

## An Electron Spin Resonance Study of the Autoxidation of Naphthols in the Presence of Hydrogen Peroxide

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A number of radicals have been obtained from polyhydroxylated naphthalenes in alkaline solution by means of autoxidation, and their e.s.r. coupling constants have been measured. A new way of generating radicals derived from naphthalene-1,2-diol is reported in which alkaline hydrogen peroxide is used, and a mechanism for the observed transformation is proposed. Radicals can be obtained from resorcinols in an analogous way.

MANY hydroxylated naphthalene derivatives occur in nature,<sup>1</sup> *e.g.* Vitamins K<sub>1</sub> and K<sub>3</sub>, and their formation and behaviour are of great potential interest. It has already

<sup>1</sup> R. H. Thompson, 'Naturally Occurring Quinones,' Academic Press, London, 1971.

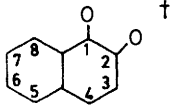
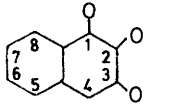
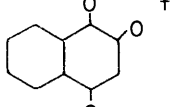
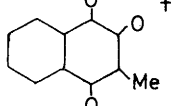
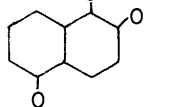
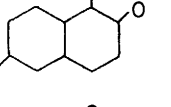
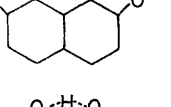
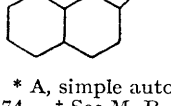
been shown that the characterisation of many such compounds can be facilitated by use of the e.s.r. spectra of the corresponding semiquinones,<sup>2</sup> which are formed

<sup>2</sup> L. H. Piette, M. Okamura, G. P. Rabold, R. T. Ogata, R. E. Moore, and P. J. Scheuer, *J. Phys. Chem.*, 1967, **71**, 29.

from the parent compounds by autoxidation or reduction, whichever is appropriate. We have prepared solutions of a number of radicals derived from hydroxylated naphthalenes by autoxidation, and have shown that their e.s.r. parameters can be used analytically to identify many of the species thus observed. Of particular interest to us were the radicals formed when

same skeleton of carbon and oxygen atoms as the starting material. In the cases of the 1,2- and the 1,4-diol, the primary radicals were observed in weak alkali but in the other cases, *i.e.* the 1,7-, 2,3-, 2,6-, and 1,5-isomers, though it was evident that some autoxidation was taking place, only secondary radicals or unresolvable complex spectra were observed. The

TABLE I

| Radical skeleton  | Method of generation | Position of oxygen in starting material | Coupling constants ( $\mu\text{T}$ ) |       |       |       |       |       |                |
|---|----------------------|---|--------------------------------------|-------|-------|-------|-------|-------|----------------|
|   |                      |   | $a_3$                                | $a_4$ | $a_5$ | $a_6$ | $a_7$ | $a_8$ | $a_{\text{H}}$ |
|    | A<br>B               | 1,2<br>1                                | 42                                   | 446   | 28    | 142   | 14    | 130   |                |
|    | A                    | 2,3                                     |                                      | 39    | 0     | 200   | 39    | 184   |                |
|    | A                    | 1,2<br>1,3<br>1,4<br>1,2,4              | 25                                   |       | 13    | 197   | 11    | 154   |                |
|   | A                    | 1,4<br>1,2,4                            | 38<br>(Me)                           |       | 26    | 208   | 13    | 151   |                |
|  | A<br>B               | 1,2,5<br>1,5<br>1,6                     | 98                                   | 494   |       | 250   | 16    | 235   |                |
|  | A<br>B               | 2,6<br>1,6                              | 58                                   | 502   | 140   |       | 36    | 140   |                |
|  | A<br>B               | 1,2,7<br>1,7<br>2,7                     | 48                                   | 497   | 48    | 243   |       | 102   |                |
|  | B                    | 1,8                                     | 75                                   | 460   | 100   | 150   | 100   |       | 52             |

\* A, simple autoxidation; B,  $\text{H}_2\text{O}_2$  + autoxidation. † See M. Adams, M. S. Blois, and R. H. Sands, *J. Phys. Chem.*, 1958, **28**, 774. ‡ See M. R. Das, H. D. Connor, D. S. Leniart, and J. H. Freed, *J. Amer. Chem. Soc.*, 1970, **92**, 2258.

hydrogen peroxide was present in the alkaline solutions, because the pattern of hydroxylation was then very different from that observed when oxygen groups are added to the naphthalene nucleus by other means (*e.g.* by using Fremy's salt<sup>3</sup>).

