25. *Reduction by Dissolving Metals. Part IV.*

By Arthur J. Birch.

Sodium in liquid ammonia dealkylates a number of aryl alkyl ethers, the ease of reaction depending on the substitution of both groups. Several catechol derivatives, including the *cyclo*hexanone acetal, substituted methylenedioxybenzenes and guaiacol methoxymethyl ether, lose an oxygen from the nucleus, giving phenol or its derivatives. Reduction of 1 : 2-, 1 : 3- and 1 : 4-dimethoxybenzene with sodium and alcohol in ammonia gives the dihydro-derivatives, together with dihydroanisoles in the case of the 1 : 2-compounds.

In Part I (*J.*, 1944, 430) it was shown that sodium in liquid ammonia has a demethylating action on *m*-tolyl methyl ether (*cf.* Freudenberg, Lautsch, and Piazolo, *Ber.*, 1941, **74**, 1886), the addition of alcohol being necessary for reduction of the ring. The relative ease of dealkylation of various phenol ethers by this process has now been studied and the results are consistent with the hypothesis that reaction occurs through a transition state which may be represented by (I, R = alkyl, R′ = aryl). This is supported by a comparison of the reaction rates with the effects of substituents on the stabilities of the negative charges in both the anions.

Under standard conditions the following comparative yields of monophenolic product were obtained : anisole 27% ; tolyl methyl ethers, *o*- 17%, *m*- 9%, *p*- 4% ; dimethoxybenzenes,

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* Most m. p's. in the literature are slightly lower than this, but a Swiss patent (*Chem. Zentr.*, 1938, **I**, 3698) gives m. p. 144·5—145·5°.

1 : 2- 89%, 1 : 3- 71%, 1 : 4- 2·5%. 3 : 4-Dimethoxytoluene gave 4-methoxy-*m*-cresol. The order of activating influence is thus *o*-methoxyl > *m*-methoxyl > hydrogen > *o*-methyl > *m*-methyl > *p*-methyl > *p*-methoxyl. In the similar fission of unsymmetrically substituted diphenyl ethers (Sowa *et al.*, *J. Amer. Chem. Soc.*, 1937, **59**, 603, 1488; 1938, **60**, 94) where the two possible transition states may be represented by (I) and (II) (R and R′ = substituted phenyl) the one which is favoured appears to be determined by the relative substitutions of the aryl anions (R and R′ respectively) rather than the phenoxide ions—as is to be expected from the higher energy required by the former—and the substituents have the same order of activating influence as above. This must therefore express the relative effects of the groups on the stability of a negative charge either on a ring carbon atom or an oxygen atom attached to it. The full significance of this conclusion, particularly the stabilising effect of *o*-methoxyl, will be discussed later in connection with the theory of ring reduction and metallation.

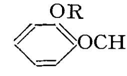
The consequence of altering R in (I, R = alkyl, R′ = aryl) was determined by an examination of several guaiacol ethers (III) which gave catechol monoalkyl ethers, the ease of removal of R being in the order $CH_2Ph, CH_2{\cdot}CO_2H > CH_3 > n\text{-}C_3H_7, iso\text{-}C_3H_7$; resorcinol methyl amyl ether (m-n-*amyloxyanisole*) gave resorcinol amyl ether. These results are in accord with the theory, since the more stable the charge on R the greater the ease of formation of (I), and it has been pointed out (Part II, *J.*, 1945, 809) that charge stability is decreased by alkylation and increased by arylation.

$\overset{-}{R}\ \overset{-}{O}R'$

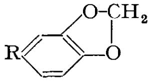
(I.)

$R\overset{-}{O}\ \overset{-}{R}'$

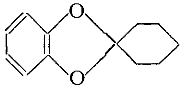
(II.)



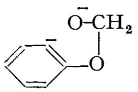
(III.)



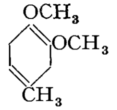
(IV.)



