J. Am. Chem. Soc. **1981**, *103*, 1041–1047

all-trans or 9-cis conformation the triplet state. The problem of photolability was discussed with emphasis on the present experimental conditions. The triplet state spectrum obtained was compared with those of intermediates occurring in the photocycle of bacteriorhodopsin. A close resemblance was found between the vibrational spectrum of the bL_{550} intermediate as reported by El-Sayed and co-workers and our triplet spectrum. Furthermore, the rate constant for triplet energy transfer from naphthalene to *all-trans*-retinal has been determined to $k_2 = 5.5 \times 10^9\ \mathrm{M^{-1}\,s^{-1}}$ and the second-order rate constant for triplet–triplet annihilation was found to be $2k_3 = 6 \times 10^9\ \mathrm{M^{-1}\,s^{-1}}$.

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Free Radical Induced Nuclear Magnetic Resonance Shifts: Comments on Contact Shift Mechanisms

Dan Draney* and Charles A. Kingsbury

Contribution from the Department of Chemistry, University of Nebraska, Lincoln, Nebraska 68588. Received May 5, 1980

Abstract: Experiments designed to test the various mechanisms proposed by Morishima et al. (*J. Am. Chem. Soc.*, 1970–1975) for the interaction of the organic radical di-*tert*-butyl nitroxide (DBNO) with various organic substrates are reported. Cyclohexane shows a strongly solvent-dependent interaction with the radical and is therefore unsuitable as an internal standard. Charge transfer, involving π systems, does not seem to be an important mechanism for induced shifts in benzophenones, as there is no evidence of ketyl formation. However, charge transfer may occur from nitroxide to *m*-dinitrobenzene. The change in bulk magnetic susceptibility of the solutions due to the addition of radical was found to cause significant shifts of NMR signals. The various models for interaction between radical and substrate are reviewed.

The effect of paramagnetic metal ions on the ^{1}H NMR chemical shifts in various organic molecules and metal complexes has been studied by Eaton[1] and by Drago[2] and their respective co-workers in the 1960's and early 1970's. LaMar[3] and Kreilick[4] have also applied NMR to studies of a variety of paramagnetic systems. More recently Roberts and co-workers[5] and Goff[6] have elucidated the effects of paramagnetic ions on ^{13}C spectra of organic ligands. Richards, Dwek, and Poindexter[7–9] and Mueller-Warmuth[10] have studied the unpaired electron distribution in paramagnetic organic systems by unique experiments involving NMR observation of microwave-irradiated molecules. Evidence for both scalar mechanisms (where odd-electron density is transmitted by polarization of bonding electrons) and dipolar mechanisms (through space) was given.

With regard to the ^{13}C mode of investigation, Morishima and co-workers[11] have recently published a series of papers on the chemical shift changes observed in a variety of molecules induced by radicals such as di-*tert*-butyl nitroxide (DBNO). Generally, a Fermi contact (scalar) interaction was invoked because of a Curie law dependence of the chemical shift change with T^{-1}. However, it is unclear whether a Curie law dependence necessarily excludes contributions from pseudocontact shifts. Horrock's work suggests that it does not.[12] In one case, Morishima did in fact propose a pseudocontact interaction.[13]

Several mechanisms were considered by Morishima and co-workers to explain the DBNO-induced shifts: (1) Hydrogen bonding between DBNO and the OH or CH bonds of the substrate; in other work, the term "spin polarization" was applied. The two terms appeared to be used interchangeably.[11a–d] (2) A spin delocalization mechanism, in which the radical donates an electron to an antibonding orbital of the substrate; i.e., to the antibonding orbital of C–X bonds (X = F, Cl, Br, or I).[11c] (3) In later work, a direct interaction between the radical and p orbitals was considered to lead to negative "spin density" on aromatic or olefinic carbons.[11a]

Morishima's work and our own experience have shown that acidic hydrogens (in the hydrogen bonding sense) undergo upfield shifts in the presence of DBNO, whereas nonacidic hydrogens exhibit a complex behavior that is not understood.[14] In some cases, no shift at all for ^{1}H is observed, although the attached ^{13}C is shifted. Due to the broadness of the ^{1}H spectra and the complexity of the spectra obtained in annular-tube experiments, ^{1}H-induced shifts will not be considered in this paper.

Our interest in ^{13}C contact shifts arose from reports by Morishima and co-workers of a correlation between contact shifts and spin–spin coupling constants.[11e] The conformational dependence of certain DBNO-induced shifts was shown to be similar to the well-known W effect in spin coupling.[13] Thus, it seemed possible

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(11) (a) Morishima, I.; Inubushi, T.; Endo, K.; Yonezawa, T. *Chem. Phys. Lett.* **1972**, *14*, 372. *J. Am. Chem. Soc.* **1975**, *97*, 2749 and references cited. (b) Morishima, I.; Toyoda, K.; Yoshikawa, K.; Yonezawa, T. *Ibid.* **1973**, *95*, 8627 and references cited. (c) Morishima, I.; Kawakami, K.; Yonezawa, T.; Goto, K.; Imanari, M. *Ibid.* **1972**, *94*, 6555. (d) Morishima, I.; Okada, K.; Yonezawa, T.; Goto, K. *Ibid.* **1972**, *94*, 4812. (e) Morishima, I.; Endo, K.; Yonezawa, T. *Ibid.* **1971**, *93*, 2048. (f) Morishima, I.; Matsui, T.; Yonezawa, T.; Goto, K. *J. Chem. Soc., Perkin Trans. 2* **1972**, 633. (g) Morishima, I.; Endo, K.; Yonezawa, T. *Chem. Phys. Lett.* **1971**, *9*, 203. *J. Chem. Phys.* **1973**, *58*, 3146.

(12) Horrocks, W. deW., Jr.; Sipe, J. P., III; Sudnick, D. In "NMR Shift Reagents"; Sievers, R. E., Ed.; Academic Press: New York, 1973. Pseudocontact shifts were shown to give a T^{-1} dependence in ordinary temperature ranges in the system tested.

