New insights into *N-tert*-butyl-α-phenylnitrone (PBN)† as a spin trap. Part 2.[1] The reactivity of PBN and 5,5-dimethyl-4,5-dihydropyrrole *N*-oxide (DMPO) toward *N*-heteroaromatic bases

Angelo Alberti,[a] Patricia Carloni,[b] Lennart Eberson,*[,c] Lucedio Greci*[,b] and Pierluigi Stipa[b]

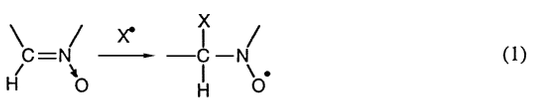
[a] *ICoCEA—CNR, Area della Ricerca, Via P. Gobetti 101, I-40129 Bologna, Italy*
[b] *Dipartimento di Scienze dei Materiali e della Terra, Università di Ancona, Via Brecce Bianche, I-60131 Ancona, Italy*
[c] *Department of Chemistry, Lund University, PO Box 124, S-221 00 Lund, Sweden*

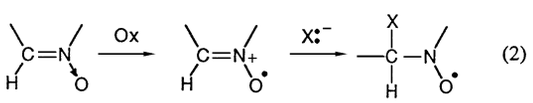
The reactions of *N-tert*-butyl-α-phenylnitrone (PBN) and 5,5-dimethyl-4,5-dihydropyrroline *N*-oxide (DMPO) with a series of *N*-heteroaromatic bases have been studied in different solvents (benzene, dichloromethane, acetonitrile) in the presence of such oxidants as PbO_2, chloranil and tetrabutylammonium dodecatungstocobalt(III)ate. In all cases spin adducts were formed and their corresponding EPR signals were recorded. The formation of the spin adducts, which mostly involves nucleophilic addition of a base to the nitrone and subsequent oxidation (Forrester–Hepburn mechanism) is also discussed and compared to conventional spin trapping and to 'inverted spin trapping'. In order to obtain further evidence for the mechanism involved some reactions were carried out using other oxidants, such as galvinoxyl and 2,2-diphenyl-1-picrylhydrazyl (DPPH).

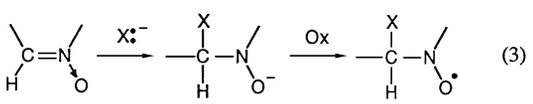
The reaction mechanisms are discussed on the basis of the redox potentials of the studied nucleophiles. Particular attention is given to the benzotriazolyl–DMPO˙ spin adduct, whose generation and decay rates were determined in the presence of some benzoquinones having different redox potentials.

Although several classes of organic compounds have been exploited as spin traps since the introduction of the technique, the majority of the spin traps employed with some success belong to the families of aliphatic and aromatic nitroso compounds and nitrones, such as *N-tert*-butyl-α-arylnitrones and 5,5-dimethyl-4,5-dihydropyrrole *N*-oxides. *N-tert*-Butyl-α-phenylnitrone (PBN) and 5,5-dimethyl-4,5-dihydropyrroline *N*-oxide (DMPO)[2] are by far the most popular compounds used in spin trapping experiments. Indeed these compounds react with virtually all radical species, readily scavenging nucleophilic (alkyls)[3] and electrophilic (alkoxyls,[4] peroxyls[5] and alkylthiyls[6]) as well as organometallic radicals.[7]

On the other hand, the observation of radical adducts from these compounds does not necessarily imply homolytic attack by a radical X˙ at the nitrone function [eqn. (1)]; in fact, PBN

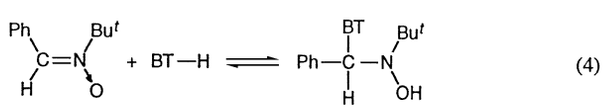

(1)

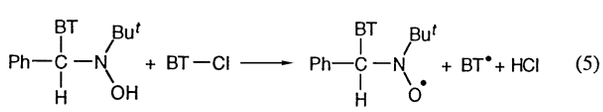

(2)

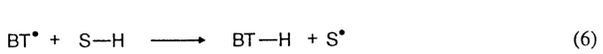

(3)

and DMPO can afford radical adducts under oxidizing conditions according to at least two alternative routes. Thus, in the presence of nucleophiles $X:^-$ spin adducts can be formed by oxidation of the spin trap to its radical cation and reaction of the latter with the nucleophile [eqn. (2)], a process denoted 'inverted spin-trapping',[8] or by addition of the nucleophile to the nitrone function followed by oxidation of the resulting adduct, a hydroxylamine derivative [eqn. (3)]. While the former mechanism has been clearly demonstrated in low-temperature matrix experiments both for PBN[9] and DMPO,[10] the latter was proposed as early as 1971 by Forrester and Hepburn[11] but little systematic study has been devoted to it. As it has been shown in detail for the formation of benzotriazolyl,[1] imidyl[8d] or trinitromethyl[8e] adducts, distinguishing between these routes is not an easy task, and it is only fair to conclude that many spin trappings purported to have proceeded through route (1) must have actually involved routes (2) and/or (3).

We recently[1] described the formation of the spin adducts between PBN and *N*-chlorobenzotriazole (BT-Cl) and identified an autocatalytic version of eqn. (3) as one of the mechanisms [eqns. (4)–(6)], where S–H is a generic hydrogen atom


(4)


(5)


(6)

donor, such as a solvent molecule. The key step, *i.e.* addition of benzotriazole to PBN, only occurred with the neutral benzotriazole, thus indicating that the equilibrium (4) is shifted to the right by protonation.

