64. *The Meta-alkylation of Aromatic Hydrocarbons by the Friedel–Crafts Reaction.*

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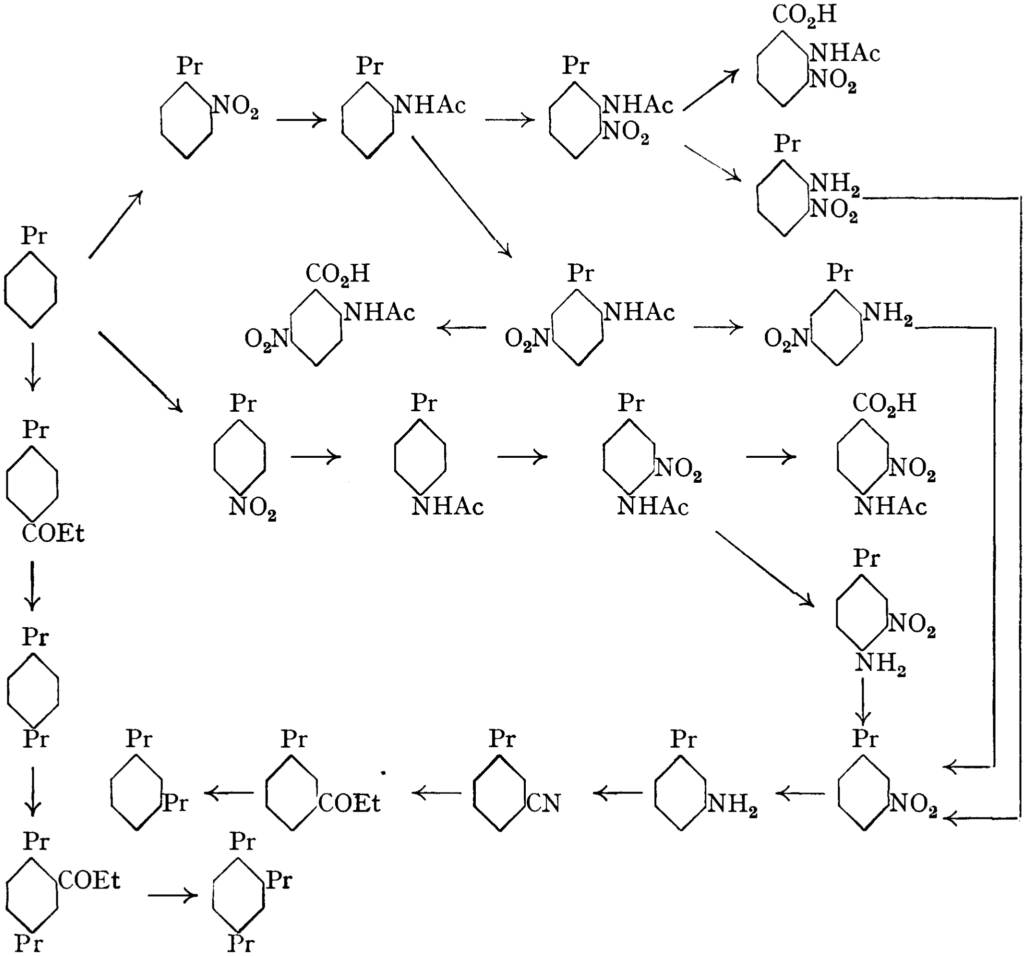
THE action of alkyl halides on the homologues of benzene in presence of aluminium chloride has frequently been investigated, and the results of earlier workers (reviewed by Holleman, "Die direkte Einführung von Substituenten in den Benzolkern," Leipzig, 1910, p. 102; compare also Shoesmith and McGechen, J., 1930, 2231), though frequently conflicting, provided strong indications of the formation of meta-derivatives. For instance, Shoesmith and McGechen (*loc. cit.*) obtained from toluene a mixture composed of 65—71% of *m-tert.*-butyltoluene with 35—30% of its *p*-isomeride.