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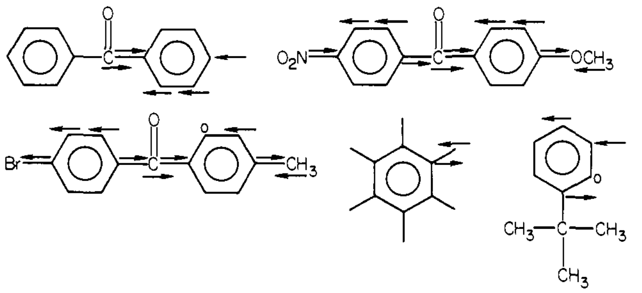
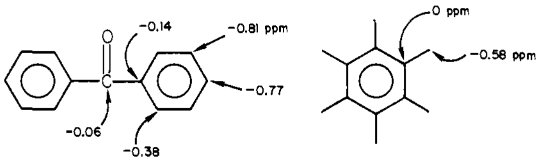
0002-7863/81/1503-1041$01.25/0

Chart I

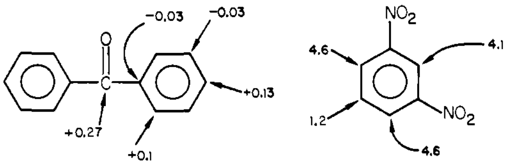
A. Observed Direction of Induced Shifts Relative to Internal Cyclohexane as Standard[a]



B. Induced Shifts (Relative to an External Standard), as Corrected for Bulk Susceptibility



C. ^{13}C Hyperfine Couplings in Benzophenone and ^1H Hyperfine Splittings in Dinitrobenzene Radical Anion[16]



[a] Diagrams represent spectral image: a leftward arrow signifies a downfield shift; a "0" signifies no shift.

that nitroxide-induced shifts might be developed into a method for the study of molecular conformation in highly substituted molecules, in which the usual NMR data are uninformative. However, this objective requires a firm understanding of the mechanisms of transmission of spin density. In particular, electron transfer to the π system of an aromatic substrate would appear to be a possible mechanism, as similar processes are well-known from both chemical reactions[15] and ESR studies.[16] Electron transfer would lead to higher spin densities than spin polarization of the π electrons by DBNO. Similar π interactions had been considered in early work by Poindexter and co-workers.[8] Initially, Morishima rejected such mechanisms because the chemical shifts of the carbons of benzene did not alternate upon interaction with a radical, as expected by Morishima for a p–π spin delocalization mechanism.[11f] However, it appeared to us that interaction of DBNO with any of the six benzene positions is equally likely, and more important, a time-averaged equivalency would result in chemical shift on the NMR time scale. Morishima later invoked a radical–π interaction in an aromatic system.[11c] Nonetheless, the range of importance of such interactions is unsettled at the present time. Also, the importance of electron transfer as opposed to spin polarization of the π electrons is not fully established.

Initial experiments involved studies of contact shifts in a class of compounds known to be strong π acceptors, i.e., benzophenones. Electron transfer forming the well-known ketyl radical anion seems likely and not merely spin polarization of the π electrons. The radical anion formed by electron transfer has been thoroughly studied by ESR techniques, and spin densities have been calculated.[16] The nitroxide-induced chemical shifts in a series of benzophenones bore no relationship to spin densities determined in relation to ESR studies (cf. Chart I). Thus, the carbonyl carbon undergoes smaller shifts than certain aromatic carbons. No relationship to ^{13}C coupling constants was apparent.[17] Thus, either a radical anion does not form or, alternatively, each carbon experiences spin density imparted by a variety of mechanisms, including π-electron transfer. The averaging of these effects may mask electron transfer. If no radical anion is formed, it may be that DBNO is a poor donor. If so, it is then difficult to believe that DBNO could donate an electron to the C–X antibonding orbital, as postulated by Morishima to explain the shifts of carbons attached to halogen.[11c]

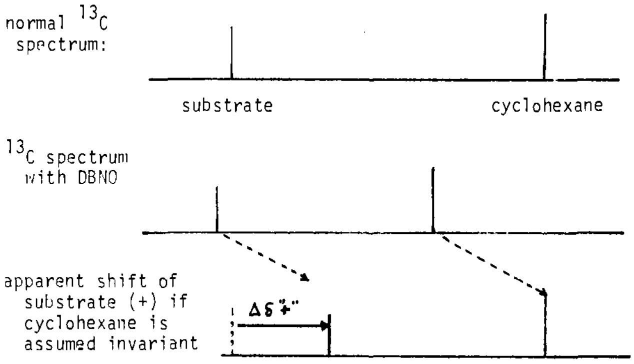


Figure 1.

Next, hexamethylbenzene and *tert*-butylbenzene were examined to see if DBNO might function in the opposite role, namely, as an electron acceptor. The induced chemical shift change of the methyls of hexamethylbenzene is smaller than and of opposite sense from the shifts of aromatic carbons (relative to internal cyclohexane as standard). While the large size of the shift of the aromatic carbon might be construed as a DBNO–π interaction,[11a] subsequent work on absolute shifts did not support this idea. In the case of *tert*-butylbenzene, a weak electron donor, the quaternary and the ipso aromatic carbons are shifted in the opposite sense than CH carbons. The results were rather similar to those for the benzophenones, which are not electron donors.

The pattern of the data, at this time, suggested that carbons attached to hydrogen(s) undergo downfield shifts (negative), although hindered CH groups were but slightly shifted. Carbons lacking an attached hydrogen were often shifted "upfield". Thus, although we disagreed with Morishima's reasons for initially excluding π interations, we are in agreement that C–H (or, possibly C–X) bonds appeared to be the site of interaction. However, in view of the sizable shifts of simple alkyl groups (methyls of *tert*-butylbenzene, for example), we became concerned about the validity of the use of cyclohexane as an internal standard. There is no reason to assume that cyclohexane is uniquely inert to DBNO. Thus, a "positive" or apparent upfield shift may merely indicate that this particular carbon of the substrate interacts with nitroxide to a lesser extent than cyclohexane and moves downfield to a lesser extent than cyclohexane (Figure 1).[18]

This hypothesis was tested by using mixtures of simple compounds and constant DBNO concentrations (hereafter 0.31 M) and an *external* standard (usually methanol in D_2O). The radical-induced shift of cyclohexane was found to be slightly downfield but also rather highly dependent upon the nature of the solution. The shift of cyclohexane was ca. 0 ppm in solutions of alkanes but up to 0.20 ppm when alcohols were present.

