215. *The Action of Methanol on Phenol in the Presence of Alumina. Formation of Anisole, Methylated Phenols, and Hexamethylbenzene.*

By N. M. Cullinane and S. J. Chard.

The reaction between methanol and phenol vapours in presence of alumina has been described as yielding hexamethylbenzene (Briner, Plüss, and Paillard, *Helv. Chim. Acta*, 1924, **7**, 1048) and anisole and *o*-cresol (Ipatiev, Orlov, and Petrov, *Ber.*, 1927, **60**, 130). It is now shown that, by using activated alumina, it is possible to control the process so as to obtain improved yields of anisole, cresols, or hexamethylbenzene. Furthermore it is shown that anisole under similar conditions yields cresols, phenol, and hexamethylbenzene.

To account for these results a mechanism is suggested involving the migration of a methyl radical from anisole to a foreign nucleus.

It is stated that methanol and phenol do not react in the presence of aluminium chloride (Tsukervanik and Nazarova, *J. Gen. Chem. Russ.*, 1937, **7**, 623) or perchloric acid (Hinsberg, G.P. 538,376). Sowa, Hennion, and Nieuwland (*J. Amer. Chem. Soc.*, 1935, **57**, 709) likewise obtained a negative result when boron fluoride was used as a catalyst at atmospheric pressure, but when the experiment was carried out in a sealed tube they obtained a fair yield of anisole. Using the same catalyst Kolka and Vogt (*J. Amer. Chem. Soc.*, 1939, **61**, 1463) found that methyl ether and phenol could be condensed to form some anisole, which was also produced from methanol and phenol in the presence of thoria as shown by Briner, Plüss, and Paillard (*loc. cit.*; cf. Sabatier and Mailhe, *Compt. rend.*, 1910, **151**, 360). It is claimed by Ipatiev, Orlov, and Petrov (*loc. cit.*) that with alumina as agent under increased pressure, in addition to anisole, *o*-cresol was formed in small yield whereas at the ordinary pressure *p*-cresol resulted.

While Briner, Plüss, and Paillard (*loc. cit.*) state that methanol and phenol do not react below 350° in the presence of alumina, it is now shown that, when activated alumina is used as catalyst, reaction actually takes place at well below this temperature; *e.g.*, at 200°, anisole is formed in moderate yield. At higher temperatures, considerable quantities of methylated phenols are produced. For example, at 345° scarcely any of the ether is obtained, the main products (in addition to phenol itself) being *o*-, *m*-, and *p*-cresols (mainly *o*-cresol) with some xylenols and higher methylated phenols. Small amounts of methylanisoles and hexamethylbenzene can also be isolated.

The anisole first produced undergoes rearrangement; this is confirmed by passing the ether itself over the catalyst at a suitable temperature, when the same compounds are formed in similar yield. The quantity of phenol present in the product is strikingly similar whether the initial material is anisole or a mixture of methyl alcohol and phenol.

Here a difference may be noted between the reactions now described and the analogous Fries reaction, von Auwers and Mauss (*Ber.*, 1928, **61**, 1495; *Annalen*, 1928, **464**, 293) having shown that, in the production of aromatic hydroxyketones from phenyl esters in the presence of aluminium chloride, the products obtained may vary when the acyl group arises from the reacting molecule (Fries) or from another molecule (Friedel–Crafts).

A synthetic aluminium silicate was also used as a catalyst, but was found not to be so effective as alumina; under comparable conditions a greater proportion of phenol was recovered and the yields of methylated phenols correspondingly reduced.

It is well known that *tert*.- and *sec*.-alkyl phenyl ethers are transformed into alkylphenols in the presence of catalysts or by the action of heat alone. The present work shows that, contrary to statements appearing in the literature (*cf.* Claisen and Eisleb, *Annalen*, 1913, **401**, 21; Porter, " Molecular Rearrangements," 1928, p. 116; Kon, *Ann. Reports*, 1933, **30**, 186; Wallis, " Organic Chemistry," Ed. Gilman, 1938, p. 748), methyl phenyl ethers are also capable of undergoing such rearrangements.

