-phenylacrylophenone is formed in 76% yield and melts at 57°. However, α-phenylacrylophenone has been reported to be a liquid by Mehr[17] and by Burr,[22] a finding which we have substantiated, while α-phenylacetophenone is a solid.[23] The analysis reported by Garry lies intermediate between that for the two compounds, but is closer to that for α-phenylacrylophenone. It seems likely, therefore, that Garry had isolated a mixture.

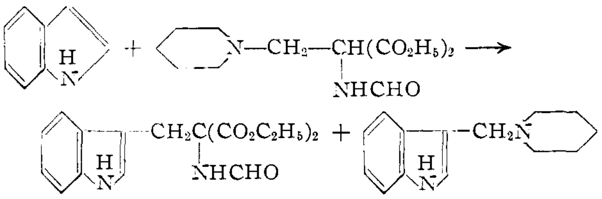
Also subjected to the reversal was the Mannich base of 2-naphthol, 1-(N-piperidylmethyl)-2-naphthol (X).[26] Upon refluxing X with piperidine for 4.5 hours a 3.7% yield of 2-naphthol was obtained. Carrying out the reaction at 180° for five hours gave 32% of crude 2-naphthol. Repeating the reaction using morpholine as the base a refluxing time of 22.5 hours afforded a crude yield of 35% of 2-naphthol.



Few examples of the base-catalyzed reversal of the Mannich reaction have come to the attention of the authors. Howton and Golding[27] and Wieland and co-workers[28,29] have reported the reversal for compounds related to the lobelia alkaloids and for lobelia alkaloids. Kermack and Muir[30] have reported what appears to be the base-catalyzed formation of 2-butanone from 1-(1′-piperidyl)-2-methyl-3-butanone. Dahlgleish[31] considers that the formation of bis-methylenelawsone from amine salts of lawsone and excess amine may be represented as a reversal of the Mannich reaction in an intermediate step.

The results of these experiments and of the work reported here are being used to guide further studies on the generality of the reaction.

ADDED IN PROOF. Since this paper was submitted, H. R. Snyder, C. Y. Meyers and D. B. Kellom (THIS JOURNAL, **75**, 4672 (1953)) have reported on a reversal of the Mannich reaction



In this paper they end a discussion as to whether water is required by showing that it is not.

H. von Euler, H. Hasselquist, G. Hanschoff and A. Glaser (*Chem. Ber.*, **86**, 969 (1953)) have reported the conversion of I to tetracyclone *via* XII without examination of the intermediates. Further, they show that methyleneanthrone (A) is converted under the same conditions to the product (B) which is obtained by treating anthrone with p-nitrosodimethylaniline. This transformation fits nicely into the reversals cited in the present manuscript.

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[21] M. Garry, *Ann. chim.*, **17**, 5 (1942). The authors are grateful to Dr. L. Mehr for bringing this point to their attention.

[22] J. G. Burr, Jr., THIS JOURNAL, **73**, 5170 (1951).

[23] The melting point has been variously reported: m.p. 60°,[24] 56°.[25]

[24] V. Meyer and L. Oelkers, *Ber.*, **21**, 1295 (1888).

[25] C. F. H. Allen and W. E. Barker, "Organic Syntheses," Coll. Vol. II, edited by A. H. Blatt, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 156.

[26] J. Decombe, *Compt. rend.*, **197**, 258 (1933).

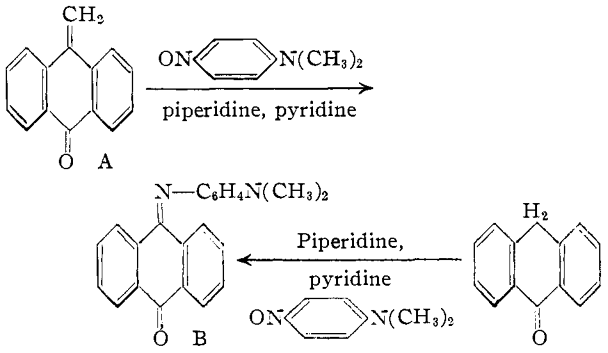
[27] D. R. Howton and D. R. V. Golding, *J. Org. Chem.*, **15**, 1 (1950).

[28] H. Wieland, *Ber.*, **54**, 1784 (1921).

