[Contribution from the School of Chemistry of the University of Minnesota]

THE JACOBSEN REACTION. V*

CLARENCE L. MOYLE and LEE IRVIN SMITH

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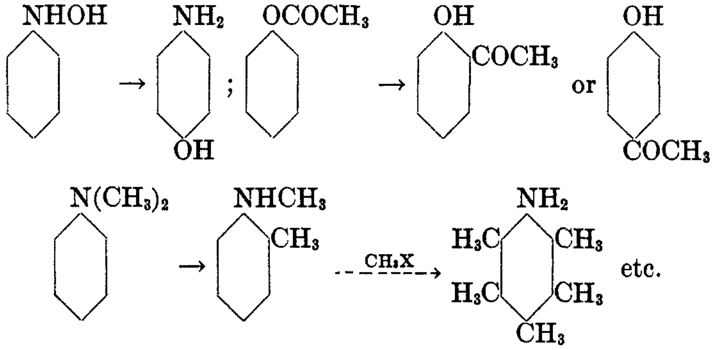
Many rearrangements of benzene derivatives are known in which a substituent migrates from some hetero element in a side-chain to a carbon atom of the ring; even carbon-to-carbon bonds can be established in this way. Thus:



Rearrangements in which the whole substituent migrates from one position to another in the ring are not so numerous, however. Chief among these are the migration of sulfonic acid groups, as in the well-known transformations of 1-naphthalenesulfonic acid into the 2-isomer; the migration of halogen atoms, and of alkyl groups. In the last case, a carbon-to-carbon bond is broken and another is reëstablished. The discussion which follows will deal with the last two types of rearrangement, and will be restricted to those benzene derivatives containing only halogen atoms, only alkyl groups, or a combination of the two, for these are the substances which undergo what has come to be known as the Jacobsen reaction, or the Jacobsen rearrangement. This name has been given to the rearrangement of the polyalkylbenzenes, the halogenated polyalkylbenzenes and the polyhalogenated benzenes which occurs when these substances are sulfonated and their sulfonic acids are allowed to stand in contact with sulfuric acid. The reaction consists in the migration of an alkyl group and/or halogen

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* Polymethylbenzenes XIX. Paper XVIII, *J. Am. Chem. Soc.* **59** (June, 1937).

atom, and was discovered by Oscar Jacobsen in 1886[1] although Herzig[2] was the first to study the rearrangement of *halogen* compounds in the presence of sulfuric acid. All of these rearrangements may be divided into two general types: (*a*) intramolecular, in which the migrating group moves from one position to another in the same molecule, and (*b*) intermolecular, in which there is a transfer of one or more groups from one molecule to another.

A. HYDROCARBONS

Migrations of alkyl groups in aromatic hydrocarbons are caused chiefly by two reagents: anhydrous aluminum chloride and concentrated sulfuric acid. Rearrangements caused by aluminum chloride do not constitute a phase of the Jacobsen reaction, but they are of interest in this connection because of the opposite orienting effects of the two reagents and because of the possibility of relationships between mechanisms for rearrangements caused by the two reagents. Aluminum chloride gives products in which the vicinal orientation of the substitutents is avoided, while sulfuric acid tends to produce the vicinal arrangement.

1. Migrations Produced by Aluminum Chloride

The common method of alkylating benzene by action of alkyl halides upon benzene derivatives in the presence of anhydrous aluminum chloride was discovered by Friedel and Crafts in 1884.[3] Shortly thereafter the methylation of benzene and its homologs was investigated in some detail by a number of workers, particularly by Oscar Jacobsen[4] and by Anschutz.[5] Jacobsen, as a result of his studies, set up the following diagram as representing the methylation of toluene.

$$\begin{tikzcd}
 & o\text{-Xylene} \arrow[dr] & & & \\
\text{Toluene} \arrow[ur] \arrow[r] \arrow[dr] & p\text{-Xylene} \arrow[r] & \text{Pseudocumene} \arrow[r] & \text{Durene} \arrow[r] & \text{Pentamethylbenzene} \\
 & m\text{-Xylene} \arrow[ur] \arrow[r] & \text{Mesitylene} \arrow[r] & \text{Isodurene} \arrow[ur] &
\end{tikzcd}$$

But Ador and Rilliet[6] could find no *o*-xylene in the product obtained by methylation of toluene, and he reported that this product consisted mainly (95 per cent.) of *m*-xylene together with a little (5 per cent.) *p*-xylene.

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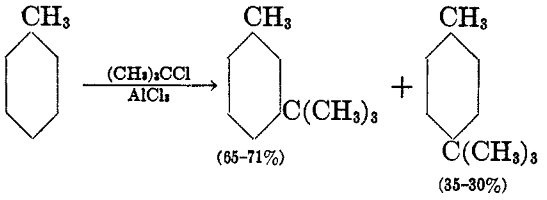
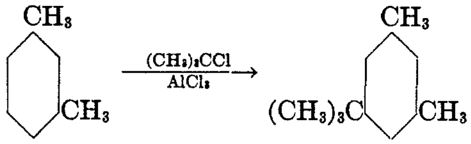
[1] JACOBSEN, *Ber.*, **19,** 1209 (1886).
[2] HERZIG, *Ber.*, **14,** 1205 (1881).
[3] FRIEDEL AND CRAFTS, *Ann. chim. phys.*, **1,** 449 (1884).
[4] JACOBSEN, *Ber.*, **14,** 2624 (1881).
[5] ANSCHUTZ, *Ann.*, **235,** 177 (1886).
[6] ADOR AND RILLIET, (*a*) *Ber.*, **11,** 1627 (1878); (*b*) *ibid.*, **12,** 329 (1879).

There was no hemimellitene (1, 2, 3) among the trimethylbenzenes, and no prehnitene (1, 2, 3, 4) among the tetramethyl benzenes. The latter statement has been verified[7] since a very careful search for prehnitene among the methylation products of (mixed) xylenes showed none present, while blank tests showed that as little as 1 per cent. of prehnitene could have been detected by the method used. There is much evidence—although some of it is conflicting—in other connections that in the Friedel-Crafts synthesis, meta derivatives are largely produced. Shoesmith and McGechen[8] obtained from toluene and *tert*-butyl chloride 65–71 per cent. *m-tert.*-butyltoluene and 35–30 per cent. of the para compound; and the well-known synthesis of 1,3-dimethyl-5-*tert.*-butylbenzene from *m*-xylene[9] is another example of meta alkylation in the Friedel-Crafts reaction. One would expect, in this case, the 1, 3, 4 isomer since this would conform to the usual orienting effects of the methyl groups in *m*-xylene. The production of the 1, 3, 5 isomer must therefore mean either that the methyl groups do not exert their usual directing effects, or that if the 1, 3, 4 compound is the primary product, it is subsequently rearranged to the 1, 3, 5 isomer by aluminum chloride. To decide this point[10] 1,3-dimethyl-4-*tert.*-butylbenzene was synthesized and subjected to the action of aluminum chloride. The only product which could be isolated (45 per cent. yield) was the 1, 3, 5 isomer.





The mechanism of this rearrangement can be viewed as an elimination of alkyl halide (since the Friedel-Crafts alkylation is known to be reversible) followed by a re-synthesis, according to the views of Anschutz[5] on methylation.

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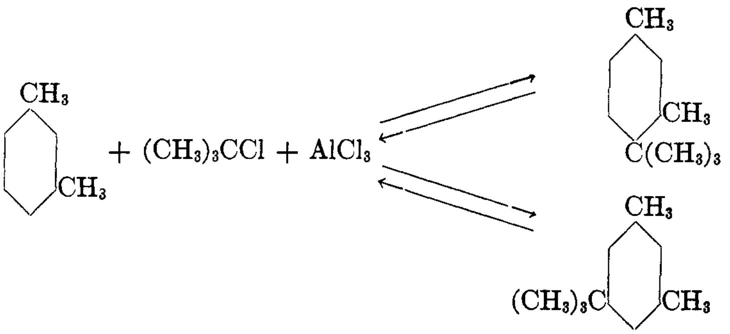
[7] O. W. Case, Ph.D. Thesis, University of Minnesota, **1931**.

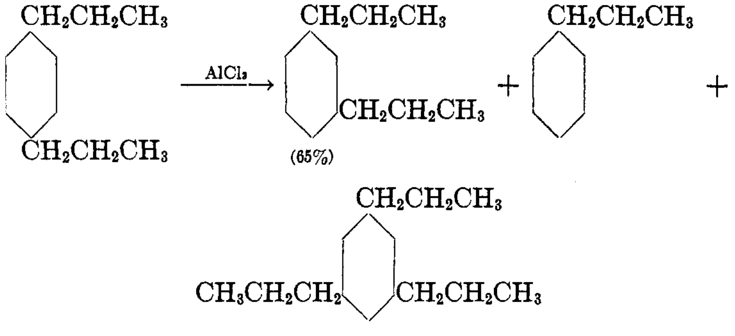
[8] Shoesmith and McGechen, *J. Chem. Soc.*, **1930**, 2231.

