Spin Trapping by Use of Nitroso-compounds. Part IV.[1] Electron Spin Resonance Studies on Oxidation with Nickel Peroxide

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The oxidation reactions of nickel peroxide were studied by use of nitrosobenzene and 2-methyl-2-nitrosopropane as spin traps. We have demonstrated by spin trapping with nitrosobenzene that nickel peroxide suspended in benzene oxidises aromatic hydrocarbons ArCHR$_2$ or Ar$_2$CHR to benzylic radicals, that radicals can similarly be formed from many compounds containing active methylene groups, and that nitroxide radicals can also be obtained from many phenols and amines. A molecule-induced homolysis occurs in the reaction of a nitroso-compound with a hydroperoxide which may be contained as an impurity in a substrate. Relationships between spectral data and structures of nitroxides formed are also discussed.

RECENTLY there has been wide interest in the application of spin trapping as a diagnosis of short-lived free radicals.[2-5] Both nitroso-compounds [equation (1)] and nitrones [equation (2)] (spin traps) react rapidly with reactive free radicals to form relatively stable nitroxides

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[1] (*a*) Part III, S. Terabe, K. Kuruma, and R. Konaka, *Chem. Letters*, 1972, 115; (*b*) preliminary communication, S. Terabe and R. Konaka, *J. Amer. Chem. Soc.*, 1969, **91**, 5655.

[2] E. G. Janzen, *Accounts Chem. Res.*, 1971, **4**, 31.

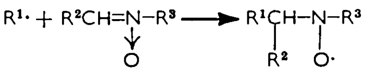
[3] M. J. Perkins, in 'Essays on Free-Radical Chemistry,' ed. R. O. C. Norman, *Chem. Soc. Special Publ.*, 1970, **24**, 97.

[4] C. Lagercrantz, *J. Phys. Chem.*, 1971, **75**, 3466.

[5] See references cited in refs. 2—4; see also: P. Tordo, M. P. Bertrand, and J.-M. Surzur, *Tetrahedron Letters*, 1970, 3399; M. G. Swanwick and W. A. Waters, *Chem. Comm.*, 1970, 930; *J. Chem. Soc.* (*B*), 1971, 1059; R. J. Holman and M. J. Perkins, *Chem. Comm.*, 1971, 244; *J. Chem. Soc.* (*C*), 1971, 2324; A. L. Bluhm, J. Weinstein, and J. A. Sousa, *Nature*, 1971, **229**, 500; J. W. Hartgerink, L. C. J. van der Laan, J. B. F. N. Engberts, and Th. J. de Boer, *Tetrahedron*, 1971, **27**, 4323; A. Rieker, P. Niederer, and H. B. Stegmann, *Tetrahedron Letters*, 1971, 3873; A. Ledwith, P. J. Russell, and L. H. Sutcliffe, *Chem. Comm.*, 1971, **964**; S. Terabe and R. Konaka, *J. Amer. Chem. Soc.*, 1971, **93**, 4306.

(spin adducts). This technique enables e.s.r. spectroscopy to be applied successfully for the detection and

$$R^1\cdot + R^2N{=}O \longrightarrow R^1R^2NO\cdot \quad (1)$$



$$R^1\cdot + R^2CH{=}\underset{\downarrow \atop O}{N}{-}R^3 \longrightarrow R^1\underset{R^2}{C}H{-}\underset{O\cdot}{N}{-}R^3 \quad (2)$$

identification of the reactive intermediates in free-radical reactions, and is especially suitable when the radical-forming reaction is so slow that concentrations detectable by e.s.r. cannot be attained.

We now describe the application of this technique to oxidations with nickel peroxide (Ni–PO).[6] Nickel peroxide prepared from nickel sulphate and sodium hypochlorite is a useful oxidant of alcohols, amines, phenols, hydrazones, sulphur compounds, phenothiazines, active hydrocarbons, and aldoximes.[7] This reagent, represented by the empirical formula $NiO_{2\cdot77}H_{2\cdot85}$, is an amorphous black powder insoluble in organic solvents. The oxidation mechanism in general involves hydrogen abstraction and hydroxyl-radical donation by nickel peroxide.[8]

In these experiments we could observe various kinds of free-radical intermediates in oxidations with nickel peroxide. We discuss here some oxidation mechanisms, and the utility of nitrosobenzene as a spin trap.

In the presence of a nitroso-compound (0·05—0·1M), the substrate (0·05—0·5M) was oxidized with nickel peroxide (0·2—1 equivalent amount of the substrate) in deoxygenated benzene at room or somewhat higher (*ca.* 60 °C) temperatures for 10—30 s, and the e.s.r. spectrum was immediately recorded at room temperature. The structures of the nitroxides formed are deduced from their e.s.r. spectra. The nitroxides studied were stable and decay of their spectra was hardly noticed during the e.s.r. measurements. None of the nitroxides given in Tables 1—3 was produced if a substrate, a nitroso-compound, or nickel peroxide was absent.[1b] The nitroxides (17)—(22) and (25), however, were obtained in the absence of nickel peroxide as mentioned below. The nitroso-compounds and substrates examined, and nitroxides formed from them, are listed in Tables 1—3 along with their *g*-values and hyperfine splitting constants. Some examples of the spectra obtained are shown in Figures 1—5.

Aromatic Hydrocarbons and Derivatives (*see Table* 1).—In the nickel peroxide oxidation of cumene in the presence of nitrosobenzene at room temperature the nitroxide spin adduct (1) was observed by e.s.r. (Figure 1). The observation of this nitroxide indicates the formation of α-cumyl radical (38). The oxidation of cumene with nickel peroxide proceeded slowly at room temperature to yield α-cumyl alcohol as the major product and αα′-bicumyl (39) as the minor product in the presence or absence of oxygen. The products were probably formed by the process shown in Scheme 1. The oxidation of cumene with nickel peroxide (8 equivalent amounts of cumene) in benzene at 80 °C for 8 h afforded benzoic acid in 29% yield.[9] It is not clear from these observations alone whether the α-cumyl radical is the intermediate to benzoic acid, but at least it is possible to say that the tertiary hydrogen atom in cumene can be abstracted by nickel peroxide. The nitroxide (1) was also produced from only cumene and nitrosobenzene if the cumene contained peroxide (probably cumyl hydroperoxide).