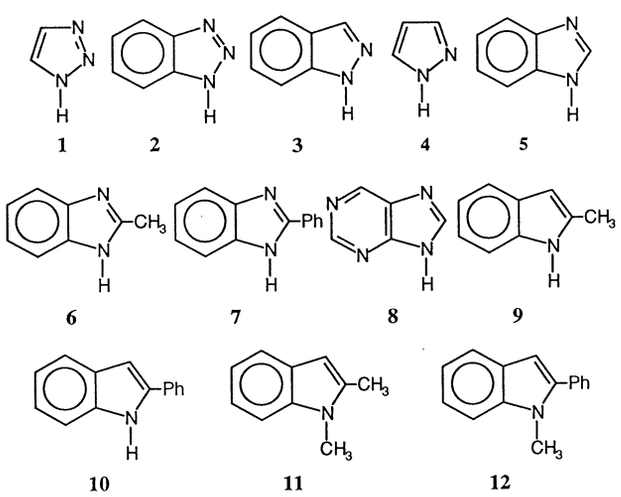
This study deals with the problem of establishing which mechanism operates under weakly oxidizing conditions in the

† IUPAC name: PBN = *N-tert*-butylbenzylideneamine *N*-oxide.

Table 1 PBN spin adducts ($R^{\bullet}$) observed by EPR spectroscopy

Substrate	Spin adduct	R	Substrate	Spin adduct	R
1	**13**	1,2,3-Triazol-1-yl	**6**	**22**	2-Methylbenzimidazol-5–yl
1	**14**	1,2,3-Triazol-2-yl	**7**	**23**	2-Phenylbenzimidazol-1-yl
2	**15**	Benzotriazol-1-yl	**8**	**24**	Purin-7-yl (or -9-yl)
2	**16**	Benzotriazol-2-yl	**8**	**25**	Purin-9-yl (or -7-yl)
3	**17**	Indazol-1-yl	**9**	**26**	2-Methylindol-3-yl
3	**18**	Indazol-3-yl (or 5-yl)	**10**	**27**	2-Phenylindol-3-yl
4	**19**	Pyrazol-1-yl	**11**	**28**	1,2-Dimethylindol-3-yl
5	**20**	Benzimidazol-1-yl	**12**	**29**	1-Methyl-2-phenylindol-3-yl
6	**21**	2-Methylbenzimidazol-1-yl			

reaction between PBN or DMPO and a number of heteroaromatic bases (**1**–**12**, **30**–**32**), which were chosen in order to



cover a wide range of redox potentials (0.5 to 2.1 V *vs.* Ag/Ag^{+}). Lead dioxide, chloranil and other benzoquinones, galvinoxyl, 2,2-diphenyl-1-picrylhydrazyl (DPPH) and tetrabutylammonium dodecatungstocobalt(III)ate were utilized as oxidants. These are all mild oxidants, not capable of forming radical cations thermally from most of the substrates used.

Results and discussion

Oxidation of PBN and compounds 1–12 by lead dioxide or chloranil

Compounds **1**–**12** were allowed to react with PBN in the presence of an oxidant in benzene, acetonitrile or dichloromethane in a sample tube placed inside the cavity of an EPR spectrometer. In all cases, with the exception of the four indole derivatives **9**–**12** the observed spectra indicated coupling of the unpaired electron with a nitrogen atom of the attacking heteroaromatic base in addition to the typical couplings with the nitrogen of the nitroxide function and the β-hydrogen atom. The resulting spin adducts (**13**–**29**) and their EPR spectral data are collected in Tables 1 and 2.

When a benzene solution of 1*H*-1,2,3-triazole **1** and PBN was treated with PbO_2 or chloranil it gave rise to an EPR spectrum consisting of the superposition of two signals due to spin adducts **13** and **14** (see Fig. 1), and the ratio of the two isomeric adducts could be determined as 3:2 through computer simulation of the experimental spectrum. On the other hand, adduct **13** was the only radical species observed upon UV irradiation of a dichloromethane solution of **1** and PBN.

Oxidation of benzotriazole **2** and PBN with chloranil in benzene similarly afforded the two isomeric adducts **15** and **16**, in *ca.* 1:1 ratio. A single radical adduct, namely **15**, was instead observed when oxidizing the mixture with lead dioxide or upon UV irradiation of **2** and PBN in CH_2Cl_2.

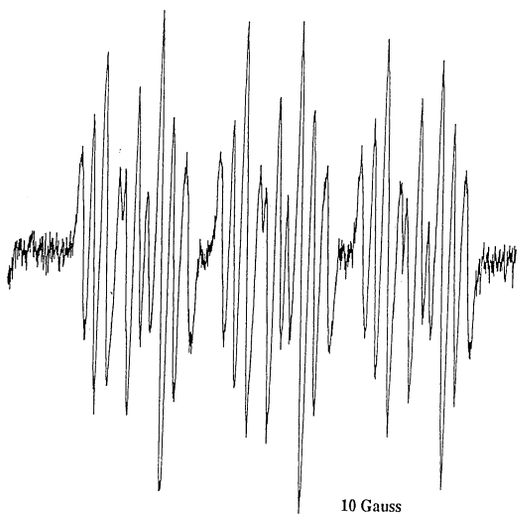


Fig. 1 EPR spectra of the PBN spin adducts **13** and **14** obtained from a benzene solution of **1** and PBN under PbO_2 treatment