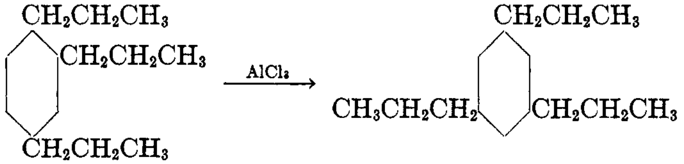
[9] Bauer, *Ber.*, **24**, 2840 (1891).

[10] Unpublished work by H. O. Perry of this laboratory.



But as Baddelcy and Kenner[11] have stated in a recent paper, such a mechanism would also involve the isomerization of the alkyl group in certain cases since, for example, aluminum chloride converts *n*-propyl chloride into isopropyl chloride. Accordingly they synthesized *m*- and *p*-di-*n*-propylbenzenes, as well as 1,2,4-tri-*n*-propylbenzene and subjected these hydrocarbons to the action of aluminum chloride.[12] The results were that the para compound was converted to the extent of about 65 per cent. into the meta compound in two hours at 100°; at the same time some *n*-propylbenzene and some 1,3,5-tri-*n*-propylbenzene were produced. Very little para compound was formed when the meta compound was so treated, but the 1,2,4-tripropyl derivative was largely converted into the 1, 3, 5 compound. In no case was any *isopropyl* derivative produced; hence the mechanism cannot involve the elimination of propyl chloride, either for the intramolecular rearrangement or for the intermolecular transfer of the propyl group.





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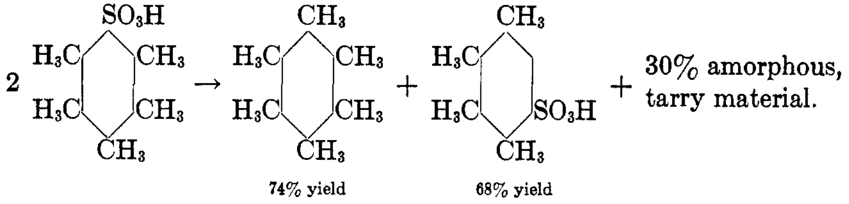
[11] Baddelcy and Kenner, *J. Chem. Soc.*, **1935**, 303.

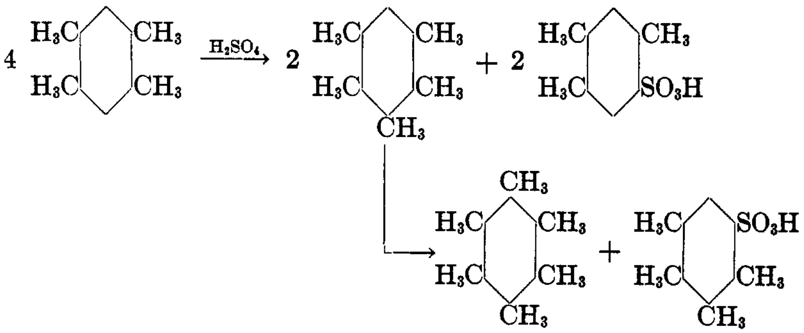
[12] See also Heise and Tohl, *Ber.*, **24**, 768 (1891).

2. Migrations Produced by Sulfuric Acid. (Jacobsen Rearrangements)

Pentamethylbenzene.[13, 14]—When pentamethylbenzene is allowed to stand in contact with concentrated sulfuric acid, the hydrocarbon first undergoes sulfonation, and then the sulfonic acid rearranges. This reaction is intermolecular and there is a transfer of a methyl group from one molecule to another.



Tetramethylbenzenes.[1, 15]—The first recorded rearrangement of a polymethylbenzene by sulfuric acid was reported by Jacobsen in 1886 in the case of durene. Jacobsen reported that durene was sulfonated by sulfuric acid slowly at 15–20° (6–10 hours) and rapidly at 80–100°, but that durenesulfonic acid in the presence of cold concentrated sulfuric acid was completely hydrolyzed to durene. When, however, durene or durenesulfonic acid was left at room temperature in contact with concentrated or fuming sulfuric acid for 4–8 days, or at 100° for 3–5 hours, sulfur dioxide was evolved, the liquid darkened and there was produced prehnitenesulfonic acid, pseudocumenesulfonic acid-5, pseudocumenesulfonic acid-6, and hexamethylbenzene, together with a brown, water-insoluble material. The main product was prehnitenesulfonic acid. On the basis of these facts Jacobsen believed that durene itself rearranged, and he represented the reaction as follows:



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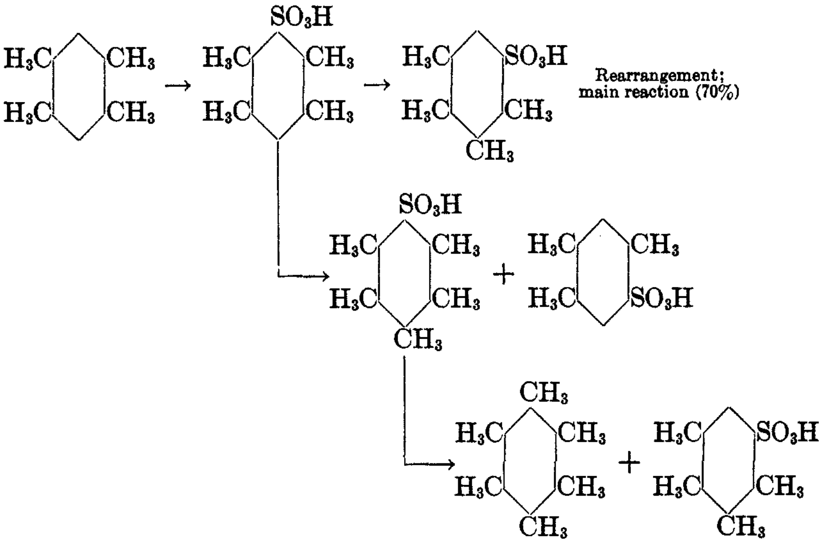
[13] Jacobsen, *Ber.*, **20**, 896 (1887).

[14] Smith and Lux, *J. Am. Chem. Soc.*, **51**, 2994 (1929).

[15] Smith and Cass, *ibid.*, **54**, 1614 (1932).

The maximum yield of prehnitene from durene according to Jacobsen's scheme is 25 per cent. Smith and Cass re-investigated this reaction; they established that prehnitenesulfonic acid was produced in 70 per cent. yield based on a direct mole-for-mole rearrangement of durene to prehnitene. The other products of the reaction were sulfur dioxide (0.356 moles per mole of durene used); CO_2 (0.0201 moles); very small amounts of pseudocumenesulfonic acid-5 and of hexamethylbenzene; and a brown amorphous material which constituted about 30 per cent. of the reaction product. Moreover, durene was found to be stable when refluxed with phosphorus pentoxide, but it rearranged in contact with sulfuric acid. Durenesulfonic acid, either hydrated or anhydrous, rearranged in contact with sulfuric acid or phosphorus pentoxide. Thus it is the sulfonic acid which rearranges, not the hydrocarbon. This is also shown by the fact that pentamethylbenzenesulfonic acid, left in a desiccator over sulfuric acid, rearranged, whereas the hydrocarbon, under the same conditions, did not rearrange. Moreover, it was found that the hydrolysis of durenesulfonic acid to durene by cold concentrated sulfuric acid was not complete until after 30 hours at 12°. Smith and Cass therefore wrote the Jacobsen reaction as follows, with the main reaction involving an intramolecular shift of a methyl group.

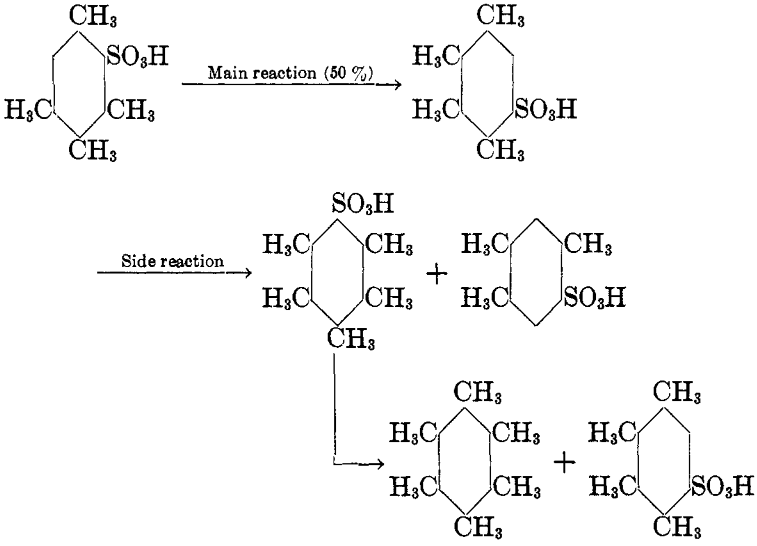


+ amorphous by-product, 15–30%.

These reactions, as well as Jacobsen's; do not account for the large amounts of sulfur dioxide evolved, nor for the amorphous by-products. Smith and

Moyle[16] have shown that the source of the sulfur dioxide is twofold: some comes from the sulfonic acid during rearrangement, and some results from the action of sulfuric acid upon the amorphous by-product.