[29] H. Wieland, C. Schöpf and W. Hermsen, *Ann.*, **444**, 40 (1925).

[30] W. O. Kermack and W. Muir, *J. Chem. Soc.*, 3089 (1931).

[31] C. E. Dahlgleish, THIS JOURNAL, **71**, 1697 (1949).



Experimental[32]

1-Ethyl-2,3,4,5-tetraphenylcyclopenta-2,4-diene (II). A.—A filtered solution of methylmagnesium bromide was prepared under nitrogen from 0.67 g. (0.0276 atom) of sublimed magnesium[33] and excess methyl bromide in absolute ether. Twenty-five ml. of dry anisole was added and the ether distilled. Tetraphenylfulvene[4] (1.0 g., 2.62 mmole) was added with stirring and the temperature was raised to 75–80°, maintained there for one hour and then raised to 100° and maintained there for one hour. The orange color of the fulvene was almost discharged. Benzene was added to the cooled reaction mixture, which was then hydrolyzed with dilute hydrochloric acid. The organic layer was separated, washed with water and concentrated to a viscous sirup at reduced pressure on the steam-bath. Trituration with cold methanol gave 0.64 g. (1.60 mmoles, 61%) of product, m.p. 178.5–181°. Chromatography on alumina gave a lower yellow band and an upper colorless band which was firmly adsorbed, both of which fluoresced blue-white under ultraviolet light.[34] Elution and concentration of the lower band afforded 0.45 g. (1.13 mmoles, 43.2%) of yellow solid, m.p. 179–180°. Admixture with authentic II showed no depression. After successive recrystallizations from cyclohexane, ethyl acetate and three times from acetonitrile (twice with active carbon), the analytical sample melted 180–181°.

Anal. Calcd. for $C_{31}H_{26}$: C, 93.42; H, 6.58. Found: C, 93.40; H, 6.76.[35]

B.—When the experiment was performed as above, using methyl iodide and Eimer and Amend magnesium "For Grignard's Reagent," the identical work-up gave 0.27 g. of crude product, m.p. 164.5–167.5°. Chromatography as above gave 0.22 g. of solid, m.p. 167.5–169.5°. Recrystallization from heptane gave colorless crystals, m.p. 169–170°; m.m.p. with 1-ethyl-2,3,4,5-tetraphenylcyclopenta-2,4-diene was 154–170°.

Anal. Calcd. for $C_{31}H_{26}$: C, 93.42; H, 6.58. Found: C, 93.08, 93.18; H, 6.69, 6.46.

1-Ethyltetraphenylcyclopentadien-1-ol (III). From 1,2,3,-4-Tetraphenylfulvene.—To the filtered Grignard reagent prepared from 1.43 g. (0.059 atom) of magnesium (Mallinckrodt "For Grignard's Reaction" grade) and 8.4 g. (0.059 mole) of methyl iodide in 30 ml. of ether was added 30 ml. of anisole and the ether was distilled. To the cooled, stirred solution was added, all at once, 2.15 g. (5.63 mmole) of tetraphenylfulvene. Under a slow stream of dry nitrogen the mixture was heated to 90–100° and maintained there for two hours. When the reaction mixture had cooled to room temperature, dry oxygen was passed through the solution for 45 min. without external cooling, then at 80–90° for 20 min. The addition of 35 ml. of ether to the cooled reaction mixture precipitated a yellow solid. Hydrolysis was effected with 40 ml. of a saturated solution of ammonium chloride. After extracting with ether and drying the organic layer over anhydrous magnesium sulfate, the ether was distilled at atmospheric pressure and the anisole was distilled at reduced pressure.

Trituration of the residual oil with petroleum ether (b.p. 28–38°) and chilling in Dry Ice gave 0.65 g. (1.57 mmoles, 27.8%) of product, m.p. 178–181°, m.m.p. with authentic dienol[4] (m.p. 189.5–190°) 184.5–188°. Several recrystallizations from petroleum ether (b.p. 90–100°) raised the melting point to 187.5–189°, m.m.p. with authentic dienol 189–190°.

Anal. Calcd. for $C_{31}H_{26}O$: C, 89.82; H, 6.32. Found: C, 90.02; H, 6.42.

