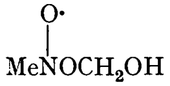
The Formation and Electron Spin Resonance Spectra of Some Cyclic Alkoxynitroxide Radicals

By **Athelstan L. J. Beckwith** * and **Michael D. Lawton**, Organic Chemistry Department, University of Adelaide, Adelaide 5000, Australia

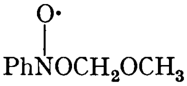
Strong signals attributed to substituted 3.4-dihydro-1*H*-2.1-benzoxazin-1-oxyl radicals are detected when aqueous solutions of titanium(III) ion. *o*-nitroarenediazonium ion. and an olefin are mixed in the flow cell of an e.s.r. spectrometer. Hyperfine splitting constants have been assigned for a number of such cyclic alkoxynitroxide radicals, and the factors which affect their magnitude. including conformational effects. have been noted. The mechanism of formation of the nitroxide radicals is thought to involve as consecutive steps. generation of *o*-nitroaryl radicals. addition to the olefin. and cyclization of the resultant 2-*o*-nitroarylalkyl radicals.

ALIPHATIC and aromatic nitro-compounds react with various organic and inorganic free radicals, Y•, to afford, among other products, addition compounds having the general formula, RN(O•)OY.[1-5] Typical examples of such nitroxides include the adduct (1) of nitromethane with the $\cdot CH_2OH$ radical derived from methanol,[1] and the adducts (2) and (3) of nitrobenzene with $\cdot CH_2OCH_3$ generated from dimethyl ether,[2] and with the phosphite radical anion,[5] $\cdot PO_3^{2-}$.



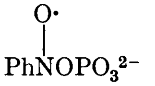
$\mathrm{Me\overset{O\cdot}{\overset{|}{N}}OCH_2OH}$

(1)



$\mathrm{Ph\overset{O\cdot}{\overset{|}{N}}OCH_2OCH_3}$

(2)



$\mathrm{Ph\overset{O\cdot}{\overset{|}{N}}OPO_3^{2-}}$

(3)

The simplest reasonable mechanism that can be formulated for the formation of alkoxynitroxides involves direct addition of the attacking radical to one of the oxygen atoms in the NO_2 group. However, the observation that adducts are formed readily by organic radicals having strong one-electron donor properties, as estimated on the basis of the stabilities of the related carbonium ions, but not by simple alkyl radicals, *e.g.* Me•, led McMillan and Norman[2] to propose that the reaction proceeds by an initial electron transfer from the radical to the nitro-compound followed by very rapid combination of the oppositely charged ions produced [equation (1)].

$$\mathrm{RNO_2 + Y\cdot \longrightarrow [RNO_2^{\cdot-} + Y^+] \longrightarrow RN(O\cdot)OY} \quad (1)$$

It is conceivable that adduct (3) and similar phosphorus-containing nitroxides are formed by the same two-step process, since the strong reducing properties of $\cdot PO_3^{2-}$ and $HPO_2^{\cdot-}$ radicals have been adequately demonstrated.[5] On the other hand, the ion pair formed by electron transfer between a nitro-compound and the radical $\cdot PO_3^{2-}$ comprises two ions, $RNO_2^{\cdot-}$ and PO_3^-, of like charge, the rate of combination of which might be expected to be less than that of diffusion from the solvent cage. The operation of a one-step addition mechanism cannot, therefore, be discounted.

We now report the results of experiments that indicate that direct addition of a radical to a nitro-group may be involved when alkoxynitroxide formation proceeds intramolecularly.

RESULTS AND DISCUSSION

Free aryl radicals add readily to olefins to afford β-arylalkyl radicals. The reaction, which is considered to be a key step in the mechanism of the Meerwein arylation of olefins, can be conveniently studied by e.s.r. spectrometry.[6] When aryl radicals are generated in a flow system in the presence of unsaturated compounds by one-electron reduction of arenediazonium salts strong signals ascribed to the appropriate adducts are detected. Thus, reduction of benzenediazonium ion in the presence of maleate or fumarate ion gives an intense doublet of doublets due to adduct (4a).[6,7]

The present investigation commenced when an attempt was made to form radical (4b) from *o*-nitrophenyl radical and maleate ion. However, mixing of aqueous solutions of *o*-nitrobenzenediazonium borofluoride, titanium(III) chloride, and ammonium maleate in the e.s.r. flow cell gave a signal that was much more complex than expected. Spectra of similarly high multiplicity were detected when *o*-nitrobenzenediazonium ion was reduced in the presence of a variety of olefins. In each case the signal was intense, even when low reactant concentrations and flow rates were used, and diminished but slowly in strength when the flow was stopped. Clearly, the radicals formed in these reactions are relatively stable.

