¹³C N.M.R. STUDIES

PART III.¹ CARBON-13 N.M.R. SPECTRA OF SUBSTITUTED ACETOPHENONES²

K. S. Dhami³ and J. B. Stothers

Department of Chemistry, University of Western Ontario, London, Ontario Received September 24, 1964

ABSTRACT

The 15.1 Mc/s ¹³C n.m.r. spectra of 55 substituted acetophenones have been examined and the chemical shifts of the various carbon nuclei determined. This series included a variety of monosubstituted cases (ortho, meta, and para) as well as several polysubstituted examples. The factors contributing to the observed shieldings of all carbon nuclei are considered. The aromatic shieldings are compared with previous results for other aromatic derivatives. The application of the carbonyl shifts to the study of steric inhibition of resonance in these derivatives is examined critically. The shieldings of the acetyl methyl and para-carbon nuclei are found to offer confirmatory evidence for the existence of steric hindrance to coplanarity of the acetyl group in several ortho-substituted cases.

INTRODUCTION

Earlier papers in this series have presented the data and our interpretations of the carbon-13 nuclear magnetic resonance (n.m.r.) signals of carbonyl groups in a wide variety of organic carbonyl compounds (1) and some ortho-substituted acetophenones (2). To investigate some of the features noted in these studies in more detail, a series of 55 substituted acetophenones has been examined by ¹³C n.m.r. spectroscopy at 15.1 Mc/s. Examples of a number of monosubstituted derivatives (ortho, meta, and para) as well as several polysubstituted compounds having at least one ortho-substituent have been included. Chemical shift values for all carbon nuclei in these compounds have been obtained except for a few cases in which the upper solubility limit was insufficient to obtain a satisfactory signal: noise ratio to allow measurements in the aromatic region. Analyses of the aromatic portions of the spectra were accomplished by intercomparisons of the variously substituted derivatives and by assuming an additive relation for the substituent effects on the aromatic nuclei on the basis of the careful studies by Lauterbur (3a-e). The resonances of the alkyl carbons were readily identified by comparisons of the observed positions with those observed for the simpler benzenoid hydrocarbons or monosubstituted benzene derivatives. The assignment of the carbonyl peaks, of course, is the easiest of all and presents no difficulty (1).

The results of this study afford a further test of the additivity of substituent effects on aromatic shieldings, first noted by Lauterbur (3b). Since the series includes 36 compounds with at least one ortho-grouping, the variations in the spectral parameters with increasing steric hindrance are easily followed and potential application of ¹³C n.m.r. techniques to the study of hindered systems is clearly indicated. In particular, an extensive test is possible for our proposed method (2) of estimating angles of twist between the planes of the aromatic ring and the carbonyl group based on the variation of the carbonyl carbon resonance position with ortho-substitution. Variations of the acetyl methyl and paracarbon shieldings also follow the trends expected for sterically hindered systems on the basis of the most probable changes in the π -electron distributions with increasing steric

¹Part I, ref. 1. Part II, ref. 2.

²These results were reported in part at the 46th Annual Conference of the Chemical Institute of Canada, Toronto, June, 1963.

³Petroleum Research Fund Predoctoral Fellow, 1962-1964.

Canadian Journal of Chemistry. Volume 43 (1965)

480

CANADIAN JOURNAL OF CHEMISTRY, VOL. 43, 1965

interference of the acetyl grouping. Further evidence for the effects of hydrogen bonding by both intra- and inter-molecular mechanisms are presented and, since the latter may involve the solvent, some results of more detailed studies of solvent effects are given to support our arguments, although a fuller discussion of these is deferred for a later publication. The spectral data for a few alkylbenzenes were required to provide estimates of the shielding properties of the ethyl, isopropyl, and *t*-butyl groups and are reported in full for the first time, although their spectra have been published (4).

EXPERIMENTAL

All spectra were obtained at 15.085 Mc/s using compounds containing carbon-13 in natural abundance. In most cases, the reference was either external CH_3I (enriched to 58% ^{13}C) or CS_2 contained in a 5 mm outside diameter tube inserted in the larger 15 mm sample tube, although in a few instances CS_2 was used as both solvent and internal reference. The spectra were calibrated by the generation of audio side bands of the reference signal on the spectrum so that peak positions could be measure by interpolation (5). The output of the audio oscillator was continuously monitored with a Hewlett Packard 522B counter. A minimum of eight separate spectra were measured in each case. The position of the CS_2 resonance signal was assigned as the origin of the chemical shift scale and no corrections for bulk susceptibility differences were included. The data are judged to be accurate to within ± 0.5 p.p.m. Other details of the experimental procedure have been reported (3a). Where possible the spectra were obtained on the neat liquids, otherwise solutions in appropriate solvents were used as noted in the text and tables. These conditions were employed to produce a maximum signal:noise ratio and sufficient model studies have been carried out to show that solvent effects, although not always negligible, are of secondary importance for any of the comparisons discussed herein.

In a few cases, double irradiation experiments were performed to assist in the spectral analysis. In these experiments, the protons coupled to the carbon nuclei under examination were irradiated at their resonance frequency near 60 Mc/s to reduce the carbon signals to singlets by heteronuclear spin-decoupling. The technique has been reviewed (6) and a detailed description of the procedure has been given (7). In the present case, a NMR Specialties, Inc. Model SD-60 decoupler was employed.

Typical traces are illustrated in Fig. 1 to show the general features of the 15.085 Mc/s carbon-13 spectra obtained.

