820. *Acid-catalysed Rearrangements of Alkyl Aryl Ethers. Part III.*[1] *Rearrangements in the Presence of Aluminium Bromide; the Mechanism of Such Rearrangements.*

By M. J. S. Dewar and N. A. Puttnam.

The rearrangement of phenyl s-butyl ether by a solution of aluminium bromide in chlorobenzene is described. The products are very different from those formed with solid aluminium chloride or sulphuric acid–acetic acid as catalyst. The mechanism of these and some related reactions is discussed and a general mechanism for the acid-catalysed rearrangements of ethers is proposed.

In the two preceding papers [1] we have given reasons for believing that rearrangement of alkyl aryl ethers to alkylphenols can take place by two routes, one intermolecular and one intramolecular, occurring simultaneously when aluminium chloride or a solution of sulphuric acid in acetic acid is used as catalyst.

[1] Parts I and II, preceding papers.

Two observations in the literature suggested that the intramolecular rearrangement might be favoured if a homogeneous solution of aluminium bromide was used as catalyst. Tarbell and Petropoulos [2] obtained in this way, from benzyl phenyl ether, a mixture of *o*-benzylphenol (55%) and phenol (45%); no *p*-benzylphenol could be detected in the product, even by infrared spectroscopy. The reaction was very fast, being complete in a few seconds at −40°. Tarbell and Petropoulos considered this to be strong evidence for an intramolecular mechanism, since benzylation [3] of phenol by the Friedel–Crafts reaction gives mainly the *para*-isomer, and since rearrangement [4] of benzyl phenyl ether with zinc chloride gave a mixture of *o*- and *p*-benzylphenol.

Hart and Elia [5] found that similar treatment of optically active α-methylbenzyl phenyl ether gave in 22% yield an optically active mixture of α-methylbenzylphenols in which the *ortho*-isomer predominated (85%). Similar rearrangement of optically active α-methylbenzyl *p*-tolyl ether gave 4-methyl-2-(α-methylbenzyl)phenol with 76% retention of configuration, implying an intramolecular mechanism.

This is surprising; for the exceptional stability of benzyl cations would be expected to facilitate an intermolecular mechanism. It seems that aluminium bromide specifically favours intramolecular rearrangements of ethers, and we therefore decided to examine its effect, in chlorobenzene solution, on phenyl s-butyl ether.

The products of this reaction were quite different from those formed [1] with solid aluminium chloride or a solution of sulphuric acid in acetic acid as catalyst. The only alkylphenols obtained were a mixture of the three isomeric mono-s-butylphenols; no dibutylphenols were formed. Moreover, the proportions of the s-butylphenols (Table 1) differed greatly from those observed with other catalysts; this is indicated by the *ortho/para* ratios quoted in Table 2.

TABLE 1. *Products (moles %) obtained by treating phenyl s-butyl ether with aluminium bromide in chlorobenzene.*

			Mono-s-butylphenols		
Time	Temp.	PhOH	*o*-	*m*-	*p*-
10 min.	70—80°	31·8	19·6	Trace	2·5
1 hr.	5—10	33·7	21·8	Trace	1·8
24 hrs.	5—10	32·8	21·8	Trace	2·0

TABLE 2. ortho/para *Ratios of mono-s-butylphenols obtained by rearranging phenyl s-butyl ether with various catalysts.*

Catalyst	$AlCl_3$ (1 mol.)	H_2SO_4–AcOH	$AlBr_3$–PhCl
Temp.	15—20°	110—120°	5—10°
ortho/para Ratio	0·24	1·0	11

Attempts were made to cause s-butyl bromide to react with phenol in the presence of aluminium bromide; after 24 hr. at 5—10° 95% of the phenol was recovered unchanged, together with a small amount (4%) of mixed butylphenols.