The variation in the DBNO-induced shift for cyclohexane is believed to be due to a competition between cyclohexane and the other components for DBNO. When the other component interacts with DBNO strongly (e.g., hydrogen bonders such as 1-propanol), a direct interaction between DBNO and cyclohexane

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Table I. DBNO[a]-Induced Shifts in ^{13}C Absorption[b] of Various Substrates

run	sample composition[c]	carbon	$\Delta\delta$, ppm	$\Delta\delta_{corr}$, ppm
1	90% heptane	1	−0.32	−1.19
		2	+0.06	−0.81
		3	+0.18	−0.69
		4	+0.22	−0.65
	10% cyclohexane	1–6	+0.02	−0.85
2	90% 2,3-dimethylbutane	1	−0.10	−0.97
		2	+0.47	−0.40
	10% cyclohexane	1–6	+0.08	−0.79
3–9[d]	90% 2,2-dimethylbutane	1	−0.11	−0.98
		2	+0.81	−0.06
		3	+0.13	−0.74
		4	−0.19	−1.06
	10% cyclohexane	1–6	+0.08	−0.79
10	50% 1-propanol	1	+0.35	−0.52
		2	−0.14	−1.01
		3	−0.20	−1.07
	40% 2,2-dimethylbutane	1	+0.18	−0.69
		2	+0.79	−0.08
		3	+0.37	−0.50
		4	+0.10	−0.77
	10% cyclohexane	1–6	+0.20	−0.67
11–12[d]	50% 1,2-dimethoxyethane	1 (CH_3)	−1.14	−2.01
		3 (CH_2)	−0.48	−1.35
	40% 2,2-dimethylbutane	1	0.00	−0.87
		2	+0.80	−0.07
		3	+0.24	−0.63
		4	−0.09	−0.96
	10% cyclohexane	1–6	+0.12	−0.75

[a] Each solution is 0.31 M in DBNO. [b] Shifts measured against external methanol; error in measurement per chemical shift measurement is ±0.02 ppm. [c] % v/v. [d] In multiple runs on the same sample composition, the largest spread of ^{13}C resonance was ±0.05; the average was ±0.02.

Table II. Effect of Diamagnetic Substrate Concentration Concentration[a] on $\Delta\delta_{corr}$

2,2-Dimethylbutane (DMB) and Pentane (P)

		DMB:P[b]		
	carbon no.	25:75 $\Delta\delta_{corr}$[c]	50:50 $\Delta\delta_{corr}$[c]	75:25 $\Delta\delta_{corr}$[c]
DMB	1	−0.96	−0.98	−0.97
	2	0.01	−0.05	−0.06
	3	−0.68	−0.72	−0.72
	4	−1.05	−1.06	−1.06
pentane	1	−1.16	−1.18	−1.15
	2	−0.73	−0.78	−0.77
	3	−0.66	−0.72	−0.70

2,2-Dimethylbutane and 1,2-Dimethoxyethane (DME)

		DMB:DME[b]		
	carbon no.	0:100 $\Delta\delta$	75:25 $\Delta\delta_{corr}$[c]	90:10 $\Delta\delta_{corr}$[c]
DMB	1		−0.89	−0.94
	2		−0.06	−0.04
	3		−0.65	−0.68
	4		−0.98	−1.04
DME	CH_3	−1.70	−2.25	−2.54
	CH_2	−1.11	−1.55	−1.77

Hexane and Tetramethylsilane

		Me_4Si:hexane[b]	
	carbon no.	10:90 $\Delta\delta_{corr}$[c]	5:95 $\Delta\delta_{corr}$[c]
hexane	1	−1.10	−1.15
	2	−0.73	−0.75
	3	−0.63	−0.64
Me_4Si	CH_3	−1.16	−1.18

[a] DBNO concentration is 0.31 M. [b] Composition by volume. [c] The computer-listed error in δ is ±0.02 ppm.

is correspondingly reduced. Cyclohexane experiences only a generalized effect of DBNO, i.e., a change in the bulk susceptibility of the medium due to addition of the paramagnetic DBNO. On the other hand, in solutions of alkanes and cyclohexane, cyclohexane competes effectively. The indirect effect (bulk susceptibility) and the direct effect are nearly equal but opposite, and little net shift is observed. Nonetheless, the sensitivity of cyclohexane to solution composition renders cyclohexane unacceptable as standard.

To a first approximation, the change in bulk susceptibility causes a uniform shift of all resonances in the sample. This uniform shift can be subtracted from the overall shift to yield the effect of a direct interaction of various carbons with DBNO.[19]

$$\Delta\delta_{corr} = \Delta\delta_{obsd} - \Delta\delta_{bulk} \qquad (1)$$

In eq 1 $\Delta\delta_{obsd}$ is the observed paramagnetic shift relative to the *external* standard. For cylindrical samples, the bulk magnetic susceptibility correction may be assessed[19]

$$\Delta\delta_{bulk} = \tfrac{2}{3}\pi(\chi_1 - \chi_0) \qquad (2)$$

The volume magnetic susceptibilities, χ_0 and χ_1 are those of the sample before and after addition of DBNO. For a given radical concentration, the difference $\chi_1 - \chi_0$ and the value of the correction are independent of the nature of the sample (provided no reaction occurs) and the resonance frequency of the nucleus observed.[19] Using annular tubes and the experimental approach and calculation of the results as described in the Experimental Section gave $\Delta\delta_{bulk} = +0.87 \pm 0.02$ ppm. The reality of this correction was tested by using molecules such as 2,2-dimethylbutane (DMB) (cf. Table I). In contrast to cyclohexane, the quaternary carbon of DMB shows a very similar paramagnetic shift, within experimental error, regardless of sample composition. Steric effects preclude close approach of DBNO, and the shift of the quaternary carbon should be almost entirely due to bulk susceptibility effects. The shift of the buried carbon, $\Delta\delta_{obsd}$ = +0.79 to +0.81 ppm, indeed lies close to the calculated value of $\Delta\delta_{bulk}$. Thus, interactions of DBNO elsewhere in the substrate do not affect the quaternary carbon a great deal. Bulk susceptibility effects were considered small in previous work,[11] although in the present study, these effects must be considered in order to evaluate the mechanism of a direct DBNO–substrate interaction.

