[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, CASE INSTITUTE OF TECHNOLOGY]

Reaction of Ferric Chloride with Sterically Hindered Aromatic Compounds[1]

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The reaction of anhydrous ferric chloride with sterically hindered aromatic compounds was studied. With mesitylene, the principal products were chloromesitylene and bimesityl. The effect of solvents, catalysts, and temperature was determined. 2,2′,3,3′,4,4′,5,5′,6-Nonamethyldiphenylmethane was the only product isolated from the pentamethylbenzene reaction. Nuclear chlorination leading to penta- and hexachlorobenzene occurred with 1,2,4,5-tetrachlorobenzene. The nature of the products is correlated with structure of the aromatic reactants, and the chemistry of the various processes is discussed.

In previous publications[2,3] the interaction of ferric chloride with simple aromatic compounds, including benzene, halobenzenes, and monoalkylbenzenes, has been reported, together with a discussion of the chemistry of the various processes involved.

The present work concerns a study of the reaction of ferric chloride with sterically hindered benzene derivatives with the aim of obtaining additional evidence to elucidate the reaction mechanisms. Mesitylene, pentamethylbenzene, and 1,2,4,5-tetrachlorobenzene were chosen for investigation in this connection.

RESULTS

Mesitylene. Mesitylene was found to react readily with ferric chloride at room temperature, yielding 26–28% of chloromesitylene, 30–38% of bimesityl, and small quantities of high-boiling oil and polymer (Table I). Chloromesitylene and bimesityl were identified by analysis, physical properties, infrared spectra, and conversion to known derivatives. The high-boiling oil contains chlorine, and appears to be a mixture from which a solid was isolated in certain instances, whose analysis corresponds to that of dichlorobimesityl.

At temperatures appreciably above room temperature, the yield of bimesityl decreased markedly, whereas the yield of chloromesitylene remained essentially constant. In the presence of catalytic amounts of aluminum chloride, chlorination was favored in accord with previous findings involving other aromatic compounds.[2,4] The use of aromatic solvents did not affect the yield of chloromesitylene in most cases, but decreased that of bimesityl. Except for some increase in the amount of polymer and a small decrease in the yield of bimesityl, the presence of oxygen did not alter the mode of reaction.

Pentamethylbenzene. The reaction of pentamethylbenzene with ferric chloride began at 20°, but proceeded very slowly even at 70°. Only a low yield of a crystalline product was obtained which was shown to be 2,2′,3,3′,4,4′,5,5′,6-nonamethyldiphenylmethane by analysis, molecular weight, infrared and NMR spectra, and comparison with authentic material. Synthesis of authentic material was accomplished by the Friedel-Crafts condensation of pentamethylchloromethylbenzene with 1,2,3,4-tetramethylbenzene in the presence of aluminum chloride. The $C_{22}H_{30}$ hydrocarbon is inert to bromine under conditions whereby pentamethylbenzene reacts with facility.

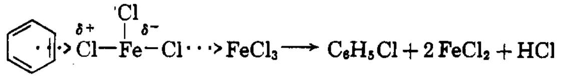
There was no evidence of products arising from nuclear chlorination or biaryl formation in the ferric chloride–pentamethylbenzene reaction.

1,2,4,5-Tetrachlorobenzene. Ferric chloride reacted[5] with 1,2,4,5-tetrachlorobenzene at 185° yielding mainly pentachlorobenzene in addition to some hexachlorobenzene. Under the drastic conditions some disproportionation may have occurred. No biphenyl-type product was found in the reaction mixture.

DISCUSSION

The competing chlorination and "dimerization" observed in the mesitylene–ferric chloride reaction bring to mind the report[6] by Yakubovich and Motsarev that phenylmagnesium bromide and ferric chloride can yield either chlorobenzene or biphenyl depending upon the reaction temperature and molar ratio of the reactants.