Discussion.—Table 1 shows that the proportions of isomers are not much affected by temperature; the differences between the *ortho/para* ratios in Table 2 cannot therefore be due to the different temperatures used in the various reactions. Nor can they be due to steric hindrance, which should be greatest in the case of aluminium bromide. The very high *ortho/para* ratio for the aluminium bromide reaction therefore strongly suggest an

[2] Tarbell and Petropoulos, *J. Amer. Chem. Soc.*, 1952, **74**, 244.
[3] See Thomas, "Anhydrous Aluminium Chloride," Reinhold Publ. Inc., New York, 1941.
[4] Short, *J.*, 1928, 528; Short and Stewart, *J.*, 1929, 553.
[5] Hart and Elia, *J. Amer. Chem. Soc.*, 1954, **76**, 3031.

intramolecular mechanism. This is further supported by the slowness of the reaction between phenol and s-butyl bromide under comparable conditions.

The proportions of isomers formed in the rearrangement of phenyl s-butyl ether, catalysed by aluminium bromide, are moreover very similar to those observed [6] in the acid-catalysed rearrangement of *N*-nitroaniline (*o*, 93; *m*, 0; *p*, 7%; *ortho*/*para* ratio, 13), a reaction which is known [6] to be intramolecular. The intramolecular rearrangement of the ether therefore leads predominantly to the *ortho*-isomer, as postulated in our two previous papers.[1]

In Part II we reviewed the work of Wallis and his collaborators on the rearrangement of optically active phenyl s-butyl ether with a sulphuric acid–acetic acid catalyst; the *o*-s-butylphenol formed had optical activity corresponding to 26% retention of configuration and 74% racemisation. Since Wallis also showed that intermolecular migration of s-butyl leads to complete racemisation, and since intramolecular migration of asymmetric alkyl groups usually takes place with complete retention of configuration, this result suggested that 26% of the rearrangement took place by the intramolecular route, and 74% by the intermolecular route.

Now the proportions of isomers formed by intermolecular migration of an s-butyl group should be the same as those formed by butylation of phenol under the same conditions; these [1] are shown in the first row of Table 3. The second row shows the proportions of isomers formed in the rearrangement catalysed by aluminium bromide (these being the mean of the values given in Table 1). If we assume that the proportions of isomers are the same for intramolecular rearrangements brought about by different catalysts, being those observed for the aluminium bromide reaction, we can calculate the products expected for the rearrangement catalysed by sulphuric acid–acetic acid, the ratio of intermolecular to intramolecular reaction being assumed to be 74 : 26. These values are shown in the third row of Table 3, and the fourth row gives the values observed (Part II). The agreement is within the limits of experimental error and confirms both the dual intermolecular–intramolecular mechanism, and the complete retention of activity in the intramolecular reaction.

TABLE 3. *Proportions of s-butylphenols in various reaction products.*

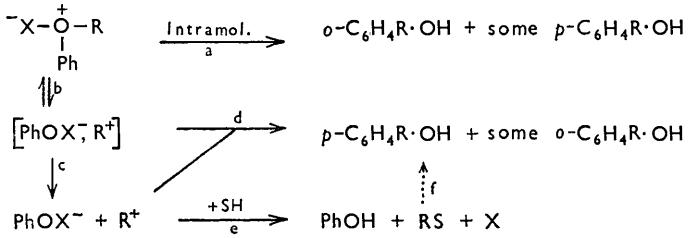
		$Bu^s \cdot C_6H_4 \cdot OH$ (%)		
Reaction		*o*-	*m*-	*p*-
$Bu^sOH + PhOH + H_2SO_4$–AcOH ...		34	4·5	61·5
$Bu^sOPh + AlBr_3$–PhCl		91	—	9
$Bu^sOPh + H_2SO_4$–AcOH	calc.	49	3	48
	obs.	47	7	46

All the available facts can now be rationalised in terms of the annexed mechanism, X being the catalyst (H^+ or aluminium halide) and SH the solvent (if any). Reaction (a) is the intramolecular rearrangement, leading to complete retention of configuration; its mechanism is considered below. Since it involves no fission into ions, it may occur quite readily even under non-polar conditions. Reaction (b) is a reversible fission of the initially formed complex into an ion pair, and (c) is the dissociation of this pair. The ions can recombine (*d*) to form racemic alkylphenols, the *p*-monoalkylphenol predominating, or they can react (*e*) with the solvent to form an alkyl derivative RS which may be able (*f*) to alkylate phenol.