2,3,4,5-Tetraphenylcyclopenta-2,4-diene (IV) from Tetraphenylfulvene (I).—A mixture of (I) (0.50 g., 1.31 mmole) and 5 ml. of piperidine (dried over potassium hydroxide) was refluxed for one hour while protected from moisture with a calcium chloride drying tube. The addition of petroleum ether (b.p. 28–38°) and chilling in Dry Ice gave IV, which, after drying over phosphorus pentoxide, weighed 0.30 g. (0.81 mmole, 61.9%) and melted 176.5–178°. Chromatography on alumina using dry benzene as solvent and eluant gave 0.24 g. (0.65 mmole, 49.5%) of a light yellow solid. Recrystallization from ethyl acetate raised the melting point to 180–181°, and no depression was observed in admixture with authentic diene.

Anal. Calcd. for $C_{29}H_{22}$: C, 94.01; H, 5.99. Found: C, 94.08; H, 5.95.

Identification of N,N'-Dipiperidylmethane.—After refluxing for one hour, a solution of I (0.50 g., 1.31 mmoles) in 5 ml. of piperidine (dried over potassium hydroxide) was chilled and treated with 50 ml. of a cold solution of 40% sulfuric acid. The mixture was refluxed under a slow stream of nitrogen for two hours, any formaldehyde being caught in two traps containing water and arranged in series. The traps were chilled in an ice-salt mixture. After refluxing, the reaction mixture was transferred to a flask arranged for steam distillation, the reaction flask being washed with 10 ml. of ethylene glycol (previously distilled) and the washings combined with the main body of material. The water in the traps was emptied into the receiver, and the adapter leading from the condenser was extended below the level of this water. The receiver was immersed in an ice-salt mixture and to obviate explosion a long safety tube was placed in the distilling flask. After about 500 ml. of distillate were collected, a suspension of 0.80 g. of methone in 150 ml. of water was added. After shaking thoroughly to effect complete solution of the methone, the whole was left to stand overnight at room temperature. The precipitate was collected by suction to give 0.246 g. (0.841 mmole, 64.2%) of methylene-bis-methone, m.p. 190.5–192°. It melted 191–192.5° after recrystallization from aqueous methanol (reported m.p. 191–191.5°).[36,37]

Anal. Calcd. for $C_{17}H_{24}O_4$: C, 69.83; H, 8.27. Found: C, 69.62; H, 8.07.

A small amount of white solid which was not further investigated was observed in the condenser during the steam distillation.

1-(N-Piperidylmethyl)-2,3,4,5-tetraphenylcyclopenta-2,4-diene (V).—I (0.50 g., 1.31 mmoles) was added to 20 ml. of piperidine previously chilled to 0°. After shaking the mixture for about five minutes to effect complete solution, distilled water was added slowly at 0°. The nearly white solid which precipitated was filtered rapidly, washed four times with cold, distilled water and dried immediately for three hours over phosphorus pentoxide at reduced pressure, m.p. 48.5–57.5° dec. The analysis was performed immediately thereafter.

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(32) Melting points are uncorrected. The analyses were performed by Dr. K. Ritter, Postfach Basel 2, Basel, Switzerland, and Dr. Francine Schwarzkopf, 62-12 79th Street, Middle Village 79, Long Island, New York.

(33) "Pure Sublimed Magnesium," Dow Chemical Company, Midland, Michigan. Alloy No. 66,200. *Anal.* Al, 0.0009%, Ca, 0.0014%; Cu, <0.0001%; Fe, 0.0005%; Mn, 0.0013%; Ni, <0.0004%; Si, <0.01%; Sn, <0.001%; Pb, <0.001%; Ba, 0.0001%; K, 0.0006%; Na, 0.0005%; Sr, <0.0005%; Zn, <0.01%; Mg, remainder.

(34) Blue-white fluorescence under ultraviolet light appears to be a diagnostic test for the tetraarylcyclopentadiene system. Tetraphenylcyclopentadiene, a number of chloro-, methyl- and methoxy derivatives of it, 2,3,4,5-tetraphenylcyclopenta-2,4-dien-1-ol, and a number of 2,3,4,5-tetraphenylcyclopentadien-1-alkyl-1-ols do fluoresce while tetracyclone, its derivatives and 2,3,4,5-tetraphenylcyclopenta-2-en-1-one do not.

(35) The yellow color persisting even in the analytical sample must have been due to an impurity since the compound is known to be colorless.[19] The analysis was not significantly affected.