Several plausible routes for chlorination by ferric chloride deserve consideration. A possible pathway might involve direct attack by positive chlorine in the form indicated



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[1] Paper VII in the series, "Reactions of Metal Halides with Organic Compounds"; an abstract of a portion of the Ph.D. thesis of C. Wu, Case Institute of Technology, 1960.

[2] P. Kovacic and N. O. Brace, *J. Am. Chem. Soc.*, **76**, 5491 (1954).

[3] P. Kovacic, C. Wu, and R. W. Stewart, *J. Am. Chem. Soc.*, **82**, 1917 (1960).

[4] (a) P. Kovacic and C. Wu, unpublished work; (b) R. W. Stewart, M.S. thesis, Case Institute of Technology, 1957.

[5] V. Thomas, *Compt. rend.*, **126**, 1211 (1898).

[6] A. Y. Yakubovich and G. V. Motsarev, *J. Gen. Chem. (U.S.S.R.)*, **23**, 1059 (1953).

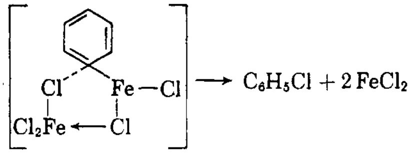
TABLE I

FERRIC CHLORIDE[a] AND MESITYLENE

C_9H_{12}, mole	Catalyst or Solvent, moles		Temp.	Time, hr.	Chloromesitylene, %[b]	Bimesityl, %[b]	Oil,[c] g.	Polymer, g.	
								Ether-insol.	Ether-sol.
1	—		18–30	1.5	28	38	3	0	4
1	—		115–120	1.5	30	10	3	2	7
1	—[d]		18–30	1	26	30	4	2.4	5
0.5[e,f]	$AlCl_3$	0.005	20	0.2[g]	51[h]	27	—[i]	0	1
0.5[e,f]	$AlCl_3$	0.005	75	0.2	88	14[h]	—[i]	0	4
0.5	C_6H_5Cl	2	16–19	2	29	19	3	2.4	8
0.5	C_6H_5Br	2	29–30	1.3	24	12	2[j]	1	3
0.5	C_6H_6	2	10–18	2	31	17	4	2.8	4
0.5	C_6H_6	3	60–70	1	57	9	2	0	3
0.5	$C_6H_5CH_3$	2	16–20	1	36	15	2	2	2

[a] 0.5 mole. [b] Based on $FeCl_3$. [c] Contains chlorine; see Experimental. [d] Oxygen was bubbled beneath the surface throughout the reaction. [e] 0.25 mole of $FeCl_3$. [f] Experiment by F. J. Donat. [g] Then overnight in a refrigerator. [h] Crude. [i] Not determined. [j] Plus 0.5 g. of solid, m.p. 130.5–131.5°; see Experimental.

An alternative scheme entails intermediate formation of organo-iron compounds.[3] This type of intermediate may be visualized as a complex, analogous to the ferric chloride dimer, which undergoes decomposition as illustrated.



Bulky groups in the *ortho* position, as in mesitylene, might well hinder the process to the extent that a competing reaction—biaryl formation—could occur.

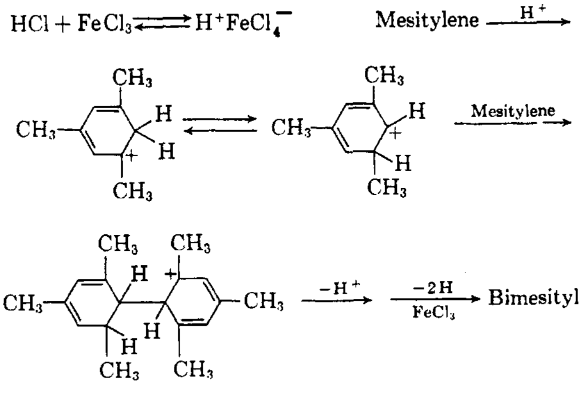
The presence of bimesityl suggests a mesityl radical precursor, since biaryls quite commonly arise by radical dimerization. In accord with this theoretical approach, the organo-iron intermediate is postulated to undergo homolytic dissociation in order to relieve the steric strain.