*Autoxidation of Naphthalenediols.*—In some cases radicals could be generated in alkaline solution by simply shaking in air, but in others no reaction could be detected either from the appearance of the solutions or by means of e.s.r.

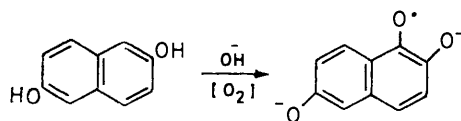
Primary radicals are defined as those containing the

remaining isomeric diols, in which the oxygen atoms were not 'conjugated' with respect to each other, did not apparently undergo autoxidation, except the 1,3-diol which did give a resolvable spectrum of a secondary radical (*i.e.* containing one more oxygen atom than the primary).

The structures of the various radicals observed were deduced mainly on the basis of production of the same species *via* different chemical pathways, *e.g.* from

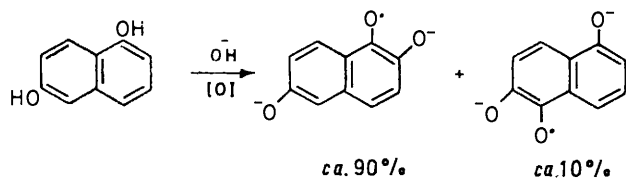
<sup>3</sup> H. Zimmer, D. C. Lankin, and S. W. Horgan, *Chem. Rev.*, 1971, 249.

different starting materials (see Table 1). In cases where this was not possible we rationalised the spectra on the basis of rules and trends inferred from the better established cases, *e.g.* Scheme 1.



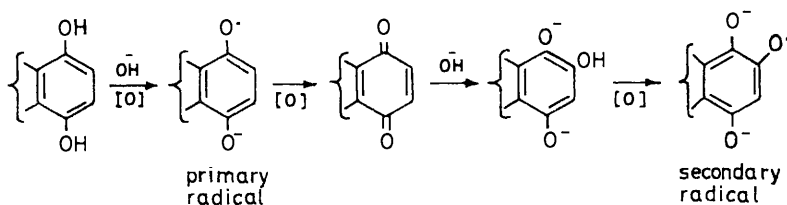
SCHEME 1

*Radicals obtained in the Presence of Hydrogen Peroxide.*—The introduction of hydrogen peroxide into alkaline solutions of hydroquinones or of catechols makes no appreciable difference to the observed e.s.r. spectra of



SCHEME 2

the semiquinones resulting from autoxidation. However, when hydrogen peroxide was introduced into alkaline solutions of naphthalenediols clear spectra were obtained in every case (*e.g.* see Figure) which correspond to oxygen being added to give eventually a 1,2-naphtho-semiquinone derivative (see Table 1). The interesting



SCHEME 3

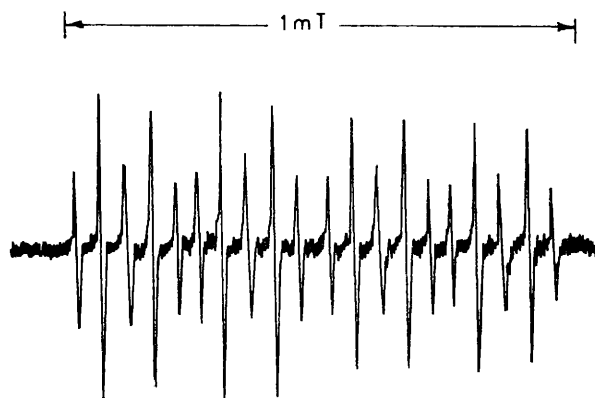
aspects of these results are that (a) the third oxygen atom was never introduced into a 4-position with respect to an  $\alpha$ -oxygen atom, and (b) the spectra indicate that oxidation occurs preferentially at a  $\beta$ -position. This pattern of substitution calls for an explanation since it is not typical of naphthalene chemistry in general, and we shall offer one after discussing the spectra of further radicals produced in the reactions, usually under more strongly alkaline conditions.