(36) E. C. Horning and M. G. Horning, *J. Org. Chem.*, **11**, 95 (1946).

(37) S. V. Lieberman and E. C. Wagner, *ibid.*, **14**, 1001 (1949).

Anal. Calcd. for $C_{35}H_{33}N$: C, 89.89; H, 7.11; N, 3.00. Found: C, 89.90; H, 6.94; N, 3.30.

When 0.0365 g. of this substance was heated at 100° for three hours at reduced pressure over phosphorus pentoxide, 0.0296 g. (98.6%) of I was obtained, m.p. 200.5–210°. After recrystallization from Skellysolve C, the fulvene melted at 208.5–211°, m.m.p. 210–212°.

2,3,4,5-Tetraphenylcyclopenta-2,4-diene (IV) from 1-(N-Piperidylmethyl)-2,3,4,5-tetraphenylcyclopenta-2,4-diene (V).—A solution of 0.30 g. (0.64 mmole) of V in 5 ml. of piperidine was refluxed for one hour while protected with a calcium chloride guard tube. Chilling in a Dry Ice-bath and adding Skellysolve A gave 0.11 g. (0.30 mmole, 46%) of IV, m.p. 175–177.5° (sintering at 160°). Chromatography on alumina with benzene as solvent and eluant gave two bands, which were colorless in visible light and blue-white fluorescent in ultraviolet light. Elution of the lower band, removal of the solvent and recrystallization from ethyl acetate gave IV, m.p. 180–181.5°, m.m.p. with authentic IV 180–181°.

1,4-Diphenyl-2,3-bis-(4′-methoxyphenyl)-fulvene (VI).—To a refluxing solution of 0.43 g. (1.0 mmole) of 2,5-diphenyl-3,4-bis-(4′-methoxyphenyl)-cyclopenta-2,4-diene (VII),[17] 12 ml. of 40% formalin solution and 20 ml. of a 1:1 mixture of benzene and methanol, there was added dropwise 12 ml. of a 4% solution of sodium methoxide in methanol. After refluxing for an additional hour, the suspension was chilled and filtered, the solids being washed once with cold methanol. The orange product (0.35 g., 0.79 mmole, 79%) sintered at 183° and melted 187–188°. The analytical sample was recrystallized from a 3:1 mixture of ethanol and benzene, m.p. 187–188°.

Anal. Calcd. for $C_{32}H_{26}O_2$: C, 86.85; H, 5.92. Found: C, 86.62; H, 6.04.

VII from VI.—A solution of VI (0.50 g., 1.13 mmoles) in 5 ml. of dry piperidine was refluxed under a calcium chloride guard tube for two hours. After chilling in a Dry Ice-bath, the addition of Skellysolve A precipitated 0.35 g. (0.81 mmole, 71.8%) of a tan solid, m.p. 211.5–217.5°. Chromatography on alumina, using benzene as solvent and eluant, gave three colorless bands which fluoresced blue-white under ultraviolet light. Elution of the lowest band gave, after the customary work-up, 0.28 g. (0.65 mole, 57.6%) of material, m.p. 221–222.5° (turbid melt). A mixture melting point with authentic diene (m.p. 221–222°[17]) showed no depression, 221–222.5° (turbid melt). After two recrystallizations from a mixture of benzene and Skellysolve C, the analytical sample melted at 221–222°, m.m.p. 221–222°.

Anal. Calcd. for $C_{31}H_{26}O_2$: C, 86.48; H, 6.09. Found: C, 86.80; H, 6.02.

The Reaction of I with *p*-Nitrosodimethylaniline. A. In Pyridine at Room Temperature.—A mixture of I (1.0 g., 2.62 mmoles), *p*-nitrosodimethylaniline (0.70 g., 4.66 mmoles), 15 ml. of pyridine (dried over barium oxide) and 5 ml. of piperidine (dried over potassium hydroxide) was left to stand at room temperature for 24 hours. Subsequent addition of water followed by filtration and alternate washings with water and methanol gave 1.28 g. of crude product. Hydrolysis of 0.50 g. of this material with concentrated hydrochloric acid gave, after extraction with benzene, drying and chromatographing on alumina (benzene as eluant), 0.25 g. (63.5% based on I) of purple solid, m.p. 219–220.5°. A mixture melting point with authentic tetracyclone was not depressed, 220.5–221°. The analytical sample was recrystallized from a mixture of benzene and methanol, m.p. 220–221°.

