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# Electron spin resonance study of phosphorus-nitroxides from 1,3-additions of silicon-phosphorus reagents to nitrones

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**This article explores a new, convenient route to β-phosphorus nitroxides. Specifically, the reaction sequence involves the novel 1,3-addition of trimethylsilyl phosphites (e.g. diethyl) or trimethylsilyl phosphines (e.g. diphenyl) to aldo-nitrones [e.g. α-phenyl-N-*tert*-butylnitrone (PBN) or 5,5-dimethyl-l-pyrroline-N-oxide (DMPO)] or keto-nitrones [e.g. 2-ethyl-5,5-dimethyl-1 pyrroline-N-oxide (2-Et-DMPO) or 2-phenyl-5,5-dimethyl-l-pyrroline-N-oxide (2-Ph-DMPO)] to form α-phosphityl- or α-phosphinyl-O-silylhydroxylamines. Acidic hydrolysis provides the corresponding hydroxylamines that are easily oxidized to the title β-phosphorus-nitroxides. ESR spectroscopic analysis revealed some very large β-phosphorus hyperfine splittings (i.e. in excess of 5 mT). For this reason and their remarkable stability (persistence) some of these nitroxides show promise as integral components in new, improved weak-field dynamic nuclear polarization (DNP) magnetometers. Copyright © 2004 John Wiley & Sons, Ltd.**

**KEYWORDS:** ESR; β-phosphorus-nitroxides (aminoxyls); α-phosphorus-O-silylhydroxylamines; nitrones; magnetometry

## INTRODUCTION

Weak-field magnetometers measure magnetic fields on land, sea, air and space. Geology,[1] aerospace exploration,[2] as well as archaeology[3] are just a few fields in which these devices find current usage. Our interest in magnetometers, however, stems from the fact that stable (persistent) free radicals play a critical role in their sensitivity. Specifically, our search is for new free radical molecules that can provide enhanced magnetometric sensitivity. In addition to their persistence, the free radical should also exhibit a large hyperfine splitting (a) in its electron spin resonance (or ESR) spectrum. The ESR parameter 'a' is associated with a phenomenon known as the dynamic nuclear polarization (DNP) effect. Dynamic nuclear polarization is a double magnetic resonance technique in which there is a transfer of electron spin polarization to the nuclear spins when the electron spin transition is stimulated. These DNP magnetometers may be thought of as NMR spectrometers in which the applied magnetic field is absent. Thus, the magnetic field of interest (e.g. from the geological site, etc.) generates the NMR signal. DNP magnetometers usually operate via detection of the $^1$H NMR signal of solvent nuclei that has been amplified by the presence of trace amounts of persistent free radicals. This is the well-known Abragam Overhauser effect.[4]

Due to their remarkable persistence, nitroxides have become the 'gold standard' for use in commercial DNP magnetometers. Two factors contribute to this stability. The first is the resonance stabilization afforded by the more polar and less polar canonical forms (Fig. 1). A second factor is steric hindrance. The bulkiness of the nitroxide flanking groups (i.e. $R_1$, to $R_6$) also enhances the free radical's lifetime (Fig. 1). This is because when nitroxides are attached to two bulky α-groups (e.g. di-tert-alkyls) a major decay route known as disproportionation is slowed or prevented altogether (Scheme 1). It is worth mentioning that some nitroxides with one β-hydrogen also may exhibit relatively long half-lives (i.e. from months to years). Spin trapping[5] with the two most popular nitrone spin traps [α-phenyl-N-*tert*-butylnitrone (PBN) and 5,5-dimethyl-l-pyrroline-N-oxide (DMPO) (Fig. 3)] may also yield spin adduct nitroxides of uncommon stability. Examples of such spin adducts that may be chromatographed (e.g. by HPLC) and/or analysed by mass spectrometry (MS) include the methyl ($^{\bullet}CH_3$[6]), 2-cyano-2-propyl [$^{\bullet}C$-$(CH_3)_2CN$][7] and trichloromethyl ($^{\bullet}CCl_3$)[8,9] adducts of PBN as well as the 2-cyano-2-propyl [$^{\bullet}C$-$(CH_3)_2CN$][7] and various alkoxyl ($^{\bullet}OR$) adducts of DMPO.[10]

It should be noted, however, that to date virtually all the nitroxides patented for use in magnetometers are

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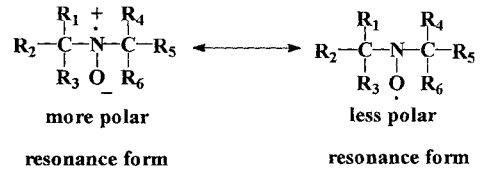
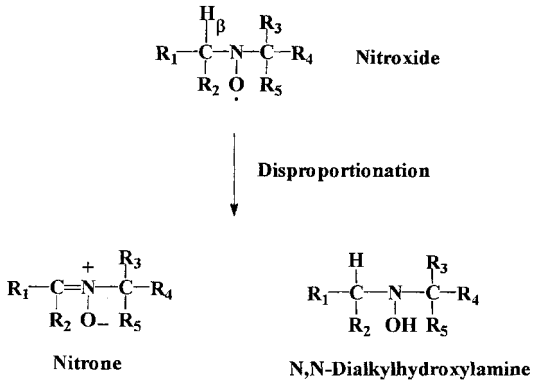



