sulfate, contained in a glass-stoppered bottle. The aldehydes reacted more vigorously than the ketones. The mixture was maintained at 5° for twenty hours and then at room temperature for four hours, whereupon it was poured into 50 cc. of ice and water in a separatory funnel. The water-insoluble layer was washed consecutively with 10% aqueous sodium hydroxide and water, and dried with sodium sulfate. This crude product was used directly for the hydrogenolysis. The yields were nearly quantitative.

Hydrogenolysis of Benzaldehyde Diethyl Thioacetal.—The hydrogenolysis was carried out on 0.01 mole of the thioacetal as described in procedure A. After a reaction period of two hours, the mixture was diluted with 300 cc. of water and distilled until the cessation of ethanol distillation. The process was repeated on the distillate and to the azeotrope distilling over was added sufficient water to separate the toluene which was collected, dried and distilled; yield 0.60 g. (65%), b. p. 110° at 750 mm., $n^{25}\text{D}$ 1.498. The generally accepted constants for toluene are: b. p. 111° at 760 mm., $n^{16}\text{D}$ 1.4978.

Hydrogenolysis of Acetophenone Diethyl Thioacetal.—The thioacetal (0.01 mole) was treated in the manner described above for the hydrogenolysis of benzaldehyde diethyl thioacetal; yield of ethylbenzene 0.70 g. (66%). b. p. 134° at 750 mm., $n^{25}\text{D}$ 1.498. The accepted constants for ethylbenzene are: b. p. 136° at 760 mm., $n^{14.6}\text{D}$ 1.4983.

Hydrogenolysis of Heptanone-2 Diethyl Thioacetal.—The hydrogenolysis was carried out on 0.01 mole of the thioacetal as described in procedure A. The reaction product was distilled out of the reaction mixture, the distillate was diluted with a large volume of water and extracted twice with ether. The ether extract was washed with 50% calcium chloride aqueous solution, then with water, dried over sodium sulfate and distilled; yield 0.50 g. (50%), b. p. 96–100° at 750 mm., $n^{25}\text{D}$ 1.390. The accepted constants for heptane are: b. p. 98.4° at 760 mm., $n^{23}\text{D}$ 1.3867.

Hydrogenolysis of Heptanal Diethyl Thioacetal.—The thioacetal (0.01 mole) was treated in the manner described above for the hydrogenolysis of heptanone-2 diethyl thioacetal; yield of heptane 0.40 g. (40%), b. p. 98–100° at 750 mm., $n^{25}\text{D}$ 1.395.

Hydrogenolysis of Benzophenone Diethyl Thioacetal.—The thioacetal (0.01 mole) was subjected to hydrogenolysis as described in procedure A. The sirup obtained on solvent removal from the centrifugate was dissolved in ether, dried with sodium sulfate, and the solvent removed; yield 1.3 g. (77%), b. p. 255° at 740 mm. A boiling point of 261–262° at 760 mm. is recorded for diphenylmethane. Further identification was afforded by the preparation[24] of the 2,4,2',4'-tetranitro derivative which after two recrystallizations from glacial acetic acid melted at 170–173° (accepted value 172°).

Identification of Acetaldehyde Formed During the Hydrogenolysis.—In one of the experiments (the hydrogenolysis of heptanal diethyl thioacetal) the gases escaping from the top of the condenser during the refluxing were bubbled through 5 cc. of a solution of 2,4-dinitrophenylhydrazine (1 g. of the hydrazine dissolved in 7 cc. of concentrated sulfuric acid, then diluted with 100 cc. of methanol followed by 25 cc. of water). After one hour, crystalline needles separated which after two recrystallizations from ethyl acetate–ethanol were identified as acetaldehyde 2,4-dinitrophenylhydrazone by melting point (161–163°) and mixed melting point (unchanged) with an authentic sample (m. p. 162–164°).

Summary

1. It is shown that the carbonyl group of aldehydes and ketones may be reduced to the hydrocarbon stage by the hydrogenolysis of their thioacetals with Raney nickel in dilute ethanol solution.

2. Examples are cited for the diethyl thioacetals of *aldehydo*-D-galactose (and its pentaacetate), *aldehydo*-D-glucose pentaacetate, *keto*-D-fructose pentaacetate, benzaldehyde, heptanal, heptanone-2, acetophenone and benzophenone.

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[24] Shriner and Fuson, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 2nd ed., 1940, p. 163.

