

can delocalize charge into the  $6\pi$  system, the tool is rather coarse and therefore ineffective in the cases where structural changes are limited, including systems which have been described as partially bridged or delocalized. For the same reasons the method must be considered ineffective in the usual solvolytic studies, wherein the solvation significantly masks the true electron demand of the carbocationic center in the solvolytic transition state unless the structural change is significant (as in the case of 7-norbornenyl or pentacyclononyl system<sup>36</sup>).

### Experimental Section

The carbocations studied in this work were generated from their alcohol precursors. The alcohols were prepared by the addition of the

(36) Brown, H. C.; Ravindranathan, M. *J. Am. Chem. Soc.* 1977, 99, 299-300.

appropriate aryl Grignard reagent to the respective ketones in ether solution. Most of the alcohols employed in this study have been reported earlier<sup>2,24</sup> except those of the cyclobutyl and nortricycyl series. All new compounds gave satisfactory analysis and spectroscopic data.

**Preparation of Carbocations.** Freshly distilled  $\text{SbF}_5$  and  $\text{FSO}_3\text{H}$  were used. To the appropriate superacid dissolved in about a twofold amount of  $\text{SO}_2\text{ClF}$  at dry ice/acetone (ca.  $-78^\circ\text{C}$ ) or petroleum ether/liquid nitrogen slush temperature ( $-140^\circ\text{C}$ ) was slowly added, with vigorous stirring, a cooled slurry or solution of the corresponding alcohol precursor in  $\text{SO}_2\text{ClF}$ , resulting in an approximately 10% solution of the ion.

<sup>13</sup>C NMR spectra were obtained with use of a Varian Associates Model FT-80 spectrometer equipped with multinuclei broad-band variable temperature probe. The chemical shifts were referenced from external capillary tetramethylsilane.

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## <sup>17</sup>O NMR Studies of Substituent and Hydrogen-Bonding Effects in Substituted Acetophenones and Benzaldehydes<sup>1a</sup>

Thomas E. St. Amour,<sup>1b</sup> Matija I. Bugar,<sup>1c</sup> Bill Valentine, and Daniel Fiat\*

Contribution from the Department of Physiology and Biophysics, University of Illinois at the Medical Center, Chicago, Illinois 60680. Received June 23, 1980

**Abstract:** <sup>17</sup>O nuclear magnetic resonance is utilized in exploring substituent effects and hydrogen-bonding interactions in <sup>17</sup>O-enriched and natural abundance aromatic carbonyl systems. Chemical shifts and line widths are presented for a wide range of mono- and polysubstituted acetophenones and benzaldehydes. The <sup>17</sup>O nuclear screening constants are highly sensitive to electronic perturbations induced by substituent groups as indicated in chemical shift ranges of 101, 60, and 13 ppm for the ortho-, para- and meta-substituted acetophenones, respectively. Intramolecular hydrogen bonding in the ortho amino and ortho hydroxy molecules results in anomalous <sup>17</sup>O chemical shifts to high field. In the case of intramolecular hydrogen-bonded compounds it is shown that for the polysubstituted acetophenones the substituent effects are much smaller and superimposed on the dominating effect of hydrogen bonding on the <sup>17</sup>O nuclear screening. Alcohol solvents induce upfield chemical shifts in acetophenone and *m*-hydroxyacetophenone, and the degree of increased shielding is dependent on solvent concentration (acetophenone undergoes a 17-ppm upfield shift upon infinite dilution in methanol). Line widths range from approximately 300 Hz (benzaldehyde) to greater than 4 kHz (2,3,4-trihydroxyacetophenone). Rate constants for carbonyl oxygen exchange in a  $\text{H}_2^{17}\text{O}$ /dioxane mixed solvent are reported for several substituted acetophenones. A good correlation of the chemical shifts of the para-substituted acetophenones with the lowest energy electronic transition implies that  $\Delta E_{\pi \rightarrow \pi^*}$  makes the dominant contribution to the <sup>17</sup>O nuclear screening. The <sup>17</sup>O chemical shifts are correlated with Hammett constants, IR carbonyl stretching bands, UV, and X-ray diffraction data.

### Introduction

The carbonyl group can be sensitive to electronic disturbances occurring at various sites in an aromatic molecule due, in large part, to its ability to enter into conjugation with adjacent  $\pi$  systems. The electron distribution in the acyl function of aromatic compounds and the electronic perturbations induced by ring substitutions have been a longstanding subject of spectroscopic investigation.<sup>2</sup> Recent applied and theoretical studies of substituted benzaldehydes and acetophenones demonstrate an active interest in these systems.<sup>3</sup>

Although substituent effects on <sup>13</sup>C,<sup>4</sup> <sup>1</sup>H,<sup>5</sup> <sup>14</sup>N,<sup>6</sup> <sup>15</sup>N,<sup>7</sup> and <sup>19</sup>F<sup>8</sup> nuclear screening constants in aromatic systems have been documented, similar systematic studies employing <sup>17</sup>O NMR have not appeared. Despite the difficulties in working with <sup>17</sup>O (due to the <sup>17</sup>O quadrupole moment,  $I = 5/2$ , and low natural isotopic abundance, 0.037%) several chemical shift studies have been

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(2) (a) Bentley, J. B.; Everard, K. B.; Marsden, R. J. B.; Sutton, L. E. *J. Am. Chem. Soc.* 1949, 71, 2957. (b) Hehre, W. J.; Radom, L.; Pople, J. A. *Ibid.* 1972, 94, 1496. (c) Miller, F. A.; Fateley, Witkowski, R. E. *Spectrochim. Acta, Part A* 1967, 32A, 891. (d) Montaudo, G.; Finocchiaro, P.; Maravigna *J. Am. Chem. Soc.* 1971, 93, 4214.

(3) (a) Young, P. R.; McMahon, P. E. *J. Am. Chem. Soc.* 1979, 101, 4678. (b) Plesnicar, B.; Smolikova, J.; Hehlicka, V.; Exner, O. *Collect. Czech. Chem. Commun.* 1978, 43, 2754. (c) Barthelemy, J. F.; Jost, R.; Sommer, J. *Org. Magn. Reson.* 1978, 11, 438. (d) Laurence, C.; Berthelot, M. *J. Chem. Soc., Perkin Trans. 2* 1979, 98. (e) Gupta, D.; Gupta, V. P. *Ind. J. Pure. Appl. Phys.* 1978, 16, 968.

(4) (a) Stothers, J. B.; Lauterbur, P. C. *Can. J. Chem.* 1964, 42, 1563. (b) Spiesscke, H.; Schnelder, W. G. *J. Chem. Phys.* 1961, 35, 731.

(5) (a) Batts, B. D.; Parsibu, S. J.; Williams, L. R. *Org. Magn. Reson.* 1977, 9, 210. (b) Beeby, J.; Sternhell, T.; Hoffman-Ostenhof, T.; Pretsch, E.; Simon, W. *Anal. Chem.* 1973, 45, 1571. (c) Bloxside, J.; Jones, J. R.; Marks, R. E. *Org. Magn. Reson.* 1970, 2, 337.

(6) Hampson, P.; Mathias, A.; Westhead, R. *J. Chem. Soc. B* 1971, 397. (7) Pregosin, P. S.; Randall, E. W.; White, A. I. *J. Chem. Soc., Perkin Trans. 2* 1972, 153.

(8) (a) Taft, R. W. *J. Am. Chem. Soc.* 1957, 79, 1045. (b) Taft, R. W.; Gillick, R. E.; Lewis, I. C.; Ehrenson, S. *J. Am. Chem. Soc.* 1960, 82, 756.

reported.<sup>9-14</sup> The sensitivity problem can be eliminated by employing <sup>17</sup>O-labeled compounds (specifically, in the aryl ketones and aldehydes studied here, enriched by an exchange reaction in a H<sub>2</sub><sup>17</sup>O-dioxane solvent).<sup>15</sup> The <sup>17</sup>O chemical shifts reported here are very sensitive to effects that modify the carbonyl electron distribution and exhibit a correlation with the Hammett substituent constants, infrared carbonyl stretching bands of substituted acetophenones, and X-ray diffraction data from ortho-substituted benzoic acids. The presence of intramolecular hydrogen-bonded chelate structures is clearly indicated by the <sup>17</sup>O data, and the chemical shifts also reflect the ortho-substituted steric interactions. The combined inductive, mesomeric, steric, and hydrogen-bonding effects play an important role in determining the <sup>17</sup>O chemical shifts of di- and trisubstituted aryl ketones and aldehydes. The high degree of sensitivity of the <sup>17</sup>O chemical shifts to the position, number, and electronic nature of the substituent is amply demonstrated in an absorption range of 150 ppm for the substituted acetophenones. The relaxation rates of these molecules also vary over a wide range (line widths vary from ca. 400-4 kHz).