Materials

Nuclear Magnetic Resonance Spectra

Acetophenone was a B.D.H. Ltd. product and the following substituted acetophenones were obtained from the Aldrich Chemical Company, Inc.: 2-hydroxy, 4-hydroxy, 2,4-dihydroxy, 2,6-dihydroxy, 2,4,6-trihydroxy, 4-methoxy, 2,4-dimethoxy, 2,4,5-trimethyl, 2,6-dimethyl-4-*t*-butyl, 4-bromo, 2,4-dichloro, 2-nitro, and 2-amino. The 3-nitro- and 4-nitro-acetophenones were Eastman-Kodak products. A sample of 2,5-di-*t*butylacetophenone was kindly supplied by Professor L. R. C. Barclay. The rest of the materials examined in this investigation are known compounds, with one exception, and all were prepared by established procedures. In each case, infrared and proton spectra were obtained to check their purity. Their physical properties and the syntheses employed are outlined in Table I together with the previously reported physical constants. All melting points were determined on a Kofler hot stage and are uncorrected. For the most part, the liquids were purified by distillation through an 18 in. Nester-Faust platinum-plated spinning band column and the refractive indices were determined on a Bausch and Lomb refractometer. The microanalysis of 2,6-diisopropylacetophenone was performed by Alfred Bernhardt and Associates, Mulheim, Germany.

DISCUSSION

To facilitate the discussion and to emphasize their similarities the results for the metaand para-substituted acetophenones are discussed together, while the ortho-substituted compounds are considered in a separate section. To permit an easier intercomparison of the figures for the various compounds, each type of carbon nucleus is discussed under a separate subheading. Finally, considerations of the application of the ¹³C n.m.r. technique to the study of sterically hindered ketones are described in the last section.

meta- and para-Substituted Acetophenones

(a) Aromatic Carbons

The shieldings observed for the aromatic carbons in acetophenone itself may be compared with those reported previously by Spiesecke and Schneider (35) and which are



F1G. 1. Spectra at 15.085 Mc/s for *p*-methoxyacetophenone (field direction as shown) direction of sweep is from left to right for these examples. (*a*) Normal spectrum with the assignments indicated; (*b*) ¹³C spectrum with simultaneous irradiation of ¹H nuclei at their respective resonance frequencies.

Can. J. Chem. Downloaded from www.nrcresearchpress.com by Scientific Library of Lomonosov Moscow State Univ.on 11/20/13 For personal use only.

included in Table II in parentheses. The agreement is within experimental error and it may be noted that the earlier data were measured using a concentric spherical cell arrangement which eliminates bulk susceptibility differences. Part of the difference between the two sets of data may be due to this factor. While these authors have unequivocally established the assignments for acetophenone by deuterium labelling, the method used for assigning specific bands in the spectra of the substituted compounds requires some explanation. The problem is twofold, (i) the bands which form portions of multiplets must be distinguished from the singlet peaks and all chemical shifts measured and (ii) the observed shifts must be assigned to specific carbon nuclei. For the first distinction, the problem is simplified by virtue of the fact that, in general, only direct ¹³C—¹H spin couplings are resolved in the spectra obtained under these experimental conditions. Thus, bands due to the aromatic nuclei bearing substituents appear as singlets, while the unsubstituted carbons give rise to doublets having coupling constants in the range, 161 ± 3 c/s.³ A further aid for selecting the components of a multiplet within a spectrum is given by the relative intensities of the bands, since the multiplets are generally skewed owing to magnetization transfer (36) so that the first peak of a doublet, for example, is more intense than the second. A scan in the opposite direction gives the reverse behavior, while

³No specific coupling constants have been included in the tables, since all were within the expected range and the present experimental method does not allow their measurement to better than ± 3 c/s.