The fact that such hydrocarbons on substitution otherwise invariably yield ortho-para-derivatives indicates that the anomalous result may be due not to "direct *meta*-substitution in the toluene nucleus" (Shoesmith and McGechen, *loc. cit.*), but to a transformation of initially formed para-derivative. An experimental basis for this view is available in the classical work of Anschütz and his collaborators (*Ber.*, 1884, **17**, 2816; 1885, **18**, 657; *Annalen*, 1886, **235**, 177) on the changes (comprising isomerisation, dealkylation, and further alkylation) undergone by various polyalkylbenzenes in presence of aluminium chloride. Anschütz (*Annalen, loc. cit.*, p. 188) connected these changes with the formation of methyl chloride and benzene from toluene and hydrogen chloride under similar conditions, and attributed isomerisation and higher alkylation to ordinary substitution by alkyl chloride formed by dealkylation. On such a view, and consistently with the maintenance of *op*-substitution, the conversion of *p*- into *m*-xylene (Mundici, *Gazzetta*, 1904, **34**, 221; Heise and Töhl, *Annalen*, 1892, **270**, 155) is perhaps most plausibly expressed as follows:

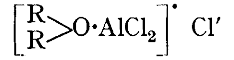
$$1:4\text{-}C_6H_4Me_2 \xrightarrow{MeCl} 1:3:4\text{-}C_6H_3Me_3 + HCl \longrightarrow 1:3\text{-}C_6H_4Me_2 + MeCl$$

Some time ago (compare *J. Soc. Chem. Ind.*, 1933, **52**, 469) one of us pointed out that such a hypothesis would also involve isomerisation of the alkyl group in suitable cases, and indicated an intention to apply this criterion. As a preliminary, we showed that *p*-*n*-propylphenol is converted by oxidation into *n*-propylquinol (J., 1934, 633), and we have now studied the behaviour of *m*- and *p*-di-*n*-propylbenzene, as well as of 1 : 2 : 4-*tri*-n-*propylbenzene*, towards aluminium chloride. Heise and Töhl (*loc. cit.*, p. 164) have already stated that the change of *n*-propylbenzene into *m*- and *p*-dipropylbenzene does not involve any modification of the propyl group, but the *m*-isomeride itself was only obtained by Heise (*Ber.*, 1891, **24**, 768) as one of the products of this reaction. In view of the importance of the matter, we have prepared the various hydrocarbons required for our purpose by methods which leave no doubt as to their constitution, and in doing so have to some extent amplified the work of Brady and Cunningham (J., 1933, 121) on the nitration of *n*-propylbenzene. The following scheme sufficiently indicates our procedure, orientations being established by reference to the known nitroacetamidobenzoic acids:



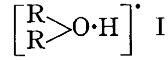
We were able to confirm the data supplied by Heise and, by using the method of separation described by him, to show that *p*-di-*n*-propylbenzene is converted to the extent of about two-thirds into the *m*-di-*n*-propylbenzene by the action of aluminium chloride for two hours at 100°. At the same time some *n*-propylbenzene and 1 : 3 : 5-tripropylbenzene were formed. Orientation of the latter was demonstrated by oxidation to trimesic acid, and there can be little doubt that the normal character of the propyl groups was preserved. Strict reversibility of the relationship between the *p*- and the *m*-isomerides cannot be expected in view of the processes of dealkylation and alkylation which also occur, and experiment showed that very little *p*-derivative was formed when *m*-dipropylbenzene was treated with aluminium chloride. 1 : 2 : 4-Tripropylbenzene was largely converted into the 1 : 3 : 5-derivative, together with lower and higher alkylated products.