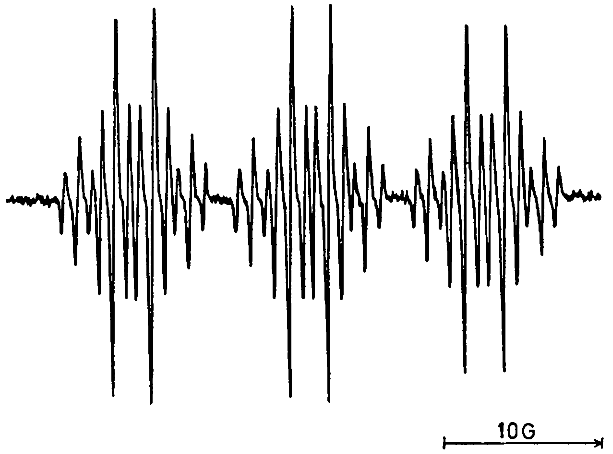
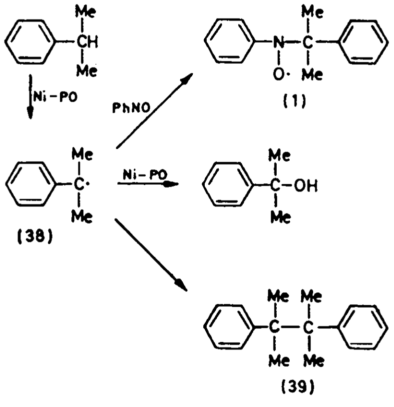


FIGURE 1 E.s.r. spectrum of α-cumyl(phenyl)nitroxide (1) in benzene. In this instance the couplings from the *N*-phenyl group alone are observed



SCHEME 1

The reaction of the hydroperoxide with a nitroso-compound is discussed later. In the case of peroxide-free s-butylbenzene, the oxidation with nickel peroxide gave the nitroxide (4). The oxidation of diphenylacetonitrile gave (5) and (6) as previously described.[1b] From these results it is recognized that benzylic tertiary hydrogen atoms tend to be abstracted by nickel peroxide.

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[6] K. Nakagawa, R. Konaka, and T. Nakata, *J. Org. Chem.*, 1962, **27**, 1597.

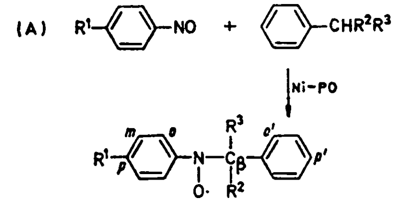
[7] See, *e.g.*, K. Nakagawa, R. Konaka, and J. Sugita, *Ann. Report Shionogi Res. Lab.*, 1969, No. **19**, 141, and references cited in ref. 8.

[8] R. Konaka, S. Terabe, and K. Kuruma, *J. Org. Chem.*, 1969, **34**, 1334.

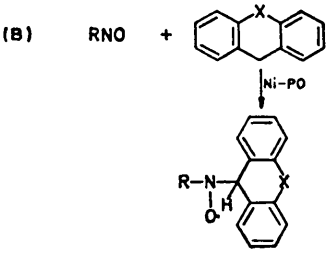
[9] J. Sugita, unpublished data.

Table 1

Spin adducts in the oxidation of aromatic hydrocarbon and derivatives with nickel peroxide in benzene (see text)



R¹	R²	R³	No.	g Value	a_N	$a_{o\text{-}H}$	$a_{m\text{-}H}$	$a_{p\text{-}H}$	$a_{\beta\text{-}H}$	Other
					Hyperfine splitting constants (G)					
H	Me	Me	(1)	2·0057	11·53	2·45	0·90	2·45		
p-Me	Me	Me	(2)	2·0057	11·50	2·58	0·90	2·58 [a]		
p-Bu^t	Me	Me	(3)	2·0057	11·47	2·45	0·89	*b*		
H	Me	Et	(4)	2·0057	11·31	2·39	0·85	2·39		0·75(1H),[c] 0·25(1H) [c]
H	CN	Ph	(5)	2·0057	11·10	2·36	0·90	2·36		0·20(1H or 3H) [d]
p-Bu^t	CN	Ph	(6)	2·0057	11·07	2·30	0·90	*b*		
H	H	Me	(7)	2·0056	10·67	2·66	0·96	2·66	5·31	0·34(3H),[c] 0·10(3H) [e]
H	H	Et	(8)	2·0056	10·71	2·67	0·94	2·67	4·00	0·34(2H) [c]
H	H	Pr^n	(9)	2·0056	10·73	2·65	0·94	2·65	3·97	0·33(2H) [c]
H	H	Pr^i	(10)	2·0056	10·76	2·68	0·95	2·68	3·52	0·22(4H) [c,e]
H	H	Ph	(11)	2·0057	10·68	2·68	0·93	2·68	3·59	
H	H	CN	(12)	2·0056	10·84	2·56	0·88	2·56	3·36	
H	H	CH_3CO	(13)	2·0055	10·62	2·67	0·94	2·67	4·21	
H	H	CH_3CO_2	(14)	2·0057	10·44	2·51	0·89	2·51	2·51	
H	H	MeO	(15)	2·0057	10·54	2·56	0·87	2·56	1·63	
H*	H	$CH_2{:}CH$	(16)	2·0056	10·76	2·65	*b*	2·65	4·71	



R	X †	No.	g Value	a_N	$a_{o\text{-}H}$	$a_{m\text{-}H}$	$a_{p\text{-}H}$	$a_{\beta\text{-}H}$	Other
					Hyperfine splitting constants (G)				
Ph	CH_2	(17)	2·0056	10·92	2·70	0·98	2·70	0·98	
Bu^t	CH_2	(18)	2·0060	14·77				0·86	*b*
Ph	O	(19)	2·0057	10·91	2·66	0·95	2·66	0·95	
Ph	S	(20)	2·0056	10·69	2·66,[f] 2·56[f]	0·90	2·66[f]	1·08	0·11(4H) [d]
Ph	C:O	(21)	2·0057	10·75	2·67	0·97	2·67	0·97	
Ph	i	(22)	2·0056	10·91	2·69	0·95	2·69	1·31	
Ph	ii	(23)	2·0057	10·58	2·06,[f] 2·63[f]	0·93	2·63	2·06[f]	0·52 (2H) [c]
Ph	iii	(24)	2·0057	10·95	2·73	0·97	2·73	0·97	
Bu^t	iv	(25)	2·0060	14·07				1·08	*b*

* 3,5-$D_2C_6H_3NO$ was used instead of *p*-$R^1C_6H_4NO$. † In X = i—iv, the substrates are not dihydroanthracene derivatives represented in equation (B), but are listed here for convenience. i, 5,12-Dihydronaphthacene; ii, tetralin; iii, 9,10-dihydrophenanthrene; iv, fluorene. The structures of spin adducts from these substrates are not shown, but it will be evident that they are similar to that illustrated in equation (B). In the case of tetralin, the tetralin-1-yl radical adduct was obtained.

[a] *p*-Methyl–hydrogen coupling. [b] Neither interaction with t-butyl or with deuterium was observed. [c] These couplings may be assigned to γ-methyl, γ-methylene, or γ-methine protons. [d] No assignment. [e] May be assigned to *o*'- and *p*'-protons. [f] *ortho*- and *para*-Protons are not equivalent, but assignments are unknown, and tentative assignments only are shown.

The oxidation of toluene and ethylbenzene with nickel peroxide is also known to produce benzoic acid in low yield.[9] However, in the oxidation of peroxide-free ethylbenzene in the presence of nitrosobenzene, no paramagnetic species was detected. In addition no nitroxide was produced from toluene, n-propylbenzene, n-butylbenzene, or isobutylbenzene, although the spectra of nitroxides (7)—(10) (Figure 2) were obtained in the absence of nickel peroxide if peroxides were not removed from the substrates. In the cases of tetralin and dihydrophenanthrene, the nitroxides (23) and (24) respectively perhaps arose from the hydroperoxide reaction (see below), since the spectrum of the nitroxide (23) was not observed in the oxidation of peroxide-free tetralin.