(V.)



(VI.)



(VII.)

Methylenedioxybenzene (IV, R = H), 3 : 4-methylenedioxytoluene (IV, R = CH_3), and safrole (IV, R = $CH_2{\cdot}CH{:}CH_2$) gave with sodium and alcohol in liquid ammonia phenol, *p*-cresol, and *p*-allylphenol, respectively. The same products were obtained in absence of alcohol, except that the last compound was partly isomerised to *p*-propenylphenol. The catechol acetal of *cyclo*hexanone (V) gave phenol and *cyclo*hexanol. Freudenberg, Klinck, Flickinger, and Sobek (*Ber.*, 1939, **72**, 226) have observed the formation of *p*-propylphenol from (IV, R = $n\text{-}C_3H_7$) and *m*-hydroxybenzoic acid from (IV, R = CO_2H) by the action of potassium in ammonia. All these results are explicable by assumption of an initial transition state of type (VI) where the negative charge on the aromatic ring is produced para- to the group more capable of stabilising it (H, rather than alkyl; CO_2H rather than H). Similarly with compounds of type (IV, R = CH:CHMe) the occurrence of oxygen removal (in this case para-) by means of sodium and alcohol is dependent on the presence of the conjugated double bond (Salway, *J.*, 1910, **97**, 2413), which must therefore exert a stabilising influence on a negative charge in the ring, and this is naturally greater in the para- than in the meta-position.

A similar fission of the methylenedioxy-ring has been observed when using Raney's aluminium–nickel alloy and aqueous alkali (Papa and Schwenk, *J. Org. Chem.*, 1945, **10**, 232), but in this case the isolation of *m*-cresol was claimed from both (IV, R = CHO) and (IV, R = CH_3). The former result has been confirmed, and is explicable if the ring is broken before reduction of the aldehyde group; in the latter case the product is, however, chiefly *p*-cresol, and the result therefore accords with a theory of electron addition, although it is possible that adsorption on the nickel plays some part.

The methoxymethyl ether of guaiacol (III, R = $CH_2{\cdot}OMe$), which has some similar structural features to the methylenedioxy-compounds, also lost oxygen from the ring by the action of sodium and ammonia, giving anisole.

As already noted, veratrole (III, R = Me) with sodium in ammonia gave guaiacol, but in presence of added alcohol the reaction took a different course (cf. Part I, *loc. cit.*), the products being a mixture of 2 : 5-dihydroanisole and a dihydroveratrole, probably the 3 : 6-, the latter giving on acid hydrolysis a mixture of phenol and anisole, and on treatment with 2 : 4-dinitrophenylhydrazine a derivative which is probably *2-methoxy-*Δ^4-cyclo*hexenone 2 : 4-dinitrophenylhydrazone*. 4-Methylveratrole gave a mixture of a dihydro-derivative, probably the 3 : 6-(VII), and dihydro-*p*-tolyl methyl ether. The loss of oxygen is probably due chiefly to direct removal of a methoxyl from the benzene ring in the expected *m*-position to the methyl, followed by reduction of the ring, and may be compared with the loss of a methoxyl from pyrogallol ethers by reduction with sodium and alcohol (Thoms and Siebeling, *Ber.*, 1911, **44**, 2135; Semmler, *Ber.*, 1908, **41**, 2556), the methoxyl here being activated by two others. Although

(VII) also lost a methoxyl by the action of sodium in ammonia the product was chiefly dihydro-*m*-tolyl methyl ether, and the process must be a direct reduction, since preliminary bond migration would result in a tetrahydro- rather than a dihydro-benzene derivative (Part III, *J.*, 1946, 593; unpublished work).

The dimethyl ethers of resorcinol and quinol were reduced normally with sodium and alcohol in ammonia with formation of dihydro-derivatives, hydrolysed by acid to dihydroresorcinol and 1 : 4-diketo*cyclo*hexane, and reduced by further action of sodium in ammonia to the enol methyl ether of *cyclo*hexanone. Pyrogallol trimethyl ether lost a methoxyl group, since hydrolysis of the product gave dihydroresorcinol.

