PERKIN 2

Synthesis and characterisation of some novel hetero-diradicals containing linked hydrazyl and aminoxyl (nitroxide) moieties

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We report the synthesis and characterisation of some novel hydrazine-derived monoradicals incorporating nitroxide **14**, nitronyl-nitroxide† **15** and imino-nitroxide **16** functions, as well as the corresponding diradicals assigned the hydrazyl-nitroxide **17**, hydrazyl-nitronyl-nitroxide **18** and hydrazyl-imino-nitroxide **19** structures. EPR, UV-Vis and electrochemical (CV) characteristics are reported, along with MS and NMR data where appropriate; pK_a and BDE values are calculated as well as the average interelectronic separation in the triplet diradicals **18** and **19** obtained *via* solid-state EPR measurement and calculations. The reactions of these compounds with short-lived radicals generated by photolysis, as well with NO and NO_2, are also reported.

Introduction

There is considerable contemporary interest in the preparation and properties of stable organic poly-radicals, not least to explore their potential as bases for new magnetic materials (*e.g.* molecular magnets, switching devices, molecular wires) and to probe the nature of the interaction between the unpaired electrons.[1–5] The majority of the stable diradicals produced thus far link two similar (or identical) moieties, as in the bis-nitroxides [see *e.g.* **1**] and nitronyl-nitroxides [see *e.g.* **2**–**4**], the bis-phenoxyl **5** and bis-semiquinone **6** and the bis-hydrazyl **7**.[6–14] A much smaller number of hetero-diradicals have been reported;[15] some recent examples include the phenoxy-nitroxide **8** and the semiquinone-nitroxide **9**. The vast majority of the diradicals so far described have either a conjugated bridge, as in **4**,[9] or a very flexible link as in the bis-nitroxide **10** studied by Falle and Luckhurst.[16]

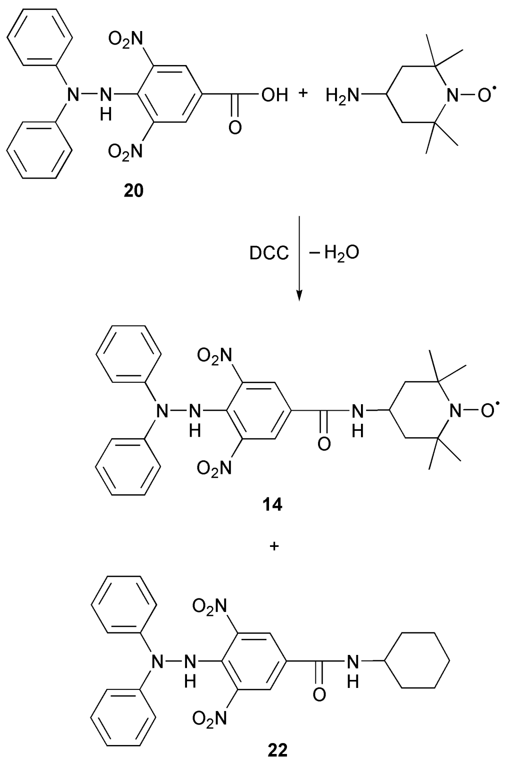
The EPR spectra obtained in solution and/or solid state generally allow a ground state triplet to be identified, with the exchange interaction (J) greater than the characteristic hyperfine splittings from each moiety (giving average hyperfine splittings); in some cases there is evidence from the solid state spectra for a significant zero-field splitting (see *e.g.* refs. 3, 4, and 7).

We set out to prepare a novel series of hydrazyl-nitroxide mono- and di-radicals with the structures shown in **14**–**19**, from appropriate precursors **11**–**13**. These were chosen so that the parent hydrazine and/or hydroxylamine could be oxidized, depending upon conditions, with the aim of determining the properties (absorption spectra, EPR spectra, electrochemical behaviour) of the mono- or di-radicals shown. We intended in particular to examine the magnitude of the magnetic interaction between the two spin sites and to explore the potential of the paramagnetic substrates and/or precursors as spin probes or spin traps. Such probes might be employed, for example, to explore simultaneously two different regions of a multiphasic or macromolecular structure or to detect two different radical species (or oxidants) present: for example, it has been asserted that the nitronyl-nitroxide radicals may be used in identification and quantification of some radicals produced *in vivo* (for example, NO and NO_2, as claimed by Kalyanaraman and co-workers).[17]

Results and discussion

(1) Synthetic strategy

In order to obtain the compounds **11**–**19**, our starting points were the two known hydrazine derivatives, 2,2-diphenyl-1-(2,6-dinitro-4-carboxyphenyl)hydrazine[18] **20** and 2,2-diphenyl-1-(2,6-dinitro-4-cyanophenyl)hydrazine **21** (see Scheme 1 and Scheme 2). For the coupling of **20** and the stable free radical 4-amino-TEMPO (Scheme 1) we obtained a good yield of **14** using 1,3-dicyclohexylcarbodiimide (DCC); using carbonyldiimidazole (CDI) or the acid chloride of **20**, the yields were



Scheme 1

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† The IUPAC name for nitronyl-nitroxide is 4,5-dihydro-4,4,5,5-tetramethyl-3-oxido-1*H*-imidazol-3-ium-1-oxyl.

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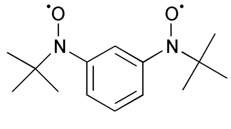
slightly decreased (see Experimental section). The cyclohexylamide by-product **22** was also isolated. The compound **11** could be obtained (but not isolated) by one-electron reduction of **14** with sodium ascorbate. The stable diradical **17** was obtained by oxidation of **14** with either lead dioxide or potassium permanganate.



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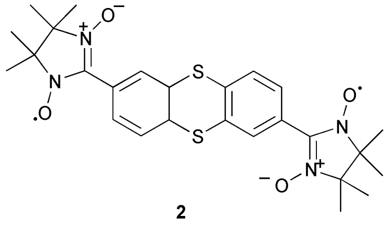

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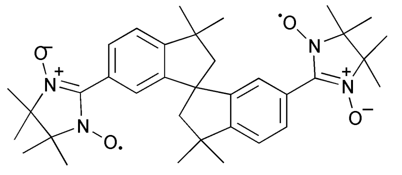

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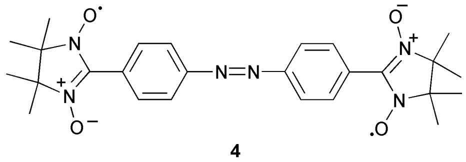

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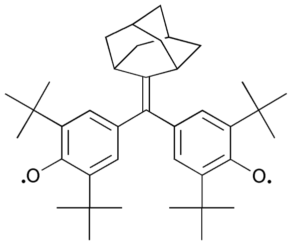

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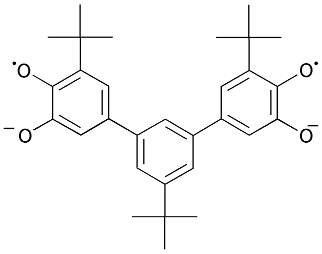

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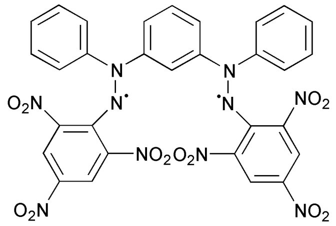

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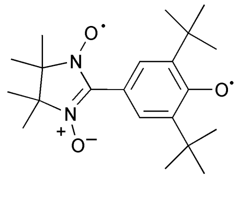

