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A RATIONALIZATION OF NITROSOARENE-OLEFIN REACTIONS

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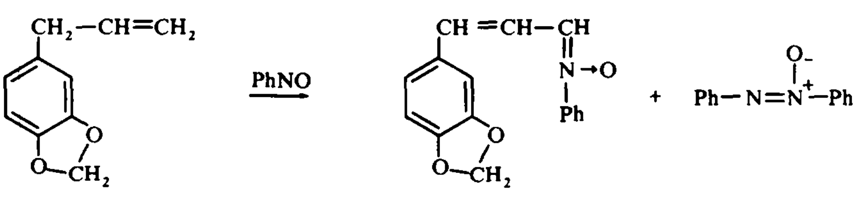
Abstract—Previously described reaction products of nitrosoarenes with olefins can be rationalized on the basis of two types of interaction dependent on whether the olefin contains an allylic H atom or not. In the former case, a reactive N-alkenyl-N-arylhydroxylamine is formed *via* an 'ene' addition reaction. This hydroxylamine may either: (i) attack the nitrosoarene to form an azoxyarene and a nitrone; (ii) decompose thermally to an N-alkenylaniline and a nitrone; (iii) undergo dehydration to an anil. The balance between these competing reactions and hence the ultimate reaction products is shown to be dependent on the nature of the substituent on the nitrosoarene.

The available literature on the reaction of nitrosoarenes with mono-olefins is conflicting and although several review articles[1,2] have appeared on the chemistry of nitroso compounds only passing mention has been made of these reactions. The reason, no doubt, lies in the fact that no systematic studies have been undertaken in this field of organic nitrogen chemistry.

The first account of the nitrosoarene-olefin reaction was given by Alessandri *et al.*[3–5] who reported the reaction of nitrosobenzene with safrole and showed the major products were the unsaturated nitrone (I) and azoxybenzene.

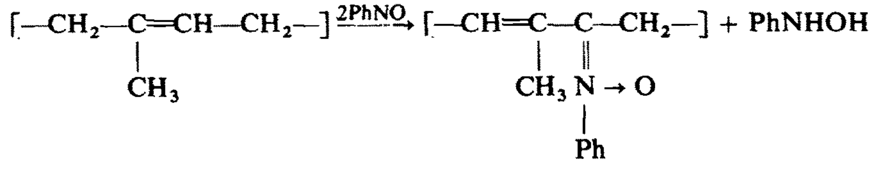


I

Alessandri reports similar reactions between nitrosobenzene and estragole, myristicin and methyleugenol, but with isosafrole, the nitrone product obtained involved cleavage of the olefinic double bond.

Experiments on the addition of nitrosobenzene to natural rubber (*cis*-1,4-polyisoprene) were also reported, but a more complete account of this was given by Bruni and Gieger[6] and Pummerer and Gündel.[7] These authors treated a homogeneous solution of rubber in benzene with a three-fold (molar) excess of nitrosobenzene and isolated azoxybenzene and a compound termed iso-rubber nitrone (II), a conjugated nitrone analogous in structure with that obtained by Alessandri from safrole.

Bruni and Geiger put forward the following equations for the reaction.



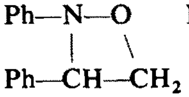
$$[\text{—}CH_2\text{—}\underset{\displaystyle CH_3}{\underset{|}{C}}\text{=}CH\text{—}CH_2\text{—}] \xrightarrow{2PhNO} [\text{—}CH\text{=}\underset{\displaystyle CH_3}{\underset{|}{C}}\text{—}\underset{\underset{\displaystyle Ph}{\underset{|}{N \rightarrow O}}}{\underset{\|}{C}}\text{—}CH_2\text{—}] + PhNHOH$$

II

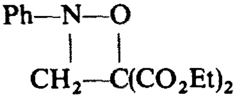
$$PhNHOH + PhNO \rightarrow Ph\overset{+}{N}(\overset{-}{O})NPh + H_2O$$

They suggested the intermediate primary hydroxylamine on the basis of azoxybenzene as a reaction product. Similar reactions were reported for *o*-, *m*- and *p*-nitrosotoluenes, *o*-nitrosophenol, and *o*-nitrosoanisole. *p*-Nitrosophenol and *p*-nitrosoanilines were reported to react readily with rubber but no account of the products was given.

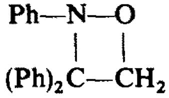
The reactions of nitrosobenzene with styrene, diethylmethylene malonate and 1,1-diphenylethylene were studied by Ingold and Weaver,[8] who claimed to have isolated the oxazetidine compounds III to V.