This work consists of an extension of preliminary studies by D. Fiat in collaboration with D. Samuel and I. Dostrovsky at the Weizmann Institute of Science, Rehovot, Israel, in 1961. In this original work the <sup>17</sup>O chemical shifts and <sup>17</sup>O-exchange rates of several substituted acetophenones and benzaldehydes were determined. The high-field <sup>17</sup>O chemical shift in *o*-hydroxybenzaldehyde was observed and ascribed to intramolecular hydrogen bonding. Some of these results have been described in a review article by D. Samuel and B. Silver.<sup>15</sup>

**Experimental Section**

All compounds were obtained from Aldrich Chemical Co., Inc., and were generally used without further purification. Several of the ketones, however, were dried and distilled in order to note any significant changes in the <sup>17</sup>O parameters; no differences outside the experimental error were observed. Purity of the methoxy- and hydroxyacetophenones was verified by <sup>13</sup>C NMR. H<sub>2</sub><sup>17</sup>O enriched to 54.75% was obtained from Monsanto Research Corp. The enriched water was distilled twice in a bulb to bulb vacuum apparatus. The water was acidified with 10 N HCl and a 10/1 (V/V) dioxane-H<sub>2</sub><sup>17</sup>O solution was used to effect exchange with the acetophenones and benzaldehydes. Typically 0.1 mL of the dioxane-H<sub>2</sub><sup>17</sup>O solution would be added to ca. 3 mL of the neat liquid or added to the solid aldehyde or ketone that was previously dissolved in dioxane. The water was not included in the mole fraction calculations since no significant difference was observed in <sup>17</sup>O spectral parameters between dried (treated with molecular sieve type 4A or recrystallized under reduced pressure for the solid molecules) and wet samples. The mole fractions reported are for the aldehyde or ketone in dioxane unless otherwise specified. At least two separately prepared samples were used to obtain the <sup>17</sup>O spectral parameters, and the average value is reported.

<sup>17</sup>O spectra were obtained on a Bruker wide bore, high power CXP-180 spectrometer operating in the Fourier transform mode at 24.4 MHz for <sup>17</sup>O. Typical spectral settings for <sup>17</sup>O are as follows: 4K data points, 90° pulse angle corresponding to ca. 6-μs pulse width, 25-kHz spectral width, 210-ms recycle delay, and normally 1000 scans for the enriched samples. The natural abundance samples typically required 20000 acquisitions for adequate resolution. Temperature was maintained at 303 K to within ±1 K. All chemical shifts are reported relative to an external tap water reference at 303 K.

**Results**

Under suitable experimental conditions it is possible to measure the kinetics of oxygen-exchange reactions in organic compounds by following the change in the area of the <sup>17</sup>O resonance signal in time.<sup>16,17</sup> Qualitatively, for the aryl aldehydes and ketones

Table I. <sup>17</sup>O Exchange Rate Constants

compd	10 <sup>5</sup> k, s <sup>-1</sup>	T, °C	pH <sup>a</sup>
<i>o</i> -hydroxyacetophenone	8.2	34	6
<i>m</i> -hydroxyacetophenone	1.5	31	4
<i>p</i> -methoxyacetophenone	1.4	31	4
<i>o</i> -aminoacetophenone	1.1	31	4

<sup>a</sup> pH values must be considered very approximate since due to the small volumes of water used these values were obtained from pH paper.

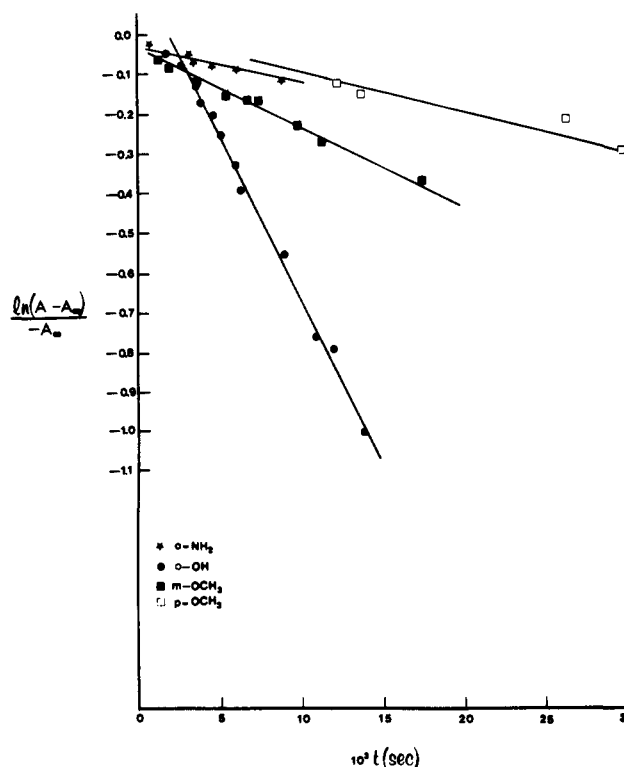


Figure 1. Experimental plots of <sup>17</sup>O exchange data used in determining the rate constants given in Table I.

studied here exchange reactions reach completion within several minutes when employing acidic H<sub>2</sub><sup>17</sup>O (pH ca. 1) and mild heating. Rate constants for several of the compounds in a mixed water (H<sub>2</sub><sup>17</sup>O)-dioxane solvent were obtained where the signal area (*A*) was equated with the concentration of the enriched aryl ketone. Rate constants (*k*) were obtained as the slope of the least-squares line of ln [(*A* - *A*<sub>∞</sub>)/-*A*<sub>∞</sub>] as a function of time. The rate constants and experimental conditions are given in Table I, and the kinetic plots are illustrated in Figure 1. The experimental errors in the rate constants are estimated to be within ±10%. It is also possible to effect carbonyl oxygen exchange by mixing H<sub>2</sub><sup>17</sup>O with the water-insoluble ketone. For example, <sup>17</sup>O-labeled *p*-aminoacetophenone (0.76 g) resulted from magnetically stirring 20% H<sub>2</sub><sup>17</sup>O (1 mL) with the ketone over a period of approximately 30 h. The advantage in this method over the use of the mixed solvent is that the enriched water can be cleanly and quickly recovered by a simple vacuum distillation. Employing the latter method, the exchange can be monitored by observing the decay of the <sup>17</sup>O carbonyl signal on exchange with naturally abundant H<sub>2</sub>O as was demonstrated by Greenzaid et al.<sup>17</sup> With use of the growth of the carbonyl signal in a water-dioxane solvent to measure kinetics, a significant error may be introduced in the area measurements of the initial signals due to a poor signal to noise ratio in the early stages of the exchange reaction. Since the ability to perform accurate <sup>17</sup>O NMR studies is dependent, in part, on using enriched samples, we might also note here that no observable oxygen occurred with the nitro or hydroxyl oxygens in the compounds containing these substituents. In addition, no exchange

(9) Sardella, D. J.; Stothers, J. B. *Can. J. Chem.* **1969**, *47*, 3089.  
 (10) Sugawara, T.; Kawada, Y.; Iwamura, H. *Chem. Lett.* **1978**, 1371.  
 (11) Delseth, C.; Kintzinger, J. P. *Helv. Chim. Acta* **1976**, *59*, 466.  
 (12) Figgis, B. N.; Kidd, R. G.; Nyholm, R. S. *Proc. R. Soc. London, Ser. A* **1962**, *A269*, 469.  
 (13) Crandall, J. K.; Centeno, M. A. *J. Org. Chem.* **1979**, *44*, 1183.  
 (14) Crandall, J. K.; Ceneno, M. A.; Borresen, S. *J. Org. Chem.* **1979**, *44*, 1184.  
 (15) Samuel, D.; Silver, B. L. *Adv. Phys. Org. Chem.* **1965**, *3*, 123.  
 (16) Greenzaid, P.; Luz, Z.; Samuel, D. *Trans. Faraday Soc.* **1968**, *64*, 2780.

(17) Reference 16, 2787.

Table II.  $^{17}\text{O}$  Carbonyl Chemical Shifts and Line Widths of Enriched Monosubstituted Acetophenones

group	$\delta^a$	line width, Hz	$\nu_{\max}^b$ , $\text{cm}^{-1}$	$\chi^c$
H	550	513	1691	0.96
<i>o</i> -OCH <sub>3</sub>	561	440		0.23
<i>m</i> -OCH <sub>3</sub>	551	876		0.61
<i>p</i> -OCH <sub>3</sub>	535	1136		0.32
<i>o</i> -OH	488	600		0.66
<i>m</i> -OH	546	1293		0.14
<i>p</i> -OH	513	1409		0.14
<i>o</i> -NH <sub>2</sub>	508	860	1653	0.26
<i>m</i> -NH <sub>2</sub>	548		1689	
<i>p</i> -NH <sub>2</sub>	511	1025	1677	0.11
<i>o</i> -CH <sub>3</sub>	579	427	1690	0.57
<i>m</i> -CH <sub>3</sub>	548	684		0.56
<i>p</i> -CH <sub>3</sub>	543	733	1687	0.56
<i>o</i> -F	562	404	1692	0.58
<i>p</i> -F	545	660	1692	0.58
<i>o</i> -Cl	586	378	1702, 1694	0.56
<i>p</i> -Cl	550	696	1692	0.56
<i>o</i> -Br	589	489	1706, 1702	0.4
<i>m</i> -Br	556	1040		0.4
<i>p</i> -Br	551	880	1693	0.23
<i>p</i> -CN	561	1087		0.22
<i>o</i> -NO <sub>2</sub>	573	880	1712, 1702	0.49
<i>m</i> -NO <sub>2</sub>	556	781	1701	0.14
<i>p</i> -NO <sub>2</sub>	567	1025	1700	0.23
$\alpha$ -Cl	541	915		0.6

<sup>a</sup> Chemical shifts reported downfield from an external water sample. <sup>b</sup> Carbonyl stretching band data obtained from Jones et al.<sup>36</sup> Acetophenones were dissolved in carbon tetrachloride. <sup>c</sup> Mole fraction of acetophenone in dioxane solvent.