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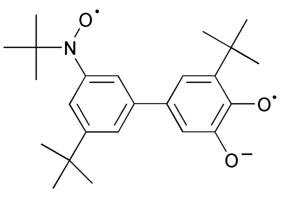

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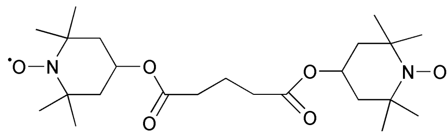

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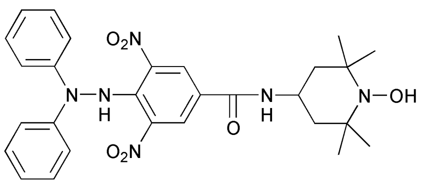

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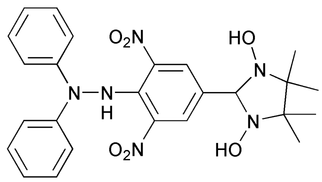

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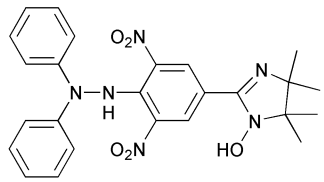

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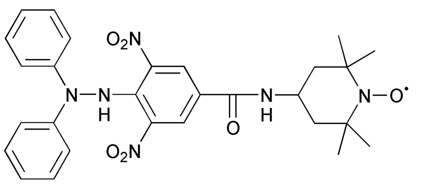

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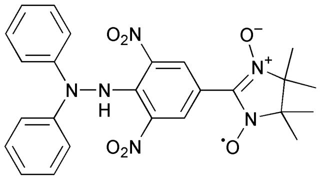

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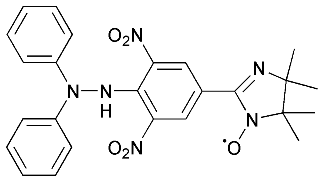

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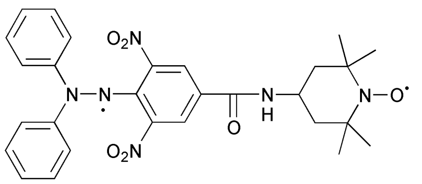

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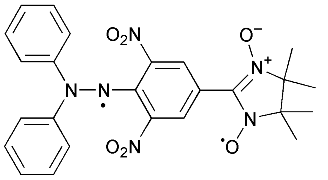

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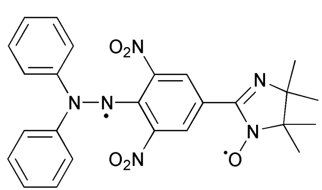

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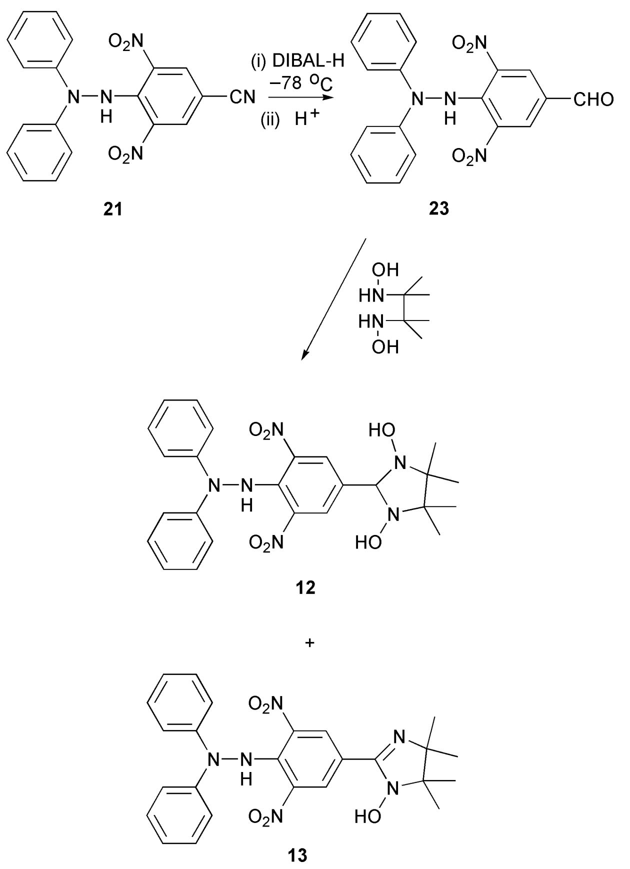


Scheme 2

In a strategy for generating the hydrazyl-nitronyl-nitroxide diradicals **18** and **19**, we attempted to prepare the corresponding hindered hydrazine containing a formyl group (it is well known that the formyl group is a precursor of nitronyl-nitroxide species). We explored the use of five different hydrazine derivatives (which contained the carboxy, acid chloride, amido, methoxycarbonyl and cyano-groups). Our attempts to convert these groups into a formyl group were unsuccesful, except for the route from the cyano-group shown in Scheme 2. Thus, the starting hydrazine **21** was converted into 2,2-diphenyl-1-(2,6-dinitro-4-formylphenyl)hydrazine **23** by reaction with diisobutylaluminium hydride (DIBAL-H) in dichloromethane (DCM) at −78 °C. The aldehyde was subsequently reacted with 2,3-bis(hydroxyamino)-2,3-dimethylbutane, leading to the precursors **12** and **13**, which were separated by column chromatography. These were oxidised to the monoradicals **15** and **16**, or to the diradicals **18** and **19**, depending on the oxidant employed (sodium periodate or potassium permanganate, respectively, see Experimental section). The oxidation process was easily monitored by TLC, UV-Vis and EPR.

(2) Physico-chemical properties of the monoradicals and diradicals

(a) Characteristic visible absorption spectra and interconversion. On oxidation, the yellow–red precursors **11**–**13** (λ_{max} = 392–482 nm; see Table 1) were converted into the monoradicals **14**–**16** with yellow–pink colour (λ_{max} = 392–496 nm), and the diradicals **17**–**19** with the characteristic purple–violet colour of the hydrazyl (λ_{max} = 505–510 nm), depending on the nature of the oxidant (see Scheme 3). For generating the monoradicals **14**–**16**, even the presence of atmospheric oxygen was found to be sufficient, especially in the case of the compound **14**; the hydroxylamines **11**–**13** were also oxidised by sodium periodate to give good yields of monoradicals **14**–**16**. The diradicals **17**–**19** were obtained starting either from the hydroxylamines **11**–**13** or from the monoradicals **14**–**16**, using the more powerful oxidants lead dioxide and potassium permanganate.

Table 1 Values of λ_{max} for **1119** in DCM

Compounds	λ_{max}/nm	Colour
11	392	Yellow
12	404	Yellow
13	482	Yellow–red
14	392	Yellow
15	505	Violet
16	496	Purple
17	486	Pink
18	507	Violet
19	510	Violet
$\mathbf{11}^-$ and $\mathbf{14}^{-a}$	620	Green
$\mathbf{12}^-$ and $\mathbf{15}^{-a}$	645	Green
$\mathbf{13}^-$ and $\mathbf{16}^{-a}$	654	Green

[a] Anions derived from the compounds **11**/**14**, **12**/**15** and **13**/**16**, respectively.