$$2MesFeCl_2 \xrightarrow[-2FeCl_2]{} 2Mes\cdot \longrightarrow \text{Bimesityl}$$

Assignment of an important role to steric factors would explain the absence of biaryls in the reaction[2,3] of ferric chloride with benzene and monosubstituted benzenes. It is also relevant to note that aryl radicals are known[7,8] to form aryl halides by reaction with ferric chloride or cupric chloride. Because of the high energy level of the aryl radical and the well known reactivity of α-hydrogens, it seems unlikely that ferric chloride would function by direct abstraction of nuclear hydrogen atoms from mesitylene. However, we have been unable to obtain evidence for the presence of a mesityl radical. No "mixed" biaryl was found when the mesitylene–ferric chloride reaction was carried out in a variety of aromatic solvents. Aromatic substitution by aryl radicals is a well established phenomenon. Although there was some increase in the amount of polymeric product, the yields of bimesityl and chloromesitylene were essentially unaffected by the presence of oxygen in the reaction mixture. Aryl radicals are reported[7,8] to react with oxygen to form phenols.

The comments[9] of Kharasch and Reinmuth on the "coupling" of the Grignard reagent may be pertinent. Although some investigators have postulated that this is a free radical reaction, the preponderance of evidence is strongly to the contrary. They conclude[9] that these processes are essentially radical reactions of second (or higher) order, with respect to the organometallic intermediate, in which the "radicals" are not free to migrate. A similar situation may pertain to the present case of bimesityl formation.

An alternative,[10] somewhat preferred reaction scheme entails intermediate formation of a sigma-complex.



From this viewpoint, the synthesis bears a striking resemblance to the Scholl reaction and to inter-

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(7) J. K. Kochi, *J. Am. Chem. Soc.*, **78**, 4815 (1956).

(8) J. K. Kochi, *J. Am. Chem. Soc.*, **79**, 2942 (1957).

(9) M. S. Kharasch and O. Reinmuth, *Grignard Reactions of Nonmetallic Substances*, Prentice-Hall, Inc., New York, N. Y., 1954, pp. 118–120.

(10) Another possibility is intermediary formation of a radical-carbonium ion from mesitylene through direct oxidation by ferric chloride. This interpretation was independently suggested by the referee.

molecular dehydrogenation of aromatic compounds to biphenyl derivatives by the action of aluminum chloride.[11] A similar mechanism may pertain[11] in the case of aluminum chloride catalysis, with the exception of the nature of the dehydrogenation step. This proposal is identical with the initial stages of the mechanism advanced[4a] for the polymerization of benzene by ferric chloride.

Conversion to both chloro and biaryl derivatives has also been noted[12] in the reaction of certain naphthols with ferric chloride in aqueous solution. There is wide agreement that this general type of oxidative, nuclear coupling proceeds through initially formed aryloxy radicals.[13]

Apparent failure of pentamethylbenzene to undergo either chlorination or "coupling" in the presence of ferric chloride is another indication of the importance of steric factors. Isolation of 2,2′,3,3′,4,4′,5,5′,6 - nonamethyldiphenylmethane from the reaction mixture demonstrates selective involvement of the least hindered side-chain in formation of the diarylmethane.

No biaryl was obtained from 1,2,4,5-tetrachlorobenzene and ferric chloride, perhaps because of the smaller steric influence of the chlorine atoms, deactivation of the nucleus by the substituents, or the elevated temperature necessary for reaction.

In contrast with ferric chloride, antimony pentachloride effected[14] only nuclear chlorination with mesitylene and pentamethylbenzene.