EXPERIMENTAL.

Demethylation under Standard Conditions.—The substance (0·083 g.-mol.) in ether (15 c.c.) was added to ammonia (150 c.c.) containing sodium (0·3 g.-mol.), stirring continued for 15 minutes, and the mixture left in a Dewar flask for 7 hours. It was worked up by adding crushed ice (about 75 g.) as rapidly as was safe, the oil extracted with ether, and the ammonia boiled from the aqueous solution, which was then acidified. The phenol was extracted with ether (4 × 50 c.c.), the solution dried, the ether removed, and the phenol distilled except in the case of quinol dimethyl ether where the amount was too small. The glycollic acids were prepared in the standard manner with chloroacetic acid and sodium hydroxide. Anisole gave phenol, 27%; b. p. 177—180°, m. p. 40°; *o*-tolyl methyl ether gave *o*-cresol, 17%, b. p. 190—195°, derived glycollic acid, m. p. 152°; *m*-tolyl methyl ether gave *m*-cresol, 9%, b. p. 195—200°, derived glycollic acid, m. p. 102°; *p*-tolyl methyl ether gave *p*-cresol, 4%, b. p. 195—200°, derived glycollic acid, m. p. 136°; veratrole gave guaiacol, 89%, b. p. 90°/12 mm., m. p. 27—30°, 3 : 5-dinitrobenzoate, m. p. 139°; resorcinol dimethyl ether gave resorcinol monomethyl ether, 71%, b. p. 95°/11 mm., glycollic acid, m. p. 115—116° (Gilbody, Perkin, and Yates, *J.*, 1901, **79**, 1410, give m. p. 115—118°); quinol dimethyl ether gave 2·5% of a phenolic product which did not crystallise but gave *p*-methoxyphenoxyacetic acid, m. p. and mixed m. p. 107°. The small yield in the last case may be due partly to low solubility, but it is sufficiently soluble to undergo nuclear reduction (see below).

The following were reduced by dissolving the substance (6 g.) and sodium (3 g.) in ammonia (100 c.c.), leaving the mixture in a Dewar flask for 4 hours, working it up as above. 4-Methylveratrole gave 3-hydroxy-4-methoxytoluene (4·7 g.), b. p. 100—103°/11 mm., m. p. 33° (Found: C, 69·4; H, 7·5. Calc. for $C_8H_{10}O_2$: C, 69·5; H, 7·2%). Guaiacol *n*-propyl ether (Cahours, *Compt. rend.*, 1877, **84**, 1195) gave catechol *n*-propyl ether (2·5 g.) as a viscous oil, b. p. 95—105°/9 mm., which may contain a little guaiacol (Found: C, 70·3; H, 8·0. Calc. for $C_9H_{12}O_2$: C, 71·1; H, 7·9%). Guaiacol *iso*propyl ether (Allan and Robinson, *J.*, 1926, 381), b. p. 98—100°/12 mm., gave *catechol* iso*propyl ether*, b. p. 100—102°/11 mm. (Found: C, 70·5; H, 7·8. $C_9H_{12}O_2$ requires C, 71·1; H, 7·9%). Guaiacol benzyl ether, b. p. 175°/11 mm., m. p. 58—59° after crystallisation from alcohol (Claisen, *Annalen*, 1925, **442**, 244, gives m. p. 62°) (Found: C, 78·4; H, 6·5. Calc. for $C_{14}H_{14}O_2$: C, 78·5; H, 6·5%), gave guaiacol (1·5 g.) b. p. 85—90°/11 mm., m. p. 26—28°, and a neutral fraction consisting of toluene (0·3 g.) and dibenzyl (0·6 g.), m. p. 51°, undepressed by an authentic specimen. 2-Methoxyphenoxyacetic acid, m. p. 119°, gave guaiacol (2·4 g.), b. p. 90°/11 mm., 3 : 5-dinitrobenzoate, m. p. 140°. m-n-*Amyloxyanisole* (resorcinol methyl amyl ether), prepared by the action of *n*-amyl bromide on the sodium salt of 3-methoxyphenol in boiling alcohol as a colourless oil, b. p. 140°/11 mm. (Found: C, 74·3; H, 9·2. $C_{12}H_{18}O_2$ requires C, 74·2; H, 9·3%), gave resorcinol amyl ether (1·4 g.), b. p. 155—160°/11 mm., which gave rise to 3-*amyloxyphenoxyacetic acid* as colourless needles from ethyl acetate–light petroleum, m. p. 95° (Found: C, 65·6; H, 7·6. $C_{13}H_{18}O_4$ requires C, 65·5; H, 7·5%).