In the oxidations of diphenylmethane, phenylacetonitrile, benzyl methyl ketone, benzyl acetate, benzyl methyl ether, and allylbenzene with nickel peroxide, the nitroxides (11)—(16) were observed respectively by spin trapping. No spin adduct was detected in the absence of nickel peroxide if peroxides contained in these substrate were removed. Since the oxidation of diphenylmethane with nickel peroxide yields benzophenone,[9] trapping of the diphenylmethyl radical suggests that the reaction proceeds by the route of Scheme 2.

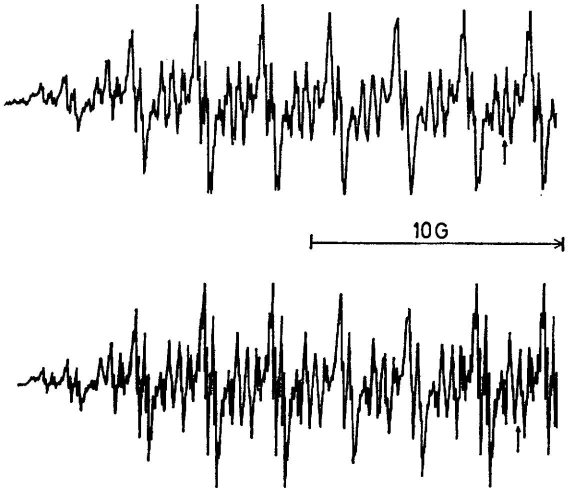
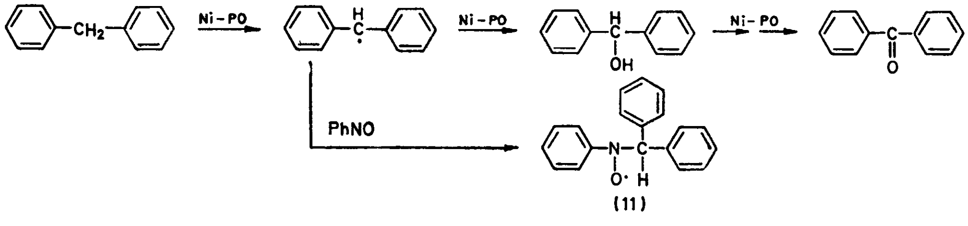


FIGURE 2 E.s.r. spectrum of α-phenylethyl(phenyl)nitroxide (7) obtained from ethylbenzene containing peroxide in benzene. Only one half the spectrum is shown: the centre is marked by an arrow. The upper spectrum is experimental and the lower is a simulation based on the coupling constants given in Table 1 and Lorentzian line-shapes. The line-widths are 0·098 G and the smallest coupling constant is 0·10 G

Treatment of phenylacetonitrile with nickel peroxide gave a polymer as the major product along with dimer, *meso*- and (±)-2,3-diphenylsuccinonitrile, *trans*- and *cis*-α,α'-dicyanostilbene, and benzoic acid as by-products.[10] Cyanophenylmethyl radical is considered to be an intermediate in this reaction,[10] and the scavenging of it supports this explanation. As noted above, nickel peroxide is capable of abstracting benzylic secondary hydrogen atoms if benzylic positions are substituted by such radical-stabilizing groups as phenyl, cyano, acyl, acyloxy, alkoxy, or allyl, but benzylic secondary hydrogen atoms in alkylbenzene cannot be abstracted.



SCHEME 2

9,10-Dihydroanthracene was oxidized with nickel peroxide in benzene to give anthracene as the major product and anthraquinone as the minor one.[8] The oxidation in the presence of nitrosobenzene or 2-methyl-2-nitrosopropane yielded the nitroxide (17) or (18) in appreciable concentration (Figure 3). It was surprising to find that the nitroxide (17) or (18) was formed in low concentration from peroxide-free 9,10-dihydroanthracene itself in the absence of nickel peroxide. This indicates that not all the 9,10-dihydro-9-anthracenyl radicals trapped are necessarily intermediates in the oxidation reaction. Similarly, in the oxidation of xanthen, thioxanthen, anthrone, 5,12-dihydronaphthacene, and fluorene with nickel peroxide the nitroxides (19), (20), (21), (22), and (25) were produced respectively, though their oxidation products were not examined. In these cases, the nitroxides were also detected in the absence of nickel peroxide (see below). Thus, in the oxidation of aromatic hydrocarbons mentioned above with nickel peroxide, the spin adducts are not always produced from the intermediate free radicals expected in the oxidation, but in fact may be the result of other non-radical reactions.

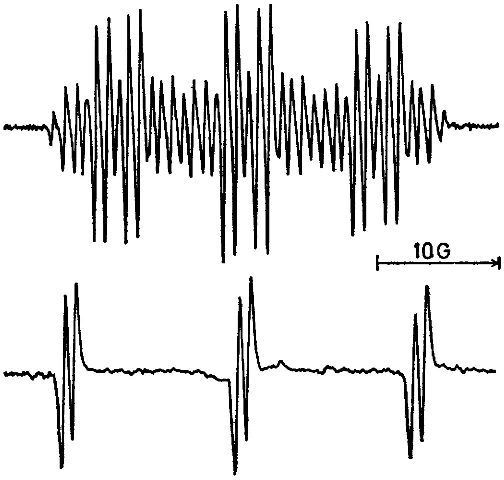


FIGURE 3 E.s.r. spectra of 9,10-dihydro-9-anthracenyl(phenyl)-nitroxide (17) (top) and 9,10-dihydro-9-anthracenyl-(t-butyl)-nitroxide (18) (bottom) in benzene

It is apparent from the above that nickel peroxide oxidations provide a convenient method for the generation of the nitroxides listed in Table 1, including a merit that the nitroxides formed do not react with nickel peroxide. Provided 2-methyl-2-nitrosopropane and α-sub-

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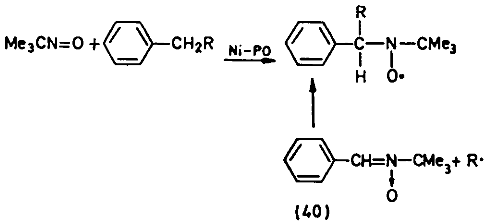
[10] J. Sugita, *J. Chem. Soc. Japan*, 1967, **88**, 668.

stituted toluenes are used, the nitroxides formed are the same as the spin adduct of R• to another effective spin trap, *N*-benzylidene-t-butylamine *N*-oxide (40).[11]

Phenols [1a] (*see Table* 2).—The oxidation of phenol with nickel peroxide has been reported to give only polymers.[12] The formation of phenoxazin-10-oxyl (26) in the presence of nitrosobenzene has previously been illustrated [1a] (see also Figure 4). An unknown e.s.r. spectrum was obtained by the use of 2-methyl-2-nitrosopropane instead of nitrosobenzene.