Whilst it can fairly be claimed that these results definitely contradict any substitution hypothesis of the kind adumbrated above, a final decision as to the real character of the changes involved is not simple. As a preliminary it is necessary to consider the general character of the changes promoted by aluminium chloride (compare Kränzlein, " Aluminium Chlorid in der organischen Chemie," Berlin, 1932). It would seem that these arise from the strong kationoid properties of the chloride, which are themselves due to the deficiency of two electrons requisite to complete the octet of the aluminium atom. As a consequence, it is able to enter into combination or association with anionoid centres (compare, *e.g.*, Walker and Spencer, J., 1904, **85**, 1106), as protons do, and so to provide a stimulus to further reaction. Thus the hydrolysis of ethers by aluminium chloride and by hydrogen iodide respectively probably depends on formation of the complexes



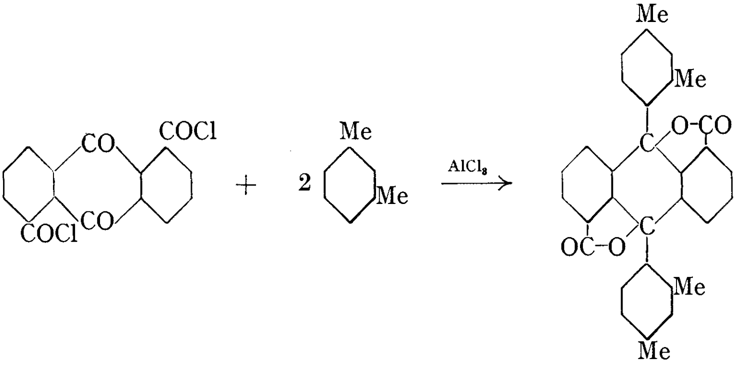
$\left[{}^{R}_{R}\!\!>\!O{\cdot}AlCl_2\right]^{\cdot} Cl'$

and



$\left[{}^{R}_{R}\!\!>\!O{\cdot}H\right]^{\cdot} I'$

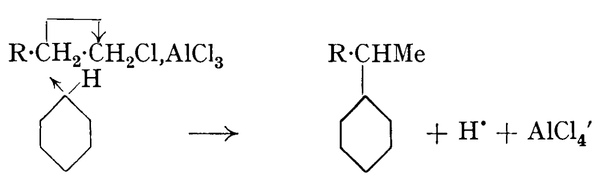
Similarly both proton and aluminium chloride stimulate the reactivity of carbonyl compounds. Thus the action of sulphuric acid in inducing condensation of carboxylic acids or other carbonyl compounds with aromatic hydrocarbons corresponds to the Friedel–Crafts reaction with acid chlorides, and it is significant that the efficiency of aluminium chloride in this connection can be reduced by the presence of such competitive anionoid centres as those of nitrobenzene and acetone (Nenitzescu and Cantuniari, *Ber.*, 1932, **65**, 807 ; *Annalen*, 1934, **510**, 269). The parallelism between the reactions of anionoid aromatic compounds (and therefore not of nitrobenzene) in presence of aluminium chloride and those of the Grignard reagent is particularly clear in the following reaction, which occurs simultaneously with the more usual type leading to ketone formation (Scholl and others, *Ber.*, 1932, **65**, 902 ; *Annalen*, 1932, **493**, 56 ; **494**, 201 ; 1934, **572**, 130, 112, 124) :



It would thus seem to be unnecessary to follow Scholl in attributing the lactone formation to tautomerism of the acid chlorides. Again, by attributing the conversion of alkyl halides into olefins to formation of the complex (I), the reaction is brought into line with the similar behaviour of the corresponding ammonium and oxonium salts :

$$R{\cdot}CH_2{\cdot}CH_2Cl \longrightarrow \underset{(I.)}{R{\cdot}CH_2{\cdot}CH_2Cl,AlCl_3} \longrightarrow R{\cdot}CH{:}CH_2 + HCl + AlCl_3$$

in presence of anionoid aromatic nuclei, an alternative method of relief of (I) occurs in alkylation of the nucleus. Whilst this is stated to involve no modification of the alkyl group at low temperatures (Gustavson, *Ber.*, 1878, **11**, 1257; Kekulé and Schötter, *ibid.*, 1879, **12**, 2279; Konovalov, *Bull. Soc. chim.*, 1896, **16**, 864; Heise, *loc. cit.*), the reaction at higher temperatures can be regarded as a particular form of the Wagner–Meerwein change, in which the aromatic nucleus figures as anion compensating the β-carbon atom for migration of a hydrogen atom with one electron :