Table III.  $^{17}\text{O}$  Carbonyl Chemical Shifts and Line Widths of Enriched Monosubstituted Benzaldehydes

group	$\delta^a$	line width, Hz	$\chi^b$
H	562	306	0.69
<i>o</i> -OCH <sub>3</sub>	555	610	0.58
<i>m</i> -OCH <sub>3</sub>	560	720	0.58
<i>p</i> -OCH <sub>3</sub>	539	830	0.58
<i>o</i> -OH	505	310	0.51
<i>m</i> -OH	559	805	0.16
<i>p</i> -OH	528	1075	0.22
<i>o</i> -Br	573	623	
<i>m</i> -Br	566	830	
<i>p</i> -Br	563	501	
<i>o</i> -NO <sub>2</sub>	576	403	0.19
<i>m</i> -NO <sub>2</sub>	572	696	0.21
<i>p</i> -NO <sub>2</sub>	580	598	0.18

<sup>a</sup>  $^{17}\text{O}$  chemical shifts are reported downfield from external water. <sup>b</sup> Mole fraction of benzaldehyde in dioxane solvent.

was observed in the acetylpyridines or acetamide and formamide derivatives under the mild reaction conditions employed here.

$^{17}\text{O}$  chemical shifts of the enriched monosubstituted acetophenones and benzaldehydes are presented in Tables II and III, and representative compounds are presented pictorially in Figure 2. It is important to report the mole fraction in conjunction with the chemical shift and line width since for some of these compounds (in particular, the molecules capable of intermolecular hydrogen bonding) the nuclear screening is a sensitive function of the dioxane concentration. The line widths are dependent on the concentration of aryl ketone or aldehyde in dioxane because the solution viscosity can change significantly. It was noted that modifying the acidity or basicity of the sample did not have an effect on the position of the carbonyl resonance (specifically, addition of up to 30  $\mu\text{L}$  NaOH or HCl to a 2-mL volume sample of *o*-methoxyacetophenone (*o*-OCH<sub>3</sub>A)). No attempt to remove the water used to effect exchange was made since it was determined that the very small water volumes employed were of no consequence in determining the chemical shift,  $\delta$ . The ortho-substituted acetophenones resonate over a range of approximately 100 ppm, and the para-substituted compounds absorb over a

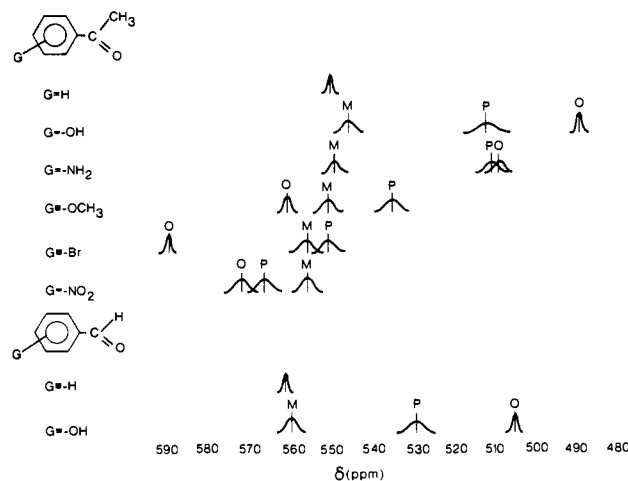


Figure 2.  $^{17}\text{O}$  chemical shifts of representative monosubstituted acetophenones and benzaldehydes measured downfield from an external water reference with relative line widths represented. O, M, and P stand for ortho, meta, and para.

Table IV.  $^{17}\text{O}$  Carbonyl Chemical Shifts and Line Widths of Enriched Polysubstituted Acetophenones and Benzaldehydes

compd	$\delta^a$	line width, Hz	$\chi^b$
2,4-dihydroxyacetophenone	459	1700	0.21
2,6-dihydroxyacetophenone	476	1013	0.21
2,3,4-trihydroxyacetophenone	466	4236	0.2
2,4,6-trihydroxyacetophenone	441	1500	0.12
2,4-dimethoxyacetophenone	539	1343	0.31
3,4,5-trimethoxyacetophenone	541	1671	0.1
2,3,4-trimethoxybenzaldehyde	545	1086	0.07
2,4,5-trimethoxybenzaldehyde	538	1160	0.05
2,4,6-trimethoxybenzaldehyde	565	1100	0.08

<sup>a</sup>  $^{17}\text{O}$  chemical shifts are reported downfield from external water. <sup>b</sup> Mole fraction of acetophenone or benzaldehyde in dioxane solvent.

60-ppm region. These rather large chemical shift ranges are to be contrasted with the 10-ppm range for meta-substituted acetophenones.

The substituted benzaldehydes are generally downfield of the corresponding acetophenone, and this difference in nuclear screening constants due to the substitution of  $-\text{CH}_3$  for  $-\text{H}$  at the  $\alpha$ -carbon is consistent over many of the compounds studied (Tables II and III). Exceptions to this occur in the cases of the *o*-OCH<sub>3</sub> and *o*-Br compounds. The chemical shift trends in the acetophenones and analogous benzaldehydes are very similar, indicating, as might be expected, that the same factors determine electron density at the carbonyl oxygen in both the aryl aldehydes and ketones.

$^{17}\text{O}$  carbonyl chemical shifts in di- and trisubstituted acetophenones and benzaldehydes are reported in Table IV. In the polyhydroxy-substituted acetophenones the resonances all appear upfield from *o*-OHA. On the other hand, the di- and trimethoxy-substituted acetophenones appear within 5 ppm of *p*-OCH<sub>3</sub>A. Similarly, 2,3,4- and 2,4,5-trimethoxybenzaldehyde resonate within a 5-ppm range centered at the *p*-methoxybenzaldehyde (*p*-OCH<sub>3</sub>B) absorption.

It was also possible to obtain  $^{17}\text{O}$  natural abundance spectra of a substantial number of these compounds, and these data are presented in Table V. It is important to note in comparing chemical shifts reported in Tables II and V that the natural abundance data can differ significantly from the chemical shifts obtained from  $^{17}\text{O}$ -labeled compounds. This may partially explain the disparities in the literature regarding  $^{17}\text{O}$  chemical shifts of the same compound reported from different groups. For natural abundance studies it is important to utilize experimental parameters that allow the maximal resolution, to average the signal until a reasonable *S/N* ratio is achieved (ca. 10:1 is usually adequate

Table V. <sup>17</sup>O Chemical Shifts of Substituted Acetophenones and Benzaldehydes at Natural Abundance<sup>a</sup>

group	$\delta^a$			
	acetophenones		benzaldehydes	
	=O	-O-	=O	-O-
H	552		568	
<i>o</i> -OH	488	90	509	85
<i>m</i> -OH <sup>c</sup>			558	92
<i>p</i> -OH <sup>c</sup>			524	108
<i>o</i> -NH <sub>2</sub>	512			
<i>m</i> -NH <sub>2</sub> <sup>d</sup>	536			
<i>p</i> -NH <sub>2</sub> <sup>d</sup>	507			
<i>o</i> -OCH <sub>3</sub>	563	56		
<i>m</i> -OCH <sub>3</sub>	548	60		
<i>o</i> -Br	586			
<i>m</i> -Br	555			
<i>p</i> -Br	548			
<i>o</i> -NH <sub>2</sub>	580			
<i>m</i> -NO <sub>2</sub>	566			
<i>p</i> -NO <sub>2</sub>	562			

<sup>a</sup> Chemical shifts are given for the neat liquids unless otherwise stated. <sup>b</sup> <sup>17</sup>O chemical shifts reported in ppm downfield from external water. <sup>c</sup> Saturated in dioxane. <sup>d</sup> Saturated in CHCl<sub>3</sub>.

for a 0.5-kHz signal), to meticulously report solution composition and other physical parameters, and to carefully report the details concerning the reference sample.<sup>18</sup> In addition, it would be useful to document the effects of utilizing a magnetic field lock and sample spinning on the <sup>17</sup>O spectrum since the utility of these precautions is not presently clear for the case of <sup>17</sup>O NMR. The experimental error in determining spectral parameters in isotopically enriched materials is significantly less than in the case of the natural abundance samples. We estimate the experimental error in determining the chemical shifts of the enriched materials to be less than 5 ppm in the case of the broadest lines studied here and for the majority of the aldehydes and ketones within  $\pm 1$  ppm. The <sup>17</sup>O-labeled acetophenone data of Sardella and Stothers<sup>9</sup> which was carried out at 1.41 T can be compared with that reported in Table II. In the case of six para-substituted acetophenones they studied, two of the chemical shifts they report differ significantly from our measurements (*p*-OCH<sub>3</sub>A,  $\delta$  548  $\pm$  4, and *p*-CH<sub>3</sub>A,  $\delta$  555  $\pm$  6) which would have masked a correlation with the Hammett para-substituent constants. Our data are in good agreement with the natural abundance, neat liquid chemical shifts for the few aromatic aldehydes and ketones reported by Christ and Diehl at 1.3 T.<sup>19</sup>

The higher field strength (4.23 T) and Fourier transform capabilities utilized in this work considerably enhance the accuracy of our results. Insufficient averaging can easily lead to experimental errors of 10 ppm in the chemical shifts of molecules at natural abundance. Naturally abundant and enriched spectra of *o*-hydroxybenzaldehyde are presented in Figure 3 for comparison. In general there is not a significant difference between the enriched and natural abundance chemical shifts; the majority of the differences being less than  $\pm 5$  ppm. Since the <sup>17</sup>O-enriched studies were carried out in a primarily dioxane solvent and the natural abundance parameters were determined as neat liquids and in various solvents (details in Table V), it would appear that a significant solvent effect is absent. <sup>13</sup>C data have demonstrated that screening constants in dioxane are in close agreement with the neat liquid values for substituted acetophenones.<sup>20</sup> Solvent effects on the carbonyl resonance of *m*-OHA and acetophenone were investigated with the results presented in Table VI. Only in the case of the alcohols does there appear to be any significant

(18) Since the <sup>17</sup>O chemical shift of water in various solvents varies considerably, it is necessary to employ an external reference sample. In addition, the isotopic composition of the external water reference should be reported since, as was pointed out by one of the reviewers, there is a significant isotope effect on  $\delta$ . For example, <sup>2</sup>H<sub>2</sub><sup>17</sup>O (99% <sup>2</sup>H, 0.037% <sup>17</sup>O) resonates 3 ppm to high field relative to tap water.