482

CANADIAN JOURNAL OF CHEMISTRY, VOL. 43, 1965

TABLE I

Physical data for the substituted acetophenones prepared for this study

			Physica	l constants		
	Mathod	Obs	erved	Rep	ported	
Substituent	of preparation	b.p./mm (m.p.)	$n_{\rm D}$ (t^0)	b.p./mm (m.p.)	$n_{\rm D} (t^0)$	Ref.
4-CH ₃	A	94/7	1.5343 (20)	60/3	1.5328 (22)	8
$4-C_2H_5$	A	82 - 84/0.5	1.5280(22)	125/20	1.5298(20)	9
$4-(CH_{3})_{2}CH$	A	89 - 91 / 0.6	1.5222(23)	68 - 72 / 0.8	1.5211(25)	10
4-(CH ₃) ₃ C	А	98 - 99 / 1.4	1.5195(25)	97 - 98 / 0.9	<u> </u>	11
4-CH₃O	A	(3839)		(38 - 39)	<u> </u>	12
4-Cl	А	103 - 104/10	1.5551(20)	138–139/15 83/4	1.5558(20)	8
4-(CH ₃) ₂ N	B1	(104–105)		(105.5) 108-110/12		13
3-CH ₂	С	73 - 74/2.9	1.5296(25)	116 - 117/26	1.5300(23.5)	14
3-CH ₃ O	$\bar{B}2$	99/4	1.5415(20)	141/23	1.5371(23)	14
3-Cl	D	88-89/4	1.5478(26)	88/4	1.5494(23)	8
3-Br	Ď	90/11	1.5740(26.5)	135 - 136 / 26	1.5755(21)	14
3-0H	Đ	(94 - 95)	<u> </u>	(95)		15
2-CH	Ĉ	51-53/1	1.5305(25)	70/4	1.5310(20)	8
2-C ₂ H ₅	Ĕŧ	117 - 120/30	1.5215(26)	99 - 103 / 13	1.5222(25)	$1\tilde{6}$
2-(CH ₃) ₂ CH	E1	77-78/3.3	1.5150(25.5)	72 - 73/2	1.5225(20)	17
2-C ₄ H ₅	F	103 - 104/0.9	1.6110(20)	104 - 105/1	,	18
2-CH ₃ O	B2	131 - 132 / 18	1.5380(23.5)	131 - 132 / 18	1.5383(23.5)	19
2-C ₂ H ₅ O	B2	77-78/0.5		(43)		20
2-Cl	G	107/14		75/4	1.5147(23)	8
2-Br	č	71 - 72/0.8	1.5669(25)	80 - 84/2	1.5683(19.5)	8
2-I	Ğ	135 - 139/5 - 6	1.6145(24)	144/15	1.6180 (20)	21a
	17.1	70 51 /1 1	1 5910 (05)	$\frac{112}{4}$	1 2004	21b
$2,3-(CH_3)_2$	EI	(0-(1/1))	1.5310 (25)	108/13	1.5334	9
$2,4-(CH_3)_2$	A	117-118/24 119/17	1.5325 (25)	122-123/27	1.5319 (24)	22
$2,5-(CH_3)_2$	A	113/17	1.5137 (25)	52/0.1	1.5290(22)	22
$2,4-(CH_{3}O)_{2}$	A	(40)		120-101/9		23
$2,5-(CH_{3}O)_{2}$	А	122 - 124/1	1.5405(26)	155 - 159 / 15		23
$2.6 - (CH_3)_2$	E1	110 - 112/23	1.5160(22)	111 - 112/23	1,5162(20)	24
$2,4,6-(CH_3)_3$	А	100 - 102/7	1.5137(25)	100 - 102/7	1.5155(20)	25
2,3,4,6-(CH ₃) ₄	А	91 - 93/1	1.5245(22)	74/0.3	1.5248(21)	26
2,3,5,6-(CH ₃) ₄	А	(74 - 75)	` ´ ´	(75)		27
2,3,4,5,6-(CH ₃) ₅	А	(85-86)	_	(87)		27
$2,6-(C_2H_5)_2$	E1	85-86/4	1.5105(26)	$\frac{86}{4}$	1.5110(21)	28
2,6-(<i>i</i> -C ₃ H ₇) ₂ *	E1	81 - 82/0.8	<u> </u>			
		(49-50)		(0 7 * 00)		00
$2,4,6-(i-C_3H_7)_3$	A	(86-87)		(87.5-88)		29
$2,6-(CH_{3}O)_{2}$	E2	(70-71)	—	118 - 120/11.5		30
a a O		110-111/1.1		(11)		0.1
2,6-Cl ₂	1-1	73/1 (41-49)	_	(44)		31
246-Br.	F2	(90-91)		(92)	_	32
2.0H-6.CH.0	B3	(57-58)	_	(60)		33
2-011-0-C1130	00	(01-00)		(00)		00

*Found for the ketone: C, 82.17; H, 9.90. Calcd. for C₁₄H₃₀O: C, 82.35; H, 9.80. Methods employed: (A) acetylation via Friedel-Crafts reaction with CH₄COCl, RH \rightarrow RCOCH₃ (28); (B1) methylation using CH₃/N₃:CO₃, Ar-NH₂ \rightarrow Ar-N(CH₃)₂ (13); (B2) methylation using (CH₃):SO₄/NaOH \rightarrow ArOCH₃ (19); (B3) methylation using (CH₃):SO₄/NaOH \rightarrow ArOCH₃ (19); (C) Grigmard reaction of CH₃MgI on the nitrile, ArCN \rightarrow ArCOCH₃ (34); (C) Grigmard reaction of CH₃MgI on the nitrile, ArCN \rightarrow ArCOCH₃ (9); (D) reaction of HX with a diazonium salt, ArN₂ \rightarrow ArX (8); (E1) reaction from the aniline, ArNH₂ \rightarrow ArBT $\stackrel{1.Mg}{\rightarrow}$ ArCOOH \longrightarrow ArCOCI $\xrightarrow{}$ ArCOCH₃ (25); (E2) reaction from the acid, ArCOOH \longrightarrow ArCOCI $\xrightarrow{}$ ArCOCH₃ (35); (F) from o-aminobiphenyl (18); (G) via reaction of the ortho-substituted benzoyl chloride with diethyl malonate (21b); (H) from the aldehyde, ArCHO \rightarrow ArCH(OH)CH₃ \rightarrow ArCOCH₃ (32).

:

the singlet peaks are unaffected. Since the intensity of a band is directly proportional to the number of contributing nuclei, measurements of relative intensities offer an additional aid. In each case, the carbonyl peak serves as a reference, representing one carbon nucleus. Many of the general features of a typical 15.085 Mc/s ¹³C spectrum are illustrated in Fig. 1a for p-methoxyacetophenone. Finally, confirmation of which particular bands constitute multiplets may be gained by heteronuclear spin-decoupling experiments to eliminate the effects of spin coupling with protons in the observed carbon spectrum. A typical result is shown in Fig. 1b. Thus, the observed chemical shifts for the various nuclei may be determined.

	Acetyl	group		Aromati	c nuclei		
Substituent	C=0	CH3	C-1	C-2,6	C-3,5	C-4	Others
H	-3.2	167.9	56.2 (55.7)*	64.4 (64.8)*	64.4 (64.8)*	61.2 (60.8)*	
Me	-3.2	166.9	`59.1 ´	64.3	64.3	49.8t	171.6
Et	3.2	167.3	59.6	64.9	64.9	43.9	164.6
							177.9
<i>i</i> -Pr	-3.4	167.4	57.4	64.7	66.4	38.8t	159.0
							169.9
t-Bu	-2.4	167.1	59.5	65.2	68.31	37.8	158.3
							162.4
OMet	-2.9	167.3	63.0	62.7	79.5	29.7	137.9
Cl	-3.0	168.0	58.2	63.7	63.7	54.6	
Brt	-3.8	166.3	58.1	62.0	62.0	66.2	
NÓ₀†	-3.3	165.9	51.71	63.5	68.7	42.4	
N(Me) ₂ t	-2.6	167.5	67.7	62.6	82.71	39.8	153.5
OH8	-4.6	167 7	62 9	61 6	77 3	30 7+	

TABLE H 13 C n.m.r. data for some para-substituted acetophenones (p.p.m.from CS₂)

*Values given by Spiesecke and Schneider (35). †(Calcd. – obsd.) more than 1.3 p.p.m. (see text). ‡Saturated solution in CHCl₂. §Saturated solution in 1,4-dioxane.