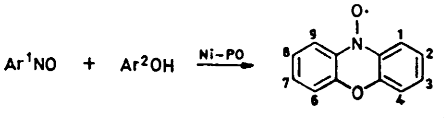


Scheme 3

It is evident from the spectrum that H(1) [or H(9)] and H(3) [or H(7)] are not equivalent but the assignments of hyperfine splitting constants are ambiguous in the literature.[13,14] The assignment was determined as shown in Table 2 by preparing 3-deuteriophenoxazin-10-oxyl from *p*-deuterionitrosobenzene. The result is consistent with the tendency estimated by HMO calculation, but inconsistent with that by McLachlan–HMO or VHF–SCF–MO calculation.[14]

Table 2

Spin adducts in the oxidation of phenols with nickel peroxide in benzene



Ar¹	Ar²	Nitroxide	*g* Value	a_N	$a_{H(1)}$	$a_{H(2,4)}$	$a_{H(3)}$	$a_{H(6,8)}$	$a_{H(7)}$	$a_{H(9)}$
				Hyperfine splitting constants (G)						
Ph	Ph	Parent (26)	2·0049	9·20	2·36	0·46	2·48	0·46	2·48	2·36
Ph 3,5-$D_2C_6H_3$	2,4,6-$D_3C_6H_2$ Ph	2,4-D_2 (27)		9·20	2·37	0·07 (D)	2·47	0·46	2·47	2·37
Ph	3,5-$D_2C_6H_3$	1,3-D_2 (28)		9·20	0·37 (D)	0·46	0·37 (D)	0·46	2·49	2·39
p-DC_6H_4	Ph	3-D (29)		9·20	2·36	0·46	0·38 (D)	0·46	2·46	2·36
Ph	*p*-$Bu^tC_6H_4$	2-Bu^t (30)	2·0049	9·38	2·4	0·47 [b]	2·5	0·47	2·5	2·4
Ph	*p*-$Bu^sC_6H_4$	2-Bu^s (31)	2·0049	9·30	2·30 [a]	0·45 [c]	2·56	0·45	2·56	2·40 [a]

[a] Assignments are uncertain. [b] No splittings resolved from the t-butyl group. [c] $a_{2\text{-CH}}$ = 0·15 G.

Phenoxazin-10-oxyls were also produced from *p*-alkylphenols (Table 2), but spectra obtained from other isomeric alkylphenols or polyalkylphenols were different from those of phenoxazin-10-oxyls although the origin of the spectrum could not be established. The oxidation of thiophenol with nickel peroxide did not give any spin adduct in the presence of nitrosobenzene. Phenyl(thiophenoxy)nitroxide was obtained during the photolysis of diphenyl disulphide in the presence of nitrosobenzene in benzene (see Table 4).

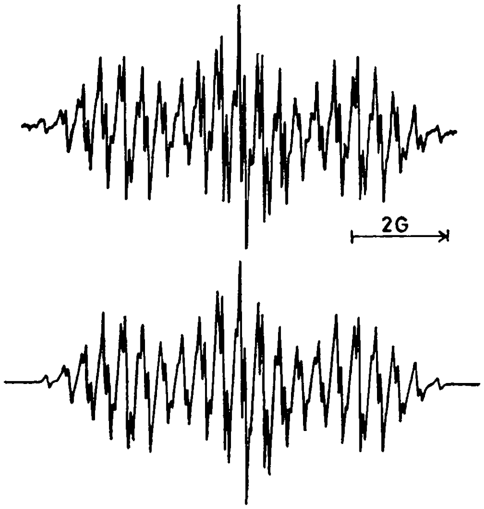


Figure 4 E.s.r. spectrum of 1,3-dideuteriophenoxazin-10-oxyl (28) in benzene. Only the central multiplet of the triplet (1 : 1 : 1) of multiplets is shown. The upper spectrum is experimental, while lower spectrum is a reconstruction based on the coupling constants in the Table 2 and Lorentzian line-shapes. Line-widths are 0·075 G

Leaver *et al.*[15] recently obtained a spectrum composed of a simple triplet upon photolysis of phenol at 300 nm in the presence of 2-methyl-2-nitrosopropane and they interpreted this spectrum in terms of the phenoxy-(t-butyl)nitroxide. The nitrogen hyperfine splitting constant (16·23 G) for the nitroxide recorded is much smaller than that (25—30 G) for t-butyl(alkoxy)-nitroxides [16] and somewhat smaller than that (16·75 G) for the thiophenoxy-(t-butyl)nitroxide,[17] and is comparable with that (15·47 G) for di-t-butylnitroxide.[18]

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[11] See, *e.g.*, E. G. Janzen and B. J. Blackburn, *J. Amer. Chem. Soc.*, 1969, **91**, 4481.

[12] J. Sugita, *J. Chem. Soc. Japan*, 1966, **87**, 603.

[13] K. Scheffler and H. B. Stegmann, *Tetrahedron Letters*, 1968, 3619.

[14] M. F. Chiu, B. C. Gilbert, and P. Hanson, *J. Chem. Soc.* (*B*), 1970, 1700.

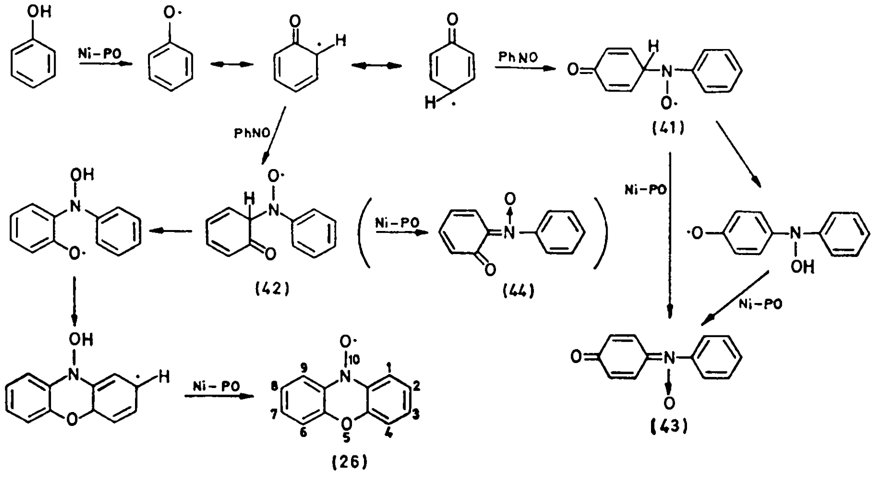
[15] I. H. Leaver, G. C. Ramsey, and E. Suzuki, *Austral. J. Chem.*, 1969, **22**, 1891.

[16] A. Mackor, Th. A. J. W. Wajer, Th. J. de Boer, and J. D. W. van Voorst, *Tetrahedron Letters*, 1967, 385.

[17] I. H. Leaver and G. C. Ramsey, *Tetrahedron*, 1969, **25**, 5669.