These experiments are the key to explaining the reactivity of almost all the compounds investigated. Considering the redox potentials of chloranil ($E_{\frac{1}{2}} = 0.02$ V *vs.* SCE in MeCN or 0.24 V *vs.* NHE; SCE = standard calomel electrode; NHE = normal hydrogen electrode),[12] and the oxidation potentials of triazole **1**, benzotriazole **2** ($E_{\frac{1}{2}ox} = 1.8$ and 1.7 V *vs.* Ag/Ag^{+} respectively) and PBN ($E_{\frac{1}{2}ox} = 1.5$ V *vs.* SCE or 1.73 V *vs.* NHE),[8d,13] we can exclude oxidation of any of these compounds by chloranil. Therefore the formation of both spin adducts **13** and **14** (or **15** and **16**) can be accounted for by assuming nucleophilic addition of triazole **1** (or benzotriazole **2**) to PBN *via* attack at nitrogen 1 or 2, respectively, followed by chloranil oxidation of the resulting hydroxylamino intermediate which undergoes H-abstraction more readily than oxidation to the corresponding radical cation.[14] Similar results were obtained with oxidants such as galvinoxyl ($E_{\frac{1}{2}} = -0.3$ V *vs.* Ag/Ag^{+} in MeCN) and DPPH ($E_{\frac{1}{2}} = 0.05$ V *vs.* Ag/Ag^{+} in MeCN), even if the formation of spin adducts was slower compared to that observed for chloranil. Lead dioxide preferentially acts as a hydrogen atom abstractor:[15] it is therefore able to oxidize the hydroxylamines, but not PBN to its radical cation to form spin adducts *via* eqn. (2).

The fact that UV irradiation of CH_2Cl_2 solutions of either **1** or **2** only leads to the formation of the N-1 adducts **13** and **15**, suggests a radical cation mechanism, the oxidant being in this case the excited singlet state of PBN itself [$E(PBN^{*}/PBN^{\bullet -})$ *ca.* 2.0 V *vs.* NHE].[8d] PBN* would thus oxidize PBN to $PBN^{\bullet +}$ which could then react with the nucleophiles **1** (or **2**) in a more selective process, producing only **13** (or **15**). A significant contribution of PBN* to the formation of the spin adducts by oxidation of any hydroxylamine present can be discarded in view of the very low concentrations of the potentially participating species.

Table 2 EPR spectral parameters of PBN spin adducts **13**–**29**

Substrate	Spin adduct	Solvent	Oxidant[a] or *hv*	a^N/G	a^{other}/G	*g*
1	**13**	Benzene	A or B	13.83	1.18 (1 H_β), 3.29 (1 N)	2.0061_5
1	**14**	Benzene	A or B	13.83	2.63 (1 H_β), 3.95 (1 N)	
1	**13**	CH_2Cl_2	*hv*	13.90	1.30 (1 H_β), 3.47 (1 N)	
2	**15**	Benzene	A or B	13.60	1.70 (1 H_β), 4.20 (1 N)	2.0061_5
2	**16**	Benzene	B	13.60	1.26 (1 H_β), 3.80 (1 N)	
2	**15**	CH_2Cl_2	*hv*	13.70	1.61 (1 H_β), 3.52 (1 N)	
3	**17**	Benzene	A or B	13.85	1.73 (1 H_β), 4.15 (1 N)	2.0061_8
3	**18**	Benzene	A or B	14.60	2.10 (1 H_β)	
3	**17**	CH_2Cl_2	*hv*	13.77	2.15 (1 H_β), 3.76 (1 N)	
4	**19**	Benzene	A or B	13.93	1.34 (1 H_β), 3.60 (1 N)	2.0015_0
4	**19**	MeCN	B	13.97	2.10 (1 H_β), 3.52 (1 N)	
4	**19**	CH_2Cl_2	*hv*	14.05	1.36 (1 H_β), 3.55 (1 N)	
5	**20**	Benzene	B	14.20	2.05 (1 H_β), 3.55 (1 N)	2.0062_3
5	**20**	MeCN	B	13.67	2.76 (1 H_β), 2.76 (1 N)	
5	**20**	CH_2Cl_2	*hv*	13.87	2.43 (1 H_β), 3.04 (1 N)	
6	**21**	MeCN	B	13.42	3.63 (1 H_β), 4.58 (1 N)	2.0062_4
6	**21**	CH_2Cl_2	*hv*	13.54	3.90 (1 H_β), 3.90 (1 N)	
6	**22**	MeCN	B	13.24	4.06 (1 H_β),	
7	**23**	Benzene	B	13.65	4.84 (1 H_β), 4.43 (1 N)	2.0062_0
7	**23**	MeCN	B	13.56	4.21 (1 H_β), 3.81 (1 N)	
7	**23**	CH_2Cl_2	*hv*	13.44	4.10 (1 H_β), 3.78 (1 N)	
8	**24**	C	B	14.03	2.24 (1 H_β), 3.98 (1 N)	2.0061_0
8	**25**	C	B	14.34	2.45 (1 H_β), 2.45 (1 N)	
9	**26**	Benzene	A or B	14.70	2.75 (1 H_β)	2.0060_0
10	**27**	Benzene	A or B	14.35	2.93 (1 H_β)	2.0060_0
11	**28**	Benzene	A or B	14.50	2.22 (1 H_β)	2.0060_0
12	**29**	Benzene	A or B	14.80	3.60 (1 H_β)	2.0060_0

[a] A = PbO_2; B = chloranil; C = MeCN–H_2O (95.5).