It is worthwhile noting that the reaction of mesitylene with ferric chloride constitutes an improved route for bimesityl synthesis. The earliest recorded attempt[15] to prepare bimesityl involved the use of bromomesitylene in the Fittig method which, instead, yielded 3,3′,5,5′-tetramethylbibenzyl and 2,4,6,3′,5′-pentamethyldiphenylmethane. Ullmann and Meyer[16] first obtained bimesityl (12% yield) by treating iodomesitylene with copper powder at 260–270°. The "coupling" of mesitylmagnesium bromide in the presence of cupric chloride[17a] or cobalt bromide[17b] increased the yield to 20–22%, but several steps were still necessary. The one-step synthesis by the ferric chloride–mesitylene method proceeds smoothly at room temperature in 30–38% yield. The simplicity and improved yield make this the preferred method for bimesityl synthesis. It is interesting that Brown and Grayson[18] obtained very small amounts of bimesityl on attempted *t*-butylation of mesitylene in the presence of ferric chloride catalyst. However, they did not discuss the mode of formation of the unexpected product.

EXPERIMENTAL[19]

Materials. Reagent grade mesitylene and anhydrous, sublimed ferric chloride powder were from Matheson Coleman and Bell. Pentamethylbenzene (95% pure) was a gift from Sinclair Chemicals, Inc.[20] 1,2,4,5-Tetrachlorobenzene (Eastman Kodak Co.) was recrystallized from methanol, m.p. 139°.

Ferric chloride and mesitylene. Ferric chloride (0.5 mole) was allowed to react with mesitylene (1 mole) at 18–30° under a nitrogen atmosphere. The evolution of hydrogen chloride was rapid. After 1.5 hr. the reaction mixture was poured onto ice; the organic material was separated, washed with water, dried over anhydrous sodium sulfate, and distilled through a 12-in. helix-packed column. Chloromesitylene, wt. 10.4 g., was collected at 93° (18 mm.) with a center fraction having b.p. 205° (750 mm.), n_D^{30} 1.5216, d^{30} 1.0336; lit.[21,22] b.p. 204–206°, n_D^{30} 1.5212, d^{30} 1.0337.

Anal. Calcd. for $C_9H_{11}Cl$: C, 69.90; H, 7.17; Cl, 22.93. Found: C, 69.97; H, 7.15; Cl, 22.90.

Nitration with 2:1 sulfuric acid–nitric acid afforded a solid derivative, m.p. 177.5°; lit.[21] dinitro derivative, m.p. 178–179°.

Bimesityl was obtained at 100–110° (0.4 mm.), wt. 25 g., as slightly wet crystals, m.p. 95–98°. Repeated crystallization from methanol yielded colorless crystals, m.p. 100.5–101°, b.p. 297° (735 mm.); lit.[16] m.p. 100.5°, b.p. 296° (735 mm.).

Anal. Calcd. for $C_{18}H_{22}$: C, 90.70; H, 9.30. Found: C, 90.75; H, 9.27.

Two derivatives were prepared[23] according to the methods of Moyer and Adams[17a]: tetranitrobimesityl, m.p. 269–270°, lit. m.p. 270–271°; 3,3′-dibromobimesityl,m.p. 111–112.5°, lit. m.p. 112–113°.

From the mother liquor of bimesityl was obtained 3 g. of viscous oil which appeared to be a mixture of bimesityl and chlorinated material. The pot residue from distillation was a brown amorphous solid, wt. 4 g.

Ferric chloride and mesitylene: Catalytic and solvent effects. The data are summarized in Table I. The temperature at which hydrogen chloride was first detected from the mesitylene–ferric chloride reaction was 18° under an atmosphere of nitrogen or oxygen, 16° in chlorobenzene, bromobenzene or toluene solvent, and 10° in benzene solvent. The fractionation of organic product was performed through an 18 in. × 6 mm. spinning band column. After bimesityl had distilled, a colorless oil and then, in certain cases, a pale yellow solid were obtained. Since the colorless oils from all experiments were of similar composition according to the infrared spectra, they were combined and fractionated into several parts. Bimesityl was obtained from the forerun

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[11] C. A. Thomas, *Anhydrous Aluminum Chloride in Organic Chemistry*, Reinhold Publishing Corp., New York, N. Y., 1941, pp. 649–59; C. D. Nenitzescu and A. Balaban, *Ber.*, **91**, 2109 (1958).