[18] R. Briere, H. Lemaire, and A. Rassat, *J. Chem. Phys.*, 1968, **48**, 1429.

Since the remarkable solvent-dependence of the nitrogen hyperfine splitting constant for nitroxides are well known,[19] the nitrogen hyperfine splitting constant would increase in the presence of phenolic hydrogen which might interact with the oxygen of the nitroxide. In addition, the nitroxide would be less stable in the presence of the acidic substance. Therefore the identification of the spectrum reported by Leaver *et al.*[15] to the t-butyl-(phenoxy)nitroxide appears very questionable. The spectrum should probably be assigned to di-t-butylnitroxide.



Scheme 4

Table 3

Spin adducts in the oxidation of amines and active methylene compounds with nickel peroxide in benzene

Nitroso-compound	Substrate	Spin adduct	g Value	Hyperfine splitting constants (G) a_N	$a_{o\text{-}H}$	$a_{m\text{-}H}$	$a_{p\text{-}H}$	$a_{\beta\text{-}H(N)}$
Bu^tNO	Carbazole	$Bu^tN(NC_{12}H_8)O\cdot$ (32) [a]	2·0059	16·77	—	—	—	1·37
PhNO	PhNHAc	PhN(Ac)NPhO· (33)	2·0054	11·61 [b]	2·60 [b] 2·73 [b]	0·89 [b]	2·60 [b]	1·67 [b]
$3,5\text{-}D_2C_6H_3NO$	PhNHAc	$PhN(Ac)N(3,5\text{-}D_2C_6H_3)O\cdot$ (34)	2·0053	11·63	2·67	*d*	2·67	1·70
$3,5\text{-}D_2C_6H_3NO$	PhNHMe	$PhNMeN(3,5\text{-}D_2C_6H_3)O\cdot$ (35)	2·0052	12·05	2·83	*d*	2·83	0·63
PhNO	$(AcCH_2\cdot)_2$	$AcCH_2\cdot CH(Ac)NPhO\cdot$ (36) [c]	2·0057	10·75	2·75	0·97	2·75	2·42
PhNO	$CH_2(CO_2Et)_2$	$EtCO_2\cdot CH_2\cdot CO_2\cdot CHMeN(Ph)O\cdot$ (37)	2·0057	10·34	2·60	0·90	2·60	5·06

[a] $NC_{12}H_8$ = Carbazol-9-yl. [b] Values from G. Binsch and C. Rüchardt, *J. Amer. Chem. Soc.*, 1966, **88**, 173. [c] Further splittings 0·51 G (1H) and 0·26 G (1H) were observed. These may be due to non-equivalent γ-protons. [d] No splitting resolved from deuterium atoms.

N-4-oxocyclohexa-2,5-dienylideneaniline *N*-oxide (43) was isolated in the oxidation of phenols with nickel peroxide in the presence of nitrosobenzene. The characterization of (43) has previously been described.[1a] The reaction path of this trapping is explained by Scheme 4. The isolation of the nitroxide (26) was unsuccessful, and evidence for the formation of *N*-6-oxocyclohexa-2,4-dienylideneaniline *N*-oxide (44) could not be obtained. The phenoxyl radical produced would attack nitrosobenzene preferentially at the *para*-position to give (43) as illustrated in Scheme 4, while in part it would add to nitrosobenzene in the *ortho*-position to afford the nitroxide (26). The primary spin adducts (41) and (42) were not detected, presumably because they were easily further oxidised.

Amines and Active Methylene Compounds (*see Table* 3).—The oxidations of carbazole and acetanilide have been mentioned.[1b] The use of 3,5-dideuterionitrosobenzene is very helpful for the analyses of complex spectra of spin adducts [the nitroxides (34) and (35)]. The observation of the nitroxide (35) (Figure 5) indicates that the *N*-methylanilino-radical is produced in the oxidation of *N*-methylaniline with nickel peroxide.

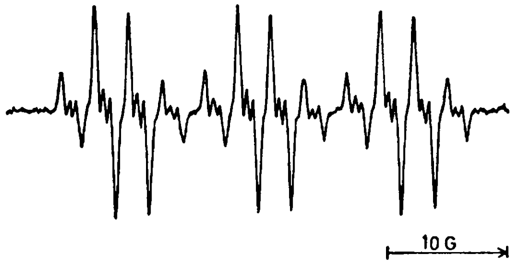


Figure 5 E.s.r. spectrum of *N*-methylanilino-(3,5-dideuteriophenyl)nitroxide (35) in benzene

The oxidation of diethyl malonate with nickel peroxide in the presence of nitrosobenzene gave the e.s.r. spec-

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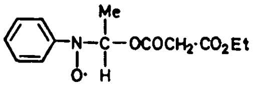
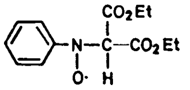
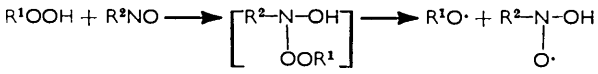
[19] See, *e.g.*, K. Mukai, H. Nishiguchi, K. Ishizu, Y. Deguchi, and H. Takaki, *Bull. Chem. Soc. Japan*, 1967, **40**, 2731; R. Briere, H. Lemaire, and A. Rassat, *Tetrahedron Letters*, 1964, 1775.

trum with hyperfine splitting constants shown in Table **3**. Since these spectral data alone could not discriminate between nitroxides (**37**) and (**45**), bis(pentadeuterioethyl) malonate was oxidised instead of diethyl malonate.

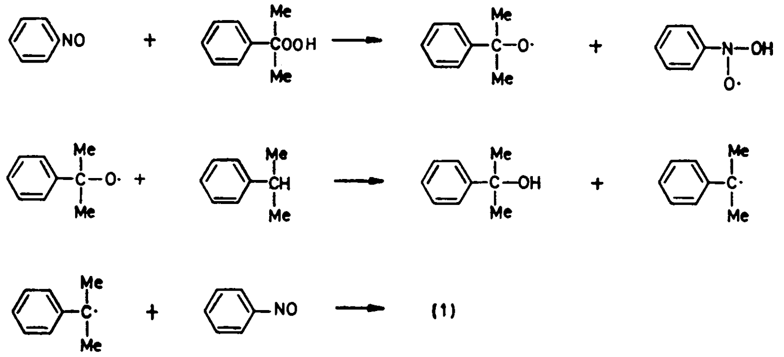

(37)

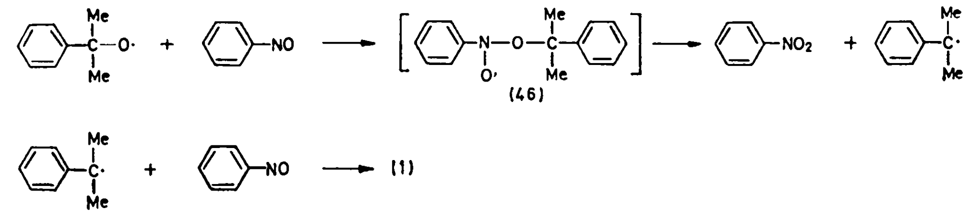

(45)

