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THE OXIDATION OF AMINES WITH SULFONYL PEROXIDES, II; ARYL REARRANGEMENT TO NITROGEN PROMOTED BY p-NITROBENZENESULFONYL PEROXIDE[1]

Robert V. Hoffman,* Reuben Cadena,[2] and David J. Poelker
Department of Chemistry
New Mexico State University
Las Cruces, New Mexico 88003

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Amine oxidations exhibit a great diversity of mechanisms which depends on the oxidant, the amine type, the pH, and/or metal additives.[3] Reaction with oxidants can occur at the nitrogen lone pair by one electron or two electron oxidation or reaction can occur at the α-carbon atom by hydrogen abstraction. A given oxidant may follow different pathways with different amines or competing pathways with the same amine. The oxidative deamination of amines by arysulfonyl peroxides, 2, has been reported to be an efficient means of degradation.[1] The relative insensitivity to amine structure exhibited by this oxidation for primary and secondary amines suggested that an invariant mechanism is operative. Furthermore, a two-step, two-electron mechanism (Eq. 1) was favored over a one-electron transfer mechanism due to the electrophilic nature of

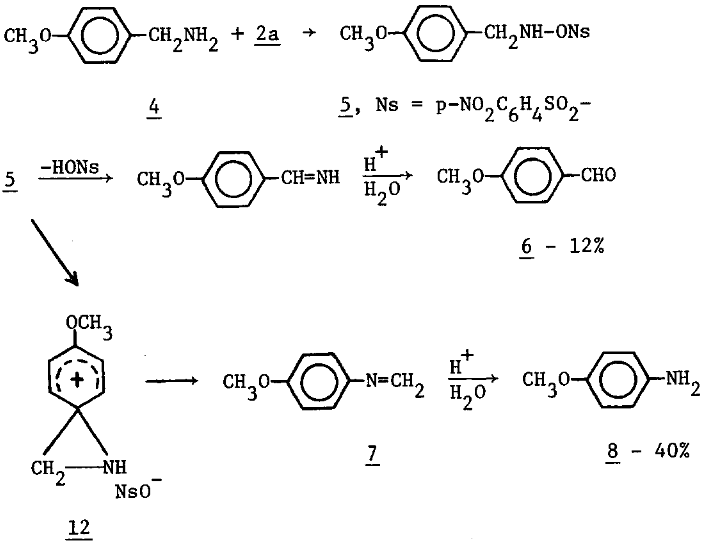
$$\underset{\underline{1}}{RCH_2NHR'} + \underset{\underline{2}}{(ArSO_2O)_2} \rightarrow \underset{\underline{3}}{RCH_2N(R')OSO_2Ar} \rightarrow RCH{=}NR' + ArSO_3H \qquad \underline{\text{Eq. 1}}$$

R = alkyl, aryl
R' = H, alkyl

2a. $Ar = p\text{-}NO_2C_6H_4$
2b. $Ar = m\text{-}CF_3C_6H_4$

sulfonyl peroxides[4] and the good leaving ability of the arylsulfonate group which would foster polar elimination in the intermediate hydroxylamine-O-sulfonate adducts, 3.[5,6]

Evidence which implicates the formation and polar decomposition of hydroxylamine-O-arylsulfonates, 3, in the reaction of amines with arylsulfonyl peroxides is herein reported. A solution of p-methoxybenzylamine, 4 (6 mmol), in ethyl acetate (30 ml) was treated with 2a (1.5 mmol) at -78°C for two hours. The solvent was removed under vacuum and the residue was hydrolyzed with aqueous acid (2.5 M HCl, 50 ml) and steam distilled. The normal oxidative deamination product, p-methoxybenzaldehyde, 6, was produced in reduced yield (12%). Examination of the base fraction of the reaction revealed the presence of p-methoxyaniline, 8, (40%). This product likely arizes by a migration of the p-anisyl group from carbon to nitrogen to yield azomethine, 7, and thus, 8, after hydrolysis (Eq. 2). In contrast the oxidation of p-methylbenzylamine, 9, yielded only a trace (< 1%) of rearrangement product 11, but mainly p-methylbenzaldehyde 10 (70%). The amount of rearrangement in these two oxidations reflects a significant difference in migratory aptitude between p-anisyl and p-tolyl groups in this oxidation.[7] These results are consistent with aryl rearrangement to electron deficient nitrogen which results from ionization of the p-nitrobenzenesulfonate group from 5 as shown in 12. Aryl rearrangement to a nitrogen



4

5, Ns = $p\text{-}NO_2C_6H_4SO_2\text{-}$

6 - 12%

7

8 - 40%

12

Eq. 2

$$p\text{-}CH_3C_6H_4CH_2NH_2 + \underline{2a} \xrightarrow[\text{hydrolysis}]{\text{after}} p\text{-}CH_3C_6H_4CHO + p\text{-}CH_3C_6H_4NH_2$$

Eq. 3

9 10 - 70% 11 - < 1%

centered free radical would yield small migratory aptitudes[9] and is thus unlikely. Aryl migration to a nitrogen cation radical, produced by electron transfer from the amine to the peroxide (Eq. 4), might be expected to show an amplification of migratory aptitudes due to the cationic nature of 15 and 16 which can contribute to the transition state for rearrangement. Electrochemical studies of the oxidation of benzylamines has shown that no resonance interaction occurs