(19) Christ, H. A.; Diehl, P. *Helv. Phys. Acta* **1963**, *36*, 170.

(20) Dhama, K. S.; Stothers, J. B. *Can. J. Chem.* **1965**, *43*, 479.

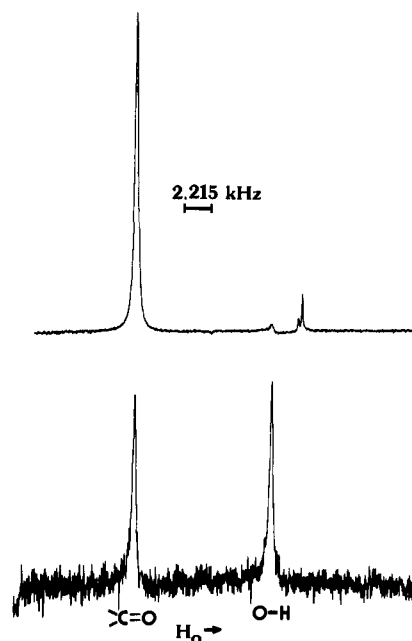


Figure 3. <sup>17</sup>O NMR spectra of enriched (top, 4000 scans,  $X = 0.68$  in dioxane) and natural abundance (bottom, 10 000 scans, neat liquid) *o*-hydroxybenzaldehyde.

Table VI. <sup>17</sup>O Chemical Shifts of Acetophenone and *m*-Hydroxyacetophenone in Various Solvents

	acetophenone		<i>m</i> -hydroxyacetophenone	
	$\delta^a$	$X^b$	$\delta^a$	$X^b$
methanol	533	0.03	528	0.03
formamide			543	0.07
<i>N,N</i> -dimethylformamide	547	0.05	544	0.1
dioxane	550	0.96	546	0.14
acetone	549	0.05	544	0.06
acetophenone			545	0.2
<i>o</i> -hydroxyacetophenone	547	0.08		
dimethyl sulfoxide	546	0.09		
chloroform	539	0.10		
propanol	538	0.09		
2-propanol	540	0.09		
butanol	541	0.11		
decanol	547	0.21		
formic acid	541	0.08		

<sup>a</sup> <sup>17</sup>O chemical shifts measured in ppm downfield from external water. <sup>b</sup> Mole fraction of solute in solvent.

effect on the positions of the acetophenone and *m*-OHA resonances. In addition, chemical shift studies as a function of solvent concentration were undertaken. Acetophenone underwent a 17-ppm upfield shift upon infinite dilution in methanol, and the curve was approximately linear.

It was also possible to observe <sup>17</sup>O resonances from the hydroxy and methoxy groups although the nitro oxygens were not resolved under the conditions employed here (Table V). The hydroxyl resonance from phenol at natural abundance has been reported as 69.3 ppm.<sup>13</sup> In general, proton-accepting solvents have the effect of inducing a downfield shift as evidenced by the chemical shift of phenol in water ( $\delta$  77), *N,N*-dimethylformamide ( $\delta$  74), and dioxane ( $\delta$  81). In comparison, the <sup>17</sup>O resonance of water also undergoes a downfield shift on participation in hydrogen bonds. It is significant to note that the benzaldehyde hydroxyl resonances appear downfield of the phenol absorptions noted above and that there is a 23-ppm absorption range depending on the position of the formyl group, indicating that the <sup>17</sup>O chemical shift of the phenolic oxygen may be sensitive to the ring substitution. However, natural abundance hydroxy and methoxy aromatic resonances are difficult to detect since they are normally at least as broad as the carbonyl line.

Table VII. Calculated and Experimental Chemical Shifts and Related Empirical Data

substituent	$H_B,^a$ eV	bond order <sup>b</sup>	$\Delta E_{n \rightarrow \pi^*},^c$ $10^{-19}$ J	$\delta_{\text{exptl}}$	$\delta_{\text{calcd}}$	$\Delta\delta_{\text{exptl}}^d$	$\Delta\delta_{\text{calcd}}^e$
NH <sub>2</sub>	8.50	1.631		511		-39	
OH	8.75	1.639	6.597	513	552	-37	-35
CH <sub>3</sub>	8.82	1.642	6.205	543	587	-7	0
H	9.24	1.653	6.205	550	587	0	0
Cl	9.14	1.651	6.244	550	583	0	-4
Br	9.13	1.649	6.148	551	592	1	5
NO <sub>2</sub>	9.24	1.678	5.927	573	615	23	28

<sup>a</sup> Energy of highest occupied orbital of mono-substituted benzene. Data taken from ref 30a. <sup>b</sup> Bond orders taken from Figure 3 in ref 30a. <sup>c</sup> UV data taken from ref 30a and 36. <sup>d</sup> Chemical shift differences relative to acetophenone at  $\delta$  550. Positive  $\Delta\delta$  denotes downfield shifts. <sup>e</sup> Chemical shift differences relative to acetophenone at  $\delta$  587. Positive  $\Delta\delta$  denotes downfield shifts.

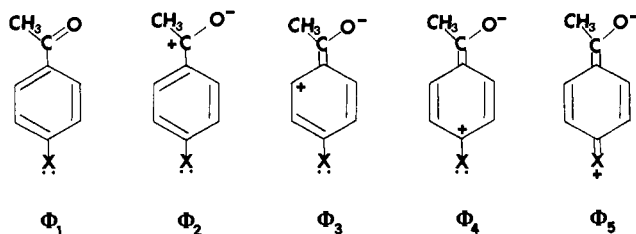
Line widths of the carbonyl resonances range from 300 Hz (benzaldehyde) to greater than 4 kHz (2,3,4-(OHA)<sub>3</sub>). In general, the ortho molecules have the sharpest lines for a given ring substitution, this trend being most pronounced for the hydroxy substituted compounds. For a given substitution the benzaldehyde normally has a sharper line than the acetophenone.

### Theory and Discussion

A complete calculation of the nuclear magnetic shielding constant ( $\sigma$ ) usually requires the LCAO-SCF-generated molecular orbital. In addition, calculation of the paramagnetic term,  $\sigma^P$ , of  $\sigma$  assumes a knowledge of all excited state eigenfunctions. Various theoretical levels of approach and the approximations employed have been discussed<sup>21</sup> and a guide to theoretical <sup>17</sup>O nuclear screening studies has appeared in a recent review article.<sup>22</sup>

For our purposes it is possible to obtain an adequate picture of the factors contributing to the observed <sup>17</sup>O chemical shifts by employing a more simplified approach. First we use the conceptually advantageous scheme of representing the molecule as a hybrid of several resonance structures. Second, we assume that the chemical shielding parameter ( $\sigma$ ) can be approximated as the sum of a diamagnetic and paramagnetic term and that  $\sigma(^{17}\text{O}) \approx \sigma^P(^{17}\text{O})$ . The benefits of this heuristic approach will be demonstrated in several interesting correlations of the <sup>17</sup>O chemical shifts with data from various spectroscopic methods. These correlations should prove fruitful in the interpretation of <sup>17</sup>O chemical shifts in other molecular systems.

Qualitatively, the electron-donating and -withdrawing characteristics of the substituent will be reflected in the stabilization of certain wave functions that contribute to the total molecular orbital in the conjugated aryl-carbonyl system. Considering the carbonyl bond to be partially polarized, <sup>+</sup>C=O<sup>-</sup>, is of proven utility in the interpretation of <sup>13</sup>C chemical shifts,<sup>23</sup> <sup>17</sup>O chemical shifts,<sup>24,25</sup> and <sup>17</sup>O quadrupole coupling constants.<sup>26</sup> The total wave function,  $\Psi$ , can be expressed as the sum of at least five resonance forms,  $\Psi = \sum_i c_i \Phi_i$ . As the electron-donating ability



of -X increases, structures  $\Phi_2 \rightarrow \Phi_5$  will be favored. The <sup>17</sup>O chemical shifts will be affected by the population distributions among the various resonance forms.

The nuclear magnetic shielding can be approximated as the sum of two terms, the paramagnetic term  $\sigma^P$  and the diamagnetic term  $\sigma^D$ ;  $\sigma = \sigma^P + \sigma^D$ .<sup>27</sup> The diamagnetic contribution to the <sup>17</sup>O nuclear screening has been estimated to be 26<sup>12</sup> and 8 ppm.<sup>28</sup> Therefore,  $\sigma^P$  is principally responsible for the <sup>17</sup>O chemical shifts and will be considered as the sole contribution to the nuclear screening,  $\sigma \approx \sigma^P$ . The average isotropic paramagnetic term for the oxygen atom can be expressed as eq 1, where  $\langle r^{-3} \rangle_{2p}$  = average

$$\sigma^P = -\frac{2}{3}(eh/mc)^2 \langle r^{-3} \rangle_{2p} \Delta E^{-1} P_u \quad (1)$$

value of the reciprocal cube of the 2p orbital radius,  $\Delta E$  = average electronic excitation energy, and  $P_u$  = the "unbalance" of the valence electrons in the p orbitals which depends on the atomic coordination number, hybridization state, and bond ionicity. Saika and Slichter<sup>29</sup> have used the approximation that  $P_u = (1 - i)$  where  $i$  is a measure of the ionic character of the bond. Clearly three factors ( $\langle r^{-3} \rangle_{2p}$ ,  $\Delta E$ , and  $p_u$ ) may be significant in determining the <sup>17</sup>O chemical shifts. We note that in the average excitation energy approximation the term that we call  $P_u$  would be replaced by  $\sum_B Q_{OB}$  where the summation over  $B$  includes the oxygen atom (O) and all other atoms in the molecule.  $Q_{OB}$  are the bond order charge density terms, and this calculation is discussed in the work of Ebraheem and Webb.<sup>21</sup> Hence use of the factor  $P_u = (1 - i)$  may be somewhat fortuitous although use of the empirical  $n \rightarrow \pi^*$  transition energies does demonstrate that the <sup>17</sup>O chemical shift differences of the para-substituted acetophenones are dominated by the lowest energy electronic transitions.