The spectrum obtained was due to a mixture of radicals. This result means that the hydrogen abstraction from the malonylmethylene group became competitive with the deuterium abstraction from the pentadeuterioethoxymethylene group because of deuterium isotope effects. Thus the structure of the nitroxide observed is assigned to the nitroxide (**37**), and it appears that the ethoxymethylene hydrogen atoms are slightly reactive towards attack by nickel peroxide. A similar result recently was reported[20] in the hydrogen abstraction by t-butoxyl radicals.


$$R^1OOH + R^2NO \longrightarrow \left[\begin{array}{c} R^2\text{—}N\text{—}OH \\ | \\ OOR^1 \end{array}\right] \longrightarrow R^1O\cdot + \begin{array}{c} R^2\text{—}N\text{—}OH \\ | \\ O\cdot \end{array}$$

Scheme 5


Scheme 6



Scheme 7

Reaction of Nitrosobenzene with Hydroperoxide.—It is known from e.s.r. spin-trapping experiments that hydrogen peroxide reacts with sulphoxides[21] and ketones[22] to give free radicals. The same type of reaction was observed with alkyl hydroperoxides.[23] Konaka *et al.* recently found that alkyl hydroperoxides reacted with nitroso-compounds as well as sulphoxide.[24] t-Butyl hydroperoxide, for example, reacts with nitrosobenzene as shown in Scheme 5, to give the spin adducts of t-butoxyl radical to nitrosobenzene.[24]

Nitrosobenzene was mixed with cumene in benzene in the absence of nickel peroxide as a control test of spin trapping, to give the nitroxide (1). However, peroxide-free cumene gave no nitroxide (1), but only a weak spectrum of phenylnitroxide. Addition of a trace amount of α-cumyl hydroperoxide to the reaction mixture described above gave rise to a strong spectrum of the nitroxide (1). Thus, the generation of the nitroxide (1) in the use of commercial cumene is attributed to α-cumyl hydroperoxide involved, and the reaction path suggested is in Scheme 6. In the reaction of nitrosobenzene and α-cumyl hydroperoxide in the absence of cumene, the nitroxide (1) was produced, suggesting that the nitroxide (1) was also formed by another process as shown in Scheme 7. Phenyl-(α-cumyloxy)nitroxide (46), which was assumed to be the primary spin adduct in the reaction of nitrosobenzene and α-cumyl hydroperoxide, could not be observed in these experimental conditions, although phenyl-(t-butoxy)nitroxide was easily observed[24] during the reaction of nitrosobenzene

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[20] M. J. Perkins, P. Ward, and A. Horsfield, *J. Chem. Soc.* (*B*), 1970, 395.

[21] C. Lagercrantz and S. Forshult, *Acta Chem. Scand.*, 1969, **23**, 811; B.-M. Bertilsson, B. Gustafsson, I. Kühn, and K. Torssell, *ibid.*, 1970, **24**, 3590.

[22] K. Torssell, *Tetrahedron*, 1970, **26**, 2759.

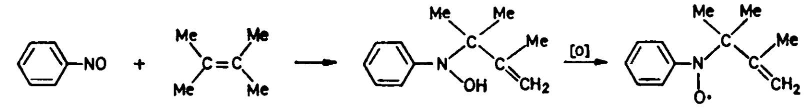
[23] R. Konaka and T. Mizuta, Abstracts, XIIth Symposium on Free-Radical Reaction (Japan), Nagoya, 1971, p. 29.

[24] R. Konaka, T. Mizuta, and S. Terabe, Abstracts, XXVIth Annual Meeting of the Chemical Society of Japan, Hiratsuka, 1972, p. 1343.

and t-butyl hydroperoxide. t-Butoxy-(t-butyl)nitroxide, which is known to be unstable,[25] may decompose to produce t-butyl radical and 2-methyl-2-nitropropane.[26] In fact, phenyl(alkoxy)nitroxides produce nitrobenzenes and alkyl radicals if alkyl radicals produced are stable as tertiary alkyl, allyl, and benzyl radicals.[27]

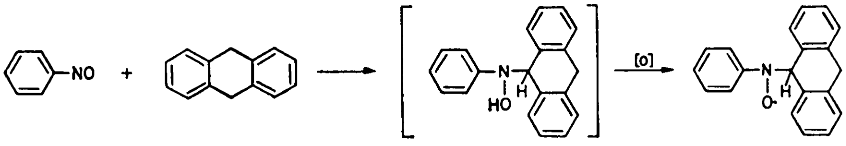
From substrates other than cumene, the nitroxides often resulted as noted above unless hydroperoxides were removed, possibly by the same way as illustrated in Scheme 6 and/or Scheme 7. Therefore, care must be taken in the spin-trapping experiments with alkylbenzenes to remove contamination by hydroperoxides.

Sullivan [28] has reported that nitrosobenzene reacts with 2,3-dimethylbut-2-ene to give phenyl-(1,1,2-trimethylprop-2-enyl)nitroxide (48) (Scheme 8). The possibility that the nitroxide (48) might be formed by the same mechanisms as illustrated in Scheme 6 and Scheme 7 was eliminated by the examination of peroxide-free 2,3-dimethylbut-2-ene. Recently, the isolation of the hydroxylamine (47) has been reported.[29] Similar examples to the formation of the nitroxide (48) were recognized for nitroxides (17)—(22) and (25), as described above. These nitroxides were recognized as being produced slowly from peroxide-free substrates in the absence of nickel peroxide. These nitroxides would not be formed by the reaction of carbanions with nitroso-compounds as noticed by Forrester and Hepburn,[30] since the solutions were neutral. The mechanism of their formation seems similar to that suggested by Sullivan.[28] The nitroxide (15), for example, might be formed as shown in Scheme 9. The intermediate hydroxylamine (49), which may be formed slowly, will be readily oxidised by unchanged nitrosobenzene or a trace of oxygen present in the reaction mixture, so that it seems to be difficult to isolate it.