**Figure 1.** Resonance structures for nitroxide (or aminoxyl) free radicals.




**Scheme 1.** Decay of nitroxides by disproportionation.

cyclic di-tert-alkylnitroxides (Fig. 2). The first three are pyrrolidine-N-oxyls (**1**),[11] piperidine-N-oxyls (**2**),[11] as well as oxazolidine-N-oxyls (**3**),[12] respectively. The next generation of nitroxides for magnetometry are deuterated and $^{15}$N-labelled versions [(**4**)[13] and (**5**)[13–15]] of the original nitroxides (**1** and **2**). Another deuterated and $^{15}$N-labelled nitroxide, an isoindoline-N-oxyl (**6**)[16,17] has also recently arrived on the magnetometry scene. Nitroxide (**6**) was synthesized and found to be superior to nitroxide (**5**) (the current radical of choice), especially in higher temperature magnetometry applications (unpublished observations). Deuteration is advantageous in magnetometry because it sharpens the ESR lines that otherwise would display long-range unresolved $^{1}$H hyperfine splittings. It is worth mentioning that free radicals for magnetometry are generally smaller molecules because the larger ones are associated with wider ESR lines due to immobilization/anisotropy. Labelling a nitroxide with $^{15}$N may help in two ways. First, it generally provides a larger ESR hyperfine splitting ($a^{15N} \sim 2.1$ mT vs $a^{14N} \sim 1.5$ mT). Second, it leads to fewer ESR lines (2 vs 3 for $^{15}$N vs $^{14}$N, respectively). It is noteworthy, however, that the DNP effect is complex[18] (higher at lower magnetic fields for $^{14}$N nitroxides). Even ESR studies at low magnetic fields are complicated. For instance, $^{14}$N nitroxides may be favoured over their $^{15}$N counterparts.[19] Therefore, some new free radicals for low-field magnetometry may require field-testing to fully gauge their utility (sensitivity). Nevertheless, because of their large (>5.0 mT) $\beta$-$^{31}$P hyperfine splittings $\beta$-phosphorus-nitroxides **(7)** (Fig. 2) have captured the interest of our group[20,21] and others.[22]

This paper examines new routes to some new and known $\beta$-phosphorus-nitroxides derived from aldo- and keto-nitrones. The sequence was discovered by recognition that the chemistries of carbonyl compounds and nitrones often parallel each other. The name of the latter actually

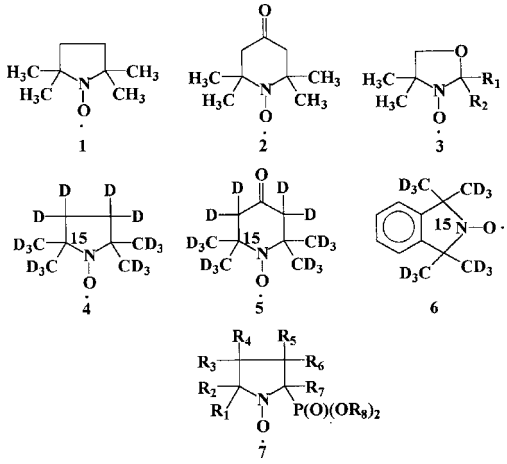
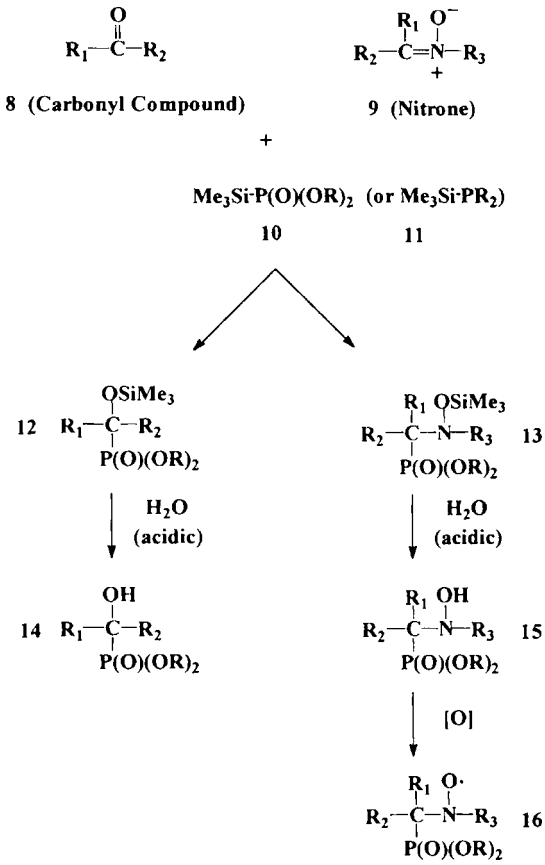



**Figure 2.** Structures of various nitroxides patented for use in DNP magnetometers.




**Scheme 2.** Addition of silicon-phosphorus reagents to carbonyl compounds and nitrones.

comes from a contraction of the term nitrogen-ketone.[23] A couple of papers[24,25] have described the reaction of carbonyl compounds (**8**) with silicon-phosphorus reagents (**10**) (Scheme 2). A check of the nitrone literature,[23,26–34] however, revealed that no one has examined the analogous reactions with nitrones (Scheme 2). While the carbonyl (**8**) and nitrone (**9**) reactions with silicon-phosphorus reagents (**10** and **11**) are likely mechanistically similar, the former is a 1,2-addition while the latter is a 1,3-addition. The

carbonyl and nitrone adducts thus are an $\alpha$-phosphityl-O-silylether (**12**) and an $\alpha$-phosphityl-O-silylhydroxylamine (**13**), respectively. Because silyl ethers (e.g. **12**) are generally hydrolysable ($H^+$) to alcohols (e.g. **14**)[25] it was reasoned that O-silylhydroxylamine (**13**) should also be easily convertible to the N,N-hydroxylamine (**15**) which in turn should be easily oxidizable to the desired nitroxide (**16**). Fortunately, this turns out to be the general case and will be discussed in detail later.