Table 3 Redox potentials $E_{\frac{1}{2}}$ for compounds **1**–**12** in MeCN–TEAP *vs.* Ag/Ag^+ (NHE = Ag/Ag^+ + 0.54 V)

Compound	$E_{\frac{1}{2}}$/V	Compound	$E_{\frac{1}{2}}$/V
1*H*-1,2,3-Triazole, **1**	1.8	2-Phenylbenzimidazole, **7**	1.0
Benzotriazole, **2**	1.7	Purine, **8**	2.1
Indazole, **3**	1.15	2-Methylindole, **9**	0.6
Pyrazole, **4**	1.7	2-Phenylindole, **10**	0.73[28]
Benzimidazole, **5**	1.1	1,2-Dimethylindole, **11**	0.5
2-Methyl-benzimidazole, **6**	1.0	1-Methyl-2-phenylindole, **12**	0.64[28]

When a mixture of indazole **3** and PBN was oxidized with PbO_2, a spectrum due to spin adduct **17** could be observed over a few days. A similar spectrum was also detected when using chloranil as oxidizing agent; however, under these conditions the EPR signal was replaced within one hour by a new and persistent spectrum which does not show any coupling of the unpaired electron with either of the heterocyclic nitrogen atoms of the indazole moiety. In the light of the known reactivity of indazoles,[16] which are known to react with electrophiles at position 3 in addition to position 1, we attribute it to the indazol-3-yl radical adduct **18**.[17] In this case, the result of the chloranil experiment indicates that replacing BT–H with indazole the equilibrium of eqn. (4) is more readily attained in the reaction with position 1 of indazole, and more slowly but completely in the reaction with position 3. The photochemical reaction of **3** and PBN in dichloromethane gave only spin adduct **17**.

Pyrazole **4**, which has the same heterocyclic moiety as indazole, somewhat surprisingly only gave rise to the spin adduct **19** whatever the oxidant used and the reaction conditions employed.

The three benzimidazoles **5**–**7** showed a very similar behaviour; in each case the spin-adduct (**20**, **21** or **23**) formed by the attack on PBN through the nitrogen of the benzimidazole nucleus was observed when performing the reaction in the presence of chloranil either in benzene or in acetonitrile. In the case of **20** there was a substantial solvent effect on the values of the spectral parameters, as is evidenced in Fig. 2. When PbO_2 was used as an oxidant in acetonitrile, the spin adducts were not obtained. A second spin adduct **22** was also observed in the reaction of **6** with PBN in the presence of chloranil. This radical was assigned to a spin adduct in which the benzimidazole **6** is added to PBN through the C-5 carbon of the benzimidazole moiety. This gives rise to a signal consisting of a triplet of doublets similar to that observed for indazole **3**. It is indeed known that the hetero ring of benzimidazoles is highly deactivated to electrophilic substitution, with the result that the few reactions which do take place, occur in the benzene ring, generally at position 5 or, to a lesser extent, at position 6.[18] Why similar adducts were not observed with benzimidazoles **4** and **6** remains an unanswered question.

Adducts **20**–**23** are probably formed through the mechanism of eqn. (3). A proper spin trapping process, involving oxidation of the substrates with formation of benzimidazole radical cations, proton loss from the latter and final trapping of the neutral benzimidazol-1-yl radical by PBN should be ruled out. In fact the large difference between the redox potentials of chloranil and of **5**–**7** (*ca.* 1.3 eV), would correspond to an endoergonicity of the ET step of *ca.* 30 kcal mol^{-1} (1 cal = 4.184 J).

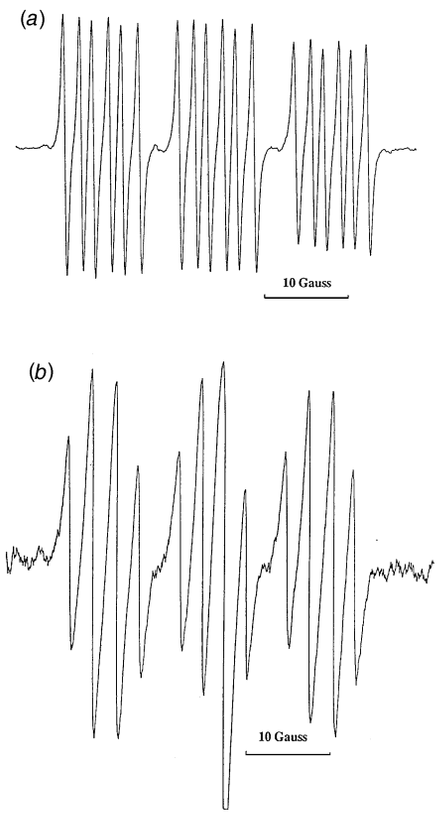


Fig. 2 EPR spectra of the PBN spin adduct **20** in benzene (*a*) or in MeCN (*b*)

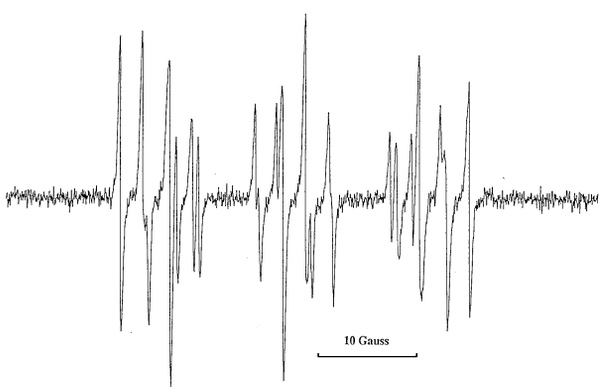


Fig. 3 EPR spectra of the PBN spin adducts **24** and **25** obtained from a MeCN–H_2O 95:5 solution of **8** and PBN under chloranil treatment

The reaction of purine **8** with PBN was carried out in 95:5 MeCN–H_2O (water having been added to dissolve **8**) in the presence of chloranil as an oxidant, and resulted in the observation of the two spin adducts **24** and **25** (see Fig. 3). Unfortunately, the EPR spectral data do not allow the assignment of a definite structure to these adducts. The high redox potential of the $\mathbf{8}^{\bullet+}$/**8** pair leaves the nucleophilic addition of eqn. (3) as the only plausible mechanism for the formation of the adducts.

