

Thesis for the Degree of Ph.D.

THE CORRELATION OF SOME ABNORMALITIES OF THE
FRIEDEL-CRAFTS' REACTION.

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was the chief constituent (the ratio of m : p being 67 : 33 expressed in parts per hundred by weight), proving that Bialobrzewski was wrong in his observation. An increase in yield of mixed tert-butyltoluenes compared with that when aluminium chloride was used as catalyst was the only difference noted.

A first examination of the problem led to the suggestion that aluminium chloride, by associating with the toluene, disturbed in some way the normal directive influence of the methyl group. Gustavson (Ber., 1879, 11, 2151; 1880, 12, 694; 1884, 16, 784) claimed that he had prepared compounds of the type $C_7H_8 \cdot AlCl_3$, but the conditions under which these were isolated were not those which obtain in the Friedel-Crafts' reaction. Menschutkin (Jour. soc. phys. chim. russe, 1909, 41, 1089; Chem. Zentr., 1910, [1], 167) later said that such compounds do not exist. Nevertheless, there might be an equilibrium of this nature:



with only a small proportion of the complex existing at one time, and assuming it to be the reactive agent, there would be virtually the same disturbance of the directive influence of the methyl group as if there were complete formation of $C_7H_8 \cdot n AlCl_3$. The normal substitution of toluene when acetyl chloride is used

may be explained by this theory, on the grounds that acetyl chloride on combining with aluminium chloride to give $\text{CH}_3\text{CO}\cdot\text{Cl}\cdot\text{AlCl}_3$ prevents completely any association between the toluene and the catalyst.

An experiment to test this theory was therefore undertaken. According to the theory any substance which prevents association of the aluminium chloride with toluene will allow the methyl group to assume its normal directive influence. Nitrobenzene is known to form a definite compound $\text{C}_6\text{H}_5\text{NO}_2\cdot\text{AlCl}_3$ (Stockhausen and Gattermann, Ber., 1892, 25, 3521), and at the same time does not undergo the Friedel Crafts' reaction (Olivier, Rec. trav. chim., 1926, 45, 817); therefore if this complex were used instead of aluminium chloride, there is a possibility that the meta-substitution might be suppressed and normal or para-substitution take place exclusively. The experiment when performed showed, however, that the complex acted differently from aluminium chloride only in giving an increased yield of the mixed tert.-butyltoluenes. The proportion of the isomerides was not materially different.

Another test of the theory was to allow acetyl chloride to react with toluene in presence of a very large excess of aluminium chloride. Under these conditions association between the toluene and the catalyst had every chance of taking place, and

hence some meta derivative might be expected in the reaction product. Again a negative result was obtained. It appeared therefore that the association of toluene with aluminium chloride could definitely be said not to be the cause of the large quantity of meta-derivative produced.

Further experiments were carried out with other alkyl halides, viz: isobutyl bromide and n-butyl chloride. Isobutyl bromide, as shown by Baur (Ber., 1891, 24, 2833), gives not isobutyl- but tert.-butyltoluenes. It was found that the meta and also the para isomeride were present in the same proportions as obtained when using tert.-butyl chloride.

n-Butyl chloride has not hitherto been employed in the Friedel-Crafts' reaction on toluene, but Schramm (Monatsh., 1888, 9, 621) and Estreicher (Ber., 1900, 33, 439) have shown, not very definitely, however, that the action between benzene and n-butyl chloride gives sec.-butylbenzene. In the case of toluene, both meta and para compounds were proved to be present in the reaction product by first separating them by means of sulphuric acid and then oxidising them to isophthalic and terephthalic respectively, which were characterised by their dimethyl esters. The ratio of meta- to para-hydrocarbon was approximately 75 to 25 parts per hundred.

There was some doubt as to the exact

constitution of the m- and p-butyltoluenes resulting from this reaction, in view of the unsatisfactory nature of the observations of Schramm and Estreicher (loc. cit.), and it was therefore decided to prepare a solid derivative from each isomeride. The compounds prepared for this purpose were the sulphonanilides which were, in turn, proved to be identical with those obtained by the same method from authentic specimens of m- and p-sec.-butyltoluenes synthesised by a method which left no doubt as to their constitution.* Here again is a case of isomerisation of a butyl group under the influence of aluminium chloride.

The investigation was extended to other monosubstituted benzenes which normally give ortho and para derivatives on further substitution, to discover if meta substitution, similar to that in the case of toluene, occurs. A summary of the work carried out on the Friedel-Crafts' reaction with halogenobenzenes is given in the following table. This table is divided into two parts, viz., (A) where alkyl halides and (B) where acyl halides were employed. The catalyst in each case was aluminium chloride.

*It was not necessary to ascertain the position of the sulphonanilido group ($C_6H_5.NH.SO_2 -$) with reference to the other groups in the nucleus, as the sulphonanilides from the unknown and the known compounds were prepared by exactly the same method.

Investigator.	Benzene derivative	Halide	Resultants.
<u>A.</u>			
1. Boedtker (Bull. Soc. Chim. 1906,[3], <u>35</u> , 826)	chlorobenzene	<u>isobutyl</u> bromide or <u>tert.-butyl</u> chloride	p-chloro- <u>tert.-butyl-</u> benzene
2. Boedtker (<i>ibid.</i> , 829)	bromobenzene	do.	p-bromo- <u>tert.-butyl-</u> benzene
3. Boedtker (<i>ibid.</i> , 831)	iodobenzene	do.	p-iodo- <u>tert.-butyl-</u> benzene
4. Gleditsch (<i>ibid.</i> , 1095)	chlorobenzene	<u>isoamyl</u> chloride	p-chloro- <u>tert.-amyl</u> benzene
5. Gleditsch (<i>ibid.</i> , 1096)	bromobenzene	do.	p-bromo- <u>tert.-</u> amyl benzene
6. Gleditsch (<i>ibid.</i> , 1097)	chlorobenzene	ethyl bromide	o- and p-chloro- ethyl benzenes
7. Gleditsch (<i>ibid.</i> , 1097)	chlorobenzene	propyl chloride	o- and p-chloro- propyl benzenes
8. Schreiner (J. pr. Chem., 1910[2], <u>81</u> , 557)	chlorobenzene	ethyl bromide	p-chloro- ethyl benzene
9. Schreiner (<i>ibid.</i>)	bromobenzene	ethyl bromide	o- and p-bromo ethyl benzenes

I N T R O D U C T I O N .

Reactions which result in the entrance of a substituent into the nucleus of the toluene molecule are known to take place normally at the ortho and para positions. Results obtained, when the Friedel-Crafts' reaction is carried out with toluene and various acyl halides, present problems of interest when considered in relation to those obtained from toluene and alkyl halides in presence of aluminium chloride, since the toluene nucleus is attacked almost exclusively in the para position by acyl halides but in the meta and para positions by alkyl halides.

An examination of the literature on the subject disclosed a number of discrepancies, as will be seen from the following résumé, showing in tabular form the observations of various workers on reactions between toluene and (A) alkyl halides and (B) acyl halides.

Investigator	Benzene derivative	Halide	Resultants.
<u>B.</u>			
10. Gautier (Bull. Soc. Chim. 1885, <u>43</u> , 603)	chlorobenzene	acetyl chloride	p-chloro- acetophenone
11. Schweitzer (Ber., 1891, <u>24</u> , 550)	bromobenzene	acetyl chloride	p-bromo acetophenone
12. Schweitzer (Ber., 1891, <u>24</u> , 551)	iodobenzene	acetyl chloride	p-iodo acetophenone
13. Wegerhoff (Annalen <u>252</u> , 6)	chlorobenzene	benzoyl chloride	p-chloro- benzophenone
14. Gomberg, Cone. (Ber., 1906, <u>39</u> , 3279)	bromobenzene	benzoyl chloride	p-bromo- benzophenone
15. Montagne (Rec. trav. chim. 1908, <u>27</u> , 336)	bromobenzene	benzoyl chloride	o- and p-bromo- benzophenones (chiefly para)

It will be noted that in none of the cases has the

occurrence of the meta isomeride along with the para been reported.

In the case of the alkyl halides, the method used for proving the position of the entering group renders the conclusion arrived at very doubtful, for the following reasons. In the first place, the method relied on to produce the necessary evidence was

oxidation of the side chain to the carboxylic group, notwithstanding the fact that the separation, for example, of m- and p-chlorobenzoic acids from one another is almost impossible in that the para compound alone can be obtained pure, and secondly, the yield of the acid (somewhat impure) in each case was exceedingly small and therefore the identification of the acid as a para derivative could not be taken as conclusive evidence that the original halogeno-hydrocarbon consisted of a para compound exclusively. On the other hand, more complete evidence is given in the cases where acyl chlorides are used and it can be taken that the para derivatives are formed almost exclusively.

Reactions were carried out, therefore, on both chloro- and bromo-benzenes with n-butyl chloride as the alkyl chloride. This latter was chosen in preference to tert.-butyl chloride, since the tert.-butyl group is extremely difficult to oxidise, whereas the sec.-butyl group, which by analogy with the reaction between n-butyl chloride and toluene is presumably the radical which enters the nucleus, can be converted to the carboxylic group with ease. Oxidation with chromic acid of the reaction product from chlorobenzene produced a solid which, from a determination of the melting-point, was clearly a mixture. Fractional crystallisation of the solid

yielded some pure p-chlorobenzoic acid and a mixture from which the second constituent could not be isolated in any degree of purity. It was, therefore, decided to attempt to separate the original product of reaction into its constituents, on the assumption that it consisted of m- and p-chloro-sec.-butylbenzenes.

Preliminary experiments were made with m- and p-chlorotoluenes to find the temperature at which concentrated sulphuric acid dissolved the meta and left the para isomeride unaffected. The acid was allowed to react at this temperature on the above mixture. Separation was achieved, although not as completely as in the case of the toluene derivatives, and both the meta and para isomerides proved to be present in the mixture. The portion unsulphonated was oxidised with chromic acid to p-chlorobenzoic acid, thus proving the presence of p-chloro-(?)-butylbenzene as one of the constituents of the reaction product. From the sulphonic acid solution the original chloro-compound was recovered, and on oxidation yielded m-chlorobenzoic acid in a state of purity. Therefore, the other component of the reaction mixture was m-chloro-(?)-butylbenzene. The two isomerides were apparently present in approximately equal quantities, although it is very probable that more of the meta compound was present than was indicated. It has already been stated that these are

most probably derivatives of sec.-butylbenzene.

In a similar way, bromobenzene and n-butyl chloride were shown to produce equal quantities of the meta and para isomerides. Again this ratio of m : p can be regarded as being only very approximate. Unfortunately in neither the case of the chloro- nor of the bromo-(?)-butylbenzenes was the barium sulphate method of separation applied with any success, for there was found to be a great similarity between the solubilities of the barium sulphates of the meta and para isomerides in both cases.

However, these results cast very grave doubts on the accuracy of the results quoted in part A of the table; therefore, Boedtker's experiment with bromobenzene and tert.-butyl chloride was carried out with a slight modification, namely, that carbon disulphide was used as solvent in place of a very large excess of bromobenzene. An improved yield resulted when one and a half molecules of bromobenzene to each molecule of tert.-butyl chloride was used in place of one molecule.