The increase in electrical conductivity observed when benzene is added to the system ethyl bromide–aluminium chloride (Wohl and Wertyporoch, *Ber.*, 1931, **64**, 1357) is in accord with this. The polymerisation of olefins is also initiated or, perhaps rather, accelerated alternatively by proton and by aluminium chloride, and would seem to depend on a " snowball " mechanism set up by these reagents :

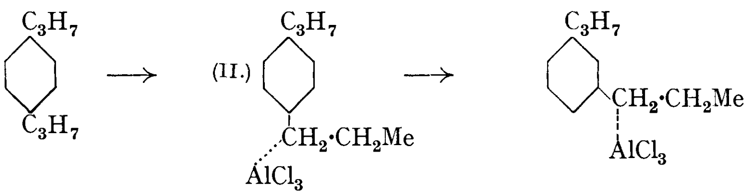
$$Me_2C{:}CH_2 \longrightarrow Me_2\overset{+}{C}{\cdot}CH_2{\cdot}AlCl_3 \longrightarrow Me_2\overset{+}{C}{\cdot}CH_2{\cdot}CMe_2{\cdot}CH{\cdot}AlCl_3$$

and so on.

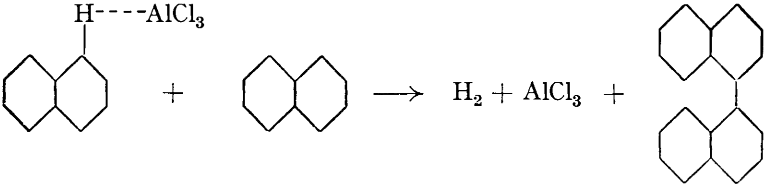
The polymerising action of boron trifluoride on olefins (D.R.-P. 264,925; Stanley, *J. Soc. Chem. Ind.*, 1931, **49**, 349T) might have been anticipated from the close relationship between the fluoride and aluminium chloride in the sense of the Periodic System. We have found, however, that boron trichloride does not promote the Friedel–Crafts reaction.

In the light of this review, it seems clear that aluminium chloride promotes reactions in virtue of its tendency to co-ordination at anionoid centres. As a result the existing dipole condition of the molecule concerned and its reactivity are enhanced. This, however, also summarises the conditions which appear from the exhaustive work of Meerwein to be responsible for the equilibrium between camphene hydrochloride and bornyl and *iso*bornyl chlorides (*Ber.*, 1920, **53**, 1815; 1922, **55**, 2500).

The following scheme represents the application of this conception to the isomerisation we have studied, the migrant being a complex of aluminium chloride with propyl :



In the *m*-derivative, however, the main anionoid centre is in the para-position to one of the alkyl groups, and it is therefore at this point that the aluminium chloride ultimately attaches itself. In this way the comparative stability of *m*-dipropylbenzene is explained. The other facts which must be accommodated by any explanation of the changes in question are, on the one hand, the conversion of naphthalene derivatives into dinaphthyls as studied extensively by Scholl (compare Kränzlein, *op. cit.*, p. 73) and including that of naphthalene itself into ββ-dinaphthyl (Homer, J., 1907, **91**, 1108; compare also the direct formation of β-ethylnaphthalene from naphthalene by the Friedel–Crafts reaction, Marchetti, *Gazzetta*, 1881, **11**, 265, 439; Roux, *Ann. Chim.*, 1887, **12**, 307) and, on the other, the dealkylation and the further alkylation, which accompany the simple isomerisation. The former could readily be explained by a direct application of the foregoing suggestion as an ordinary case of substitution, followed by isomerisation :



Such a formulation, however, can hardly be extended to the transference of alkyl groups from one aromatic nucleus to the other, and this is most simply attributed to radical formation, of which, indeed, in other directions such dismutation has been employed as a criterion. Nevertheless, it must not be assumed that this in any way invalidates our general thesis as to the essential character of these reactions. Radical formation is one of the results which might ensue from the condition represented by (II), and the stability of *pp'p''*-trinitrotriphenylmethyl (Ziegler and Boye, *Annalen*, 1927, **458**, 248) illustrates the way in which electron-avidity may contribute to radical formation. For the present, therefore, it seems best to regard the various experimentally observed results as consequences of varying degrees of the same general dipolar condition induced by aluminium chloride.