Can. J. Chem. Downloaded from www.nrcresearchpress.com by Scientific Library of Lomonosov Moscow State Univ on 11/20/13 For personal use only.

The assignment of particular shieldings to specific nuclei within the molecule is based primarily on the previous results of extensive investigations of several aromatic series. Lauterbur (3a-e) has been the principal contributor to this field and was the first to point out the apparent additivity of substituent effects on aromatic carbon shieldings (3b). His studies of several polysubstituted benzenes show that the combined effects of a methyl group with other methyls (3a), methoxyl (3b), iodo (3c), amino and dimethylamino (3d), and nitro groups (3e) are additive to a high degree of precision (ca. ± 1 p.p.m.) provided the substituents are not ortho with respect to each other. (It may be noted that the aromatic carbons for these various series absorb over a total range of almost 70 p.p.m.) More recently, Savitsky (37) has shown that comparable results are obtained for some para-disubstituted benzenes, p-X-C₆H₄-X, where X = F, Cl, Br, and Ac, and with somewhat less precision (ca. 2 p.p.m. maximum deviation) for some para-substituted anisoles, p-Y-C₆H₄OMe, where Y = Br, Cl, CHO. Comparable results were obtained from an extensive survey of the spectra of 40 substituted anisoles (38), the full details of which will be published in due course.

Assuming that an additive relation holds for the meta- and para-substituted acetophenones, we have assigned the observed shifts as shown in Tables II and III utilizing the substituent effects which are available for the appropriate monosubstituted benzenes

CANADIAN JOURNAL OF CHEMISTRY, VOL. 43, 1965

	Acety	group			Aromati	ic nuclei			
Substituent	C=0	CH₃	C-1	C-2	C-3	C-4	C-5	C-6	Others
Н	-3.2	167.9	56.2	64.4	64.4	61.2	64.4	64.4	
Me	-2.7	167.7	55.9	65.5	55.9	60.3	65.5	68.3	172.3
OMe	-3.3	167.3	55.1	81.1*	34.0	74.0*	64.1	74.0	138.5
Cl	-2.6	167.0	54.8	63.7	58.7	60.3	63.7	66.0	
Br	-2.6	166.7	55.0	62.9*	71.2	57.3	62.9	66.0	_
NO2†	-2.8			—					
OH‡	-4.9	—- §	(53.9)	(78.6)	(35.1)	<u> </u>	(62.6)	(72.9)	

TABLE III

¹³C chemical shifts for some meta-substituted acetophenones (in p.p.m.from CS₂)

*(Calcd. — obsd.) more than 1.3 p.p.m. (see text). †Saturated solution in CHCl3, but too dilute to obtain aromatic chemical shifts. ‡Saturated solution in 1,4-dioxane, but too dilute to measure aromatic shifts precisely.

\$Absorption lost in solvent signals.

(3b, 35). For the effects of the acetyl group, we have employed values obtained by averaging the present results and those reported by Spiesecke and Schneider (35). Since the necessary shielding data for the alkylbenzenes, $R-C_6H_5$ where R = Et, *i*-Pr and *t*-Bu, were not available, although their spectra have been published (4), these spectra were determined and the figures appear in Table IV. For the most part, the deviations between the calculated and observed shifts are less than ± 1.3 p.p.m. and those cases for which the differences are larger are indicated in the tables. It may be that a part of these discrepancies arises from the fact that our observed shieldings are not corrected for bulk susceptibility differences. In general, however, it appears that the combined substituent effects on the aromatic carbon nuclei for the meta- and para-substituted acetophenones are additive to a reasonable approximation. Some typical results for this comparison are shown in Fig. 2 in which the difference between the calculated and observed shifts is given beside the various aromatic nuclei.





\$

Can. J. Chem. Downloaded from www.nrcresearchpress.com by Scientific Library of Lomonosov Moscow State Univ on 11/20/13 For personal use only.

ne e gegener de la charac

		Aromat	ic nuclei		
Substituent	C—X	ortho	meta	para	Others
H Et*	$\begin{array}{c} 65.0 \\ 48.9 \end{array}$	65.0 (67.7	$65.0 \\ 63.4)$	65.0 67.3	164.8
<i>i</i> -Pr*	45.2	67.6	65.7	67.6	177.7 159.8 169.5
t-Bu*	42.8	68.3	65.3	68.3	$158.1 \\ 162.1$

TABLE IV ¹³C chemical shifts of monosubstituted benzenes (in p.p.m. from CS₂)

*The reader is referred to ref. 4 for typical spectra of these compounds.

(b) Carbonyl Carbons

The assignment of the carbonyl peak in these spectra is straightforward in all cases since it appears as a clear single band at the lowest field position. The most striking feature of the carbonyl carbon resonance positions for the meta- and para-substituted acetophenones is the apparent lack of sensitivity toward the variety of polar substituent groups examined. All carbonyl peaks fall in the range, -3.2 ± 0.6 p.p.m., with the exception of the two hydroxy derivatives at -4.6 and -4.9 p.p.m. which constitute separate cases and are discussed in conjunction with their corresponding ortho-derivatives in a later section. While the present series is more extensive, our earlier reports (1, 2) have noted the absence of substituent effects on the carbonyl resonance position and this feature has been discussed in detail (2). Although it is conceivable that solvent effects may mask a weak substituent effect, the influence of the substituent on the carbonyl shielding must be very small since the observed difference between the p-NO₂ and p-NMe₂ derivatives is only 0.7 p.p.m. (both in CHCl₃). An indication that chloroform tends to lower the carbonyl shielding relative to that in a less polar medium has been given for acetophenone (1) and, as a further example, we find the carbonyl peak for the p-NMe₂ derivative at 0.8 p.p.m. higher field in benzene solution relative to chloroform solution. Thus, it is clear that our original observation of no pronounced substituent effect holds.

