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^{1}H, ^{2}H, ^{19}F AND ^{31}P NMR AND ESR INVESTIGATIONS OF ARYL-t-BUTYL NITROXIDES

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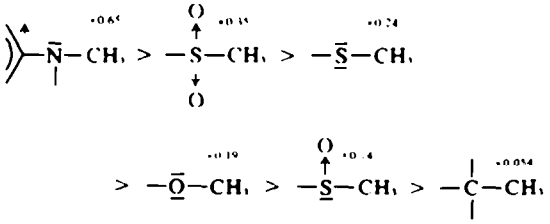
Abstract—Aspects of translocation of spin to fluorine and phosphorus are discussed. $(2p\text{-}3d)_\pi$ overlap in phosphorus is insignificant. Spin polarization and $(2p\text{-}3p)_\pi$ overlap are opposing spin transfer mechanisms for phosphorus. The ^{31}P NMR spectrum of the nitroxide from **7a** shows some features which are not fully understood. Some gain in resolution of the NMR spectra can be achieved by deuteration, but it is considerably lower than predicted.

Spin polarization predicts a negative spin density at hydrogen of the $\uparrow C\text{-}H$ fragment. In the $\uparrow C\text{-}\bar{X}$ fragment the spin delocalization mechanism, $\bar{C}\text{-}X\uparrow$, (synonymous to charge transfer, resonance or $(p\text{-}p)_\pi$ overlap) opposes spin polarization. It was demonstrated earlier[1-4] for X = F that spin is transmitted predominantly in the π-system, as predicted by the resonance formalism. It soon became clear that this is an oversimplification. Contrary to expectations, all fluorines in pentafluorophenyl - t - butyl nitroxide have positive hfs, and this is also the case for the fluorine in 2 - methyl - 5 - fluorophenyl - t - butyl nitroxide.[3] In these radicals the nitroxide group is rotated out of the plane by the *ortho*-substituent.

The planar 3 - fluorophenyl - t - butyl nitroxide and 3 - trifluoromethyl - phenyl - t - butyl nitroxide have negative F-hfs.[2] Since the aromatic hydrogens and methyls of these sterically hindered nitroxides indicate alternating signs of spin in the aromatic carbon ring skeleton, the findings above are difficult to rationalize by the simple resonance formalism. In the very moment π-conjugation is hindered and σ-transmission becomes important, no simple prediction concerning the sign of the spin can be made. We became interested in determining the sign of hfs of the 5-trifluoromethyl group in the sterically hindered nitroxide from the hydroxylamine **5**, as compared with the corresponding Me derivative. The results are reported in this work.

In an earlier work of this series,[1] the effect on spin transfer of successive removal of lone pairs was investigated. The spin transfer decreases in the series:



The $(p\text{-}n)_\pi$ conjugation is an effective mechanism for spin transfer, which also became evident for the OMe group when it was forced out of conjugation by two *ortho*-substituents.[3] The hfs of the Me decreased considerably and, furthermore, homohyperconjugation seems to be insignificant. Somewhat unexpectedly, the sulfono group is also an effective spin transmittant, despite the fact that it has no lone pair. All β-hfs are positive in the series, but one is not allowed to draw any definite conclusions from that about the sign of spin on the α-atom.† However, one is rather confident that the sign of net spin on N, O, S and SO is positive in accordance with the prediction of $(p\text{-}n)_\pi$ conjugation as a dominant factor in spin transfer; cf. fluorine in a planar system. For the α-C, it is negative, but for the SO_2 group it could be positive or negative, depending upon the mechanism operating. An efficient $(p\text{-}d)_\pi$ overlap or involvement of antibonding orbitals places spin of a positive sign on S, whereas, if spin polarization is dominant, this should give a negative sign. $(p\text{-}d)_\pi$ overlap was found to be insignificant for silicon.[4] We have chosen to investigate the significance of spin polarization, $(p\text{-}p)_\pi$ and $(p\text{-}d)_\pi$ overlap in the second row elements by ^{31}P NMR and ESR studies of nitroxides **6** and **7** containing 3-valent and 4-valent phosphorus, respectively.