The product of reaction, after sulphonation and treatment of the sulphonic acid with barium carbonate, yielded two barium sulphates differing greatly in solubility, a fact which suggested the method of separation of meta and para isomerides which has already been mentioned in the case of the

tert.-butyltoluenes. The more insoluble of the two salts was converted with ease to a sulphonanilide which proved identical with that prepared from authentic m-bromo-tert.-butylbenzene. In a similar manner the more soluble barium salt was shown to be a derivative of p-bromo-tert.-butylbenzene. Boedtker's observation is faulty because not only was the m-isomeride produced in the reaction, but was found to constitute about 70% of the total yield of mono-substituted derivatives.

Anisole which, like toluene and chloro- and bromobenzenes, contains a substituent with an ortho-para directive influence, was also investigated. It is interesting also because it is known to combine with aluminium chloride to give a well defined crystalline complex (Hartmann and Gattermann, Ber., 1892, 25, 3531). Previous work (Baur, Ber., 1894, 27, 1618) showed that a para-substituted derivative was obtained from a Friedel-Crafts' reaction between anisole and isobutyl bromide.

The product resulting from the action between n-butyl chloride and anisole contained p-(?)-butyl anisole, as shown by its oxidation to anisic acid, but the yield of the acid was so small that it could not be said with certainty that the whole consisted of the para derivative. Sulphuric acid of a strength which would separate m- and p-tolyl

Investigators.

Halide.

Resultants.

A.

1. Friedel, Crafts (Ann. Chim. [6], <u>1</u> , 461)	methyl chloride	m-xylene
2. Ador, Rilliet (Ber., 1879, <u>11</u> , 1627)	methyl chloride	o-, m- and p-xylenes. Chiefly meta
3. Jacobsen (Ber., 1882, <u>14</u> , 2624)	methyl chloride	o-, m- and p-xylenes. Chiefly ortho
4. Defren (Ber., 1895, <u>28</u> , 2648)	ethyl chloride	No product identified.
5. Silva (Bull. Soc. Chim., 1885, <u>43</u> , 322)	<u>n</u> -propyl chloride	p-propyltoluene
6. Genvresse (Bull. Soc. Chim., 1893, [3], <u>9</u> , 225)	<u>n</u> -propyl bromide	m- and p- <u>i</u> sopropyltoluene. Chiefly meta
7. Kelbe (Annalen, 1881, <u>210</u> , 25)	<u>i</u> sopropyl iodide	m- <u>i</u> sopropyltoluene
8. Kelbe, Pfeiffer (Ber., 1886, <u>19</u> , 1724)	<u>i</u> sobutyl bromide	m- and p- <u>t</u> ert.-butyltoluenes
9. Baur (Ber., 1891, <u>24</u> , 2833)	<u>t</u> ert.-butyl chloride	m- <u>t</u> ert.-butyltoluene
10. Bialobrzewski (Ber., 1897, <u>30</u> , 1773)	<u>t</u> ert.-butyl chloride (in pres. of FeCl ₃)	p- <u>t</u> ert.-butyltoluene
11. Essner and Gossin (Bull. Soc. Chim. 1884, <u>42</u> , 213)	opt.act. amyl chloride opt.inact. amyl chloride	m- and p- <u>t</u> ert.-amyltoluenes chiefly meta

methyl ethers left practically all of the reaction product unaffected, which again suggests that only the para isomeride is formed. It must be admitted that the identification of the product is not satisfactory.

EXPERIMENTAL.

The aluminium chloride used in the Friedel-Crafts' reactions was a yellow product obtained by subliming commercial aluminium chloride from a wide combustion tube in a current of dry hydrogen chloride.

The reaction between *tert.*-butyl chloride and toluene in presence of aluminium chloride.

(Baur, Ber., 1891, 24, 2833).

Toluene (125 gm.) distilled over sodium and boiling at 110 - 111° was stirred with aluminium chloride (10 gm.) in a flask from which moisture was excluded, and cooled to 0°. *tert.*-Butyl chloride (25 gm.) was added from a tap-funnel at such a rate that the temperature was maintained at 0 - 5°. After the addition of the chloride, which took about one hour, the mixture was stirred (4 hours) and then poured into water. The toluene layer was separated, washed with caustic soda solution, followed by water, and dried over calcium chloride. After removal of the toluene by distillation, the product of reaction was fractionated, and the fraction of b.p. 180 - 197° collected. A yield of 46% of that expected was

obtained. In some experiments the mixture was allowed to stand for 48 hours at 0° but the yield was much decreased, being only about 28%.

Separation of the isomers by means of concentrated sulphuric acid.

According to the "Enzyklopädie der technischen Chemie", 12, 127, m-xylene can be separated from p-xylene by shaking the mixture repeatedly with an equal weight of concentrated sulphuric acid. The meta-isomeride is dissolved whilst the para- is practically unaffected. Since the tert. butyl-toluenes are similar in constitution to the xylenes, it appeared probable that a separation of the tert.-butyl toluenes could be effected. A slight modification of the method was introduced.

Five grams of the product from the Friedel-Crafts' reaction were stirred vigorously at ordinary temperature with 8 c.c. of concentrated sulphuric acid for 3 - 4 hours. Some heat was developed at first and most of the oil dissolved. The mixture was poured into water and the unchanged oil extracted with ether. On removing the ether, 1.5 gm. (30% of the total) of hydrocarbon was obtained. From the solution of the sulphonic acid 3 gm. (60%) of hydrocarbon were recovered on the addition of an equal volume of concentrated sulphuric acid and distilling

over the hydrocarbon in a current of superheated steam.

Oxidation of the portion soluble in concentrated sulphuric acid.

(Cf. Kelbe and Pfeiffer, Ber., 1886, 19, 1724).

The 3 g. of hydrocarbon recovered from the sulphonic acid were boiled for three days under a reflux with 120 c.c. of dilute nitric acid (d 1.2), the mixture poured into water, extracted with ether, and the ether, in turn, extracted with sodium carbonate solution. On acidifying the alkaline solution with dilute hydrochloric acid, the acid was precipitated. After crystallising the acid a few times from light petroleum (b.p. 40 - 60°) a pure product of m.p. 126.5 - 127° was obtained. It crystallised in plates, and when mixed with an authentic specimen of m-tert.-butylbenzoic acid, melted at 126.5 - 127°.

Oxidation of the portion insoluble in concentrated sulphuric acid.

The 1.5 g. of hydrocarbon undissolved by the sulphuric acid were boiled with dilute nitric acid (d 1.2) and treated in exactly the same manner as above. After a few crystallisations of the crude acid which resulted, a solid of m.p. 162 - 163° was obtained. A mixed mp. with p-tert.-butylbenzoic acid was 162.5 - 163.5°

The reaction between tert.-butyl chloride
and toluene in presence of ferric chloride.

(Białobrzewski, Ber., 1897, 30, 1773).

Anhydrous ferric chloride was prepared by passing dry chlorine over heated iron wire contained in a wide combustion tube, and trapping the sublimed ferric chloride in a bottle cooled by a blast of air.

Toluene (125 g.) and ferric chloride (12 g.) were agitated and cooled to 0° and tert.-butyl chloride (25 g.) added, so that the temperature did not rise appreciably. After the addition, stirring was continued for 4 hours, and towards the end of this time the temperature was allowed to rise to that of the room. The product was poured into water and distilled in steam to separate the oil from ferric chloride. The toluene layer of the distillate was separated, washed with dilute caustic soda solution, followed by water, dried over calcium chloride, and the toluene removed by distillation. The residue on being fractionated gave 28 g. of a liquid of b.p. 180 - 197°. Another experiment yielded 30 g. The yield was, therefore, 70 - 75% of that expected.

On treating the liquid (30 g.) with concentrated sulphuric acid, 8.5 g. remained undissolved, whilst 20 g. were recovered from the sulphonic acid as described above. This latter was distilled and 15 g. collected over the range 185 - 195°. By this method,

Investigator.

Halide.

Resultants.

B.

12. Essner and Gossin (Bull. Soc. Chim., 1884, <u>42</u> , 95)	acetyl chloride	m- and p-tolyl methyl ketones. Chiefly meta
13. Claus (Ber., 1886, <u>19</u> , 234)	acetyl chloride	p-tolyl methyl ketone
14. Verley (Bull. Soc. Chim., 1897, <u>17</u> , 909)	acetyl chloride	p-tolyl methyl ketone
15. Sorge (Ber., 1902, <u>35</u> , 1069)	acetyl chloride	p-tolyl methyl ketone
16. Elbs (J. pr. Chem., 1887, <u>35</u> , 466)	benzoyl chloride	o- and p-tolyl phenyl ketones. Chiefly para
17. Bourcet (Bull. Soc. Chim., 1896, [3], <u>15</u> , 945)	benzoyl chloride	m- and p-tolyl phenyl ketones. Chiefly para: trace meta.

In the résumé the following points were considered to be worthy of special attention. The quantitative aspect of the subject has been ignored save in condensations with acyl chlorides which are generally regarded as giving completely the para derivative except in one particular instance (12). There are, however, in addition to the lack of information about the quantities of

therefore, it was possible to separate from the reaction product 28% of what was apparently the p-isomeride and 70% of the meta.

Conversion of the portion soluble in concentrated sulphuric acid to m-tert.-butylbenzoic acid.

The hydrocarbon (15 g. of b.p. 185 - 195°) was heated to boiling in a flask fitted with a condenser and an inlet tube dipping below the surface of the liquid. Bromine vapour (18 g.) was passed into the liquid through the inlet tube, by means of a current of dry air. The product was distilled in vacuo, yielding 13 g. of a slightly lachrymatory liquid boiling from 92 - 132°/10 mm.

Without further purification, the 13 g. of liquid were boiled with 600 c.c. of KMnO_4 solution (4%) until the colour had disappeared. The liquid was cooled and sulphur dioxide passed in until the manganese dioxide was completely removed. Towards the end of this process, the acid was precipitated. It was extracted away with ether, and in turn, removed from the ethereal solution with aqueous sodium carbonate. This solution, on acidification, yielded 3 g. of crude acid of m.p. 115 - 117°. Recrystallised from light petroleum (b.p. 40 - 60°), it had m.p. 124.5 - 125.5°, and mixed with m-tert.-butylbenzoic acid, gave a m.p. of 124.5 - 125.5°.

Conversion of the portion insoluble in concentrated sulphuric acid to p-tert.-butylbenzoic acid.

After bromination and oxidation of the sulphuric acid insoluble portion, a small quantity of acid of mp. 160 - 163° after being crystallised from light petroleum, was obtained. (Mixed m.p. with p-tert.-butylbenzoic acid 162 - 164°).

Separation of the isomers by conversion to the barium sulphonates.

This method, discovered towards the end of the research when working with bromo-tert.-butylbenzenes, gave a much more reliable and accurate estimate of the proportion of meta to para isomeride in the mixture than that obtained by the sulphonation method.