The aluminium bromide reaction. The experimental evidence suggests that this took place almost entirely by the intramolecular route (a); this is not surprising, since the ionisation (b) should be suppressed in the non-polar solvent (chlorobenzene) used, and since any ions that were formed could be removed irreversibly by reaction with the solvent to form alkylchlorobenzenes. In this case reaction (f) cannot occur. Our mechanism

[6] Hughes and Jones, *J.*, 1950, 2678.

implies that rearrangement of optically active phenyl s-butyl ether should take place with complete retention of configuration; this is being investigated.



The sulphuric–acetic acid reaction. Here the reaction appears to take place mainly (74%) by the intermolecular path with complete racemisation, and partly (26%) by the intramolecular path with complete retention of configuration. Acetic acid is a much more polar solvent than chlorobenzene, so the new reaction (b) is faster than reaction (a). In this case reaction of the carbonium ion with the solvent gives an alkyl acetate which can alkylate phenol in presence of the acid catalyst; racemic alkylphenols can be formed by both reactions (d) and (f).

The first product of the ionisation (b) is, however, not an ion pair, but a combination of a cation (R^+) and a neutral molecule (PhOH); the reverse reaction (b) can be largely suppressed by the competing reactions (d) and (e). This means that the original ether is not significantly racemised by reversible ionisation; the intramolecular reaction (a) can therefore give alkylphenols with a very high retention of optical activity.

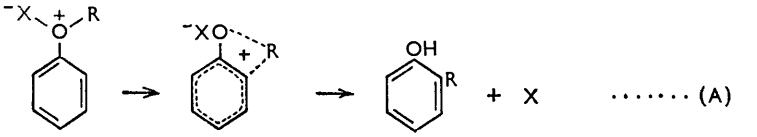
The aluminium chloride reaction. The experimental evidence suggests that (*a*) racemisation is complete, (*b*) most of the reaction is intermolecular, but part takes place by the intramolecular route, (*c*) the proportion of intramolecular reaction is greater, the smaller the amount of catalyst, and (*d*) rearrangement of n-butyl phenyl ether gives the same products as does the s-butyl ether, but in amounts that suggest a greater proportion of intramolecular reaction. It is explained by our reaction scheme if in this case reaction (b) is rapid and reversible, converting the starting material into racemic phenyl s-butyl ether. This would not be surprising; the ionisation (b) should occur very readily on the ionic surface of the catalyst. Observation (c) can be explained if the intramolecular reaction occurs solely in solution, being catalysed by dissolved aluminium chloride whose concentration in solution must be constant (it being present in excess). The rate of the intramolecular reaction should be independent of the amount of catalyst used, whereas the rate of the surface-catalysed intermolecular rearrangement should be proportional to the amount of catalyst. The relative importance of the intramolecular reaction should therefore be greater, the less the total amount of catalyst.

Observation (d) can be explained if aluminium chloride is more soluble in n-butyl phenyl ether than in phenyl s-butyl ether; this seems likely, since co-ordination between the former ether and aluminium chloride should be less sterically hindered.

This interpretation can be checked in several ways. First, the optically active phenyl s-butyl ether should racemise faster than it rearranges; secondly, the solubility of aluminium chloride in n- and s-butyl phenyl ether could be measured; thirdly, the reaction could be carried out in solvents in which the solubility of aluminium chloride varied. Experiments along these lines are in progress. It might seem that our mechanism would also require a rapid isomerisation of n-butyl phenyl ether to phenyl s-butyl ether; this, however, is not the case since the s-butyl ether rearranges much more rapidly [1] and would be removed as soon as it was formed. We could detect no isomerisation in a sample of n-butyl phenyl ether after partial rearrangement over aluminium chloride.