---

[1] W. E. Griffiths, G. F. Longster, J. Myatt, and P. F. Todd, *J. Chem. Soc.* (*B*), 1966, 1130; 1967, 533.

[2] M. McMillan and R. O. C. Norman, *J. Chem. Soc.* (*B*), 1968, 590.

[3] D. J. Cowley and L. H. Sutcliffe, *J. Chem. Soc.* (*B*), 1970, 569.

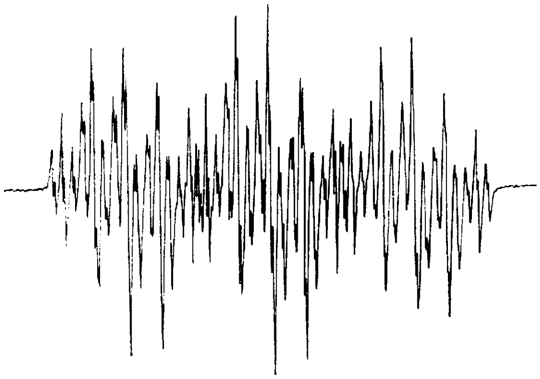
[4] E. G. Janzen and J. L. Gerlock, *J. Amer. Chem. Soc.*, 1969, **91**, 3108.

[5] A. L. J. Beckwith, *Austral. J. Chem.*, 1972, **25**, 1887.

[6] A. L. J. Beckwith, *Intrascience Chem. Reports*, 1970, **4**, 127.

[7] A. L. J. Beckwith and R. O. C. Norman, *J. Chem. Soc.* (*B*), 1969, 403.

The general features of the various spectra recorded are illustrated well by the signal obtained (Figure) when *o*-nitrobenzenediazonium ion was reduced in the presence of ammonium acrylate. It has a *g* value of 2·0045 and comprises a large triplet (1 : 1 : 1), a 1 : 4 : 6 : 4 : 1 quintet, a 1 : 2 : 1 triplet, and a very small doublet splitting. The major triplet is clearly due to interaction of the unpaired electron with nitrogen; the other splittings arise from interactions with protons, and their number is such as to indicate that both aromatic and aliphatic protons are involved. On the basis of the multiplicity of the spectrum and the similarity of the coupling constants (Table) to those previously determined for arylalkoxynitroxides [2,3] and appropriately substituted nitroarene radical anions [8] we conclude that the reaction of *o*-nitrophenyl radical with acrylate ion gives the cyclic alkoxynitroxide (5a) and that products of the same general type are formed from other olefins by treatment with *o*-nitrobenzenediazonium ion. However, radicals (5b) and (5c) which contain a CO_2^- substituent in the 7- and 6-positions were formed from acrylate ion and the diazonium salts derived from 4-amino-3-nitrobenzoic acid and 3-amino-4-nitrobenzoic acid, respectively.



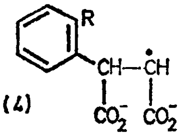
E.s.r. spectrum of the radical (5a) generated from *o*-nitrophenyl radical and acrylate ion

Hyperfine splitting constants (mT) of cyclic alkoxynitroxide radicals [a]

Radical	a_N	a_3	a_4	$a_{5(7)}$	a_6	a_8
(5a)	1·585	0·02	0·355	0·11	0·355	0·355
(5b)	1·569		0·350	0·105	0·330	0·330
(5c)	1·425		0·362	0·12		0·345
(6a)	1·545		0·35	0·115	0·35	0·35
(6b)	1·565		0·395	0·11	0·345	0·345
(6c)	1·545		0·35	0·115	0·35	0·35
(6d)	1·545		0·355	0·113	0·355	0·355
(6e)	1·405			0·11	0·35	0·35
(6f)	1·515		0·235	0·11	0·345	0·345
trans-(6g)	1·55		0·11	0·11	0·357	0·333
cis-(6g)	1·55		0·265	0·11	0·357	0·333

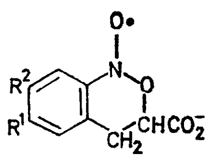
[a] Radicals had *g* values in the range 2·0044—2·0046.