The mixture of tert.-butyltoluenes (20 g.) was vigorously agitated with 40 c.c. of concentrated sulphuric acid until most of the oil had dissolved. Complete solution was obtained by heating the mixture on the water bath for a few minutes, when it was poured into water contained in a porcelain basin and the whole heated on a sand-bath. Barium carbonate was added until all the acid was neutralised. The aqueous solution was filtered from the solid whilst still hot, and the latter extracted with five litres of water in two portions, the solid filtered off and

well washed with hot water. The filtrates were mixed and the water evaporated off. It was noted that a salt began to crystallise when the volume of the solution was reduced to about five litres. Evaporation was continued until approximately one litre of solution remained, and the solid, which had crystallised out, filtered off. The solution was then evaporated to 150 - 200 c.c. and the small quantity of salt, which had crystallised, removed by filtration. This, along with that already obtained, had a weight of 26 g. (Found: Ba, 23.0. $(C_{11}H_{15}SO_3)_2Ba$ requires Ba, 23.2%). No more solid appeared until the filtrate was evaporated to dryness, and 14 g. of the more soluble barium sulphonate were recovered. (Found: Ba, 23.4%). The difference in solubility of the two barium sulphonates was clearly marked and a good separation was obtained. (Note: the barium sulphonates were dried at 140 - 150° before weighing.)

Recovery of the hydrocarbon from the more insoluble barium sulphonate and oxidation to m-tert.-butylbenzoic acid.

The barium salt (26 g.) was mixed with about 300 c.c. of 50% sulphuric acid and distilled in superheated steam. The distillate was extracted with ether and, after removal of the latter, 12.5 g. of oil were obtained. The hydrocarbon was found to have a b.p. of 188.5 - 190°.

One gram of the oil was dissolved in 15 c.c. of glacial acetic acid and 10 g. of chromic acid in the same solvent slowly added to the boiling solution. After boiling for about two hours, the liquid was poured into water and extracted away with ether. The ethereal solution, in turn, was extracted with sodium hydroxide solution. When the latter was acidified, a small quantity of acid was precipitated which, without crystallisation, had a m.p. of 126 - 127° and did not depress the m.p. of m-tert.-butyl benzoic acid.

Recovery of the hydrocarbon from the more soluble barium sulphonate, and oxidation to p-tert.-butylbenzoic acid.

The method of hydrolysis was identical with that described above. Three grams of hydrocarbon only distilled over because some decomposition took place. When one gram of this oil was oxidised with chromic acid, a small quantity of acid resulted which, when crystallised from light petroleum, melted at 164 - 165°, and was shown to be identical with p-tert.-butylbenzoic acid by a mixed melting-point determination.

Note: Chromic acid was used as oxidising agent, in the hope that the yield of acid would be

larger than that obtained by the other methods, but very little improvement was met with.

These last two experiments show that the more insoluble and the soluble barium sulphonates are derived from m- and p-tert.-butyltoluenes respectively. Therefore, in the mixture from this Friedel-Crafts' reaction the ratio of meta to para isomeride is 65 : 35. The proportion of the meta isomeride should be rather higher, as a small quantity of the barium sulphonate (approximately one gram, assuming the solubility as 5 g. per litre at 100°) is unavoidably mixed with that of the para isomeride. The ratio 67% meta to 33% para would probably be more accurate.

Separation of the tert.-butyltoluenes produced in the reaction, where aluminium chloride was catalyst, by the barium sulphonate method.

The method was applied in exactly the same way as described on p. 22. From 18.5 g. of the hydrocarbons, 23 g. of the more insoluble barium sulphonate and 13.5 of the more soluble salt were obtained, indicating 62% of the meta and 38% of the para isomeride in the mixture. Allowing for the small quantity of the barium sulphonate of the meta compound admixed with that of the para, the ratio would become m- : p- as 65 : 35.

isomerides produced when toluene reacts with alkyl halides, several contradictory statements. For instance, there will be seen from the table discrepancies in the results obtained in (1), (2) and (3); in (5), (6) and (7); in (8) and (9); in (12), (13), (14) and (15); and in (16) and (17). Perhaps the most unaccountable result was that obtained by Bialobrzewski (10) when ferric chloride was used as catalyst and p-tert.-butyltoluene resulted (Cf. Baur (9)).

In order to correlate some of these abnormalities which appear in the above table, a series of reactions were carried out first with tert.-butyl chloride and toluene in presence of aluminium chloride with the production of tert.-butyltoluenes, since it was considered the most satisfactory halide to work with, in view of its comparative non-volatility. As has already been stated, in none of the cases quoted had any reasonably accurate estimate of the proportion of meta to para isomeride been made, and as the extent to which meta substitution takes place has much importance theoretically, and practically, in the preparation of artificial musk, i.e. 2:4:6-trinitro-m-tert.-butyltoluene, a method was devised for the separation of the isomerides.

The presence of the meta and para isomerides

The reaction between *tert.*-butyl chloride and toluene in presence of $C_6H_5.NO_2.AlCl_3$ as catalyst.

The catalyst was prepared by dissolving 10 g. of aluminium chloride in 18 g. (an excess) of nitrobenzene (cf. Olivier, Rec. trav. chim., 1926, 45, 817). The reaction was carried out in the same way as in the absence of nitrobenzene, with the same quantities of *tert.*-butyl chloride and toluene. From the first fractionation, 43 g. of liquid, boiling at 195 - 200°, were obtained. This contained much nitrobenzene.

Removal of the nitrobenzene.

The oil (43 g.) was placed in a flask with 36 g. of tin and heated on the water bath. Concentrated hydrochloric acid (68 c.c.) was added in small portions, so that the liquid boiled gently. After the addition of the acid, the mixture was heated for 2 hours on the water bath, being frequently agitated. Water was added and the oil extracted away with ether. After evaporation off of the ether, the product was fractionated and 29 g. of liquid collected between 185° and 195°, i.e., a 70% yield of *tert.*-butyltoluenes. Two additional experiments yielded 24 and 25 g. of hydrocarbon respectively, representing approximately 60% of that expected.

Separation of the isomers.

Twenty-five grams of the oil were treated with 30 c.c. of concentrated sulphuric acid in exactly the same way as before. Nine grams (36%) were undissolved by the acid, and 11 g. (44%) recovered from the sulphonic acid. The latter distilled at a temperature of 187 - 190°.

Conversion of the portion soluble in concentrated sulphuric acid to m-tert.-butyl benzoic acid.

The hydrocarbon (8.5 g.) was brominated in the manner described on p. 21, when 5 g. of a liquid (b.p. 110 - 135°/10 mm.) were obtained. Oxidation of this with KMnO_4 solution (4%) yielded 3 g. of crude acid of m.p. 119 - 122°. When purified by crystallisation from light petroleum, this substance had m.p. 125 - 126°, and when mixed with m-tert.-butyl benzoic acid, gave a m.p. of 125.5 - 126.5°.

Conversion of the portion insoluble in concentrated sulphuric acid to p-tert.-butylbenzoic acid.

From 9 g. of the oil, 3 g. of bromo-derivative were obtained which, when treated with boiling KMnO_4 solution, yielded an acid of m.p. 110 - 115°. Crystallisation from light petroleum raised

the m.p. to 163 - 164°. (Mixed m.p. with p-tert.-butylbenzoic acid: 164 - 164.5°).

The reaction between acetyl chloride and toluene in presence of aluminium chloride.

(Essner, Gossin, Bull. Soc. Chim., 1884, 42, 95; Verley, Bull. Soc. Chim., 1897 [3], 17, 909; Claus, Ber., 1886, 19, 234; Boesken, Rec. trav. chim., 1897, 16, 313).

Toluene (125 g.) and aluminium chloride (33.5 g.) were stirred together at a temperature of 0 - 5°, and acetyl chloride (20 g.) slowly added. The subsequent treatment was the same as in the other Friedel-Crafts' reactions. The ketone was distilled and the fraction b.p. 223 - 227° collected. The yield of product was 70% of that expected.

Conversion of the ketone to its dibromo-derivative.

(Verley, loc. cit.)

The ketone (5 g.) was dissolved in chloroform (20 g.) and bromine (4 c.c.) added, drop by drop, to the cooled solution. Hydrogen bromide was evolved copiously. The mixture was well washed with water to remove acid, dried, and the chloroform evaporated off.

The violet-coloured, crystalline mass which remained gave, after one crystallisation from 95% alcohol, rhombic plates of m.p. 98 - 99°. Three more crystallisations from alcohol did not alter the m.p., so it appeared to be a single compound.

Oxidation of the dibromo-compound.

(Cf. Roberts, J.C.S., 1916, 109, 793).

The solid (4 g.) was added to 28 c.c. of sodium hypobromite solution (4 %) at ordinary temperature and almost immediately the odour of bromoform was perceptible. After standing overnight, unchanged dibromo-compound and bromoform were extracted away with ether. The aqueous layer acidified with dilute hydrochloric acid and the precipitated acid filtered off. (Yield: 1g, i.e. 50% of that expected). After crystallisation from aqueous alcohol, it had m.p. 181 - 182° and did not depress the m.p. of authentic p-toluic acid.

The reaction between acetyl chloride and toluene in presence of a large excess of aluminium chloride.

The reaction was carried out in the same way as before except that three times the quantity of aluminium chloride was used. The yield of oil

boiling from 220 to 227° was 76% of that expected.

Dibromination of the ketone.

Twenty-five grams of the liquid were treated with bromine (20 c.c.) in the manner described when 40 g. of the dibromo compound (m.p. 98 - 99°) representing a yield 73% of that expected, were obtained. There were 10 g. of uncrystallisable residue. Again p-tolyl methyl ketone was formed almost exclusively.

The reaction between isobutyl bromide and toluene in presence of aluminium chloride.

(Kelbe and Pfeiffer, Ber., 1886, 19, 1724).

Isobutyl bromide was treated with toluene in presence of aluminium chloride in exactly the same way as was tert.-butyl chloride, and gave a 30% yield of hydrocarbon of b.p. 180 - 195°. On sulphonation of 12 g. of the oil, 3.5 g. (30%) were recovered unchanged, and 5 g. from the hydrolysis of the sulphonic acid.

Bromination of the portion soluble in concentrated sulphuric acid yielded 1 g. of bromo-compound (b.p. 105 - 135°/10 mm.) which, by oxidation with aqueous KMnO_4 , was converted to an acid (0.3 g.) of m.p. 122.5 - 124°. The m.p. was raised to

was proved by their oxidation to m- and p-tert.-butyl benzoic acids respectively. The hydrocarbons were separated by a modification of the method used on the industrial scale for the separation of p-xylene from the ortho and meta isomerides by means of concentrated sulphuric acid. As will be seen later, a more accurate method was discovered, which depended on the fact that the barium sulphonates of m- and p-tert.-butyltoluenes showed a remarkable difference in solubility. Fractional crystallisation of these salts effected practically complete separation of the two. From the barium sulphonates the hydrocarbons could be recovered with scarcely any loss. The proportion of meta to para-isomeride in the monosubstituted derivatives was 65% to 35% respectively.

The observation made by Bialobrzewski (Ber., 1897, 30, 1773), viz. that toluene and tert.-butyl chloride in presence of anhydrous ferric chloride yield only p-tert.-butyltoluene, is somewhat surprising as it is difficult to understand why ferric chloride should act differently from aluminium chloride in catalysing the reaction. The above experiment was repeated with ferric chloride, and the product subjected to the same treatment as was applied to that from tert.-butyl chloride, toluene and aluminium chloride, when it was found that m-tert.-butyltoluene

126 - 126.5° when the acid was crystallised from light petroleum, (Mixed m.p. with m.-tert.-butylbenzoic acid 126.5 - 127°).

