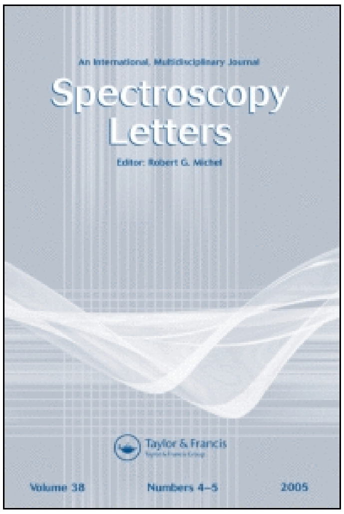

Spectroscopy Letters
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597299

The Internal Steric Push-Effect: Its Consequences on the Reactivity of Carbonyl Functions in 3-Substituted Phthalic Anhydrides

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To cite this Article Kayser, Margaret M.(1988) 'The Internal Steric Push-Effect: Its Consequences on the Reactivity of Carbonyl Functions in 3-Substituted Phthalic Anhydrides', Spectroscopy Letters, 21: 8, 831 — 840

To link to this Article: DOI: 10.1080/00387018808082345

URL: http://dx.doi.org/10.1080/00387018808082345

SPECTROSCOPY LETTERS, 21(8), 831-840 (1988)

THE INTERNAL STERIC PUSH-EFFECT: ITS CONSEQUENCES ON THE REACTIVITY OF CARBONYL FUNCTIONS IN 3-SUBSTITUTED PHTHALIC ANHYDRIDES

Key Words: Regioselectivity, Carbonyl Group, Nucleophilic Addition, Phthalic Anhydrides

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Abstract:

The enhanced reactivity of the meta carbonyl function vis-a-vis nucleophiles in 3-substituted phthalic anhydrides is interpreted in terms of an internal steric effect. A through-space interaction between the substituent and the carbonyl function causes a displacement of electrons in the C=O bond from the oxygen to the carbon atom with simultaneous deactivation of the carbon atom toward nucleophilic attack and the oxygen atom toward complexation with a counter ion.

Introduction

Intramolecular steric effects are generally well understood and are predictable by molecular mechanics calculations. The interactions of proximate polar groups are more complex due to the possibility of electronic interactions, in addition to simple steric effects.

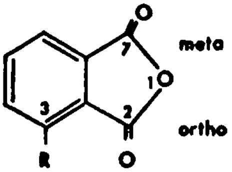
The object of the research reported in this paper is to determine how the proximity of the substituent to the carbonyl group in 3-substituted phthalic anhydrides affects the reactivity of this function vis-à-vis nucleophiles. Previously reported [1] ab initio and Extended Hückel calculations for some model phthalic anhydrides have shown that a correlation exists between the relative reactivities of the two carbonyl groups and the electronic character of substituents. The experimental results from metal hydride reductions of phthalic anhydrides suggested, however, that other than electronic effects must also be implicated in the regioselectivity control [2].

The chemical shifts in nuclear magnetic resonance are observable phenomena which are believed to be the result of the through-bond, as well as through-space interactions. The latter interactions involve non-bonded repulsions, dipole-dipole attractions, charge-transfer processes, hydrogen bonding and solvent effects. As a result, the ^{13}C chemical shifts for the two carbonyl groups in 3-substituted phthalic anhydrides should reflect not only the electronic properties of the substituents, but also various proximity effects and thus provide realistic experimental estimation of the intrinsic reactivity of the carbonyl group.

The ^{13}C chemical shifts for a number of 3-substituted phthalic anhydrides and the corresponding lactones were measured. The results are shown in Tables I and II. The assignments of the two

TABLE I

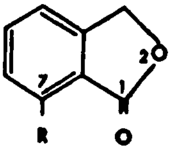
^{13}C NMR Data for Substituted Phthalic Anhydrides

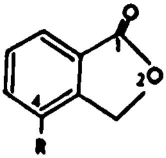


		(ortho)		(meta)	
Anhydride	R	$\delta(C{=}0)_2$	(^{17}O)	$\delta(C{=}0)_7$	(^{17}O)
	H	163.8	(374)	163.8	(374)
	F	159.5	(385)	162.2	(376)
	Cl	159.5	(386)	161.1	(375)
	Br	160.1	(385)	160.9	(374)
	I	160.6	(382)	161.0	(373)
	OCH_3	160.3	(383)	162.6	(371)
	t-Bu	162.7	(396)	163.3	(367)
	CH_3	163.0	(383)	163.1	(372)
	NO_2	165.8	(395)	167.0	(377)

TABLE II

^{13}C NMR Data for 7-phthalides and 4-phthalides





7-Phthalide	R	$(C{=}0)_1$	(^{17}O)	4-Phthalide	R	$(C{=}0)_1$	(^{17}O)
	H	171.3	(320)		H	171.1	(320)
	F	166.0	(334)		F	169.0	(325)
	Cl	167.8	(335)		Cl	169.8	(327)
	Br	168.0	(334)		Br	169.9	(327)
	I	168.7	(330)		Cl	170.3	(327)
	OCH_3	168.9	(333)		OCH_3	170.8	(323)
	CH_3	171.3	(332)		CH_3	171.5	
	NO_2	165.3	(327)		NO_2	168.4	(325)

^{13}C signals for the anhydrides studied were made by analogy with the signals for the corresponding isomeric lactones.