Among the compounds studied, indoles **9**–**12** possess the lowest oxidation potentials (0.5 to 0.7 V *vs.* Ag/Ag^+) and the corresponding spin adducts **26**–**29** (all formed by attack at the position 3 of the indole moiety) may be obtained *via* different routes. By using PbO_2, the spin adducts are hardly formed indicating a very slow nucleophilic addition of the indole to PBN and subsequent oxidation of the adduct by PbO_2. When using chloranil, a very deep-violet colour was observed; as the same colour is also observed by mixing only indoles with chloranil,[19] the formation of a CT complex appears likely. The relatively low endoergonicity of the indole–chloranil ET step, *ca.* 20 kcal mol^{-1} makes the formation of an indole radical cation possible.

Table 4 EPR spectral data for spin adducts formed in the reaction between a heteroaromatic base (0.1 mol dm^{-3}), DMPO (0.025 mol dm^{-3}), and $Co^{III}W$ (0.001–0.002 mol dm^{-3}), in dichloromethane or acetonitrile

Base	Solvent	a^N/G	a^{other}/G	Reaction period[a]/min
1	MeCN	13.22	15.02 (1 H_β), 4.54 (1 N)	5
1	CH_2Cl_2	13.3	14.30 (1 H_β), 4.57 (1 N)	20
2	MeCN	13.5	15.40 (1 H_β), 3.86 (1 N)	10
2	CH_2Cl_2	13.36	13.96 (1 H_β), 4.03 (1 N)	10
$Bu_4N^+\mathbf{2}^-$	MeCN	No signal		
$Bu_4N^+\mathbf{2}^{-b}$	MeCN	13.4	15.4 (1 H_β), 3.84 (1 N)	
3[c]	MeCN	13.7	15.6 (1 H_β), 3.6 (1 N)	
5	MeCN	13.5	16.30 (1 H_β), 3.20 (1 N)	120
5	CH_2Cl_2	13.1	16.40 (1 H_β), 3.52 (1 N)	120
8	A	No signal[d]		
30	MeCN	13.3	15.10 (1 H_β), 3.91 (1 N)	20
31	MeCN	13.2	15.10 (1 H_β), 4.50 (1 N)	40
32	CH_2Cl_2	13.0	17.60 (1 H_β), 4.80 (1 N)	

[a] Approximate time for change from yellow to blue. [b] Equivalent amount of TFA added. [c] Only with UV light. [d] HO–DMPO$^\bullet$ seen with chloranil. A: MeCN–H_2O (95:5).

Oxidation of PBN and 2 by tetrabutylammonium dodecatungstocobalt(III)ate

Extensive studies[20] have shown that the dodecatungstocobalt(III)ate ion, $[Co^{III}W_{12}O_{40}]^{-5}$ (to be denoted $Co^{III}W$ in the following) is an almost ideal outer-sphere ET reagent toward organic molecules as a result of the screening of the Co^{III} ion by a sheath of tungsten oxide octahedra. Thus only very weakly basic and non-nucleophilic oxygen atoms are exposed toward other species. In organic solvents, the tetrabutylammonium salt has a relatively low redox potential, $E_{\frac{1}{2}}(Co^{III}/Co^{II})$ being *ca.* 0.2 V *vs.* SCE in CH_2Cl_2 or acetonitrile[21] (0.43 V *vs.* NHE). Since the oxidants used above possess reactivities other than outer-sphere ET, it was of some interest to test $Co^{III}W$ as well.

Treatment of a mixture of PBN and **2** in dichloromethane by the Bu_4N^+ salt of $Co^{III}W$ in the dark gave no signal of **15** and **16** during the first 3 h. The yellow sample was then kept in the dark at 22 °C; after 24 h a weak signal due to **15** appeared and it grew for the period it was monitored (*ca.* 100 h). During this period, the colour of the solution turned to green due to the formation of the $Co^{II}W$ species (blue). Thus $Co^{III}W$ appears to be a slowly reacting ET oxidant toward the hydroxylamine intermediate(s) formed; alternatively, the position of the equilibrium is strongly situated to the left leading to a low rate of the second-order reaction between the hydroxylamine and $Co^{III}W$.

The irradiation (UV) of a similar solution of PBN, **2** and the Bu_4N^+ salt of $Co^{III}W$ within 1 min led to the observation of a very strong spectrum of **15**. As demonstrated earlier,[8c] the formation of the spin adduct in this type of reaction most likely proceeds by excitation of PBN to PBN*, which is oxidized to $PBN^{\bullet+}$ by $Co^{III}W$. The nucleophile subsequently reacts with $PBN^{\bullet+}$ to give the spin adduct.