When the portion insoluble in concentrated sulphuric acid was brominated, 4 g. of a liquid of b.p. 100 - 135/10 mm. was obtained and yielded on oxidation 1.8 g. of an acid of m.p. 75 - 80°. This acid, after two crystallisations from light petroleum, had m.p. 162.5 - 163.5° which did not change when the acid was mixed with p-tert.-butylbenzoic acid.

The reaction between n-butyl chloride and toluene in presence of aluminium chloride.

A mixture of toluene (250 g.) and aluminium chloride (20 g.) was stirred at 0° and n-butyl chloride (50 g.) added slowly. From the product, 42 g. of liquid distilling at 185 - 211° were collected. On refractionation, 37 g. of the liquid distilled between 190° and 208°, the major part having b.p. 198 - 202°. In this and in other experiments a yield of 45% was obtained.

Sulphonation of this liquid.

When the product of the above reaction was treated with cold concentrated sulphuric acid in the usual manner, 25% of it was undissolved, and this fraction on distillation boiled at 200 - 203°.

(Found: C, 89.0; H, 10.9. $C_{11}H_{18}$ requires C, 89.1; H, 10.9%). The hydrocarbon recovered from the sulphonic acid had a b.p. of 197 - 200°. (Found: C, 89.2; H, 10.9%).

Bromination of the portion soluble in concentrated sulphuric acid and oxidation of the bromo-derivative.

Nineteen grams of the hydrocarbon were brominated at its boiling-point in the way described (p. 21). Fifteen grams of a liquid of b.p. 90 - 120°/10 mm. were obtained.

The bromo compound (15 g.) was boiled with 500 c.c. of aqueous $KMnO_4$ (4%) and treated in the usual manner. Much unchanged oil (10 g.) was recovered from the ethereal extract. The acid was observed to be rather insoluble in ether. After extraction with sodium carbonate solution and acidification of this extract, 2 g. of acid were obtained which on crystallisation from aqueous alcohol did not melt below 260°. It sublimed when heated in a flame, and was sparingly soluble in ether. These properties correspond with those of a phthalic acid. It was converted to the methyl ester by the passage of hydrogen chloride into a suspension of one gram of the acid in 20 c.c. of methyl alcohol for about 2 hours. The ester was precipitated by the addition of water, filtered off and crystallised from 30% alcohol. The

slender plates obtained melted at 63 - 64°. This is the m.p. of the dimethyl ester of isophthalic acid. Isophthalic acid was, therefore, the product of the oxidation, proving that one of the compounds from the Friedel-Crafts' reaction was a meta derivative.

Bromination of the hydrocarbon insoluble in concentrated sulphuric acid, and oxidation of the bromo-derivative.

The hydrocarbon (5 g.) was treated with bromine (2 c.c.) in the manner already described, when one gram of liquid distilling at 50 - 70°/9 mm. was obtained.

The bromo-compound (1 g.) was boiled with aqueous KMnO_4 (4%) and treated as before. The acid which was practically insoluble in ether sublimed on heating in a flame. It was converted to the methyl ester in the same way as was isophthalic acid. The ester crystallised from 95% alcohol in slender plates of m.p. 140.5 - 141°. This was the dimethyl ester of terephthalic acid, and therefore the other product of the Friedel-Crafts' reaction was a para derivative.

Attempts were made to prepare a solid derivative of m-(?)-butyltoluene, in order to prove its constitution definitely.

Nuclear bromination of the m-(?)-butyltoluene.

Twenty grams of the oil were brominated at ordinary temperatures with 23 g. of bromine in the same apparatus as used in the other brominations. A small piece of aluminium-mercury couple was used as catalyst. The mixture, after bromination, was washed well with water, dried, and distilled under reduced pressure. Three fractions were collected, viz: at 70 - 102°; 102 - 115° and 115 - 150°, at 8 mm. The middle fraction being the largest, was redistilled, and 8.5 g. of liquid (b.p. 108 - 113°/ 8 mm.) were collected. This contained only a trace of hydrolysable bromine, but the sodium test showed a considerable quantity of non-hydrolysable bromine.

Conversion of the bromo compound to a Grignard derivative, and attempt to make a carboxylic acid from the latter.

The bromo-compound (8.5 g.) was dissolved in dry ether, one gram of magnesium turnings added, and the whole warmed. When the reaction was complete, carbon dioxide was passed in for 15 hours, but only a feeble, if any, reaction took place. Ice and

dilute hydrochloric acid were added, the ethereal layer separated and extracted with sodium carbonate solution. Acidification of the alkaline solution yielded a viscous oil which did not crystallise even on cooling in a mixture of ice and salt. As a satisfactory acid was not obtained, the method was abandoned.

The sulphenanilide of m-(?) -butyltoluene.

The sodium sulphonate of m-(?) -butyltoluene.

Part of the sulphonic acid obtained during the separation of the meta and para isomerides was first treated with excess of calcium carbonate - (1) to precipitate the sulphuric acid as calcium sulphate, and (2) to form the calcium sulphonate. The solid was removed from the hot solution by filtration, and the filtrate gave a solution of the sodium salt on the addition of the requisite amount of sodium carbonate, the precipitate of calcium carbonate being filtered off. This aqueous solution was evaporated to about 100 c.c. when the salt which had crystallised was separated.

This sodium salt was analysed to see if it was the sodium salt of a monosulphonic acid. A weighed quantity of the substance was first heated gently until decomposition was complete and all volatile matter driven off. A few drops of

concentrated sulphuric acid were added and the heating continued. If the residue was not quite white when all the acid was evaporated, the procedure was repeated until all the carbon was oxidised and only sodium sulphate remained. (Found: Na, (I) 8.8, (II) 8.9. $C_{11}H_{15}O_3SNa$ requires Na, 9.2%).

The salt was, therefore, derived from a monosulphonate of m-(?)-butyltoluene.

The sulphonic chloride of m-(?)-butyltoluene.

Five grams of the sodium sulphonate were added to 5 g. of phosphorus pentachloride and heated on the water-bath until a viscous oil was obtained. Iced water was added and the sulphonic chloride extracted with ether, washed well with water, and dried over calcium chloride. The ether was removed and the sulphonic chloride distilled under reduced pressure. It was obtained as a viscous oil of b.p. 160 - 164°/9 mm. (Found: Cl, 14.1; $C_{11}H_{15}O_2SCl$ requires Cl, 14.4 %).

Conversion to the sulphonanilide.

On adding an excess of aniline to the sulphonic chloride, reaction took place immediately with liberation of heat and the separation of aniline hydrochloride. The mixture was heated for a short time on the steam bath to make sure that reaction was complete. Dilute hydrochloric acid was added to

remove excess of aniline and dissolve the aniline hydrochloride. On standing for some time, the sulphonanilide, which was precipitated as a viscous oil, solidified. After a few crystallisations from 95% alcohol the substance was obtained in rhombic prisms of m.p. $119.5 - 120^{\circ}$. (Found: N, (I) 4.45, (II) 4.52. $C_{17}H_{21}O_2NS$ requires N, 4.62%).

Synthesis of m-n-butyltoluene.

A mixture of 100 g. m-bromotoluene, 100 g. n-butyl bromide, 200 c.c dry benzene and 30 g. of sodium in thin slices was heated on the water bath until reaction commenced. The mixture was cooled if reaction became too vigorous. When reaction had somewhat abated, the whole was heated for six hours on the water bath. The benzene solution was separated from the bluish solid, which was, in turn, washed twice with benzene. The benzene solution was washed with water, dried, distilled and the fraction distilling at $195 - 210^{\circ}$ collected; 43 g. were obtained. This liquid was found to contain bromine, probably in the form of m-bromotoluene. To remove this compound, the liquid was dissolved in dry ether, 5 g. of magnesium added, and the whole heated on the water bath. Some reaction was observed to take place. Ice and dilute hydrochloric acid were added, and the

ethereal layer separated, and from it 21 g. of m-n-butyltoluene of b.p. 202 - 205° were obtained. Niemczyski (Bull, Acad. Sci. Cracovie, 1900; Chem. Zentr., 1900, [2], 468) quotes the b.p. as 197 - 198°.

Sulphonanilide of m-n-butyltoluene.

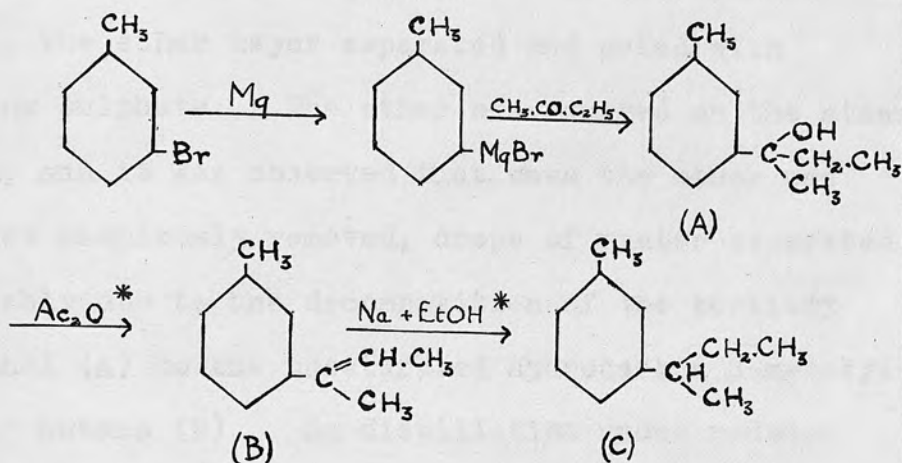
Fifteen grams of m-n-butyltoluene were sulphonated at ordinary temperature, and the sulphonic acid converted into the sodium salt. The latter was treated with the theoretical quantity of phosphorus pentachloride in the usual way. The sulphonic chloride which resulted had a b.p. of 162 - 167°/10 mm., and yielded, with excess of aniline, a sulphonanilide which after a few crystallisations from 95% alcohol had a m.p. 130 - 130.5°. It crystallised in rhombic prisms.

(Found: N, 4.51. $C_{17}H_{21}O_2SN$ requires N, 4.62%).

The mixed m.p. with the sulphonanilide of m-(?)-butyltoluene of unknown constitution was 100 - 102°, i.e., the two were not identical.

Synthesis of m-sec.-butyltoluene.

This was carried out according to the reactions summarised in the following scheme:



m-Bromotoluene with magnesium followed by the action of methyl ethyl ketone gave an unstable tertiary alcohol (A) and this, with acetic anhydride, was converted to β -m-tolyl- \triangle^2 -butene (B) which was reduced by sodium and ethyl alcohol to m-sec.-butyltoluene (C).

m-Tolyl methyl ethyl carbinol.