(47) (48)

SCHEME 8



(49) (15)

SCHEME 9

Hyperfine Splitting Constants and g-Values of Spin Adducts to Nitrosobenzene.—It is generally accepted that the nitrogen hyperfine splitting constants depend substantially on the group adjacent to the nitrogen atom. The structural dependence of nitrogen coupling constants of various phenylnitroxides is summarized in Table 4 along with *g*-values and *ortho*- and *para*-hydrogen coupling constants. The spectral data of secondary and tertiary alkyl(phenyl)nitroxides and amino(phenyl)-nitroxides are taken from data in Tables 1—3. Although primary alkyl radicals were not trapped in this study, the nitrogen hyperfine splitting constants for primary alkyl(phenyl)nitroxide generated by another method are smaller than 10·5 G. The nitrogen hyperfine splitting constants for phenyl-, t-butoxy(phenyl)-, thiophenoxy(phenyl)-, and acyl(phenyl) [31]-nitroxides, which were also generated by other methods, are shown for comparison. Trapped species can be predicted to a certain extent solely by the nitrogen hyperfine splitting constants as long as the solvent is limited to benzene. The nitrogen hyperfine splitting constants are considered to vary with the coplanarity of the phenyl group and the nitroxyl group in alkylphenylnitroxides. Though, for example, the 9,10-dihydro-9-anthracenyl group appears considerably bulky, the nitrogen hyperfine splitting constant in the nitroxide (17) is smaller than those in the nitroxides (1), (4), and (5). Such a finding shows that the phenyl group is twisted from the plane of the nitroxyl group less in the nitroxides (17), (19), (20), (21), and (22) than in (1), (4), and (5). The slightly smaller values of the nitrogen hyperfine splitting constants in the nitroxides, (14), (15), and (37) than those in other secondary alkyl(phenyl)nitroxides may be due to the influence of the greater electronegativity of the acyloxy- and alkoxy-groups on β-carbon atoms. The *g*-values observed are slightly dependent on the structure of nitroxides (see Table 4). These values serve as a complementary parameter in the identification of the nitroxide.

The magnitude of *ortho*- and *para*-hydrogen hyperfine splitting constants also vary substantially according to

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[25] A. Mackor, Th. A. J. W. Wajer, Th. J. de Boer, and J. D. W. van Voorst, *Tetrahedron Letters*, 1967, 385.

[26] D. F. Bowman, J. L. Brokenshire, T. Gillan, and K. U. Ingold, *J. Amer. Chem. Soc.*, 1971, **93**, 6552.

[27] T. Mizuta and R. Konaka, unpublished data.

[28] A. B. Sullivan, *J. Org. Chem.*, 1966, **31**, 2811.

[29] G. T. Knight, *Chem. Comm.*, 1970, 1016.

[30] A. R. Forrester and S. P. Hepburn, *J. Chem. Soc.*, (*C*), 1971, 701.

[31] A. Mackor, Th. A. J. W. Wajer, and Th. J. de Boer, *Tetrahedron*, 1968, **24**, 1623.

the substituent on the nitrogen in *N*-substituted phenylnitroxides as shown in Table 4. Since the coupling constants of ring hydrogens depend chiefly on the spin density on the phenyl group, these could be related to the coplanarity of the phenyl and nitroxyl groups in alkyl(phenyl)nitroxides. In most cases the coupling constants of *ortho*- and *para*-hydrogens are the same, but in some cases they differ slightly, *e.g.*, in the nitroxides (20), (23), and (33). The difference would be due to the restricted rotation of the phenyl group around the N–Ph bond in *N*-substituted phenylnitroxides.

TABLE 4

Spectral data of *N*-substituted phenylnitroxides in benzene at room temperature (25 °C) [a]

R in PhN(R)O·	*g* Value	a_{N}/G	$a_{o,p\text{-}\mathrm{H}}$/G
H [b]	2·0055	9·64	3·12 [c]
Primary alkyl [d]	2·0055—2·0057	<10·5	2·8
Secondary alkyl		10·3—11·0	2·5—2·7
Tertiary alkyl		11·1—11·5 (12·3) [h]	2·4—2·5
Amino	2·0052—2·0054	11·6—12·1	2·6—2·8
Bu^{t}O [e]	2·0048	14·58	2·93
PhS [f]	2·0059	11·42	2·52
RCO [g]	2·0065	7·3—7·7	1·5—1·6

[a] Summarized from Tables 1—3. See text also. [b] $a_{m\text{-}\mathrm{H}}$ = 1·04 G, a_{NH} = 12·45 G. For the values in toluene see, Th. A. J. W. Wajer, A. Mackor, Th. J. de Boer, and J. D. W. van Voorst, *Tetrahedron Letters*, 1967, 1941. [c] Average value of 3·26 G, 3·26 G, and 2·83 G. [d] Benzyl(phenyl)nitroxide in toluene: *g* = 2·0056, a_{N} = 10·40 G, $a_{o,p\text{-}\mathrm{H}}$ = 2·80 G (3H), $a_{m\text{-}\mathrm{H}}$ = 0·94 G (2H), $a_{\beta\text{-}\mathrm{H}}$ = 5·65 G (2H); ethyl(phenyl)nitroxide in benzene: *g* = 2·0055, a_{N} = 10·53 G, $a_{o,p\text{-}\mathrm{H}}$ = 2·81 G (3H), $a_{m\text{-}\mathrm{H}}$ = 0·95 G (2H), $a_{\beta\text{-}\mathrm{H}}$ = 7·84 G (2H). [e] $a_{m\text{-}\mathrm{H}}$ = 0·99 G (2H). For the value in trichlorofluoromethane, see ref. 16. [f] $a_{m\text{-}\mathrm{H}}$ = 0·86 G (2H). [g] Ref. 31. [h] The nitrogen hyperfine splitting constant for t-butyl(phenyl)nitroxide has been reported to be 12·3 G (see ref. 20).

The most important values for the identification of alkyl(phenyl)nitroxides are those of β-hydrogens, because the number of hydrogens attached to the β-carbon atom is directly given by the multiplicity of the splitting pattern. The most effective factor influencing the magnitude of β-hydrogen hyperfine splitting constants is the dihedral angle between the p_z orbital on the nitrogen atom and the C_{β}–H bond.[32] Another possible factor is the electronegativity of the substituent on the β-carbon atom. The decrease in the magnitude of β-hydrogen hyperfine splitting constants in the nitroxides, (7) > (8) ≈ (9) > (10), is probably due to the variation of steric factors in the alkyl part of the α-alkylbenzyl group, because the electronegativities of α-alkylbenzyl groups in these nitroxides are considered to be almost the same. The small values of β-hydrogen hyperfine splitting constants in the nitroxides (17), (19)—(22), and (24) indicate that the dihedral angle between the p_z orbital and the C_{β}–H bond is close to 90°. On the other hand, remarkably smaller values in the nitroxides (14) and (15) than in the nitroxides (7)—(10) are probably due largely to the greater electronegativity of oxygen than of carbon, because acetoxy- and methoxy-groups are not expected to be bulkier than n-propyl and isopropyl groups.

In the spectra of alkyl(phenyl)nitroxides, the hyperfine splitting constants by the γ-methyl, γ-methylene, or γ-methine hydrogen atoms were often observed [see the nitroxides (4), (7)—(10), and (36)], although these couplings are not observed unless the linewidth is small. Long-range couplings thus also serve to identify the spin adduct in some cases.

Amino(phenyl)nitroxides can easily be distinguished by the splitting pattern attributable to the β-nitrogen atom. Not enough spectral data for amino(phenyl)nitroxides are available to estimate the structure of amino-radicals trapped.

In the case of tertiary alkyl(phenyl)nitroxides the splitting due to tertiary alkyl group is generally not observed, and so the identification of trapped radical is difficult. The distinction among tertiary alkyl, alkoxy-, thiophenoxy-, and acyl groups is possible, however, from nitrogen hyperfine splitting constants and *g*-values. The hyperfine splitting constant of γ-hydrogen atoms, if observed, may be available to elucidate the structure of the spin adduct [see nitroxide (4)].