Coupling constants for all the radicals studied are given in the Table. In most cases the value of a_N, the nitrogen hyperfine splitting factor, was found to lie within the range 1·545—1·585 mT. The arylnitroxides (2) and (3) have very similar values for a_N. However, the data for radical (5c) show that a_N is lowered by the presence of a CO_2^- substituent in the *para*-position with respect to the nitroxide group, an observation which accords with previous results for nitroxides derived from *p*-nitrobenzoic acid.[1,5] Surprisingly, radicals (6e) and (6f) derived from *o*-nitrobenzenediazonium ion and 3,3-dimethylacrylate ion also show low values of a_N. The reasons for this are not clear; possibly the high degree of substitution in the oxazine ring distorts it in such a way as to enhance the conjugation between the nitroxide group and the aromatic nucleus.



(4)

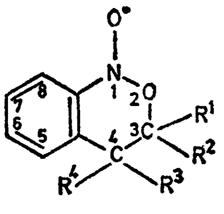
a; R = H
b; R = NO_2



(5)

a; $R^1 = R^2 = H$
b; $R^1 = H$; $R^2 = CO_2^-$
c; $R^1 = CO_2^-$; $R^2 = H$

The assignments for the proton couplings listed in the Table are consistent with the observed multiplicities of the absorption peaks and are based on the magnitudes of the splitting factors which are generally similar to those exhibited by protons occupying analogous positions in arylnitroxides [1,5] and nitroarene radical anions.[8,9]



(6)

	R^1	R^2	R^3	R^4
a;	Me	CO_2^-	H	H
b;	H	CO_2^-	H	Me
c;	H	Ac	H	H
d;	Me	Me	H	H
e;	H	CO_2^-	Me	Me
f;	Me	Me	H	CO_2^-
g;	H	CO_2^-	H	CO_2^-
h;	H	H	H	H

Each of the radicals derived from acrylate (5a—c) and methacrylate ions (6a), from methyl vinyl ketone (6c), and from isobutene (6d) showed triplet coupling of *ca.* 0·35 mT attributed to the presence of two benzylic protons at the 4-position. We conclude that these radicals have the structures expected on the basis of initial attack by *o*-nitroaryl radicals at the unsubstituted termini of the C=C bonds of the olefinic reactants. Separate experiments have indicated that these substrates exhibit the same regiospecificity in their reactions

[8] H. Fischer, ' Magnetic Properties of Free Radicals,' Landolt-Börnstein New Series, Springer-Verlag, Berlin, 1965, Group II, vol. 1.

[9] D. H. Geske, J. L. Ragle, M. A. Bambenek, and A. L. Batch, *J. Amer. Chem. Soc.*, 1964, **86**, 987.

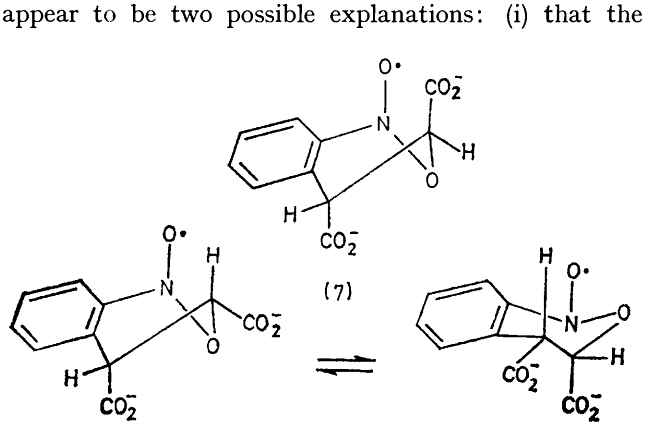
with other aryl radicals.[7,10] As expected on the basis of the proposed structures, which provide no mechanism for the delocalization of the free spin onto the 3-position, there is little detectable interaction with protons at that position and only in the case of radical (5a) formed from acrylate ion could a coupling constant be determined.

The spectral information available from these experiments does not allow one to distinguish between structure (6b), proposed for the product formed from crotonate ion, and its isomer in which the substituents at the 3- and 4-positions are interchanged. However, a separate experiment in which benzenediazonium borofluoride was reduced in the presence of ammonium crotonate gave a spectrum showing two large doublet splittings ($a_{\alpha\text{-H}}$ 2·025, $a_{\beta\text{-H}}$ 1·180 mT) and a small quartet splitting (a_{CH_3} 0·085 mT) thus indicating that the only radical formed has the methyl protons in the γ-position. This demonstration that phenyl radical attack on crotonate ion occurs exclusively at the end of the C=C bond remote from the carboxylate group leads us to favour structure (6b) for the product formed from *o*-nitrophenyl radical.