(Cf. Rupe and Burgin, Ber., 1911, 44, 1219)

Seven grams of dry magnesium turnings and 50 g. m-bromotoluene in 150 c.c of dry ether were

* The symbols "Ac" and "Et" denote throughout the radicals $\text{CH}_3\text{CO}-$ and C_2H_5- respectively.

allowed to react in the usual manner. To the Grignard compound were added slowly 21 g. of methyl ethyl ketone (b.p. 78.5 - 79.5°) in 30 c.c. of dry ether. After standing overnight the magnesium compound was decomposed with ice and dilute hydrochloric acid, the ether layer separated and dried with sodium sulphate. The ether was removed on the steam bath, and it was observed that when the ether was almost completely removed, drops of water separated, probably due to the decomposition of the tertiary alcohol (A) to the unsaturated hydrocarbon β -m-tolyl- \triangle^2 -butene (B). On distillation under reduced pressure, the largest fraction came over at 85 - 95°/12 mm. This b.p. is much lower than that expected when compared with that of p-tolyl methyl ethyl carbinol (b.p. 108.5 - 109°/10 mm, Rupe and Bürgin, loc. cit.). Bromine water was instantly decolorised by the compound, indicating unsaturation. It was considered more convenient to convert the crude product directly to the unsaturated hydrocarbon.

β -m-tolyl- \triangle^2 -butene.

The crude m-tolyl methyl ethyl carbinol was boiled with about $2\frac{1}{2}$ times its weight of acetic anhydride for 3 hours. The mixture was poured into water and the oily layer separated, washed with caustic soda solution, then with water, and dried.

The oil was fractionally distilled under diminished pressure and the fraction of b.p. 90 - 94°/12 mm. collected. This liquid was found to be unsaturated. (Found: C, (i) 86.2, (ii) 86.1; H, (i) 9.3, (ii) 9.4. $C_{11}H_{14}$ requires C, 90.4; H, 9.6%). The discrepancies between the theoretical percentages of carbon and hydrogen and those observed must be due to impurities which did not appear in the reduced hydrocarbon (q.v.).

m-sec.-Butyltoluene.

(For method of reduction see Klages, Ber., 1902, 35, 2642).

The β -m-tolyl- \triangle^2 -butene was reduced by dissolving it in ten times its volume of absolute alcohol and adding its own weight of sodium in small portions, so that the temperature of the alcohol was maintained at the boiling point. The product was poured into water and the oil extracted away with ether. After removal of the latter, the oil was distilled and the fraction of b.p. 194 - 198° collected. On the addition of bromine water, very little evidence of unsaturation was observed.

Sulphonanilide of m-sec.-butyltoluene.

Twenty-four grams of the hydrocarbon were sulphonated by the usual method, and converted by means of barium carbonate to the barium sulphonate,

of which 27 g. were obtained. It was observed that this salt was sparingly soluble in hot water. Twenty grams of this compound on treatment with phosphorus pentachloride yielded the sulphonic chloride (11 g. distilling at 162 - 166°/11 mm.). This compound with aniline in excess, gave the sulphonanilide which, after two crystallisations from 95% alcohol, had a m.p. 120.5 - 121°, and which did not depress the m.p. of the sulphonanilide from the m-(?) - butyltoluene of unknown constitution. This observation proved that the unknown readily sulphonated compound was identical with m-sec.-butyltoluene.

The sulphonanilide of the p-(?) - butyltoluene obtained from the Friedel-Crafts' reaction with toluene and n-butyl chloride.

Ten grams of the para hydrocarbon separated from the meta isomeride by means of cold concentrated sulphuric acid in which it is insoluble were heated (vigorous stirring) on the water bath with 15 c.c. of concentrated sulphuric acid for 1 - 2 hours. The sulphonic acid so obtained was converted to the barium salt which was very soluble in water and did not begin to crystallise until the solution was almost evaporated to dryness. The barium salt (18.5 g.) was mixed with 15 g. of phosphorus pentachloride and allowed to react

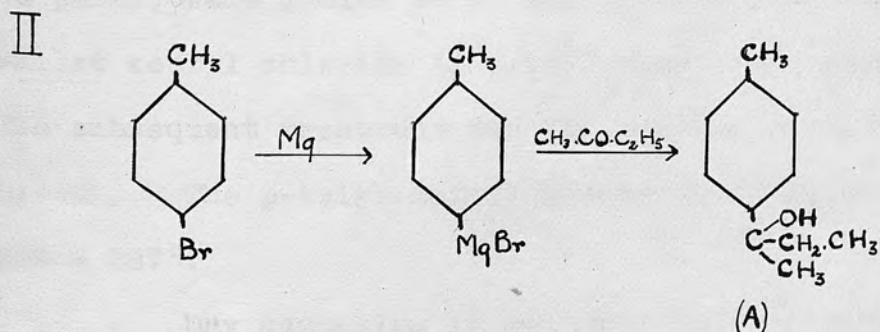
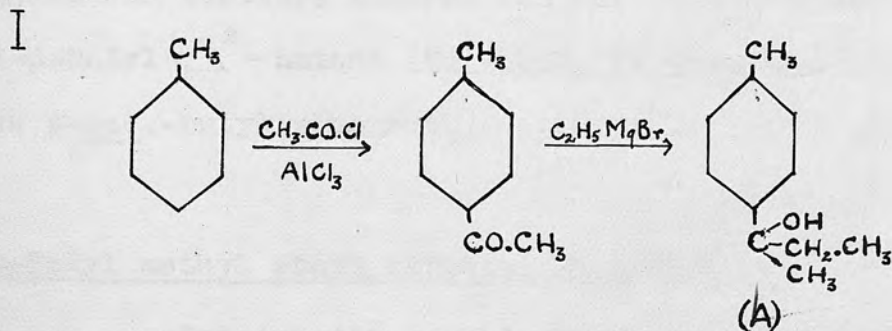
in the usual way. Nine grams of sulphonic chloride (b.p. 166 - 170°/14 mm.) were collected.

(Found: Cl, 14.4. $C_{11}H_{15}O_2SCl$ requires Cl, 14.4%).

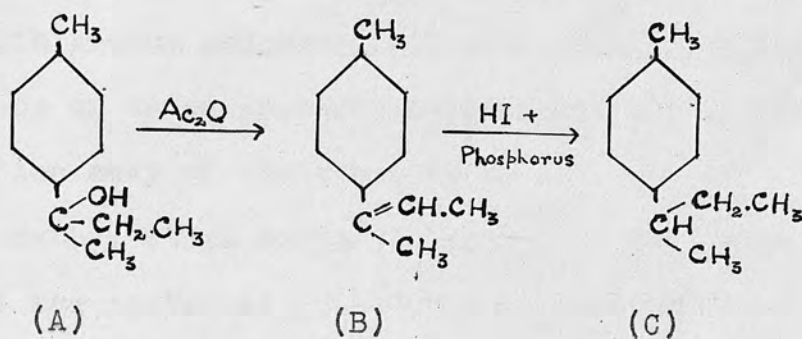
Excess of aniline converted the sulphonic chloride to sulphonanilide which, after purification by crystallisation from 95% alcohol, had m.p. 123.5 - 124.5°. The crystalline form of this sulphonanilide was rhombic prisms. (Found: N, (i) 4.54, (ii) 4.55. $C_{17}H_{21}O_2NS$ requires N, 4.62%).

Synthesis of p-sec.-butyltoluene.

In this synthesis p-tolyl methyl ethyl carbinol, one of the intermediate compounds, was prepared by two methods which may be outlined as follows:-



The p-tolyl methyl ethyl carbinol (A) was prepared (i) by the action of p-tolyl methyl ketone, prepared from acetyl chloride and toluene, on ethyl magnesium bromide, and (ii) by methods similar to those employed in the case of the meta isomeride (p. 39). The remainder of the synthesis followed the scheme:



where the tertiary alcohol (A) was converted to β-p-tolyl- Δ^2 -butene (B) which, in turn, was reduced to p-sec.-butyltoluene (C).

p-Tolyl methyl ethyl carbinol by method I.

Toluene (15 parts) and aluminium chloride (5 parts) were cooled to 0° and stirred vigorously whilst acetyl chloride (3 parts) was added slowly. The subsequent treatment was the same as given on p. 28. The p-tolyl methyl ketone distilled at 226 - 227°.

Dry magnesium (1 mol) was covered with

dry ether, and ethyl bromide (1 mol) mixed with dry ether slowly added so that reaction did not become too violent. When reaction was complete, *p*-tolyl methyl ketone (1 mol), dissolved in dry ether, was slowly dropped into the mixture which was cooled in ice. The mixture was allowed to stand overnight, and the Grignard compound decomposed with dilute hydrochloric acid. The ethereal layer after separation was well dried with sodium sulphate, but even after this treatment, drops of water appeared towards the end of the evaporation away of the ether as in the case of *m*-tolyl methyl ethyl carbinol (p. 40). The crude carbinol was converted to the unsaturated hydrocarbon (B) without previous distillation.

p-Tolyl methyl ethyl carbinol by method II.

(Rupe and B^urgin, Ber., 1911, 44, 1219)

A mixture of *p*-bromotoluene (1 mol), magnesium turnings (1 mol) and 450 c.c. dry ether was warmed gently on the water bath. Reaction soon set in and became so vigorous that it was necessary to cool the mixture in ice. Rupe and B^urgin (loc. cit.) had difficulties with this reaction, especially when working with large quantities, difficulties which were not experienced. To the Grignard compound was slowly run in methyl ethyl ketone (1 mol) dissolved in ether. The mixture was allowed to stand overnight and then

treated in the usual way. The ethereal layer was separated, dried, and the crude carbinol obtained on removal of the ether by distillation.

β -p-Tolyl- \triangle^2 -butene (B). (Rupe and B"urgin, loc.cit.)

p-Tolyl methyl ethyl carbinol (2 parts) was boiled for 3 hours with acetic anhydride (5 parts), after which the mixture was cooled, poured into water, neutralised with caustic soda with cooling, the oil extracted with ether, and the ethereal solution dried. The oil, when fractionally distilled, boiled between 90° and $94^\circ/10\text{mm}$. (Rupe and B"urgin give b.p. $93.5 - 94^\circ/10 \text{ mm}$.)

p-sec.-Butyltoluene.

Attempts were made to reduce the unsaturated hydrocarbon in the same way as was β -m-tolyl- \triangle^2 -butene (p. 41), but very incomplete reduction took place. Sodium amalgam was no more successful as reducing agent. Hydriodic acid and red phosphorus, however, reduced the compound.

β -p-Tolyl- \triangle^2 -butene (3 parts), hydriodic acid of b.p. 127° (12 - 13 parts) and red phosphorus (1 part) were heated to boiling when a vigorous reaction took place and some free iodine was liberated. After boiling for some time, the mixture was poured into water, and filtered ~~with ether~~ to remove the

phosphorus, the latter being well washed with ether to remove the hydrocarbon. The ethereal layer of the filtrate was separated, well washed with aqueous caustic soda, dried, and the ether removed by distillation. The oil, though colourless at ordinary temperatures, became violet-coloured on boiling, due to the decomposition of some iodine compound. Iodine was also contained in the distillate. The latter was distilled over sodium, and pure ^{p-}sec.-butyltoluene of b.p. 195 - 197° was obtained (cf. Wallach, Annalen, 1917, 414, 207, 211, who quotes the b.p. as 196 - 197°).

Sulphonanilide of p-sec.-butyltoluene.

p-sec.-Butyltoluene (10 g.) was sulphonated on the water bath with 15 c.c. concentrated sulphuric acid in the usual manner. Two layers separated, but the whole dissolved on pouring into water. This sulphonic acid was converted to the barium salt which was observed to be very much more soluble than the barium sulphonate of the meta isomeride. Nineteen grams of the barium sulphonate were obtained and yielded 12 g. of sulphonic chloride (b.p. 160 - 164°/13 mm.). (Found: Cl, 14.2. $C_{11}H_{15}O_2SCl$ requires Cl, 14.4%).