Both empirical<sup>12</sup> and theoretical<sup>28</sup> correlations of <sup>17</sup>O chemical shifts with the lowest energy electronic transitions for the carbonyl chromophore ( $n \rightarrow \pi^*$ ) have appeared. None of these studies, however, included aromatic carbonyl molecules. On the other hand, Sardella and Stothers<sup>9</sup> concluded from a very limited <sup>17</sup>O chemical shift study of substituted acetophenones that a consistent explanation in terms of the  $\Delta E_{n \rightarrow \pi^*}$  factor is not possible and thus  $\langle r^{-3} \rangle_{2p}$  was invoked to explain the observed shifts. A reexamination of their optical data with  $\delta(^{17}\text{O})$  presented here indicates that their interpretation requires modification.

Dominance of the polarized structures relative to resonance form  $\Phi_1$  intuitively should lead to a decrease in  $\pi$  bond order and a correlation with carbonyl stretching band data.<sup>30</sup> The bond order of the carbonyl group will decrease steadily with increasing electron migration from benzene ring to the acyl function, and the tendency for orbital mixing to occur will depend on the energy difference between the highest occupied orbital of benzene and the lowest unoccupied orbital of the carbonyl group (Table VII).<sup>30,31</sup> Changes in  $\langle r^{-3} \rangle_{2p}$  and modifying the electronic energies will result in changes in  $\pi$  bond order and  $\delta(^{17}\text{O})$ .

In general, as the  $\pi$ -electron-donating ability (according to the Hammett constants) of a para substituent in substituted acetophenones increases, the  $n \rightarrow \pi^*$  transition shifts to higher ener-

(21) Ebraheem, K. A. K.; Webb, G. A. *Prog. Nucl. Magn. Reson. Spectrosc.* **1977**, *11*, 149.

(22) St. Amour, T.; Fiat, D. *Bull. Magn. Reson.* **1980**, *1*, 118.

(23) Llinas, M.; Wilson, D. M.; Klein, M. P. *J. Am. Chem. Soc.* **1977**, *99*, 6846.

(24) Burgar, M. I.; St. Amour, T. E.; Fiat, D. *J. Phys. Chem.* **1981**, *85*, 525.

(25) Reuben, J. *J. Am. Chem. Soc.* **1969**, *91*, 5725.

(26) Cheng, C. P.; Brown, T. L. *J. Am. Chem. Soc.* **1979**, *101*, 2327.

(27) Slichter "Principles of Magnetic Resonance"; Springer-Verlag: New York, 1979.

(28) Ebraheem, K. A. K.; Webb, G. A. *J. Magn. Reson.* **1977**, *25*, 399.

(29) Saika, A.; Slichter, C. P. *J. Chem. Phys.* **1954**, *22*, 26.

(30) (a) Tanaka, J.; Nagakura, S.; Kobayashi, M. *J. Chem. Phys.* **1956**, *24*, 311. (b) Ditchfield, R.; Del Bene, J. E.; Pople, J. A. *J. Am. Chem. Soc.* **1972**, *94*, 703.

(31) Nagakura, S.; Tanaka, J. *J. Chem. Phys.* **1954**, *22*, 236.

gies.<sup>30a</sup> Ditchfield et al.<sup>30b</sup> in an ab initio MO study of  $n \rightarrow \pi^*$  transition energies in small, acyclic molecules found for XCHO molecules that the excitation energies are found to decrease in the order  $X = \text{NH}_2, \text{OH}, \text{F}, \text{and } \text{CH}_3$ . Note that  $\pi$  donation by X according to the Hammett para-substituent constant decreases in the order  $\text{NH}_2 > \text{OH} > \text{CH}_3 > \text{F}$ . In the molecules studied by Ditchfield et al.<sup>30b</sup> there are four effects (due to  $\pi$  donation and  $\sigma$  withdrawal) that need to be considered in a rationalization of the theoretically predicted  $n \rightarrow \pi^*$  transition energies. At least in the case of the para-substituted aromatic compounds studied here the  $\pi$  donation will be the important mode of transmitting information concerning the ring substituent. There are two main effects due to  $\pi$ -electron donation by the substituent: (a) an increase of the  $\pi^*$  one-electron orbital energy and (b) an increase in the negative charge on the carbonyl oxygen which indirectly causes the oxygen lone pair to be less tightly bound. We might note here that b suggests that the  $\langle r^{-3} \rangle_{2p}$  and  $\Delta E^{-1}_{n \rightarrow \pi^*}$  factors in  $\sigma^P$  may very well be dependent upon each other and may be separated into distinct, independent terms (for example, assuming  $\langle r^{-3} \rangle_{2p}$  remains constant while  $\Delta E^{-1}_{n \rightarrow \pi^*}$  varies) only as a very rough approximation.

With a blue-shifted  $n \rightarrow \pi^*$  transition eq 1 predicts  $\sigma^P$  will decrease if  $\langle r^{-3} \rangle_{2p}$  and  $P_u$  remain constant. Calculated values for  $\sigma^P$  using eq 1 are given in Table VII.  $\Delta E^{-1}_{n \rightarrow \pi^*}$  values are empirical (reference given in Table VII) and we use  $\langle r^{-3} \rangle_{2p} = 1/24(4.55/a_0)^3$  where 4.55 is the appropriate value for the effective oxygen nuclear charge according to Slater's rules. The  $P_u$  factor in (1) is estimated by analogy with Saika and Slichter<sup>29</sup> as  $(1 - i)$  where  $i$  is taken as 0.46 (the estimated carbonyl bond polarity for acetone).<sup>32</sup>  $P_u = 0$  corresponds to the spherically symmetric closed-shell case,  $O^{2-}$ . A rigorous evaluation of  $\sigma^P$  would require a LCAO-MO calculation of the  $P_u$  factor as we have pointed out before. Although, the calculated shifts appear reasonably close to the experimental values (in particular,  $\Delta\delta_{\text{exptl}} \approx \Delta\delta_{\text{calcd}}$ ) this is deceptive since electronic transitions other than the  $n \rightarrow \pi^*$  have been ignored and the chemical shifts are calculated relative to  $O^{2-}$  instead of  $\text{H}_2\text{O}$  at 0 ppm. Consideration of the  $\pi \rightarrow \pi^*$  and  $\sigma \rightarrow \pi^*$  transitions would have the effect of increasing the paramagnetic shift. Given the crude method of calculation, the shift differences are reasonably close and clearly indicate that  $\Delta E^{-1}_{n \rightarrow \pi^*}$  is the dominant factor in determining the <sup>17</sup>O nuclear screening for the para-substituted acetophenones. It has been reported that the  $\Delta E^{-1}_{n \rightarrow \pi^*}$  term does not predict the proper  $\delta(^{17}\text{O})$  trend for the ortho-substituted acetophenones.<sup>9</sup> However, UV data for only one mono- and one di-ortho-substituted acetophenone were presented, and we feel that this conclusion was unwarranted and certainly does not prove that  $\sigma^P$  is determined by  $\langle r^{-3} \rangle_{2p}$ .

Although we did not explicitly consider contributions to  $\delta(^{17}\text{O})$  from bonding orbitals centered on other atoms, their effect is indirectly exerted through modifying  $\Delta E^{-1}_{n \rightarrow \pi^*}$ , carbonyl bond order, and bond ionicity. The contribution of the radial term is difficult to ascertain since for changes in the electron-donating properties of the substituent it predicts changes in  $\sigma^P$  in the same direction as those predicted by the electronic energy term; i.e., electronic factors stabilizing valence bond structures  $\Phi_2 \rightarrow \Phi_5$  will have the effect of decreasing  $\langle r^{-3} \rangle_{2p}$  and increasing  $\Delta E^{-1}_{n \rightarrow \pi^*}$  both of which result in chemical shifts to high field. Finally, although we have treated  $P_u$  as a constant, it might be expected to decrease in association with stabilization of  $\Phi_2 \rightarrow \Phi_5$ . However, a theoretical study in the SCF-MO INDO approximation for  $\delta(^{17}\text{O})$  in nitroalkanes shows that variation in  $P_u$  is 1 order of magnitude less than changes in  $\Delta E$ .<sup>33</sup>

In the discussion that follows we will freely use the qualitative framework provided by the wave functions  $\Phi_2 \rightarrow \Phi_5$  in relation to  $\delta(^{17}\text{O})$ . As we have mentioned, this approach is conceptually advantageous. In summary, factors stabilizing  $\Phi_2 \rightarrow \Phi_5$  result in upfield <sup>17</sup>O chemical shifts due to a reduction in  $\sigma^P$ . Note that if there is a shift in the orbital populations favoring structure  $\Phi_2$

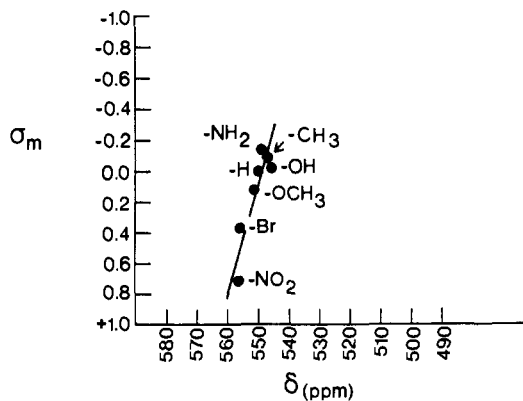


Figure 4.  $\delta(^{17}\text{O})$  in ppm vs.  $\sigma_m$  for the meta-substituted acetophenones. The values for the meta-substituent constant are taken from: Jaffe, H. *Chem. Rev.* **1953**, 53, 191.

significant downfield shifts in the carbonyl <sup>13</sup>C chemical shift might be expected.

