89. *The Action of Aluminium Chloride on Some Phenyl Ethers.*

By G. Baddeley.

The alkylation of the phenol nucleus is shown to be exclusively in the *p*-position in the presence of aluminium chloride, whereas that of the phenol homologues is directed by the alkyl groups present in the nucleus. Ethylation occurs more readily than methylation and the products of the former are very readily isomerised.

Anisole and a molecular proportion of aluminium chloride form an oxonium complex, which decomposes above 40° with the evolution of methyl chloride, $\mathrm{C_6H_5{\cdot}\overset{+}{O}(Me),\overset{-}{A}lCl_3 \longrightarrow C_6H_5{\cdot}O{\cdot}AlCl_2 + MeCl}$, and phenol is obtained quantitatively after 2 hours at 100°. Hydrogen chloride is evolved when two molecules of the chloride are used and, after an hour at 100°, phenol (68%), *p*-cresol (16%), *o*-4-xylenol (8%), and hemimellithenol (5%) are formed on the addition of ice. The methylating agent is probably $\mathrm{MeCl,AlCl_3}$ and the formation of *p*- to the exclusion of *o*-cresol indicates the magnitude of the inductive effect of the oxyaluminochloride group. Similarly, a mixture of phenol, diethyl ether, and excess of aluminium chloride furnishes *p*-ethylphenol (15%) and no *o*-isomeride after 3 hours at 100°. Table I shows the effect of various amounts of reagent at 100° on *p*-tolyl methyl ether, and Table II summarises the action of reagent (1·1 mols.) at 100° on the methyl ethers of several phenols and indicates that, as must be expected, nuclear-attached alkyl groups retard the decomposition of the oxonium complex and produce a more reactive nucleus towards electrophilic attack.

Table I.

Mols. $\mathrm{AlCl_3}$.	Unchanged methyl ether, %.	*p*-Cresol, %.	*o*-4-Xylenol, %.	Hemimellithenol, %.
0·5	50	50	—	—
1·25	—	40	40	10
2·0	—	30	40	20

Table II.

Methyl ether of—	Reaction time (hrs.).	Products.
Phenol	2	Phenol (95%)
m-Cresol	3	*m*-Cresol (80%) + *o*-4-xylenol (15%)
m-5-Xylenol	5	*m*-5-Xylenol (70%) + hemimellithenol (20%) and higher homologues (10%)

The methylation of *p*-tolyloxyaluminium chloride is directed by the nuclear-attached methyl group (the electromeric effect of the oxygen atom being suppressed by its oxonium condition : $\mathrm{Ar{\cdot}O{\cdot}AlCl_2,Ar{\cdot}\overset{+}{O}{:}\overset{-}{A}lCl_2}$) and this is in accord with the isomerisation of *o*-tolyl methyl ether to *p*-xylenol (38%), contaminated with some *o*-3-xylenol, and *iso*-ψ-cumenol (24%). The formation of the last has limited theoretical significance, since trimethylphenols can isomerise under the conditions of the experiment (J., 1943, 528); this does not apply to the cresols and xylenols. Again, *p*-tolyl ethyl ether, heated with excess of the reagent at 100° for a few minutes, produces 2-ethyl- (27%) and 2 : 6-diethyl-*p*-cresol (18%); these two products (26% and 31% respectively) are also obtained by the action of ethyl bromide and aluminium chloride at 20° for 3 days. A similar treatment of 4-ethylphenol with methyl bromide yields some 6-ethyl-*m*-cresol.

The same phenol homologues are formed by the methylation of *p*- and *m*-cresols respectively. A mixture of equal amounts of their methyl ethers reacts vigorously for a few minutes at 125° with excess of aluminium chloride and the cresol fraction, after separation from *o*-4-xylenol and higher homologues, contains *m*- (54%) and *p*-cresol (46%). The interconversion of these cresols (*loc. cit.*) under these conditions is not appreciable and the methylation of *p*-tolyloxyaluminium chloride must be at least as ready as that of the *m*-isomeride.