(c) Acetyl Methyl Carbons

In all of these spectra a quartet appears centered at 167 ± 1.0 p.p.m. with a coupling constant of 127 ± 2 c/s (the highest field multiplet in Fig. 1*a*, for example) and for most cases an unambiguous assignment of this multiplet to the acetyl methyl carbon nucleus can be made directly. Since the compounds bearing polar groups exhibit no large changes in the resonance position for the acetyl methyl quartet, it follows that its shielding is also unaffected by alkyl groups in the meta- and para-positions. In the case of alkylated derivatives with other bands in this region, the acetyl methyl resonance was assigned to correspond with the other cases. The increased shielding of the acetyl methyl carbon in conjugated ketones by ca. 4 p.p.m. relative to saturated analogues has been noted and discussed (1). It is possible that the total range of these shifts listed in Tables II and III is increased somewhat by a small effect of the chloroform solvent relative to the pure liquids but this effect would not appear to exceed ca. 1 p.p.m. (see Table VII, ref. 1).

(d) Other Carbons

The observed shieldings and coupling constants for the various nuclei in the substituent groupings are found to be in close agreement with the data obtained for the corresponding

monosubstituted benzenes. The figures in Table II for the ethyl, isopropyl, and *t*-butyl groups may be compared with those in Table IV while the results for the different types of methyl carbons agree closely with those given by Lauterbur for toluene, 171.8 (3*a*), anisole, 138.4 (3*b*), and N,N-dimethylaniline, 152.6 p.p.m. (3*d*). The observed coupling constants for these various carbons were OCH₃, 147 \pm 2; N—CH₃, 134 \pm 2; C—CH₃, C—CH₂—C, and C—CH—, 127 \pm 2 c/s, in close agreement with other results (3*a*-*e*).



FIG. 3. Deviations between observed and calculated shielding data for aromatic carbon nuclei in some ortho-substituted acetophenones.

ortho-Substituted Acetophenones

(a) Aromatic Carbons

Following the procedure outlined above for the meta- and para-substituted cases, the assignments of the observed spectral bands to the various aromatic carbons in the ortho derivatives have been made as listed in Tables V and VI. As Lauterbur has established for several other examples, the additivity of the indirect effects of substituents on the ring carbons appears to break down with ortho substitution. In the present series of monosubstituted acetophenones the differences between the observed and calculated shifts are appreciably larger, on the average, than those discussed for the meta- and paraderivatives. In addition these differences appear to increase with increasing size of the group ortho to acetyl, clearly suggesting the existence of steric interference between substituent groups. To indicate the magnitude of these differences, some examples are shown in Fig. 3 together with a few more highly substituted compounds. While the larger deviations from the calculated values tend to introduce a greater uncertainty in the specific assignments, intercomparison of the data for the monosubstituted derivatives with those for the more highly substituted cases provide some support for our assignments. Examination of ortho-derivatives labelled with deuterium would, of course, allow unequivocal assignments but this has not been done. The assignments for the symmetrically substituted cases (i.e., 2,6-disubstituted) are unambiguous.

Four of the examples, having similarly positioned substituents, display particularly striking deviations of the observed chemical shifts from those calculated by the additivity relation. These are 2,3-dimethyl-, 2,3,4,6-tetramethyl-, 2,3,5,6-tetramethyl-, and 2,3,4,5,6-pentamethylacetophenone, each of which has three or more contiguous, substituted

aromatic carbons. It can be seen that for each of these compounds, at least one of the aromatic nuclei bearing a methyl group absorbs at considerably higher field than the less highly methylated compounds. For the four examples, these signals appear at 58.5, 59.9, 64.8, and 65.1 p.p.m., respectively. The last two figures are virtually the same as that of benzene itself although the effect of a methyl group is usually ca. -9 p.p.m. Lauterbur has noted this remarkable change in durene and hexamethylbenzene (3a). While this particular case is perhaps an extreme example, it serves to illustrate the complexity of the problem which must be solved before a rational explanation of the origins of these substituent effects can be offered.

Apart from the changes in chemical shift for the para-carbon (C-4), the observed trends are difficult to interpret on the basis of present knowledge and further discussion does not seem warranted. A detailed discussion of the para-carbon shieldings is included in the section on steric inhibition of conjugation below.

TABLE V ¹³C chemical shifts for substituted acetophenones bearing one ortho-substituent (in p.p.m. from CS₂)