COLUMBUS, OHIO RECEIVED MARCH 8, 1944

[CONTRIBUTION FROM THE EASTERN REGIONAL RESEARCH LABORATORY[1a]]

Pyrolysis of Nicotine to Myosmine

BY C. F. WOODWARD, ABNER EISNER AND PAUL G. HAINES

Two new processes have been developed in this Laboratory for the preparation of nicotinic acid from nicotine. One involves the catalytic, vapor-phase, air oxidation of nicotine to nicotinonitrile,[1b] which is hydrolyzable to either nicotinic acid[2] or nicotinamide,[3] whereas the second employs the catalytic, liquid-phase, sulfuric acid oxidation of nicotine directly to nicotinic acid.[4]

It appeared that an alternative method could be employed for a stepwise conversion of nicotine to nicotinic acid which would utilize a preliminary pyrolysis of the alkaloid to β-alkyl and β-alkenyl pyridines prior to oxidation of these products.

This paper discloses the results obtained in a study of the pyrolytic reaction. Preliminary experiments indicated that the yields of such products as β-picoline, β-ethylpyridine, and β-vinylpyridine were too low to justify the utilization of this reaction in the preparation of nicotinic acid from nicotine. This investigation revealed, however, that myosmine (III) can be produced in fair yields, and most of the data herein reported were obtained in an attempt to determine the optimum pyrolytic conditions for the production of this rare alkaloid.

Brief references to the pyrolysis of nicotine have been made previously by Cahours and Étard,[5] but the two experiments reported were

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(1) (a) This is one of four Regional Research Laboratories operated by the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, United States Department of Agriculture. Article not copyrighted.

(1) (b) Woodward, Badgett and Willaman, accepted for publication in *Ind. Eng. Chem.*

(2) McElvain and Goese, THIS JOURNAL, **63**, 2283 (1941).

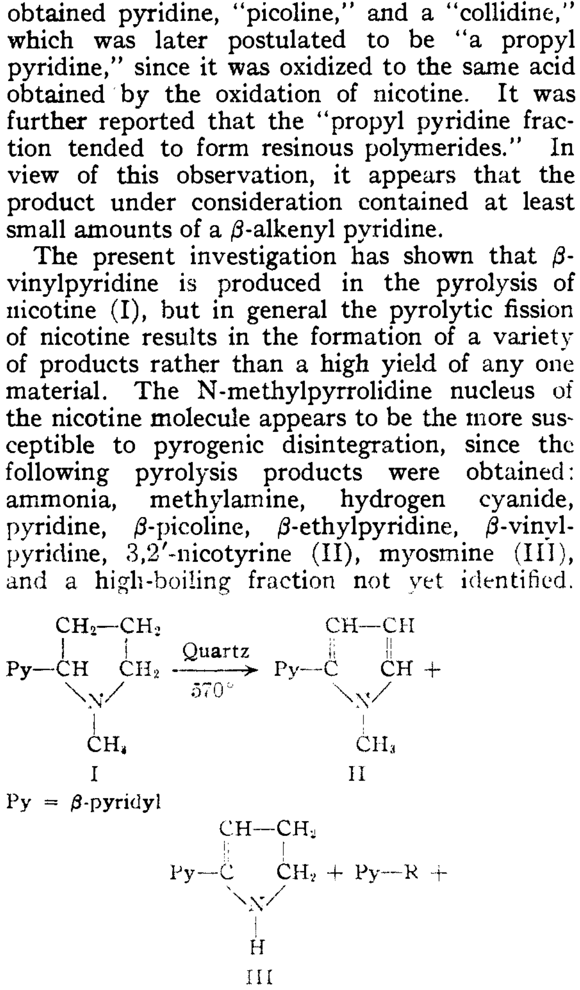
(3) Krewson and Couch, *ibid.*, **65**, 2256 (1943).

(4) Woodward, Badgett and Kaufman, accepted for publication in *Ind. Eng. Chem.*

(5) Cahours and Étard, *Compt. rend.*, **90**, 275 (1880); **92**, 1079 (1881).

apparently only incidental to the investigation of the reaction of nicotine with sulfur and selenium. In these procedures, nicotine was passed through an iron pipe filled with porcelain chips while the reactor was "heated to dark red" on one occasion and to "cerise red" in the other experiment. In addition to appreciable quantities of unchanged nicotine, these investigators obtained pyridine, "picoline," and a "collidine," which was later postulated to be "a propyl pyridine," since it was oxidized to the same acid obtained by the oxidation of nicotine. It was further reported that the "propyl pyridine fraction tended to form resinous polymerides." In view of this observation, it appears that the product under consideration contained at least small amounts of a β-alkenyl pyridine.