In conclusion, there can be little doubt that the results obtained in the cases of the di- and tri-propylbenzenes will be reproducible in other cases, so that from the purely preparative point of view a convenient means is revealed of obtaining hydrocarbons otherwise only accessible by a laborious process such as that described for *m*-di-*n*-propylbenzene.

EXPERIMENTAL.

The yield of propiophenone, b. p. 123°/25 mm., was increased from 50 to 88·5% by addition, until no further evolution of hydrogen chloride occurred, of further aluminium chloride (*ca.* 30 g.) to the product obtained when a mixture of propionyl chloride (150 g.) and benzene (180 g.) had been added with vigorous stirring to a suspension of aluminium chloride (150 g.) in carbon disulphide (200 c.c.). Reduction of the ketone by Clemmensen's method furnished *n*-propylbenzene, b. p. 160° (yield, 80%). This hydrocarbon (204 g.), submitted to conditions analogous to those applied to benzene, yielded, besides unchanged material (20 g.), *p*-*n*-propylpropiophenone (196 g.), b. p. 145°/18 mm. (*semicarbazone*, needles from light petroleum, m. p. 140°. Found : C, 66·7; H, 8·3; N, 18·1. $C_{13}H_{19}ON_3$ requires C, 66·9; H, 8·2; N, 18·0%), and a fraction (20 g.), b. p. 220°/20 mm. *p*-Di-*n*-propylbenzene, b. p. 110°/20 mm., obtained from *p*-propylpropiophenone in 50% yield by Clemmensen's method, was characterised by its sulphonamide, m. p. 105° (Heise, *Ber.*, 1891, **24**, 709, gives 106°), and converted into 2 : 5-*dipropylpropiophenone*, b. p. 160°/15 mm. (Found : C, 82·0; H, 9·7. $C_{15}H_{22}O$ requires C, 82·5; H, 10·1%). Yield, 60%. 1 : 2 : 4-*Tripropylbenzene*, b. p. 135°/20 mm., was obtained from the ketone in 60% yield (Found : C, 87·9; H, 11·6. $C_{15}H_{24}$ requires C, 88·2; H, 11·8%).

Nitration of n-*Propylbenzene*.—This has been studied by Brady and Cunningham (*loc. cit.*), who experienced the tendency to formation of the 2 : 4-dinitro-derivative and prepared from this the *o*-nitro-derivative, b. p. 133—136°/26 mm. In our experiments, *n*-propylbenzene (75 g.) was added gradually to an ice-cooled mixture of sulphuric acid (200 c.c., *d* 1·8), nitric acid (112 c.c., *d* 1·4), and water (50 c.c.), the temperature being maintained below 15°. After ½ hour, the upper layer furnished fractions (1) 78 g., b. p. 133—140°/20 mm., (2) 8 g., b. p. 140—150°/20 mm., (3) 33 g., b. p. 150—160°/20 mm., (4) 40 g., b. p. 150°/1 mm.