Finally, t-butyl-phenyl, d_5, nitroxide was prepared in order to determine the gain in resolution obtained by deuterium labelling.

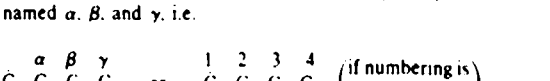
Synthesis. The hydroxylamine **5** was synthesized according to Scheme 1 and the phosphorus compounds according to Scheme 2.

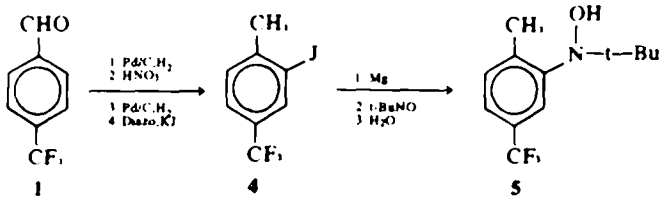
The nitroxides were generated by silver oxide oxidation of the hydroxylamines.

Results. The ESR spectrum of the nitroxide from **5** could not be resolved, but the hfs splittings could be obtained from the ^{1}H and ^{19}F NMR spectra (Table 1). The CF_3 group shows a small splitting of the same magnitude and sign as the Me derivative. Unless certain favourable conformations dominate, the hfs along an alkyl chain quickly attenuates. The high $^{4}H/^{4}CH_3$ value at the *meta* position of the hindered 2,5-dimethylphenyl nitroxide is indicative of a σ-spin transfer, and this is prevailing in the 2 - methyl - 5 - trifluoromethylphenyl nitroxide.

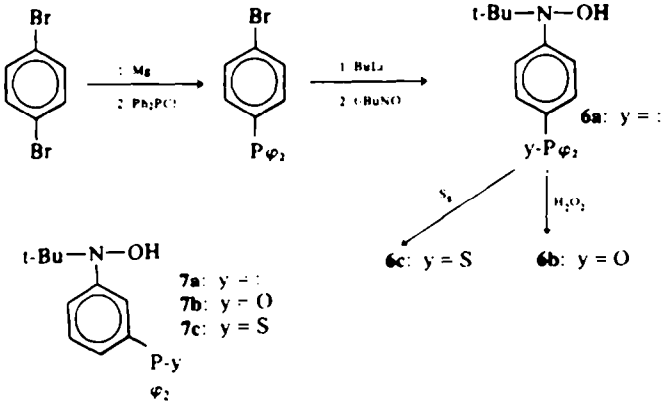
The ESR spectra of the radicals **6a, b, c** and **7a, b, c** show that the hfs of quaternized ^{31}P is larger than those of trivalent phosphorus. This is in concordance with the

†We suggest that ESR spectroscopists also use the logical notation that substituents (H, F, etc.) on α, β, or γ carbons be named α, β, and γ, i.e.





Scheme 1.



Scheme 2.

Table 1. Hyperfine splitting constants (gauss) obtained for Ar$\dot{N}$-t-Bu by ESR and NMR spectroscopy