III



IV

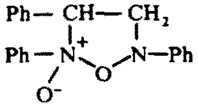


V

These structural assignments were criticized by Lapworth,[9] and more recent work[10] substantiates Lapworth's criticism.

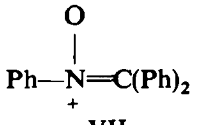
No further reports in this field were published until the early 1960's, when Hamer and Macaluso[11] reported the reactions of *p*-nitronitrosobenzene, or *p*-bromonitrosobenzene with cyclopentene, cyclohexene, isobutene, butene-1, butene-2, triphenylethylene and stilbene: the only products they were able to isolate were the *p*-substituted azoxybenzenes. The reactions proceeded equally well in ethanol, chloroform, carbon tetrachloride or the alkene as solvent. The 'lost' oxygen could not be accounted for by the oxidation of either the solvent or the nitrosobenzenes.

Griffin and Hepfinger[12] reinvestigated the work of Ingold. They found that the reaction of nitrosobenzene with styrene proceeded *via* an unstable adduct (VI) produced by the addition of two molecules of nitrosobenzene to one molecule of styrene.



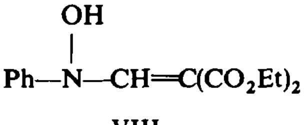
VI

This adduct subsequently broke down resulting in the overall cleavage of the olefinic double bond to yield α,N-diphenylnitrone: a similar reaction to that observed by Alessandri for isosafrole. The reaction of nitrosobenzene with 1,1-diphenylethylene and diethylmethylene malonate[10] was shown not to give the oxazetidine ring system as postulated by Ingold, but rather the nitrone (VII) and hydroxylamine (VIII) respectively, products suggested by Lapworth.



$$\mathrm{Ph{-}\underset{+}{\overset{\overset{\displaystyle O}{|}}{N}}{=}C(Ph)_2}$$

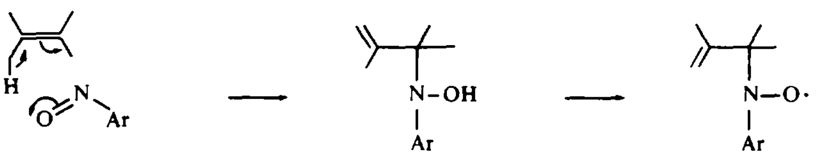
VII



$$\mathrm{Ph{-}\overset{\overset{\displaystyle OH}{|}}{N}{-}CH{=}C(CO_2Et)_2}$$

VIII

The reaction of various substituted nitrosobenzenes with 2-methylpentene-2 and 2,3-dimethylbutene-2 was the subject of a paper by Sullivan[13] who suggested that the nitroso group underwent an 'ene' addition to the olefin to yield in the latter case the unsaturated hydroxylamine intermediate (IX). He further suggested that this intermediate hydroxylamine could then be oxidised by air or unreacted nitroso compound to the alkenyl aryl nitroxide (X) which was detected by ESR spectroscopy.

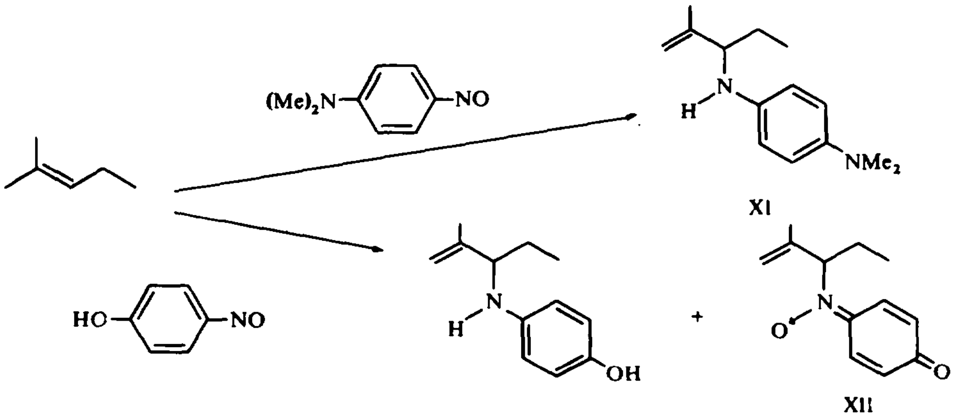


IX X

Evidence in favour of the proposed reaction was obtained by reduction of the total reaction product, from which N-(1,1,2-trimethyl-2-propenyl) aniline was obtained, but work-up of the reaction product before reduction resulted in azoxybenzene as the only identifiable product.