The investigation of the ethylation of phenol and its homologues is complicated by the ready isomerisation of those homologues containing an ethyl group (*loc. cit.*). As shown above, ethylation under the mildest conditions gives products which correspond to those obtained on methylation, but, *e.g.*, the more vigorous ethylation of phenol by diethyl ether and aluminium chloride produces 3 : 5-diethylphenol (Jannasch and Rathjen, *Ber.*, 1899, **32**, 2392). The products of the ethylation of *p*-cresol by the same reagents are shown in Table III, which indicates that the 5-ethyl-*m*-cresol is probably formed by the isomerisation of 2-ethyl-*p*-cresol.

TABLE III.

Ethylation of *p*-cresol by diethyl ether (1 mol.) and aluminium chloride (5 mols.).

Temp.	Time (hrs.).	2-Ethyl-*p*-cresol, %.	5-Ethyl-*m*-cresol, %.
75—80°	4	9	—
80	48	—	45
100	1·0	18	—
100	3·5	—	40

Similarly, the 5-ethyl-*m*-cresol (38%) obtained by the ethylation of *m*-cresol at 100° for 30 hours is probably derived from the 6-isomeride. The ethylated cresols from both *p*- and *m*-cresol and diethyl ether are accompanied by an equal amount of alkali-insoluble substances (b. p. 138°/20 mm.), which are being investigated.

Alkylation occurs in the *o*-position to the oxyaluminochloride group only when the *p*- and both *m*-positions are occupied by alkyl groups, and the reactions of phenoxyaluminium chloride and its homologues with alkylating agents, brominating agents (J., 1943, 525), and aluminium chloride (*loc. cit.*) show a close resemblance to one another; the reactions with acylating agents are now shown to be due to a more vigorous electrophilic attack.

The optimum yield of *p*-hydroxy-ketone is obtained when the phenyl ester is rearranged at the lowest temperature compatible with a useful rate of reaction (Rosenmund and Schnurr, *Annalen*, 1928, **460**, 56); again, under identical conditions, phenyl benzoate, owing to its much slower isomerisation (due to the mesomeric effect of the phenyl group), affords more *p*-hydroxy-ketone than does the corresponding acetate (95 and 50% respectively). The attack of *m*-4-xylenyl methyl ether by acid chlorides can be directed by the methyl groups (Auwers, *Ber.*, 1928, **61**, 1495; *Annalen*, 1928, **464**, 293); an excess of aluminium chloride ensures the oxonium condition of the ether oxygen atom, and benzoyl chloride provides more *m*-methoxy-ketone than does acetyl chloride. The action of nitrobenzene on the Fries rearrangement and on the Friedel–Crafts reaction is explained in a later communication.

These researches originated in a suggestion that the *m*-alkylation of an alkyl-benzene is due, at least in part, to the isomerisation of the product of *p*-substitution (Kenner, *J. Soc. Chem. Ind.*, 1933, **42**, 470). This suggestion was subsequently substantiated (Kenner and Baddeley, J., 1935, 307).

EXPERIMENTAL.

In the following experiments the resulting phenol homologues were identified by their melting points and mixed melting points and/or those of their *p*-nitrobenzoates.

(1) Anisole (22 g.) was heated with aluminium chloride (56 g., 2 mols.) at 100° for an hour. The product was poured on ice and extracted with ether, the extract shaken with dilute caustic soda solution and dried (calcium chloride), and the ether removed. The solid residue (1·5 g.) crystallised from light petroleum (b. p. 60—80°) in colourless prisms (m. p. 125°), and was soluble in hot alkali and reprecipitated by acid. These properties are those of pentamethylphenol (Hofmann, *Ber.*, 1885, **18**, 1826). The caustic soda washings were acidified with dilute sulphuric acid, an ethereal extract of them dried (calcium chloride), and the residue, after removal of the ether, fractionally distilled under reduced pressure (20 mm.): phenol (b. p. 80—85°, 13·5 g.), *p*-cresol (b. p. 100—105°, 3·0 g.), *o*-4-xylenol (b. p. 120—125°, 2·0 g.), and hemimellithenol (m. p. 109°, 1·5 g.) were obtained.

(2) Phenol (25 g.), diethyl ether (25 g., 1·27 mols.), and aluminium chloride (100 g., 2·8 mols.) were heated at 100° for 3 hours. The product was treated in the manner described in (1) and phenol (18 g.), *p*-ethylphenol (4 g.), and an unidentified residue (5 g.) were obtained.