Compound, Ar	Method[a]	a_N	a_2	a_3	a_4	a_5	a_6	$a_{t\text{-}Bu}$	Substituent	Refs
6a	ESR[b]	11.6	2.22	0.89	—	0.89	2.22		2.26 (P)	
6b	ESR	11.6	2.15	0.86	—	0.86	2.15		3.28 (P)	
	NMR			+0.84		+0.84		−0.030		
6c	ESR	11.6	2.22	0.90	—	0.90	2.22		3.35 (P)	
7a	ESR	12.4	1.95	—	1.95	0.87	1.95		<0.1 (P)	
	NMR								(−3.2 KHz)	
7b	ESR	12.4	1.86	—	1.86	0.89	1.86		1.37 (P)	
	NMR								+1.2 (P)	
									(−9.06 KHz)	
7c	ESR	12.2	2.02	—	2.02	0.89	2.02		1.40 (P)	
	NMR								+1.1 (P)	
									(−8.4 KHz)	
5	ESR	13.7							−0.06 (5-CF_3)	
	NMR		—	+0.64	−0.63	—	−0.82	−0.23	+0.25 (2-CH_3)	
3-trifluoromethylphenyl	NMR		−1.92	—	−1.92	+0.85	−1.92	−0.062	−0.62	2
2,5-dimethylphenyl	ESR	13.5							−0.1 (5-CH_3)	6
	NMR		—	+0.57	−0.37	—	−0.77	−0.24	+0.23 (2-CH_3)	
3,5-di-t-butylphenyl	ESR[c]	13.3	1.71	—	1.71	—	1.71		(3,5-t-Bu)	
	NMR		−1.78	—	−1.78	—	−1.78	−0.11	<0.01	
phenyl	NMR		−1.84	+0.83	−1.72	+0.83	−1.84	−0.09		
phenyl, d_5	NMR		−0.28	+0.13	−0.27	+0.13	−0.28	−0.09		

[a]The ESR measurements were carried out in DMSO, 25°C.
[b]These values are uncertain because of secondary oxidation.
[c]cf. Ref. 7.

opposing mechanisms formulated above. The spectrum of **6a** was difficult to analyze, since it contained the two superimposed spectra of **6a** and **6b**. In **7a** the effects balance each other so that the ^{31}P hfs is ~0 (Fig. 1a). Quaternization with, e.g. sulphur brings the ^{31}P hfs to 1.40 gauss and spin polarization predicts a positive sign. This was demonstrated by observing the magnitude of the low field shift in the ^{31}P NMR spectrum (Fig. 2, Table 1). The splitting constants calculated from the ^{31}P NMR spectra of the O and S derivatives agree reasonably well with the ESR data. This means that $(p\text{–}d)_\pi$ overlap for phosphorus is insignificant. d-Orbital participation is a matter of controversy; however, our findings are in agreement with some recent investigations[5,8–10] of the second row elements.

We were not able to observe the ^{31}P absorptions in the NMR spectra of **6a, b, c** because of the large shifts and corresponding very broad lines and instabilities of the radicals.