*Further Secondary Radicals and Dimers.*—From our previous work on semiquinones<sup>4</sup> we expect secondary radicals to be formed in strong alkali *via* the sequence shown in Scheme 3. This development during the autoxidation applies as much to 1,2- as to 1,4-quinones. However, it seems from our present results that there is an appreciable possibility of dimerisation in the sense of two naphthalene units becoming joined together. Exactly what emerges in the e.s.r. spectrum depends on the balance between this dimerisation<sup>5</sup> and further

<sup>4</sup> P. Ashworth and W. T. Dixon, *J.C.S. Perkin II*, 1972, 1130.

<sup>5</sup> A. I. Scott, *Quart. Rev.*, 1965, 1.

oxidation. The rule which seems to apply is that radicals dimerise through the positions of highest spin

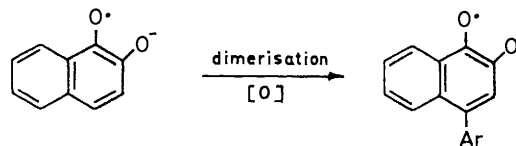


The e.s.r. spectrum of the species obtained from the action of alkaline hydrogen peroxide on naphthalene-2,7-diol

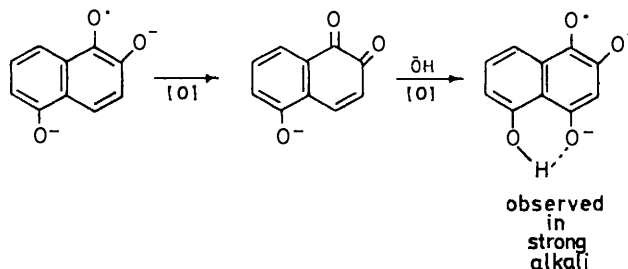
density but the rate of dimerisation depends also on the degree of steric hindrance at that position. For example an intense spectrum of the dimer from naphthalene-1,2-diol (Scheme 4) was observed. In this case there was minimal steric hindrance at the 4-position.

In other cases we can rationalise the results by postulating that steric effects are important in slowing down the dimerisation so that further oxidation of the semiquinone can take place. Thus sometimes steric

effects appear to prohibit dimerisation altogether, *e.g.* with naphthalene-1,2,5-triol only the secondary radical was observed in strong alkali (Scheme 5).



SCHEME 4



SCHEME 5

In 1,4-naphthoquinone derivatives, the primary radicals have no positions of high spin density (*i.e.* all the proton coupling constants are less than *ca.* 0.4 mT) and so no dimerisation occurs.

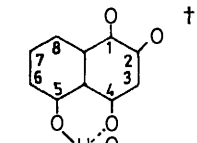
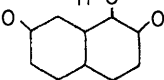
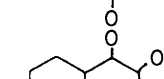
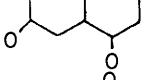
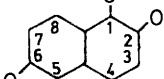
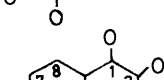
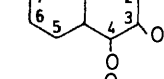
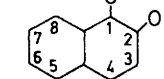
## DISCUSSION

The patterns of the sets of coupling constants were much as expected and it is clear that the overall spin distribution is much more affected by a further oxygen

The ease of formation of secondary radicals is similar to that in the autoxidation of catechol or of hydroquinone. The activating effect of the second ring is however illustrated by the formation of a secondary radical from naphthalene-1,3-diol, whereas its monocyclic analogue, resorcinol, is inert under similar conditions.

The autoxidations in the presence of hydrogen peroxide were the most interesting for us, both from the

