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^{17}O NMR Spectroscopic Study of Steric Hindrance in Phthalic Anhydrides and Phthalides

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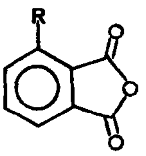
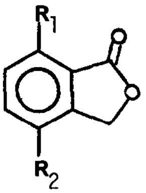
Summary: ^{17}O NMR data for sterically hindered phthalic anhydrides and phthalides showed unusual deshielding effects which were correlated with in-plane bond angle distortions (X-ray results and MM2 calculations); indicative of van der Waals repulsions.

^{17}O nmr spectroscopy is rapidly gaining attention as an important method for studying ground state molecular structure and bonding.[2] A number of ^{17}O nmr studies have been focused on electronic effects in homologous series;[3] others have investigated conformational effects.[4] Recently, a quantitative relationship has been demonstrated between deshielding effects in ^{17}O chemical shift data and torsional angles (X-ray) for aromatic nitro compounds;[5] thus torsional relationships are accessible by this methodology. However, deshielding effects observed for the ^{17}O chemical shift data for sterically hindered heteroaromatic N-oxides,[6] where torsional effects should be limited, indicated that additional factors can influence the chemical shifts. To investigate non-torsional factors, phthalic anhydrides[7] were chosen since the system has a well-defined, planar geometry and is expected to show a large chemical shift range. In addition, in certain cases the two anhydride carbonyls have been reported to exhibit differential reactivity.[8] We report ^{17}O NMR data for a series of 3-substituted phthalic anhydrides (**1a-1c**) and corresponding phthalides (**2-3**) which clearly show that the chemical shifts are sensitive to steric hindrance.



1a R=H
1b R=CH_3
1c R=$C(CH_3)_3$



2a R_1=R_2=H
2b R_1=CH_3, R_2=H
2c R_1=$C(CH_3)_3$, R_2=H
3 R_1=H, R_2=$C(CH_3)_3$

The ^{17}O nmr data (natural abundance, CH_3CN, 75°) for **1-3** are summarized in Table 1.[9,10]

Table I. ^{17}O NMR Data (±1 ppm) for Phthalic Anhydrides (**1a-c**) and Phthalides (**2-3**) in CH_3CN at 75°.

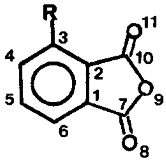
Anhydrides			Lactones		
Cmpd.	$\delta(C{=}O)^a$	$\delta(-O-)^b$	Cmpd.	$\delta(C{=}O)^c$	$\delta(-O-)^d$
1a	374	263	**2a**	320	170
1b	383 372^e	264	**2b**	332	170
1c	396 367^e	262	**2c**	346	168
			3	319	173

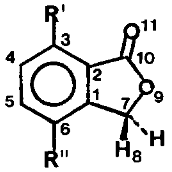
a) Band widths $\nu_{1/2}$=129±7 Hz. b) $\nu_{1/2}$=142 ±5 Hz.
c) $\nu_{1/2}$=160 ±6 Hz. d) $\nu_{1/2}$=137 ±9 Hz.
e) Signal for carbonyl meta to alkyl group.

For both **1b** and **1c**, two well-defined ^{17}O signals for the sterically different carbonyl groups, separated by 11 and 29 ppm, respectively, were observed. The single bond oxygen for all the anhydrides appeared at 263±1 ppm. The ^{17}O data for the two t-butyl phthalides (**2c**, **3**) allow the assignment of the downfield carbonyl signal in the substituted anhydrides to the carbonyl adjacent to the substituent Note that the "carbonyl" signal for **2c** is downfield of that of **3** by 27 ppm. The downfield shifts noted for for **1b**, **1c**, **2b** and **2c** cannot be due to electronic effects. Previous work on benzoate systems has shown that the electronic effect of an alkyl group on the carbonyl resonance is modestly shielding (2 ppm)[11]. The deshielding effect in both series for the ortho-methyl group is 9-12 ppm while a similarly located t-butyl group produces a 22-27 ppm shift. The molecules are expected to be planar. However, since the magnitudes and direction of these shift differences are similar to those attributed to torsional variations,[5,12] this possibility must be evaluated. Results[12] for sterically hindered acetophenones show that a torsional rotation of the carbonyl group of at least 20° would be required to yield the deshielding of 25 ppm observed for the chemical shifts in **1c** and **2c**. Molecular mechanics calculations[13] (MM2) for **1-3** predicted that the molecules were planar. In addition, the calculations showed no significant changes in bond lengths within each series of compounds. However, the calculations did predict substantial in-plane distortions of the bond angles in both rings (Table II) in close proximity to the R group at the juncture of the two rings. To obtain independent corroboration of the predicted geometry, the crystal structure[14] of the most distorted anhydride, 3-t-butylphthalic anhydride, **1c**, was obtained. All atoms in **1c**, with the exception of t-butyl methyl groups, were planar.