The sulphonanilide prepared from this compound crystallised in rhombic prisms of m.p. 124.5 - 125° from 95% alcohol. When mixed with the sulphonanilide

of the p-(?)-butyltoluene of unknown constitution a m.p. of 123.5 - 124.5° was obtained. This proved definitely that p-sec.-butyltoluene is the other product of the Friedel-Crafts' reaction between toluene and n-butyl chloride.

The reaction between n-butyl chloride and chlorobenzene in presence of aluminium chloride.

Chlorobenzene (60 g.), aluminium chloride (20 g.) and carbon disulphide (250 c.c.) were vigorously stirred and cooled to 0°, when n-butyl chloride (50 g.) was added slowly. Evolution of hydrogen chloride did not commence until almost all the chloride had been added. The mixture was allowed to stand for about 24 hours at 0° and then treated in exactly the same way as the products from the other Friedel-Crafts' reactions. On distillation of the residue, after removal of carbon disulphide, 40 g. of an oil of b.p. 215 - 225° were collected. (Found: Cl, 20.6. C₁₀H₁₃Cl requires Cl, 21.1%).

Separation of the isomerides.

A separation of the isomerides was attempted in the following way. Twenty grams of the oil were vigorously agitated with 40 c.c. of concentrated sulphuric at 75 - 80° for half an hour. (Note: it had already been observed that under these circumstances

m-chlorotoluene dissolved whilst p-chlorotoluene was practically unaffected). Eight grams of oil (40% of the total) were undissolved, whilst 9 g. (45%) were recovered from the sulphonic acid by distilling in superheated steam. In this distillation sufficient sulphuric acid was added to the solution of the sulphonic acid to raise its boiling-point to 150 - 160°.

Oxidation of the portion which had dissolved in the sulphuric acid.

Two grams of the oil were dissolved in 50 c.c. of glacial acetic acid and heated to boiling. A solution of chromic acid prepared by dissolving 12 g. in 7 c.c. of water and 35 c.c. acetic acid was slowly added, drop by drop, to the boiling solution. When all the solution had been run in and the liquid was quite green, the mixture was poured into water. This solution was extracted with ether and from the latter there was removed with sodium hydroxide solution one gram of an acid, which was precipitated from the alkaline solution on acidification. The solid had m.p. 154 - 155°. When crystallised from water it melted at 155.5 - 156° alone and when mixed with m-chlorobenzoic acid.

Oxidation of the portion unaffected by the sulphuric acid.

Two grams of this oil, when oxidised

according to the method described above, yielded one gram of an acid of m.p. 216° . Crystallisation of the compound from water raised its m.p. to $238.5 - 239.5^{\circ}$. (Mixed m.p. with p-chlorobenzoic acid $239 - 240^{\circ}$).

From the recognition of the two acids as m- and p-chlorobenzoic acids, the ease of oxidation of the chlorinated hydrocarbons, and by analogy with the production of sec.-butyltoluenes, it was concluded that the products of the Friedel-Crafts' reaction were m- and p-chloro-sec.-butylbenzenes.

When separation of the isomerides was attempted by converting to the barium sulphonates, it was found that the solubilities of these salts were too similar to allow of their being separated by fractional crystallisation.

The reaction between n-butyl chloride and bromobenzene in presence of aluminium chloride.

This reaction was carried out in exactly the same manner as was the reaction when chlorobenzene was used, and the quantities of materials employed were: bromobenzene, 85 g.; n-butyl chloride, 50 g.; aluminium chloride, 20 g.; and carbon disulphide, 250 c.c. The product, of which a 50% yield was obtained, distilled over the range $236 - 250^{\circ}$. (Found: Br, 37.2.

$C_{10}H_{13}Br$ requires Br, 37.6%).

Separation of the isomerides.

Twenty grams of the oil were agitated with 40 c.c. of concentrated sulphuric acid at 95° for 1 hour. (In a preliminary experiment with m- and p-bromotoluenes it was found that under these conditions the para isomeride was unaffected whilst the meta dissolved.) Nine grams (45% of the total) of oil were extracted away unchanged with ether and 9 g. (45%) were recovered from the sulphonic acid by the same method as used in the experiment with chlorobenzene (p. 49).

Oxidation of the separated portions of the reaction product.

The method used in both oxidations has already been described on p. 49, where the two chloro-(?)-butylbenzenes were the compounds so treated.

From 2 g. of the oil recovered from the sulphonic acid 0.9 g. of an acid of m.p. $155.5 - 156^{\circ}$, without being crystallised, was obtained. This compound was pure m-bromobenzoic acid as shown by a determination of a mixed melting point with an authentic specimen of that acid.



In a similar way, 2 g. of the unsulphonated oil were oxidised to an acid (1 g.) the m.p. of which was approximately 236°. The acid when crystallised from 95% alcohol gave a m.p. of 254.5 - 255° and did not depress the m.p. of authentic p-bromobenzoic acid.

These two results show very definitely that both m- and p-bromo-(?)-butylbenzenes are the products of this reaction. Most probably the butyl group of doubtful constitution is secondary-butyl, by analogy with the case of the sec.-butyltoluenes produced from toluene and n-butyl chloride in presence of aluminium chloride (pp. 42 and 48).

Separation of the isomerides by the barium sulphonate method was attempted but was unsuccessful, as again the similarity in solubility between these salts was too great to effect their separation. The estimate of the ratio m : p given by the sulphonation method of separation cannot be taken as accurate, since the p-bromobenzoic acid from the oxidation was obviously impure and probably contained some of the meta compound.

The reaction between tert.-butyl chloride and bromobenzene in presence of aluminium chloride.

(Boedtker, Bull. Soc. Chim., 1906, [3], 35, 829)

A mixture of bromobenzene (65 g.), aluminium

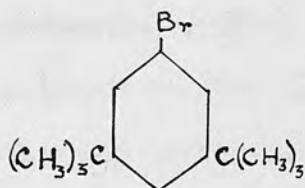
chloride (10 g.) and carbon disulphide (125 c.c.) was stirred together and cooled to 0°. tert.-Butyl chloride (25 g.) was added slowly, when reaction started almost immediately, copious fumes of hydrogen chloride being evolved. Subsequent procedure was the same as in previous Friedel-Crafts' reactions. When the carbon disulphide had been removed by distillation the residue was distilled under reduced pressure, when excess of bromobenzene distilled first, and then the boiling point rose to 87°/8 mm. and the fraction (b.p. 87 - 106°/8 mm.) was collected separately. Forty-one grams of oil, representing a 70% yield of that expected, were obtained.

Separation of the isomerides.

The improved method of separation of meta and para isomerides by means of the barium salts of the corresponding sulphonic acids was employed in this case, when it proved to be extraordinarily efficient. (See pp. 22 - 23 for a description of the method, where it was used for the separation of m- and p-tert.-butyltoluenes). To sulphonate the oil it was treated with twice its volume of fuming sulphuric acid (5 parts sulphuric acid containing 15% free SO₃ : 2 parts concentrated acid).

From 20 g. of the oil, 22.5 g. of the

sparingly soluble barium sulphate which was afterwards proved to be that of *m*-bromo-tert.-butylbenzene (Found: Ba, 19.2. $(C_{10}H_{12}BrSO_3)_2Ba$ requires Ba, 19.05%) and 9.5 g. of the barium sulphate of the corresponding *para* compound (Found: Ba, 19.5%) were obtained. After sulphonation of the original oil, a small quantity (0.5 g.) remained, which could not be sulphonated. This was probably a polysubstituted derivative of bromobenzene, possibly 1-bromo-3:5-ditert.-butylbenzene:



(the tert.-butyl group preventing substitution ortho to itself: Shoesmith and Mackie, J.C.S., 1928, 2334).

The weights of barium sulphates obtained proved that the *m*-bromo-derivative was present with the *para* compound in a ratio of 70 to 30. This ratio is not quite correct because a small quantity of the sulphate from the *meta* compound was unavoidably present in that of the *para*.

The constitution of the two components of the reaction product was proved by converting them to the corresponding sulphonanilides and identifying these with sulphonanilides prepared from *m*- and *p*-bromo-tert.-butylbenzenes respectively.

Sulphonanilide prepared from the more insoluble barium sulphonate.

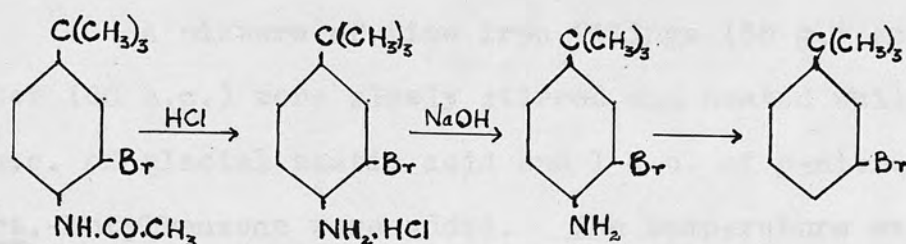
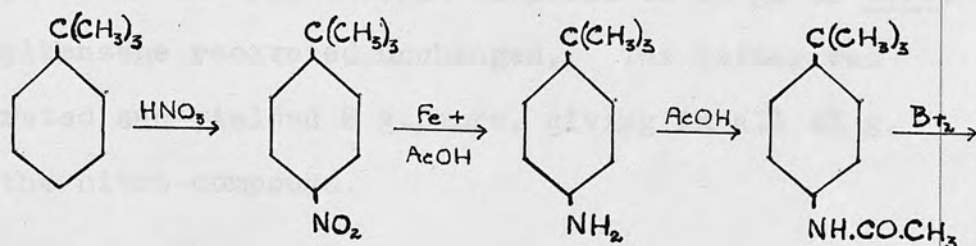
Five grams of the sulphonate were heated on the water bath with 3 g. of phosphorus pentachloride until the mass became quite liquid. The sulphonic chloride, of which 3.7 g. were obtained, was isolated in the usual manner. This compound solidified on cooling. (Found: Cl, 11.3. $C_{10}H_{12}O_2SClBr$ requires Cl, 11.4%).

The sulphonanilide which resulted from the action of excess aniline on the above compound had m.p. 156 - 157.5° before crystallisation. After crystallisation from 95% alcohol it melted at 160 - 160.5°. The yield was 90% of that expected, calculated on the quantity of barium salt used. (Found: Br, 21.3. $C_{18}H_{18}O_2SNBr$ requires Br, 21.7%).

Synthesis of m-bromo-tert.-butylbenzene.

(Cf. Organic Synthesis, 6, 16).

The method was similar to that employed for the preparation of m-bromotoluene from p-toluidine. The following scheme shows the stages of the synthesis:



A slight modification of the usual method had to be made, as difficulty was met with in isolating 3-bromo-4-amino-tert.-butylbenzene hydrochloride in a state of purity.

p-Nitro-tert.-butylbenzene.

tert.-Butylbenzene (45 g.) was vigorously stirred at ordinary temperature and an equal weight of nitric acid (d 1.52) added during two hours. The mixture was poured into water and the oil extracted with ether. After washing with water and sodium carbonate solution the ether was removed, and the residue distilled under diminished pressure.

