357. *The Oxidation of Aromatic Hydrocarbons and Phenols by Trifluoroperoxyacetic Acid.*

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Benzene homologues other than toluene undergo electrophilic hydroxylation on treatment with trifluoroperoxyacetic acid. Further oxidation then occurs, to give quinones. An alkyl group in the *para*-position with respect to the hydroxyl group introduced migrates so that the *para*-quinone can be formed.

By starting with the phenols, good yields of some quinones have been obtained.

In practically all the known examples of the hydroxylation of aromatic hydrocarbons the reactions are ascribed to attack either by free radicals such as hydroxyl or benzoate radicals, or by addition of the so-called "double-bond reagents" followed by the elimination of water [1,2] to give the phenol. In some cases it is claimed that these double-bond reagents function simply as sources of hydroxyl radicals.[1] When the oxidation proceeds beyond the quinol stage without leaving a trace of earlier products as, for example, when dichromates are used as oxidising agents, free radicals are again postulated as intermediates.[3]

There are two cases where it is suggested that an electrophilic reaction has occurred. In one of these the hydroxyl cation was produced from hydrogen peroxide in acetic–sulphuric acid and used to prepare mesitol from mesitylene.[4] In the other, where peroxybenzoic acid was the oxidant,[5] there is little detail given and only polycyclic aromatic compounds were used. Peroxyacetic acid, which like peroxybenzoic acid is used to afford glycols from olefins and is also accepted for this purpose as an electrophilic reagent,[6] has been said to give no quinone from aromatic hydrocarbons [7] and, when it is used in a modified form simply as hydrogen peroxide and glacial acetic acid, reaction has occurred under such conditions that no decision on the mechanism has been possible. When peroxyacetic acid is used on phenols [8] the first step in the attack is at the *ortho*-position and, by analogy with the action of acyl peroxides on phenols, may occur by a bimolecular "four-centre" process.[9]

Since trifluoroperoxyacetic acid is a much better oxidising agent than any of the non-fluorinated peroxyacids,[10] and since Bourne *et al.*[11] have shown that the mixed anhydrides derived from trifluoroacetic acid are ionised slightly into negative trifluoroacetate ions and positive acylium ions, it seemed that if the other peroxyacids could be considered as electrophilic reagents then trifluoroperoxyacetic acid was likely to be an excellent source of positive hydroxyl ions. This was confirmed by treating certain benzene homologues with about 1½ equivalents of trifluoroperoxyacetic acid at 0°. The peroxy-acid was prepared *in situ* by adding "high-test peroxide" to a solution of the hydrocarbon and trifluoroacetic anhydride in methylene chloride. Since the equilibrium in which trifluoroperoxyacetic acid is formed is set up instantaneously,[10] $(CF_3\cdot CO)_2O + H_2O_2 \rightleftharpoons CF_3\cdot CO_3H + CF_3\cdot CO_2H$, it was not necessary to form it before mixing with the hydrocarbon

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[1] Waters, *Ann. Reports*, 1945, **42**, 130.

[2] Schoental, in Biochemical Symposium No. 5, 1949, p. 3 (Biological Oxidation of Aromatic Rings), ed. R. T. Williams; Cook and Schoental, *J.*, 1950, 47; Cross and Heiberg, *Ber.*, 1900, **33**, 2015; Perret and Perrot, *Helv. Chim. Acta*, 1945, **28**, 558; Milas, *J. Amer. Chem. Soc.*, 1937, **59**, 2342.

[3] Waters, *Trans. Faraday Soc.*, 1946, **42**, 184; Gee, *ibid.*, 197; Cason, "Organic Reactions," ed. R. Adams *et al.*, John Wiley, New York, 1948, Vol. IV, p. 305.

[4] Derbyshire and Waters, *Nature*, 1950, **165**, 401.

[5] Roitt and Waters, *J.*, 1949, 3060.

[6] Swern, "Organic Reactions," Ed. by R. Adams *et al.*, John Wiley, New York, 1953, Vol. VII, p. 378.

[7] Arnold and Larsen, *J. Org. Chem.*, 1940, **5**, 250.

[8] Boeseken and Metz, *Rec. Trav. chim.*, 1935, **54**, 345.

[9] Walling and Hodgdon, *J. Amer. Chem. Soc.*, 1958, **80**, 228.

[10] Emmons, *ibid.*, 1954, **76**, 3468, 3470; Emmons, Pagano, and Freeman, *ibid.*, p. 3472; Emmons and Pagano, *ibid.*, 1955, **77**, 89, 4557; Emmons and Lucas, *ibid.*, p. 2287.

[11] Bourne, Randles, Stacey, Tatlow, and Tedder, *ibid.*, 1954, **76**, 3206 and earlier papers.

solution. In later experiments it was found that trifluoroacetic acid could be used instead of the anhydride: the yields were lower by one-third but the same products were obtained and its use avoids the losses incurred in preparing the anhydride.