The signals recorded when *o*-nitrophenyl radical was generated in the presence of 3,3-dimethylacrylate ion revealed the presence of two nitroxides in the approximate relative concentrations of 4 : 1. The major product was that, (6f), expected from initial attack of the aryl radical at the terminus of the C=C bond adjacent to the carboxylate group, whilst the minor was isomer (6e) formed by addition to the other terminus. Probably the stabilizing effect of the two methyl groups on an adjacent radical centre, steric hindrance, and the expected electrophilicity of the *o*-nitrophenyl radical all have an effect in determining the observed preference of reaction at the 2-position. Interestingly, the $\cdot$OH radical also reacts preferentially at the 2-position in dimethylacrylate ion, whereas $\cdot\text{PO}_3{}^{2-}$ and $\text{HPO}_2{}^{-\cdot}$, which are expected to be relatively nucleophilic, add mainly at the 3-position.[5] The phenyl radical reacts with dimethylacrylate ion mainly by hydrogen atom transfer to afford a substituted allyl radical.[10]

The same complex signal comprising overlapping spectra for two radicals present in approximately equal concentration was recorded when *o*-nitrobenzenediazonium borofluoride was reduced in the presence of either maleate or fumarate ion. The two spectra had the same multiplicity and identical hyperfine splitting factors except for that attributed to interaction of the free electron with protons at the 4-position. We suggest that the two radicals are the *cis*- and *trans*-isomers of nitroxide (6g). Because of electrostatic repulsion between the two charged substituents the *trans*-nitroxide is expected preferentially to assume the conformation (7) in which the plane of the C(4)–H bond lies close to that of the aromatic ring. The *cis*-isomer is expected to be more evenly distributed between the two possible conformations (8a) and (8b); the contribution of the latter increases the net interaction of 4-H, as compared with that in the *trans*-isomer, with the unpaired electron in the aromatic π system.

Although nitroxide (6b) generated from crotonate ion should also exist in *cis*- and *trans*-forms, the e.s.r. signal could not be resolved into two distinct spectra. There appear to be two possible explanations: (i) that the reaction affords only one isomer, probably the *cis*, which preferentially assumes that conformation in which the 4-proton is in a pseudo-axial orientation, or (ii) that both *cis*- and *trans*-isomers are formed but the relative populations of the possible conformers are such as to give, for each isomer, approximately the same net interaction of 4-H with the unpaired electron.



(7)

(8a)

(8b)

Although either explanation is compatible with the relatively high value of a_4 observed, we prefer the latter since there is no obvious reason why the crotonate ion should not resemble maleate and fumarate ions in forming both *cis*- and *trans*-nitroxides.

There is one further detail of structure which deserves comment. The pair of protons at the 4-position in each of the monosubstituted radicals (5a—c) and (6c) gives rise to triplet multiplicity in the e.s.r. spectra and hence must be approximately magnetically equivalent. Apparently, in each case, the two possible stable conformers are approximately equally populated and we conclude therefore that there is no strong conformational preference for substituents at the 3-position.

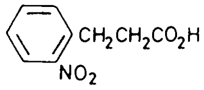
Attempts were made to generate the parent nitroxide radical (6h) from 3-*o*-nitrophenylpropionic acid (9). However, no signal was detected when a solution of the nitro-compound (9) and lead tetra-acetate in dichloromethane was irradiated with u.v. light in the e.s.r. cavity at low temperature. When $\text{SO}_4{}^{-\cdot}$ radicals were generated in the presence of the carboxylate anion derived from (9) by mixing solutions of ammonium persulphate and titanium(III) chloride in the flow cell[11] a weak, poorly resolved spectrum was detected. Since it was similar to the much more intense signal obtained by warming the nitro-acid (9) with glucose in aqueous alkali, we believe it to be due to the radical anion (10) which has a_{N} 1·44, $a_{3'(5')}$ 0·337, $a_{4'(6')}$ 0·117, and a_{CH_2} 0·275 mT. Apparently the reaction of Ti$^{\text{III}}$ with the

---

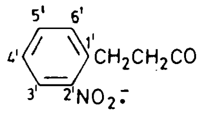
[10] A. L. J. Beckwith, unpublished observations.

[11] R. O. C. Norman, P. M. Storey, and P. R. West, *J. Chem. Soc.* (*B*), 1970, 1087.

nitro-compound (9) competes with its oxidation by persulphate ion.