[12] I. S. Ioffe, *J. Gen. Chem.* (*U.S.S.R.*), **7**, 2715 (1937); *Chem. Abstr.*, **32**, 2931 (1938).

[13] S. L. Cosgrove and W. A. Waters, *J. Chem. Soc.*, 1726 (1951).

[14] P. Kovacic and A. K. Sparks, *J. Am. Chem. Soc.*, **82** 5740 (1960).

[15] M. Weiler, *Ber.*, **33**, 334 (1900).

[16] F. Ullmann and G. M. Meyer, *Ann.*, **332**, 38 (1904).

[17] (a) W. W. Moyer and R. Adams, *J. Am. Chem. Soc.*, **51**, 630 (1929); (b) H. Gilman and M. Lichtenwalter, *J. Am. Chem. Soc.*, **61**, 957 (1939).

[18] H. C. Brown and M. Grayson, *J. Am. Chem. Soc.*, **75**, 20 (1953).

[19] Melting points and boiling points are uncorrected. Elemental analyses were determined by Drs. Weiler and Strauss, Oxford, England, and the NMR spectrum by Dr. L. F. Johnson, Varian Associates, Palo Alto, Calif.

[20] We wish to thank Dr. R. R. Chambers for samples of this material.

[21] V. R. Fittig and S. Hoogewerff, *Ann.*, **150**, 323 (1869).

[22] F. Brown, J. M. A. de Bruyne, and P. Gross, *J. Am. Chem. Soc.*, **56**, 1291 (1934).

[23] Experiment by F. J. Donat.

fractions. Microanalyses showed an increasing chlorine content with increasing boiling point, but apparently separation of chlorinated material from bimesityl was incomplete. The pale yellow solid (dichlorobimesityl?) obtained from the mesitylene–ferric chloride–bromobenzene reaction was recrystallized from ethanol as colorless needles, m.p. 130.5–131.5°.

Anal. Calcd. for $C_{18}H_{20}Cl_2$: C, 70.36; H, 6.56; Cl, 23.08. Found: C, 70.51; H, 6.64; Cl, 22.80.

Ferric chloride and pentamethylbenzene. The reaction of ferric chloride (0.25 mole) and pentamethylbenzene (0.5 mole) started at 20° but proceeded very slowly even at higher temperatures. The reaction mixture was kept at 20–50° for 2 hr., at 65–70° for another 2 hr., then treated with dilute hydrochloric acid, and filtered. The solid organic material was taken up in ether, leaving 4 g. of black, infusible solid. Distillation of the organic material gave an 83% recovery of pentamethylbenzene. Crystallization of the pot residue from cyclohexane yielded 4 g. of colorless crystals, m.p. 181.5–182°. The analytical sample melted at 182.5–183.5°.

Anal. Calcd. for $C_{22}H_{30}$: C, 89.80; H, 10.20; mol. wt., 270. Found: C, 89.82; H, 10.14; mol. wt., 271.

The presence of a single nuclear hydrogen was indicated by the infrared spectrum. The NMR spectrum revealed the presence of the following types of hydrogen in the indicated ratio: nuclear/methylene/methyl = 1/2/28.

This compound was inert to bromine in glacial acetic acid at room temperature in the presence of aluminum chloride; pentamethylbenzene yielded bromopentamethylbenzene readily under the same conditions. An attempt at nitration failed to yield the desired derivative.