A 30—40% conversion of alkylbenzenes into a mixture of phenols and quinone was effected. This was separated after methylation, a process which caused the loss of most of the quinone, the yield of which had to be determined by eluting a separate portion of the original reaction mixture through an alumina column with methylene chloride or light petroleum. Except in the case of mesitylene, liquid chromatography could not be used to separate the whole mixture because the phenols are very strongly adsorbed on activated alumina and when deactivated alumina is used it is not a feasible method.[12]

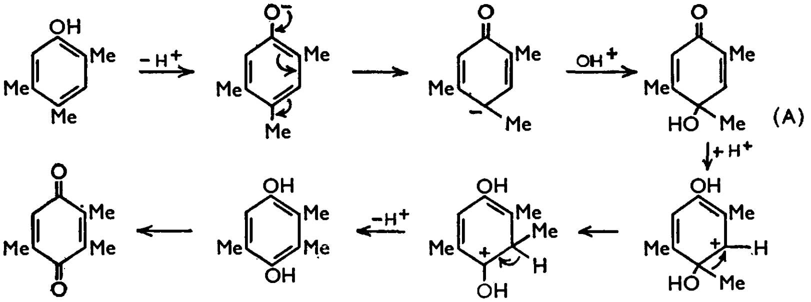
The aqueous layer from the reaction contained only trifluoroacetic acid and traces of a gum; no appreciable breakdown of the aromatic ring or tar formation appeared to have occurred.

The proof that electrophilic hydroxylation occurs came from the reactions with *m*-xylene and 1,2,4-trimethylbenzene. In the former the products were 2,6- and 2,4-xylenol and *m*-xyloquinone in yields of approximately 15%, 35%, and 20% respectively based on the amount of hydrocarbon used. They were identified mainly by gas–liquid chromatography after calibration of the column with authentic specimens of the methyl ethers and quinones. This method would not differentiate between methyl 2,4- and 3,5-xylyl ether but the infrared spectrum showed no trace of the latter. *m*-Xyloquinol was also isolated in the form of its dimethyl ether, but this is almost certainly all formed by methylation of the quinone and accounts for its disappearance.[13]

Oxidation of 1,2,4-trimethylbenzene gave 2,3,6- and 2,4,5-trimethylphenol, and the quinone. Again gas–liquid chromatography would not differentiate between methyl 2,4,5- and 2,3,5-trimethylphenyl ether, but the infrared spectrum showed that the 2,3,5-isomer was absent.

It has not yet been possible to confirm the mechanism by the hydroxylation of toluene because, under conditions necessary to initiate reaction, reaction is vigorous, giving a complex mixture which is not easy to separate. Benzene behaves similarly. In this connection the inability of Bourne *et al.*[11] to acylate benzene and toluene with mixed anhydrides is worth noting.

When mesitylene is oxidised it gives mesitol in good yield together with a small amount of 2,3,5-trimethylbenzoquinone. The latter probably results from the formation and rearrangement of mesityl " quinole "; this compound itself has not been isolated from the reaction mixture but by treating 2,4,5-trimethylphenol with trifluoroperoxyacetic acid the corresponding 2,4,5-trimethyl" quinole " (A) has been isolated in about 10% yield. The mechanism for the complete process is probably as annexed.



Bamberger and Rising [14] claim to have isolated very small amounts of this and other " quinoles " by the oxidation of benzene homologues with Caro's acid. They rearranged

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[12] Schneider and Oberkobusch, *Brennstoff-Chem.*, 1951, **32**, 110.

[13] Rao, Rao, and Seshadri, *Proc. Indian Acad. Sci.*, 1948, **27**, *A*, 245.

[14] Bamberger and Rising, *Ber.*, 1900, **33**, 3636; 1903, **36**, 2028.

them in the presence of either acid or alkali but this has not previously been confirmed because other workers [15] have been unable to repeat their preparation of the "quinoles." Attempts to prepare other "quinoles" by means of trifluoroperoxyacetic acid are now being made.

Since fairly high yields of quinones were obtained, even under unsuitable conditions, in the cases where their formation was possible without rearrangement, we compared this use of peroxytrifluoroacetic acid with other methods of preparing quinones. Certain phenols (*o*- and *m*-cresol, 2,3-dimethylphenol) gave only resins, while others gave 50—80% yields of quinone. In these reactions the temperature was allowed to rise after addition of the peroxide, and the colour changed through red to black (presumably formation of semiquinones), then to orange-yellow during about 8 hours, whereafter the quinone was obtained almost pure. The method generally gives a better yield than does chromic acid, it is easier to isolate and purify the product, and in some cases, *e.g.*, 2,3,5-trimethylphenol, chromic acid will not effect direct oxidation and either Fremy's salt [16] or the route through the azo-dye [17] has to be used.