From the ESR data of **7a**, one expects a small shift in

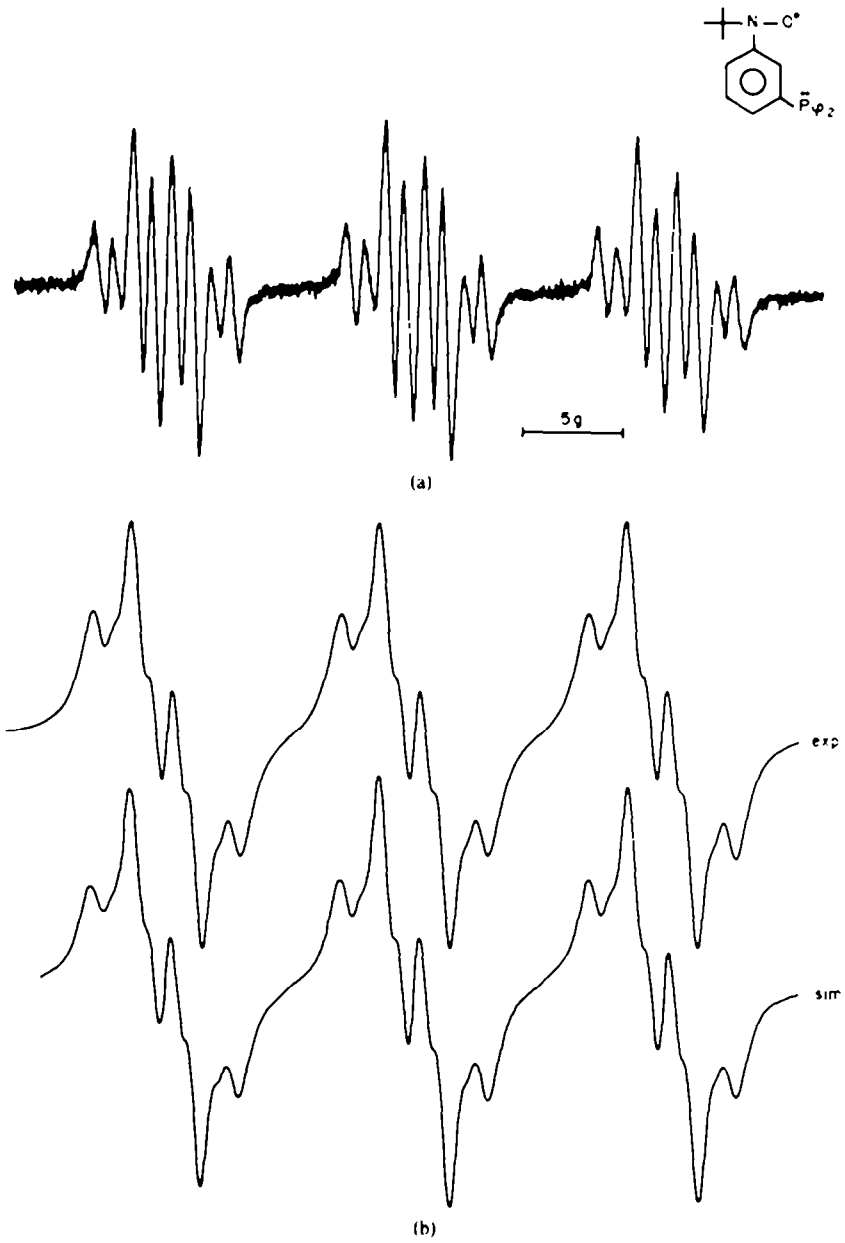


Fig. 1. (a) ESR spectrum of t-butyl-3-diphenylphosphinophenyl nitroxide from **7a**. (b) ESR spectra, experimental and simulated, (hfs from 1a.), of the same radical obtained in preparative scale and purified by TLC (see text).

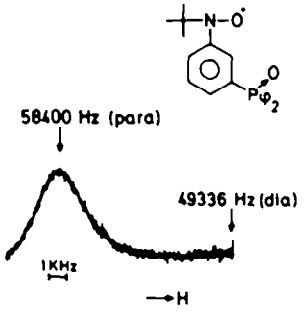


Fig. 2. ^{31}P NMR spectrum of the nitroxide radical from **7b**.

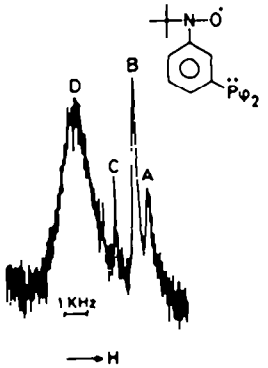


Fig. 3. ^{31}P NMR spectrum of t-butyl-3-diphenylphosphinophenyl nitroxide from **7a**. B and C are diamagnetic **7a** and **7b**, respectively. D is the nitroxide, and A is not identified (*cf* text).

the ^{31}P NMR spectrum. 80–90% of the total absorption is located in a broad band, D, shifted 3.2 KHz (~0.4 gauss) downfield which has no equivalent in the ESR spectrum

($a_p < 0.1$ gauss). Two of the narrow peaks were identified as diamagnetic **7a**, B, and **7b**, C. The unidentified peak A is believed to originate from decomposition products (Fig. 3). A freshly prepared sample of the nitroxide was chromatographed on a preparative TLC plate and the main fraction showed in the ESR, besides line broadening, again the same hfs as an original preparation (Fig. 1b). Thus, in this very case with a trivalent phosphorus, the NMR and ESR methods give different results. If this depends on the non-validity of the McConnell–Chesnuts relation[1] or the widely different experimental conditions (neat liquid for NMR; 10^{-3} M in DMSO for ESR) remains to be seen.