Experimental

Carbon-13 spectra were obtained on a Varian HA-100 and Fourier transform NMR spectrometer. Samples of anhydrides and lactones were run in $CDCl_3$ in 5-mm sample tubes and were locked on deuterium.

Each spectrum was noise decoupled at 100 MHz to eliminate $^{13}C-^{1}H$ coupling. Chemical shifts are reported relative to TMS as zero.

Materials

The anhydrides prepared in a few-step syntheses were reduced by a variety of simple and complex metal hydrides to the corresponding lactones. The mixtures were separated by chromatography and the lactonic products were purified by crystallization and sublimation as reported previously [3].

Discussion

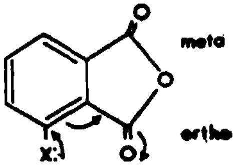
A small upfield shift of the carbonyl signal of about 2.5 ppm generally accompanies dehydration of the diacid to the corresponding anhydrides. It seems to be the net result of two opposing phenomena: the shielding "anhydride effect" [4], and the deshielding "five-member ring effect" [4]. The shielding of the anhydride carbonyl may be due to the elimination of hydrogen bonding on going from the diacid to anhydride [5a], or it may be linked to the effect of the acetoxy group which, by withdrawing electrons from the carbonyl carbon, opposes polarization of the π-electrons by the carbonyl oxygen. The similar upfield shift of carbonyl carbon is observed in α-haloketones and aryl halides [5b, 6]. To our knowledge, no satisfactory rationalization for the deshielding five-member ring effect has been proposed. Nevertheless, the experimental results indicate that carbonyl carbon atoms in five member ketones, lactones [5c] and anhydrides [4] resonate downfield from carbonyl carbons in six-member rings or straight-chain compounds. Thus, the small upfield shift observed upon dehydrating a diacid to the corresponding five-member anhydride may be due to the somewhat more important contribution of the "anhydride effect" cancelling the five-member ring effect.

The above interpretation is supported by the fact that, upon reduction of five-member cyclic anhydrides to the corresponding lactones, an important downfield shift of 8-9 ppm is observed (see Table I).

Substituent effects

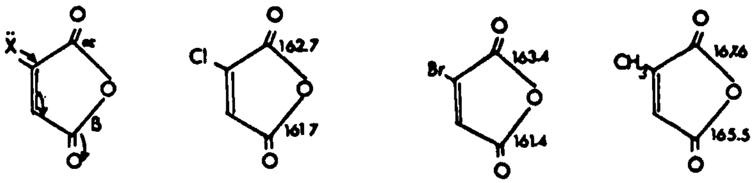
The halogens (F, Cl, Br, I), methyl and methoxy substituents cause a weak upfield shift of carbonyl carbons in anhydrides and lactones (Table I and II). The effect is slightly larger for the ortho- than for the meta-carbonyl carbon atom. For the NO_2 group a downfield shift of carbonyl carbons is observed. This shift is smaller for the ortho carbonyl group.

The observed slight shielding of the two carbonyl carbon atoms in 3-halo and 3-methoxy phthalic anhydrides (relative to the unsubstituted compound) suggests a weak mesomeric electron donating effect of these substituents 1, while the deshielding observed in 3-nitrophthalic anhydride is consistent with the electron with-



1

drawing character of NO_2 group. The resonance effects, however, cannot account for the somewhat higher shielding of the ortho (v.s. meta) carbonyl carbon atom in the investigated compounds. Although mesomeric effects were successfully employed to explain the slight shielding of the β-carbonyl relative to the α-carbonyl in chloro, bromo and methyl maleic anhydrides 2 [4], such an interpretation does not appear to be correct for 3-substituted phthalic anhydrides.



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In the latter compounds the observed shielding of the ortho-carbonyl carbon atom is accompanied by simultaneous deshielding of the oxygen atom of this function, as was demonstrated by a ^{17}O NMR study [7]. The ^{13}C upfield shift does not appear to be the result of the through-bond electronic effects, (similar to those observed in -haloketones and acyl halides [5b,6] since electron-donating and electron withdrawing groups alike shield the carbon and deshield the oxygen atom of the ortho-carbonyl function. Nor does it appear to be caused by mesomeric effects, which would shield the oxygen as well as the carbon atom as shown in 1. On the other hand, there is ample evidence that the observed shielding has its origins in the intra molecular van der Waals interactions between the carbonyl function and the neighbouring substituent.

The net result can be interpreted as a displacement of electronic density from the oxygen toward the carbon atom in the carbonyl function. In the process, oxygen becomes "less" nucleophilic and the carbon atom "less" electrophilic than the oxygen and carbon atoms in the meta-carbonyl group. In view of the above it may be expected that the ortho-function should be less reactive towards nucleophilic additions, particularly in metal hydride reductions, in which simultaneous or prior association of the oxygen with a counter ion promotes nucleophilic addition to the carbon atom of the carbonyl group.