EXPERIMENTAL

m-*Xylene*.—(*a*) To trifluoroacetic anhydride (30 g.) and *m*-xylene (16 g.), dissolved in methylene chloride (50 ml.) and cooled to 0°, 85% hydrogen peroxide (6 ml.) was added with stirring during 30 min. Stirring was continued at 0° for 24 hr., the colour changing through dark red to yellow. The mixture was then neutralised with solid sodium hydrogen carbonate after addition of a few ml. of water. After separation, the aqueous layer was extracted with methylene chloride (3 × 10 ml.) and the extracts were added to the rest of the organic layer.

The aqueous layer was then acidified with dilute sulphuric acid and extracted continuously with methylene chloride. Drying and distillation of the methylene chloride and the trifluoroacetic acid left only a minute amount of a gum. The methylene chloride solutions were dried ($MgSO_4$) and distilled, to give (i) methylene chloride, (ii) *m*-xylene (10 g.), b. p. $<90°/20$ mm., and (iii) a red oily residue (5·6 g.).

A sample of this red oil (1·0 g.) was eluted through a column of activated alumina with methylene chloride, to give *m*-xyloquinone (0·25 g.), m. p. 71°, mixed m. p. 72°. The phenolic constituents remained on the column and could not be removed quantitatively even on continuous extraction with methyl alcohol.

Methylation of the red oil (3 g.) in methanol (6 ml.) with dimethyl sulphate (3 g.) and a 30% aqueous solution of sodium hydroxide (7 g.) first at $-5°$ and then under reflux gave, after ether-extraction, a dark liquid (2·5 g.) which was examined by gas–liquid chromatography in a column (length 232 cm., internal diameter 6 mm.) packed with 12 g. of a mixture of "Apiezon L" (4 pt.) and "Celite 545" (10 pt.). With the column at 194°, a nitrogen flow-rate of 38 ml./min., inlet pressure being atmospheric and a vacuum of -22 cm. being applied at the outlet, the mixture separated into three main components with peak-maximum times of 6½ min., 8 min., and 17½ min. respectively. Comparison of these chromatograms with those of authentic specimens and with those of mixtures of the product and authentic specimens showed that the components were methyl 2,6-xylyl ether, either the 2,4- or the 3,5-xylyl ether or a mixture of the two, and *m*-xyloquinol dimethyl ether respectively.

The methyl ethers were condensed out of the nitrogen stream after passing through the column, and infrared analysis of the second component showed that it consisted mainly of the 2,4-isomer, $\nu_{max.}$ (no solvent) 1040, 877, 804, 754, 710 $cm.^{-1}$ (authentic specimen 1039, 877, 804, 754, 710), together with a little 2,6-isomer, $\nu_{max.}$ (no solvent) 1094, 1068, 1018, and 771 $cm.^{-1}$ (authentic specimen 1093, 1064, 1015, 768), due to overlapping with the first peak, but that the 3,5-isomer was absent (no band at or near 952 or 691 $cm.^{-1}$ as for an authentic specimen).

From the yields of methyl ethers (85%) obtained by methylation of the authentic phenols, the areas of the peaks obtained by chromatography, and the amount of quinone isolated by liquid chromatography, it was calculated that the red oil (5·6 g.) from *m*-xylene (6 g.) contained 2,6-xylenol 1 g., 2,4-xylenol 2·5 g., *m*-xyloquinol 0·7 g., and *m*-xyloquinone 1·4 g.

(*b*) Repetition of the experiment with *m*-xylene (12·9 g.), trifluoroacetic acid (20 g.), methylene chloride (50 ml.), and 85% hydrogen peroxide (5·3 ml.) gave recovered *m*-xylene

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[15] Cosgrove and Waters, *J.*, 1951, 388.

[16] Teuber and Rau, *Chem. Ber.*, 1953, **86**, 1036.

[17] Smith, Opie, Wawzonek, and Prichard, *J. Org. Chem.*, 1939, **4**, 318.

(9·3 g.) and a red oil (3·3 g.) which contained 2,6- (0·75 g.) and 2,4-xylenol (0·75 g.), *m*-xyloquinol (0·7 g.), and *m*-xyloquinone (0·8 g.).

1,2,4-*Trimethylbenzene*.—Trifluoroacetic anhydride (33 g.), 1,2,4-trimethylbenzene (19 g.), and 85% hydrogen peroxide (6·5 ml.) in methylene chloride (50 ml.) gave recovered hydrocarbon (12 g.) and a red oil (6·2 g.) which contained 2,5,6- (1 g.) and 2,4,5-trimethylphenol (1·3 g.) and the quinone (1·7 g.) (*monosemicarbazone*, m. p. and mixed m. p. 252°; Found: C, 57·6; H, 6·3. $C_{10}H_{13}O_2N_3$ requires C, 58·0; H, 6·3%). A fourth component was probably the quinol; its dimethyl ether was eluted so slowly from the gas–liquid chromatography column that it was not collected.