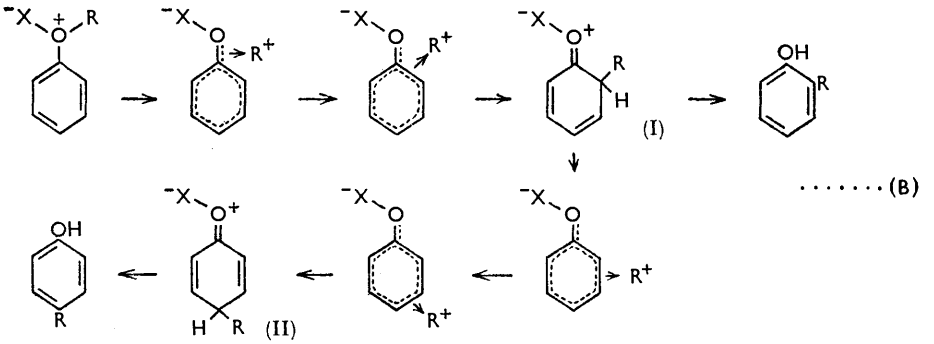
Mechanism of the intramolecular rearrangement. The intramolecular acid-catalysed rearrangement of alkyl aryl ethers cannot take place by a classical mechanism, involving

a cyclic transition state, for the latter would contain an impossibly strained four-membered ring (cf. A).



(A)

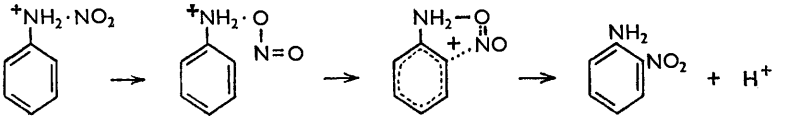
Much the most likely mechanism for this rearrangement, and for the analogous intramolecular acid-catalysed rearrangement of *N*-nitroaniline[6] is the π-complex mechanism suggested by one of us some years ago.[7] Since the problem has recently been reviewed[8] no details need be given here; the proposed mechanism in the present case may be written as in (B). Here (I) is the Wheland intermediate for *ortho*-substitution in



(B)

phenol. Since it must be a precursor of the intermediate (II) for *para*-substitution, the rearrangement leads mainly to the *ortho*-isomer. In direct electrophilic substitution of phenol the more favourable intermediate (II) can be formed directly and so *para*-substitution predominates.

The *N*-nitroaniline rearrangement probably takes place in a similar manner. Hughes and James suggested an alternative mechanism in which the nitroaniline first isomerised to phenylhydroxylamine nitrite, which then rearranged *via* a cyclic transition state (III). This mechanism is unacceptable, for two reasons. First, it postulates a reaction which has no analogy and is contrary to the known chemistry of nitramides. If nitramides were to rearrange in presence of acid to hydroxylamine nitrites, they would give rise to products



(III)

which are never observed. Nor can one suppose that the rearrangement is specifically assisted in the case of *N*-nitroaniline by a neighbouring-group participation by phenyl; for such participation would meet the very stereochemical difficulties that the Hughes mechanism was designed to avoid. Secondly, the mechanism does not account for the simultaneous formation of *p*-nitroaniline by a process which, as Hughes and Jones themselves pointed out, must also be intramolecular.