	Acety	group			Aromat	ic nuclei			
Substituent(s)	C=0	CH ₃	C-1	C-2	C-3	C-4	C-5	C-6	Others
2-CH ₃ 2-C ₂ H ₅	-6.5 -6.9	$164.2 \\ 164.3$	56.1 57.0	$56.1 \\ 49.8$	64.0	$\frac{62.4}{62.5}$	67.7 68.7	$\begin{array}{c} 62.4 \\ 62.5 \end{array}$	172.5 166.5
2- <i>i</i> -C ₃ H ₇	-8.0	164.3	55.1	46.6	68.1	63.0	68.1	66.3	$164.4 \\ 170.0$
$\begin{array}{c} 2\text{-}C_{6}\text{H}_{5} \\ 2\text{-}C\text{H}_{3}\text{O} \\ 2\text{-}C_{2}\text{H}_{5}\text{O}^{*} \\ 2\text{-}Cl \\ 2\text{-}Br \\ 2\text{-}I^{*} \\ 2\text{-}NO_{2} \\ 2\text{-}OH \\ 2\text{-}OH \\ 2\text{-}3\text{-}(CH_{3})_{2} \end{array}$	$\begin{array}{r} -9.6 \\ -5.0 \\ -5.9 \\ -6.5 \\ -8.0 \\ -5.5 \\ -11.6 \\ -7.5 \\ -7.8 \end{array}$	$\begin{array}{c} 163.0\\ 161.8\\ 160.9\\ 163.3\\ 163.1\\ 163.8\\ 164.4\\ 167.1\\ 165.7\\ 163.7 \end{array}$	$\begin{array}{c} 65.1\\ 64.5\\ 55.7\\ 52.6\\ 47.4\\ 57.1\\ 73.6\\ 75.3\\ 53.4 \end{array}$	$\begin{array}{r} 34.3\\ 34.3\\ 61.2\\ 70.5\\ 102.2\\ 47.8\\ 31.0\\ 42.7\\ 58.5 \end{array}$	$\begin{array}{c} 81.4\\ 80.2\\ 66.3\\ 61.0\\ 54.4\\ 70.0\\ 74.2\\ 77.8\\ 55.8\end{array}$	$59.7 \\ 59.2 \\ 62.6 \\ 61.0 \\ 61.1 \\ 62.7 \\ 57.0 \\ 59.2 \\ 61.2$	$\begin{array}{c} 73.1 \\ 72.7 \\ 66.3 \\ 65.1 \\ 64.5 \\ 59.5 \\ 74.2 \\ 75.7 \\ 68.6 \end{array}$	$\begin{array}{c} 63.2\\ 62.2\\ 66.3\\ 65.1\\ 64.5\\ 66.2\\ 62.8\\ 61.1\\ 68.6 \end{array}$	138.2 — — — — 173.0 177.2
$2,4-(CH_3)_2$	-5.8	164.9	52.0	58.7	63.1 64.2	55.2	67.6	63.1	$173.0 \\ 173.0 \\ 172.8 $
2,3-(CH ₃) ₂ 2,4,5-(CH ₃) ₃ 2,5-(<i>t</i> -C ₄ H ₉) ₂ †	-5.5 -15.3	$164.7 \\ 161.6$	59.6	57.9	61.8	53.9	57.9	60.2	172.8 172.8 174.5 157.5
$2,4-(CH_3O)_2^*$	-2.8	161.8	72.7	32.3	95.7	29.2	88.0	61.3	161.6 137.9 127.0
2,5-(CH ₃ O) ₂ *	-4.5	162.2	65.3	40.1	79.9	74.1	40.1	79.9	137.9 138.3 138.3
2,4-Cl ₂ 2,4-(OH) ₂ ‡	$-3.9 \\ -10.1$	$\frac{162.9}{168.9}$	$\begin{array}{c} 60.8 \\ 78.6 \end{array}$	$56.8 \\ 27.4$	$\begin{array}{c} 63.1 \\ 89.0 \end{array}$	$56.8 \\ 27.4$	$\begin{array}{c} 66.1 \\ 83.9 \end{array}$	$\begin{array}{c} 63.1 \\ 58.6 \end{array}$	

Can. J. Chem. Downloaded from www.nrcresearchpress.com by Scientific Library of Lomonosov Moscow State Univ on 11/20/13 For personal use only.

*Saturated solution in CHCl₂, †In CHCl₂ solution. ‡Saturated solution in 1,4-dioxane.

(b) Carbonyl Carbons

The striking feature of the carbonyl shieldings for the ortho-substituted acetophenones is the wide range over which these peaks absorb, -2.8 to -15.3 p.p.m., in direct contrast to the results for the meta- and para-derivatives. The values listed in Tables V and VI serve to extend the number of examples included in our previous report (2) in which a detailed discussion of the earlier observations was presented. The application of these

487

	Acetyl	groups			Aromat	ic nuclei			
Substituents	C==0	CH3	C-1	C-2	C-3	C-4	C-5	C-6	Others
2,6-(CH ₃) ₂ 2,4,6-(CH ₃) ₃ 2,3,4,6-(CH ₃) ₄	-12.9 -13.4 -13.5	162.0 161.7 161.0	$50.8 \\ 53.1 \\ 57.9$	$61.0 \\ 60.8 \\ 59.9$	$65.6 \\ 64.4 \\ 52.3$	$65.6 \\ 55.4 \\ 52.3$	$\begin{array}{r} 65.6\\64.4\end{array}$	$61.0 \\ 60.8 \\ 59.9$	$174.8 \\ 174.0 \\ 173.6(2) \\ 162.2 \\ 1$
2,3,5,6-(CH ₃) ₄ *	-14.2	159.4	48.3	64.8	58.6	60.8	58.6	64.8	169.3 176.0(2) 172.1(2)
$2,3,4,5,6-(CH_3)_5*$	-14.1	158.1	50.4	65.1	59.2	59.2	59.2	65.1	174.4
$(t-C_4H_9)^*$	-13.3	160.0	52.1	60.5	67.0	41.6	67.0	60.5	158.2 174 7
$2,6-(C_2H_5)_2$	-13.0	161.5	51,1	54.8	67.2	64.4	67.2	54.8	167.1
2,6-(<i>i</i> -C ₃ H ₇) ₂ *	-13.5	160.8	51.3	49.5	69.3	63.3	69.3	49.5	177.4 158.5 166.8
2,4,6-(<i>i</i> -C ₃ H ₇) ₃ †	-13.8	160.8	53.7	49.8	72.4	43.9	72.4	49.8	$159.6 \\ 168.9$
2,6-(CH ₃ O) ₂ * 2,6-Cl ₂ †	-6.8 - 5.2	$\begin{array}{c}161.2\\162.6\end{array}$	$\begin{array}{c}51.3\\53.1\end{array}$	$\begin{array}{c} 36.2\\ 63.4\\ \end{array}$	$\begin{array}{c} 88.4 \\ 64.5 \end{array}$	$\begin{array}{c} 61.4\\ 62.7\\ \end{array}$	$88.4 \\ 64.5$	$\begin{array}{c} 36.2\\ 63.4 \end{array}$	137.3
2,4,6-Br3‡ 2,6-(OH)2† 2-OH-6-CH3O‡	$-7.2 \\ -12.0 \\ -11.9$	$162.4 \\ 160.6 \\ 159.3$	$50.5 \\ 84.5 \\ 81.8$	$74.0 \\ 31.1 \\ 28.5$	$58.5 \\ 86.0 \\ 82.6$		$58.5 \\ 86.0 \\ 91.6$	$74.0 \\ 31.1 \\ 31.7$	 137.3
2,4,6-(OH) ₃ †	-10.4	160.4	88.5	27.4	98.0	27.4	98.0	27.4	_