By measuring the NMR of t-butyl phenyl nitroxide as neat liquid, it was possible to resolve the *ortho* and *para* splittings. They coalesced on dilution with chloroform. The *o*- and *p*-deuterons are well resolved, but the gain in resolution is lower than predicted, ~6.5; *expt. ca.* 1.1 for the *m*-deuterons and 2.6 for the *o*- and *p*-deuterons, as measured by the relative line width ratio of the ^1H and ^2H NMR spectra.

From this and earlier work in this series it is evident that formalisms such as spin polarization, charge transfer, $(p–p)_\sigma$ and $(p–d)_\sigma$ overlap, hyper- and homo-hyperconjugation as visualized are unreliable to predict sign of spin.

EXPERIMENTAL

The NMR measurements were performed on a Varian XL-100-15 spectrometer with accessories for recording the ^2H and ^{31}P spectra, and the ESR measurements on a Varian E3 instrument. NMR spectra of the radicals were run on neat liquids or the radical was diluted with a small amount of chloroform.

The m.ps and b.ps are not corrected.

Generation of the radicals for the ESR measurements. The radicals appeared immediately in a DMSO soln of the corresponding hydroxylamine on addition of a small amount of dil NaOHaq.

p-Trifluoromethyl-toluene, **1**. p-Trifluoromethyl-benzaldehyde (10 g, 57.5 mmole) in MeOH (25 ml), conc H_2SO_4 (3 ml), and water (1 ml) was reduced over Pd/C (5%, 0.5 g) with H_2 for 6 hr at 25° and 3.5 atm. After filtration, water (150 ml) was added and the soln was extracted with CH_2Cl_2 (2 × 50 ml), washed with water (60 ml) to remove most of the MeOH, and dried over $MgSO_4$. The solvent was carefully evaporated and the remainder distilled giving p-trifluoromethyl-toluene (7.4 g crude product, 80%).

2-Iodo-4-trifluoromethyl-toluene, **4**. **1** (11.7 g crude product) was added to a mixture of conc H_2SO_4 (47 ml), and conc HNO_3 (35 ml). The soln was heated with stirring to 55–60° for 1 hr. Hydrolysis with ice (500 ml), extraction with CH_2Cl_2 (2 × 50 ml), drying ($MgSO_4$), and evaporation yielded **2** (12.3 g, 82% crude yield).

Compound **2** (12.3 g) was hydrogenated in EtOH (50 ml) over Pd/C (5%, 0.9 g) for 3 hr at 25° and 3.5 atm. Filtration and evaporation gave 9.0 g of 2-amino-4-trifluoromethyltoluene, **3**, which was purified by dissolution in petrol ether with active carbon. Evaporation of the solvent yielded **3** (8.1 g, 77% crude yield) which solidified in the freezer.

Compound **3** (10.77 g, 61.5 mmole) was stirred in water (54 ml) and conc H_2SO_4 (8.6 ml)—the sulphate precipitated—and $NaNO_2$ (4.24 g, 61.5 mmol) in water (20 ml) was added at 0–5°. The soln was stirred for 1 hr at 0–5° and urea (0.2 g), KI (13.3 g, 102 mmole) in water (20 ml) and conc. H_2SO_4 (2 ml) were then added at 0–5°. After 4 hr the N_2-generation stopped and the mixture was then heated and maintained at 80° for 5 min. Some $NaHSO_3$ was added. The mixture was extracted with CH_2Cl_2 (2 × 40 ml), washed with a sat. $NaHCO_3$ aq, dried ($MgSO_4$), and solvent evaporated. Distillation gave **4** (9.8 g) b.p. 83–85°/14 Torr (lit.[2] 65–66°/4.8 Torr). NMR (CCl_4): δ 2.45 (3 H, s); 7.36 (2 H, q).