The trends discernible in Table II show that as the R group gets larger, the angles represented particularly by entries **1**, **2**, **3** and **4** get larger and the ones represented by entries **5**, **7**, **13** get smaller. The carbonyl group peri to the R-group shows significant bond angle variation with R-group size, whereas the relatively unhindered carbonyl group is essentially unaffected. Presumably the in-plane distortions observed reflect minimization of van der Waals interactions. Recently, a correlation[15] has been found between the local van der Waals steric energy and the chemical shift of a resonant nucleus within several classes of compounds. Chesnut has suggested[15] that the repulsive van der Waals interactions lead to a contraction of the orbitals on the resonant nucleus with a corresponding increase in r^{-3} of the paramagnetic term

Table II. Calculated (MM2) Bond Angles for Anhydrides 1a-c and Phthalides 2a-c, 3.





Entry		Angle Degrees				Angle Degrees			
	Type	1a	1b	1c	(X-ray)	2a	2b	2c	3
1	C_2C_3R	121	122	125	(124.7)	121	122	125	121
2	$C_3C_2C_{10}$	129	130	133	(132.9)	128	129	131	126
3	$C_2C_{10}O_{11}$	126	126	128	(133.3)	125	126	128	125
4	$C_2C_{10}O_9$	109	110	111	(107.4)	111	112	112	111
5	$O_{11}C_{10}O_9$	123	123	120	(119.3)	123	122	119	123
6	$C_7O_9C_{10}$	103	103	103	(110.3)	107	107	107	107
7	$C_1C_2C_{10}$	108	107	105	(105.7)	108	107	105	109
8	$C_2C_1C_7$	108	108	109	(109.6)	109	110	111	107
9	$C_1C_7O_8$	126	126	126	(132.0)	--	--	--	--
10	$C_1C_7O_9$	109	109	109	(107.0)	102	102	101	103
11	$O_8C_7O_9$	123	123	123	(121.0)	--	--	--	--
12	$C_2C_3C_4$	116	115	113	(113.7)	116	115	113	116
13	$C_6C_1C_7$	129	128	126	(126.8)	130	129	125	131
14	C_1C_6R''	--	--	--		120	120	121	123

resulting in a net deshielding effect. The trends noted in Table II parallel the carbonyl ^{17}O chemical shift data. The predicted distortions for the phthalides **2a-c** parallel those observed for **1a-c**, whereas little distortion of the carbonyl angles for **3** was estimated. The carbonyl ^{17}O data for the phthalides reflects this trend (Table II). For all five compounds no distortion of the bond angle involving the single oxygen (entry **6**) was predicted by the calculations; the ^{17}O data for O_9 is essentially constant in each series (Table I). Comparison of the MM2 data and the X-ray results for **1c** shows they are in reasonable agreement. The two methods are in poorest agreement for the angles represented by entries **3**, **6** and **9**; MM2 calculations underestimated the bond angles for the anhydride although the trends are consistent with ^{17}O data.

Differential reactivity of carbonyl functions in similar systems has been observed and explanations for these differences have included steric blocking of the attacking reagents as well as the influence of electronic effects of the substituents.[8] The present data clearly show that steric interactions in these systems are not limited to steric blocking but also include molecular distortions, which should affect the reactivity of the carbonyl functions. An interpretation of the ^{17}O data for the anhydrides suggests that there is greater double bond character at the hindered (peri) carbonyl oxygen while the other carbonyl oxygen has a greater charge density (single-bond character). Thus, the peri-carbonyl would be expected to exhibit a lower reduction potential whereas the unaffected carbonyl would be more likely to complex Lewis acids. This combination of effects must be considered in explanations of reactivity data. Thus, the ^{17}O nmr data has provided new insights into the nature of the regiospecificity in these hindered systems. Furthermore, these results suggest that the unusual ^{17}O NMR data reported[6] for sterically hindered N-oxides involve a similar deshielding mechanism indicative of analogous interactions.

^{17}O NMR chemical shifts are more sensitive than those of ^{13}C and ^{15}N. Thus, it is clearly an important method for detection of the effects of steric hindrance on the molecular structure of organic systems. Study of other even more highly hindered molecules is underway.

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