Part B of Chart I gives the $\Delta\delta_{corr}$ values for benzophenone and for hexamethylbenzene. The complexion of the results is altered by correction for bulk susceptibility. In fact, no positive (upfield) shifts at all are observed that might be ascribed to "negative spin density" (vide infra). Carbons lacking an attached hydrogen show approximately zero induced shifts. No effect of DBNO either as a donor or as an acceptor to π systems is evident. No correlation exists with ketyl odd-electron spin densities. DBNO may polarize the aromatic π electrons, and, in fact, such an interaction seems quite likely, in view of results to be presented later. However, the sp^2 carbon can only sense the odd-electron density via a secondary polarization of σ electrons, whose orbital has a finite coefficient at carbon.[16] However, as seen from the DMB data, such indirect effects are small.

Concentration Dependence. Morishima showed that the induced shift of various substrates is linear with respect to the concentration of added DBNO. Varying the concentration of substrate at constant radical concentration also leads to interesting results (cf. Table II).

If both the solvent and solute are alkanes, as for pentane and 2,2-dimethylbutane (DMB), increasing the concentration of one component with respect to the other has little effect. The two alkanes have roughly equal affinity for DBNO. The chemical

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Table III. DBNO[a]-Induced Shifts for ^{13}C

substrate[b]	solvent	carbon position	$\Delta\delta_{corr}$,[c] ppm
tetramethylene-ethylenediamine	hexane	CH_3	−1.53
		CH_2	−0.79
triethylamine	hexane	CH_3	−1.20
		CH_2	−0.83
tributylphosphine	cyclohexane	1	−0.88
		2	−0.70
		3	−0.79
		4	−1.25
dimethyl sulfide	hexane	CH_3	−3.54
m-xylene	hexane	1,3	−0.20
		2	0.96
		4,6	−1.11
		5	−1.16
m-xylene	$CDCl_3$	1,3	−0.03
		2	−0.33
		4,6	−0.43
		5	−0.49
		$\mathit{C}DCl_3$	−19.5
m-dinitrobenzene	$CDCl_3$	1,3	−0.39
		2	−0.58
		4,6	−2.20
		5	−2.69
		$\mathit{C}DCl_3$	−17.6

[a] Radical concentration 0.31 M. [b] Concentrations of substrate (in order): 10% (v/v), 20% (v/v), 50% (v/v), 10% (v/v), 1.0 M, 1.0 M, 1.0 M. [c] Error in line position, 0.02 ppm.

Table IV. DBNO[a]-Induced ^{31}P,[b] ^{11}B,[c] and ^{19}F[d] Shifts

substrate[e]	solvent	δ_{corr}, ppm	notes
$[CH_3(CH_2)_3]_3P$	cyclohexane	−1.67	
$[c\text{-}C_6H_{11}]_3P$	cyclohexane	−0.03	
$Ph_2PCH_2CH_2PPh_2$	benzene	−1.36	
$(CH_3CH_2O)_3P$[f]	hexane	−2.12	
$(CH_3O)_3P$	hexane	−2.40	
$(CH_3CH_2CH_2CH_2O)_3B$	cyclohexane	+0.22	
p-XC_6H_4F[f]	cyclohexane		
$X = OCH_3$		−1.15	δ_F[d] = 48.8 ppm
$X = CH_3$		−1.17	42.7
$X = H$		−1.20	37.2
$X = COCH_3$		−1.46	30.9
$X = NO_2$		−1.83	27.6

[a] 0.31 M in DBNO in each case. [b] Triphenylphosphine was the external standard. [c] Tetrafluoroborate ion in D_2O was the external standard. [d] Trifluoroacetic acid was the external standard; the chemical shifts reported were measured in the absence of radical and are upfield from trifluoroacetic acid. [e] Concentrations (in order): 50% (v/v), 0.71 M, 0.25 M, 1.0 M, 1.0 M, 2.0 M, and 2.0 M for each substituent X. [f] In contrast, $(CH_3CH_2O)_3P{=}O$ (neat) undergoes an induced shift of only −0.24 ppm.

shift, δ_{corr}, is the average of the chemical shifts of complexed and uncomplexed species (SR and S, respectively).[20]

$$\delta_{corr} = \frac{(SR)\delta_{SR} + (S)\delta_S}{(S) + (SR)} \tag{3}$$

If the equilibrium constant for complexation is very small, (SR) is also small and (S) is essentially the stoichiometric concentration of substrate added, $(S)_{stoi}$. Thus

$$\delta_{corr} = [(SR)\delta_{SR} + (S)\delta_S]/(S)_{stoi} \tag{4}$$

$$\delta_{corr} = (SR)\delta_{SR}/(S)_{stoi} + \delta_S \tag{5}$$

$$\Delta\delta_{corr} = (SR)\delta_{SR}/(S)_{stoi} \tag{6}$$

If the equilibrium relationship for the interaction of substrate and radical holds

$$K = (SR)/(S)(R) \tag{7}$$

Thus

$$\Delta\delta_{corr} = K(R)\delta_{SR} \tag{8}$$

If the equilibrium constant is indeed small, (R) also reflects $(R)_{stoi}$ and the chemical shift appears functionally independent of substrate concentration. A similar expression may be derived for both components of mixtures of two similar substrates such as two alkanes.

For a two-component mixture where one component has a high affinity for nitroxide, as indicated by the high shifts for dimethoxyethane (DME) of DMB/DME mixtures, a concentration effect is indeed found (cf. Table II). The $\Delta\delta_{corr}$ values for DMB become less negative as the concentration of DME increases from 10 to 25% (except for the quaternary carbon of DMB). However, the ^{13}C resonances of DME are also less shifted at the higher DME concentrations, particularly at 100% DME. The radical concentration (R) of eq 8 is reduced by complexation with DME present in solution, and the shift $\Delta\delta_{corr}$ averaged over all DME molecules is reduced due to lesser probability of complexation of DBNO with each fresh increment of DME.

