

ORGANIC CHEMISTRY OF SUPEROXIDE. II
OXIDATION OF β -NAPHTHYLAMINE - POSSIBLE INVOLVEMENT OF THE HYDROXYL RADICAL

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ABSTRACT Of a selection of aromatic monoamines examined only β -naphthylamine was oxidized by potassium superoxide and formed dibenzo[a,h]phenazine, dibenzo[a,i]phenazine and 1-hydroxy-2,2'-azonaphthalene, the latter product indicating that the hydroxyl radical may be involved in superoxide oxidations.

The ubiquity of Superoxide Dismutase in aerobic organisms is widely considered to indicate a cytotoxic role for the superoxide species $[O_2^{\cdot-}]^1$. However a satisfactory chemical explanation for the toxicity of $O_2^{\cdot-}$ is not presently available in spite of much research on the topic. Chemical investigations have, in fact, shown that $O_2^{\cdot-}$ is a rather mild and selective species² although it does show a preference for oxidizing thiol groups³. One attractive hypothesis to account for its alleged toxicity is the possibility that it can act as a source of hydroxyl radicals $[HO^{\cdot}]^4$, which are powerful and indiscriminate oxidants.

In view of the importance of this matter considerable efforts have been made to observe hydroxylation promoted by $O_2^{\cdot-}$ using both enzymic and chemical systems⁴. The latter have been mainly unsuccessful, for example no evidence of hydroxylation was observed for aromatic compounds⁵.

Following our work on the diamines³ we have examined the action of $O_2^{\cdot-}$ on aromatic monoamines. Of a range of amines chosen (aniline, *o*-methoxyaniline, *o*-chloroaniline, *o*-nitroaniline, α -naphthylamine and β -naphthylamine) only β -naphthylamine was oxidized using the following procedure.

β -Naphthylamine (I) (860 mg - 6 m moles) in purified dry toluene (200 ml) containing potassium superoxide (1.8 g - 24 m moles) was heated at 80° with vigorous stirring for 8 hrs, under nitrogen. Tlc analysis indicated the formation of three products with no starting material remaining. The reaction mixture was cooled, quenched with water and the solvent layer was collected, washed with water, dried, and concentrated to a syrup which crystallized on standing.

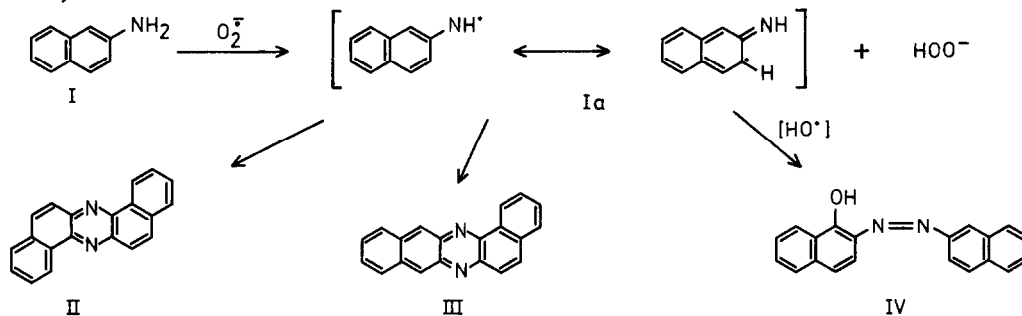
Orange crystals (210 mg - 25% yield) were collected, mp 286-88° and the compound was identified as dibenzo[a,h]phenazine (II) (lit mp 284°)⁶. Found C, 85.4; H, 4.4; N, 10.1%. Calc. for $C_{20}H_{12}N_2$, C, 85.7; H, 4.3; N, 10.0%. Nmr, ms and ir data supported the structure.

The residual material was separated by preparative layer chromatography into two bands using ethyl acetate/petrol (1:1) as developing solvent. The lower band, on extraction yielded a yellow crystalline compound (110 mg - 13% yield), mp 245-6°, which was identified as dibenzo[a,i]phenazine (III), (lit mp 247°)⁷. High resolution ms gave m/e 280.0981 (M^+), $C_{20}H_{12}N_2$ has m/e = 280.1000 (M^+). Nmr and ir spectra supported this assignment.

Extraction of the upper band yielded a red crystalline compound (240 mg - 30% yield)

mp 166-7^o, identified as 1-hydroxy-2,2'-azonaphthalene (IV) (lit mp 168^o). Found C, 80.4; H, 4.9; N, 9.4%. Calc. for C₂₀H₁₄N₂O, C, 80.5; H, 4.7; N, 9.4%. Ms, nmr and ir data supported the assignment.

It is proposed that the formation of II, III and IV involves the initial abstraction of hydrogen from I by O₂^{•-} to give an intermediate radical Ia which couples with a carbon centered radical to give II and III, and with another nitrogen centered radical to give, after further reactions, IV.



The formation of IV, presumably derived from 2,2'-azonaphthalene, is strongly suggestive of the participation of HO• in O₂^{•-} oxidations. It is not clear how HO• arises in the system, however if a concerted two hydrogen atom abstraction occurs, as has been claimed elsewhere⁹, then HO• could be produced [AH₂ + O₂^{•-} → HO⁻ + HO• + A].

It is noteworthy that when α-naphthylamine is treated similarly no trace of reaction is observed, thus O₂^{•-} illustrates the great difference in chemical reactivity of the naphthylamines. It shows that the β-isomer is much more susceptible to hydrogen abstraction and radical initiated processes. This difference may be significant in respect of the variations in carcinogenic activity of the compounds.

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