TABLE VI

¹³C chemical shifts for substituted acetophenones bearing two ortho-substituents (in p.p.m. from CS₂)

*Saturated solution in CS2. †Saturated solution in 1,4-dioxane. ‡Saturated solution in CHCl3.

Can. J. Chem. Downloaded from www.nrcresearchpress.com by Scientific Library of Lomonosov Moscow State Univ on 11/20/13 For personal use only.

carbonyl results to the estimation of the extent of steric inhibition of conjugation in these hindered systems is illustrated in the final section of this paper.

Further comments, however, regarding the different media employed are in order. Since it was impossible to obtain all of the spectra using the neat liquid, solutions in various solvents were required for examination. Since preliminary solvent studies had indicated that data obtained in either dioxane or carbon disulfide solution are in close agreement with the neat liquid values (1), these were the solvents employed, if possible. In the case of the former, recent work has confirmed our conclusion (39). To examine the effect of chloroform, which was employed in a few cases to obtain concentrations sufficient for detection of the spectra, on the carbonyl carbon resonance position, some compounds were measured in different solvents. These figures in Table VII indicate clearly that, although there is a small but definite deshielding of the carbonyl carbon, the effect of chloroform as a solvent is much smaller than the changes caused by orthosubstitution. It seems likely that the effect of chloroform is due to hydrogen bonding of the carbonyl oxygen and the proton of the solvent.

(c) Acetyl Methyl Carbons

The shieldings of the acetyl methyl carbons in the ortho-substituted acetophenones follow trends similar to those exhibited by the carbonyl carbon nuclei as the results in Tables V and VI show. The resonance position of these nuclei moves to lower field, relative to that of acetophenone, as the bulk and (or) number of the ortho-substituents increases such that this carbon absorbs over the range, 159.3–168.9 p.p.m. The variation of these shifts roughly follows that of the carbonyl carbon for this series of ortho-substituted compounds. The trend is illustrated in Fig. 4, for a number of the alkyl-substituted

		Solvents					
Substitution	CHC13	$C_4H_8O_2^*$	CS2	Other			
Nil	-4.5	-3.1		$-2.9(C_6H_6)$			
$4 - N(CH_3)_2$	-2.6			$-1.8(C_6H_6)$			
2,6-Čl ₂	-6.0	-5.2		(• •,			
$2,6-(CH_{3}O)_{2}$	-7.8		-6.8				
$2_{1}6 - (C_{2}H_{5})_{2}$	-14.0	-13.2	13.1	$-12.2(C_6H_6)$			
$2,4,6-(i-C_3H_7)_3$	-15.1	-13.8					
$2_{16} - (CH_{3})_{2} - 4 - (t - C_{4}H_{9})$	-13.3		-12.3				
2,3,5,6-(CH ₃) ₄	-15.3		-14.2				
2,3,4,5,6-(CH ₃) ₅	-15.7		-14.1				

TABLE VII ¹³C carbonyl shieldings of various acetophenones in different solvents (p.p.m. from CS₂)

acetophenones examined. The apparent slope of this plot indicates that the shielding of the acetyl methyl carbon is somewhat less sensitive to the influence of the ortho-grouping than the carbonyl carbon shielding. The possible significance of the variation of the acetyl methyl chemical shift with the nature of the ortho-group is discussed in a later section.



 F_{1G} . 4. Plot of observed resonance positions of carbonyl carbon nuclei vs. those of the acetyl methyl carbon nuclei for a number of ortho-alkylated acetophenones.

(d) Other Carbons

The observed chemical shifts for the methoxyl carbon nuclei are in the range, 137.8 \pm 0.5 p.p.m. in agreement with the data for the meta- and para-derivatives above and with the results reported by Lauterbur previously (3b). Apparently there is no effect of

ortho-substitution on these shieldings. A more extensive study of the spectra of substituted anisoles has shown that substitution at both positions ortho to the methoxyl group is required to change its shielding from the typical value near 138 p.p.m. (38).

In the case of the alkyl substituent groups, however, the chemical shifts of the carbons bonded directly to the aromatic ring and flanked by one or more ortho-groups show small but significant differences from those in the corresponding meta- and para-substituted compounds. In general, the effect of ortho-substitution is one of shielding at these α -carbons. Intercomparisons of the figures in Tables V and VI with those in Tables II, III, and IV show that this effect on primary carbon is ca. 1 p.p.m., on secondary carbon, ca. 2 p.p.m., and on tertiary carbon ca. 4 p.p.m. for methyl, ethyl, and isopropyl groups, respectively. In the last two cases, the β -carbons do not appear to be affected. For the more highly substituted compounds, the data indicate that this trend is accentuated in compounds bearing three substituents on contiguous aromatic carbons (i.e., 1,2,3trisubstitution). For example, for 2,3-dimethylacetophenone, the two aromatic methyl carbons appear at 177.2 and 173.0 p.p.m., the first of which may be assigned to the 2-methyl carbon flanked by two substituents. Similar shifts were found for acetyldurene (2,3,5,6-tetramethylacetophenone).