## RESULTS AND DISCUSSION

In this study the reaction of four nitrones (Fig. 3) with two silicon-phosphorus compounds (Fig. 4) was examined. The two aldo-nitrones were $\alpha$-phenyl-N-*tert*-butylnitrone (PBN) **(17)** and 5,5-dimethyl-l-pyrroline-N-oxide (DMPO) (**18**), whereas the two keto-nitrones were 2-ethyl-5,5-dimethyl- l-pyrroline-N-oxide (2-Et-DMPO) (**19**) and 2-phenyl-5,5-dimethyl-l-pyrroline-N-oxide (2-Ph-DMPO) **(20)**. The silicon-phosphorus compounds used were diethyl trimethylsilyl phosphite **(21)** and diphenyl(trimethylsilyl) phosphine **(23)** (Fig. 4). The $^1$H and $^{13}$C NMR data for the nitrones (**17**–**20**) are collected in Table 1 while the $^1$H, $^{13}$C and $^{31}$P NMR data for the silicon-phosphorus (**21** and **23**) and related compounds (**22** and **24**) are listed in Table 2. Key $^1$H, $^{13}$C and $^{31}$P NMR spectroscopic data for phosphorus adducts (**25**) and (**26**) (Fig. 5) derived from the 1,3-addition of diethyl trimethylsilyl phosphite (**21**) and diphenyl (trimethyl) phosphine (**23**) to nitrone (**17**) (PBN), respectively, are listed in Table 3. The ESR spectral data for the various $\beta$-phosphityl- and $\beta$-phosphinyl-nitroxides (**27**–**35**) (Fig. 6) derived from nitrones (**17**–**20**) are presented in Table 4. Representative ESR spectra of some phosphorus-nitroxides from the 1,3-additions (i.e. **27, 31** and **32**) are given in Figs 7–9, respectively.

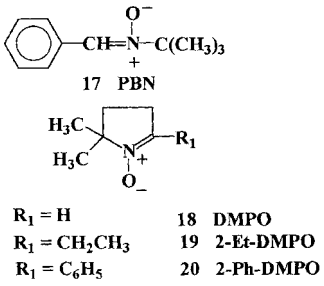



**Figure 3.** Structures of the nitrones used in this study.

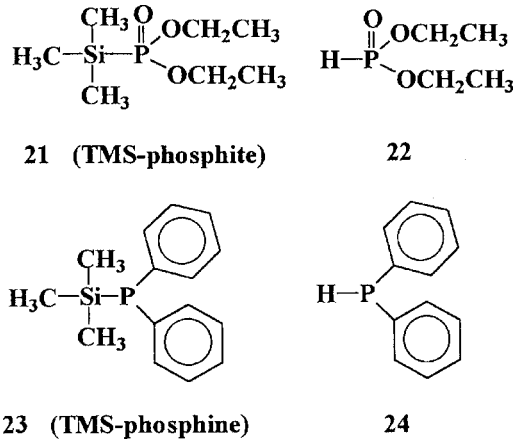



**Figure 4.** Structures of the silicon-phosphorus reagents and related compounds.

## EXPERIMENTAL

The aldo-nitrones $\alpha$-phenyl-N-tert-butylnitrone (PBN) (**17**) and 5,5-dimethyl-l-pyrroline-N-oxide (DMPO) (**18**) were purchased from the Aldrich chemical company. The

**Table 1.** The $^1$H and $^{13}$C NMR data for the nitrones (**17**–**20**)[a,b]

| | |
|---|---|
| Nitrone **17** (PBN) | $^1$H NMR: 1.26 (s, 9H, methyls), 7.17–7.23 (m, 4H, *nitronyl*, and *meta*, and *para-aryls*), 8.47 (d, 2H, *ortho-aryls*, $J^1H$-$^1H$ = 8.20 Hz)<br>$^{13}$C NMR:28.16 (methyls), 70.53 (*tert-butyl* quaternary), 127.82, 128.31,128.57,128.75,129.62 (*nitronyl* and aryls except aryl quaternary), 132.43 (aryl quaternary) |
| Nitrone **18** (DMPO) | $^1$H NMR:1.16 (s, 6H, 5-methyls), 1.42 (t, 2H, $C_4$, $J^1H$-$^1H$ = 7.20 Hz), 1.80 (t of d, 2H, $C_3$, $J^1H$-$^1H$ = 7.20 Hz, $J^1H$-$^1H$ = 2.67 Hz), 6.40 (t, 1H, *nitronyl*, $J^1H - {}^1H$ = 2.67 Hz)<br>$^{13}$C NMR: 23.92 ($C_3$), 25.24 (5-methyls), 33.81 ($C_4$), *72.75* ($C_5$), 129.00 *(nitronyl)* |
| Nitrone **19** (2-Et-DMPO) | $^1$H NMR: 0.82 (t, 3H, ethyl $CH_3$, $J^1H$-$^1H$ = 7.60 Hz), 1.21 (s, 6H, 5-methyls), 1.40 (t, 2H, $C_4$, $J^1H$-$^1H$ = 7.40 Hz), 1.94 (t, 2H, $C_3$, $J^1H$-$^1H$ = 7.20 Hz), 2.35 (q, 2H, ethyl $CH_2$, $J^1H$-$^1H$ = 7.74 Hz)<br>$^{13}$C NMR: 9.25 (ethyl $CH_3$), 20.36 (ethyl $CH_2$), 25.18 (5-methyls), 25.48 ($C_3$), 32.13 ($C_4$), 72.77 ($C_5$), 141.82 *(nitronyl)* |
| Nitrone **20** (2-Ph-DMPO) | $^1$H NMR: 1.24 (s, 6H, 5-methyls), 1.38 (t, 2H, $C_4$, $J^1H$-$^1H$ 7.40 Hz), 2.32 (t, 2H, $C_3$, $J^1H$-$^1H$ = 7.40 Hz), 7.18 (m, 3H, *meta-* and *para-* aryls), 8.56 (d, 2H, *ortho-aryls*, $J^1H$-$^1H$ = 8.26 Hz)<br>$^{13}$C NMR: 25.61 (5-methyls), 26.25 ($C_3$), 31.64 ($C_4$), 75.31 ($C_5$), 127.09, 128.44, 129.40 (aryls except aryl quaternary), 131.15 (aryl quaternary), 135.30 *(nitronyl)* |

[a] The chemical shifts ($\delta$) in ppm for the $^1$H and $^{13}$C spectra are relative to external $(CH_3)_4Si$ and/or internal $C_6D_6$. All spectra were recorded at room temperature.