The rearrangement of isodurene was really discovered by Töhl[17] who however, did not recognize in his isolation of prehnitene that a rearrangement of isodurene had actually occurred. The rearrangement was investigated by Smith and Cass,[15] who found that the rearrangement was quite analogous to that of durene.



+ amorphous by-product (28%)

Prehnitene[15] is merely sulfonated by sulfuric acid, and the sulfonic acid does not rearrange.

No polymethylbenzenes up to the tetramethylbenzenes are rearranged by sulfuric acid or other sulfonating agents: toluene, the three xylenes and the three trimethylbenzenes merely yield sulfonic acids which are quite stable toward sulfuric acid. Hexamethylbenzene was shown by Jacobsen[1] and by Smith and Cass[15] to be stable toward sulfuric acid.

Few ethyl derivatives of benzene have been studied, but Töhl and Karchowski[18] prepared 5-ethylpseudocumene and subjected the hydrocarbon to the action of sulfuric acid. They concluded that no rearrangements

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[16] Smith and Moyle, *ibid.*, **55**, 1676 (1933).

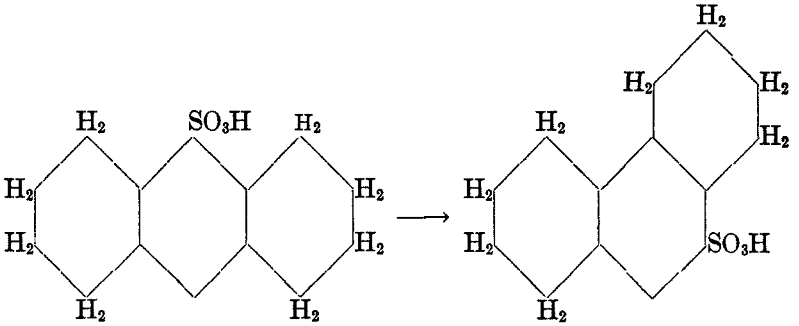
[17] *Ber.*, **21**, 904 (1888).

[18] Töhl and Karchowski, *Ber.*, **25**, 1530 (1892).

occurred, but their conclusion was based upon the fact that the sulfonic acids, when converted to the dibromo compounds, gave compounds which did not show marked depressions in melting points when mixed with each other or with dibromo-5-ethylpseudocumene prepared from the original hydrocarbon. This evidence is of little value as a proof of structure since it has been demonstrated[16] that the perbromopolymethylbenzenes when mixed with each other do not give significant depressions in melting points. Moreover, work in progress in this laboratory[19] indicates that both ethylpseudocumene and ethylmesitylene rearrange, and that the ethyl group is lost during the process.

Pentaethylbenzene was found by Töhl[17] to rearrange, and the rearrangement produced hexaethylbenzene and 1,2,3,4-tetraethyl benzene, analogous to the products obtained from pentamethylbenzene.

Octahydroanthracene.—Schroeter and Götzsky[20] found that this hydrocarbon, in the presence of sulfuric acid, rearranged to give octahydrophenanthrene.



The rearrangement occurred only in sulfuric acid solution; heating the sodium sulfonate merely produced the original hydrocarbon, octahydroanthracene.

B. Halogen Derivatives

1. Iodo compounds.—Neumann[21] observed that aromatic iodo compounds rearranged in the presence of sulfuric acid, and from iodobenzene he obtained *p*-diïodobenzene and benzenesulfonic acid. He claimed that no evolution of iodine or of carbon dioxide occurred, and noticed only small amounts of sulfur dioxide. Similar rearrangements were observed in the case of *o*- and *p*-iodotoluene.

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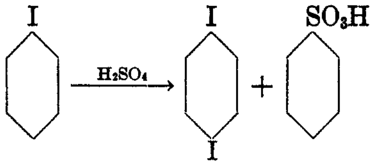
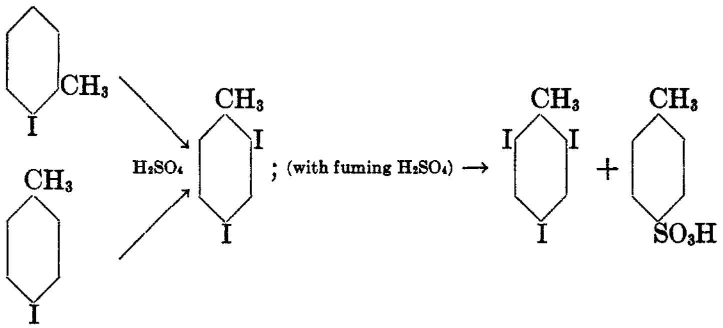
[19] Matthew Kiess, unpublished work.

[20] Schroeter and Götzsky, *Ber.*, **60**, 2035 (1937).

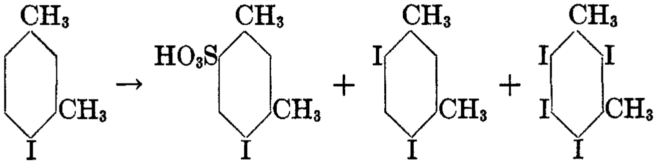
[21] Neumann, *Ann.*, **241**, 33 (1887).





Cass[7] verified Neumann's results in the case of iodobenzene, but he was able to show that both iodine and hydriodic acid were evolved. Boyle[22] stated that *p*-diïodobenzene was converted to a tri- and a tetraiodobenzene by hot fuming sulfuric acid, although no experimental details were given.

Hammerich[23] as well as Töhl and Bauch[24] found that 4-iodo-*m*-xylene, after contact with sulfuric acid for one week, gave polyiodo-*m*-xylenes.



It is interesting to note, in this connection, that no rearrangements have been reported in the case of *o*- and *p*-xylenes or any of their halogen derivatives.

Kurzel[25] investigated the rearrangement of 5-iodopseudocumene in the presence of concentrated or fuming sulfuric acid; he isolated two diïodopseudocumenes, an iodopseudocumenesulfonic acid, and pseudocumenesulfonic acid-5.

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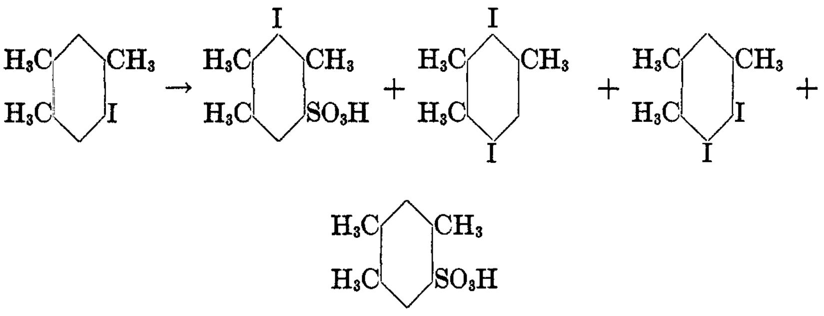
[22] Boyle, *J. Chem. Soc.*, **95**, 1683 (1909).

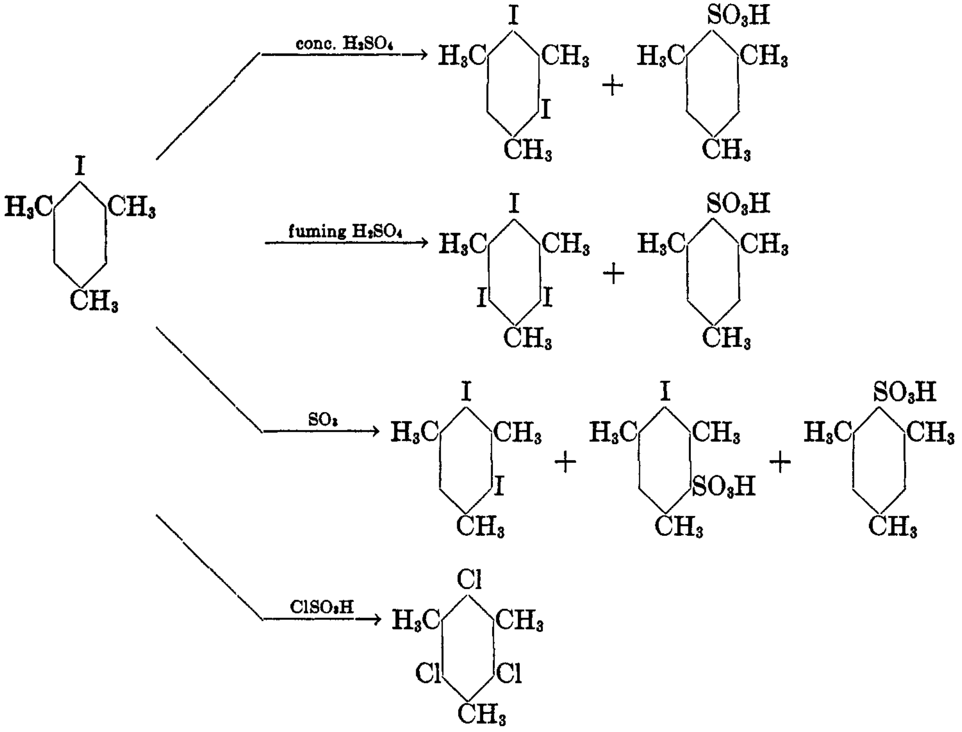
[23] Hammerich, *Ber.*, **23**, 1634 (1890).