As the reactions now described take place in the vapour phase the methyl group doubtless migrates as a neutral radical (*cf.* Hickinbottom, *Nature*, 1938, **142**, 830; 1939, **143**, 520). Furthermore in the transformation of *tert*.-alkyl or benzyl phenyl ethers by the action of heat the migrating group has been observed in some cases to become attached to a foreign nucleus (cf. Behaghel and Freiensehner, *Ber.*, 1934, **67**, 1368; Hickinbottom, *loc. cit.*). This suggests that the rearrangements described in the present work are not intramolecular in nature. Moreover the formation of phenol cannot be explained on such a basis. Neither can the phenol obtained be formed by fission of the anisole molecule to give phenol and olefin as intermediate products of the reaction, for the ethylene thus formed if it reacted with phenol would yield ethyl not methyl derivatives. Nor is it likely that scission of the ether occurs as a side reaction, as noted by Sprung and Wallis (*J. Amer. Chem. Soc.*, 1934, **56**, 1715) in the rearrangement of *sec*.-butyl *p*-tolyl ether, since when anisole is passed over the catalyst only negligible quantities of gases are evolved. It is true that rather more gaseous products are obtained from phenol and methanol but these no doubt arise from the alcohol, which is present in excess and is known to give such products under the conditions of the experiment.

It is considered therefore that migration of a neutral methyl radical to a foreign nucleus takes place, the reaction being thus not a true rearrangement. The production of phenols, methylated phenols and methylanisoles can be accounted for by reactions of the following type:

$$C_6H_5{\cdot}OMe + C_6H_5{\cdot}OMe = C_6H_5{\cdot}OH + MeC_6H_4{\cdot}OMe \qquad C_6H_5{\cdot}OMe + C_6H_5{\cdot}OH = C_6H_5{\cdot}OH + MeC_6H_4{\cdot}OH$$

$$C_6H_5{\cdot}OMe + MeC_6H_4{\cdot}OH = C_6H_5{\cdot}OH + Me_2C_6H_3{\cdot}OH \qquad MeC_6H_4{\cdot}OMe + C_6H_5{\cdot}OH = MeC_6H_4{\cdot}OH + MeC_6H_4{\cdot}OH$$

An attempt was next made to prepare hexamethylbenzene in as large a yield as possible. Apart from the preparation of this compound by Briner, Plüss and Paillard (*loc. cit.*) in 49% yield, earlier described methods are somewhat tedious. The hydrocarbon, in 70% yield, was obtained when a mixture of phenol and a large excess of methanol was heated at 375° in contact with activated alumina. The yield was considerably reduced when aluminium silicate was substituted as catalyst. The Swiss authors claim that carbon monoxide and hydrogen, which were apparently the only gaseous products they observed, are responsible for the reduction involved in the operation. In the experiments now described, however, though the former gas was formed in some quantity very little hydrogen was collected, in addition to methane (containing some ethane), carbon dioxide and ethylene. In any case these gases arise, in part at least, from the decomposition of the alcohol itself.

EXPERIMENTAL.

Type C activated alumina was used in most of the experiments. When, however, ordinary activated alumina was used the results showed little variation. All the catalysts were supplied by Messrs. Peter Spence and Sons, Ltd.

When the alumina was first used a preliminary run-through was carried out, the products being discarded. This was desirable because the catalyst took a little time to settle down; as it contained some sulphate there was a possibility that sulphur compounds might be formed. The same process was carried out with the silicate; at first there was a considerable evolution of ammonia and no products were collected until ammonia ceased to be formed. The same catalyst was used several times. Briner, Plüss, and Paillard (*loc. cit.*), on the other hand, used fresh alumina for each operation.