However, it is also quite possible that equilibrium relationships (cf. eq 7) do not in fact hold and that a momentary contact interaction is merely governed by diffusional constraints, as pointed out by Poindexter some years ago.[9] This possibility is particularly worthy of consideration for the alkane components.

Table II also illustrates the effect of DBNO on the tetramethylsilane/hexane system. Me_4Si is of interest with regard to the ability of the radical to interact with unoccupied d orbitals. Silanes have been shown to interact with amines under certain conditions.[21] Me_4Si however, does not appear to interact strongly with the open-shell DBNO. The alkane chemical shifts do not indicate that the silane associates strongly with the radical.

The finding that the interaction of certain substrates with DBNO gave concentration-dependent chemical shifts that could be interpreted in terms of association equilibria also led to a brief investigation of competition effects for π systems. As shown in Table III, *m*-xylene undergoes sizable induced shifts in hexane solution, even though the number of interacting C–H groups is small compared to that in alkanes such as DMB. Steric hindrance is evident in the slightly smaller shift for C_2 compared to the other protonated carbons. The same substrate undergoes substantially smaller shifts in $CDCl_3$ solution, where the solvent is known to interact strongly with DBNO (cf. the large shift for $\mathit{C}DCl_3$). A similarly substituted molecule, *m*-dinitrobenzene, on the other hand, undergoes significantly larger shifts even in $CDCl_3$, and the shift of the solvent is corresponding reduced (−17.6 ppm), indicative of the fact that the substrate is competing effectively with the solvent for DBNO. As *m*-dinitrobenzene is a well-known electron acceptor from many ESR and chemical reaction studies, electron transfer from DBNO might well be expected.[15] A molecule lacking CH groups, bromopentafluorobenzene undergoes much larger shifts for the ortho (−2.11 ppm), meta (−2.67 ppm), and para (−2.43 ppm) fluorines than the monosubstituted fluorobenzenes listed in Table IV ($\Delta\delta_{corr}$ ca. −1.2 to −1.9 ppm). If, as Morishima suggests,[11c] fluorines interact weakly with DBNO, an electron transfer to the π system would seem to be the most likely mechanism that accounts for the roughly equivalent shift of all fluorines.

Interactions of n Electrons with DBNO. Interactions with nonbonded electron pairs are known to stabilize radical cations formed by oxidation of thioethers.[22] Sulfur and phosphorus

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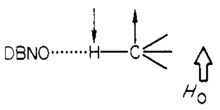
(20) Feeney, J.; Birdsall, B.; Roberts, G. C. K.; Burgen, A. S. V. In "NMR in Biology"; Dwek, R. A., et al., Eds.; Academic Press: London, 1977; p 113.

(21) Sommer, L. H. "Stereochemistry, Mechanism, and Silicon"; McGraw-Hill: New York, 1965; p 22.

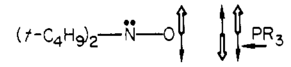
(22) (a) Musker, W. K.; Wolford, T. L.; Roush, P. B. *J. Am. Chem. Soc.* **1978**, *100*, 6146. (b) Asmus, K.-D.; Bahnemann, D.; Fischer, Ch.-H.; Veltwisch, D. *Ibid.* **1979**, *101*, 5322. (c) Glass, R. S.; Duchek, J. R.; Klug, J. T.; Wilson, G. S. *Ibid.* **1977**, *99*, 7349.

Chart II[a]

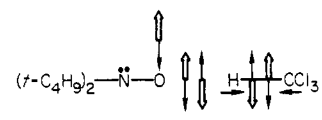
Morishima's Spin Polarization Model



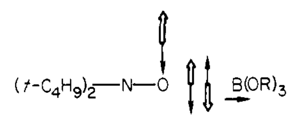
Spin Polarization of the Phosphorus Lone Pair



Hydrogen Bonding through the Nitroxide Lone Pair



Lewis Acid-Base Association through the Nitroxide Lone Pair



[a] $\underset{\leftarrow}{X}$, transverse arrow signifies direction of NMR shift of nucleus X (negative, in this case; ⇧, magnetic moment due to electron spin; ↓, preferred electron spin; $\overset{\Uparrow}{H_0}$, applied magnetic field.

showed particularly strong interactions, while oxygen was somewhat less effective. A two-center, three-electron bond was believed to be responsible. The odd electron was found to be antibonding, as the bond order increased upon oxidation to the dication.

Examination of the DBNO-induced shifts for compounds containing heteroatoms (cf. Tables I–III) indicates that these molecules interact with the radical quite strongly. As indicated earlier, the dimethoxyethane (DME) shifts are much more negative than the shifts for similarly situated carbons in alkanes. The shifts for DME are larger than those found in 1-propanol. Thus, the effect of oxygen cannot be explained solely by its ability to participate in hydrogen bonding, although hydrogen bonding is also an important effect in alcohols.[11c] The uncorrected data for various benzophenones (Chart I) also showed a much larger effect for methoxyl carbons than for any other type of carbon in the molecule. In addition to ethers, other types of molecules having heteroatoms exhibit similar shifts, e.g., tetramethylethylenediamine, tributylphosphine, and, in particular, dimethyl sulfide. Dimethyl sulfide gave the largest shift for ^{13}C of any compound in this study (−3.65 ppm), excepting chloroform.

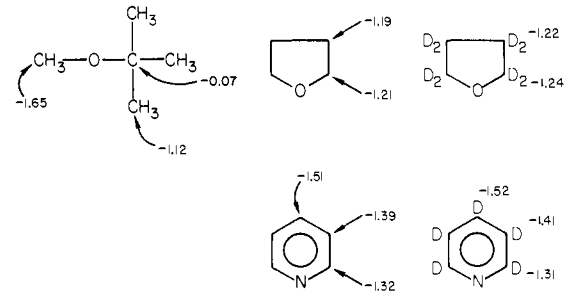
In the absence of steric effects, the induced shift of methyl groups compared to methylene groups is roughly in the ratio 3:2 for many compounds. The 3:2 ratio persists for triethylamine, but for tributylphosphine, the methylene group nearest phosphorus is more highly shifted than other methylenes. (cf. Table III).