On redistillation, (1) furnished practically pure *o*-nitropropylbenzene, b. p. 133°/20 mm. (Found : N, 8·6%), from which *o*-propylaniline, b. p. 112°/20 mm., was prepared by means of tin and hydrochloric acid. o-*Propylacetanilide* crystallised from light petroleum in needles, m. p. 93° (Found : C, 75·0; H, 8·9; N, 8·0. $C_{11}H_{15}ON$ requires C, 74·6; H, 8·5; N, 7·9%) (Piccinini and Cannozzi, *Gazzetta*, 1898, **28**, 95, assign m. p. 104—105° to the acetyl derivative of the base they prepared from 2-methyldihydroindole by reduction with hydriodic acid and phosphorus). Evidence of orientation was obtained when the anilide (17·5 g.) was gradually added to a mixture of nitric acid (50 g., *d* 1·5) and glacial acetic acid (18 g.) at 10°, and the solution left for 12 hours at the ordinary temperature. The solid, isolated by means of water was hydrolysed in 2 hours by boiling hydrochloric acid (40 c.c., *d* 1·17), and the mixture distilled in steam. The weak base thus removed was 2-*nitro*-6-*propylaniline*, yellow needles, m. p. 60° (Found : C, 60·1; H, 6·9; N, 15·6. $C_9H_{12}O_2N_2$ requires C, 60·0; H, 6·7; N, 15·6%), and furnished an *acetyl* derivative, needles, m. p. 140° (Found : C, 59·7; H, 6·5; N, 12·7. $C_{11}H_{14}O_3N_2$ requires C, 59·5; H, 6·3; N, 12·6%). The last was converted by oxidation at 80° with aqueous potassium permanganate in presence of magnesium sulphate into 3-nitro-2-acetamidobenzoic acid, m. p. 180°, from which the ethyl ester, m. p. 102°, was prepared by use of diazoethane. The acid and its ester did not depress the melting points of authentic specimens derived from 3-nitro-*o*-toluidine. 4-*Nitro*-2-*propylaniline* was isolated from the solution remaining after removal of the isomeride just described, and obtained in pale yellow needles, m. p. 97° (Found : C, 60·0; H, 6·9; N, 15·7%), from which an *acetyl* derivative, needles, m. p. 159°, was prepared (Found : C, 59·8; H, 6·5; N, 12·6%). This yielded 5-nitro-2-acetamidobenzoic acid, m. p. 216°, and its ethyl ester, m. p. 153°, which were each formally identified by comparison with authentic specimens.

Fraction (3), b. p. 154°/20 mm. on redistillation, was p-*nitropropylbenzene* (Found : N, 8·6. $C_9H_{11}O_2N$ requires N, 8·5%). *p*-Propylaniline boiled at 112°/20 mm. and furnished an *acetyl* derivative, needles, m. p. 96° (Found : C, 74·3; H, 8·7; N, 8·0. $C_{11}H_{15}ON$ requires C, 74·6; H, 8·5; N, 7·9%). By adding it (38 g.) rapidly at 30—40° to a cooled and stirred mixture of nitric acid (118 c.c., *d* 1·4) and sulphuric acid (47 c.c., *d* 1·8) and leaving the mixture for ½ hour 2-*nitro*-4-*propylacetanilide*, yellow needles, m. p. 77°, was obtained (Found : C, 59·2; H, 6·7; N, 12·7. $C_{11}H_{14}O_3N_2$ requires C, 59·5; H, 6·3; N, 12·6%), from which 3-nitro-4-acetamidobenzoic acid, m. p. and mixed m. p. 221°, and its ethyl ester, m. p. and mixed m. p. 95°, were prepared. 2-*Nitro*-4-*propylaniline*, obtained from the acetyl derivative by hydrolysis with 50% sulphuric acid, separated from light petroleum in orange prisms, m. p. 36° (Found : C, 60·3; H, 6·9; N, 15·7. $C_9H_{12}O_2N_2$ requires C, 60·0; H, 6·7; N, 15·6%).

Fraction (4) was shown to be 2 : 4-dinitropropylbenzene (Found : N, 13·3%) by reduction to 2-nitro-4-aminopropylbenzene, m. p. 59° in accordance with the datum of Brady and Cunningham (*loc. cit.*).

m-Nitropropylbenzene (Brady and Cunningham, *loc. cit.*) was conveniently prepared by converting a mixture of *o*- and *p*-nitropropylbenzene, as obtained by the above process of nitration, into a mixture of the three nitropropylacetanilides described above. Hydrolysis of this (223 g.) with sulphuric acid (450 c.c., *d* 1·8) and water (810 c.c.) yielded a solution, which was diazotised (sodium nitrite, 76 g.; water, 112 c.c.), added gradually to boiling alcohol (5600 c.c.), and heated on the steam-bath for ½ hour; *m*-nitropropylbenzene (110 g.), b. p. 150°/20 mm., was isolated. The following constants were determined at 17° : *d* 1·0898; n_D 1·5334; α_D 31° 43′; γ (drop weight) 39·66; γ (drop number) 39·40. m-*Propylaniline*, b. p. 112°/20 mm., 230°/760 mm. (Found : N, 10·5. $C_9H_{13}N$ requires N, 10·4%), was characterised by an *acetyl* derivative, m. p. 53° (Found : C, 74·9; H, 8·7; N, 8·1. $C_{11}H_{15}ON$ requires C, 74·6; H, 8·5; N, 7·9%), and was converted by the Sandmeyer process into m-*propylbenzonitrile*, b. p. 127°/20 mm., which was lighter than water (Found : N, 9·8. $C_{10}H_{11}N$ requires N, 9·65%).