Anal. Calcd. for $C_{29}H_{20}O$: C, 90.59; H, 5.24. Found: C, 90.20; H, 5.00.

When the hydrolysis was repeated for duplicability, in addition to tetracyclone, m.p. 221.5–222.5°, there was obtained a small amount of the dimethylaminoanil of tetracyclone which, after recrystallization from a mixture of benzene and petroleum ether (b.p. 90–100°), melted at 224.5–227° (reported 217–218°,[4] 224–226°).[38]

B. **In Benzene at Reflux Temperature.**—A mixture of 0.50 g. (1.31 mmoles) of I, 0.35 g. (2.33 mmoles) of *p*-nitrosodimethylaniline and 0.22 g. (2.6 mmoles) of piperidine (dried over potassium hydroxide) in 15 ml. of dry benzene was refluxed for 0.5 hour under a calcium chloride guard tube. After cooling, 20 ml. of concentrated hydrochloric acid and 20 ml. of benzene were added and the mixture was refluxed for 0.5 hour. The aqueous layer was separated, washed with benzene and discarded. The combined organic layers were washed with water until neutral. After drying the benzene layer over anhydrous magnesium sulfate, it was chromatographed on alumina, using benzene as developer. The lowest band, orange, gave 0.28 g. (0.73 mmole, 56%) of I, m.p. 210–212°, mixture melting point with authentic I 211–215.5°. The second band, purple, gave 0.093 g. (0.242 mmole) of tetracyclone, m.p. 221.5–223°. The melting point of authentic tetracyclone was not depressed. The yield of tetracyclone was 41.8%, based on I consumed.

β-(N-Piperidyl)-α-phenylpropiophenone (VIII).—A mixture of 10.6 g. (0.051 mole) of α-phenylacrylophenone[17] (b.p. 193–195° (12 mm.)), 4.4 g. (0.052 mole) of dry piperidine and 15 ml. of methanol was kept at room temperature for one hour, then chilled. A cake formed at this point. Trituration with cold methanol, filtration and washing with cold methanol gave 12.6 g. (0.043 mole, 84.4%) of VIII, m.p. 89.5–90°. Recrystallization from ethanol raised the melting point to 90–90.5°.[39]

α-Phenylacetophenone from VIII. A. Using Piperidine.—A mixture of 2.0 g. (6.80 mmoles) of VIII and 10 ml. of dry piperidine was refluxed for 3.5 hours, chilled and acidified with dilute hydrochloric acid. The mixture was extracted with ether and the ether extract washed with water until neutral. After drying with anhydrous magnesium sulfate, removal of the ether afforded 0.060 g. (0.31 mmole, 4.4%) of α-phenylacetophenone, m.p. 50–55° (m.m.p. 53–56.5° with authentic material). The oxime melted at 94–95°; m.m.p. with authentic oxime (m.p. 95.5–96.5°[40]) was 96.5–96.5°.

B. **Using Aniline.**—A mixture of 0.76 g. (1.93 mmoles) of the Mannich base and 5 ml. of distilled aniline was refluxed under a calcium chloride guard tube for 3.5 hours. After chilling, the reaction mixture was acidified with dilute hydrochloric acid and extracted with ether. The ether extract was washed with dilute hydrochloric acid, then with water until neutral and dried over anhydrous magnesium sulfate. After filtration and removal of the solvent, 0.25 g. (1.28 mmoles, 66%) of yellow product was obtained, m.p. 53.5–55.5° (sintering at 50°). Recrystallization from aqueous methanol gave nearly colorless crystals, m.p. 51–55° (sintering at 50°) (m.m.p. 54–56.5° with authentic desoxybenzoin).

2-Naphthol from X. A. Using Piperidine at Reflux.—A mixture of 2.0 g. (7.56 mmoles) of the Mannich base of 2-naphthol[26] and 15 ml. of dry piperidine was refluxed for 4.5 hours under a calcium chloride guard tube. After chilling, the reaction mixture was acidified with dilute hydrochloric acid and then extracted with benzene. The benzene layer was washed with dilute acid, then with water and dried over anhydrous magnesium sulfate. Removal of the solvent *in vacuo* under nitrogen gave 0.040 g. (0.26 mmole, 3.7%) of tan solid, m.p. 116–119.5°. Recrystallization from carbon tetrachloride gave pink crystals of 2-naphthol, m.p. 121.5–122.5°; m.m.p. with authentic 2-naphthol was 121.5–122.5°.