TABLE 2

| Radical skeleton  | Method of generation | Position of oxygen in starting material | Coupling constants ( $\mu\text{T}$ ) |       |       |       |       |       |       |
|---|----------------------|---|--------------------------------------|-------|-------|-------|-------|-------|-------|
|   |                      |   | $a_3$                                | $a_4$ | $a_5$ | $a_6$ | $a_7$ | $a_8$ | $a_H$ |
|    | A                    | 1,2,5                                   | 28                                   |       |       | 260   | 10    | 214   | 39    |
|    | A                    | 1,7                                     | 60                                   |       | 10    | 200   |       | 164   |       |
|    | A                    | 1,4,6                                   | 40                                   |       | 40    |       | 84    | 150   |       |
|    | A                    | 1,2,5                                   | 33                                   | 150   |       |       | 33    | 150   |       |
|   | B                    | 2,3                                     |                                      |       | 103   | 73    | 73    | 103   |       |
|  | A                    | 1,2                                     | 30                                   |       | 17    | 120   | 13    | 107   |       |
|  | A                    | 2,6                                     | 70                                   | 520   |       |       | 40    | 150   |       |
|  | B                    | 1,7                                     | 62                                   |       | 20    | 216   |       | 80    |       |

\* A, simple autoxidation; B,  $\text{H}_2\text{O}_2$  + autoxidation. † See ref. 2.

atom attached to the skeleton than by an additional aryl or alkyl group. Thus we were able to characterise the dimers without much difficulty, since their coupling constants are similar to those of the monomeric radicals except that one hydrogen atom is missing. As is the case with monocyclic semiquinones, hydroxy-substituents appear to increase spin density on positions *para* to themselves.<sup>4</sup>

point of view of the mechanism, and because they afforded a way of obtaining a series of 1,2-semiquinones which would otherwise have been difficult to prepare in detectable quantities.

A general observation in these experiments was that, even in the cases when no autoxidation took place in alkaline aqueous solution (as far as one could tell from the absence of colour change or of an e.s.r. signal),

resolved e.s.r. spectra were immediately detectable on addition of hydrogen peroxide. This showed that hydrogen peroxide was active at some early stage in the reactions leading to the observed radicals. A

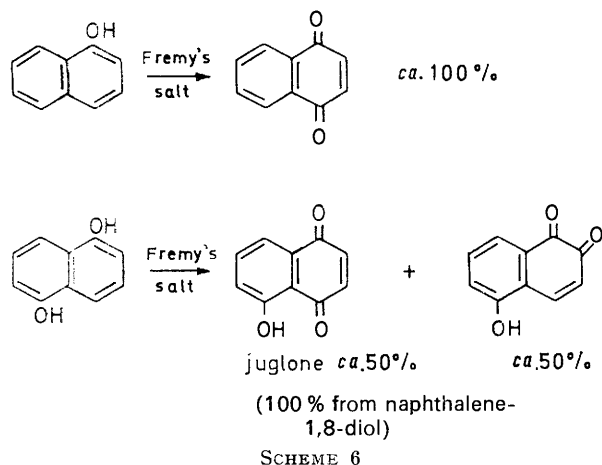
necessary alkaline conditions, we feel that hydrogen peroxide cannot be involved in a free-radical step and therefore propose a simple reaction between hydrogen peroxide, or its anion  $\text{HO}_2^-$ , with the ionised naphthol

TABLE 3

| Radical skeleton | Method of generation * | Position of oxygen in starting material | Coupling constants ( $\mu\text{T}$ ) |       |       |       |       |       |       |
|------------------|------------------------|---|--------------------------------------|-------|-------|-------|-------|-------|-------|
|                  |                        |   | $a_2$                                | $a_3$ | $a_5$ | $a_6$ | $a_7$ | $a_8$ | $a_H$ |
|                  | A †                    | 1,4                                     | 324                                  | 324   | 65    | 58    | 58    | 65    |       |
|                  | A ‡                    | 1,4                                     | 300 (Me)                             | 235   | 62    | 68    | 68    | 76    |       |
|                  | A §                    | 1,4,5                                   | 390                                  | 270   |       | 80    | 30    | 112   | 80    |
|                  | A                      | 1,4,6                                   | 442                                  | 278   | 60    |       | 164   | 0     |       |

\* A, simple autoxidation. † See footnote ‡, Table 1. ‡ Vitamin K<sub>3</sub>. § See ref. 2.

second point is that only 1,2-semiquinones were observed, although under the conditions of our experiments 1,4-semiquinones would be long-lived and would also have been observed had they been formed to any appreciable extent. This pattern of reaction products (or rather intermediates in the overall oxidation) is