Synthesis of 2,2′,3,3′,4,4′,5,5′,6-nonamethyldiphenylmethane. In 150 ml. of carbon disulfide were dissolved 4.4 g. (0.022 mole) of pentamethylchloromethylbenzene, m.p. 81.5–83° (prepared[24] by the method of Aitken, Badger, and Cook[25]), and 3 g. (0.022 mole) of 1,2,3,4-tetramethylbenzene (95% pure, Chemicals Procurement Co.). After introduction of 0.1 g. of aluminum chloride at 26°, the reaction mixture was allowed to stand for 17 hr. with occasional stirring. The organic layer was separated after addition of water, dried, and distilled to remove the solvent. The residue consisted of 0.7 g. of yellow crystals and 2 g. of brown oil which solidified on standing. The yellow crystals were crystallized twice from cyclohexane yielding colorless crystals, m.p. 179–180°. A mixture melting point with the crystalline product from the pentamethylbenzene–ferric chloride reaction was 180–181°. Their infrared spectra were identical. Isolation of pure material from the 2 g.-portion by attempted crystallization from cyclohexane was not successful.

Ferric chloride and 1,2,4,5-tetrachlorobenzene. The reaction of ferric chloride (0.25 mole) and the tetrachlorobenzene (0.5 mole) began at 185°. After being maintained at 185–198° for 2 hr., the hot reaction mixture was poured into dilute hydrochloric acid with stirring. The organic material was triturated repeatedly with dilute hydrochloric acid, and then distilled to remove unchanged tetrachlorobenzene. The majority of the distillation residue was dissolved in hot glacial acetic acid. About 1 g. of insoluble, gray crystals remained which was crystallized from methanol–acetic acid, m.p. 218–221°; lit.[5] hexachlorobenzene, m.p. 226°. The addition of aqueous alcohol to the original glacial acetic acid solution gave 13 g. of crude pentachlorobenzene, m.p. 70–80°. Recrystallization from glacial acetic acid and then from ethanol yielded colorless needles, m.p. 86.5–87°; lit.[5] m.p. 86°.

Acknowledgment. We gratefully acknowledge the support of this work by the National Science Foundation.

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(24) Prepared by C. E. Stephan.

(25) R. R. Aitken, G. M. Badger, and J. W. Cook, *J. Chem. Soc.*, 331 (1950).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, CASE INSTITUTE OF TECHNOLOGY]

Reaction of Ferric Chloride with Xylenes[1]

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The course of the ferric chloride–xylene reaction has been investigated. *p*-Xylene yielded 2,5,2′,5′,4″-pentamethyltriphenylmethane (I), in addition to chloro-*p*-xylene, (*p*-methylbenzyl)-*p*-xylene (II) and di(*p*-xylyl)methane (III). 4-Chloro-*m*-xylene and 2,2′,4,4′-tetramethylbiphenyl were obtained from *m*-xylene. The principal product from *o*-xylene consisted of polymer, along with 4-chloro-*o*-xylene in low yield. Yields of chloroxylene were in the order, *m*- $\gg$ *o*- $>$ *p*-xylene. Aluminum chloride in catalytic amounts promoted the chlorination reaction. Correlations are drawn between the nature of the products and structure of the aromatic reactant.

Studies of the reaction of ferric chloride with simple aromatic compounds, such as benzene, halobenzenes, and monoalkylbenzenes,[2–4] have shown that a number of competing reactions may occur: nuclear chlorination, side-chain attack leading to diphenylmethane-type compounds, disproportionation, and polymerization. Among the aromatic hydrocarbons, mesitylene is thus far unique in that biaryl formation also occurs.[5]

The present investigation was aimed at obtaining further insight into the relationship between mode of reaction and aromatic structure by extending the reaction scope to the xylenes.

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(1) Part VIII in the series, *Reactions of Metal Halides with Organic Compounds;* this paper is abstracted in part from the Ph.D. thesis of C. Wu, Case Institute of Technology, 1960.

(2) P. Kovacic and N. O. Brace, *J. Am. Chem. Soc.*, **76**, 5491 (1954).

(3) P. Kovacic, C. Wu, and R. W. Stewart, *J. Am. Chem. Soc.*, **82**, 1917 (1960).

(4) P. Kovacic and C. Wu, unpublished work.

(5) P. Kovacic and C. Wu, *J. Org. Chem.*, **26**, 759 (1961).