[b] The NMR parameters for these nitrones have been reported previously in the literature (c.f. references 20, 21 and references cited therein).

**Table 2.** The $^{1}H$, $^{13}C$, and $^{31}P$ NMR data for the silicon-phosphorus reagents (**21** and **23**) and related compounds (**22** and **24**)[a,b]

Silicon-phosphorus compound (**21**) (diethyl trimethylsilyl phosphite)
$^{1}H$ NMR: 0.19 (s, 9H, Si-$CH_3$), 1.09 (t, 6H, ethyl $CH_3$, $J^{1}H$-$^{1}H = 7.00$ Hz), 3.76 (m, 4H, ethyl $CH_2$)
$^{13}C$ NMR: 1.43 (s, Si-$CH_3$), 17.11 (d, ethyl $CH_3$, $J^{13}C$-$^{31}P = 4.72$ Hz), 56.67 (d, ethyl $CH_2$, $J^{13}C$-$^{31}P = 9.33$ Hz)
$^{51}P$ NMR: −7.70 (p, phosphityl P, $J^{31}P$-$^{1}H = 8.29$ Hz)

Silicon-phosphorus compound (**22**) (diethyl phosphite)
$^{1}H$ NMR: 0.96 (t, 6H, ethyl $CH_3$, $J^{1}H$-$^{1}H = 7.00$ Hz), 3.78 (m, 4H, ethyl $CH_2$), 6.60 (d, 1H, phosphityl H, $J^{1}H$-$^{31}P = 683.83$ Hz)
$^{13}C$ NMR: 16.24 (d, ethyl $CH_3$, $J^{13}C^{-31}P = 6.01$ Hz), 61.20 (d, ethyl $CH_2$, $J^{13}C$-$^{31}P = 5.50$ Hz)
$^{31}P$ NMR: 7.32 (d of p, phosphityl P, $J^{31}P$-$^{1}H = 683.93$ Hz, $J^{31}P$-$^{1}H = 9.23$ Hz) Silicon-phosphorus compound (**23**) [diphenyl (trimethylsilyl)phosphine]
$^{1}H$ NMR: 0.13 (d, 9H, Si-$CH_3$, $J^{1}H$-$^{31}P = 4.80$ Hz), 7.02 to 7.09 (m, 6H, aryls), 7.49 to 7.53 (m, 4H, aryls)
$^{13}C$ NMR: −1.11 (d, Si-$CH_3$, $J^{13}C$-$^{31}P = 12.59$ Hz), 127.69 to 137.27 (aryls)
$^{31}P$ NMR: −56.32 (s, phosphinyl P)

Silicon-phosphorus compound (**24**) (diphenylphosphine)
$^{1}H$ NMR: 7.00 to 7.60 (m, l0 H, aryls)
$^{13}C$ NMR: 127 to 137 (aryls, estimated)
$^{31}P$ NMR: −40.29 (d of multiplets, phosphinyl P, $J^{31}P$-$^{1}H = 215.59$ Hz)

[a] The chemical shifts ($\delta$) in ppm for the $^{1}H$ and $^{13}C$ spectra are relative to external $(CH_3)_4Si$ and/or internal $C_6D_6$. The chemical shifts for the $^{31}P$ spectra are relative to external $H_3PO_4$. All spectra were recorded at room temperature in $C_6D_6$.

**Table 3.** The key $^{1}H$, $^{13}C$, and $^{31}P$ parameters for the $\alpha$-phosphorus-O-silylhydroxylamines (**25** and **26**) derived from nitrone (**17**) (PBN) and the silicon-phosphorus compounds (**21** and **23**)[a]

$\alpha$-Phosphorus-O-silylhydroxylamine (**25**)
$^{1}H$ NMR: 4.19 (d, diastereomeric CH, $J^{1}H$-$^{31}P = 25.15$ Hz), 4.21 (d, diastereomeric CH, $J^{1}H$-$^{31}P = 25.16$ Hz). Note: the $^{31}P$ coupling disappeared upon $^{31}P$ decoupling
$^{13}C$ NMR: 56.79 (d, CH, $J^{13}C$-$^{31}P = 31.09$ Hz)
$^{31}P$ NMR: 24.06 (broad s, phosphityl P)

$\alpha$-Phosphorus-O-silylhydroxylamine (**26**)
$^{1}H$ NMR: 5.19 (d, CH, $J^{1}H$-$^{31}P = 4.40$ Hz). Note: the $^{31}P$ coupling disappeared upon $^{31}P$ decoupling
$^{13}C$ NMR: 69.43 (broads, CH)
$^{31}P$ NMR: −9.44 (broad s, phosphinyl P)

[a] The chemical shifts ($\delta$) in ppm for the $^{1}H$ and $^{13}C$ spectra are relative to external $(CH_3)_4Si$ and/or internal $C_6D_6$. The chemical shifts for the $^{31}P$ spectra are relative to external $H_3PO_4$. All spectra were recorded at room temperature in $C_6D_6$.