Oxidation of DMPO and compounds 1–3, 5, 8, 30–32 by tetrabutylammonium dodecatungstocobalt(III)ate

Since the low rate observed in the PBN/**2**/$Co^{III}W$ experiment might be due to a combination of a slow rate of the forward reaction and the low concentration of $Co^{III}W$, resulting in a slow second-order reaction, it was expected that the nucleophile addition to DMPO would be more favourable due to the relief of strain in going from the unsaturated to the saturated five-membered ring upon addition of **2**. This expectation was fulfilled. When the above experiment was repeated with DMPO, **2** and $Co^{III}W$ in dichloromethane, an EPR signal (see Table 4)

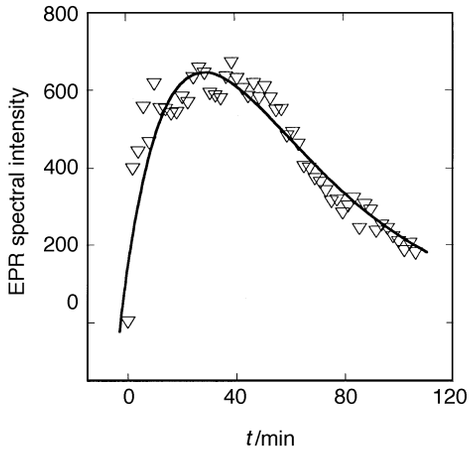


Fig. 4 Time development of the absolute intensity of the EPR spectral signal of the *N*-benzotriazol-1-yl–adduct of DMPO (left-most line of the signal) from a solution of DMPO (0.025 mol dm^{-3}), **2** (0.133 mol dm^{-3}) and the Bu_4N^+ salt of $Co^{III}W$ (initially *ca.* 1 mmol dm^{-3}) in acetonitrile. Five spectra were accumulated per point. The curve represents the best fit of a double exponential function to the data points with the rate constants given in the text.

assigned to a benzotriazolyl adduct of DMPO immediately developed. The solution became blue after 10–15 min, signalling the complete consumption of the $Co^{III}W$. A check experiment with $Co^{III}W$ and either DMPO or **2** showed no consumption of oxidant after 30 min. When the tetrabutylammonium salt of **2** was used in a similar experiment, no signal of the spin adduct developed during 1 h and no colour change was observed. Addition of 1 equiv. of trifluoroacetic acid immediately induced the formation of the spin adduct.

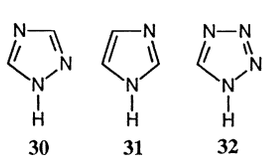
The reaction was also performed in acetonitrile, affording the same benzotriazolyl–DMPO spin adduct (see Table 4); the biphasic time development of the signal is shown in Fig. 4. The rate constants $k_{up} = 0.03(1)$ and $k_{down} = 0.04(1)$ min^{-1} are identical within the limits of experimental error. A duplicate experiment gave $k_{up} = 0.04(1)$ and $k_{down} = 0.06(2)$ min^{-1}. This indicates that the formation of the spin adduct is the rate-determining step and thus controls the rate of its decay.

In separate experiments [$Co^{III}W$] was monitored by UV–VIS spectroscopy at 22 °C, showing that its disappearance followed pseudo-first-order behaviour at constant $[DMPO]_o$ and $[\mathbf{2}]_o \gg [Co^{III}W]_o$ [eqn. (7)].

$$-d[Co^{III}W]/dt = k_{obs}[Co^{III}W] = -k[Co^{III}W][DMPO]_o\,[\mathbf{2}]_o \quad (7)$$

From six runs at varying initial concentrations of DMPO and **2**, an approximate value of k was obtained as 0.32(8) dm^6 mol^{-2} s^{-1}. The value of k obtained from the EPR experiment of Fig. 4 is 0.16(4) dm^6 mol^{-2} s^{-1} and from its duplicate 0.20(4) dm^6 mol^{-2} s^{-1}. The agreement between the results of the two methods is satisfactory in view of the less than ideal concentration conditions necessary to run the reaction.

Table 4 also gives hyperfine splitting (hfs) constants for spin adducts between DMPO and **1**, **3**, **5**, 1*H*-1,2,4-triazole **30**, imidazole **31** and 1*H*-tetrazole **32** in acetonitrile and dichloromethane generated by the $Co^{III}W$ method. Purine **8** did not give a spin adduct under these conditions.



Oxidation of DMPO and 2 by benzoquinones

In order to study the effect of varying the redox potential of the oxidant, a series of benzoquinones were allowed to react with a solution of benzotriazole **2** and DMPO in acetonitrile under as standardized conditions as possible. The initial intensity of the signal was recorded, and the rate of disappearance of the signal monitored in a few typical cases. The results are shown in Table 5. The spin adduct proved much less persistent when generated by the strong oxidant, 2,3-dichloro-4,4-dicyanobenzoquinone (DDQ), which has an $E°(Q/Q^{\bullet -})$ at least 0.5 V more positive than the other benzoquinones employed. This finding is in line with the fact that nitroxyl radicals have $E°(R_2N–O^{\bullet}/R_2N–O^+)$ between 0.6 and 0.8 V *vs.* SCE[22] (0.83 and 1.03 V *vs.* NHE).

Table 5 Generation of the benzotriazolyl–DMPO$^{\bullet}$ spin adduct by treatment of DMPO (0.025 mol dm^{-3}) and **2** (0.1 mol dm^{-3}) in acetonitrile with a benzoquinone Q (0.02–0.04 mol dm^{-3}) in the dark, and determination of its decay rate constant, k_{decay}

Substituent in quinone (Q)	$E°(Q/Q^{-1})$/ V *vs.* SCE	Intensity[a]	k_{decay} of spin adduct/min^{-1}
2,3-Dichloro-4,5-dicyano-	0.51	250	0.50
Tetrachloro-	0.02	120	2.7×10^{-4}
2,3-Dichloro-	−0.18	130	—
None	−0.51	130	1.5×10^{-4}
Tetramethyl-	−0.76	64	—

[a] See Experimental.