Thirty-five grams of p-nitro-tert.-butylbenzene resulted (b.p. 125 - 130°/10 mm.), in addition to 10 g. of tert.-butylbenzene recovered unchanged. The latter was nitrated and yielded 8 g. more, giving in all 43 g. of the nitro-compound.

p-Amino-tert.-butylbenzene.

A mixture of fine iron filings (50 g.) and water (60 c.c.) were slowly stirred and heated whilst 3 c.c. of glacial acetic acid and 1 c.c. of p-nitro-tert.-butylbenzene were added. The temperature was raised to 90° and 43 g. of p-nitro-tert.-butylbenzene run in during the course of 3 hours. After heating for a further 2 hours the amine was distilled in steam and extracted from the distillate with ether. The ethereal layer was extracted with dilute hydrochloric acid and the amine precipitated from this solution with ammonia. The amine was extracted with ether, dried, and distilled under reduced pressure. The liquid collected had b.p. 101°/8 mm. and weighed 31 g.

p-Acetamido tert.-butylbenzene.

The amine (31 g.) was boiled for 2 hours with 90 c.c. of glacial acetic acid when the acetamido compound was formed. It was not isolated but brominated in the acetic acid solution.

3-Bromo-4-acetamido-tert.-butylbenzene.

To the thoroughly agitated solution of p-acetamido-tert.-butylbenzene cooled to 50° were added 12 c.c. of bromine so that the temperature remained at 50 - 55°. When the bromine was added, the mixture was stirred for a further half-hour and then poured in a thin stream into 2 litres of water which was vigorously stirred and contained 5 g. of sodium bisulphite. The precipitated acetamido compound was filtered off and dried.

3-Bromo-4-amino-tert.-butylbenzene hydrochloride.

The crude 3-bromo-4-acetamido-tert.-butylbenzene was dissolved in 40 c.c. of 95% alcohol and heated to boiling, when 40 c.c. of concentrated hydrochloric acid were added and the boiling continued for 3 hours. On cooling the solution 13 g. of a hydrochloride separated. This was washed with ether to remove impurities. The amine liberated from this compound with aqueous caustic soda did not give m-bromo-tert.-butylbenzene after diazotisation in alcoholic solution and heating the solution of the diazonium compound with copper powder. The liquid obtained had b.p. 90 - 105°/8 mm., whereas m-bromo-tert.-butylbenzene has a b.p. about 85°/8 mm. Apparently, the hydrochloride which had separated

consisted chiefly of that from a dibrominated p-amino-tert.-butylbenzene. The mother liquors of the hydrochloride still contained a considerable quantity of the amine, so were treated as follows.

Water was added to the alcoholic solution and the whole distilled in steam to remove alcohol and the ethyl acetate formed during the hydrolysis of the acetamido compound. Sodium hydroxide was added to the liquid in the distillation flask until the amine was completely precipitated. Steam distillation was continued, and the amine in the distillate extracted with ether and purified by extracting it from the ether with dilute hydrochloric acid, and liberating it again by means of ammonia. It was extracted away with ether, and the ethereal solution dried. After removal of the ether the amine was fractionally distilled under reduced pressure.

p-Amino-tert.-butylbenzene distilled first (b.p. about $100^{\circ}/8$ mm.) and then the temperature rose and the supposed 3-bromo-4-amino-tert.-butylbenzene collected from $115 - 131^{\circ}/8$ mm. (chiefly $129 - 131^{\circ}/8$ mm.). This was the required product, since a small quantity when shaken with acetic anhydride gave the acetamido compound which, when crystallised from aqueous alcohol, melted at $153 - 155^{\circ}$, and which did not depress the m.p. of an authentic specimen of 3-bromo-4-acetamido-tert.-butylbenzene. The amine was, therefore the

compound required.

m-Bromo-tert.-butylbenzene.

To a cold mixture of 38 c.c. of absolute alcohol and 10 c.c. of concentrated sulphuric acid, 12 g. of the amine were added and the whole cooled to 0°. Sodium nitrite (6 g.) in 8 c.c. of water was slowly dropped in, so that the temperature was maintained below 10°. The mixture was stirred for 20 minutes after the addition. Copper powder (2 g.) was added and the mixture gently heated on the water bath, when acetaldehyde and nitrogen were liberated. When the violence of the reaction had abated, the mixture was heated for a further half-hour on the water bath. Water was added and the whole steam distilled. The heavy oil was extracted with ether, washed twice with sodium hydroxide solution and then with water. The ether was removed by evaporation and the residue washed once with concentrated sulphuric acid and then with sodium carbonate solution. It was extracted with ether, dried, and distilled. A few drops of tert.-butylbenzene distilled first, but soon the temperature rose and 4.5 g. of m-bromo-tert.-butylbenzene of b.p. 85 - 86.5°/8 mm. were collected.

Sulphonanilide of m-bromo-tert.-butylbenzene.

m-Bromo-tert.-butylbenzene (4.5 g.) yielded the barium sulphonate (6.5 g.) after sulphonation with fuming sulphuric acid (5 parts sulphuric acid containing 15% free SO_3 : 2 parts concentrated acid) and treatment of the sulphonic acid with barium carbonate in the manner already described. Phosphorus pentachloride converted this barium salt to the sulphonic chloride which without distillation was treated with excess of aniline. The sulphonanilide so obtained crystallised in rhombic prisms from 95% alcohol and had m.p. $160 - 160.5^\circ$, both alone and when mixed with the sulphonanilide prepared from the more insoluble barium sulphonate obtained from the product of the Friedel-Crafts' reaction between bromobenzene and tert.-butyl chloride. This proved that the portion of the reaction product which gave this barium sulphonate and which was present to the extent of 70% of the monosubstituted derivatives was m-bromo-tert.-butylbenzene. This is in absolute contradiction to the statement of Boedtker (loc. cit.) that only the para isomeride is produced in the reaction. In addition, the difficulties reported by Boedtker were not encountered.

Sulphonanilide from the more soluble barium sulphonate.

The sulphonic chloride prepared from this barium sulphonate by the action of phosphorus pentachloride boiled at 171 - 172°/8 mm. (Found: Cl, 11.4. $C_{10}H_{12}O_2SClBr$ requires Cl, 11.4%). It yielded, as in the other cases, a sulphonanilide of m.p. 151 - 153° after one crystallisation from 95% alcohol from which it separated in long rhombic prisms. (Found: Br, 21.3. $C_{16}H_{18}O_2SNBr$ requires Br, 21.7%).

Sulphonanilide of p-bromo-tert.-butylbenzene.

p-Bromo-tert.-butylbenzene (5 g.) was sulphonated with sulphuric acid (10 c.c.) of the same strength as was used for the meta isomeride. The barium salt of the sulphonic acid was prepared and, when treated with phosphorus pentachloride, gave a sulphonic chloride of b.p. 172 - 173°/8 mm. which solidified on cooling. Excess of aniline reacted with the compound to give the sulphonanilide which crystallised from 95% alcohol in long rhombic prisms of m.p. 152.5 - 153.5°. When this was mixed with a sample of the sulphonanilide obtained from the more soluble barium sulphonate, the m.p. was unaffected, thus proving the constitution of this portion of the oil to be p-bromo-tert.-butylbenzene.

The reaction between *n*-butyl chloride and anisole in presence of aluminium chloride.

(Cf. Baur, Ber., 1894, 27, 1618).

The reaction was carried out according to the method given by Baur, but no appreciable evolution of hydrogen chloride took place, even after heating for 12 hours on the water bath. The following method was adopted.

Thirty grams of anisole, 40 g. of aluminium chloride and 125 c.c. of carbon disulphide were agitated and cooled to 0°. During the cooling, crystals of the compound of anisole and aluminium chloride separated (Hartmann and Gattermann, Ber., 1892, 25, 3531). *n*-Butyl chloride (25 g.) was slowly added and after some time hydrogen chloride was evolved. The mixture was left over-night at 0° and then the temperature allowed to rise to about 15°. The mixture was treated in the usual manner and after the removal of the carbon disulphide, the oil which remained was fractionally distilled under reduced pressure, when a fraction of b.p. 95 - 115°/12 mm. was collected. Distillation of this fraction at ordinary pressure yielded 11g. of oil of b.p. 220 - 230°. (Found: C, 80.2; H, 9.92. $C_{11}H_{16}O$ requires C, 80.5; H, 9.83%).

Oxidation of the product of the above reaction.

An attempt to oxidise the reaction product with chromic acid was carried out. The method was identical with that used in the case of m-chloro-(?)-butyltoluene which is described on p. 49. From the oxidation of 2 g. of the oil no acid was isolated, but 0.5 g. of a sweet-smelling oil was recovered from the ethereal extract. From the appearance of the oxidation mixture it was evident that some oxidation had taken place, so further oxidation of this oil was attempted with potassium permanganate. Four grams of potassium permanganate dissolved in 50 c.c. of water were boiled with the oil till the colour of the former had disappeared. The manganese dioxide was removed with sulphur dioxide and the precipitated solid extracted away with ether. The ether was, in turn, extracted with sodium carbonate solution and the alkaline extract acidified. The small quantity of acid which was precipitated had m.p. 182.5 - 183.5 alone and together with an authentic specimen of anisic acid. This proved that a p-methoxy derivative was present.

In order to see if there was any meta isomeride present, the sulphonation method of separation was applied. Preliminary experiments were carried out with m- and p-tolyl methyl ethers to

discover which strength of sulphuric acid dissolved the meta isomeride and left the para unaffected at ordinary temperature. A mixture of $4\frac{1}{2}$ parts concentrated sulphuric acid and one part of water gave the desired result.

On stirring 10 g. of the product of the Friedel-Crafts' reaction with 30 c.c. of acid of the above strength for one hour and pouring the mixture into water, 9 g. of oil undissolved by the sulphuric acid were recovered. This would indicate that little or none of the oil consists of the meta isomeride although, of course, the evidence is not conclusive.

The important observations in the preceding pages are summarised below:

1. The proportions of m- and p-tert.-butyl-toluenes produced in the reaction between tert.-butyl chloride and toluene with aluminium chloride as catalyst have been estimated.

2. The proportions of m- and p-tert.-butyl-toluenes in the same reaction with ferric chloride as catalyst have been estimated.

3. The observation of Bialobrzewski was shown to be definitely wrong by proving that m-tert.-butyl-toluene was a product of the reaction mentioned in (2), and that it was present to the extent of 65% of the total monosubstituted derivatives.

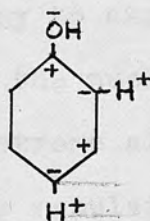
4. The reaction between n-butyl chloride and toluene was carried out for the first time, and m- and p-sec.-butyltoluenes shown to be products of the reaction.

5. The reactions between n-butyl chloride and both chloro- and bromobenzenes were carried out for the first time, and m- and p-derivatives of the halogeno-benzenes shown to be formed in both cases.

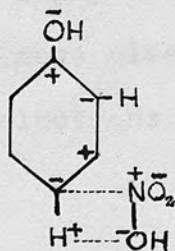
6. tert.-Butyl chloride and bromobenzene, when allowed to react in presence of aluminium chloride, were shown to produce m- and p-bromo-tert.-butyl-benzenes in a proportion of 70% to 30% respectively, which disagrees with the result of Boedtger who reported that the p-derivative only was formed.