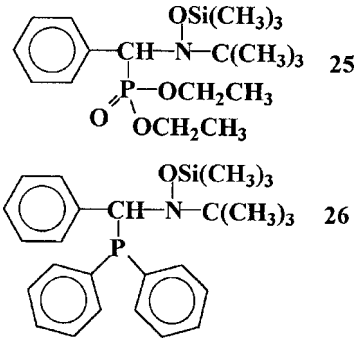



**Figure 5.** Structures of the $\alpha$-phosphorus-O-silylhydroxylamines derived from $\alpha$-phenyl-*N*-*tert*-butylnitrone (PBN) and silicon-phosphorus reagents detected by NMR spectroscopy.

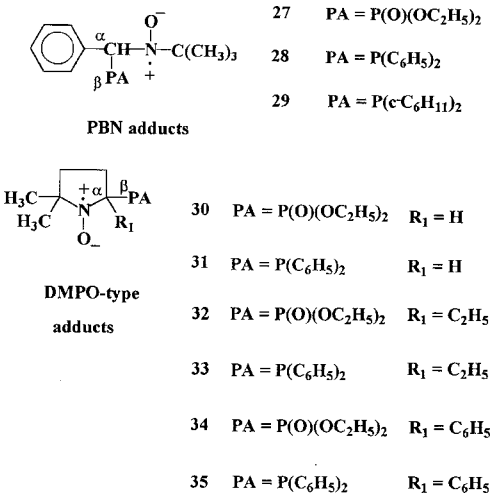



**Figure 6.** Structures of the 0-$^{31}P$ phosphityl- and phosphinyl-nitroxide adducts (PA = phosphorus addend).

keto-nitrones 2-ethyl- 5,5-dimethyl-l-pyrroline-N-oxide (2-Et-DMPO) (**19**) and 2-phenyl-5,5-dimethyl-l-pyrroline-N-oxide (2-Ph-DMPO) (**20**) were synthesized as described, respectively in two previous papers.[21,35] The two silicon-phosphorus reagents diethyl trimethylsilyl phosphite (**21**) and diphenyl(trimethylsilyl)phosphine (**23**) were obtained from the Aldrich chemical company. Since diethyl trimethylsilyl phosphite (**21**)[36] may be synthesized

**Table 4.** ESR hyperfine splittings for the [$\beta$-$^{31}$P] phosphityl and phosphinyl nitroxide adducts in benzene at room temperature[a]

| Nitrone | Nitroxide | $^{31}$P adduct | $a^N$ | $a\beta^H$ | $a\beta^{31P}$ | Refs. |
|---|---|---|---|---|---|---|
| PBN | **27** | $P(O)(OEt)_2$ | 1.448 | 0.3075 | 2.445 | This work |
| PBN | **27** | $P(O)(OEt)_2$ | 1.465 | 0.306 | 2.433 | 66 |
| PBN | **27** | $P(O)(OEt)_2$ | 1.450 | 0.294 | 2.431 | 20 |
| PBN | **27** | $P(O)(OEt)_2$ | 1.475 | 0.318 | 2.475 | 67 |
| PBN | **28** | $P(Ph)_2$ | 1.425 | 0.325 | 1.838 | This work |
| PBN | **29** | $P(C_6H_{11})_2$ | 1.439 | 0.335 | 1.211 | 66 |
| DMPO[b] | **30** | $P(O)(OEt)_2$ | 1.32 | 1.69 | 4.50 | 68 |
| DMPO | **31** | $P(Ph)_2$ | 1.391 | 1.846 | 3.729 | This work |
| 2-Et-DMPO | **32** | $P(O)(OEt)_2$ | 1.350 | — | 5.400 | This work |
| 2-Et-DMPO | **32** | $P(O)(OEt)_2$ | 1.350 | — | 5.425 | 21 |
| 2-Et- | **33** | $P(Ph)_2$ | 1.381 | — | 4.250 | This work |
| 2-Ph- | **34** | $P(O)(OEt)_2$ | 1.353 | — | 3.429 | This work |
| 2-Ph-DMPO[c] | **34** | $P(O)(OEt)_2$ | 1.367 | — | 3.459 | 51 |
| 2-Ph- | **34** | $P(O)(OEt)_2$ | 1.347 | — | 3.458 | 20 |
| 2-Ph-DMPO | **35** | $P(Ph)_2$ | 1.349 | — | 2.727 | This work |

[a] The hyperfine splittings (a) are listed in millitesla (mT).

[b] This $\beta$-phosphityl nitroxide was not observed. Instead, DMPOX$^\bullet$(2-oxo-5,5-dimethylpyrrolidine-N-oxyl) was seen ($a^N = 0.650$ mT, $a\gamma^{2H} = 0.325$ mT).

[c] This nitroxide was formed by the addition of phenyl radicals (from benzoyl peroxide) to 2-(diethylphosphityl)-5,5-dimethyl-1-pyrroline-N-oxide.