Anal. Calcd. for $C_{10}H_8O$: C, 83.32; H, 5.59. Found: C, 83.53; H, 5.68.

B. **In Sealed Tube.**—A mixture of 2.0 g. (7.56 mmoles) of the Mannich base and 20 ml. of dry piperidine was heated in a sealed tube at 180° for 5 hours. A work-up identical with that in A above afforded 0.35 g. (2.42 mmoles, 32%) of tan solid, m.p. 96–112° after sintering at 90°. After recrystallization from carbon tetrachloride and then from a mixture of benzene and Skellysolve B, pink crystals were obtained, m.p. 115–116.5° (m.m.p. with authentic 2-naphthol was 115–119°). Dissolving the solid in 10% sodium hydroxide (charcoal) and reprecipitating with acetic acid gave a white solid which was recrystallized from carbon tetrachloride; m.p. 115.5–119°, m.m.p. 120–121° with authentic 2-naphthol (m.p. 122–123°). The picrate[41] melted at 156–157° dec. (reported[41] 155.5–156.8°).

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[38] K. Ziegler and B. Schnell, *Ann.*, **445**, 266 (1925).

[39] C. Mannich and D. Lammering, *Ber.*, **55**, 3510 (1922), reported m.p. 91°. Their product was prepared from α-phenylacetophenone, formaldehyde and piperidine hydrochloride.

[40] E. Beckmann and E. Gunther, *Ann.*, **252**, 44 (1889).

[41] S. P. Mulliken, "A Method for the Identification of Pure Organic Compounds," Vol. I, first edition, John Wiley and Sons, Inc., New York, N. Y., 1904, p. 108.

C. Using Morpholine.—A solution of 2 g. (7.56 mmoles) of the Mannich base and 10 ml. of morpholine (b.p. 127–129°) (distilled from barium oxide) was refluxed for 22.5 hours under a guard tube packed with sodium hydroxide. After chilling, the reaction mixture was acidified with dilute (1:1) hydrochloric acid and then extracted with benzene. The extract was washed with dilute acid, then with water until neutral and finally extracted with 5% sodium hydroxide. Acidification of the basic solution with acetic acid gave a solid which was washed and dried, 0,38 g. (2.64 mmoles, 35%). After recrystallization from carbon tetrachloride the solid melted at 115–119°. The melting point was not changed significantly by additional recrystallizations.

The 1-benzeneazo derivative melted at 131–132° (reported 128.5–129.5°;[42] 133°,[43] 134°.[44-46]

Anal. Calcd. for $C_{16}H_{12}N_2O$: C, 77.40; H, 4.87; N, 11.29. Found: C, 77.72; H, 4.79; N, 11.57.

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[42] R. Möhleau and E. Strobach, *Ber.*, **33**, 804 (1900).

[43] M. Betti and G. Leoncini, *Gazz. chim. ital.*, **30, II**, 164 (1900).

[44] C. Liebermann, *Ber.*, **16**, 2858 (1883).

[45] B. Fischer and H. Wimmer, *ibid.*, **20**, 1577 (1887).

[46] G. Ciusa and U. Pestalozza, *Gazz. chim. ital.*, **41I**, 391 (1911).

BROOKLYN 1, NEW YORK

[CONTRIBUTION FROM KOPPERS CO., INC., MONOMER FELLOWSHIP AT MELLON INSTITUTE]

Steric Hindrance. I. 2,6-Dimethylacetophenone and 2,6-Dimethylstyrene[1]

BY L. H. SCHWARTZMAN AND B. B. CORSON

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The spectra of 2,6-dimethylacetophenone and 2,6-dimethylstyrene show the effect of diortho substitution. These compounds were synthesized from 2-iodo-*m*-xylene *via* the lithiumalkyl derivative and acetaldehyde. 2,6-Dimethylacetophenone fails to respond to the usual diagnostic tests for a ketone, but it takes part in the Schmidt reaction to yield 2,6-dimethylacetanilide. 2,6-Dimethylstyrene is more difficult to hydrogenate than styrene, and it is oxidized to 2,6-dimethylbenzoylformic acid under conditions which convert styrene to benzoic acid.