Methylenedioxybenzene, 3 : 4-Methylenedioxytoluene, Piperonal, and Safrole.—(A) To methylenedioxybenzene (7 g.) in ammonia (150 c.c.) and alcohol (10 g.) was added sodium (5 g.) in small pieces. The product (4·1 g.) was phenol. 3 : 4-Methylenedioxytoluene (prepared by methylenation of homocatechol, Baker, *J.*, 1931, 1765) similarly gave *p*-cresol, identified as *p*-tolyloxyacetic acid, m. p. 134—136°, undepressed by an authentic specimen, m. p. 135—136°. The same products were obtained in both cases if the alcohol was omitted, but safrole in presence of alcohol gave *p*-allylphenol, b. p. 113—115°/9 mm., 3 : 5-dinitrobenzoate, m. p. 97°, and in absence of alcohol an admixture of this with *p*-propenylphenol, m. p. 93° (from alcohol) (Found: C, 80·4; H, 7·5. Calc. for $C_9H_{10}O$: C, 80·6; H, 7·4%). Both these substances on methylation and oxidation with potassium permanganate in acetone gave *p*-methoxybenzoic acid, m. p. and mixed m. p. 180—181°.

(B) 3 : 4-Methylenedioxytoluene (4 g.) was reduced with Raney's alloy (30 g.) in aqueous sodium hydroxide (200 c.c., 10%) and alcohol (100 c.c.) (cf. Papa and Schwenk, *loc. cit.*) and gave *p*-cresol (0·7 g.), identified by conversion into *p*-tolyloxyacetic acid, m. p. 132—134°, undepressed by an authentic specimen, m. p. 135—136°. Methylenedioxybenzene similarly gave phenol. Piperonal (5 g.) by the same process gave a phenolic fraction, b. p. 190—200° (2·9 g.), which on treatment with sodium hydroxide and chloroacetic acid gave a derivative, m. p. 85—95°, undepressed by *m*-tolyloxyacetic acid, m. p. 102°. After six crystallisations from water the small amount of material remaining had m. p. 127—130°, undepressed by *p*-tolyloxyacetic acid, m. p. 135—136°. The phenol was probably a mixture of *m*- and *p*-cresol with the former predominating. Methylation and reduction with sodium and alcohol in liquid ammonia followed by acid hydrolysis gave a ketone, the 2 : 4-dinitrophenylhydrazone of which had m. p. 172—174° and the semicarbazone m. p. 200—202°, both undepressed by authentic derivatives of 3-methyl-Δ^2-*cyclo*hexenone.