A diagram of the apparatus is shown. The silica tube was filled with the catalyst (about 300 g.), which was held in place by a perforated porcelain disc. A pyrex glass sheath contained the thermometer reading to 550°. A Mariotte bottle ensured a constant dropping rate; the capillary tube was of 1 mm. bore. The catalyst tube was heated by an mainly solid, as in the preparation of hexamethylbenzene, a short air condenser, maintained at a temperature sufficient to melt the solid and prevent clogging, was used.

The fractionating column was 2 ft. long, and consisted of a silica tube packed with glass cylinders about 6 mm. in length and of equal width. It was electrically heated and efficiently insulated; the temperature was controlled by a Sunvic Unit and observed by means of two thermometers resting in glass tubes inserted one at each end of the jacket. The temperature of the latter was maintained at about 5° below the b. p. of the fraction required. The still-head was of the total condensation, variable take-off type (Whitmore and Lux, *J. Amer. Chem. Soc.*, 1932, **54**, 3451).

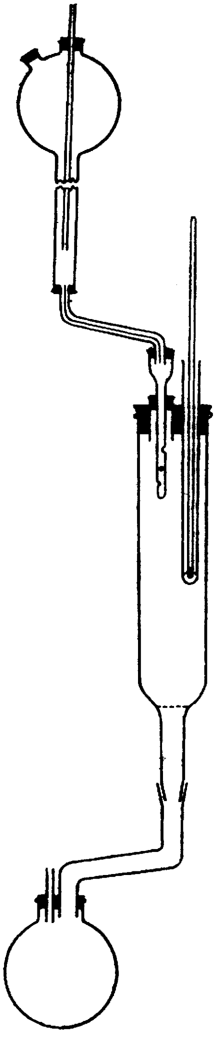
Formation of Anisole.—Phenol (282 g.) mixed with commercial 98% methanol (118 g., 1·2 mols.) was dropped at a rate of 160 c.c. per hour upon the catalyst, the temperature being maintained at 200°. Heat was evolved during the reaction. The product (370 g.), consisting of a yellowish oil and a more mobile layer, was well shaken with excess of 20% aqueous sodium hydroxide, a light-brown oil forming on the surface. This was separated, taken up in ether and the solution washed with successive quantities of 20% sodium hydroxide solution until free from phenols. The ether solution was dried with anhydrous sodium sulphate and distilled. Anisole (56 g., 50% yield calculated on the phenol consumed) distilled at 155°; there was no higher boiling product.

The alkaline extracts were made acid with concentrated hydrochloric acid and the precipitated oil separated and distilled; phenol (185 g.) was obtained. This was mixed with methanol (77 g., 1·2 mols.) and passed over the catalyst as before. Anisole (35 g.) was obtained, and phenol (120 g.) recovered. The total yield of anisole in 5 operations was 139 g.

Formation of Nuclear Methylated Phenols.—Phenol (211 g.) mixed with methanol (88 g., 1·2 mols.) was passed over the catalyst at 345°, the dropping rate being 130 c.c. per hour. The product (285 g.), consisting of an oily and an aqueous portion, contained scarcely any unreacted alcohol. A large excess of 20% aqueous sodium hydroxide was added, the mixture was well shaken, and, after standing at room temperature for 12 hours, a small oily layer separated. This was extracted with ether, phenols were removed with alkali and the ether solution fractionally distilled up to 210°. Anisole, b. p. 155° (about 1 g.), and methylanisoles (6 g.; the *o*-isomer, b. p. 175°, and the *p*-isomer, b. p. 202°, were identified) were collected. The undistilled portion, an oily solid, was washed with small quantities of methanol and recrystallised from ethanol. Colourless plates of hexamethylbenzene (6 g.), m. p. 165°, separated (Found: C, 88·65; H, 11·1. Calc. for $C_{12}H_8$: C, 88·9; H, 11·1%). The analysis was carried out by Dr. G. Weiler.

On addition of excess of concentrated hydrochloric acid to the alkali-soluble portions a brownish oil separated. This was taken up in ether and the aqueous layer extracted thrice with the same solvent. After removal of ether and water, the fractions obtained were (*a*) up to 189°, mostly phenol (5 g.), (*b*) 189—205° (180 g.), (*c*) above 205°, xylenols with some higher methylated phenols (20 g.).