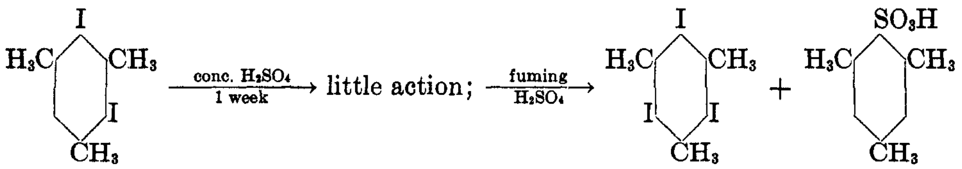
[24] Töhl and Bauch, (*a*) *ibid.*, **23**, 3117 (1890); (*b*) *ibid.*, **26**, 1105 (1893).

[25] Kurzel, *ibid.*, **22**, 1586 (1889).



Iodomesitylene was investigated by Töhl and Eckel[26] who studied the effects produced by varying the reagent.





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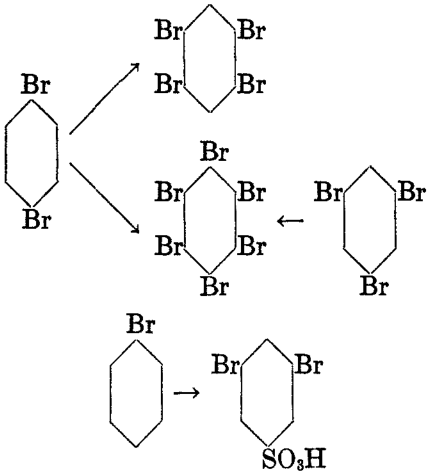
[26] Töhl and Eckel, *ibid.*, **26**, 1099 (1893).

The last reaction is good evidence that sulfonation precedes the rearrangement, for fuming sulfuric acid, required to sulfonate the diïodo compound, is also required to bring about the rearrangement.

Iodopentamethylbenzene was decomposed when subjected to the action of sulfuric acid. Iodine was evolved, and a black tarry decomposition product was formed.[27]

2. Bromo compounds.—Bromobenzene, when refluxed for eight hours with concentrated sulfuric acid, was reported by Herzig[2] to give large amounts of sulfur dioxide and carbon dioxide, together with small amounts of a dibromobenzenesulfonic acid, which Herzig thought was the 1, 3, 5 compound. *p*-Dibromobenzene gave the same gaseous products, together with some 1,2,4,5-tetrabromobenzene and a small amount of hexabromobenzene. From 1,3,5-tribromobenzene, Herzig obtained hexabromobenzene. Herzig explained these transformations by assuming that the halogen was eliminated as nascent bromine, which then acted as a brominating agent.



An attempt by Jackson and Gallivan[28] to nitrate 1,2,4,5-tetrabromobenzene in the presence of sulfuric acid, resulted in the production of hexabromobenzene.

By the action of concentrated sulfuric acid at 230° upon 4,6-dibromo-*m*-xylene, Jacobsen[29] obtained 2,4-dibromo-*m*-xylene. Whether a bromine atom or a methyl group migrated cannot be determined, for the same product would result in either case. The rearrangement of 5-bromo pseudocumene was also investigated by Jacobsen[30] who sulfonated a large

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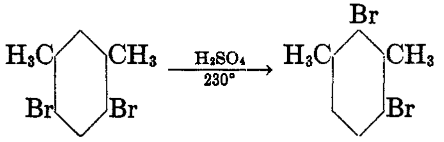
[27] C. L. Moyle, M. S. Thesis, University of Minnesota, 1932.

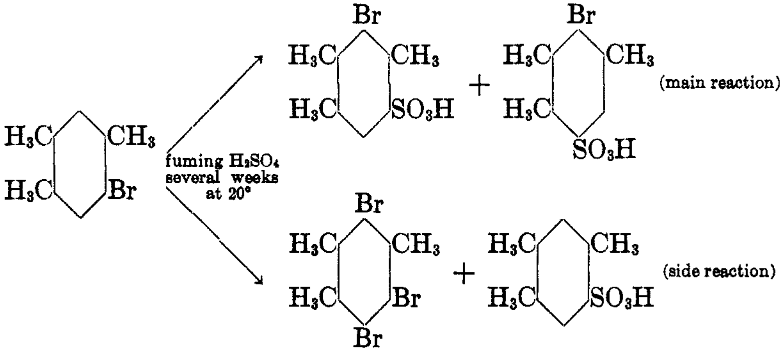
[28] Jackson and Gallivan, *Am. Chem. J.*, **18**, 251 (1896).

[29] Jacobsen, *Ber.*, **21**, 2827 (1888).

[30] Jacobsen, *ibid.*, **22**, 1580 (1889).

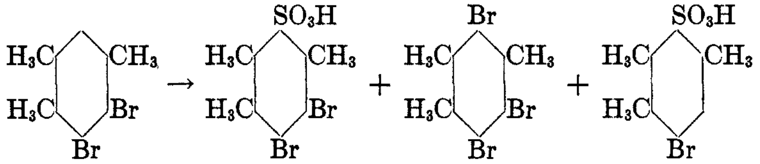
amount (450 g.) of the substance with fuming sulfuric acid (2300 g.) and kept the solution at room temperature for several weeks. The main reaction led to 3-bromopseudocumenesulfonic acid-5, which could have been produced by migration of either a methyl group or a bromine atom.





Smith and Moyle[31] found that 5-bromopseudocumene rearranged largely to 3-bromopseudocumenesulfonic acid-5 together with a small amount of tribromopseudocumene, but contrary to the work of Jacobsen, no pseudocumenesulfonic acid-5 could be found in the product.

When 5,6-dibromopseudocumene was subjected to the action of chlorosulfonic acid[32] the substance was not only sulfonated, but 6-bromopseudocumenesulfonic acid-3 and tribromopseudocumene were obtained.



Töhl and Eckel[26] found that the action of sulfuric acid upon bromomesitylene consisted not only of sulfonation, but that there was a migration of bromine, leading to dibromomesitylenesulfonic acid and mesitylenesulfonic acid as by-products, a point which had been overlooked by Rose.[33]

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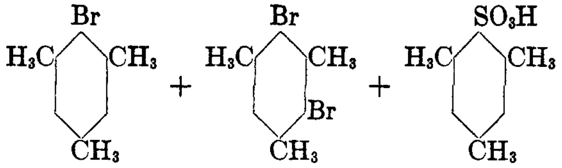
[31] Smith and Moyle, *J. Am. Chem. Soc.*, **58,** 1 (1936).

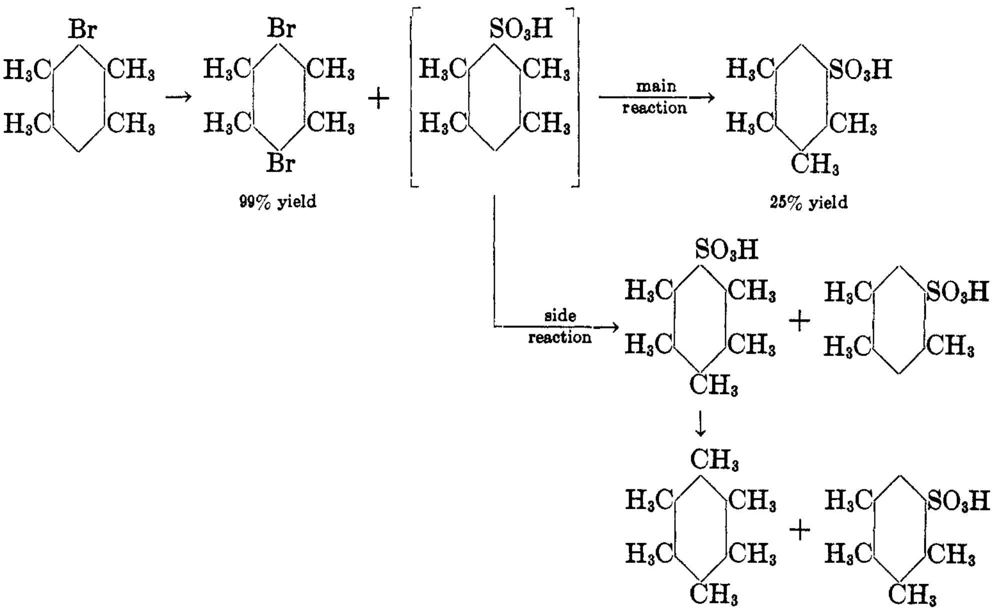
[32] Jacobsen, *Ber.*, **19,** 1221 (1889).

[33] Rose, (*a*) *Ann.*, **164,** 63 (1872); (*b*) *Ber.*, **26,** 1102 (1893).



Smith and Moyle[31] verified the results of Töhl and Eckel concerning the rearrangement of bromomesitylene, but in addition it was found that either dibromo- or tribromomesitylene could be produced, depending upon the temperature.