An alternative interpretation of Sullivan's ESR data has been given by Russell[14] but this need not invalidate the proposed 'ene' mechanism. Indeed, the latter is supported by the work of Cain *et al.*[15, 16] who investigated the reaction of *p*-nitrosoanilines with simple mono-olefins and found the major products to be N-alkenyl-*p*-phenylenediamines (XI).

A similar reaction for *p*-nitrosophenol has been studied by Pepper,[17] who was also able to isolate and identify an N-alkenyl *p*-benzoquinoneimine-N-oxide (XII), which is tautomeric with an unsaturated nitrone.

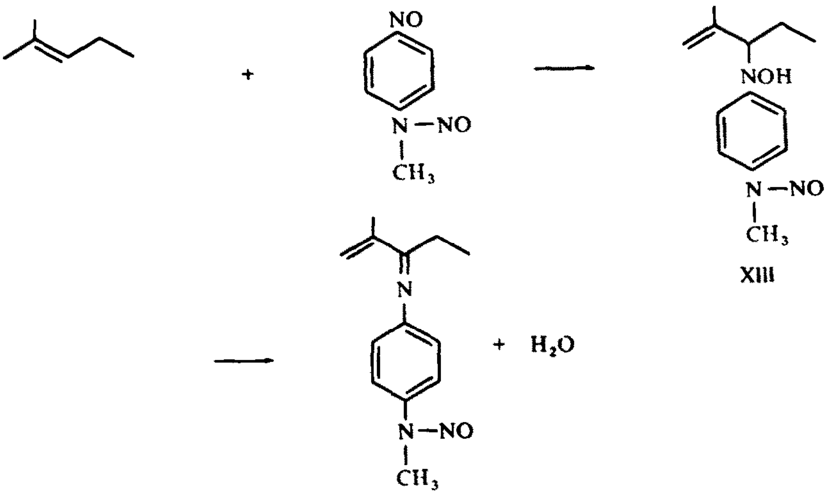


XI

XII

The 'ene' nature of these reactions has been confirmed by Knight. By careful work-up under favourable conditions, N-alkenyl-N-phenylhydroxylamines can be isolated from the reaction of nitrosobenzenes with allylic olefins.[18] Under less favourable conditions where the hydroxylamine cannot be isolated, the kinetic parameters, substantial effects and absence of substantial solvent effects, point strongly to an 'ene' addition. Further confirmation of the 'ene' reaction is found by examining the effect of olefin structure on rate and the correspondence between olefin structure and the alkenyl groups developed in the products.[19, 20] A recent publication by Haszeldine *et al.*[21] describes the isolation of an N-alkenyl-N-aryl hydroxylamine from the reaction of pentafluoronitrosobenzene and various allylic olefins formed via an 'ene' addition.

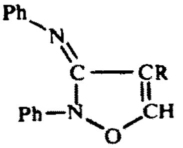
The reaction of N, 4-dinitroso-N-methylaniline with 1-methylcyclohexene, 2-methylpentene-2, and squalene has been investigated by Zherebkova *et al.*[22] The postulate that the reaction proceeds via the C-nitroso moiety which undergoes an 'ene' reaction to give an intermediate unsaturated hydroxylamine (XIII). They suggest that the secondary hydroxylamine dehydrates to give an unsaturated anil product (XIV).



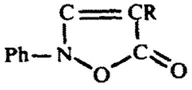
XIII

XIV

The addition of nitrosobenzene to α-methylstyrene and methyl methacrylate has been studied by Hepfinger and Kolak.[23] The products of the reactions were shown to be 4-substituted 3-phenylimino-4-isoxazolines (XV) and 4-substituted-2-phenyl-3-isoxazolin-5-ones (XVI).



XV



XVI

R = Ph or CO.O CH_3

The formation of these products is consistent with a pathway involving oxidation and rearrangement of an initially formed β,γ,-unsaturated hydroxylamine followed by further reaction of nitrosobenzene with the cyclized product.

From this review of the literature it is apparent that no single coherent scheme appears to cover all the known facts, or will account for products as diverse as anils, amines, nitrones and azoxyarenes often variously reported as the major products. One feature does, however, emerge: that any rationalization of the reactions of nitrosoarenes with alkenes must recognize the occurrence of two distinct types of initial interaction between the nitroso compound and olefin, dependent on the olefin structure.

