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ORGANIC CHEMISTRY OF SUPEROXIDE. I.
OXIDATIONS OF AROMATIC COMPOUNDS.

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Potassium superoxide is a selective oxidant for aromatic compounds with the order of susceptibility of substituent groups being $-SH > -NH_2 > -OH$. Only *o*- and *p*- disubstituted amines and phenols are oxidized but monosubstituted thiols react.

Following the recent discovery of the important enzyme Superoxide Dismutase[1] considerable attention has been paid to the organic chemistry of the superoxide radical-ion[2] to evaluate its role in biological systems. In this context its reaction with catechol derivatives[3] is particularly interesting since the products obtained are similar to those formed in biological oxidation by mono-oxygenase enzymes. Preliminary results are now presented for the action of superoxide on related disubstituted aromatics and also for some monosubstituted aromatics.

o-Phenylenediamine (1 g) in dry toluene (100 ml) was stirred under N_2 at 25° with excess KO_2 (2 g) for 48 hrs. Residual KO_2 was destroyed by cautious addition of water, and the toluene extract, after concentration, was chromatographed in a short column of t.l.c. grade silica gel. The only significant product formed was a red crystalline compound, m.p. 135°, identified as 2,2'-diaminoazobenzene.

The other compounds listed in Table 1, when similarly treated with KO_2 gave the products indicated.

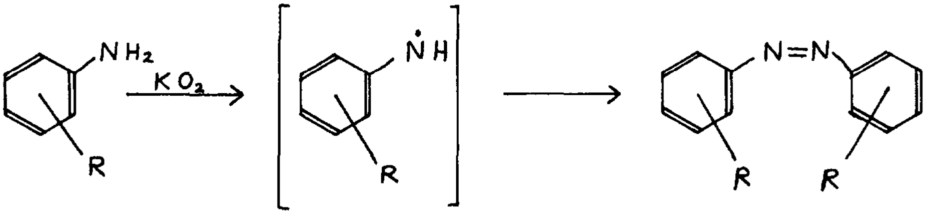
Table 1

Reactant	Product[†]	m.p.	Crude Yield (%)
o-Phenylenediamine	2,2'-Diaminoazobenzene	135°	70
p-Phenylenediamine	4,4'-Diaminoazobenzene	252°	40
m-Phenylenediamine	No reaction	-	-
o-Aminophenol	2,2'-Dihydroxyazobenzene	174°	70
p-Aminophenol	4,4'-Dihydroxyazobenzene	218°	35
m-Aminophenol	No reaction	-	-
o-Aminothiophenol	2,2'-Diaminodiphenyldisulphide	93°	85
Thiophenol	Diphenyldisulphide	60°	80
Toluene-3,4-dithiol	Dimethyldibenzo-(1,2,5,6)-tetrathiocin	192-195°	60
Phenol	No reaction	-	-
Aniline	No reaction	-	-
o-Methoxyaniline	No reaction	-	-

[†] All compounds had satisfactory elemental analysis; i.r., mass and n.m.r. spectra were fully in accord with structures presented.

The reactions of *o*- and *p*-phenylenediamines with superoxide are different from the reactions reported for the analogous compounds catechol[3] and hydroquinone[4], which give ring cleavage products and *p*-benzoquinone respectively. The latter reactions have been interpreted in terms of an initial hydrogen abstraction by $O_2^{\cdot -}$ from the reactants. Although direct evidence is lacking a similar process is suggested in the present case, where it is envisaged that $O_2^{\cdot -}$ abstracts a hydrogen atom from the amino group. Subsequent reactions, at present unknown, then take place to yield the observed products.

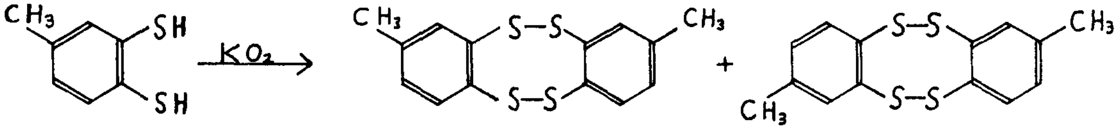
This process is repeated for *o*- and *p*-aminophenol, where formation of azo derivatives indicates preferential reaction of the amino group. It is significant that conjugated disubstitution is required for oxidation, since aniline, phenol, *m*-phenylenediamine and *m*-aminophenol failed to react with the reagent.



R = $-NH_2$ or $-OH$ in
o- or *p*- position

Introduction of a thiol group directs the reaction to another path as seen by formation of the disulphide from *o*-aminothiophenol. Thus the susceptibility to attack by $O_2^{\cdot -}$ appears to be in the order $-SH > -NH_2 > -OH$ in aromatic molecules, and thiophenol was the only monosubstituted aromatic compound to react. Clearly $O_2^{\cdot -}$ is a relatively weak but rather selective reagent and this point may have considerable significance in biological systems.

Oxidation of toluene-3,4-dithiol with $O_2^{\cdot -}$ was notable as it provided a good yield of the novel dibenzo-(1,2,5,6)-tetrathiocin. High resolution mass spectrum, m/e - 307.985, $C_{14}H_{12}S_4$ requires m/e - 307.982. The i.r. spectrum indicated absence of SH while the n.m.r. spectrum had two signals for $-CH_3$ suggesting a mixture of isomers.



Further studies are under way to investigate the mechanisms of these reactions and to explore the selectivity of $O_2^{\cdot -}$ towards other organic compounds.

References

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