Attempted reduction with Raney's alloy gave only a trace of phenolic product from safrole.

cyclo*Hexanone Catechol Acetal.*—Catechol (10 g.), *cyclo*hexanone (10 g.), benzene (40 c.c.), and sulphuric acid (3 drops) were heated under reflux for 2 hours, the water formed being removed by slow distillation of the solvent. The mixture was then poured into aqueous sodium hydroxide, and the oil extracted with ether and distilled (8 g.), b. p. 125°/10 mm., m. p. 47° from aqueous alcohol (Slooff, *Rec. Trav. chim.*, 1935, **54**, 999, gives m. p. 41°) (Found: C, 75·8; H, 7·6. Calc. for $C_{12}H_{14}O_2$: C, 75·8; H, 7·4%). This substance (5·5 g.) and sodium (3 g.) in ammonia (150 c.c.) were left for 10 hours, and worked up as usual. The neutral material (2·0 g.), b. p. 160°, was *cyclo*hexanol (3 : 5-dinitrobenzoate, m. p. 110°), and the phenolic product phenol (2·2 g.), giving phenoxyacetic acid, m. p. 98°.

Guaiacol Methoxymethyl Ether.—This was prepared in 26% yield by refluxing the sodium salt of guaiacol (1 mol.) with chloromethyl ether (1 mol.) in ether for 1 hour and direct distillation, finally under reduced pressure; b. p. 113—115°/11 mm. (cf. Hoering and Baum, D.-R.P., 1907, 209,608). This substance (6 g.) in ether (15 c.c.) was added to ammonia (80 c.c.), and sodium (2·8 g.) added in small pieces until a permanent blue was obtained. Worked up as usual, the neutral oil (2·8 g.), b. p. 40°/11 mm., $n_D^{18°}$ 1·5204, was anisole, identified by demethylation to phenol (phenoxyacetic acid, m. p. 98°). The phenolic fraction (0·4 g.) was chiefly guaiacol.

Veratrole.—Veratrole (17 g.) in alcohol (25 g.) and ammonia (250 c.c.) was reduced with sodium (9 g.). The product gave (i) b. p. 30—60°/10 mm. (5·1 g.), and (ii) b. p. 60—85°/10 mm. Fraction (i) was chiefly 2 : 5-dihydroanisole, since it gave in good yield Δ³-*cyclo*hexenone 2 : 4-dinitrophenylhydrazone, m. p. 133°; fraction (ii) was redistilled, giving (*a*) b. p. 72—76°/10 mm. (3·6 g.), and (*b*) b. p. 83—85°/10 mm. Fraction (*a*) was 3 : 6-*dihydroveratrole* (Found: C, 68·9; H, 8·6. $C_8H_{12}O_2$ requires C, 68·6; H, 8·6%). On treatment with cold alcoholic 2 : 4-dinitrophenylhydrazine sulphate it gave 2-*methoxy*-Δ⁴-cyclo*hexenone* 2 : 4-*dinitrophenylhydrazone* as red prisms from ethyl acetate–alcohol, m. p. 187—188° (Found: C, 51·0; H, 4·5. $C_{13}H_{14}O_5N_4$ requires C, 51·0; H, 4·6%). Fraction (*b*) was unchanged veratrole. 3 : 6-Dihydroveratrole (3 g.) and sodium (1·5 g.) in ammonia (35 c.c.) for 1 hour gave 2 : 5-dihydroanisole, b. p. 155—160° (1·2 g.), identified by conversion into Δ³-*cyclo*hexenone 2 : 4-dinitrophenylhydrazone, m. p. 133°.