Rearrangements of benzyl phenyl ethers. The extraordinary facility[2,5] with which

[7] Dewar, *J.*, 1946, 406; " The Electronic Theory of Organic Chemistry," Oxford, 1949.
[8] Dewar, " Theoretical Organic Chemistry (Kekulé Symposium)," Butterworths, London, 1959.

benzyl phenyl ethers rearrange in presence of aluminium bromide suggests that these reactions may differ from the corresponding rearrangements of alkyl aryl ethers. There is a formal similarity [8] between the rearrangement of benzyl phenyl ether to *o*-benzylphenol, and that of a hydrazobenzene derivative to an *o*-semidine. This is being investigated.

Experimental

For general directions see Parts I and II.[1]

o-s-Butylphenol.—A solution of but-2-enyl phenyl ether, b. p. 55°/0·5 mm., n_D^{19} 1·5210 (9·5 g.), in diethylaniline (60 ml.) was boiled under reflux for 4 hr. When cold, the solution was poured into hydrochloric acid and extracted with light petroleum (b. p. 40—60°). The hydrocarbon layer was extracted with Claisen solution [potassium hydroxide (350 g.) in water (250 ml.) made up to 1 l. with methanol]; acidification and distillation gave *o*-1-methylallylphenol, b. p. 76°/2 mm., n_D^{21} 1·5382 (phenylurethane, m. p. 88—89°). Hydrogenation over 10% palladised charcoal in ethanol gave *o*-s-butylphenol which was shown by infrared spectroscopy to be identical with that synthesised earlier.[1]

Aluminium Bromide Solution.—A solution of anhydrous aluminium bromide in chlorobenzene was prepared, filtered, and stored under nitrogen in absence of moisture; 1 g. of solution contained 0·19 g. of the bromide.

Rearrangement of Phenyl s-Butyl Ether.—(a) *At* 70°. Aluminium bromide solution (157·4 g., 0·11 mole of aluminium bromide) was added with stirring to a solution of phenyl s-butyl ether (16·5 g., 0·11 mole) in chlorobenzene (20 g.). The mixture became hot (70°) and hydrogen bromide was evolved. After 10 min. the reaction was stopped by addition of water (500 ml.). The organic layer was taken up in light petroleum (b. p. 40—60°) and extracted with Claisen solution. Acidification gave a phenolic product (7 g.) which were fractionated in a 15 ml. " Towers " semimicro-apparatus. Fraction (i) (3 g.), b. p. 50—6°/1·5 mm., gave a phenylurethane, m. p. 126·5° alone or mixed with *ON*-diphenylurethane. Fraction (ii) was shown (infrared) to be a mixture of phenol and *o*-s-butylphenol. Fraction (iii), b. p. 78—80°/1 mm., gave a phenylurethane, m. p. 85°, alone or mixed with *o*-s-butylphenyl phenylurethane (corresponding aryloxyacetic acid, m. p. and mixed m. p. 112°). The last fraction was shown (infrared) to be mainly *o*-s-butylphenol with some *p*-s-butylphenol and traces of the *meta*-isomer.

(b) *At* 5—10°. The rearrangement was repeated with excess of chlorobenzene (300 ml.), the temperature was kept at 5—10°. After 1 hr. the phenolic products (7·5 g.) were separated as above and analysed by infrared spectroscopy.

(c) *At* 5—10° *for* 24 *hr.* Experiment (b) was repeated but the mixture was stirred for 24 hr. before addition of water. The phenolic products (7·4 g.), separated in the usual manner, were analysed spectroscopically.

Alkylation of Phenol by s-Butyl Chloride.—(*a*) Aluminium bromide solution (79 g., 0·055 mole) was added to mixture of phenol (5·2 g., 0·055 mole) and s-butyl bromide (7·5 g., 0·055 mole) in chlorobenzene (150 ml.) as described in (b) above. The reaction was stopped after 1 hr.; the phenolic products (4·9 g.) were shown (infrared) to be phenol with a very small amount of s-butylphenols. (*b*) The alkylation was repeated, but allowed to occur for 24 hr. before addition of water. The phenolic material was shown to be phenol with 4—5% of s-butylphenols.

Queen Mary College, Mile End Road,
London, E.1.

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