The Jacobsen reaction of the monobromotetramethylbenzenes[16]—bromodurene,[34] bromoisodurene, and bromoprehnitene[35]—consisted of migration of a bromine atom from one molecule to another to give the corresponding dibromo derivative. Removal of the bromine atom left the sulfonic acid of the hydrocarbon, and since both durene and isodurene rearranged to prehnitene, the final bromine-free product in all three cases was prehnitenesulfonic acid. The dibromo compounds were obtained in excellent yields (80–100 per cent.); prehnitenesulfonic acid resulted in yields of from 25 to 80 per cent. Sulfur dioxide was evolved, and there was produced as usual the insoluble brown amorphous powder which represented 25–30 per cent. of the weight of the total product. The course of these reactions was outlined by Smith and Moyle[16] as follows:



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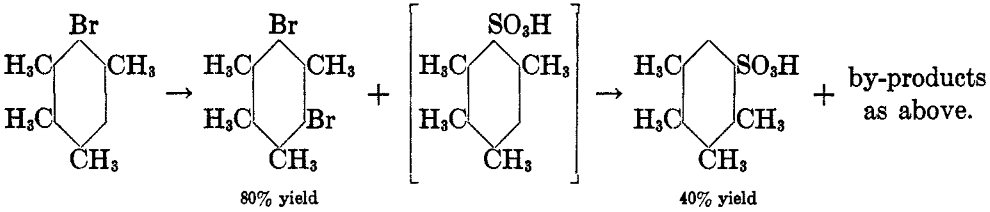
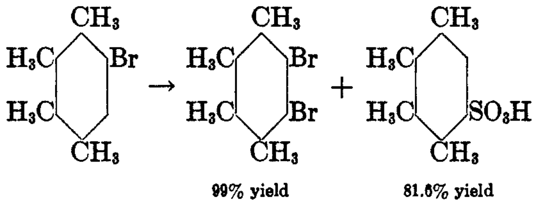
[34] JACOBSEN, *Ber.*, **20**, 2837 (1887).

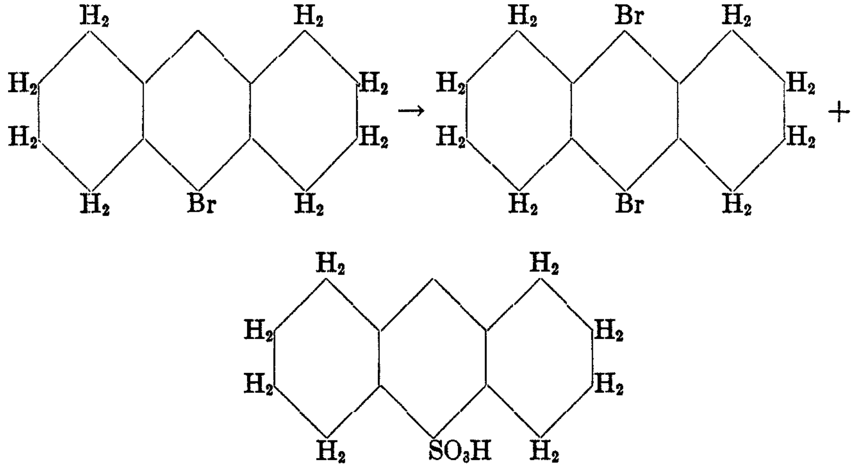
[35] TÖHL, *ibid.*, **25**, 1527 (1892).





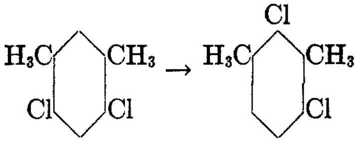
The three isomeric dibromotetramethylbenzenes, as well as bromopentamethylbenzene, did not rearrange when in contact with sulfuric acid, although all underwent a very slow oxidation (decomposition) accompanied by evolution of sulfur dioxide.

Schroeter and Götzky[20] have reported that 9-bromoöctahydroanthracene, when treated with fuming sulfuric acid at 50–60° for a short time, gives the dibromo compound together with a sulfonic acid. The structure of the sulfonic acid was not determined; if, as assumed, it were actually a derivative of octahydroanthracene, it is likely that longer contact with sulfuric acid would have produced octahydrophenanthrenesulfonic acid.

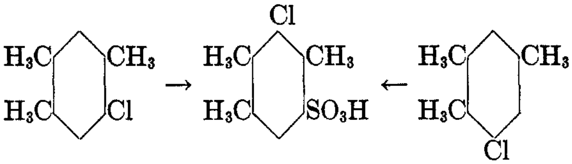


3. Chloro compounds.—Chlorobenzene in contact with sulfuric acid merely sulfonates, and no rearrangement occurs.[7] However, 4,6-dichloro-

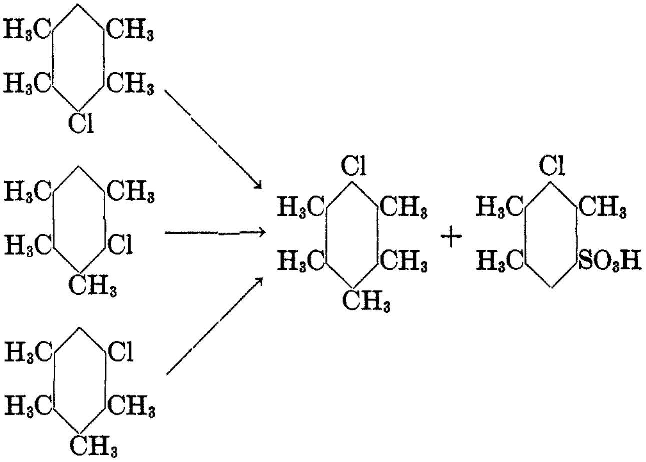
m-xylene[36] behaves in a manner analogous to that of the corresponding dibromo compound and rearranges into 2,4-dichloro-*m*-xylene.



Töhl and Müller[37] observed that 5-chloropseudocumene, when treated with fuming sulfuric acid gave a liquid chloropseudocumene, but they did not determine the structure of the product. Smith and Moyle[31] investigated the action of sulfuric acid upon the three monochloropseudocumenes. They found that 5- and 6-chloropseudocumene rearranged into 3-chloropseudocumene and that the last compound was stable toward sulfuric acid. In these cases, the migrating group was the chlorine atom, and the methyl groups were unaffected.



In the rearrangement of chlorodurene, reported by Töhl[38] a methyl group migrated, and the products were 3-chloropseudocumenesulfonic acid-5 and chloropentamethylbenzene. Smith and Moyle[31] investigated the rearrangements of the three chlorotetramethylbenzenes and found that all of them gave chloropentamethylbenzene and 3-chloropseudocumenesulfonic acid-5.



Thus the rearrangements of the chlorotetramethylbenzenes involve migration of a methyl group, whereas those of the bromotetramethyl-

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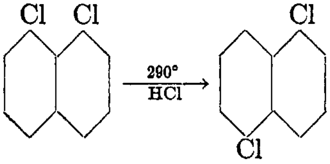
[36] Koch, *ibid.*, **23**, 2318 (1890).

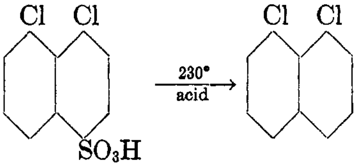
[37] Töhl and Müller, *ibid.*, **26**, 1108 (1893).

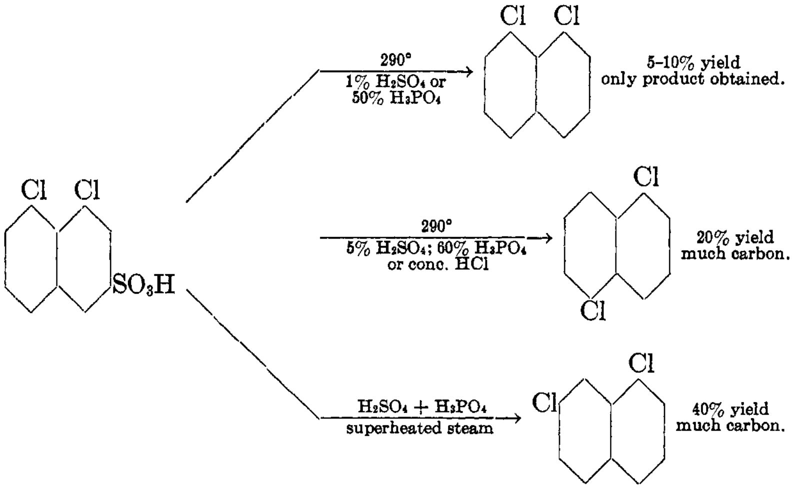
[38] Töhl, *ibid.*, **25**, 1527 (1892).

benzenes involve migration of the halogen atom. It is likely that these migrations constitute, in some cases at least, but the first step and that more than one migration occurs before the final products are reached.