DISCUSSION OF RESULTS.

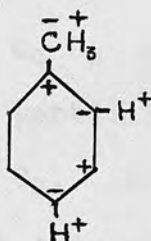
One of the most important theories which have been advanced to account for the reactivity of the ortho and para positions during substitution in, for example, phenol, halogeno-benzenes and toluene, is that of Lapworth (Mem. Manchester Phil. Soc., 1920, 64, ii, 1). This theory postulates that certain atoms ("key atoms") of the substituent induce alternating polarity through the chain of carbon atoms. Thus, in phenol where the "key atom" is negative oxygen, the effect can be represented in a diagram as follows:



The hydrogen atoms attached to the ortho and para carbon atoms are regarded as possessing an induced positive polar charge and are therefore readily replaced by the nitro group according to the reaction:



The driving force of the reaction is the tendency of the hydrogen to combine with the hydroxyl to form unionised water. In toluene, which is the compound of special interest in this research, the "key-atoms" are the positive hydrogen atoms of the methyl groups and therefore as may be seen from the diagram



the ortho and para positions are again those which are reactive.

Robinson, somewhat later (J.C.S., 1926, 401), propounded another theory to explain the reactivity of certain positions in the nucleus. He assumed that there is a shift of electrons along the carbon chain, due to the attraction or repulsion of electrons by the atoms of the substituent. In the case where the electrons are repelled, an excess of negativity appears only on the ortho and para carbon atoms because such cannot exist on the meta carbon atom without disturbing the system of stable octets. The following quotation from Robinson's paper (J.C.S., 1926, 409) will make the mechanism more clear: "In the case of a group A which repels electrons more than hydrogen

does, we have the arrangement

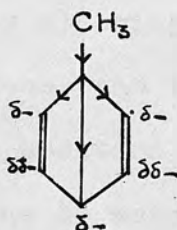


Here the crowding of electrons round C_α will facilitate, by repelling $C_\alpha C_\beta$ covalency electrons, the polarisation of that particular butadienoid* system which starts with C_α . The electron will be captured by C_β (process a : o-substitution) or, if not, a $C_\alpha C_\beta$ covalency electron will become a $C_\beta C_\gamma$ covalency electron (process b). C_γ , to recover its normal covalency, must then correspondingly relinquish an electron to C_δ (process c : p-substitution). An alternative statement is that the ring carbon atom around which the density of electrons is greatest most easily becomes the positive end of a conjugated polarised complex. The applications will be obvious - toluene and tert.-butylbenzene belong to the same category." (The repulsion of electrons from the $-\text{CH}_3$ group is borne out by the fact that whilst CH_3^+ has been discovered in the positive ray tubes, CH_3^- never appears. J.C.S., 1926, 402). According to this

*Note: By a butadienoid system is meant $-\text{C}=\text{C}-\text{C}=\text{C}-$, a system which occurs in butadiene.

theory, it is at the ortho and para positions in toluene that electrons accumulate. The carbon atoms will readily attract the nitro-group of nitric acid and expel a proton to form water with the hydroxyl group. The meta carbon atom in this reaction is quite neutral, a fact which agrees with general observations.

A modification of the theory has been made by Ingold (Rec. trav. chim., 1929, 48, 805) who suggests that repulsion of electrons may take place from the methyl group directly towards the ortho and para positions in toluene if the Dewar formula is assumed.



To explain the production of a small quantity of meta isomeride during nitration of toluene he assumes a relaying of negativity from the ortho or para position to the meta.

It is quite obvious that none of these theories can give any explanation of the preponderance of meta isomerides which is produced when toluene is submitted to the Friedel-Crafts' reaction with alkyl halides. Acyl halides, on the other hand, behave

quite normally except in that they give little or no ortho isomeride. Boeseken (Rec. trav. chim., 1904, 23, 98) has put forward the suggestion that steric hindrance, due to the size of the complex $\text{CH}_3\text{CO.Cl.AlCl}_3$, prevents ortho substitution taking place.

It has already been stated on p. 6 that the abnormality in the production of meta compounds by direct substitution of toluene by alkyl halides in presence of aluminium chloride was at first considered to be due to the association of the toluene with the catalyst. This view was soon seen to be quite untenable, since (i) no alteration in the position of substitution was brought about on preventing this possible association by allowing the catalyst to combine with nitrobenzene, and (ii) the acetyl group did not enter the meta position when every opportunity was given to the toluene to associate with aluminium chloride.

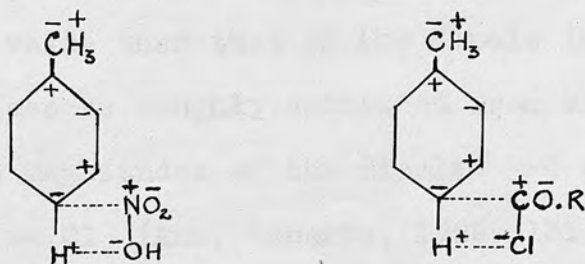
Unfortunately very little is known of the mechanism of the Friedel-Crafts' reaction. Originally (see p. 6) it was thought that the explanation was to be found in a combination of the aluminium chloride with the benzenoid derivative which, on treatment with an alkyl or acyl halide, yields hydrogen halide and an alkylated or acylated benzene derivative. Such a view was shown to be untenable, as aluminium chloride in combination with another compound is less

reactive than in the free state (Boeseken, Rec. trav. chim., 1904, 23, 105; Olivier, Rec. trav. chim., 1926, 45, 817)*. Boeseken (Rec. trav. chim., 1905, 24, 6) postulated an activation of the hydrocarbon and the organic halide by the aluminium chloride, but gave no indication of how such an activation can take place. A ternary compound of hydrocarbon, organic halide and catalyst, from which hydrogen halide is eliminated, was assumed by Schmidlin and Lang (Ber., 1912, 45, 902) to explain the reaction. There is an important difference between alkyl and acyl halides in the reaction, namely, that a definite complex is formed between aluminium chloride and acyl halide, whilst the existence of a similar complex with alkyl halides has never been demonstrated. Also, one molecule of aluminium chloride to one molecule of halide is necessary to drive the reaction to completion when acyl halides are employed, whereas a much smaller proportion of catalyst suffices in the case of alkyl halides.

* The increased production of monosubstituted toluenes found when the complex $C_6H_5NO_2 \cdot AlCl_3$ was catalyst was very probably due to a decreased catalytic activity which would tend to minimise further substitution. Cf. Olivier, Rec. trav. chim., 1926, 45, 817.

The reaction between toluene and acyl halides in presence of aluminium chloride.

In these reactions the chlorides contain the group $\text{>C}=\text{O}$, which according to the latest measurements (Ann. Reports, 1929, 131) is a dipole of considerable magnitude with the positive end on the carbon atom. The acyl group $\text{R}-\overset{\text{O}}{\underset{\text{O}}{\parallel}}{\text{C}}-$, which is about to enter the nucleus of toluene is, therefore, comparable with the nitro-group, as is illustrated below:



Whilst in the first case the driving force of the reaction may well be the formation of unionised water, in the second case it is the formation of unionised hydrogen chloride. Thus, on the theories of Lapworth, Robinson and Ingold, there would be expected, as in the case of the nitration of toluene, a preponderance of ortho and para derivatives. The para derivative is produced and the suggested reason for the

non-appearance of the ortho isomeride has been given on p. 71.

The reaction between toluene and alkyl halides in presence of aluminium chloride.

The case of an alkyl chloride reacting with toluene under the influence of aluminium chloride is quite different in that it is no longer a question of a strongly polarised radical which is entering the toluene nucleus. tert.-Butyl chloride, for example, probably contains a dipole, which however has a very much smaller value than that of the dipole in acetyl chloride, as can be roughly estimated from the figures given for the magnitudes of the dipoles $\text{C} = \text{O}$, $\text{C} - \text{CH}_3$, $\text{C} - \text{Cl}$ (Ann. Reports, 1929, 131). The explanation of the appearance of such a considerable quantity of meta compound by substitution in the toluene nucleus by an alkyl group, when compared with the results obtained from a reaction with an acyl group, is to be sought in the difference between the state of polarisation of the former group and that of the latter. A non-polarised group would have no more tendency, *prima facie*, to enter the ortho and para positions of toluene, although these are rendered negative by the methyl group (see pp. 67-70) than it would to enter the meta.

During the Friedel-Crafts' reaction with an alkyl halide it is obvious, since the hydrocarbon and alkyl halide will not react alone, that at the moment of reaction there must be three molecules, viz., hydrocarbon, alkyl halide and aluminium chloride, in proximity to each other, sufficiently close to permit of reaction taking place. This is similar to Schmidlin and Lang's suggestion (p. 72), except that definite compound formation is not assumed. However, activation of the hydrocarbon and halide must be regarded as being caused by the catalyst.

Where toluene is the hydrocarbon in question, there are three positions, ortho, meta and para, which can be activated, and with regard to the meta and para positions there is no reason for assuming other than equal activation. The ortho position is somewhat different, as the steric influence of the methyl group may prevent a sufficiently close approach of the aluminium chloride molecule to produce activation. It appears most probable, however, that the steric influence would entirely prevent both a molecule of the catalyst and of the alkyl halide approaching at the same time near enough to the ortho carbon atom to allow reaction to take place. Therefore, no ortho substituted derivative would be expected.

Now, the extent to which reaction takes place at either the meta or para carbon atom depends not only on the degree of activation of these atoms but also on the number of times there are collisions between the alkyl halide, aluminium chloride and the carbon atom. In the first place, there are two carbon atoms meta to the methyl group of toluene, whereas there is only one para. This doubles the chance of reaction at the meta position. In the second place, the steric influence of the methyl group tends to repel both the molecules of the aluminium chloride and the alkyl halide in such a way that an accumulation of these molecules will occur round the meta carbon atom, resulting in an increased opportunity for that atom to react. In other words, the molecules of alkyl halide which, in the absence of the steric influence, would have attacked the ortho position, largely transfer their attack to the meta position.

Thus we have two effects both tending to produce the meta compound in larger proportion than the para. Since the tert.-butyl group, on which the work was carried out, cannot be considered to be altogether without polarity, there is probably a residue of affinity for the group on the para carbon atom, due to the negativity induced there by the

methyl group of the toluene. This would increase the proportion of para isomeride formed.

Exactly the same arguments can be presented to explain the formation of the large proportion of meta compounds when both chloro- and bromobenzenes undergo the Friedel-Crafts' reaction with alkyl halides. The results obtained from the butylation of anisole were not sufficiently definite to indicate the quantities of meta and para compounds produced. However, a larger proportion of para isomeride is to be expected, as the reactivity of para position in anisole, as shown by its nitration (Annalen, 1850, 74, 299; Ber., 1919, 52, 1476), is very much greater than that of the same position in toluene, a factor which might cause more reaction at the para carbon atom.

Finally, it may be concluded that the reason for the absence of any discussion in communications on substitution in the benzene nucleus, of the large proportion of meta compounds produced in the experiments quoted in this thesis, is to be found in the fact that this abnormal substitution is obviously not dependent on the directive influence of the substituent in the nucleus.