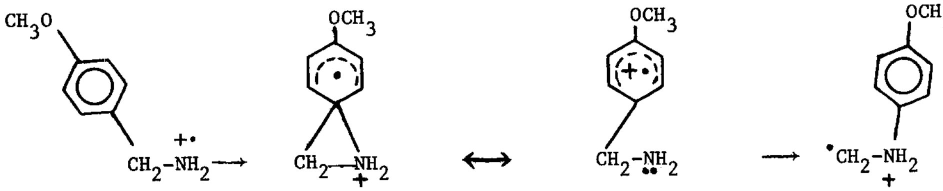
$$p\text{-}CH_3OC_6H_5CH_2NH_2 + \underline{2a} \xrightarrow[\text{transfer}]{e^-} p\text{-}CH_3OC_6H_4CH_2\overset{+\bullet}{N}H_2 + NsO^- + NsO^\bullet$$

13

$$\underline{13} \xrightarrow[\text{fast}]{-H^+} p\text{-}CH_3OC_6H_4\dot{C}H\text{-}\overset{\bullet\bullet}{N}H_2 \xrightarrow{ox} \text{products}$$

Eq. 4

14



13 15 16 13a

during the formation of the nitrogen cation radical, 13, therefore migration via 15 would have to occur after the initial electron transfer.[10a] Furthermore the formation of the cation radical is normally followed by very rapid proton loss to give a neutral radical, 14.[10] Neither 13 nor the rearranged ion radical 13a is resonance stabilized whereas proton loss gives a neutral,stabilized radical product, 14. It is therefore reasonable to assume that proton loss is favored by product stability and that aryl rearrangement in the radical cation is of lesser importance.

When tritylamine, 17, was reacted with 2a, benzophenone anil, 19, was isolated and hydrolysis of the mixture yielded benzophenone (60%) (Eq. 5). The observed aryl rearrangement is consistent with the formation of tritylhydroxylamine-O-p-nitrobenzenesulfonate, 18, and subsequent Stieglitz rearrangement.[9] That 18 is an intermediate in the conversion of 17 to 19 is

$$\underset{\underline{17}}{(C_6H_5)_3CNH_2} + \underline{2a} \rightarrow \underset{\underline{18}}{(C_6H_5)_3CNHONs} \rightarrow \underset{\underline{19}}{(C_6H_5)_2C{=}NC_6H_5} \xrightarrow[H_2O]{H^+} (C_6H_5)_2CO \qquad \underline{\text{Eq. 5}}$$

consistent with the results obtained when tritylhydroxylamine, 20, was treated with p-nitrobenzenesulfonylchloride, 21, (Eq. 6).

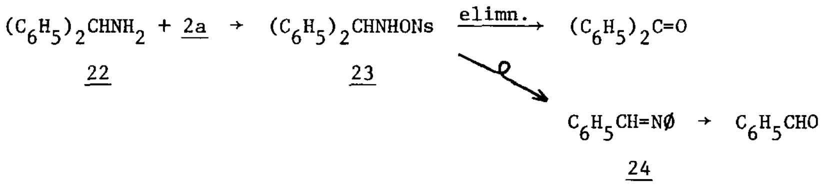
$$\underset{\underline{20}}{(C_6H_5)_3CNOH} + \underset{\underline{21}}{NsCl} \xrightarrow[Et_3N,\ 0°]{ether} \underline{18} \rightarrow \underline{19} \xrightarrow[H_2O]{H^+} (C_6H_5)_2CO \qquad \underline{\text{Eq. 6}}$$

Thus 18 is produced by the condensation of 20 and 21 and undergoes rearrangement to 19 (50%), analogous to the chemistry observed for the conversion of 17 to 19 by 2a. Of further interest is that 18 is not susceptible to homolytic N-O bond cleavage. No tritylamine, 17, is produced from 18 when it is generated from 20 and 21 (Eq. 7). Since nitrogen centered radicals are good abstracting species,[11] N-O homolysis would be predicted to yield some 17. The absence

$$\underline{18} \rightarrow (C_6H_5)_3C\dot{N}H \xrightarrow{RH} \underset{\underline{17}}{(C_6H_5)_3CNH_2} \qquad \underline{\text{Eq. 7}}$$

of 17 in the product mixture discounts N-O bond homolysis and is further indication that hydroxylamine-O-arylsulfonates decompose to products by polar mechanisms.

The oxidation of benzhydrylamine (22) with 2a yielded a mixture (82%) of benzophenone (43%) and benzaldehyde (57%) (Eq. 8). In this substrate, intermediate 23 undergoes competetive



$$\begin{array}{llll} \underset{\underline{22}}{(C_6H_5)_2CHNH_2} + \underline{2a} \rightarrow \underset{\underline{23}}{(C_6H_5)_2CHNHONs} & \xrightarrow{elimn.} & (C_6H_5)_2C{=}O & \qquad \underline{\text{Eq. 8}} \\ & \searrow^{\phi} & & \\ & & \underset{\underline{24}}{C_6H_5CH{=}N\phi} \rightarrow C_6H_5CHO & \end{array}$$

elimination and rearrangement, the latter predominating. The formation of conjugated anil 24 is apparently the driving force for rearrangement to overcome normally facile elimination, and suggests that product character is significantly manifested in the transition state. This is in accord with kinetic studies currently in progress which also indicate a late transition state for polar hydroxylamine-O-sulfonate decomposition.

From the studies described, the oxidation of amines by sulfonyl peroxides likely involves the formation of hydroxylamine-O-sulfonates 3 which undergo polar decomposition accompanied by aryl migration to electron deficient nitrogen when a) a very good migrating groups are present, 4; b) where elimination is impossible due to the lack of α-protons, 17; c) where product stability favors rearrangement, 22.

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