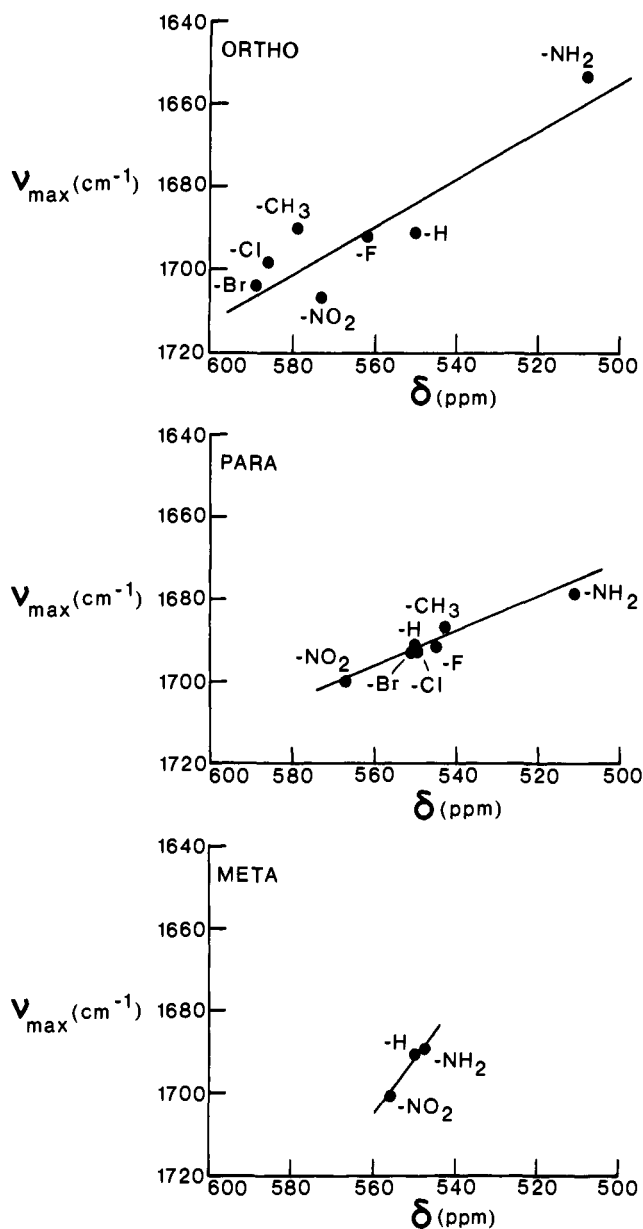
**Meta-Substituted Molecules.** The chemical shift range for the meta benzaldehydes (13 ppm) and meta acetophenones (10 ppm) is considerably less than in the ortho and para compounds, indicating a reduced sensitivity to the electronic nature of the substituted group. Inductive effects are transmitted with equal effectiveness from both the meta and para positions although resonance effects are most efficiently transmitted from the para position. Thus the difference in shift ranges between the meta and para molecules is most likely due to the mesomeric effect, and, in particular, the contribution to the nuclear screening due to structure  $\Phi_5$ , which is not possible for the meta compounds, can account for the diamagnetic shifts for a given ring substitution in the para molecules. There is a correlation between the <sup>17</sup>O chemical shifts and the Hammett substituent constants,  $\sigma_m$ , although the correlation is not as pronounced as for the para compounds (Figure 4). The correlation coefficients for  $\delta^{\text{meta}}(^{17}\text{O})$  vs.  $\sigma_m$  is 0.89 for the acetophenones and 0.96 for the benzaldehydes. The linear relationship between the meta <sup>17</sup>O screening constants and carbonyl stretching frequencies is shown in Figure 5.

**Para-Substituted Molecules.** The chemical shift ranges for the para-substituted acetophenones and benzaldehydes are both approximately 60 ppm, indicating a high sensitivity to the mesomeric and inductive effects exerted by the para substitution.

<sup>1</sup>H NMR studies have been used in the estimation of the barrier to internal rotation about the  $C_1-C_\alpha$  bond in benzaldehyde and its substituted derivatives and is a measure of the resonance interaction of the aromatic  $\pi$  electrons and the oxygen lone pair of the carbonyl group.<sup>34,35</sup> The correlation is illustrated in the free energy of activation for internal rotation for benzaldehyde (7.9 kcal/mol), *p*-OCH<sub>3</sub>B (9.2 kcal/mol), and *p*-N(CH<sub>3</sub>)<sub>2</sub>B (10.8 kcal/mol). The increased double bond character of the  $C_1-C_\alpha$  bond was attributed to an increased contribution from canonical form  $\Phi_5$  relative to the wave function distribution in benzaldehyde. The IR carbonyl vibrational data reproduced from Jones, et al.<sup>36</sup> in Table I gives the highest stretching frequency for *p*-NO<sub>2</sub>A and the lowest frequency for *p*-NH<sub>2</sub>A. Qualitatively, there is a greater degree of carbonyl double bond character in the *p*-NO<sub>2</sub>A molecule or  $\Phi_1$  makes a greater contribution to  $\Psi$  for the *p*-NO<sub>2</sub>A molecule relative to the orbital population distribution in *p*-NH<sub>2</sub>A. Increased contribution from  $\Phi_1$  would lead to downfield <sup>17</sup>O chemical shifts and in fact the IR and NMR data are strongly correlated (Figure 5). Although the carbonyl stretching frequencies are insensitive to the different halogen substitutions, the <sup>17</sup>O chemical shifts are in accord with the Hammett constants with respect to

(32) Coulson, C. A. "Valence"; Oxford University Press: New York, 1961; p 159.  
 (33) Moniz, W. B.; Poranski, C. F., Jr. *J. Magn. Reson.* **1973**, 11, 62.

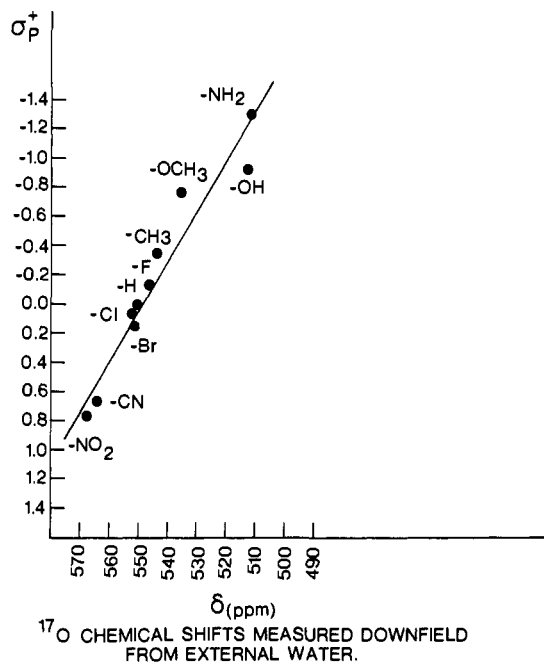
(34) Anet, F. A. L.; Ahmad, M. *J. Am. Chem. Soc.* **1964**, 86, 119.  
 (35) Klincck, R. E.; Marr, D. H.; Stothers, J. B. *Chem. Commun.* **1967**, 409.  
 (36) Jones, R. N.; Forbes, W. F.; Mueller, W. A. *Can. J. Chem.* **1957**, 35, 504.



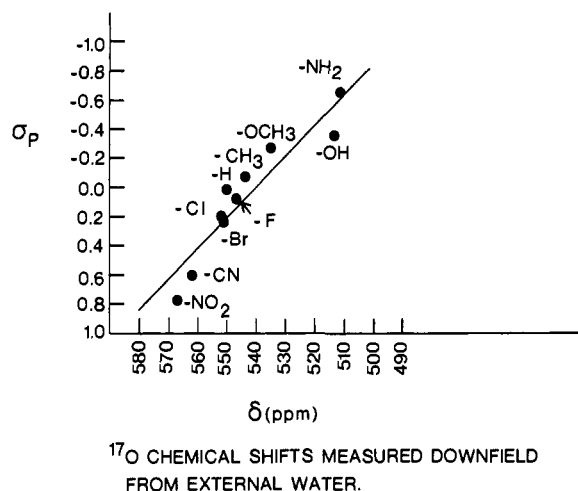
**Figure 5.** IR carbonyl stretching bands plotted against  $^{17}\text{O}$  chemical shifts for the substituted acetophenones. The infrared values are taken from ref 36.

the various para-halogenated acetophenones.