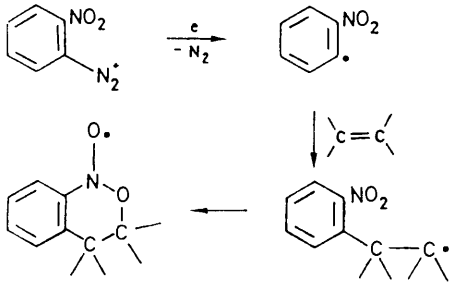


(9)



(10)

The mechanism of the formation of cyclic nitroxides from diazonium salts and olefins appears to involve three consecutive steps (Scheme): (i) generation of *o*-nitroaryl radicals by reduction of the diazonium ion, (ii) addition to C=C bonds in the substrate to afford β-arylalkyl radicals, and (iii) cyclization of the latter by direct addition of the radical centre to the nitro-group. Evidence for the first two steps comes from previous work [6,7] and from the observation that maleate and fumarate ion give identical products thus indicating that addition to the double bond and cyclisation are not concerted. Since there is no evidence to suggest that β-arylalkyl radicals of the type postulated as intermediates in these reactions are sufficiently powerful one-electron donors to reduce nitroarenes to radical anions we believe that the cyclization occurs in a single addition step, and not *via* an ion pair as previously suggested for intermolecular formation of alkoxynitroxides.[2]



SCHEME

Attempts to isolate stable nitroxides from the effluent from the flow experiments described above were unsuccessful. Appropriate extraction procedures yielded only tarry materials shown by t.l.c. to comprise complex mixtures of compounds, formed presumably by decomposition and/or oxidation–reduction reactions of the initially formed nitroxides. The recognition of the rapid cyclization of β-*o*-nitroarylalkyl radicals accounts for the low yields of products previously obtained on attempted application of the Meerwein arylation reaction to *o*-nitroarenediazonium salts.[12] For example, the reaction of *o*-nitrobenzenediazonium ion with acrylic acid affords only 6% of the expected product; better yields are obtained when the *meta*- and *para*-substituted diazonium salts are employed.[13]

EXPERIMENTAL

A Varian E9 e.s.r. spectrometer, with 100 kHz modulation and an X band klystron, was used in conjunction with a silica flow-cell which enabled three solutions to be mixed simultaneously shortly (*ca.* 0·05 s) before entering the cavity.[14] Total flow rates were in the range 100—250 ml min^{-1}. The instrument was calibrated by the addition of Fremy's salt (g 2·0055; a_N 1·309 mT) to one of the reactant solutions. Analysis of complex spectra and signals comprising overlapping spectra was facilitated by spectral simulation using a suitable computer programme.

Materials.—*o*-Nitrobenzenediazonium borofluoride was prepared from *o*-nitroaniline by the usual procedure.[7] 4-Amino-3-nitrobenzoic acid was prepared by nitration of *p*-acetylaminobenzoic acid followed by hydrolysis of the product.[15] 3-Amino-4-nitrobenzoic acid was similarly prepared from *m*-acetylaminobenzoic acid. Since both these acids afforded, on diazotisation, diazonium borofluorides which were too soluble to be isolated by the usual methods, the crude diazonium salt solutions obtained by treating the acids dissolved in 30% sulphuric acid with sodium nitrite, were used directly for the generation of radicals. 3-*o*-Nitrophenylpropionic acid was prepared by nitration of 3-phenylpropionic acid.[16] All the olefins and other reagents used were commercial samples.

Generation of Radicals.—The solutions contained (i) 0·01M-*o*-nitrobenzenediazonium borofluoride, and (ii) 0·01M-titanium(III) chloride. 0·02M-Disodium ethylenediaminetetra-acetate, the olefinic compound (*ca.* 0·04M) and sufficient ammonia were added to give the required pH (8—9).

We thank Dr. J. McGarry for technical assistance and Dr. F. R. Hewgill for making available a computer programme for spectral simulation. The project was supported by the Australian Research Grants Committee.

[3/1253 *Received*, 15*th June*, 1973]

---

[12] C. S. Rondestvedt, *Org. Reactions*, 1960, **11**, 189.

[13] J. Rai and K. B. L. Mathur, *J. Indian Chem. Soc.*, 1947, **24**, 413.

[14] R. O. C. Norman and P. R. West, *J. Chem. Soc.* (*B*), 1969, 389.

[15] F. Ullmann and F. Mauthner, *Ber.*, 1903, **36**, 4026.

[16] M. Walter, H. Besendorf, and O. Schnider, *Helv. Chim. Acta*, 1963, **46**, 1127.