The larger effect for sulfides than for ethers and for phosphines than for amines is consistent with Morishima's findings for halogen-substituted carbons, C–X (X = I > Br > Cl > F).[11d] The larger shifts for carbons attached to heavy atoms are not outside the realm of expectation for a mechanism involving electron transfer to antibonding C–X orbitals, although there is some question as to why nonbonding orbitals at X would not be utilized. It is again noteworthy that tetramethylsilane shows little effect, despite the availability of d orbitals. Although oxygen compounds are less highly shifted than dimethyl sulfide, the oxygen compounds are shifted more than hydrocarbons and amines. A basic question remains as to why an electron-deficient oxygen (as in nitroxides) would donate an electron to a filled-shell oxygen–carbon bond (as in ethers).

A number of alternative models are possible: (1) an electron transfer in the opposite sense, from ether oxygen to nitroxide;[8] (2) a spin polarization of the heteratom lone pair, which is transmitted to neighboring carbons; (3) complexation of DBNO with the molecule with generalized spin polarization of the C–H bonding electrons (perhaps pseudocontact shifts). A likely candidate for this complexation is formation of a short-lived two-center, three-electron bond,[22] particularly for phosphorus and sulfur. Alternatively, no model at all need be invoked if the local magnetic susceptibility of a DBNO–ether complex were different from that of free DBNO. The fact that the quaternary carbons of *tert*-butyl methyl ether and of 2,2-dimethylbutane are both unshifted whereas the other carbons of the ether are more highly shifted argues against the variable magnetic susceptibility hypothesis. Nonetheless, this point deserves more extensive study, as the lack of shift could result from a cancellation of effects.

Chart III

Carbon-13 Shifts Induced by DBNO



With regard to the other possible models, the equivalent induced shifts of the α and β carbons of tetrahydrofuran (THF) (cf. Chart III) is not consistent with spin polarization of the lone pair, as the effect should attenuate as polarization is passed down the carbon chain. The data for *tert*-butyl methyl ether cannot be reconciled with electron transfer from oxygen to DBNO. If this were the case, both α carbons should be shifted, not just CH_3O. In view of the conflicting data, no present model seems particularly strong. The observed shifts probably result from a combination of mechanisms including pseudocontact shifts.[23]

The one molecule that shows a really large induced shift for both carbon and hydrogen is chloroform. Morishima showed that the induced shift for $CHCl_3$ (uncorrected) is larger than that for CCl_4. Thus, an interaction with C–Cl cannot be responsible for the entire shift, and thus hydrogen bonding to C–H would seem to be involved.[11d] Lim and Drago have studied the hydrogen-bonding characteristics of DBNO.[24] Their observation that nitrogen undergoes an increase in spin density on hydrogen bonding is significant. This suggests that the basic mechanisms for association involves hydrogen bonding through an oxygen lone pair. Morishima's calculations, on the other hand, suggest that the induced shift results from direct interaction of the odd electron with hydrogen via a spin polarization. Although the two points of view are not mutually exclusive, it is not immediately obvious from the latter model why hydrogen should be shifted upfield and carbon downfield, although it seems clear from the former model (Chart II) involving electron pair association in the classical hydrogen bonding sense.

Our data indicate a larger shift for carbon ($\Delta\delta_{corr} = -19.4$ ppm) than for hydrogen ($\Delta\delta_{corr} = +1.0$ ppm)9 Furthermore, the carbon shift depends upon whether chloroform or deuteriochloroform is used (i.e., $CDCl_3$, = −18.7 ppm). These two molecules hydrogen bond equally fully.[25] The difference constitutes an isotope effect upon the induced shift. Isotope shifts have been studied by Gutowsky and co-workers, and reviewed by Batiz-Hernandez and Bernheim.[26,27] Recently, Jameson has provided a theoretical

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(23) The small difference in g tensor values of DBNO (which would lead to but a small pseudocontact shift) may become enhanced if complexation of DBNO occurs to a substrate: Pearson, G. A., private communication.

(24) Lim, Y. Y.; Drago, R. S. *J. Am. Chem. Soc.* **1971**, *93*, 891.

(25) Green, R. "Hydrogen Bonding by C-H Groups"; Halstead Press: New York, 1974; pp 15, 16.

(26) Batiz-Hernandez, H.; Bernheim, R. A. *Prog. Nucl. Magn. Reson. Spectrosc.* **1967**, *3*, 63.

interpretation of the phenomenon.[28] Briefly, the different internuclear separations in the isotopically substituted molecules (as well as the differing force constants for the C–H vs. C–D bonds) lead to different charge distributions at the vibrational extreme.[28] Usually the effect is most pronounced for light nuclei, such as $^1H/^2H(D)$. The observation of an isotope effect on the induced shift in $CH(D)Cl_3$ is consistent with the idea that a specific interaction of DBNO with C–H(D) occurs. The interaction with the longer C–H bond appears to transmit spin density to carbon more efficiently, in contrast to the effect of bond length on coupling constants.[29]

On the other hand, when THF is compared to THF-d_8, no isotope effect is found (Chart III). The *deuterated* species gives the greater shift. However, the results are within the combined experimental error of the two observations, ±0.04 ppm. An isotope shift of the same percentage as found in $CH(D)Cl_3$ would yield a 0.08-ppm larger shift for the protic compound. Thus, sizable induced shifts for hydrogen *and* carbon, as well as significant isotope effects for carbon, occur principally for C–H(D) bonds well recognized to be hydrogen bonding in the classical sense.[30]

For weakly hydrogen-bonding C–H bonds, such as the α C–H bonds of pyridine, the induced shift again shows no isotope effect (cf. Chart III). Other C–H(D) bonds of the molecules also fail to show isotope shifts greater than experimental error.

With regard to the model for the hydrogen-bonding interaction (as well as other models; cf. Scheme II), the caution recently stated by Drago should be reviewed.[31] The electron spin vector lies *opposed* to the applied field (preferentially), but the magnetic moment vector due to the unpaired electron lies in the opposite sense, aligned with the magnetic field. It is the magnetic moment, not spin per se, that causes variation in the effective magnetic field at the nucleus under observation and thus affects chemical shift. Early work referred to electron "spin" orientations although magnetic moment was actually displayed in diagrams. References to positive and negative "spin density" are similarly hard to follow.