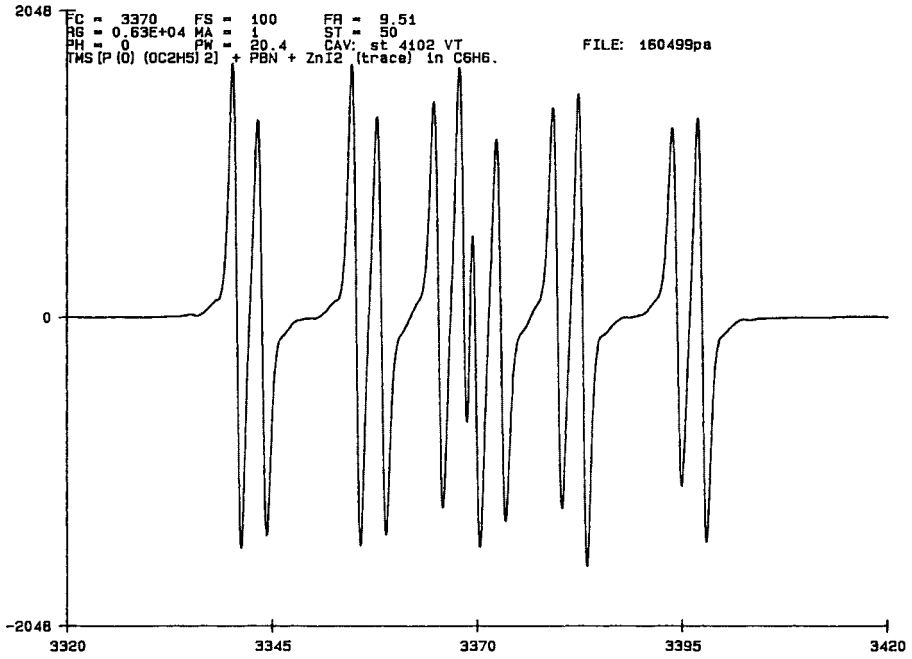



**Figure 7.** ESR spectrum of the diethylphosphityl-nitroxide adduct of PBN (**27**) in $C_6H_6$.

from sodium diethylphosphite [Na P(O) $(OEt_2)$] and trimethylsilyl chloride ($Me_3SiC1$) other non-commercially available silicon-phosphorus reagents should be available by variation of the alkyl groups (e.g. ethyl vs methyl, etc.).

## Syntheses for NMR examination

Production of the 1,3-adducts ($\alpha$-phosphorus-O-silylhydroxy lamines) (**25** and **26**) (Fig. 5) from the silicon-phosphorus reagents (**21** and **23**) and nitrone (**17**) (PBN) was conducted as follows: an equimolar (1.25 mmol) solution of the silicon-phosphorus reagent and nitrone (as well as a catalytic amount of $ZnI_2$[37]) in 5 ml of $C_6D_6$ was refluxed for 3 h. The crude reaction mixture was analysed by $^1$H, $^{13}$C and $^{31}$P NMR.

## Syntheses for ESR examination

An equimolar (0.125 mmol) solution of the silicon-phosphorus reagent and nitrone (including a catalytic amount of $ZnI_2$[37]) in 5 ml of $C_6H_6$ was refluxed for 3 h.