t-Butyl - 2 - methyl - 5 - trifluorophenyl hydroxylamine, **5**, was prepared from the Grignard compound of **4** and t-nitrosobutane in a yield of 17%, m.p. 99–105° (acetonitrile). NMR ($CDCl_3$): δ 7.81 (1 H, br, s); 7.17 (2 H, AB spectrum); 2.21 (3 H, s); 1.14 (9 H, s). (Found: C, 58.1; H, 6.53. Calc. for $C_{12}H_{16}ONF_3$: C, 58.3; H, 6.42%).

p - N - t - Butylhydroxylaminophenyl - diphenylphosphine, **6a**. To p - Bromophenyl - diphenylphosphine[13] (10.0 g) in dry ether (200 ml) BuLi (28 ml, 15% in hexane) was added under N_2 at −30°. After stirring for 25 min at −20° to −10°, the temp. was raised to 0° and t-nitrosobutane (4.0 g) in dry THF (20 ml) was added. The mixture was hydrolyzed with ice-water (200 ml), the layers were separated, and the ether phase was dried ($MgSO_4$) and evaporated. The semi-solid residue was recrystallized in acetonitrile giving **6a** (5.65 g, 55%), m.p. 167–170°. The m-derivative **7a**, m.p. 134–135°, was prepared in the same way and the yield was 57%. (Found: C, 75.40; H, 6.90; N, 4.01. Calc. for **7a**, $C_{22}H_{24}ONP$: C, 75.65; H, 6.93; N, 4.01%).

6a showed two spots on TLC ($CHCl_3$, 3% MeOH). Purification over silica gave the pure compound, m.p. 164°. The other fraction proved to be the phosphinoxide **6b**, m.p. 194°C.

The phosphinoxides **6b** *and* **7b**. The corresponding phosphine **6a** or **7a** (1.8 g) dissolved in EtOH/CH_2Cl_2 (20 ml 1:1) was oxidized with H_2O_2 (28%, 1 ml) at 5° for 4 hr. Water was added and the organic phase separated, dried (Na_2SO_4), and evaporated. Recrystallization from acetonitrile gave **6b**, m.p. 194°, and **7b**, m.p. 188–192°, respectively, in a yield of *ca.* 70–80%. (Found for **6b**: C, 72.4; H, 6.56; N, 3.86, and for **7b**: C, 71.9; H, 6.68. Calc. for $C_{22}H_{24}O_2NP$: C, 72.4; H, 6.64; N, 3.84%).

The thiophosphines **6c** *and* **7c**. The phosphine **6a** or **7a** (0.6 g) was stirred with S (0.25 g) in CH_2Cl_2 (6 ml) for 28 hr. Evaporation of the solvent and dissolution in MeOH, filtration, and evaporation gave the sulphide **6c** or **7c** which was recrystallized from acetonitrile, m.p. 151 and 138°, respectively. The yields were *ca.* 60%. (Found for **6c**: C, 69.20; H, 6.37, and for **7c**: C, 69.03; H, 6.43; N, 3.67. Calc. for $C_{22}H_{24}ONPS$: C, 69.29; H, 6.34; N, 3.67%).

t-Butyl-phenyl, d_5, *hydroxylamine and the nitroxide* were prepared from bromobenzene, d_5, and t-nitrosobutane via the Grignard reaction, m.p. 123°. The hydroxylamine (0.6 g) was oxidized in benzene (4 ml) at 0–3° with silveroxide (0.6 g) for 25 min with good stirring. The solvent was rapidly evaporated *in vacuum* and the NMR spectrum of the red viscous radical was recorded at −10° as quickly as possible (within 10–15 min) in order to minimize linewidth broadening caused by decomposition. The other nitroxides were generated in the same way. CH_2Cl_2 was also used as solvent for the oxidation with silveroxide.

3,5-Di-t-butyl-phenyl-t-butyl hydroxylamine was prepared from 3,5-di-t-butyl-bromobenzene[14] via the Grignard reagent and t-butyl nitrosobutane in ether. The yield was 18% and the m.p. 126° (from acetonitrile). (Found: C, 77.68; H, 11.17. Calc. for $C_{18}H_{31}NO$: C, 77.97; H, 11.18%).

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