^{31}P and ^{11}B Nuclei. In assessing the interaction between DBNO and heteroatoms with lone pairs, it seems advisable to observe the heteroatom directly rather than ^{13}C nuclei elsewhere in the molecule. Studies on molecules with observable ^{31}P nuclei are recorded in Table IV along with limited data on a ^{11}B compound in which the heteroatom has no lone pair.

In the case of phosphines and phosphites, ^{31}P undergoes a strong induced shift, particularly when compared to the less polarizable ^{19}F compounds (also in Table IV). The effect of steric hindrance is shown by the small shift for tricyclohexyl phosphine. In these compounds, a chemical reaction is possible which creates a new P–O bond between phosphorus and DBNO, as suggested by the work of Bentrude and others.[32] However, odd-electron density would then exist in a d orbital, which could only affect the ^{31}P by spin polarization. As with benzophenones, only a small effect would result.

Comparing ^{31}P shifts to other nuclei is possible through consideration of "reduced shifts", $\Delta\delta_{corr}/\mu$, where μ is the magnetic moment of the nucleus in question. The general range of reduced ^{31}P shifts (−3.0 to −4.2) is significantly greater than those of ^{19}F (−0.9 to −2.0) or carbon (ca. −2.3 in the case of alkanes).[33] The importance of lone pairs is underscored by observation of the

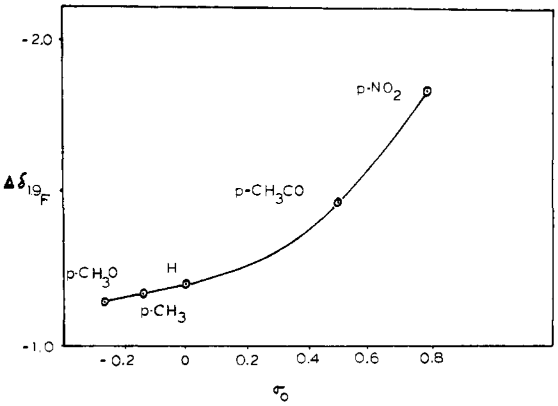

Figure 2. Plot of the DBNO-induced chemical shifts for ^{19}F vs. Taft's σ_0 constants.

induced shift of ^{11}B in tributyl borate. This acidic nucleus, like the hydrogen of $CHCl_3$ undergoes an upfield shift (+0.22 ppm). The reduced shift, however, (+0.2) is very small. Regrettably, other boron compounds tested destroyed the nitroxide.[34] The model for DBNO interaction with boron (Chart II) emphasizes an acid–base interaction using the nitroxide lone pair. Like the $C\mathit{H}Cl_3$ shift, the boron shift is quite small.

Other compounds lacking a lone pair, e.g., triethyl phosphate, are shifted but slightly (−0.24 ppm) compared to phosphines or phosphites. For the latter, a spin polarization mechanism (Chart II) seems adequate to explain the results. Similar behavior was observed in the ENDOR studies of Richards and co-workers.[7–9] These data provide strong evidence that lone pairs are important sites for interaction with the radical.

^{19}F Compounds. The DBNO-induced shifts for ^{19}F in a group of monosubstituted fluorobenzenes is given in Table IV. Electron-withdrawing substitutents markedly increase the magnitude of the paramagnetic shift. A correlation was attempted between $\Delta\delta_{corr}$ and various types of Hammett parameters. In view of the sizable number of possible interactions between DBNO and these aromatic compounds, the lack of a linear correlation is not surprising. However, a smooth curve is observed (Figure 2) that is remniscent of a gradual change in mechanism similar to Hammett plots in certain reaction mechanism studies.[35,36] The large effect of nitro and acetyl substituents suggests that an electron transfer from the radical to the aromatic system occurs. Compounds with neutral or electron-donating groups also show a sizable shift, perhaps indicative of a direct ^{19}F–DBNO interaction.

^{19}F and ^{13}C shifts within the same molecule were compared for hexafluorobenzene. The nonprotonated aromatic carbon showed a small shift ($\Delta\delta_{corr}$ = −0.56 ppm), while the ^{19}F shift (−2.80 ppm) was even larger than the ^{19}F shifts in pentafluorobromobenzene. The difference between carbon and fluorine is considerably smaller when reduced shifts are considered (−1.60 vs. −2.13 ppm), but the magnitude of the ^{13}C shift is still less than that of the fluorine. This observation is consistent with direct DBNO interaction with the fluorine lone pairs and π delocalization.

Conclusions

(1) In view of the tendency for DBNO to induce chemical shift changes in inert substances, internal standards are not recommended.

(2) In the present study, bulk susceptibility effects were found to be important. Morishima and co-workers considered such effects to be small.[11] The latter would indeed be expected at the very low DBNO concentrations (ca. 10^{-5} M) claimed by Morishima to produce sizable shifts. This concentration is less than (paramagnetic) oxygen solubility in organic solvents.[37]

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[27] (a) Pendelbury, M.; Phillips, L. *Org. Magn. Reson.* **1972**, *4*, 529. (b) Lambert, J. B.; Griefenstein, L. G. *J. Am. Chem. Soc.* **1974**, *96*, 5120.

[28] Jameson, C. *J. Chem. Phys.* **1977**, *66*, 4983.

[29] Solkan, V.; Sergeyev, N. *Org. Magn. Reson.* **1974**, *6*, 200.

[30] Shahidi and Farrell (Shahidi, F.; Farrell, P. G. *J. Chem. Soc., Chem. Commun.* **1978**, 455) have shown that isotope effects upon another type of complexation, i.e., charge-transfer complexation, are very small (less than 0.2 kJ/mol); see also: Clark, T.; Chardrasekhari, J.; Schleyer, P. von R. *Ibid.* **1980**, 265. The lesser amplitude of the C–D vibration and the greater electropositivity of deuterium were suggested as reasons for the difference.

[31] Drago, R. S.; Zunk, J. I.; Richman, R. M.; Perry, W. D. *J. Chem. Educ.* **1974**, *51*, 371.

[32] Bentrude, W. G.; Khan, W. A.; Murakami, M.; Tan, H.-W. *J. Am. Chem. Soc.* **1974**, *96*, 5566 and references cited.