The present investigation has shown that β-vinylpyridine is produced in the pyrolysis of nicotine (I), but in general the pyrolytic fission of nicotine results in the formation of a variety of products rather than a high yield of any one material. The N-methylpyrrolidine nucleus of the nicotine molecule appears to be the more susceptible to pyrogenic disintegration, since the following pyrolysis products were obtained: ammonia, methylamine, hydrogen cyanide, pyridine, β-picoline, β-ethylpyridine, β-vinylpyridine, 3,2′-nicotyrine (II), myosmine (III), and a high-boiling fraction not yet identified.



Py = β-pyridyl

HCN, NH_3 and CH_3NH_2

R = CH_3, C_2H_5 and C_2H_3 (vinyl)

The pyrolysis of nicotine over quartz at 570° produced a fair yield of myosmine but only small quantities of other identifiable reaction products. Pyridine was not isolated under these experimental conditions, but it was produced in low yields when the pyrolysis temperature was increased to 700° or when the quartz contact material was replaced by activated alumina at 500°. These latter conditions were too drastic for the obtention of myosmine.

In addition to being the principal pyrolysis product obtained with a quartz contact material at 570°, myosmine was of particular interest from an historical as well as a theoretical viewpoint. This base was first isolated from cigar smoke by Wenusch and Schoeller,[6] and since the alkaloid had never been found in the *Nicotiana* genus it was postulated by these investigators that myosmine was probably formed from nicotine during the smoking process. Although our experiments were conducted in the absence of air, the pyrolysis of nicotine to myosmine lends some credence to this theory.

The myosmine obtained from cigar smoke was assigned formula III by Späth, Wenusch, and Zajic.[7] This structural configuration was later confirmed synthetically by Späth and Mamoli.[8] N-Benzoylpyrrolidone was condensed with ethyl nicotinate, and the resulting 3-nicotinyl-N-benzoylpyrrolidone-2 was heated with concentrated hydrochloric acid. The latter reaction involved hydrolysis, decarboxylation, and ring closure to the desired product (III). Myosmine was prepared by a similar procedure in the present investigation, and the picrate derivative was found to be identical with the picrate of the pyrolysis material.

A study of the pyrolytic reactions of nicotine and resulting products, such as nicotyrine, directs attention to the pyrogenic behavior of N-substituted pyrroles and pyrrolidines. The pyrolysis of N-substituted pyrroles yields two types of reaction products. One reaction course, exemplified by the isomerization of N-acetylpyrrole to 2-acetylpyrrole, involves a migration of the substituting group from the 1 to 2 position.[9] The pyrogenic conversion of N-methylpyrrole to pyridine illustrates a second reaction type resulting in ring enlargement.[10] In this reaction the formation of a six-membered ring is apparently preceded by isomerization to 2-methylpyrrole. Similar reactions have not been reported in the pyrrolidine series.

Insofar as the authors are aware, the pyrolytic conversion of nicotine to myosmine is a new type of reaction. Since the formation of methane was not established, it is not known whether myosmine is produced by the direct elimination of methane from nicotine or by a more involved reaction. The fact that Meisenheimer and Schütze[11] obtained fair yields of methane and 2-propylquinoline by continued refluxing of N-methyl-2-propyldihydroquinoline at 270° may be indicative of the simpler reaction mechanism.

Experimental

Apparatus.—The iron reactor employed in most of the pyrolysis experiments consisted of a 4-foot length of 1-inch iron pipe maintained in a vertical, tubular, electrically heated furnace. An iron "Y" tube was connected to the upper opening of the reactor. The top of the vertical side of this fitting was provided with a cap, which served as a support for a sealed-in iron thermocouple well. The

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(6) Wenusch and Schoeller, "Fachliche Mitteilungen der Österreichischen Tabakregie," **2**, 15 (1933).

(7) Späth, Wenusch and Zajic, *Ber.*, **69**, 393 (1936).

(8) Späth and Mamoli, *ibid.*, **69**, 757 (1936).

(9) Ciamician and Magnaghi, *ibid.*, **18**, 416, 1828 (1885).

(10) Pictet, *ibid.*, **37**, 2792 (1904); **38**, 1947 (1905).