In the case of olefins not possessing α-methylenic H atoms an unstable adduct is formed as reported by Griffin and Hepfinger for the reaction of nitrosobenzene with styrene,[12] this type of reaction is well covered in that paper and will not be considered further. In the case of simple olefins containing α-methylenic H atoms, the initial stage appears to be an 'ene' addition with rearrangement of the double bond to give an alkenyl hydroxylamine. Therefore, in these cases, in order to understand the nature of the final reaction products one must consider the chemistry of these initially formed secondary hydroxylamines. Since there are no descriptions of the chemistry of alkenyl aryl hydroxylamines, the subsequent course of the reactions must be inferred from the chemistry of alkyl aryl hydroxylamines. The latter have themselves received only meagre study and relevant information is available only on their decomposition and oxidation.

The thermal decomposition of various N-*p*-phenyl-substituted N-benzylhydroxylamines have been recently studied[19, 20] and the stoichiometry of the equation given by earlier workers confirmed.[24, 25]

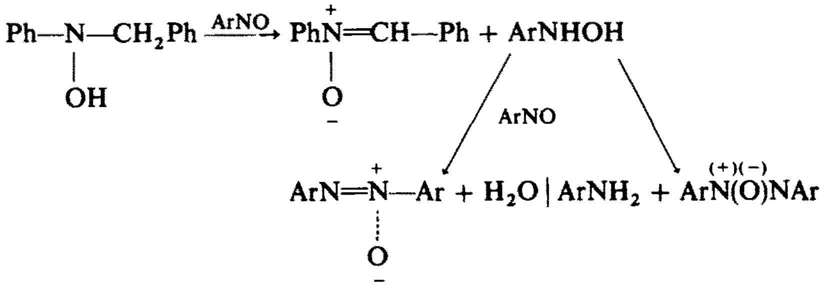
$$2\,\mathrm{ArN(OH)CH_2R} \rightarrow \mathrm{ArNHCH_2R} + \mathrm{Ar}\overset{+}{\mathrm{N}}(\overset{(-)}{\mathrm{O}})\mathrm{:CH{-}R} + \mathrm{H_2O}$$

The rate of decomposition was shown to be second order in hydroxylamine and to be markedly affected by the nature of the substituent, *p*-electron-releasing substituents increasing the rate of decomposition, (a Hammett σ *vs* log k_2 correlation being linear with a slope of $-2{\cdot}8$). The thermal decomposition of *p*-substituted-N-phenylhydroxylamines has also been studied[19, 20] and shown to give as products anilines and azoxyarenes with a similar rate correlation to that found with the disubstituted hydroxylamines.

Some dehydration has been observed in the decomposition of the disubstituted hydroxylamine and indeed dehydration, together with oxidation by excess nitroso compound has been postulated as the fate of the intermediate hydroxylamine produced in the base-catalysed reaction of nitrosobenzenes with active methylene compounds.[26]

Knight and Loadman[27] have recently made a thorough study of the oxidation of N-benzyl-N-phenylhydroxylamine by various *p*-substituted nitrosobenzenes and have shown that α,N-diphenylnitrone and *p*-substituted azoxybenzenes are formed in a quantitative, second order reaction (a).

In cases where the nitrosobenzene had strongly electron-donating substituents the yield of azoxy compound was not quantitative, but the primary amine derivatives could be readily observed in the reaction mixtures. An outstanding feature of this reaction is its high sensitivity to the nature of the *p*-substituent of the nitrosobenzene and a ρ value of $+4{\cdot}3$ was obtained from a Hammet σ *vs* log k_2 plot.