[33] The reduced shifts are obtained by dividing the shift ($\Delta\delta_{corr}$) by the magnetic moment (μ) of the nucleus in nuclear magnetons and multiplying by 2. The resulting quantity is in units of Hz/$\hbar$.

[34] Kochi, A. J. *Acc. Chem. Res.* **1974**, *7*, 351.

[35] Shorter, J. "Correlation Analysis in Organic Chemistry"; Clarendon Press: Oxford, 1973; Chapter 4.

[36] Coke, J. L.; McFarlane, F. E.; Mourning, M. C.; Jones, M. G. *J. Am. Chem. Soc.* **1969**, *91*, 1154.

(3) We are in agreement with Morishima about the effect of DBNO on good hydrogen bond donors, such as $CHCl_3$, in which large shifts are noted for both carbon and for hydrogen. However, with regard to nonacidic C–H bonds, the evidence is less clear. The ^{13}C induced shift depends in a roughly statistical manner on x of CH_x; yet if heteroatoms with lone pairs are present, the shift is greater than for hydrocarbons of similar general structure. A combination of pseudocontact shifts, spin polarization effects, and possibly variable magnetic susceptibility effects perhaps should be investigated. However, the term "hydrogen bonding" does not seem warranted in these cases.

(4) The observance of steric effects suggests that a direct interaction of DBNO with many types of C–H bonds (nonacidic) is present.

(5) The interaction of DBNO with NMR-active nuclei with lone pairs is sizable, particularly for polarizable nuclei such as ^{31}P. A spin polarization mechanism seems adequate to explain the results.

(6) For molecules with C–X bonds, we disagree that addition of a DBNO electron to the antibonding σ orbital is very important. Compounds such as $(CH_3)_3CX$ (X = Cl, Br) show only a small induced shift (ca. −0.2 ppm), although a large shift for methyl is observed (ca. −1.5 ppm). Better electron acceptors than Cl show only small effects.

(7) Regrettably, this technique is not easily applied to most questions of conformational analysis in view of the different types of interaction possible. In retrospect, the use of paramagnetic inorganic ions such as nickel would have been better, as complexation occurs only a specific site.

Experimental Section

Magnetic Susceptibility Measurements. The coaxial sample cell method of Malinowski and Pierpaoli[19] was used to measure the change in volume magnetic susceptibility induced by the addition of 0.31 M DBNO. The separation in frequencies of the "spinning side bands" observed for nuclei in the outer, annular region can be related to the volume susceptibilities of the central solution (χ_{center}), the annular solution ($\chi_{annular}$), and the glass of the central tube

$$\frac{\nu_m}{\nu_0} = \frac{2\pi}{Kr^2}[a^2\chi_{center} + (b^2 - a^2)\chi_{glass} - b^2\chi_{annular}] \qquad (9)$$

Here ν_0 is the spectrometer frequency, r is the mean radius of the annular region, a and b are the inner and outer radii of the center tube, and ν_m is the frequency separation between the main peak and the first side bands. The K is the argument of the Bessel function relationship

$$J_0^2(K)/J_1^2(K) = I_0/I_1 \qquad (10)$$

where I_0 and I_1 are the intensities of the main peak and the first side bands, respectively, and the values of J_0 and J_1 are obtained by consulting a table of Bessel functions.

The NMR spectrum of the annular reference is run first with the sample in the central tube and then again with only air in the central tube.

$$\chi_{sample} = \chi_{sample} - \chi_{air} = \frac{r^2}{a^2 2\pi\nu_0}[(K\nu_n)_x - (K\nu_m)_{air}] \qquad (11)$$

Here ν_m is the frequency separation between the main peak and the first side bands (twice the sample rotation rate), and $(K\nu_m)_x$ and $(K\nu_m)_{air}$ are values with the sample and only air in the central tube, respectively.

NMR Spectra. The data were collected with a Varian XL-100. The measurements using external standards utilized coaxial 8- and 12-mm tubes with the reference and lock materials in the outer tube and the sample in the inner one. Repetition of runs showed that reproducibility was good (Table I).

The compounds used in the study were predominantly commercial samples. The ethanol was removed from the chloroform by passing the liquid through a short column of activated alumina. The DBNO was prepared by a method in the literature.[38] VPC of DBNO disclosed no contaminants.

The initial work on benzophenones utilized a range of DBNO concentrations. In this work, a linear dependence of induced chemical shift on DBNO concentration was evident.[11] In one set of runs (^1H), the effect of external magnetic field was measured by running the same sample at 60, 90, and 100 MHz. The variations were small and very close to experimental error in line position. In initial studies, a 5000-Hz spectral width was used, but in later studies, only the minimum spectral width was used to incorporate peaks of interest, plus the external standard peaks, in order to minimize error in line position. In a typical run, a 1-kHz spectral width was used, with a 4-s pulse repetition rate, and a tip angle of ca. 50° (this was unnecessarily low). Approximately 1000 transients were collected, using a full (8K) data table; the error in line position under these conditions was ±0.25 Hz (ca. 0.01 ppm). In ^{13}C runs at 25.2 MHz, methanol was the external standard (the same sample was used for runs with an without DBNO, so that error in methanol position was minimized). For the ^{31}P runs at 40.5 MHz, triphenylphosphine was the external standard; for ^{19}F runs at 94.1 MHz, TFA was used, and for ^{11}B runs at 32.1 MHz, $Et_4N^+BF_4^-$ was used. In all work, the normal probe temperature of the XL-100 instrument was used, ca. 26 °C. Previous work has shown that probe temperature is quite constant from run to run. The data reported came from NMR samples that showed no extraneous peaks due to impurities in the substrate or diamagnetic contaminants of DBNO. Considering the data on benzophenones in Chart I, a total of ca. 15 benzophenones (various substituents) were run, but the data were rather similar to that displayed in Chart I.

Acknowledgment. We thank Dr. Edmund Malinowski, Dr. G. A. Pearson, and Dana Durham for helpful discussions.

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(37) Garrard, W. "Solubility of Gases and Liquids"; Plenum Press: New York, 1976; p 73.

(38) Hoffman, A. K.; Feldman, A. M.; Gelbulm, E.; Henderson, A. "*Organic Syntheses*"; Baumgarten, H. E., Ed.; Wiley: New York, 1973; Collect. Vol. V, p 355.