The methyl ethers of 2,5,6- and 2,4,5-trimethylphenol had peak maximum times of 6 min. 50 sec. and 8 min. 50 sec. respectively when eluted through the gas–liquid chromatography column at 202° (nitrogen flow rate 38 ml./min.; inlet pressure atmospheric; outlet vacuum −13·5 cm.).

Methyl 2,4,5-trimethylphenyl ether, $\nu_{\text{max.}}$ (no solvent) 1271, 1214, 1100, 873, 841 cm.$^{-1}$ (authentic, 1275, 1215, 1099, 877, 845 cm.$^{-1}$), was differentiated from the 2,3,5-trimethyl isomer [authentic, $\nu_{\text{max.}}$ (no solvent) 1189, 1151, 1117, 964, 832 cm.$^{-1}$] by comparing its infrared spectrum with those of authentic specimens. There was no 2,3,5-trimethyl isomer in the reaction mixture.

Mesitylene.—Trifluoroacetic acid (19 g.), mesitylene (18·7 g.), and 85% hydrogen peroxide (6 ml.) in methylene chloride (50 ml.) gave recovered mesitylene (14 g.) and a red oil (4·5 g.) which on elution through an alumina column with methylene chloride gave the quinone (0·75 g.) (monosemicarbazone, m. p. and mixed m. p. 252°) and crude mesitol (3·5 g.) which, purified by sublimation, had m. p. 70° and mixed m. p. 70°.

Preparation of 2,4,5-*Trimethyl" quinole "*.—2,4,5-Trimethylphenol (9·7 g., 0·07 mol.) and trifluoroacetic acid (10 g., 0·07 mol.) in methylene chloride (50 ml.) were treated with 85% hydrogen peroxide (8·2 ml., 0·28 mol.) at room temperature with stirring. After 24 hr. the mixture was neutralised with sodium hydrogen carbonate. The aqueous layer was separated and extracted with methylene chloride. The united extracts, when dried ($MgSO_4$) and evaporated, left a red oil (6·7 g.) which was eluted through an alumina column (36 cm. × 2 cm.) with methylene chloride until the first coloured fraction was completely removed. Evaporation gave a yellow-brown oil (2·67 g.), which was treated with a few ml. of ether and left exposed to the air. White crystals of " 2,4,5-trimethylquinole " [14] (1·04 g.; m. p. 113°) separated. After recrystallising from water and subliming it had m. p. 116° (Found C, 71·1; H, 8·4. Calc. for $C_9H_{12}O_2$: C, 71·0; H, 7·9%) and formed a *benzoate*, m. p. 93° (from alcohol and water) (Found: C, 75·2; H, 6·5. $C_{16}H_{16}O_3$ requires C, 75·0; H, 6·3%). The infrared spectrum of the quinole showed $\nu_{\text{max.}}$ (KBr discs) 3522 (OH) 1650 cm.$^{-1}$ (C=O) and no benzene absorption (1610—1450, 3500—3000 cm.$^{-1}$).

Oxidation of Phenols to Quinones.—(a) 2,6-*Xylenol*. To 2,6-xylenol (10 g.) and trifluoroacetic acid (10 g.) in methylene chloride (50 ml.) at room temperature were added, all at once, 10 ml. of 85% hydrogen peroxide. The mixture was stirred and within 30 min. the heat of reaction caused the methylene chloride to reflux. During the next 7 hr. the temperature gradually fell and the colour changed through red to black and then orange-yellow. The last stage was completed by refluxing the mixture for 30 min. After neutralisation with aqueous sodium hydrogen carbonate and extraction of the aqueous layer with methylene chloride, the combined methylene chloride fractions were dried ($MgSO_4$) and evaporated, to give almost pure *m*-xyloquinone (8·6 g., 77%), m. p. 69°. Recrystallisation from ethanol or ether gave a specimen with m. p. 71° (mixed m. p. 72° with an authentic specimen [17] of m. p. 74·5°) (lit., 73°).

(b) 3,5-*Xylenol*. The phenol (8·2 g.) gave crude *m*-xyloquinone (5·3 g., 57%) which was purified by elution, with methylene chloride, through alumina to give pure *m*-xyloquinone (5·2 g.), m. p. and mixed m. p. 74°.

(c) p-*Xylenol*. The phenol (8·4 g.) gave crude *p*-xyloquinone (4·8 g., 50%), m. p. 120°. Recrystallised from ethanol it had m. p. and mixed m. p. 124°.

(d) 2,3,5-*Trimethylphenol*. This phenol (10 g.) gave a crude quinone (7 g.) (monosemicarbazone, m. p. 252° and mixed m. p. 252°).

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