(11) Meisenheimer and Schütze, *ibid.*, **56**, 1353 (1923).

other opening of the "Y" tube was employed for addition of the nicotine. The thermocouple well was centered in the iron reactor and extended down through a bed of quartz chips. This well was supplied with a movable thermocouple in order that the temperature could be determined at any point within the heated zone. About 350 cc. of 4- to 6-mesh quartz chips was maintained in a 34-inch length of the heated reactor. At a maximum temperature of 570° within the quartz bed, a 15° temperature differential (555-570°) was observed over a 12-inch length of the reactor. The volume of quartz within this temperature range was 124 cc., and this value was employed in the corresponding space-velocity calculations below. The bottom of the reactor was connected to a receiving train, which consisted in turn of a 1-liter 2-neck flask immersed in an ice-bath, a water-cooled condenser, a dry-ice trap, and an exhaust tube leading to a well-ventilated hood. In experiments at 550° or lower, the iron reactor was replaced by a Pyrex-glass tube of equal size.

Procedure.—The following data, unless otherwise indicated, were taken from Experiment 6 (Table I) to illustrate the experimental procedure. Nitrogen was passed through the apparatus for a period of fifteen minutes before the pyrolysis. Two hundred and fourteen grams of nicotine was then added, at a uniform rate over a period of one hundred and ninety minutes, to the iron reactor, which was maintained at a temperature of 570°. Although a total of 350 cc. of 4- to 6-mesh quartz was employed as a contact material in the heated reactor, only 124 cc. of this volume was within the temperature range of 555-570°. After all the nicotine had been added, the apparatus was again flushed with nitrogen to remove volatile products from the reactor.

The 201 g. of liquid condensate collected in the ice-cooled receiver was fractionally distilled through a helix-packed column (2.2 × 50 cm.) equipped with a reflux head. Several of the fractions were obtained in too small a quantity to be reliably identified by redistillation. In view of these small amounts and the possibility of an azeotropic distillation, each fraction was characterized by means of its picric acid derivative.

Identification of Pyrolysis Products

The identity of the derivatives of all pyrolysis products reported below was confirmed by the fact that the melting points remained unchanged when the derivatives were mixed with authentic specimens.

Myosmine and Nicotyrine.—Since this investigation resolved itself into a determination of the optimum pyrolytic conditions for the production of myosmine, the data relating particularly to myosmine are summarized in Table I. In view of the fact that other identified pyrolysis products were obtained in low yields in all experiments, these values have not been included in the table. Thirty grams of myosmine distilled at 119.0 to 130.0° (4.3 mm.). After recrystallization from water, the picric acid derivative of this fraction melted at 183.0 to 184.0°. An additional 5 g. of myosmine was obtained from higher boiling fractions. On cooling to 5°, all these fractions crystallized. The 35 g. represents an 18.1% conversion on the basis of the weight of the original nicotine and 33.3% of the theoretical yield on the basis of nicotine consumed in the pyrolysis experiment. A 90% recovery of pure product could be obtained by twice recrystallizing the combined myosmine fractions from petroleum ether cooled in an acetone-dry-ice mixture.

TABLE I

EFFECT OF PYROLYLIC CONDITIONS ON YIELDS OF MYOSMINE

Expt.	Max. temp., °C.	Nicotine, g.	Time, min.	Space velocity[a]	Myosmine produced, % of theoretical On basis of nicotine added	Myosmine produced, % of theoretical On basis of nicotine destroyed
1[b]	500	201.8	170	166	2.33	13.0
2[b]	600	200.6	220	144	17.5	24.6
3[c]	700	200.3	240	199	0	0
4[c]	600	213.5	200	228	16.4	21.0
5[c]	650	218.4	190	259	3.3	..
6[c]	570	214	190	233	18.1	33.3
7[c]	550	220	325	136	16.5	31.5
8[c]	570	611	380	332	14.1	28.9

[a] Cc. of nicotine at reaction temperature per hour divided by cc. of contact material. [b] Glass reactor used. Iron reactor used.

To remove steam-volatile bases, the crude myosmine was subjected to steam distillation through a six-ball Snyder column. Although Wenusch and Schoeller[6] reported myosmine to be steam volatile, it was observed that the alkaloid did not distill azeotropically with water. With an efficient fractionating column, the base was still retained in the distillation flask when test portions of the aqueous distillate were no longer alkaline. This is in agreement with Smith's observations[12] that nicotine distilled azeotropically with water while nornicotine and anabasine did not. The latter two alkaloids contain a cyclic secondary amino group, as does myosmine.

Portions of the steam distillate were taken at varying intervals and treated with picric acid. The melting points of the picrates showed that nicotine was the principal contaminant in the early stages of the distillation, while traces of 3,2′-nicotyrine were obtained in subsequent portions. The suspected nicotyrine picrate melted at 169.0 to 170.0°.