Table 2 Electrochemical values [E_{ox}, E_{red}] obtained for the biradicals **17**–**19** and the anions $\mathbf{11}^-$–$\mathbf{13}^-$ by CV in acetonitrile (in V *vs.* Ag/Ag$^+$)

Compound	$E_{1ox/red}$/V	$E_{2ox/red}$/V	$E_{3ox/red}$/V
$\mathbf{11}^-$	0.173/0.097	0.745/0.634	1.023/—
$\mathbf{12}^-$	0.107/0.077	0.836/0.613	0.972/0.883
$\mathbf{13}^-$	0.130/0.095	0.677/0.613	1.070/—
17	0.180/0.110	0.800/0.640	1.060/—
18	0.149/0.052	0.714/0.636	0.981/0.903
19	0.143/0.012	0.695/0.617	1.039/—

We also found that the monoradicals and diradicals could be reduced to the corresponding parent hydroxylamine-hydrazines [**11**–**13**], using ascorbic acid, cysteine, glutathione or, even better sodium ascorbate, as judged by TLC, UV-Vis and EPR spectroscopy. The diradicals were found to be selectively reduced by hydroquinone to the corresponding monoradicals.

In basic media, compounds **11**–**16** were all found to give the corresponding anions, with green colour (λ_{max} = 620–654 nm), *via* a reversible process (see Table 1).[18–20]

(b) pK_a values. Because the colours of the hydrazines change as a function of pH, it was straightforward to determine the pK_a values for the N–H group by visible spectroscopy, as described elsewhere.[18–20] The pK_a values of the hydrazinic N–H groups were thus determined as 7.82 (± 0.05), 8.07 (± 0.05) and 8.33 (± 0.05), for the compounds **11**–**13**, respectively.

(c) Cyclic voltammetry. Cyclic voltammetry measurements were performed in acetonitrile with inert platinum electrodes on the compounds **11**–**19**, as well as on the corresponding sodium salts of the compounds **11**–**13**. For the compounds **11**–**16** the shape of the voltammograms reflects the multistep oxidation–reduction and protonation–deprotonation processes. The clearest voltammograms were obtained in the case of the diradicals **17**–**19** (see Fig. 1) and for the anions $\mathbf{11}^-$–$\mathbf{13}^-$; only small differences (usually no more than ± 20 mV) were observed between these two series of CVs. Note that, at the starting potential, with the compounds **17**–**19**, the corresponding anions of the hydrazyl moiety are present; in the case of compounds $\mathbf{11}^-$–$\mathbf{13}^-$ the nitroxide moiety is present, due to air oxidation. By comparison with the results for the anions $\mathbf{11}^-$–$\mathbf{13}^-$, and the behaviour of similar hydrazine and hydroxylamine compounds (as well as results obtained here for DPPH, its relatives, and TEMPO radicals),[21–23] we attribute the first wave to oxidation of the hydrazine nitrogen ($N^-/N^•$), the second wave to the oxidation of the nitroxide moiety ($NO^•/NO^+$), and the third wave to the formation of the nitrogen cation ($N^•/N^+$). Thus, these three peaks correspond to the

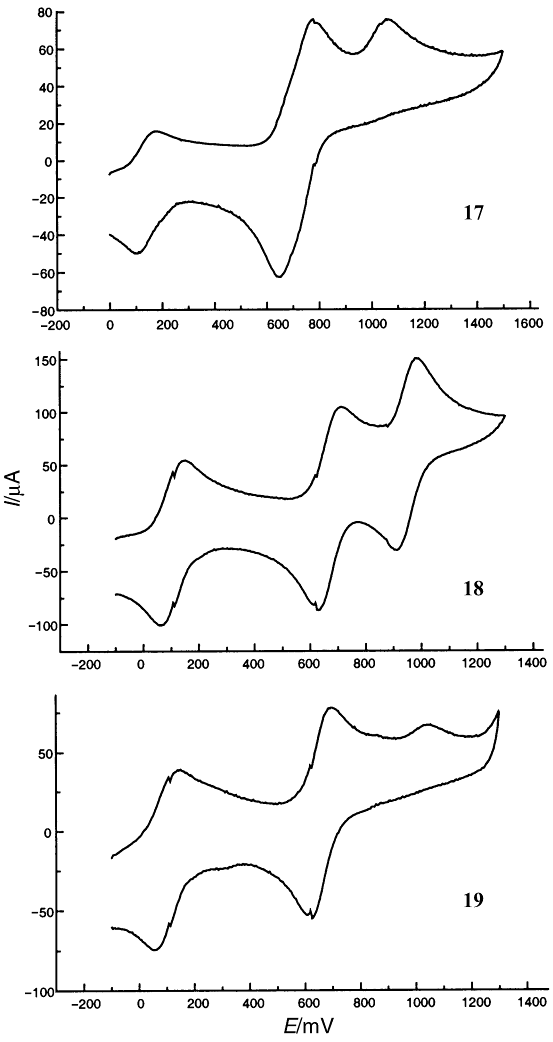


Fig. 1 Cyclic voltammograms of the diradicals **17**, **18** and **19** recorded in acetonitrile (*vs.* Ag^+/Ag).

oxidation processes which result in the formation of hydrazyl radical, nitroxide cation and of a hydrazyl nitrogen cation. Table 2 shows the oxidation and reduction potentials for the compounds **17**–**19**, as well as for the anions $\mathbf{11}^-$–$\mathbf{13}^-$.

Table 3 EPR parameters for the mono- and di-radicals **14**–**19** [a]

Compound	a_N(nitroxide)	a_N(hydrazyl)	a_H	g
14	1.550	—	0.045(4)	2.0062
15	0.743(2)	—	—	2.0068
16	0.892/0.437	—	—	2.0061
17	1.550		0.045(4)	2.0059
		1.247/0.418		2.0048
18	0.740(2)			2.0065
		1.247/0.399		2.0049
19	0.864/0.432			2.0059
		1.340/0.445		2.0049

[a] Hyperfine splittings a/mT and g value; solvent: toluene.

$$\text{R–H} \rightleftharpoons \text{R}^- + \text{H}^+ \quad (1)$$

$$\text{R}^- \rightleftharpoons \text{R}^\bullet + \text{e}^- \quad (2)$$

$$\text{R–H} \rightleftharpoons \text{R}^\bullet + \text{H}^+ + \text{e}^- \quad (3)$$

(d) Evaluation of BDE values for N–H and O–H groups. Our approach to the calculation of the N–H and O–H bond dissociation energies (BDE) is based on a cycle represented by eqns. (1)–(3) and the analysis presented in references 21 and 22; the BDE values (in kcal mol^{-1}) are related to the appropriate pK_a and E_{ox} values (in V) [reactions (1) and (2)] *via* the relationship given by the semi-empirical eqn. (4), with modification to

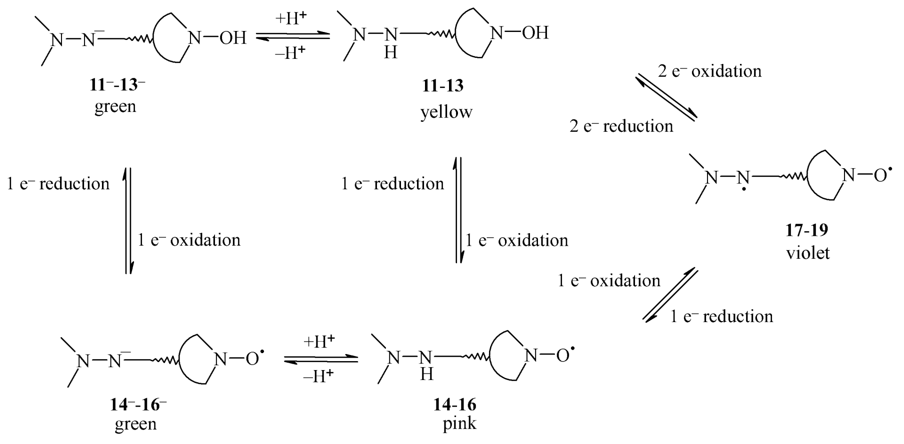
$$\text{BDE} = 1.37\text{p}K_a + 23.06E_{ox} + 56 \quad (4)$$

allow for the solvent employed; the constant 56 is appropriate when E_{ox} is referenced to the standard hydrogen electrode.[21–23]

BDE values calculated in this way for the N–H groups in the compounds **11**–**13** are 75.45, 75.08, and 75.30 kcal mol^{-1} (*cf.* a value of *ca.* 80 kcal mol^{-1} reported for DPPH itself).[23] These values are identical within experimental error. For the O–H groups, the literature data for typical E_{ox} and pK_a values (*ca.* −2.0 V and 31, respectively) lead to an estimated BDE value of 70.0 kcal mol^{-1}.[21] The difference between the BDE values for oxidation of the O–H and N–H groups underpins the use of different oxidants to obtain the corresponding mono- or di-radicals selectively, starting from a given precursor.