Swain and Lupton<sup>37</sup> have calculated that the resonance contribution for  $\sigma_p$  is 53% and for  $\sigma_p^+$  66%.  $\delta$  plotted as a function of  $\sigma_p^+$  results in a somewhat better straight line than  $\delta$  vs.  $\sigma_p$  as evidenced by the correlation coefficients of 0.96 and 0.92 for the  $\sigma_p^+$  and  $\sigma_p$  graphs, respectively (Figures 6 and 7). An opposite trend occurs for the benzaldehydes, however, where the correlation coefficients are 0.99 for  $\delta$  vs.  $\sigma_p$  and 0.94 for  $\delta$  vs.  $\sigma_p^+$ . The acetophenone correlation coefficients are probably somewhat better due to a larger  $^{17}\text{O}$  data base which indicates that mesomeric effects play the dominant role in determining the electron density at the carbonyl oxygen. Comparison with the  $^{17}\text{O}$  data for the meta compounds suggests that  $\delta$  provides a qualitative measure of the contribution of structure  $\Phi_5$  to  $\Psi$  for the para-substituted compounds. The least-squares line relating the  $^{17}\text{O}$  chemical shifts to the optical data is given by  $\delta = 1.4815\lambda(n \rightarrow \pi^*) + 73.23$  and is illustrated in Figure 8. For a variety of organic carbonyl compounds the correlation between chemical shift and lowest energy electronic transition yields a slope of approximately 3 ppm/nm.<sup>12</sup> There is a good deal of scatter in the region 300–340



**Figure 6.**  $\delta(^{17}\text{O})$  in ppm vs.  $\sigma_p^+$  for the para-substituted acetophenones. The values for  $\sigma_p^+$  are taken from: Okamoto, Y.; Inukai, J.; Brown, H. C. *J. Am. Chem. Soc.* **1958**, *80*, 4979.



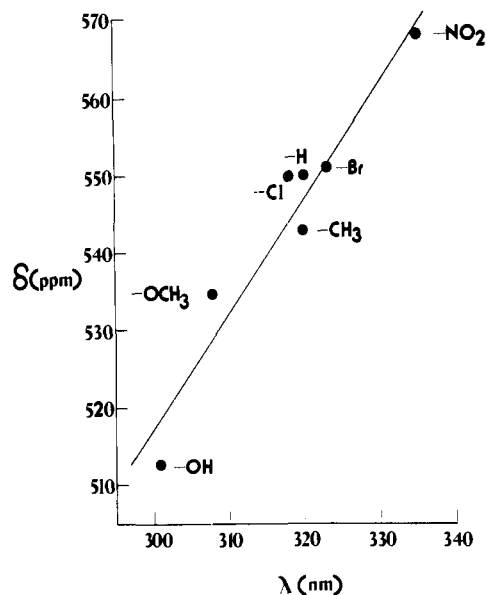
**Figure 7.**  $\delta(^{17}\text{O})$  in ppm vs.  $\sigma_p$  for the para-substituted acetophenones. The values for  $\sigma_p$  are taken from: Jaffe, H. *Chem. Rev.* **1953**, *53*, 191.

nm for the aliphatic and cyclic ketones in the correlation line obtained by Figgis, Kidd, and Nyholm.<sup>12</sup> The correlation line in Figure 8 is well within the scatter of points for the aldehydes and ketones in Figure 2 of ref 12 and conforms quite nicely with their curve.

The proximity of the 2,3,4- and 2,4,5-( $\text{OCH}_3\text{B}$ ) and  $p\text{-OCH}_3\text{B}$  resonances indicates that the para substitution is the dominant factor in determining oxygen nuclear shielding for equivalent ortho substitutions (Table IV). The influence of the para position is also demonstrated in comparing 2,4-( $\text{OCH}_3\text{A}$ )<sub>2</sub>, 3,4,5-( $\text{OCH}_3\text{A}$ )<sub>3</sub> and  $p\text{-OCH}_3\text{A}$  which resonate within a 6-ppm range.

**Ortho-Substituted Molecules.** The strongest perturbation of the electronic structure of the carbonyl bond occurs upon varying the ortho substitutions. The ortho-substituted compounds resonate over regions of 110 and 71 ppm for the acetophenones and benzaldehydes, respectively. There are two groups of ortho-substituted acetophenones classified according to  $\delta$ : one group resonates upfield of ca. 510 ppm whereas the other compounds resonate downfield from ca. 560 ppm (Figure 2 and Table II). Similarly, there are two regions of carbonyl stretching bands: the  $o\text{-NH}_2\text{A}$  being considerably red shifted with respect to the other compounds (Figure 5). Carbonyl  $^{13}\text{C}$  chemical shifts of the  $o\text{-OHA}$  and

(37) Swain, C. G.; Lupton, E. C. *J. Am. Chem. Soc.* **1968**, *90*, 4328.



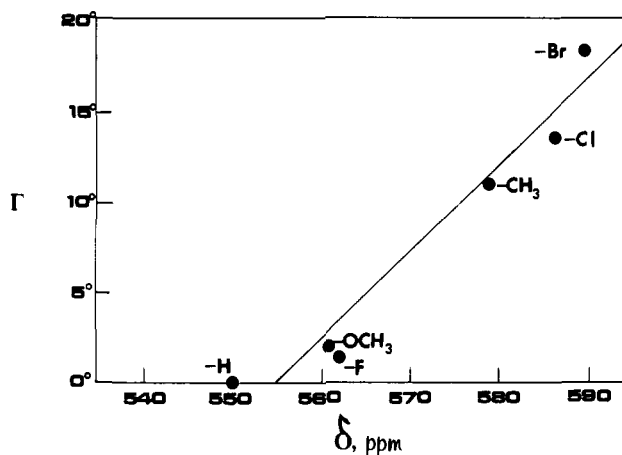
**Figure 8.**  $\delta(^{17}\text{O})$  in ppm vs.  $\lambda$  in nm (lowest energy electronic transitions,  $\Delta E^{-1}_{n \rightarrow \pi^*}$ ) for the para-substituted acetophenones. UV data were taken from ref 30 and 36.

*o*-NH<sub>2</sub>A molecules are deshielded relative to other ortho-substituted acetophenones.<sup>23</sup> Comparison with other spectroscopic data indicates that the <sup>17</sup>O screening constants are determined by essentially two main effects: (1) steric effects that determine the resonance positions of the downfield group of ortho molecules and (2) intramolecular hydrogen-bonding effects are responsible for the high-field absorptions.

**Steric Effects.** A substantial literature devoted to the quantitative treatment of the ortho effect has appeared and amply demonstrates the difficulty in presenting a simple characterization of the nature of this effect.<sup>38-40</sup> Our analysis is based primarily on the steric inhibition of resonance effect and appears to have some semiquantitative predictive value although electrical effects which are known to be important have been ignored.<sup>41-44</sup> However, we did not find any striking correlations between a large number of sets of ortho substituent constants that have been shown to be due to pure electrical effects<sup>43</sup> and  $\delta(^{17}\text{O})$ .

Steric interactions between the ortho substitution and the formyl or acetyl groups prevent electron migration from the ortho-substituted ring to the acyl function. Increasing deviation from a coplanar configuration between the ring and the carbonyl group results in a significant downfield shift for both the carbonyl <sup>13</sup>C<sup>45</sup> and <sup>17</sup>O nuclei. As the bulk and/or number of nonhydrogen bond donating ortho substituents increases, the carbonyl carbon shifts to lower field, and this trend is presumably due to the prevention of positive charge delocalization or a redistribution of resonance populations favoring increased contributions from  $\Phi_1$  and  $\Phi_2$  to  $\Psi$ . The contributions from canonical forms  $\Phi_3 \rightarrow \Phi_5$  are decreased and the <sup>17</sup>O paramagnetic screening constant increases; the increased contribution from  $\Phi_2$  induces the <sup>13</sup>C downfield shift. An examination of Table III indicates the effect of two ortho substituents on the <sup>17</sup>O-screening constant. Although the 2,3,4- and 2,4,5-(OCH<sub>3</sub>B)<sub>3</sub> molecules absorb with 5 ppm of *p*-OCH<sub>3</sub>B, 2,4,6-(OCH<sub>3</sub>B)<sub>3</sub> resonates 25-ppm downfield from *p*-OCH<sub>3</sub>B, demonstrating the effect of increased steric hindrance in the case of two ortho substitutions on the <sup>17</sup>O nuclear screening.

A comparison of the interplanar angle,  $\Gamma$ , between the aromatic ring and the carboxyl group of ortho-substituted benzoic acids



**Figure 9.** <sup>17</sup>O chemical shifts of ortho-substituted acetophenones vs.  $\Gamma$ , the angle between the carboxyl group and the ortho-substituted ring in substituted benzoic acids obtained from X-ray diffraction data. Crystallographic data was taken from ref 38.

and <sup>17</sup>O chemical shifts of ortho-substituted acetophenones demonstrates a strong correlation between  $\Gamma$  and  $\delta$  (Figure 9). The interplanar angles compiled by Charton<sup>38</sup> are from X-ray diffraction studies, and it is suggested that  $\Gamma$  is a function of the van der Waals radius of the ortho substituent. This is the strongest evidence that the differences in the <sup>17</sup>O chemical shifts in the low-field group of ortho-substituted acetophenones can be explained in terms of a decrease in delocalization due to increasing deviations from coplanarity. An assumption implicit in this correlation is that the interplanar angle between the acetyl and the ortho-substituted ring is very similar to the angle observed in the ortho-substituted benzoic acids.

An alternative explanation has been offered for the IR carbonyl stretching band data of the ortho-substituted acetophenones by Jones et al.<sup>36</sup> and is based on the interplay of a steric and electrostatic ortho effect that results in a dynamic equilibrium between the cis and trans isomers (the ortho group may be cis or trans to the carbonyl oxygen). Their interpretation assumes that the stereoisomers are planar although an examination of molecular models (CPK) indicates that planarity either is not possible or results in a highly strained configuration. The weakness of an interpretation based purely on steric inhibition of resonance should also be made clear. For example, ortho substitution in the (OCH<sub>3</sub>B)<sub>3</sub> does not cause a significant downfield shift relative to *p*-OCH<sub>3</sub>B as might be expected from the steric inhibition of conjugation arguments.