The steam-distillation residue was made strongly alkaline and extracted many times with ether. The ether extract was dried over anhydrous sodium carbonate and filtered, and the filtrate was then saturated with dry hydrogen chloride until precipitation was complete. The filtered myosmine dihydrochloride was dissolved in sodium hydroxide. Pure myosmine was obtained by extracting the alkaline solution with ether, drying the extract over anhydrous sodium carbonate, removing the drying agent by filtration, and then evaporating the solvent. After being pressed on a porous plate, the residual myosmine melted at 44.0 to 45.0°, which is in agreement with the melting point reported by Späth and Mamoli.[8] *Anal.* Calcd. for $C_9H_{10}N_2$: C, 73.97; H, 6.85; N, 19.18. Found: C, 73.74; H, 6.87; N, 19.38. The picric acid derivative melted at 183.0 to 184°, which agrees with the melting point observed by Späth, Wenusch and Zajic.[7]

The identity of this material was conclusively established by comparison with the picrate of synthetic myosmine. Three and four-tenths grams of N-benzoylpyrrolidone-2 was condensed with 2.7 g. ethyl nicotinate, according to the method of Späth and Mamoli.[8] The reaction mixture was then refluxed for forty-two hours with 60 cc. of 48% hydrobromic acid. After the acid reaction mixture was made strongly alkaline, the solution was thrice extracted with ether, and the ether extract was then dried over anhydrous calcium sulfate. The drying agent was then removed by filtration, and the filtrate was concentrated on a steam-bath. The 0.7 g. of residual oil was treated with an aqueous solution of picric acid. After two recrystallizations from water, the precipitated picrate melted at 183.0 to 184.5° and was identical with the picrate from the purified pyrolysis product because the mixture had the same melting point.

Hydrogen Cyanide, Ammonia and Methylamine.—The presence of hydrogen cyanide in the pyrolysis products was detected in the exit gases. Distillation of the liquid condensate in the receiver resulted in the sublimation of ammonium cyanide, which crystallized on the cold finger of the reflux head. The formation of ammonia in pyrolysis Experiment 4 was confirmed by allowing the products collected in the dry-ice trap to distill into water. Phenyl thiourea melting at 156 to 157.5° was produced when the solution was treated with phenyl isothiocyanate. A similar procedure in Experiment 7 resulted in the formation of methyl phenyl thiourea, which melted at 112 to

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(12) Smith, *Ind. Eng. Chem.*, **34**, 231 (1942).

113°, and thereby established the presence of methylamine.

Pyridine.—Pyridine was not isolated from the pyrolysis products of nicotine over quartz at temperatures of 600° or lower. Pyridine was obtained, however, when nicotine was pyrolyzed at 700° in the presence of quartz or at 500° over activated alumina. The picric acid derivative melted at 168.5 to 170°.

β-Picoline.—Only 1.4 g. of the product distilled at 100 to 135°. Although this fraction appeared to have no definite boiling point, it was shown to be principally β-picoline by its picric acid derivative, which melted at 148.0 to 149.0°. The 4.1 g. distilling at 135.0 to 155.0° was shown to be β-picoline by the same procedure.

β-Ethylpyridine.—The 7.0-g. fraction distilling at 155 to 180° was probably a mixture of β-ethylpyridine and β-vinylpyridine. Repeated recrystallization of the picric acid derivative of this fraction did not yield a pure picrate. Redistillation of the fraction gave a distillate which again yielded an inseparable mixture of picrates, while the residue in the distillation flask yielded a picrate melting at 141 to 143°. The latter compound was identical with β-vinylpyridine picrate.

In Experiment 8, however, the fraction distilling at 155 to 180° yielded a picrate which melted at 128.0 to 129.5°. Since this is the reported melting point of β-ethylpyridine picrate, a synthetic sample of β-ethylpyridine was prepared by the following procedure:

A solution of 7.6 g. of β-acetylpyridine hydrochloride[13] dissolved in 30 ml. of water was added to a solution of 5.6 g. of semicarbazide hydrochloride and 8.0 g. of sodium acetate in 30 ml. of water. After being warmed on the steam-bath for twenty minutes and then cooled in an ice-bath, the semicarbazone acetate salt precipitated. The yield of product after drying *in vacuo* was 13.1 g.