m-*Propylpropiophenone* was prepared by adding the nitrile (36 g.) to a solution prepared from ethyl bromide (54 g.), magnesium (12 g.), and ether (140 c.c.), and finally boiling the mixture for ½ hour. The ketone (36 g.), b. p. 145°/20 mm. (Found : C, 81·3; H, 8·8. $C_{12}H_{16}O$ requires C, 81·8; H, 9·1%), furnished a *semicarbazone*, plates, m. p. 128° (Found : N, 8·2. $C_{13}H_{19}ON_3$ requires N, 18·0%), and was converted by Clemmensen's method into *m*-dipropylbenzene, b. p. 105°/20 mm. (yield, 80%). This was identified by its disulphonamide, m. p. 195° (Heise, *loc. cit.*, gives 195°).

Action of Aluminium Chloride on Hydrocarbons.—(a) p-*Dipropylbenzene*. A mixture of the hydrocarbon (62 g.) and aluminium chloride (21 g.), heated on the steam-bath for 22 hours, darkened considerably, but some solid aluminium chloride remained, covered by a black oil, and an upper layer of a pale brown oil. The last became colourless, but evolved little heat, on treatment with water, whereas the black oil reacted vigorously. Fractionation of the products, however, showed them to be essentially the same. On refractionation the following main products were obtained from both layers : (1) 7 G., b. p. 67°/20 mm., identified as *n*-propylbenzene by conversion into 2-nitro-4-aminopropylbenzene, m. p. 59°. (2) 15 G., b. p. 105°/20 mm., sulphonated by twice its volume of fuming sulphuric acid (*d* 1·9) without cooling, and finally at 100° for 10 minutes. On concentration of a solution of the lead salts of the resulting sulphonic acids, that of *p*-dipropylbenzenesulphonic acid crystallised, and was identified by conversion into the sulphonamide, m. p. 105°. From the liquor the lead salt of *m*-dipropylbenzenedisulphonic acid was obtained on evaporation, and converted into the disulphonamide,

m. p. 195°. The weights of the two salts indicated that the fraction consisted of 65% of *m*- and 35% of *p*-dipropylbenzene. (3) 7 G., b. p. 135°/20 mm. Oxidation with nitric acid (1 vol., *d* 1·4) and water (3 vols.) at 160—200° yielded an acid, m. p. 345—350°, from which ethyl trimesate, m. p. 133°, was prepared.

(b) m-*Dipropylbenzene*. A similar experiment was carried out, and the fraction, b. p. 105°/20 mm., shown to be essentially unchanged *m*-derivative, with a very small proportion of the *p*-isomeride.

(c) 1 : 2 : 4-Tripropylbenzene (25 g.) after treatment with aluminium chloride for 4 hours at 100° yielded : (1) 7·5 g., b. p. 90—120°/20 mm., essentially *m*-dipropylbenzene, with a very little *p*-derivative; (2) 3·5 g., b. p. 120—130°/20 mm.; (3) 3·5 g., b. p. 131—140°/20 mm.; (4) 3·0 g., b. p. 140—170°/20 mm.

(2) and (3) on refractionation yielded a main fraction, b. p. 133°/20 mm., from which almost pure trimesic acid, m. p. 355° (compared with 372° for the pure acid), was obtained, and characterised by its ethyl ester, m. p. 128° before recrystallisation and m. p. 133° after one recrystallisation from alcohol. (2) and (3) were therefore mainly 1 : 3 : 5-tripropylbenzene. (4) was not examined, but, by analogy with the results obtained by Anschütz, probably consisted of tetrapropylbenzene.

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