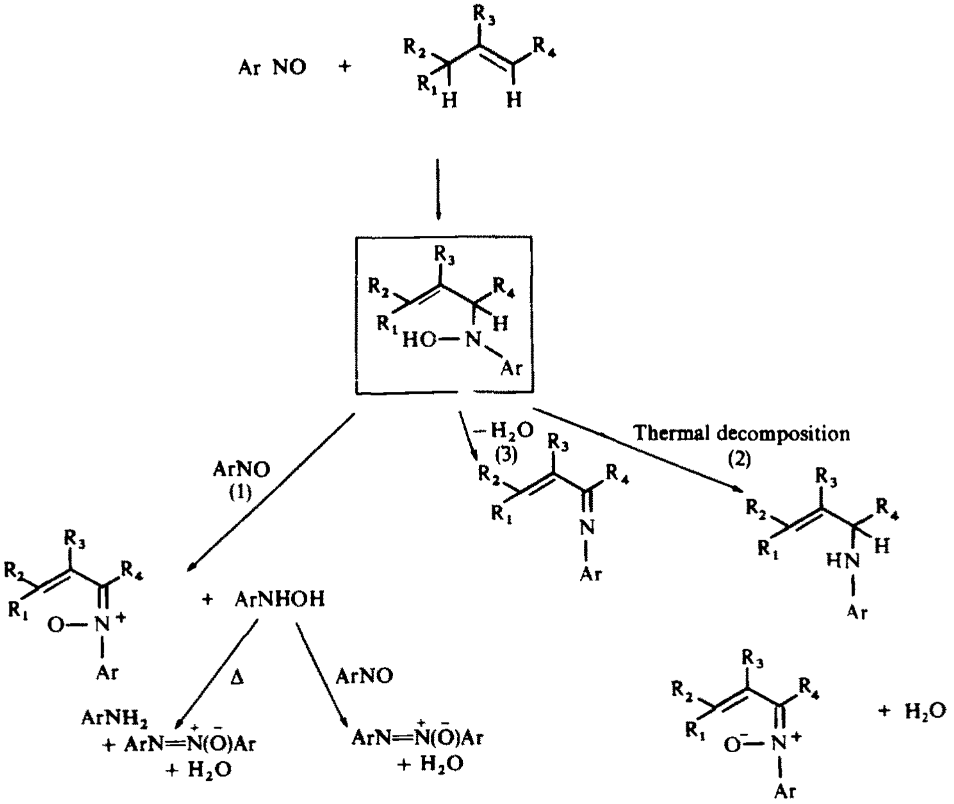


$$\underset{\mathrm{OH}}{\mathrm{Ph{-}N{-}CH_2Ph}} \xrightarrow{\mathrm{ArNO}} \underset{\mathrm{O^-}}{\mathrm{Ph\overset{+}{N}{=}CH{-}Ph}} + \mathrm{ArNHOH}$$

$$\xrightarrow{\mathrm{ArNO}} \underset{\mathrm{O^-}}{\mathrm{ArN{=}\overset{+}{N}{-}Ar}} + \mathrm{H_2O} \mid \mathrm{ArNH_2} + \mathrm{Ar\overset{(+)(-)}{N}(O)NAr}$$

(a)

Hence, from our present understanding of hydroxylamine chemistry there are three distinct routes whereby the secondary hydroxylamine produced from the 'ene' reaction of aromatic nitroso compounds and mono-olefins can react;



When neutral or electron-withdrawing substituents are present in the aromatic ring, pathway (1) is mainly followed to provide the nitrones and azoxyarenes as observed by Alessandri,[3–5] Bruni,[6] Pummerer,[7] Hamer[11], and Sullivan.[13] When electron-releasing substituents are present in the aromatic ring the main effect is markedly to slow the rate through pathway (1) whilst reciprocally enhancing the rates of thermal decomposition *via* pathway (2) so that the main products observed, as we have found,[15, 16] are the alkenyl arylamines as well as nitrones which, in the case of p–OH, can exhibit themselves as N-alkenyl quinoneimine-N-oxides.[17]

Although we have not observed it, dehydration of the hydroxylamine (pathway (3)) cannot be discounted in a general description of this chemistry. Russian workers claim that it can occur,[22] and the dehydration of intermediate hydroxylamines seems a necessary process in the formation of anils from acyl-activated methylene compounds and nitrosoarenes.[26] However, we consider the evidence for the anil structure of Zherebkova *et al.* to be inconclusive and that a nitrone structure is equally consistent with their published spectroscopic data. The only anomaly in this reaction scheme appears to be the reaction of nitrosobenzene with isosafrole reported by Alessandri.[4] In this case, although an 'ene' addition is possible it would involve addition in an electronically unfavourable direction and hence the reaction takes a similar course to that described by Griffin and Hepfinger for the styrene-nitrosobenzene reaction.

The failure of Sullivan, Hamer, and ourselves to isolate the αβ-unsaturated nitrones is perhaps not too surprising since these compounds are known to undergo addition reactions,[28] to cyclize,[29] and may even react further to yield more complex products,[23, 30] except when the nitrones are internally stabilized by extensive conjugation,[3] or tautomerization.[12] Spectroscopic and chemical analyses of the irresolvable residues from our olefin/nitrosoarene reactions,[17, 20] are in line with the suggestion that more complex nitrone-type products may be formed.

Thus, it is believed that we have been able to evolve a scheme which may rationalize a great deal of the hitherto diverse observations made in the past concerning the reaction of nitrosoarenes with olefins containing α-methylenic hydrogen atoms.

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