The constituents were identified after suitable fractionation by the usual tests, further confirmation being afforded by the preparation of the following derivatives: phenol picrate, m. p. 83°, *o*-cresol *m*-nitrobenzoate, m. p. 97°, trinitro-*m*-cresol, m. p. 110°, *p*-tolyloxyacetic acid, m. p. 136°. The phenol was determined by the crystallising-point method, *o*-cresol by the method of Potter and Williams (*J. Soc. Chem. Ind.*, 1932, **51**, 59T), *m*-cresol by Raschig's method (*Z. angew. Chem.*, 1900, **13**, 759).



When the 189—205° fraction was redistilled using the column the product now boiling above 205° consisted of xylenols, and *p*-cresol was estimated by difference (confirmed by Lederer's method, G.P. 79,514). These results were further supported by analyses carried out by Dr. W. Idris Jones of Powell Duffryn Ltd., to whom we are greatly indebted. The yields were: phenol, 51 g.; *o*-cresol, 54 g.; *m*-cresol, 24 g.; *p*-cresol, 29 g.; higher methylated phenols, mostly xylenols, 47 g. The gaseous products were evolved slowly, and contained in addition to nitrogen: methane (containing some ethane) 17%, carbon dioxide 13·7%, carbon monoxide 12·4%, ethylene 4·9%, oxygen 4·3%, hydrogen 2·6%.

When the experiment was carried out at 300°, the other conditions being the same, the products were anisole (12 g.), methylated anisoles (4 g.), hexamethylbenzene (4 g.), phenol (102 g.), *o*-cresol (35 g.), *m*-cresol (16 g.), *p*-cresol (21 g.), xylenols and higher methylated phenols (42 g.).

When aluminium silicate ($1Al_2O_3 : 2SiO_2$) was used in place of alumina, the quantities and experimental conditions being the same as above (345°), the product (278 g.) yielded anisole (8 g.), methylanisoles (12 g.), hexamethylbenzene (2 g.), phenol (63 g.), and cresols with higher methylated phenols (100 g.). The evolution of gas was slow, the mixture containing methane (with some ethane) 40·2%, ethylene 6·6%, oxygen 4·2%, hydrogen 2·8%, carbon monoxide 2·2%, carbon dioxide 1·8%.

Action of Alumina on Anisole.—Anisole (242 g.) was passed over the catalyst at 320° at a rate of 130 c.c. per hour. To the product (214 g.) excess of 20% sodium hydroxide was added, a small quantity of oil remaining undissolved. The mixture was thoroughly extracted with ether, and the extract washed free from alkali-soluble constituents. The solution contained anisole (1 g.), methylanisoles (9 g.), and hexamethylbenzene (4 g.). The alkaline solutions contained phenol (49 g.), *o*-cresol (61 g.), *m*-cresol (18 g.), *p*-cresol (23 g.), and higher methylated phenols, mostly xylenols (48 g.). Only traces of gases were evolved in this experiment.

Preparation of Hexamethylbenzene.—A mixture of phenol (50 g.) and methanol (400 g.) was dropped upon activated alumina at 375°, at a rate of 250 c.c. per hour. The receiver contained a yellowish oily solid together with water and unchanged methanol. The solid, after being pressed on a porous plate and washed with small quantities of methanol, yielded almost pure hexamethylbenzene (60 g.), m. p. 165°; it was slightly soluble in cold methyl and ethyl alcohol, more readily soluble in hot alcohol, glacial acetic acid, acetone, ether and benzene. The other products (not more than 5 g.) were not further investigated.

During this operation gases were evolved at a fairly rapid rate and contained carbon monoxide (25·4%), methane (containing some ethane) (16·9%), carbon dioxide (6·0%), oxygen (4·4%), ethylene (3·6%), and hydrogen (2·9%).

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UNIVERSITY COLLEGE, CARDIFF.

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