(3) EPR spectra

(a) Monoradicals 14–16. Fig. 2 shows the isotropic EPR spectra of the stable monoradicals **14**–**16** recorded in toluene at different temperatures. For the monoradical **14** the spectra show the expected simple triplet (a_N 1.550 mT) altogether with the proton hyperfine splitting ($a_{4H} = 0.045$ mT) discernible on the low field line at 273 K. As expected the nitronyl-nitroxide **15** has two equivalent nitrogen splittings (see Table 3), these being inequivalent in the imino-nitroxide **16**. All the spectra show anisotropic broadening as the temperature is lowered, the patterns of **15** and **16** being particularly distinctive. The frozen samples provide no extra information.



Scheme 3

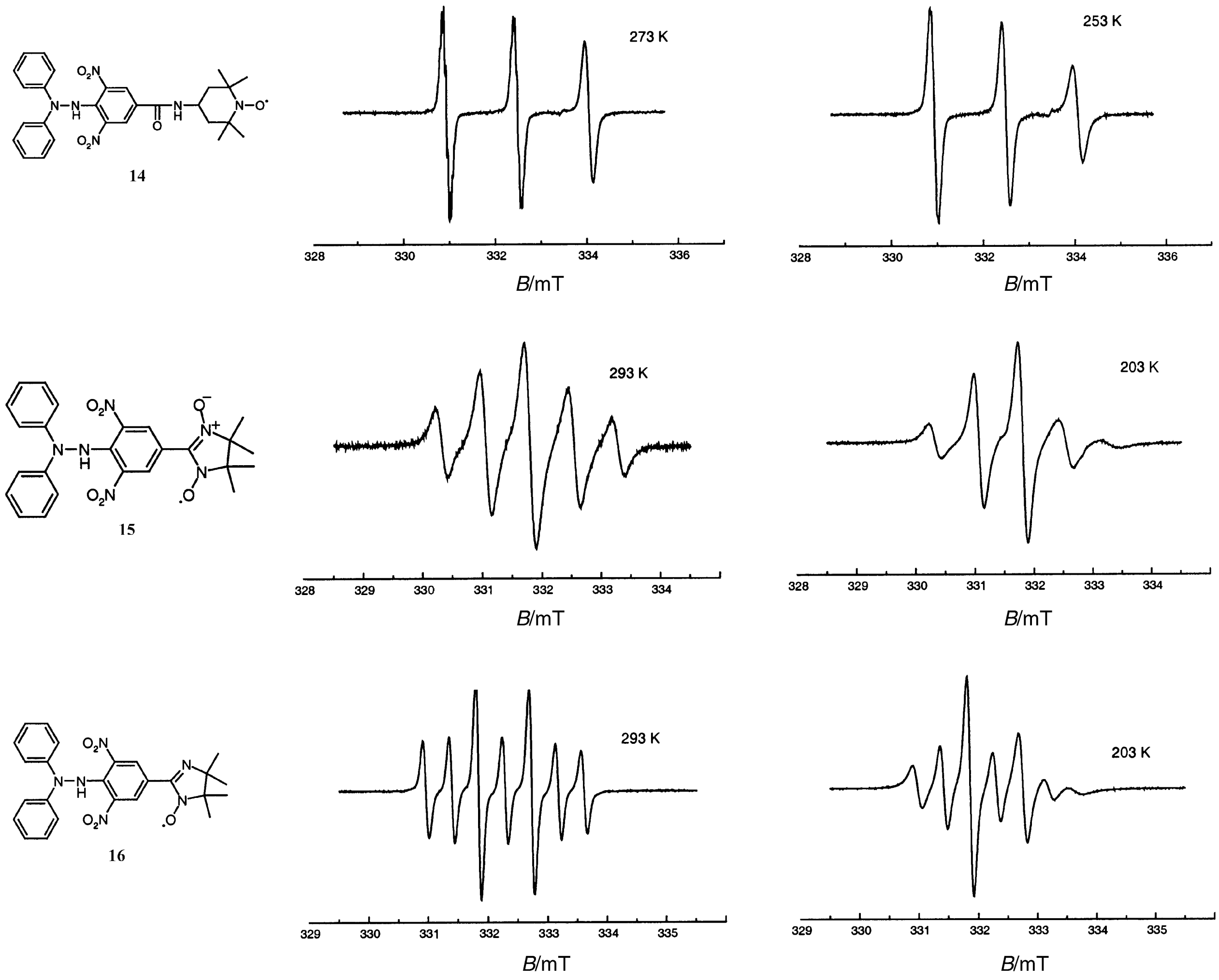
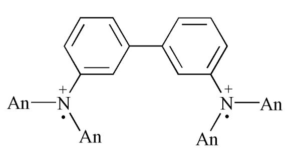


Fig. 2 EPR spectra of the monoradicals **14**–**16** in toluene (10^{-3} M) at selected temperatures.

(b) Diradicals 17–19. Oxidation of **14** or **11** led to the detection of the unconjugated hydrazyl-nitroxide diradical **17** with an EPR spectrum at room temperature consisting of a mixture (1 : 1) of nitroxide and hydrazyl signals (effectively simulated with the parameters listed in Table 3; see Fig. 3). The broad anisotropic spectrum obtained from the frozen sample showed no discernible features, and there was no detectable $\Delta m_s = 2$ signal (which could be characteristic of a triplet state). Thus we have no evidence from these experiments for significant interaction between the two unpaired electrons.[24–26] This may reflect the relatively large separation between the two spin sites (see below).

Oxidation of **12** or **15** with potassium permanganate or lead dioxide similarly led to the formation of the diradical **18**, with the EPR spectrum shown in Fig. 4 [the peaks marked * are due to the presence of the imino-nitroxide radical **16**, probably formed through oxygen loss in the compound **15** (see later)]. The spectrum can be simulated by overlap of the signals from a hydrazyl and nitronyl-nitroxide diradical (*i.e.* with the two radical types present in almost equal concentration) with parameters shown in Table 3; it is notable that the observation of two superimposed and distinct free-radical spectra indicates that the exchange interaction (J) is less than the typical hyperfine couplings [unlike *e.g.* diradicals **2**–**4**]. The spectra broadened on lowering the temperature but gave a sharp line in the solid state. No $\Delta m_s = 2$ features were detectable (which could help characterise a triplet spectrum). However, the appearance of two pairs of peaks (marked x) in the solid state spectrum are characteristic of a triplet (with zero-field splitting $D = 7.65$ mT) superimposed on a sharp singlet spectrum attributed to a monoradical (with a g value 2.0037 characteristic of a hydrazyl). This behaviour, and the appearance of the composite spectrum, resembles that for some structurally related diradicals, including **2**, and especially, the diradical-cations from the diamino-biphenyl derivatives **24** and **25**.[27]



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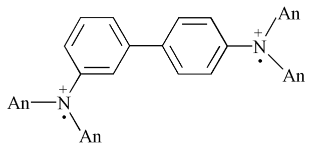

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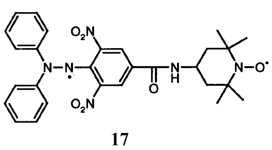
(An = anisyl)

As with the latter, for which J is also small (no averaging observed for the individual hyperfine splittings), $\Delta m_s = 2$ lines are not anticipated given the low value of D.[27] If we make the assumption that the zero-field splitting in this system can be approximated by a point-dipole model with $2D = 3g^2\mu_B{}^2(1/r^3)$ [28] we estimate an average electron-electron separation of 6 Å.