Merits and Demerits of Nitrosobenzene as a Spin Trap.—Since a general comparison of the effectiveness of various spin traps has been made by Janzen,[2] the characterization of nitrosobenzene as a spin trap is briefly discussed. The main advantages of the use of nitrosobenzene are the following. (i) Nitrosobenzene is accessible and is easily handled; for example, it exists in active monomeric form to some extent in solution and is not susceptible to photolysis by u.v. irradiation of 365 nm or light of longer wavelength, whereas 2-methyl-2-nitrosopropane is easily decomposed by both red and u.v. light to give di-t-butylnitroxide[25,33] which complicates the spectra in the most interesting region. Only u.v. irradiation at below 310 nm gives diphenylnitroxide.[34] (ii) Spin adducts are usually stable for several hours or more. (iii) The absorption lines in the spectra of spin adducts are very sharp, hence small hyperfine splitting constants can be resolved (see Figure 2). Accordingly, the patterns of these spectra are useful in the identification of the trapped radicals just as in the fingerprint region of i.r. spectra. The main disadvantage of the use of nitrosobenzene is that spectra of spin adducts are more complex than are those from other nitroso-compounds. Analysis of the spectra is not very difficult, but superimposed spectra are too complex to be interpreted. This problem can be considerably avoided by use of 3,5-dideuterionitrosobenzene instead of nitrosobenzene, but this alteration causes line broadening owing to unresolved coupling by deuterium (see Figure 5).

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[32] See, *e.g.*, E. G. Janzen, *Topics Stereochem.*, 1971, **6**, 177.

[33] Th. A. J. W. Wajer, A. Mackor, Th. J. de Boer, and J. D. W. van Voorst, *Tetrahedron*, 1967, **23**, 4021.

[34] K. Maruyama, R. Tanikaga, and R. Goto, *Bull. Chem. Soc. Japan*, 1964, **37**, 1893; P. B. Ayscough, R. C. Sealy, and D. E. Woods, *J. Phys. Chem.*, 1971, **75**, 3454.

EXPERIMENTAL

E.s.r. Spectra.—An inverted U-type mixing cell described by Russell *et al.*[35] was used for all experiments. Benzene (*ca.* 1 ml) containing 0·1—0·2M-nitroso-compound, and nickel peroxide (0·2—1 equivalent amount of the substrate) were placed in one arm of the mixing cell. Into the other arm was placed benzene (*ca.* 1 ml) containing 0·1—1M-substrate. After being degassed with commercial high-purity argon for 15 min, the mixing cell was inverted, and solutions and nickel peroxide were thoroughly mixed at room temperature or somewhat higher (*ca.* 60 °C) for 10—30 s, and allowed to fill a 6 mm i.d. cylindrical quartz cell (for non-polar substrates) or a flat quartz sample cell (for polar substrates). Spectra were immediately recorded at room temperature on a Varian V-4502-15 *X*-band spectrometer with 100 kHz magnetic field modulation. A Varian F-8 nuclear fluxmeter and a Takeda Riken TR-5578 frequency counter were employed to monitor the magnetic field H. The microwave frequency ν was determined by combining a Takeda Riken TR-3001 digital frequency counter plug-in, a TR-3011 M frequency counter, and a TR-5578 frequency counter. The g-value was calculated from the equation $g = (h/\beta)(\nu/H)$, where H and ν were both measured directly, and the coefficient h/β was experimentally determined so as to reproduce the value $g = 2{\cdot}00550$ for Frémy's salt.[36]

The nitrogen hyperfine splitting constants and g-values in Tables 1—3 were the average values of at least three measurements, and other hyperfine splitting constants were determined by the spectral simulations. The simulation of spectra was carried out with a Facom 270—20/30 computer and an IBM 1627 type-plotter. In order to carry out the simulation, a Lorentzian or a Gaussian wave-form was selected, and the tail was extended to $8W$, where W is the assumed line-width for all the absorption bands.

Reagents.—Compounds were mostly commercial, purified where necessary by crystallisation or distillation. In order to remove the contaminated hydroperoxides aromatic hydrocarbons were filtered through a column of active aluminium oxide. Nickel peroxide was prepared by the method of Nakagawa *et al.*,[6] and its available oxygen content was $0{\cdot}318 \times 10^{-2}$ g-atom g^{-1}. Nitrosobenzene was recrystallised from ethanol and stored in the dark at −20 °C, and 0·1M-benzene solution gave no paramagnetic impurity. 3,5-Dideuterionitrosobenzene, 4-deuterionitrosobenzene, *p*-nitrosotoluene,[37] and *p*-t-butylnitrosobenzene were prepared by the oxidation of corresponding anilines with neutralised Caro's acid. *p*-t-Butylnitrosobenzene was a green liquid which solidified at temperatures lower than *ca.* −10 °C to give a green solid. 3,5-Dideuterioaniline was obtained from 2,3,4,5,6-pentadeuterioaniline by a method similar to that of Russell *et al.*,[38] by which 2,4,6-trideuterioaniline was obtained from aniline, and 4-deuterioaniline was prepared by the reduction of 4-bromoaniline with tri-n-butyltin deuteride. 2-Methyl-2-nitrosopropane was synthesized by Emmons' procedure.[39] 3,5-Dideuteriophenol and 2,4,6-trideuteriophenol were obtained by the diazotisation and hydrolysis of corresponding anilines.

Oxidation of Cumene with Nickel Peroxide.—Cumene (240 mg, 2 mmol) and nickel peroxide (630 mg, 2 equiv. of cumene) in benzene (5 ml) were stirred under argon or in air at room temperature for 1 day. Nickel peroxide was filtered off and the benzene solution was examined by g.l.c. (Shimazu GC-5APTF, 1·5 m × 3 mm i.d. packed glass columns with 3% OV-1 on Gaschrom Q and 3% Apiezon L grease on Chromosorb W, programmed from 80 to 180 °C at 5 °C min^{-1}). The solution mostly consisted of unchanged cumene along with small amounts of three compounds. α-Cumyl alcohol was the major product (*ca.* 80%), and other products were α,α′-bicumyl (*ca.* 5%) and an unidentified compound (*ca.* 15%). Substantial differences were not recognized between the reactions under an argon atmosphere and in air. α-Cumyl alcohol and α,α′-bicumyl were identified by comparison with authentic samples.

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[2/1160 *Received*, 22*nd May*, 1972]

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[36] J. A. Adams and J. R. Thomas, *J. Chem. Phys.*, 1964, **39**, 1904.

[37] J. Hamer and M. Ahmad, in ' 1,4-Cycloaddition Reactions,' ed. J. Hamer, Academic Press, New York, 1967, p. 448.

[38] G. A. Russell, E. J. Geels, F. J. Smentowski, K.-Y. Chang, J. Reynolds, and G. Kaupp, *J. Amer. Chem. Soc.*, 1967, **89**, 3821.

[39] W. D. Emmons, *J. Amer. Chem. Soc.*, 1957, **79**, 6522.