The semicarbazone acetate salt was reduced to β-ethylpyridine by the general method of Wolff and Kishner. Thirteen grams of the semicarbazone acetate salt was mixed with 15.6 g. of sodium ethylate in a distillation flask, which was then heated in an oil-bath. As the oil-bath temperature was gradually increased to 180°, a few grams of liquid distilled which had the smell of alcohol and formed no picrate. The 2.8 g. of liquid distillate obtained at a bath temperature of 180 to 220° formed a picrate melting at 128.5 to 130.0° (cor.) after two crystallizations from water. Stoehr[14] reported 128.0 to 130.0° as the melting point of β-ethylpyridine picrate. The melting point was not depressed when this picrate was mixed with the suspected β-ethylpyridine picrate from the nicotine pyrolysis.

β-Vinylpyridine.—About 0.7 g. of the pyrolysis product distilled at 57.0 to 66.0° (2.7 mm.). The picric acid derivative melted at 142.0 to 144.0°, which is in agreement with the reported melting point of β-vinylpyridine picrate. An authentic sample of β-vinylpyridine was prepared by the dehydration of 3-(α-hydroxyethyl)-pyridine with phosphorus pentoxide.[15] The picrate of the synthetic material melted at 142.0 to 144.0°, and was identical with the picric acid derivative of the pyrolysis product.

Nicotine.—A total of 97.4 g. of unchanged nicotine was recovered from the reaction mixture. The major portion distilled at 104 to 109° (4.9 mm.). The limited number of experiments herein reported indicated that the highest yields of myosmine were obtained under experimental conditions which did not completely destroy the nicotine.

Unidentified Fraction and Residue.—The 4.1-g. fraction distilling at 152.0 to 165.0° (2.8 mm.) was not soluble in water or distillable with steam. No crystalline derivatives were obtained with methyl iodide or picric acid.

The 46.0 g. of distillation residue solidified to an amorphous mass on cooling. No nicotinic acid was isolated from the oxidation products when this residual, resinous material was oxidized with alkaline permanganate. This negative result may indicate that the pyridine nucleus of the nicotine molecule was partially destroyed in the pyrolysis but no conclusive evidence was obtained to confirm this assumption.

Summary

1. Ammonia, methylamine, hydrogen cyanide, pyridine, β-picoline, β-ethylpyridine, β-vinylpyridine, and 3,2′-nicotyrine have been obtained in small quantities from the pyrolysis products of nicotine.

2. Myosmine, a comparatively rare alkaloid, has been obtained in fair yields by the pyrolysis of nicotine over quartz at 570°.

3. A new synthesis of β-ethylpyridine is described.

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[13] Strong and McElvain, THIS JOURNAL, **55**, 816 (1933).

[14] Stoehr, *J. prakt. Chem.*, [2] **45**, 38 (1892).

[15] Iddles, Lang and Gregg, THIS JOURNAL, **59**, 1945 (1937).

PHILADELPHIA, PA. RECEIVED FEBRUARY 7, 1944

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Dissociation of Hexaarylethanes. XVI.[1] Alkyl and Halogen Derivatives

BY C. S. MARVEL, H. W. JOHNSTON, J. W. MEIER, T. W. MASTIN, JOHN WHITSON AND CHESTER M. HIMEL

Earlier papers in this series[2] have shown that in general unsymmetrically substituted hexaarylethanes are less dissociated than are closely related symmetrically substituted ethanes. Thus, di-*p*-*t*-butylphenyltetraphenylethane is dissociated to the extent of 7.5 ± 1% and tetra-*p*-*t*-butylphenyldiphenylethane to the extent of 8.5 ± 1% under the same conditions where hexa-*p*-*t*-butylphenylethane is dissociated to the extent of 20–25%.[2] Likewise di-*p*-tolyl-tetra-*p*-*t*-butylphenylethane and di-*p*-*t*-butylphenyl-tetra-*p*-tolylethane show equal degrees of dissociation of 5 ± 1%. We were accordingly very much surprised to find in the present work that a variety of alkyl substituted hexaarylethanes with mixed *m*- and *p*-substitution showed in general a higher degree of dissociation than many related hexa-*p*-alkylphenylethanes. We have no theory to account for the unexpected values which are reported here, for the work was stopped before a sufficiently large variety of compounds could be studied to make generalization significant.

The *p*-*t*-butyl group seems to have a very marked effect in promoting dissociation in the

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[1] For the fifteenth communication in this series, see THIS JOURNAL, **66**, 415 (1944).

[2] Marvel, Kaplan and Himel, THIS JOURNAL, **63**, 1892 (1941); Marvel and Himel, *ibid.*, **64**, 2227 (1942).