Oxidation of either **13** or **16** under similar conditions led to the formation of diradical **19**, as judged by superposition of the EPR spectrum of the imino-nitroxide (with two different nitrogen splittings) and one broadened hydrazyl moiety (in the ratio 1 : 1, see Fig. 5). Again, the signal broadened then narrowed on cooling, giving a single relative sharp line in a solid matrix, with extra resonances typically of a triplet



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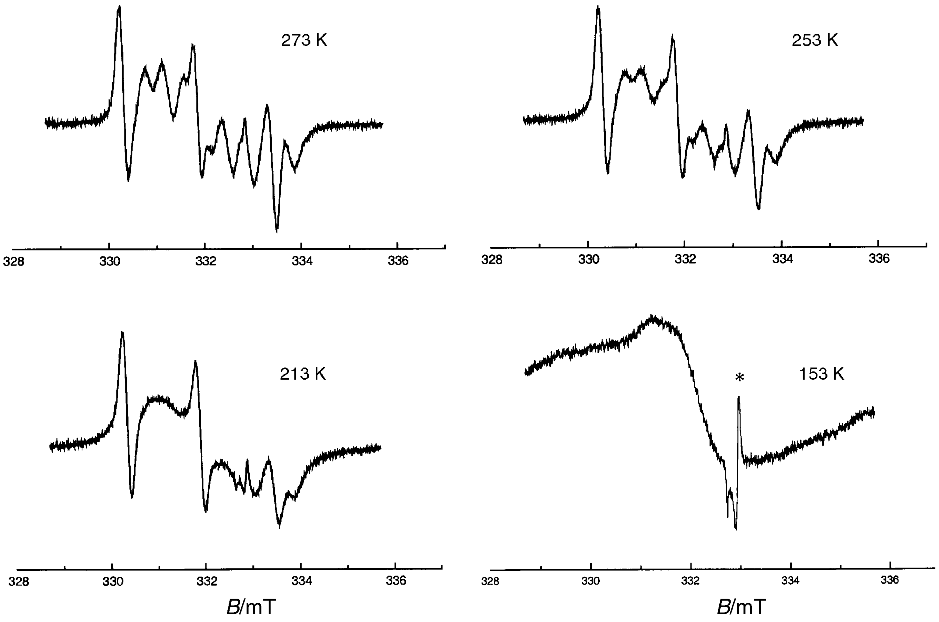
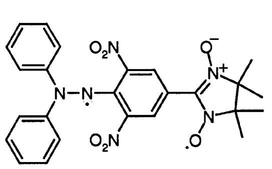


Fig. 3 EPR spectra of the diradical **17** in toluene (10^{-3} M) at selected temperatures (* = peak due to the quartz cell).



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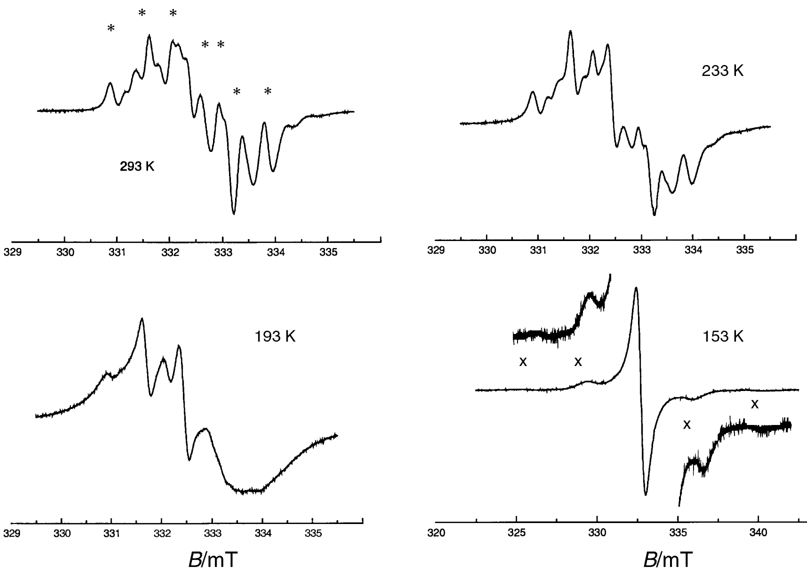


Fig. 4 EPR spectra of diradical **18** in toluene (10^{-3} M) at selected temperatures [peaks marked * are assigned to the radical **16**, and the peaks marked x are associated with the triplet species (see text)].

($D = 7.60$ mT, but with no detectable $\Delta m_s = 2$ transitions). As for **18** the zero-field splitting suggests an average electron–electron separation of spins of about 6 Å, again with low exchange interaction J (no averaging of the hyperfine splittings).

Surprisingly, prolonged oxidation (1–2 days, with PbO_2 or $KMnO_4$) of the substrates **12**, **13**, **15**, and **16** led in each case to the production of an EPR spectrum characteristic of a mixture of **15** and **16**, with a predominance of the latter (imino-nitroxide): no evidence for hydrazyl radicals was obtained. These results are discussed further below.

(4) Structure determination: quantum mechanical calculations

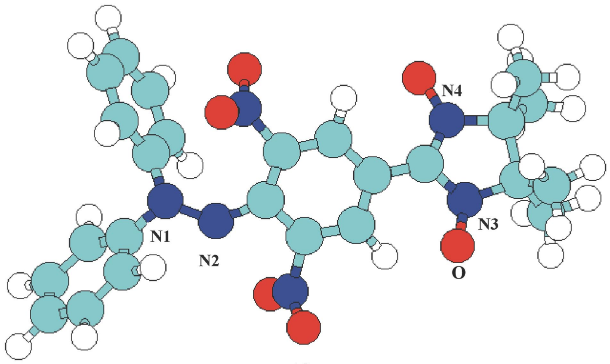
In order to obtain more detailed information about the structure of the diradicals, molecular orbital calculations were performed using Hyperchem and Spartan Pro packages.[29,30] The geometry of the compounds **14**–**19** was first approximated using molecular mechanic (MM+) force fields, and then optimised using one of the semi-empirical methods described below. The determination of the calculated spin population was carried out using semi-empirical quantum mechanics, employing AM1, PM3 and MINDO/3 methods. The values obtained using Hyperchem and the AM1 semi-empirical method were found to be generally in better agreement with the experimental data, as judged by comparison of the observed hyperfine splittings with those calculated using Q values ($Q^{N}_{NN} = 2.28$, $Q^{N}_{NO} = 3.31$ mT)[31,32] for the hydrazyl and nitroxide moieties, respectively; the calculated hydrazyl nitrogen splittings are particularly close for all species, but for the nitroxides, the nitrogen splittings calculated for the imino N in the imino-nitroxide appear to be over-estimated by the approach. The results obtained for the compounds **11**–**19** are compiled in Table 4; the optimised structure of the compound **18** is shown below.