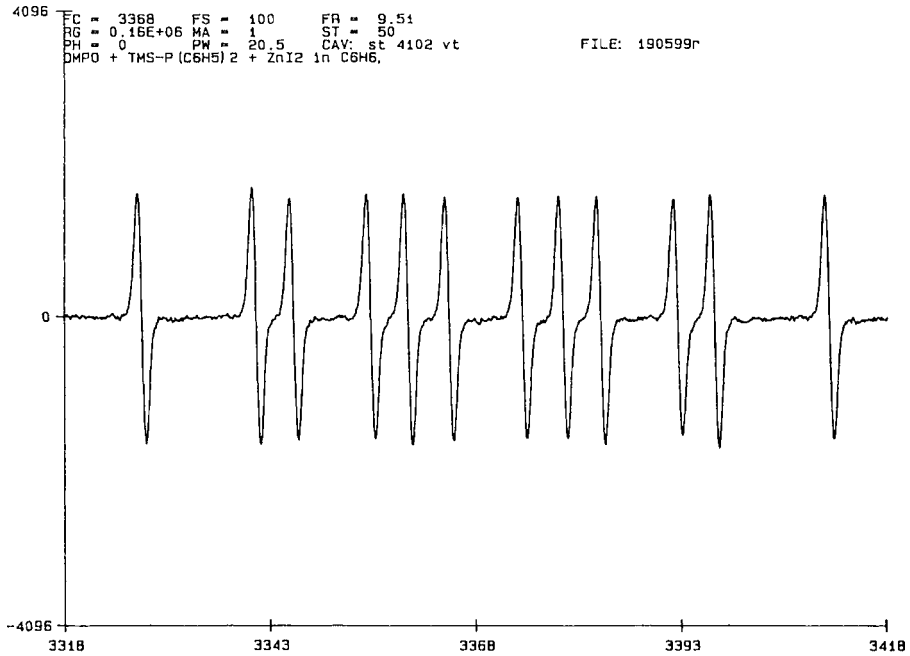



**Figure 8.** ESR spectrum of the diphenylphosphinyl-nitroxide adduct of DMPO (**31**) in $C_6H_6$.

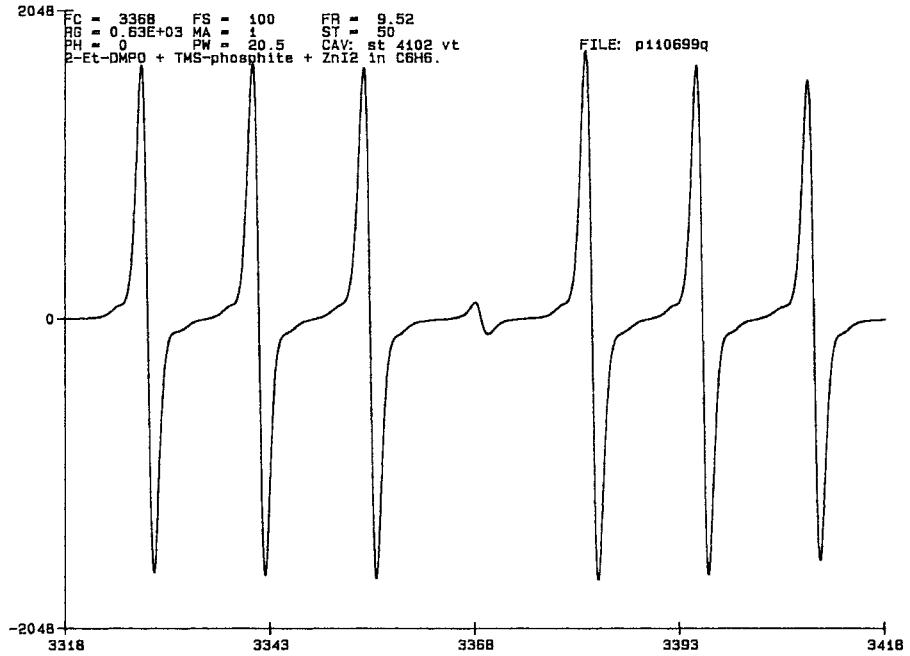



**Figure 9.** ESR spectrum of the diethylphosphityl-nitroxide adduct of 2-Et-DMPO (**32**) in $C_6H_6$.

After cooling to room temperature the mixture was treated with 5 ml of 0.1 M HCl. The organic layer was separated and treated with several milligrams of lead dioxide and anhydrous $Na_2SO_4$ (0.25 g). The filtered $C_6H_6$ solution was placed into a round, quartz ESR cell and purged with argon (g) for 15 min. The mixture was then examined by ESR.

## NMR and ESR spectroscopy

The $^1H$, $^{13}C$ and $^{31}P$ spectra were obtained at ambient temperature using a Bruker spectrometer operating at approximately 400, 100 and 162 MHz, respectively. The ESR spectra were recorded at room temperature using a Bruker ER 200 D instrument operating at around 9.8 GHz (i.e. X-band) and centre field (337.5 mT).

## NMR results

Since the 1,3-addition of silyl-phosphorus reagents to nitrones is virtually unknown in the literature, it was decided to use NMR spectroscopy to identify some of these adducts. In contrast to some related studies where the 1,3-addition of trimethylsilyl cyanide to nitrones proceeds in high yield (95%)[37] the reaction of silicon-phosphorus reagents (**21** and **23**) (Fig. 4) to nitrone (**17**) (PBN) gave **25** and **26** (Fig. 5) in low yield (<10%) and relatively complex NMR spectra. It is noteworthy though that no attempt was made to

optimize the yields. Nevertheless, by recording the NMR spectra ($^1$H and $^{13}$C) of the nitrones (Table 1) and the silicon-phosphorus reagents ($^1$H, $^{13}$C and $^{31}$P) (Table 2) in the reaction solvent (i.e. benzene) it was possible to identify the 1,3-adducts of PBN (**25** and **26**) by focusing on the methine (i.e. CH) peak in the $^1$H and $^{13}$C NMR spectra and the phosphityl and phosphinyl peaks in the $^{31}$P NMR spectra (Table 3). Though the 1,3-adducts (**25** and **26**) are new to the literature, comparison with the $^{31}$P NMR chemical shifts of related compounds was helpful in the assignment of these peaks.[38] For instance, diethyl phosphityl compounds of the R-P(O)$(OEt)_2$ type (R = alkyl) exhibit $^{31}$P NMR peaks around 21 ppm (±10). This compares favourably with the observed peak at 24.06 ppm for compound **25**. Diphenyl phosphinyl compounds[R-P$(C_6H_5)_2$] (R = alkyl) show $^{31}$P NMR peaks around −12 ppm (±10). This is also close to the observed peak at −9.44 ppm for compound **26**.

## ESR results

The phosphorus-nitroxides (**27**–**35**, except **29** and **30**) (Fig. 6) were synthesized according to the 1,3-addition, acidic hydrolysis, oxidation sequence outlined in Scheme 2. The ESR spectral data are collected in Table 4. Specifically, diethyl phosphityl (**27**, **32**, **34**) and diphenyl phosphinyl (**28**, **31**, **33**, **35**) nitroxide adducts of all the aldo- and keto-nitrones except for the diethyl phosphityl adduct of DMPO (**30**) were observed. In place of the expected adduct (**30**) the oxidation product, an acyl nitroxide or nitroxone, known as DMPOX$^\bullet$ (2-oxo-5,5-dimethyl-pyrrolidine-N-oxyl) was detected. The ESR hyperfine splittings ($a^N = 0.650$ mT, $a\gamma^{2H} = 0.325$ mT in $C_6H_6$) are well known. This result reflects the susceptibility of aldo-nitrones to oxidation at the nitronyl-carbon [−CH=N$^+$(O$^-$)]. Formation of an oxo (C=O) group at the nitronyl-carbon of keto-nitrones is blocked. That DMPO is oxidized to DMPOX$^\bullet$ while PBN is not oxidized to PBNOX$^\bullet$ is likely due to the overall higher lability of DMPO versus PBN.[5] The phosphorus-nitroxides from the aldo-nitrones (**27**–**31**) all exhibit 12 line triplet of doublet of doublet patterns due to the nitrogen, $\beta$-hydrogen (hfs), and $\beta$-phosphorus nuclei (Table 4). Examples of these ESR spectral patterns are illustrated in Figs 7 and 8 (the diethylphosphityl adduct of PBN (**27**) and the diphenylphosphinyl adduct of DMPO (**31**)).

The phosphorus-nitroxides from the keto-nitrones (**32**–**35**) show 6 line triplet of doublet patterns due to the nitrogen and (3-phosphorus nuclei (Table 4). A case in point is the diethylphosphityl adduct of 2-Et-DMPO (**32**) (Fig. 9). (A small peak in the centre of the spectrum is due to a di-*tert*-alkyl nitroxide of unspecific structure.) While the nitrogen (and $\beta$-hydrogen where applicable) hyperfine splittings for all the phosphorus adducts did not vary much between the phosphityl and phosphinyl adducts, significant changes were observed in the $\beta$-phosphorus splittings. Phosphorus adducts of PBN exhibited $\beta$-phosphorus splittings around 2.5 mT (**27**), whereas those of phosphinyl adducts varied from 1.2 mT (**29**) to 1.8 (**28**). DMPO phosphityl adducts (e.g. **30**) show a robust $\beta$-phosphorus splitting (4.5 mT) while the phosphinyl adduct (**31**) is significantly smaller at 3.7 mT. An even larger ($\beta$-phosphorus splitting (around 5.4 mT) is observed for the phosphityl adduct of 2-Et-DMPO (**32**). The corresponding phosphinyl adduct (**33**) has a $\beta$ -phosphorus splitting of 4.3 mT.