There are some interesting observations in the literature on the migration of chlorine atoms in certain naphthalene derivatives. Thus Armstrong and Wynne[39] found that when 1,8-dichloronaphthalene was heated to 290° with hydrochloric acid, it was converted into 1,5-dichloronaphthalene. This isomerization did not occur below 200°, but it was noticeable at 250° and complete at 290°. No isomerization occurred when the chloronaphthalene was heated alone, with water, or with phosphoric acid at 300°, but it did occur when sulfuric acid was used, and under these conditions there was considerable carbonization. None of the isomeric dichloronaphthalenes showed any tendency to change under any of the conditions used by Armstrong and Wynne. The 4-sulfonic acid of 1,8-dichloronaphthalene when hydrolyzed by acid at 230°, gave only 1,8-dichloronaphthalene, but the 3-sulfonic acid, which could not be hydrolyzed below 285°, gave no less than three isomeric dichloronaphthalenes.







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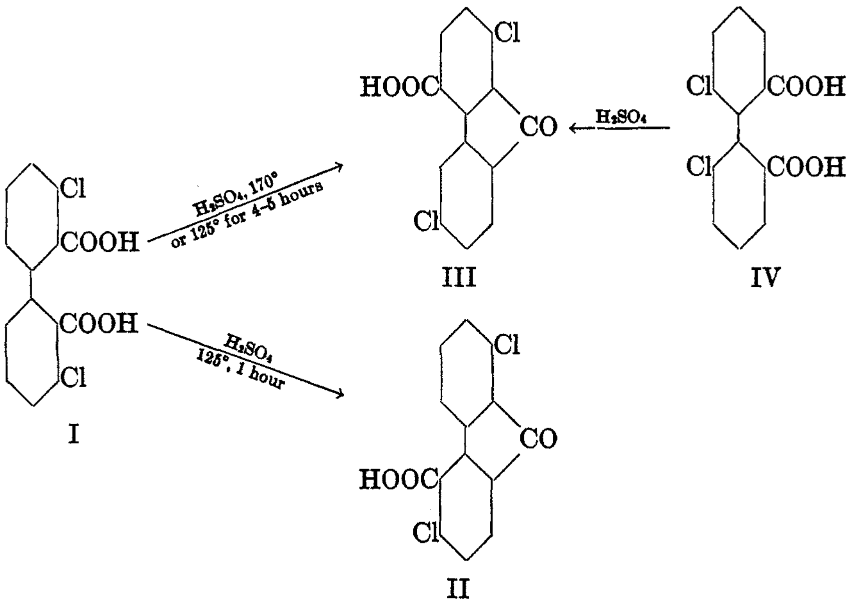
[39] Armstrong and Wynne, *Chem. News*, **76**, 69 (1897).

Of the trichloronaphthalenes, the 1, 2, 8 isomer was the only one which rearranged when heated with hydrochloric acid. The course of the rearrangement was not determined.

Recently, Huntress and his students[40] have investigated the migrations of chlorine atoms which occur when certain dichlorodiphenic acids are heated with sulfuric acid. Thus 3,3′-dichlorodiphenic acid (I) when heated with sulfuric acid at 125° for one hour, gives the expected product, 1,6-dichlorofluorenone-5-carboxylic acid (II) in quantitative yield. But if the time of heating is prolonged (4–5 hours), or if higher temperatures are used, the product is the isomeric 1,6-dichlorofluorenone-4-carboxylic acid (III), a substance which is also obtained from 5,5′-dichlorodiphenic acid (IV). It was also found that both the 1,6- (V) and the 1,8- (VI) dichlorofluorenones, when heated with sulfuric acid gave the rearrangement product, 3,6-dichlorofluorenone (VII). Phosphoric acid does not cause the rearrangement, but does cause the ring closure, giving in every case the expected product. It follows that the rearrangement occurs after the ring closure. The work is still incomplete, but it will be interesting to learn whether or not a sulfonation is involved. If so, the reaction becomes a typical Jacobsen rearrangement of chlorine produced by sulfuric acid; if not, the reaction must be assigned to some other class.



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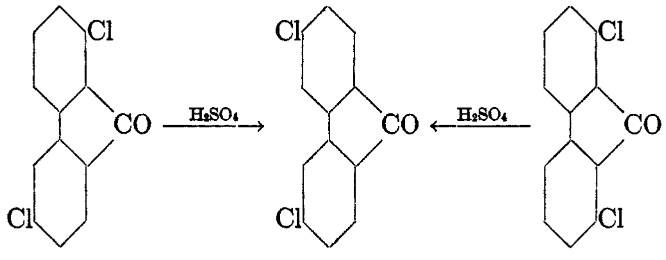
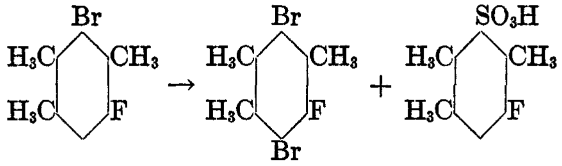
[40] HUNTRESS *et al.*, *J. Am. Chem. Soc.*, **58**, 1514 (1936).

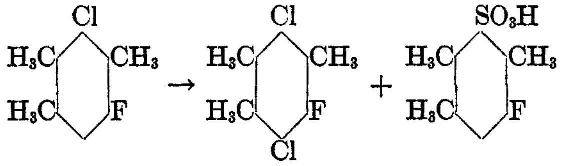


V VII VI

4. Fluoro compounds.—The only fluorine compounds to be investigated so far are studied by Töhl and Müller,[37] and in this group are also the only mixed halogen compound which have been studied. 5-Fluoropseudocumene was sulfonated by sulfuric acid, but the sulfonic acid remained unaffected by sulfuric acid when in contact with it for three months. The action of sulfuric acid upon 3- (or 6-) iodo-5-fluoropseudocumene caused decomposition with evolution of iodine; no rearranged product was found. However, 3- (or 6-) bromo-5-fluoropseudocumene rearranged with migration of the bromine atom:

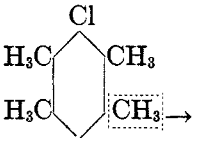


while the corresponding chloro-fluoro compound rearranged with migration of chlorine, and the methyl groups were unaffected.

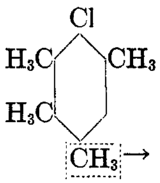


DISCUSSION

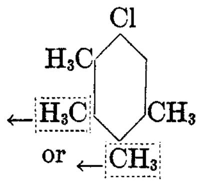
The three chlorotetramethylbenzenes, chlorodurene (I), chlorisodurene (II), and chloroprehnitene (III), rearrange to give the same products, *viz:* chloropentamethylbenzene and 3-chloropseudocumenesulfonic acid-5. In each case a methyl group migrates in such a manner that the same chlorotrimethylbenzene results. These rearrangements can be compared with that of pentamethylbenzene (A) in which a methyl group also migrates. But the situation becomes more involved when the rearrangement of chlorodurene is compared with those of bromodurene (B) and of 3-chloro-5-fluoropseudocumene (C).



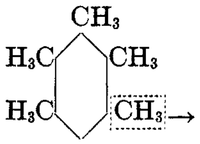
I



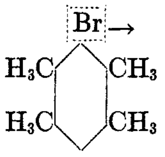
II



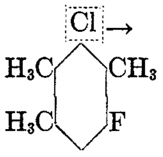
III



A



B

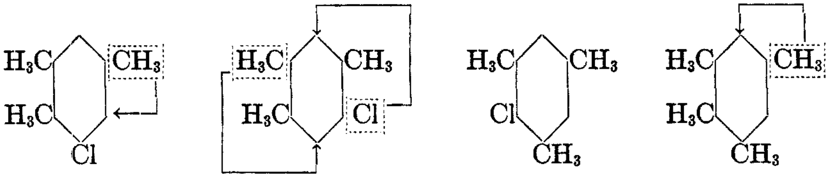


C

It is not known, of course, which methyl group migrates in pentamethylbenzene. In the analogs I and A, a methyl group migrates, while in B and C, the halogen atom is the labile group. The rearrangements of I, B, and C show the different courses which the rearrangement may take when one substituent is replaced by another. In I the methyl group migrates; in B the bromine atom moves, and in C the chlorine atom migrates and leaves a non-vicinal tetrasubstituted benzene, 5-fluoropseudocumene.

A methyl group can be removed from either I or II (as shown) in such a way that 3-chloropseudocumene results directly. But the rearrangement of III is more complex and must involve at least two migrations. If either of the marked methyl groups were to be removed, the product would be a chloropseudocumene which would itself then rearrange into 3-chloropseudocumene. Methyl group 1 cannot be the one removed, because the first product would then be 4-chlorohemimellitene, a substance which does not undergo the Jacobsen rearrangement. No 4-chlorohemimellitene could be found among the rearrangement products of III. Removal of the methyl group at 4 would give 5-chlorohemimellitene as the first product. Unfortunately this compound has not been available for study and hence nothing can be said concerning this possibility.

Two chlorotrimethylbenzenes are unstable toward sulfuric acid, the 6- and the 5-chloropseudocumene both rearranging to 3-chloropseudocumene. On the other hand, 4-chlorohemimellitene and chloromesitylene do not rearrange. If the latter is compared with isodurene, the migration of a methyl group would be expected. However, if the assumption is made that the chlorine atom is the only group in a chlorotrimethylbenzene that can move then chloromesitylene should be a stable substance. This assumption has some basis in the fact that halogen is the labile group when 3-chloro-5-fluoropseudocumene, bromomesitylene, or 5-bromopseudocumene rearrange.