The calculations indicate a significant torsion angle (between the dinitrobenzene ring and the N–O bond) for the diradical **17**, but a much lower value for **19**, suggesting that in the latter the benzenic ring is nearly coplanar with the nitroxide bond. For **18** and **19** the computed distance between the radical centres (the nitrogen atom of the hydrazyl and the oxygen atom

Table 4 Calculation of spin populations (p-orbital) in mono- and di-radicals, and calculated distance between spins and torsion angles

Compd.	N1 (Hydrazine)	N2 (Hydrazyl)	N3 (Nitroxide)	N4 (Nitronyl or imino)	O (Nitroxide)	Distance between spins/Å[a]	Torsion angle/°[b]
14	0.017	0.021	0.271	—	0.659	—	—
15	−0.009	−0.011	0.353	0.318	0.494	—	—
16	0.006	−0.037	0.346	0.592	0.497	—	—
17	0.270	0.602	0.248	—	0.669	10.05	76.10
18	0.307	0.504	0.346	0.329	0.510	6.19	35.74
19	0.244	0.698	0.313	0.568	0.506	6.50	4.90

[a] Distance between the hydrazyl atom (N2) and oxygen-nitroxide (O). [b] Angle between the dinitrobenzene plane and N–O bond.



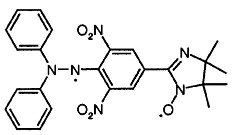
18

of the nitroxide) is *ca.* 6 Å, consistent with the conclusions from the use of the point-dipole approximation discussed earlier. For the diradical **17**, the calculated value is *ca.* 10 Å, which would be expected to lead to a much lower, presumably undetectable value of D, $<$ *ca.* 2 mT (*n.b.* substantially larger distances can be probed *via* pulse techniques, *e.g.* in some alkyne linked bis-nitroxides).[30]

(5) Investigation of mono- and di-radicals as potential probes or scavengers

(a) Selectivity in radical reactions. From the observations described earlier, we can make certain conclusions about the oxidation of the hydrazine and hydroxylamine functions. Thus, the hydroxylamine group is more easily oxidised than the hydrazine group, as shown by the cyclic voltammograms and by the BDE values, as well as the experiments carried out with different oxidants, the stronger oxidant (potassium permanganate) being required for the oxidation of hydrazine. As expected, the reverse phenomenon is apparent for the reduction of the diradicals or monoradicals, the weaker reducing agent (hydroquinone) transforming the diradicals to the monoradicals, and the stronger reducing agents (*e.g.* sodium ascorbate) transforming both di- and mono-radicals to the corresponding hydroxylamines.

(b) Reaction of the compounds 12–19 with short-lived radicals generated by photolysis. We also studied the reaction of the compounds **12**–**19** with the short-lived radicals generated by photolysis of di-*tert*-butyl peroxide (t-BuO$^{\bullet}$), AIBN ($^{\bullet}CMe_2CN$) and acetone (to give Me$^{\bullet}$ and MeCO$^{\bullet}$) or acetone in the presence of propan-2-ol (to give $^{\bullet}CMe_2OH$). The results can be summarised as follows. Compound **12** reacts with any of the short-lived radicals generating first the persistent monoradical **15**, evidently *via* H-abstraction; **15** is subsequently converted slowly into the diradical **18** *via* H-abstraction, as well as **16** *via* oxygen loss (we believe that occurs *via* addition at the nitroxide oxygen, followed by loss of the alkoxy fragment, see Scheme 4). When we employed the monoradical **15** the same result was obtained, namely the initial observation of a mixture of radicals **16** and **18**. Starting from **18**, the main product was found to be a nitronyl-nitroxide [*cf.* **16**]; we believe that, following deoxygenation to **19** the loss of the hydrazyl function may reflect attack of R$^{\bullet}$ on the ring, followed by tautomerisation to regenerate the aromatic hydrazine as noted for NO_2 (see below). In a related fashion, compound **13** led to a mixture of **16** and **19**, formed *via* H-abstraction; starting from **16**,



19

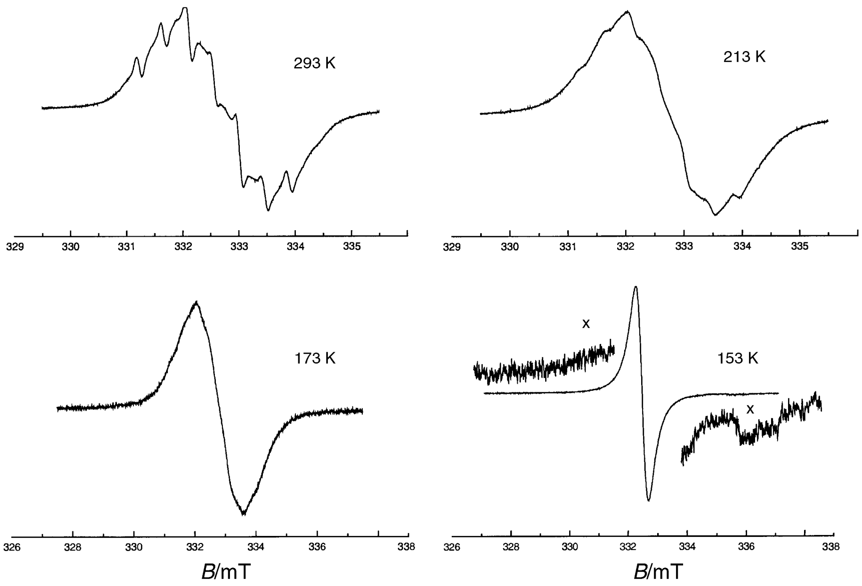
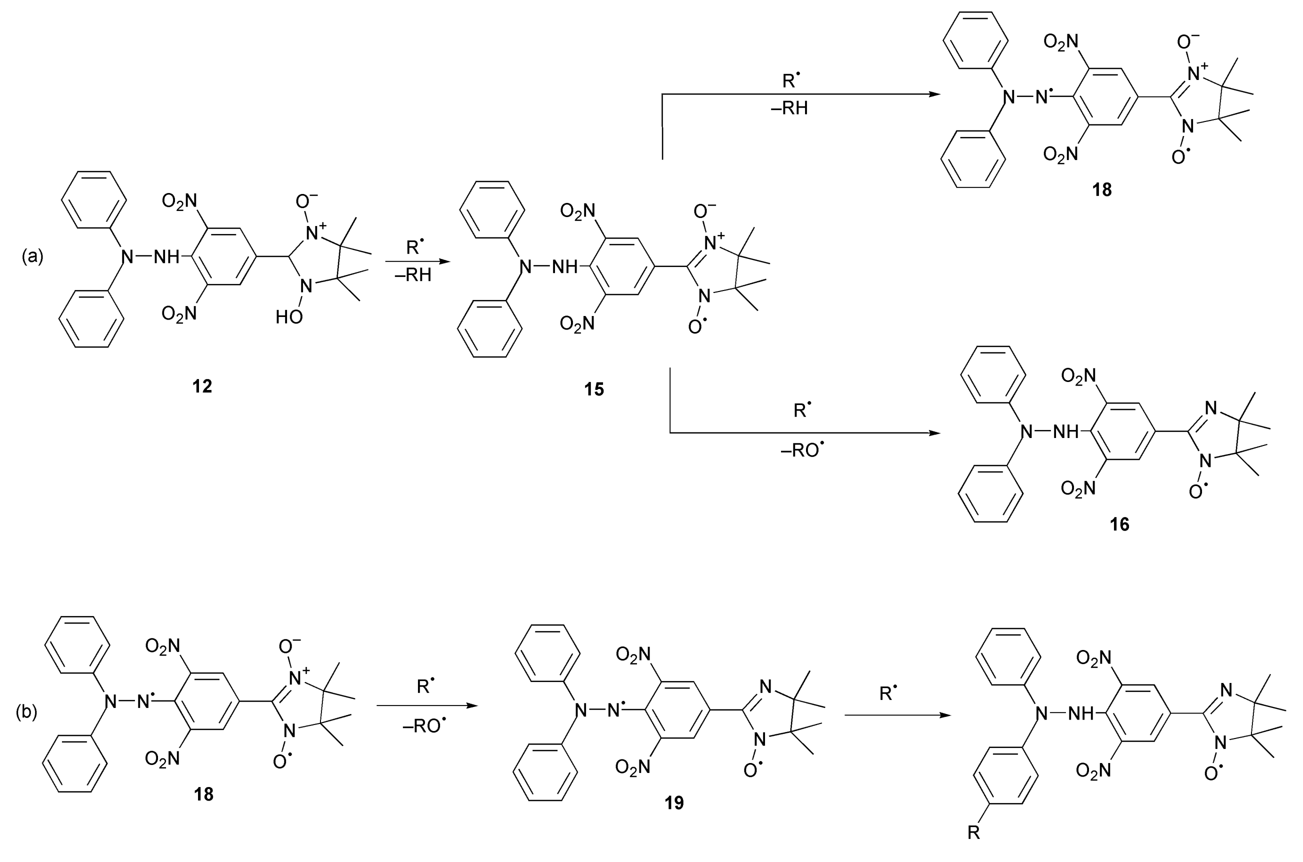
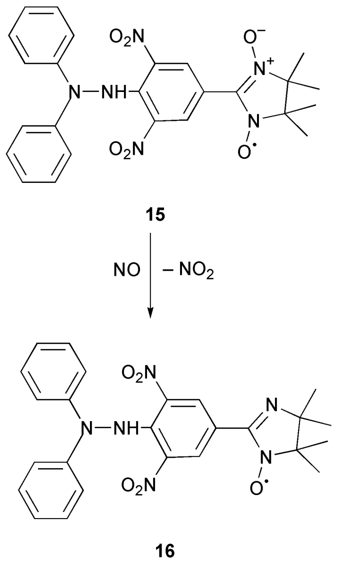