Conclusions

The reaction between PBN or DMPO with a range of heterocyclic N–H bases in the presence of a weak oxidant represents a typical case of the Forrester–Hepburn mechanism, *i.e.* addition of the base to the spin trap to give a hydroxylamine derivative, followed by oxidation of the latter. The initial addition process is presumably an equilibrium, as shown by the kinetic dependence of the consumption of the oxidant on both $[spin\ trap]_o$ and $[base]_o$ in the case of the DMPO/**2**/$Co^{III}W$ reaction.

This reaction type has several advantages for studying the Forrester–Hepburn mechanism. The reaction produces relatively persistent spin adducts with characteristic EPR spectra, thus allowing for easy monitoring of the spin adduct. The oxidants employed are weak and cannot undergo electron transfer from either of the other reaction components, thus excluding competition from the radical cation mediated mechanism.

Experimental

EPR experiments were carried out on a Varian E-4 spectrometer or the upgraded version ESP-3220-200SH of a Bruker ER200D spectrometer. PBN, DMPO, chloranil, benzoquinones, galvinoxyl, DPPH and compounds **1**–**5** and **8**–**11** were purchased from Aldrich and used as received. Compounds **6**,[23] **7**,[23] **12**,[24] lead dioxide[25] and tetrabutylammonium dodecatungstocobalt(III)ate[21] were prepared according to literature procedures.

EPR measurements

The reactions in Ancona were performed using an inverted U cell similar to that described in the literature.[26] PBN (1 mg, 5 μmol) and the appropriate nucleophile (50 μmol) were put in one of the two inverted legs and dissolved in 1 ml of solvent. PbO_2 (10 mg), or chloranil (0.5 mg, 2 μmol), or galvinoxyl (0.4 mg, 1 μmol), or DPPH (0.4 mg, 1 μmol) were put into the other leg in 1 ml of solvent. The two solutions were carefully degassed with nitrogen or argon, mixed and then transferred immediately into the EPR cavity. The experiments performed under irradiation were carried out in the same way irradiating the EPR cavity with a 70 W mercury lamp.

The reactions at Lund were performed in quartz tubes of 1.0 mm inner diameter in the lower part. A solution of DMPO or

PBN (17.5 μmol, 0.025 mol dm^{-3}) and heteroaromatic base (70 μmol, 0.1 mol dm^{-3}) in 0.70 ml of the appropriate solvent was filled into the tube and bubbled with argon for 1 min, after which time the Bu_4N^+ salt of $Co^{III}W$ (0.001–0.002 mol dm^{-3}) or the benzoquinone (0.02–0.04 mol dm^{-3}) was added. After bubbling for another min, the tube was sealed and transferred to the EPR cavity. The kinetic experiments were performed by the automation routine of the Bruker software. A 50 W mercury lamp was used for runs under irradiation.

Kinetics by UV–VIS spectroscopy

Solutions containing weighed amounts of **2** (10–80 mg) and DMPO (4–8 mg) in 3.00 ml of acetonitrile were prepared. Each reaction was started by the addition of 10–15 mg of the Bu_4N^+ salt of $Co^{III}W$ and the course of the reaction monitored at 22 °C by an HP-8452A spectrophotometer, equipped with standard kinetics software. First-order kinetics were obeyed, and the third-order rate constants computed from six runs with different starting concentrations of **2** and DMPO were 0.22, 0.38, 0.37, 0.44, 0.27 and 0.26 dm^6 mol^{-2} s^{-1}, average value 0.32(8) dm^6 mol^{-2} s^{-1}.

Voltammetric experiments

The electrochemical studies were carried out at room temp. in a three electrode cell described elsewhere,[27] using nitrogen purged MeCN solutions of the compounds studied (10^{-3} mol dm^{-3}), containing 0.1 mol dm^{-3} tetraethylammonium perchlorate (TEAP). Cyclic voltammetric experiments on compounds **1**–**9**, **11**, galvinoxyl and DPPH were performed in the range of sweep rate 0.1–0.5 V s^{-1} using a stationary platinum disk (AMEL 492) of *ca.* 1 mm diameter as working electrode and a platinum wire as auxiliary electrode. Ag/0.1 mol dm^{-3} $AgClO_4$–MeCN/sintered glass disk/0.1 mol dm^{-3} TEAP–MeCN/sintered glass disk was used as reference electrode. The experiments were performed using a multipolarograph AMEL 472/WR coupled with a digital *x/y* recorder AMEL 863.

Acknowledgements

The Italian Ministero dell'Università e della Ricerca Scientifica e Tecnologica (MURST) (L. G.), the Swedish Natural Science Research Council (L. E.) and the Knut and Alice Wallenberg Foundation (L. E.) are gratefully acknowledged for financial support.