**Hydrogen-Bonding Interactions.** The results in Table VI demonstrate that alcohols, which possess a proton-donating group, generally induce high-field <sup>17</sup>O chemical shifts. With respect to the resonance of *m*-OHA and acetophenone in dioxane, dilution in methanol results in a 17-ppm upfield shift for acetophenone and a 18-ppm upfield shift for *m*-OHA. In addition, in the case of molecules where the possibility for the formation of an intramolecular hydrogen bond exists, we find that the <sup>17</sup>O resonance is significantly shielded with respect to similar molecules that cannot form the intramolecular hydrogen-bonded chelate structure. For example, *o*-OCH<sub>3</sub>A resonates at  $\delta$  561 and *o*-OHA resonates at  $\delta$  488. Note that the chemical shift differences between *p*-OCH<sub>3</sub>A and *p*-OHA is only 22 ppm and between *m*-OCH<sub>3</sub>A and *m*-OHA there is a 5-ppm difference. Similar chemical shift differences occur for the substituted benzaldehydes (Table III). Clearly, hydrogen-bonding effects on the <sup>17</sup>O nuclear screening are considerably larger than the substituent effects. In the cases of intramolecular hydrogen bonding, the hydrogen bond dominates the <sup>17</sup>O nuclear screening constant and the substituent effects are superimposed on this stronger interaction. This is most clearly demonstrated in comparing the mono- and polyhydroxy-substituted acetophenones. The effect of a para-substituted hydroxyl group in 2,4-(OHA)<sub>2</sub> results in a 29 ppm increased shielding relative to *o*-OHA. The addition of a meta hydroxyl group to 2,4-(OHA)<sub>2</sub>

(38) Charton, M. *Prog. Phys. Org. Chem.* **1971**, *8*, 235.

(39) Unger, S. H.; Hansch, C. *Prog. Phys. Org. Chem.* **1976**, *12*, 91.

(40) Fujita, T.; Nishioda, T. *Prog. Phys. Org. Chem.* **1976**, *12*, 49.

(41) Charton, M. *J. Am. Chem. Soc.* **1969**, *91*, 619.

(42) Reference 41, p 624.

(43) Reference 41, p 6649.

(44) Bastos, M. P.; do Amaral, L. *J. Org. Chem.* **1979**, *44*, 980.

(45) Dhama, K. S.; Stothers, J. B. *Tetrahedron Lett.* **1964**, *12*, 631.



results in a 7-ppm low-field shift relative to the 2,4-(OHA)<sub>2</sub> resonance at 459 ppm (Table IV). It is also worthwhile to note that intermolecular hydrogen bonding via the 3- and 4-ring-substituted hydroxyl groups in 2,3,4-(OHA)<sub>3</sub> is responsible for the 4.2-kHz line width observed for this molecule (Table IV).

It is useful to briefly review previous spectroscopic studies in light of our results employing <sup>17</sup>O NMR. The anomalous downfield shifts observed in <sup>13</sup>C NMR of the carbonyl carbon in molecules capable of intramolecular hydrogen bonding in acetophenones have been reported.<sup>46</sup> Proton NMR data have indicated that the trans form predominates except in the cases of *o*-OHB and *o*-NH<sub>2</sub>B where coupling constant and chemical shift data indicate that intramolecular hydrogen bonding favors the cis conformation.<sup>46</sup> These data suggest that in the case of a proton-donating ortho substituent the formyl oxygen prefers an orientation in close juxtaposition to the ortho group. A contribution to the oxygen nuclear screening variation due to hydrogen bonding can be an increase in the energy of a *n* → *π*\* electronic redistribution where the *n* orbital is stabilized by the hydrogen bond. A proton-donating group can hydrogen bond to the carbonyl oxygen lone pair, and the *n* → *π*\* transition now requires additional energy (relative to the nonhydrogen-bonded state) to rupture the hydrogen bond and thus greater energy overall to promote an *n* electron to the *π*\* orbital.

IR and NMR spectroscopic data qualitatively support the hypothesis that the strength of the hydrogen bond can be correlated with the observed trend in <sup>17</sup>O chemical shifts. In support of the contention that *o*-OHA forms a stronger intramolecular hydrogen bond than the *o*-NH<sub>2</sub> molecule, it was found that the carbonyl carbon in *o*-OHA resonated at -11.6 ppm from CS<sub>2</sub> and the *o*-NH<sub>2</sub>A resonance occurred at -7.5 ppm (increasing negativity corresponds to increased <sup>13</sup>C deshielding).<sup>23</sup> This 4-ppm downfield shift in *o*-OHA probably reflects a stronger intramolecular hydrogen bond. Preliminary data from this laboratory show that addition of water to any of the methoxy-substituted acetophenones results in downfield <sup>13</sup>C chemical shifts and the changes in the nuclear screening are dilution dependent. The O-H out-of-plane bending deformation also provides information concerning intramolecular hydrogen bonds. The IR measurements compiled by Nyquist<sup>47</sup> indicate that a stronger intramolecular hydrogen bond is present in *o*-OHA than in *o*-OHB and an energy difference of approximately 1 kcal/mol in favor of the ketone has been calculated by Koelle and Forsen.<sup>48</sup> Hydroxyl proton chemical shifts<sup>49</sup> and C=O stretching bands<sup>49</sup> also support the conclusion that the stronger hydrogen bond occurs in *o*-OHA in accord with the <sup>17</sup>O data.

**Line Widths.** The theory relevant to <sup>17</sup>O relaxation rates is discussed in a recent review article.<sup>22</sup> Carbonyl oxygen line widths may vary by more than 1 order of magnitude over the series of aryl aldehydes and ketones reported here. Although a detailed study of factors contributing to T<sub>1</sub> and T<sub>2</sub> relaxation in these systems will be presented in a subsequent communication, a brief discussion will be given here.

The substituted benzaldehyde has a characteristically sharper line than the analogous acetophenone. There are at least four possible explanations for this observation: (1) the rotational anisotropy of the aromatic aldehyde is modified by the substitution of the methyl group for the hydrogen atom with the net effect of increasing the rotational correlation times in the acetophenones; (2) there may be a contribution due to intramolecular rotation of the formyl or acetyl group to the relaxation; (3) a difference in quadrupolar coupling constants between the aryl ketones and aldehydes may account for the observed relaxation rate differences; and (4) differences in macroscopic solution viscosity may be important. Considering the nonsubstituted molecules, viscosity differences between benzaldehyde (1.39 cp) and acetophenone (1.62 cp) at 298 K cannot fully account for the observed line width differences.<sup>50</sup> Conclusions drawn from available <sup>17</sup>O NQR data are that coupling constants in the systems studied here probably do not vary by more than ±4% and thus (3) is quantitatively inadequate.<sup>26</sup> IR experiments show that the energy of activation for internal rotation is large and therefore internal rotations probably do not contribute to the effective correlation times.<sup>34</sup> We conclude from this short discussion that the differences in relaxation rates between the aldehydes and ketones are at least partially due to changes in the rotational diffusion tensor components and bulk viscosity effects.

### Conclusion

This work demonstrates that the <sup>17</sup>O nuclear screening at an acyl substitution reflects the electron-donating and -withdrawing properties of the ring substituent quite well. The <sup>17</sup>O chemical shifts are consistent with and complementary to a wide range of spectroscopic data, and the potential of <sup>17</sup>O NMR for monitoring electronic effects in conjugated *π* systems is significant. In addition, the fact that the <sup>17</sup>O nuclear screening response to hydrogen bonding is specific and large in magnitude suggests that this method may be extremely important in studies of solvent-solute interactions in studies of biological molecules. In particular we note that the application of <sup>17</sup>O NMR to problems of peptide conformation in solution clearly has a role in future studies.

Finally, we note that the interpretation given here is in general agreement with a recent NQR study of organic carbonyl compounds.<sup>26</sup> The carbonyl *π* bond character is important in determining <sup>17</sup>O quadrupolar coupling constants, asymmetry parameters, and nuclear screening constants, and a combination of both <sup>17</sup>O NMR and NQR data over a given series of molecules should lead to a highly satisfactory characterization of the carbon-oxygen bond in various electronic environments. Although our analysis showed that at least for the para-substituted acetophenones,  $\Delta E^{-1}_{n \rightarrow \pi^*}$  makes a significant contribution to the nuclear screening, more extensive theoretical studies are required to distinguish contributions from the three variable factors in  $\sigma^P$ . Molecular orbital calculations for several substituted acetophenones<sup>51</sup> indicate that there is a general qualitative agreement between our results and the calculated oxygen spin densities.

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(46) Smith, W. B.; Deavenport, D. L.; Ihrig, A. M. *J. Am. Chem. Soc.* **1972**, *94*, 1959.

(47) Nyquist, R. A. *Spectrochim. Acta* **1964**, *19*, 1655.

(48) Koelle, U.; Forsen, S. *Acta Chem. Scand., Ser. A* **1974**, *A28*, 531.

(49) Porte, A. L.; Gutowski, H. S.; Hunsberger, I. M. *J. Am. Chem. Soc.* **1960**, *82*, 5057.

(50) Weast, R. C., Ed. "Handbook of Chemistry and Physics"; CRC Press: Cleveland, Ohio, 1971.

(51) Rieger, P. H.; Fraenkel, G. K. *J. Chem. Phys.* **1962**, *37*, 2811.