The rearrangements of two bromotrimethylbenzenes have been investigated—5-bromopseudocumene and bromomesitylene. The former rearranged chiefly to 3-bromopseudocumene, with a small by-product of tribromopseudocumene; the latter rearranged entirely intermolecularly giving mesitylene and polybromomesitylenes.

The Jacobsen reaction does not appear to be an extensive reaction. With few exceptions it is limited to the halogen derivatives of benzene, the halogen derivatives of methylated benzenes, the tetramethylbenzenes (durene and isodurene), pentamethylbenzene, pentaethylbenzene, and possibly to mixed alkyl benzenes. In general, four substituents must be attached to the ring except when halogen alone is present. The substituents which have so far been shown capable of migration are I, Br, Cl, CH_3, C_2H_5 and SO_3H. No Jacobsen rearrangements are known in which an amino, nitro, acetyl, methoxyl or carboxyl group is present in the molecule (except perhaps for the recent work of Huntress). Moreover, the conditions which bring about the rearrangement appear to be quite limited. Many reagents have been tried,[31] but the only reagent of general applicability is some form of sulfuric acid, and it is not possible to replace more than a small proportion of the sulfuric acid by something else. The following table shows some data regarding the effect of changing the reagent upon the products obtained. The material used was a tetramethylbenzene mixture, about 90 per cent. isodurene and 10 per cent. durene both of which give prehnitene on rearrangement. In only three cases was any considerable yield of prehnitene obtained; all the others gave essentially unchanged material.

The ease of rearrangement of various substituents changes with the nature of the compounds. In the case of the monochloro- and monobromotetramethylbenzenes, the data show the relative ease of migration to be Br > CH_3 > Cl, but in the case of halogenated trimethylbenzenes, the halogen always migrates if any rearrangement occurs, and the relative

TABLE

SUMMARY OF THE EFFECT OF DIFFERENT REAGENTS UPON REARRANGEMENT OF TETRAMETHYLBENZENES[a]

EXPT.	REAGENT AND CONDITIONS	TEMP., °C.	TIME, HRS.	TAR[b] G.	OIL[b] G.	A[c]	B[c]	C[d]	D[d]
1	50 ml. 20% fuming H_2SO_4	86	8	5.0		31.5	7.0	24.0 (48%)	
2	75 ml. 20% fuming H_2SO_4; pass in SO_2 with stirring	85	6	0.5		32.9	12.2	25.8	
3	50 ml. 20% fuming H_2SO_4 to sulfonate; then add 18 ml. water	65	20		18.0	23.0	5.5		34.0
4	75 ml. 20% fuming H_2SO_4 to sulfonate; then add 50 ml. CH_3COOH	85	10	2.0		40.2	4.8		31.5
5	50 ml. 20% fuming H_2SO_4 to sulfonate; then add 50 ml. 100% H_3PO_4	65	20	5.2	16.0	15.2	4.8		24.6
6	50 ml. 20% fuming H_2SO_4 to sulfonate; then add 300 ml. conc. H_2SO_4	80	15	23.5		12.3	3.0	6.6	
7	50 ml. 20% fuming H_2SO_4 to sulfonate; 35 g. Na_2SO_4 in 50 ml. conc. H_2SO_4	65	30	4.2		34.6	6.2	25.2	
8	40 ml. 20% fuming H_2SO_4 to sulfonate; then add 1 g. $HgSO_4$	65	15	5.8		28.0	8.2		21.0

[a] Fifty grams of the mixed tetramethylbenzene filtrate used in each experiment except No. 8, in which 40 g. was used.

[b] The reaction product was poured onto ice and the tar and oil (if any) were separated.

[c] Sulfuric acid was added to the aqueous filtrate from *b*, and the precipitated prehnitene sulfonic acid was filtered off. It was dissolved in water (100 cc.) and sulfuric acid (30 cc.) and hydrolyzed with steam at 145°. Column A gives the weight of crude product in the distillate; column B gives the weight of residue.

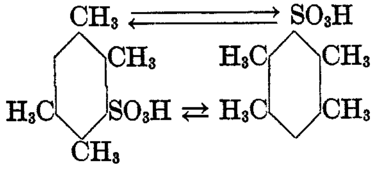
[d] Column C gives the weight of pure prehnitene obtained by fractionation of the oil in the distillate from *c*. Column D gives the weight of mixed tetramethylbenzenes obtained in the experiments in which the Jacobsen rearrangement either did not occur, or was incomplete.

ease of migration appears to be $Br > Cl > CH_3$. But slight changes in conditions and in the nature of the compound may cause great differences in the ease of rearrangement—for example, pentamethylbenzenesulfonic acid rearranges readily, but its methyl ester does not rearrange at all.

Attempts to formulate a mechanism for the reaction, or even to formulate with certainty the course of the reaction, are complicated by the fact that sulfuric acid can act as a reagent in so many different reactions—oxidation, sulfonation, hydrolysis, polymerization, and the like. In all the Jacobsen reactions so far observed, there resulted large amounts of a tarry amorphous solid which accounted for approximately one-third of the starting material. The source of this material is not definitely known, but this by-product resulted only when sulfur dioxide was evolved, and the amount appeared to be roughly proportional to the amount of sulfur dioxide. Rapid rearrangements (chloro- and bromotetramethylbenzenes), accompanied by only small amounts of sulfur dioxide, gave good yields of products and much less of the amorphous by-product than did the slower rearrangements. Moreover, if a substance that rearranged rapidly was allowed to stand in contact with sulfuric acid for a long time, the evolution of sulfur dioxide continued and the longer the time, the smaller the yield of rearranged product and the greater the amount of amorphous material. Hence it appears that the amorphous by-product is a result of the action of sulfuric acid upon all the organic materials present. The source of the sulfur dioxide appears to be not only sulfuric acid, but also the sulfonic acids themselves. The reaction is always accompanied by a series of characteristic color changes: first red, then deepening to reddish-brown, and finally black.

Three mechanisms have so far been suggested for the Jacobsen reaction. Herzig[2] explained the production of dibromobenzene from bromobenzene by assuming the elimination of (nascent) bromine which then acted as a brominating agent. While a plausible explanation for some rearrangements of halogenated compounds, this mechanism fails when attempts are made to apply it to the halogen-free compounds unless by "nascent" groups, one means transient radicals.

Jacobsen[41] suggested that prehnitene resulted from durene through an exchange of a methyl group of one molecule for the sulfonic acid group of another molecule, thus:



This "mechanism" involves exchanges among four groups, and it does not, of course, explain the stability of the final product, prehnitene.

Recently Schroeter and Götzky[20] proposed that the rearrangement takes place because of longitudinal and transversal oscillations within the

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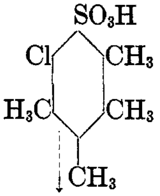
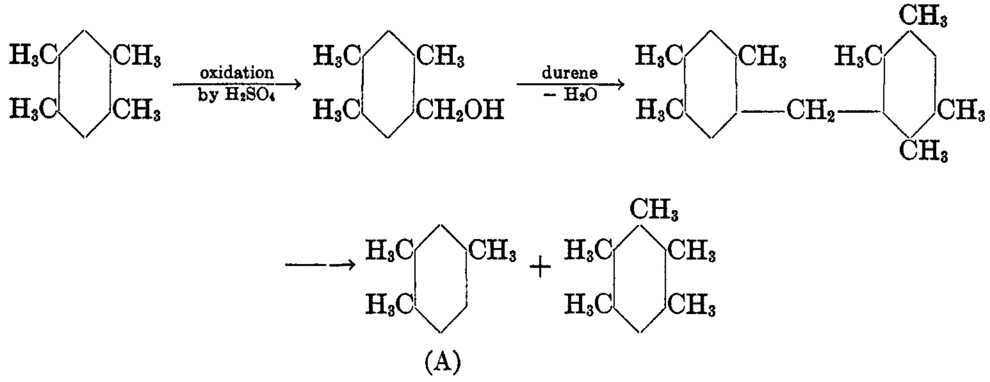
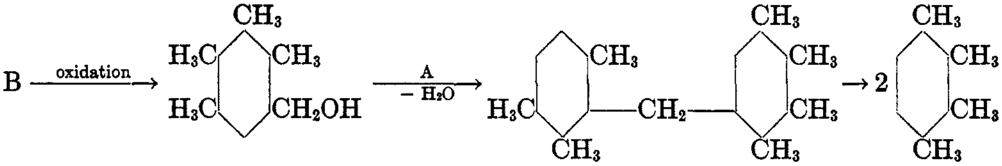
[41] Jacobsen, *Ber.*, **19**, 1215 (1886).

molecules. This idea cannot explain migrations of groups within a molecule, and although it can be applied to pentamethylbenzene, it cannot be used to explain the rearrangement of chloroprehnitene unless the assumption is made that the bond of a substituent in the para position to the sulfonic acid group is also broken by the longitudinal vibrations within the molecule. Schroeter's mechanism cannot be applied to the rearrangements of the bromotetramethylbenzenes without considerable modification.