References

1 P. Carloni, L. Eberson, L. Greci, P. Sgarabotto and P. Stipa, *J. Chem. Soc., Perkin Trans. 2*, 1996, 1297.
2 For reviews, see (*a*) E. G. Janzen, *Acc. Chem. Res.*, 1971, **4**, 31; (*b*) M. J. Perkins, *Adv. Phys. Org. Chem.*, 1980, **17**, 1; (*c*) V. E. Zubarev, V. N. Belevskii and L. T. Bugaenko, *Russ. Chem. Rev.*, 1979, **48**, 729; (*d*) E. G. Janzen, in *Advances In Free Radical Chemistry*, ed. D. D. Tanner, vol. 1, JAI Press, London, 1990, ch. 6.
3 (*a*) S. Kubow, E. G. Janzen and T. M. Bray, *J. Biol. Chem.*, 1984, **259**, 4447; (*b*) E. G. Janzen, *J. Magn. Reson.*, 1973, 510.
4 J. G. Pacifici and H. L. Browíng, *J. Am. Chem. Soc.*, 1970, **92**, 5231.
5 L. Ueno, M. Kohono, K. Mitsuta, Y. Mizuta and S. Kanegasaki, *J. Biochem.*, 1989, **105**, 905.
6 C. Mottley and R. Mason, in *Biological Magnetic Resonance 8, Spin Labeling Theory and Applications*, ed. L. Berliner and J. Reuben, Plenum Press, New York, London, 1989, ch. 10.
7 (*a*) P. Riviere, S. Richelme, M. Riviere-Baudet, J. Satge, M. J. S. Gynane and M. F. Lappert, *J. Chem. Res.* (*S*), 1978, 218; (*b*) L. Grossi, L. Lunazzi and G. Placucci, *J. Chem. Soc., Perkin Trans. 2*, 1983, 1831; (*c*) R. G. Gasanov, L. V. Ivanova and R. Kh. Freidlina, *Izv. Akad. Nauk SSSR*, 1984, 938.
8 (*a*) L. Eberson, *J. Chem. Soc., Perkin Trans. 2*, 1992, 1807; (*b*) L. Eberson and M. Nilsson. *Acta Chem. Scand.*, 1993, **47**, 1129; (*c*) L. Eberson, *J. Chem. Soc., Perkin Trans. 2*, 1994, 171; (*d*) L. Eberson, J. Lind and G. Merenyi, *J. Chem. Soc., Perkin Trans. 2*, 1994, 1181; (*e*) L. Eberson, M. P. Hartshorn and O. Persson, *J. Chem. Soc., Perkin Trans. 2*, 1996, 141.
9 V. E. Zubarev and O. Brede, *J. Chem. Soc., Perkin Trans. 2*, 1994, 1821; 1995, 2183.
10 H. Chandra and M. C. R. Symons, *J. Chem. Soc., Chem. Commun.*, 1986, 1301.
11 A. R. Forrester and S. P. Hepburn, *J. Chem. Soc.* (*C*), 1971, 701.
12 (*a*) F. M. Martens, J. W. Verhoeven, R. A. Gase, U. K. Pandit and Th. J. de Boer, *Tetrahedron*, 1978, **34**, 443; (*b*) R. Foster, *Organic Charge Transfer Complexes*, Academic Press, London, 1969.
13 G. L. McIntire, H. N. Blount, H. J. Stronks, R. V. Shetty and E. G. Janzen, *J. Phys. Chem.*, 1980, **84**, 916.
14 (*a*) H. Sayo, S. Ozaki and M. Masui, *Chem. Pharm. Bull. Jpn.*, 1973, **21**, 1988; (*b*) P. E. Iversen and H. Lund, *Anal. Chem.*, 1969, **41**, 1322.
15 (*a*) A. Alberti, L. Greci, P. Stipa, P. Sgarabotto and F. Ugozzoli, *Tetrahedron*, 1987, **43**, 3031; (*b*) P. Carloni, L. Cardellini, L. Greci, P. Stipa and A. Faucitano, *Gazz. Chim. Ital.*, 1989, **119**, 621.
16 A. Katritzky, in *Handbook of Heterocyclic Chemistry*, Pergamon Press, Oxford, New York, 1985, p. 339.
17 The remote possibility that **18** be in fact the indazol-5-yl adduct of PBN, resulting from attack at the condensed aromatic ring[18] cannot be excluded.
18 M. R. Grimmet, in *Comprehensive Organic Chemistry*, ed. P. G. Sammes, Pergamon Press, Oxford 1979, vol. 4, p. 357.
19 B. Sabourault, D. Abenhalm and J. Bourdaìs, *J. Heterocycl. Chem.*, 1976, **13**, 241.
20 (*a*) M. Bietti, E. Baciocchi and J. B. F. N. Engberts, *J. Chem. Soc., Chem. Commun.*, 1996, 1307; (*b*) E. Baciocchi, M. Bietti and S. Steenken, *J. Chem. Soc., Perkin Trans. 2*, 1996, 1261; (*c*) E. Baciocchi, M. Bietti and M. Mattioli, *J. Org. Chem.*, 1993, **58**, 7106; (*d*) E. Baciocchi, M. Crescenzi, E. Fasella and M. Mattioli, *J. Org. Chem.*, 1992, **57**, 4684; (*e*) L. Eberson, *J. Am. Chem. Soc.*, 1983, **105**, 3192.
21 L. Eberson and P. Carloni, *Acta Chem. Scand.*, 1991, **45**, 373, and references reported therein.
22 W. Sümmerman and U. Deffner, *Tetrahedron*, 1975, **31**, 593.
23 C. Berti, M. Colonna, L. Greci and L. Marchetti, *J. Heterocycl. Chem.*, 1979, **16**, 17.
24 M. Colonna, L. Greci and M. Poloni, *J. Chem. Soc., Perkin Trans. 2*, 1981, 628.
25 R. Kunh and I. Hammer, *Chem. Ber.*, 1950, **83**, 413.
26 G. A. Russell, E. G. Janzen and E. T. Strom, *J. Am. Chem. Soc.*, 1964, **86**, 1806.
27 (*a*) R. Andruzzi, A. Trazza, L. Greci and A. Marchetti, *Ann. Chim.* (*Rome*), 1979, **69**, 583; (*b*) R. Andruzzi and A. Trazza, *J. Electroanal. Chem.*, 1977, **77**, 101; 1978, **90**, 389.
28 C. Berti, L. Greci, R. Andruzzi and A. Trazza, *J. Org. Chem.*, 1982, **47**, 4895.

Paper 6/08004I
Received 26*th November* 1996
Accepted 15*th January* 1997