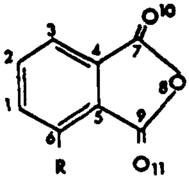
This conclusion matches reasonably well the experimental results obtained in metal hydride reductions of the 3-substituted phthalic anhydrides, carried out in the absence of an effectively chelating counter-ion [3].

Recently Li and Chesnut [8] reported that a good correlation exists between the local van der Waals steric energy (as calculated by MM2 force field calculations) and the chemical shifts of the resonant nuclei in β, γ, and γ positions. The relationship associates a repulsive interaction with deshielding effects and attractive interactions with shielding effects.

The important repulsive interactions between the 3-substituents and the ortho carbonyl function in phthalic anhydrides ensue from the rigid geometry of these compounds, which forces the carbonyl and the 3-substituent into close proximity.

TABLE III

MM2 Calculations for 3-substituted phthalic anhydrides



Type	Angle (Degrees)				
	F	Cl	Br	I	t-Bu
C_5C_6R	121.82	122.69	123.12	123.56	124.8
$C_5C_9O_{11}$	125.87	126.04	126.14	126.19	127.69
$C_5C_9O_8$	110.30	110.51	110.59	110.62	111.28
$C_4C_7O_8$	110.23	110.21	110.19	110.18	109.14
$C_4C_7O_{10}$	125.55	125.57	125.59	125.61	125.82

The MM2 calculations [9] for several of 3-substituted phthalic anhydrides predict that the substituent and the neighbouring carbonyl group remain co-planar and within the plane of the aromatic ring. To alleviate the imposed crowding there is an in-plane distortion of the bond angles of the substituent and the carbonyl function. The observed angle distortion increases with the increasing steric demand of the substituent (see Table III), in agreement with repulsive van der Waals interaction between these two groups.

Baumstark and co-workers have shown that, for 3-methyl and 3-t butyl phthalic anhydrides, the magnitude of the calculated in-plane distortion parallels the deshielding observed in ^{17}O chemical shift data [10]. Furthermore, the force-field-predicted geometry was confirmed by the crystallographic data reported for 3-t-butylphthalic anhydride [10].

In substituted maleic anhydrides, the interaction between the substituent and the α-carbonyl function is quite different. The two groups are splayed and the actual non-bonded distance between the substituent and the carbonyl function is larger than in 3-substituted phthalic anhydrides. The observed ^{13}C signals for 1-carbonyl are shifted downfield with respect to the β-carbonyl <u>2</u>, thus making C-1 a better target for nucleophilic attack. These predictions correlate well with the experimental results showing preferential reduction of the β-carbonyl function in a series of substituted maleic anhydrides [11].

In conclusion, we should point out that the diminished reactivity of the ortho carbonyl groups vis-à-vis nucleophiles in 3-substituted phthalic anhydrides may be linked to the internal steric "push effect" which causes the displacement of electrons in the C=O bond from the oxygen to the carbon atom. This phenomenon, associated with the particular geometry of 3-substituted phthalic anhydrides, <u>can be detected</u> by ^{13}C <u>nmr</u>. It is possible that it may be operative in other rigid systems of similar geometry.

REFERENCES

1. M.M. Kayser, and O. Eisenstein, Can. J. Chem. 1981, <u>59</u>, 2457-2462.

2. M.A. Makhlouf, and B. Rickborn, J. Org. Chem. 1981, <u>76</u>, 4810-4811.

3. C. Soucy, D. Favreau, and M.M. Kayser, J. Org. Chem. 1987, <u>52</u>, 129-134.

4. K.L. Williamson, M.V. Hasan, and D.R. Clutter, J. Mag. Res. 1978, 30, 367-383.

5. J.B. Stothers, Carbon-13 NMR Spectroscopy, Academic Press New York and London, 1972; (a) p. 297; (b) p. 303; (c) pp 289, 300.

6. G.C. Levy, R.W. Lichter and G.L. Nelson, Carbon-13 Nuclear Magnetic Resonance Spectroscopy 2nd Ed. John Wiley and Sons Inc., New York, 1980, p. 140.

7. D.W. Boykin, A.L. Baumstark, M.M. Kayser and C.H. Soucy to appear in Can. J. Chem. 1987, 65, 1214.

8. S. Li and D.B. Chesnut, Magn. Res. Chem. (1986), 24 93-100, ibid, 1985, 23, 625.

9. MM2 1977 (Allinger-QCPEI), 395, MMPI Pi (Allinger-QCPE 318) + Model Parameters (Still) + More Atoms and Trial Constants by K.E. Gilbert and T.J. Gajewski Indiana University.

10. A.L. Baumstark, P. Balakrishnan and D.W. Boykin, Tetrahedron Letters (1986), 27, 3079.

11. M.M. Kayser, L. Breau, S. Eliev, P. Morand and H.S. Ip. Can. J. Chem. 1986, 64, 104-109.

Date Accepted: 06/08/88
Date Received: 07/19/88