4-*Methylveratrole.*—This substance (18 g.) in alcohol (55 g.) and ammonia (400 c.c.) was reduced with sodium (18 g.). The product gave two main fractions: (i) b. p. 68—73°/14 mm., and (ii) b. p. 83—85°/14 mm. (7·5 g.). The former must be chiefly 2 : 5-dihydro-*p*-tolyl methyl ether, since hydrolysis with dilute acid gave a ketone, 2 : 4-dinitrophenylhydrazone, m. p. 122°, undepressed by the derivative of 4-methyl-Δ³-*cyclo*hexenone, and converted by boiling with alcoholic sulphuric acid to the derivative of 4-methyl-Δ²-*cyclo*hexenone, m. p. 174°, undepressed by an authentic specimen. Fraction (ii) was 4-*methyl*-3 : 6-*dihydroveratrole* (Found: C, 70·1; H, 9·1. $C_9H_{14}O_3$ requires C, 70·1; H, 9·1%). After this (2·3 g.) had been refluxed with 10% hydrochloric acid (5 c.c.), it gave a phenolic fraction (0·8 g.), b. p. 190—200°, which is probably a mixture of *m*- and *p*-cresol since it gave a glycollic acid, m. p. 85—110°, which after several crystallisations from water gave *p*-tolyloxyacetic acid, m. p. 134—136°, undepressed by an authentic specimen. The neutral product (0·6 g.), b. p. 175—180°, appears to be a mixture of *p*- and *m*-tolyl methyl ether. Addition of 4-methyl-3 : 6-dihydroveratrole (5 g.) to sodium 4 g.) in ammonia (100 c.c.) gave some low-boiling product, apparently a hydrocarbon, and a fraction b. p. 60°/12 mm. (1·8 g.) (Found: C, 77·4; H, 9·5. Calc. for $C_8H_{12}O$: C, 77·4; H, 9·7%), which must be 2 : 5-dihydro-*m*-tolyl methyl ether, since after hydrolysis with dilute hydrochloric acid it gave 3-methyl-Δ²-*cyclo*hexenone, semicarbazone m. p. and mixed m. p. 200—201°.

Quinol Dimethyl Ether.—This substance (13 g.) in alcohol (25 g.) and ether (40 c.c.) was added to ammonia (250 c.c.) and reduced with sodium (12 g.). The product (12 g.), 2 : 5-*dihydroquinol dimethyl ether*, b. p. 78°/12 mm., recrystallised from light petroleum (b. p. 40—60°) as colourless prisms, m. p. 54° (Found: C, 68·7; H, 8·5. $C_8H_{12}O_2$ requires C, 68·6; H, 8·6%). Refluxing with 10% hydrochloric acid for an hour, followed by chloroform extraction and recrystallisation from ethyl acetate–light petroleum gave 1 : 4-diketo*cyclo*hexane as long colourless prisms, m. p. 78°. The dihydro-ether (5 g.) and sodium (3 g.) in ammonia (50 c.c.) for two hours gave Δ¹-cyclo*hexene methyl ether*, b. p. 40°/14 mm. (2·4 g.) (Found: C, 75·4; H, 10·7. $C_7H_{12}O$ requires C, 75·0; H, 10·7%), identified by conversion into *cyclo*hexanone 2 : 4-dinitrophenylhydrazone, m. p. 161°.

Resorcinol Dimethyl Ether.—Reduced as for quinol dimethyl ether, this substance gave 2 : 5-*dihydroresorcinol dimethyl ether* (12 g.), b. p. 95°/18 mm. (Found: C, 68·6; H, 8·5. $C_8H_{12}O_2$ requires C, 68·6; H, 8·6%). This was hydrolysed by heating on the steam-bath with an equal volume of water containing a few drops of hydrochloric acid for 45 minutes, and finally in an open vessel to remove methyl alcohol. The residue was taken up in chloroform, dried, the solvent removed, and the solid crystallised from ethyl acetate–light petroleum (b. p. 40—60°) as large colourless prisms, m. p. 105°, undepressed by an authentic specimen of dihydroresorcinol. The dihydro-ether (5 g.) further reduced with sodium as for dihydroquinol dimethyl ether, gave *cyclo*hexanone enol methyl ether, b. p. 36°/12 mm., converted into *cyclo*hexanone 2 : 4-dinitrophenylhydrazone, m. p. 162°. Pyrogallol trimethyl ether, reduced as for quinol dimethyl ether, gave an oil, b. p. 85—90°/13 mm., which on hydrolysis with hot dilute hydrochloric acid gave dihydroresorcinol, m. p. and mixed m. p. 105°.

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