Fig. 5 EPR spectra of diradical **19** in toluene (10^{-3} M) at selected temperatures [the peak marked x is associated with the triplet species (see text)].



Scheme 4

compound **19** was first obtained, but prolonged irradiation led to the removal of the hydrazyl function (as noted for **18**). Reaction of the compound **14** led to the diradical **17**, which then lost the hydrazyl function *via* reaction with short-lived radicals (*cf.* Scheme 4b).

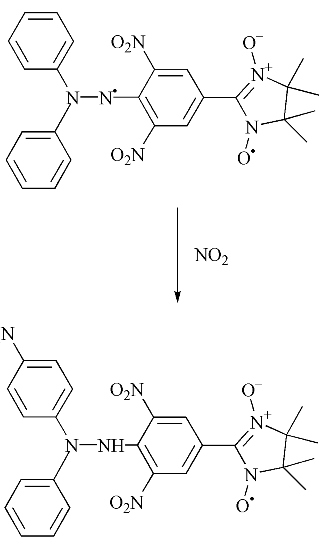


Scheme 5

(c) Reaction with NO or NO_2. We finally employed EPR spectroscopy to investigate the reactions of the mono- and di-radicals in the presence of NO or NO_2. With NO, there was no evidence of reaction with the compounds **12**–**14** or the diradicals **17** and **19**. On the other hand, reaction of **15** and **18** led to the detection of the EPR spectrum of the imino-nitroxide **16**. We believe that this reflects the occurrence of a deoxygenation reaction for **15**, similar to the reported conversion of nitronyl-nitroxide to imino-nitroxide[17] (see Scheme 5), and as noted above for free-radical reactions. We conclude that NO is unable to oxidise N–H or O–H functions. However, the apparent reaction of **18** to give the hydrazyl-nitroxide **16** is at first sight surprising. We believe that the observation may reflect the production of NO_2 following deoxygenation of the nitronyl function in **18** (see below). Thus, reactions of all the substrates **12**–**19** with NO_2 led to marked changes in the spectra: for **14** and **17** the spectra were rapidly removed, no new spectrum being detectable. For all other substrates, the new EPR spectrum appeared to be characteristic of **16** [as with the reaction of **15** or **18** with NO]. The conversion of **12** or **13** to nitroxides whose spectra are characteristic of monoradicals **15** or **16** (or close analogues) is understandable if NO_2 can both bring about hydrogen-atom abstraction from an N–H or O–H bond, and hence give nitrous acid and NO [which converts **15** into **16**], and also remove the hydrazyl species as shown in Scheme 6.

Experimental

Solvents and starting materials were purchased from Lancaster or Aldrich. The UV-Vis spectra were recorded at ambient temperature in dichloromethane (DCM) using a Hitachi U-3000 spectrophotometer. EPR spectra were normally recorded in deoxygenated toluene using both JEOL-RE1X and Bruker ESP 300 spectrometers. Cyclic voltammetry was performed on solutions of the compounds in dry acetonitrile (10^{-2} M) under nitrogen on a Princeton Applied Research Potentiostat 273A, with Pt electrodes (wire) as working and auxiliary electrodes, and Ag/Ag^+ as reference electrode (scan rate 0.05–0.75 V s^{-1}) and supporting electrolyte $(C_4H_9)_4N^+BF_4^-$ (0.1 M). pK_a values of compounds were determined in a methanol–water mixture (1 : 1), as previously described.[19] TLC was performed on silica gel plates (Merck). Compounds **20**, **21** and 2,3-bis(hydroxyamino)-2,3-dimethylbutane were synthesized as reported in the



Scheme 6

literature.[33] The measurement of EPR constants is described elsewhere.[34–36]

Synthesis of 23

To a solution of **21** (3.8 g, 10 mmoles) in 200 mL DCM and cooled to −78 °C, was added dropwise, under nitrogen, a solution of 10 mL DIBAL-H (0.1 M in toluene, 10 mmoles). The mixture was stirred for one hour, then left to warm to room temperature (approx. 1 h), washed with diluted hydrochloric acid, dried over anhydrous sodium sulfate, and the solvent removed under vacuum. Chromatography on a silica gel column with benzene as eluent led to the isolation of **23**. Yield 2.5 g, 70%. $R_f = 0.40$ (silica gel/toluene). EI-MS: *m*/*z* 378 (M^+), 168 ($((C_6H_5)_2N^+)$), 77 ($C_6H_5^+$). CI-MS: *m*/*z* 379 (MH^+), 168 ($((C_6H_5)_2NH_2^+)$). IR: ($CHCl_3$) 798, 1192, 1230, 1297, 1541, 1620, 1703, 2838, 2928, 3035, 3077, 3297 cm^{-1}. ^{1}H-NMR δ ($CDCl_3$): 7.10–7.40 (10H, phenyl, multiplet), 8.15 (1H, CH-*meta*, singlet, broad), 8.80 (1H, CH-*meta*, singlet, broad), 9.86 (1H, NH, singlet), 10.08 (1H, CHO, singlet). UV-Vis λ_{max}(DCM): 395 nm. In basic media the corresponding anion with $\lambda_{max} = 583$ nm was obtained. On oxidation with potassium permanganate or lead dioxide the corresponding hydrazyl radical was obtained with $\lambda_{max} = 495$ nm and EPR coupling constants $a_{N1} = a_{N2} = 0.9$ mT and $g = 2.0037$.