(3) *p*-Tolyl methyl ether (36 g.), heated with aluminium chloride (20 g., 0·5 mol.) at 100° for 2·75 hours, gave *p*-cresol (19 g.) and its methyl ether (14 g.).

(4) *p*-Tolyl methyl ether (10 g.) and the reagent (15 g., 1·25 mols.), heated at 100° for 3 hours, produced *p*-cresol (3·5 g.), *o*-4-xylenol (4·0 g.), and hemimellithenol (1·0 g.).

(5) *p*-Tolyl methyl ether (26 g.) and the reagent (56 g., 2 mols.), heated at 100° for an hour, yielded *p*-cresol (8 g.), *o*-4-xylenol (9·5 g.), hemimellithenol (5 g.), and a substance (m. p. 125°, 2 g.) which was soluble in dilute caustic soda solution only on warming and was probably pentamethylphenol.

(6) Anisole (10 g.) and aluminium chloride (14 g., 1·1 mols.) were carefully mixed together at 20°; no gas evolution

occurred and long colourless needles were obtained. The evolution of methyl chloride was complete after 2 hour 100° and phenol (8 g.) was obtained.

(7) *m*-Tolyl methyl ether (25 g.) and the reagent (31 g., 1·1 mols.) no longer evolved gases after 2·5 hours at 1 and *m*-cresol (17 g.) and *o*-4-xylenol (4 g.) were obtained.

(8) *m*-5-Xylyl methyl ether (16 g.) and the reagent (18 g., 1·1 mols.) no longer evolved gases after 5 hours at 1 and provided *m*-5-xylenol (10·5 g.), hemimellithenol (3 g.), and the above-mentioned product (2 g.), m. p. 125°.

(9) *o*-Tolyl methyl ether (49 g.) and the reagent (120 g.) were heated on the steam-bath for 4 hours. After pour on ice, the components of the product were separated by repeated fractional distillation under 15 mm., *o*-cresol (b 85—90°, 10 g.), *p*-xylenol together with some *o*-3-xylenol (b. p. 100—105°, 19 g.), *iso*-ψ-cumenol (b. p. 120—125°, 13 and residue (6 g.) being obtained. The *o*-3-xylenol in the *p*-xylenol fraction was identified by its *p*-nitrobenzoate.

(10) The evolution of hydrogen chloride from a mixture of *p*-tolyl ethyl ether and the reagent (95 g., 2 mols.) complete after 10 minutes at 100°. *p*-Cresol (b. p. 95—100°, 17 g.), 2-ethyl-*p*-cresol (b. p. 130—135°, 13 g.), and 2 diethyl-*p*-cresol (b. p. 150°, 10 g.) were obtained on fractionation at 20 mm.

(11) *p*-Cresol (33 g.), ethyl bromide (33 g.), and aluminium chloride (84 g.) were kept at room temperature for 3 da *p*-Cresol (18 g.), 2-ethyl-*p*-cresol (11 g.), 2 : 6-diethyl-*p*-cresol (13 g.), and residue (3 g.) were obtained.

(12) A mixture of *p*-ethylphenol (75 g.), methyl bromide (40 c c.), and aluminium chloride (230 g.) was kept at ro temperature for 2 days and then warmed on the steam-bath for 5 minutes. A yellow precipitate, insoluble in eth was formed when the product was poured on ice. The ether-soluble material was dried (calcium chloride) and fr tionally distilled at 20 mm. Phenol (b. p. 80—85°, 8 g.), *p*-ethylphenol (b. p. 115—120°, 33 g.), 6-ethyl-*m*-cresol (b. 130—135°, 7 g.), a product which gave no solid *p*-nitrobenzoate and was not identified (b. p. 140—145°, 10 g.), a residue (3 g.) were obtained.

(13) *p*-Tolyl methyl ether (24·5 g.), *m*-tolyl methyl ether (24·5 g.), and aluminium chloride (112 g.) were plac in an oil-bath at 130°; after 5 minutes, the evolution of hydrogen chloride being nearly complete, the mixture w rapidly cooled. The cresol fraction (b. p. 198—202°, 14·3 g.) was separated from higher-boiling homologues by fractior distillation and found by quantitative analysis (J., 1943, 528) to contain 54% of *m*- and 46% of *p*-cresol.