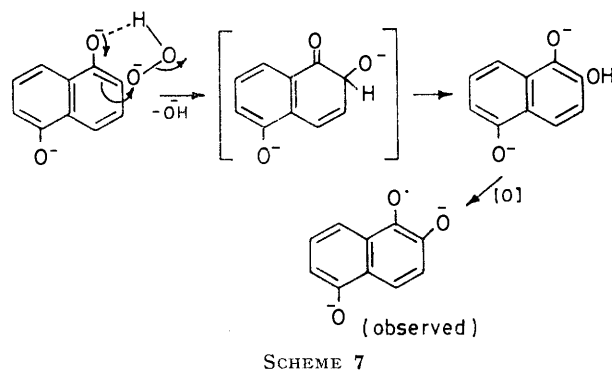


completely different from that observed in the usual radical reactions of naphthols, *e.g.* with Fremy's salt, chromic acid, peracetic acid, *etc.*, in which oxidation occurs preferentially at the 4-position<sup>6</sup> (Scheme 6).

In view of the two foregoing points, together with the

<sup>6</sup> L. F. Fieser and M. Fieser, 'Reagents for Organic Synthesis,' Wiley, New York, 1967, p. 550.

(Scheme 7). The functions of the second ring and a second hydroxy-group seem to be to activate the site of attack. We deduced this point from further experi-

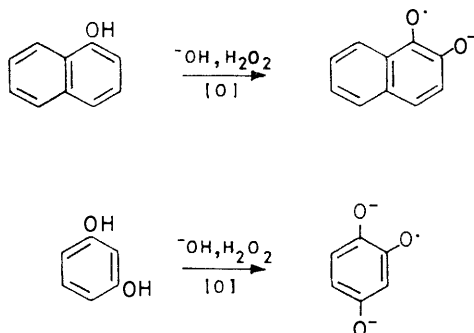


ments, for  $\beta$ -naphthol and various phenols did not react whereas resorcinols and  $\alpha$ -naphthol, though they were not autoxidised in alkali, after addition of hydrogen peroxide gave the corresponding semiquinones (Scheme 8).

If the mechanism is correct then the lack of attack on the 4-position can be attributed partly to the fixation of the double bonds in the naphthalene skeleton, for the 1,2- and 3,4-bonds are similar in length to the C=C bond in ethylene.<sup>7</sup> The resulting bond alternation

<sup>7</sup> *E.g.* see *Chem. Soc. Special Publ.* No. 18, 'Interatomic Distances,' 1958.

could damp out mesomeric effects markedly in comparison with the situation in benzenoid compounds in which the C-C bonds do not usually vary much in length. Another factor favouring *ortho* attack is the



SCHEME 8

possibility of hydrogen bonding between the hydroperoxy-group and the neighbouring oxygen atoms.

If we regard the 1,2-linkage as a double bond, the addition of  $\text{H}_2\text{O}_2$  or  $^-\text{O}_2\text{H}$  is similar to an analogous step in the oxidation of purpurogalloquinone by hydrogen peroxide,<sup>8</sup> which involves attack by  $\text{H}_2\text{O}_2$  on a quinonoid structure; it also resembles the attack on a tertiary carbon atom by peroxide in the oxidation of phthaleins.<sup>9</sup>

The main difference here is that the reaction involves the 'reduced' form of the naphthols and not the quinones.

An alternative mechanism involving catalysis by transition metal ions seems unlikely since it does not explain why even activated phenols did not react nor why the presence of an excess of ethylenediamine tetraacetate in the solutions made no observable difference to the intensities of the spectra obtained with alkaline hydrogen peroxide solutions.

#### EXPERIMENTAL

Autoxidations were normally carried out in 50% aqueous methanol containing sodium hydroxide (2% w/v), but for the observation of secondary radicals at least 10% sodium hydroxide was required.

Quinones were reduced in 90% dimethylformamide with alkaline dithionite.

In the hydrogen peroxide experiments the solutions contained aqueous 2% alkali and 5% hydrogen peroxide.

The solutions studied were about  $10^{-3}\text{M}$  with respect to the naphthalene derivatives.

[3/2305 Received, 9th November, 1973]

<sup>8</sup> P. D. Collier, *J. Chem. Soc. (B)*, 1968, 1494.

<sup>9</sup> E. McKeown and W. A. Waters, *J. Chem. Soc. (B)*, 1966, 6679.