The sterically hindered compounds, 2,6-dimethylacetophenone (IV) and 2,6-dimethylstyrene (II), were prepared from 2-iodo-*m*-xylene *via* the Grignard reaction; lithium was found to be preferable to magnesium.

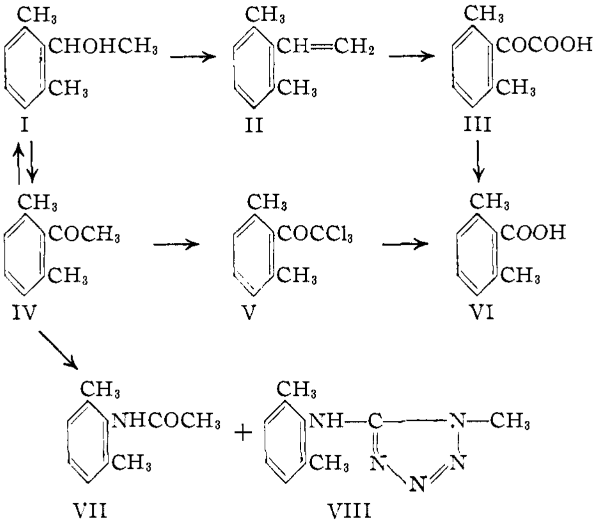
2,6-Dimethylphenylmagnesium iodide treated with acetaldehyde to give anomalous results. In one experiment, very poor yields of 2,6-dimethylphenylmethylcarbinol (I) and 2,6-dimethylstyrene (II) were obtained; in another experiment, the product, still in poor yield, was the ether of 2,6-dimethylphenylmethylcarbinol.

The infrared spectrum of α,α'-di-[2-*m*-xylyl] ethyl ether indicated the presence of an ether linkage and vicinal trisubstituted aromatic rings. Hydrolytic cleavage of the ether with hydrobromic acid produced 2,6-dimethylphenylmethylcarbinol (I) and its dehydration product, 2,6-dimethylstyrene (II).

Fuson, Rabjohn, Schenk and Wallace[2] treated mesitylmagnesium bromide with acetaldehyde and obtained a small yield of the corresponding carbinol, but the major product was a compound which they assumed to be the ether of the carbinol, on the basis of analysis.

In contradistinction to the behavior of the magnesium complex, the lithium derivative of 2-iodo-*m*-xylene gave a high yield of 2,6-dimethylphenylmethylcarbinol (I), and although this carbinol is readily dehydrated, we were able to prepare its 3,5-dinitrobenzoate and phenylurethan derivatives,

Carbinol I was oxidized to 2,6-dimethylacetophenone (IV), which resembles the similarly hindered acetomesitylene in that it fails to give the usual carbonyl reactions.[3] Attempts to prepare the 2,4-dinitrophenylhydrazone and oxime derivatives of 2,6-dimethylacetophenone failed.



The infrared spectrum of 2,6-dimethylacetophenone shows strong ketocarbonyl absorption at 5.95 μ and an intense band at 12.9 μ, the latter being characteristic of the vicinal trisubstituted benzene ring. The ultraviolet spectrum of acetophenone (Fig. 1) displays well-defined absorption at 239 mμ, whereas acetomesitylene and 2,6-dimethylacetophenone show poorly-defined absorption in the ultraviolet, with maximum absorption well below 240 mμ.[4] These spectra are consistent with the concept of steric inhibition of resonance owing to diortho substitution, which inhibits coplanarity of the "first excited state" (ionic state), thus increasing the energy of the ionic state relative to the ground state and shifting the absorption maximum to shorter wave lengths.

Kohler, Stone and Fuson[5] made use of the Grig-

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[1] Presented before the 124th meeting of the American Chemical Society, Chicago, Illinois, September 6–11, 1953.

[2] R. C. Fuson, N. Rabjohn, W. J. Schenk and W. E. Wallace, *J. Org. Chem.*, **9**, 187 (1944).

[3] P. de Jong, *Rec. trav. chim.*, **61**, 539 (1942); L. I. Smith and C. Guss, THIS JOURNAL, **59**, 804 (1937).

[4] M. T. O'Shaughnessy and W. H. Rodebush, *ibid.*, **62**, 2906 (1940).

[5] E. P. Kohler, J. F. Stone and R. C. Fuson, *ibid.*, **49**, 3181 (1927).