(14) *p*-Cresol (54 g.), diethyl ether (37 g., 1 mol.), and aluminium chloride (210 g., 5 mols.), heated at 75—80° f 4 hours, yielded only *p*-cresol and 2-ethyl-*p*-cresol (b. p. 132—135°/20 mm., 6 g.). When a similar mixture was heat at 80° for 48 hours, 5-ethyl-*m*-cresol (b. p. 130°/20 mm., 30 g.) and an alkali-insoluble fraction (b. p. 140°/20 mm., 32 were obtained. The latter fraction, which readily decolorises bromine water and permanganate and remains unchang when refluxed for 5 hours with hydriodic acid (*d* 1·7), is being investigated.

When a similar reaction mixture was heated at 100° for 1·6 hours, the alkali-soluble fraction consisted of *p*-cres and 2-ethyl-*p*-cresol (12 g.). The further addition of aluminium chloride to the hot reaction mixture quickened tl liberation of hydrogen chloride and augmented the yield of the alkali-insoluble fraction.

When the reaction mixture was heated at 100° for 3·5 hours, *p*-cresol (8 g.), 5-ethyl-*m*-cresol (27 g.), and an unident fied fraction (b. p. 138—140°/20 mm., 15 g.) were obtained.

(15) *m*-Cresol (27 g.), diethyl ether (25 c.c.), and aluminium chloride (105 g.), heated at 100° for 30 hours, produce 5-ethyl-*m*-cresol (13 g.) and an alkali-insoluble fraction (b. p. 138—140°/20 mm., 18 g.).

2 : 6-*Diethyl*-p-*cresol*, obtained by the Clemmensen reduction of 4-hydroxy-2 : 6-diethylbenzaldehyde (Jannasc and Rathjen, *Ber.*, 1899, **32**, 2393), crystallised from light petroleum (b. p. 60—80°) in needles m. p. 59° (Found : 80·3; H, 10·0. $C_{11}H_{16}O$ requires C, 80·5; H, 9·7%).

6-Ethyl-*m*-cresol, b. p. 134°/20 mm., was obtained by the Clemmensen reduction of 4-hydroxy-2-methylacetophenon

2-*Ethyl*-p-*cresol*.—5-Methoxy-2-methylphenylmagnesium bromide reacted with ethyl sulphate to give a poor yiel of 2-ethyl-*p*-tolyl methyl ether, b. p. 105°/20 mm., which was demethylated with hydriodic acid.

4-Ethyl-*m*-cresol was obtained by the Clemmensen reduction of 2-hydroxy-4-methylacetophenone.

Table for the identification of phenol and its homologues.

			p-Nitrobenzoate.		
	B. p./20 mm.	M. p.	M. p.	% N found.	% N calc.
Phenol	80°	42°	129°	5·8	5·8
o-Cresol	92	30	94	5·6	5·45
m- ,,	101	12	87	5·5	,,
p- ,,	101	37	100	5·4	,,
c-3-Xylenol	114	75	104·5	5·3	5·2
o-4- ,,	125	63	128	5·3	,,
m-2- ,,	104	49	99	5·35	,,
m-4- ,,	110	26	113	5·3	,,
m-5- ,,	120	64	109	5·35	,,
p- ,,	110	74	88	5·3	,,
o-Ethylphenol	101	—	57	5·2	,,
m- ,,	120	—	68	5·2	,,
p- ,,	120	47	80	5·25	,,
4-Ethyl-*m*-cresol	111	45	88	5·0	4·9
5-Ethyl-*m*- ,,	130	54	84	5·0	,,
6-Ethyl-*m*- ,,	134	—	116	5·0	,,
2-Ethyl-*p*- ,,	134	—	116	4·9	,,
3-Ethyl-*p*- ,,	111	—	98	5·0	,,
Hemimellithenol	135	109	147	4·9	,,
iso-ψ-Cumenol	126	95			
3 : 5-Diethylphenol	140	77			
2 : 6-Diethyl-*p*-cresol	151	59			

THE COLLEGE OF TECHNOLOGY, MANCHESTER.

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