Synthesis of the compounds 12 and 13

To a solution of **23** (378 mg, 1 mmole) dissolved in a mixture of DCM–methanol (3 : 2 v/v, 100 mL) was added 2,3-bis-(hydroxyamino)-2,3-dimethylbutane (296 mg, 2 mmole) and the mixture left overnight at room temperature. A further quantity of 2,3-bis(hydroxyamino)-2,3-dimethylbutane was then added (300 mg, 2 mmole), and the reaction mixture was allowed to stand for several days. The mixture was washed with dilute hydrochloric acid and the separated organic phase was dried over anhydrous sodium sulfate. After removal of the solvent under vacuum, separation chromatography on a silica gel column, using first benzene in order to remove the unreacted compound **23**, then ethyl acetate, led to the isolation of the compounds **12** and **13**. Compound **12**: yield 50 mg. $R_f = 0.61$ (silica gel/ethyl acetate). ESI-MS: *m*/*z* 508 (M^+). IR ($CHCl_3$): 1191, 1228, 1333, 1492, 1536, 1630, 2349, 3028, 3574 cm^{-1}. ^{1}H-NMR δ ($CDCl_3$): 1.10–1.30 (12H, CH_3, multiplet), 4.72 (1H, CH-imidazole, singlet), 7.10–7.40 (10H, phenyl, multiplet), 8.16 (2H, CH-*meta*, singlet, broad), 9.66 (1H, singlet, NH). UV-Vis λ_{max}(DCM): 404 nm. In basic media the corresponding anion with $\lambda_{max} = 645$ nm is obtained. Compound **13**: yield 200 mg. $R_f = 0.21$ (silica gel/ethyl acetate). ESI-MS: *m*/*z* 491 (MH^+). IR ($CHCl_3$): 798, 1228, 1360, 1491, 1540, 1627, 2348, 3028, 3295, 3692 cm^{-1}. ^{1}H-NMR δ ($CDCl_3$): 1.13–1.25 (12H, CH_3, multiplet), 5.30 (1H, CH-imidazole, singlet), 7.10–7.40 (10H, phenyl, multiplet), 9.10 (2H, CH-*meta*, singlet), 9.77 (1H, NH, singlet). UV-Vis λ_{max}(DCM): 482 nm. In basic media the corresponding anion with $\lambda_{max} = 654$ nm is obtained.

Synthesis of the monoradical 14

To 394 mg (1 mmole) 2,2-diphenyl-1-(2,6-dinitro-4-carboxyphenyl)hydrazine[15] dissolved in 25 mL DCM was added 206 mg (1 mmole) DCC and then 171 mg (1 mmole) 4-amino-TEMPO free radical. The reaction mixture was allowed to stand at room temperature for three days, and was then concentrated by partial removal of the solvent: chromatography on a silica gel column first with DCM as eluent, then a mixture of DCM–methanol 9 : 1 gave **14** with a yield of 200 mg (~40%) and *ca.* 100 mg compound **22**. The replacement of the DCC with CDI led to the same monoradical **14**, but in lower yield (25%). Instead of 2,2-diphenyl-1-(2,6-dinitro-4-carboxyphenyl)-hydrazine the corresponding acid chloride (in the presence of pyridine) can be used, with an average yield of 30%. $R_f = 0.10$ (silica gel, eluent DCM–methanol 9 : 1). Compound **14**: ESI-MS *m*/*z* 547 (M^+). UV-Vis λ_{max} (DCM): 392 nm. IR ($CHCl_3$): 3005, 2979, 1667, 1626, 1600, 1540, 1492, 1318, 1260, 760, 698 cm^{-1}. EPR: $a_N = 1.550$ mT; $a_H = 0.045$ mT; *g* value 2.0063. Compound **22**: $R_f = 0.15$ (TLC silica gel (Merck), eluent DCM–methanol 9 : 1). IR ($CHCl_3$): 2936, 2858, 1704, 1620, 1540, 1248, 808, 674 cm^{-1}. CI-MS: *m*/*z* 170 ($((C_6H_5)_2NH^+)$), 83 (cyclohexyl). ^{1}H-NMR δ ($CDCl_3$): 9.81 (NH, singlet), 8.57 (CH-*meta*, singlet, broad), 7.95 (CH-*meta*, singlet, broad), 7.10–7.40 (phenyl, multiplet), 0.70–1.40 (alkyl, multiplet). ^{13}C-NMR δ ($CDCl_3$) CH: 120.37, 125.29, 129.30, 56.53, 50.19; CH_2: 24.48, 25.17, 25.95, 32.28, 30.91; C: 165.17, 153.65, 146.36, 139.65. Oxidation gave the corresponding free radical with EPR coupling constants $a_{N1} = a_{N2} = 0.900$ mT and *g* value 2.0062.

Synthesis of the monoradicals 15 and 16

To 10 mg of the compounds **12** or **13** dissolved in 10 mL DCM was added 200 mg sodium periodate and the mixtures stirred for about one hour. After filtration and removal of the solvent under vacuum the solid radicals were obtained. Compound **15**: $R_f = 0.73$ (silica gel/DCM). UV-Vis λ_{max}(DCM): 496 nm. EPR: $a_{N1} = a_{N2} = 0.743$ mT and *g* value 2.0068. Compound **16**: $R_f = 0.73$ (silica gel/DCM). UV-Vis λ_{max}(DCM): 486 nm. EPR: $a_{N1} = 0.437$, $a_{N2} = 0.892$ mT and *g* value 2.0061.

Synthesis of the diradical 17

100 mg of monoradical **14** dissolved in 50 mL DCM was stirred with solid potassium permanganate (5 g) and anhydrous sodium sulfate (5 g) for 2 hours; the solution was filtered off and the solvent removed under reduced pressure using a rotary evaporator. Yield of **17** 90 mg. $R_f = 0.49$ (silica gel, eluent DCM–methanol 9 : 1). UV-Vis λ_{max}(DCM): 505 nm. EPR: $a_N = 1.550$, $a_{N1} = 1.247$, $a_{N2} = 0.418$, $a_H = 0.045$ mT and *g* values 2.0059 and 2.0048.

Synthesis of the diradicals 18 and 19

To 10 mg of the compounds **12** or **13** dissolved in 10 mL DCM was added 500 mg solid potassium permanganate or lead dioxide and the mixtures stirred for about 24 h. After filtration and removal of the solvent under vacuum the solid radicals were obtained. For a pure sample of diradical further purification by TLC (silica gel/ DCM) is required. Compound **18**: $R_f = 0.73$ (silica gel/DCM). UV-Vis λ_{max}(DCM): 507 nm. EPR: $a_{N1} = 0.740$, $a_{N2} = 0.740$, $a_{N3} = 1.247$, $a_{N4} = 0.399$ mT and *g* values 2.0065 and 2.0049. Compound **19**: $R_f = 0.73$ (silica gel/ DCM). UV-Vis λ_{max}(DCM): 510 nm. EPR: $a_{N1} = 0.864$,

$a_{N2} = 0.432$, $a_{N3} = 1.340$, $a_{N4} = 0.445$ mT and g values 2.0059 and 2.0049.

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