Finally, the phosphityl (**34**) and phosphinyl (**35**) adducts of 2-Ph-DMPO show $\beta$-phosphorus splittings around 3.5 mT and 2.7 mT, respectively. In summary, the $\beta$-phosphorus hyperfine splitting is consistently and significantly larger for the phosphityl versus the phosphinyl nitroxide adducts of the respective nitrone. As mentioned in the Introduction Section some ESR parameters influence the performance of a free radical in magnetometry applications. And since the $\beta$-phosphorus hyperfine splitting for the phosphorus-nitroxides from the cyclic nitrones (**30**–**35**) (2.7–5.4 mT) are larger than those from PBN (**27**–**29**) (1.2–2.5 mT) the former are favoured. Among the phosphorus adducts from the cyclic nitrones those from 2-Et-DMPO and 2-Ph-DMPO (i.e. **32**–**35**) are expected to elicit a stronger DNP effect than those from the corresponding ones from DMPO (**30**, **31**) because they display fewer ESR lines (6 vs 12). A further consideration is the persistence of the various phosphorus-nitroxide adducts. Nitroxide adducts of DMPO (**30**, **31**) are expected to be less persistent, especially because they are prone to decomposition by disproportionation Scheme 1. Keto-nitrone adducts (**32**–**35**) cannot degrade via this route.

The most persistent phosphorus-nitroxides are 2-Et-DMPO-R$^\bullet$ (**32**, **33**) and 2-Ph-DMPO-R$^\bullet$ (**34**, **35**) whose stabilities are very similar. The next most stable are the adducts of PBN (**27**–**29**) with those of DMPO (**30**, **31**) the least stable. Qualitatively, the phosphorus adducts of the aldo-nitrones (**27**–**31**) were ESR detectable for hours to days while the corresponding ones for the keto-nitrones (**32**–**35**) were observable for weeks to months. Little difference in persistence was observed between the phosphityl and phosphinyl adducts of the same nitrones. In summary, of all the phosphorus-nitroxides synthesized in this study, the best candidate for magnetometry would appear to be the phosphityl-nitroxide adduct of 2-Et-DMPO (**32**). Related phosphorus adducts of 2-alkyl-DMPO[20–22] have also been synthesized for these purposes.

## CONCLUSIONS

The design and synthesis of phosphorus-nitroxides (mainly $\beta$-$^{31}$P nitroxides) is an active research field. New $\beta$-$^{31}$P labelled spin traps[20,21,39–51] and spin probes[46,52–54] have recently appeared in the literature. At least three papers[20–22] deal specifically with magnetometry. Controlled/living stable free radical mediated polymerization using ordinary nitroxide spin probes such as 2,2,6,6 tetramethyl-piperidine-1- oxyl(TEMPO)[55–58] and TMIO (1,1,3,3,-tetramethyl-isoindoline-N-oxyl[59] have been studied by ESR and HPLC, respectively. $^{15}$N NMR has also been used to investigate polymerizations using $^{15}$N-labelled TEMPO derivatives.[60] Interestingly, some cyclic and non-cyclic $\beta$-phosphorus nitroxides have found their way to the scientific and industrial forefronts.[61,62] Our study here has shown that new and known $\beta$-phosphityl- and $\beta$-phosphinyl-nitroxides may be conveniently prepared by a novel 1,3-addition (of silicon-phosphorus reagents), acidic hydrolysis, oxidation sequence. In the case of PBN (**17**) it was possible to identify

the intermediate $\alpha$-phosphityl (**25**) and $\alpha$-phosphinyl (**26**) silylhydroxylamines by $^{1}H$, $^{13}C$ and $^{31}P$ NMR spectroscopy (Table 3). These assignments were made much easier by recording the $^{1}H$ and $^{13}C$ of the nitrones (Table 1) as well as the silicon-phosphorus reagents (Table 2). The ESR spectral parameters of the phosphorus-nitroxide adducts (**27**–**35**) from diethyl trimethylsilyl phosphite (**21**) and diphenyl(trimethylsilyl)phosphine (**23**) and the aldo-nitrones [PBN (**17**) and DMPO (**18**)] and the keto-nitrone [2-Et-DMPO (**19**) and 2-Ph-DMPO (**20**) were recorded and are collected in Table 4. It is noteworthy that the phosphityl adduct of DMPO (**30**) was not observed. In its place the oxidation product DMPOX$^{\bullet}$ (2-oxo-5,5-dimethylpyrrolidine-N-oxyl) was seen. In terms of persistence, the number of ESR lines, and the relatively large ($\beta$-phosphorus hyperfine splitting, it appears that the phosphityl adduct of 2-Et-DMPO (**32**) represents the best prototypical nitroxide examined here for use in magnetometry. Finally, it is worth mentioning that we are currently searching for phosphorus-centred radicals (e.g. $^{\bullet}PR_2$, etc.) because these species may exhibit even larger hyperfine splittings (10–100 mT).[63] The challenge, so far, has been to synthesize phosphorus-centred radicals[64,65] with sufficient persistence to be useful in real life magnetometric applications. Finally, it should be noted that the ESR hyperline splittings (hfs) of some known $\beta$-phosphorus nitroxides are collected in Table 4.[51,55–68] High magnitude ESR lines such as those from $^{31}P$ nuclei (spin 1/2) generally lead to better DNP responses, although the effect may be complicated.

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