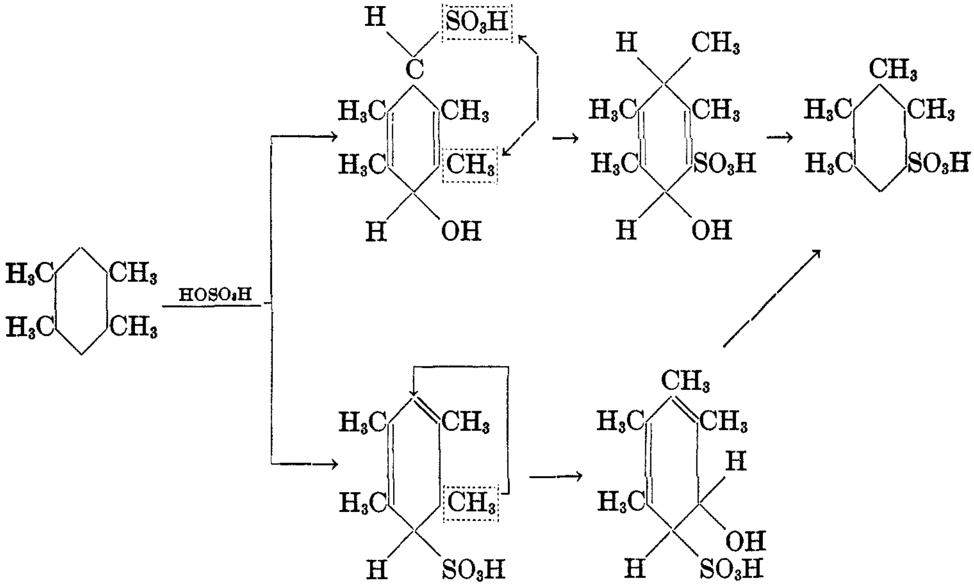
The authors have considered three other formulations of the mechanism of the Jacobsen reaction. The first of these involved formation and subsequent cleavage of diphenylmethane derivatives, thus transferring a methyl group. Applied to durene, the scheme may be outlined somewhat as follows:





By assuming a series of similar intermediates, the other products could be accounted for by means of concurrent reactions. The mechanism of the cleavage was a matter for some speculation, since it involved the addition of two hydrogen atoms. According to this mechanism, a mixture of one mole of pentamethylbenzene and one mole of pseudocumene should lead to two moles of prehnitene. An experiment conducted upon a mixture of pentamethylbenzene (0.338 moles) and pseudocumene (0.417 moles) led to prehnitene (0.125 moles) in an amount no greater than that which would have been obtained from the pentamethylbenzene alone. Enough pentamethylbenzene and pseudocumene were recovered which, together with the other products, accounted for practically all the material used. Hence it does not appear that the mechanism of the transfer of the methyl group can involve chain-ring compounds related to diphenylmethane.

The second scheme involved the addition of sulfuric acid as hydroxyl and SO_3H to ortho or para positions in the benzene nucleus; the quinoid intermediate so produced then rearranged to give the final product.

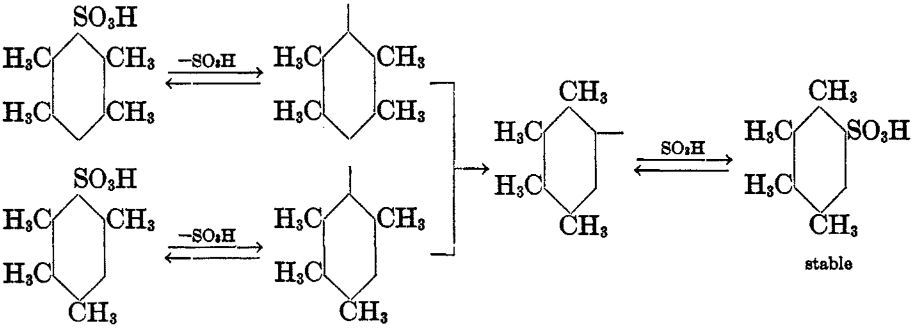


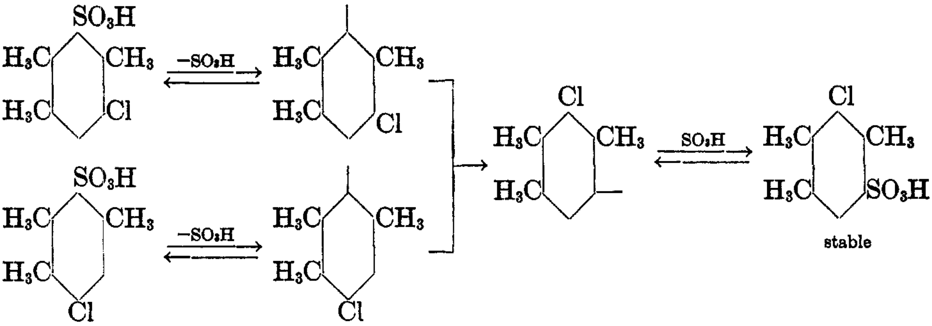
This mechanism has the advantage that it is analogous to the known rearrangements of quinols, and while there are some objections, it has decided possibilities. It does not explain the stability of chloromesitylene or of 5-fluoropseudocumene unless one assumes that these substances do not add sulfuric acid, or if they do, the quinoid intermediate decomposes to give the original products again. Moreover, this mechanism would not hold for the rearrangements of the dry sulfonic acids by phosphorus pentoxide, because in this case formation of addition compounds is impossible unless it is assumed that hydrolysis of the sulfonic acid by traces of water takes place.

No mechanism has been found which will explain satisfactorily all the available data. The main points to be considered in formulating a mechanism are the following:

1. Whether or not, in any given case, a rearrangement will occur, and why.
2. Both the intermolecular and intramolecular types of rearrangement must be explained, and predictions made as to when they will occur.
3. Which groups will migrate in a given compound, and why.
4. The non-rearrangement of chloromesitylene, 5-fluoropseudocumene, 5-aminopseudocumene, 5-nitropseudocumene, *p*-bromodiphenyl, 2,3-dimethylnaphthalene, the xylenes, the trimethylbenzenes, and all the hexasubstituted benzenes.
5. The stability of 3-chloropseudocumene and the other products obtained from the Jacobsen reactions.
6. The rearrangement of certain of the sulfonic acids when the dry substances are mixed with phosphorus pentoxide, and the evolution of sulfur dioxide under these conditions.
7. The inhibiting action of phosphoric and acetic acids when mixed with the sulfuric acid used.
8. The evolution of sulfur dioxide, the colors during the reaction, and the formation of the amorphous by-product as well as its nature.

From the information available at present, the ease with which the sulfonic acids rearrange seems possibly to be related to the ease with which the sulfonic acids can be hydrolyzed. The sulfonic acids of durene, isodurene and pentamethylbenzene (which rearrange) are all easily hydrolyzed at lower temperatures than prehnitene, chloromesitylene and 3-chloropseudocumene (which do not rearrange). How far this generalization will hold is a matter to be determined by experiments. If one invokes transient radicals as intermediates, then the extent of radical formation might logically be connected with the ease with which the sulfonic acids are hydrolyzed. Thus:





The free radicals rearrange to give the most stable structure, and the same stable structure will be obtained from all those radicals which have the same number and kind of substituents attached to the ring. According to this mechanism, 3-chloropseudocumene is a more stable structure than chloromesitylene, even though the latter (because the sulfonic acid does not dissociate into radicals) is not capable of rearrangement. In agreement with the predictions of this theory, all the chlorotrimethylbenzenes which can rearrange give the same product, 3-chloropseudocumene. It would be expected in some cases that the free radicals would combine to give a diphenyl derivative and in two cases such products have been observed: a cómpound having the composition $C_{20}H_{24}Cl_2$ (dichloroöctamethyldiphenyl?) was obtained as a by-product from the rearrangement of chloroisodurene, and from the rearrangement of 6-chloropseudocumene there was obtained a high-melting substance (m.p. 168–169°) which possibly is a diphenyl derivative. Moreover, the free radicals would be susceptible to oxidation and polymerization, which would account for the amorphous by-product.

Finally, in studying the Jacobsen reactions it is necessary that the structures of the reaction products should be established beyond any doubt. In preparing many of these substances for purposes of comparison, sulfonation is often used as one of the steps in the synthesis; since this is also the condition under which the Jacobsen reaction occurs, great care must be taken to show that no rearrangements have occurred during the syntheses. The papers of Smith and Moyle[16, 31] contain detailed experiments which show that mixture melting points of the halogenated polymethylbenzenes cannot be relied upon as a method of identification and the detailed proof of the structure of many of the reaction products is also given in these papers.

SUMMARY

This paper contains a discussion of the Jacobsen rearrangement. The material is reviewed historically and the limits of the reaction, the nature of the products, and the possible mechanisms are discussed. A table is given showing the effect of changes in the nature of the reagent upon the rearrangement of a mixture of durene and isodurene.