Hydroxy-Substituted Acetophenones

A number of derivatives bearing hydroxyl groups have been included in this series and the results obtained differ somewhat from those found for the other examples. One would expect that hydrogen bonding involving the hydroxyl proton and the carbonyl oxygen is probably responsible for these differences. In the monosubstituted cases, the orthohydroxyl group is seen to lower the carbonyl shift substantially (by ca. 7 p.p.m.) relative to the meta- and para-derivatives, while the acetyl methyl shielding is unaffected. Presumably the slightly lower carbonyl peak position in the meta- and para-derivatives relative to acetophenone is due to electron-withdrawing intermolecular hydrogen bonding while much more effective intramolecular interaction occurs in the ortho-case. The carbonyl carbon absorbs at significantly lower field for the ortho-amino derivative relative to acetophenone. Although the appropriate model compounds $(3-NH_2)$ and $4-NH_2$) were not examined, it is reasonable that the intramolecular hydrogen bonding of the type, N-H-O=C, is responsible, at least in part, for the observed shift. In those compounds bearing two ortho-hydroxyl groups, the acetyl methyl shielding is reduced indicating steric interference between the acetyl methyl and the second substituent. The carbonyl resonance position is little affected by the second ortho-hydroxyl grouping. It does seem reasonable that hydrogen bonding between a carbonyl group and an ortho-hydroxyl would not be seriously affected if the carbonyl group was hindered from attaining coplanarity with the ring provided it was not twisted too far from this plane. For reasons that are presented in detail below, we would suggest that the second hydroxyl group does not cause a severe twist of the carbonyl group away from the aromatic ring plane although there is little doubt that these two groups are not coplanar. While both inter- and intramolecular H bonding will contribute to the shift of the carbonyl carbon nucleus in these cases, it is not possible to show with the present evidence the extent of the contribution of the former factor for the ortho-substituted cases. Studies of the dilution effect on these shifts are required but these present a practical difficulty due to the low sensitivity of the present technique.

Steric Inhibition of Conjugation

In the preceding section, some spectral features pointing to the existence of steric interference between substituent groupings in the compounds having ortho-substitution

490

have been mentioned. A number of these observations suggested the possibility of a semiquantitative approach to the estimation of the extent of steric inhibition of conjugation in these derivatives. In the preceding part of this series (2), a method has been proposed which is alternative to, and possesses certain advantages over, the more usual means of predicting angles of twist between the carbonyl group and the aromatic ring. With the results for a larger number of derivatives now in hand, a critical assessment of this proposed method may be undertaken.

We have already demonstrated the variation of the carbonyl carbon shielding with the size of the ortho-grouping, as estimated by van der Waal's radii or covalent radii (see Fig. 2, ref. 2) and the additional data in Tables V and VI offer further support for this relation. The rationale of the arguments leading to the conclusion that the carbonyl resonance position reflects the degree of steric interference in these ketones has been given and need not be reiterated. Secondary and confirmatory evidence for these ideas derived from other observed trends in these spectra was not presented in detail previously, however, and requires further amplification.

The deviations from additivity of substituent effects on the aromatic carbon shieldings in the ortho-substituted acetophenones were noted above and the difficulty of presenting a clear evaluation of all of these differences was mentioned. One possible exception, however, is the variation of the para-carbon (i.e. C-4) chemical shifts with changes in the substituent group. There are two reasons which suggest that a rational interpretation of these shieldings is possible. First, Spiesecke and Schneider (35) have demonstrated that there is a good correlation of the para-carbon shifts with the Hammett σ_P parameter for a number of monosubstituted benzenes. This result indicates that these ¹³C shifts reflect the π -electron density distribution at this position and Lauterbur has confirmed this conclusion by comparing the calculated π -electron densities with the para-carbon shifts for several examples (3a-e, 40). Secondly, the effect of various substituents at the metacarbon in monosubstituted benzenes is small, less than 1 p.p.m. for the substituents included in our series with the exception of the halogens and hydroxyl. These two facts suggest that the shielding of the para-carbon in the acetophenones will reflect variations in the extent of electron withdrawal at this position by the acetyl group, which would be caused by steric hindrance to co-planarity of the carbonyl group and the aromatic ring. In acetophenone, the para-carbon absorbs ca. 4 p.p.m. toward lower field from the resonance position of pure benzene and it is reasonable that this low field shift is primarily due to conjugative electron withdrawal by acetyl from the para-position. Thus, any factor hindering this conjugation would be expected to reduce the effect of the acetyl group at the para-carbon which would mean an increased shielding and, therefore, a shift to a value closer to that of pure benzene.

Can. J. Chem. Downloaded from www.nrcresearchpress.com by Scientific Library of Lomonosov Moscow State Univ on 11/20/13 For personal use only.

An examination of the data for the para-carbon nuclei, however, does not necessarily support this proposal unless the effects of the other substituents are taken into account. To allow an easier comparison, the pertinent shielding data are collected in Tables VIII and IX and the "corrected" figures, allowing for the effects of the other substituents, are included. In general, the para-carbon shifts move to higher field with increasing size and (or) number of ortho-groups, in agreement with expectations. Probably the most reliable data are those for the mono- and 2,6-di-substituted compounds, since the "corrections" for the substituents in these positions are relatively small. Because of the breakdown of the additivity relation for ortho-substituted derivatives, the significance of the "corrections" used for the examples having groups at the 3-, 4-, and 5-positions is questionable. As an example, the corrected figures for tetramethyl- and pentamethyl-acetophenone do not agree well with those for less highly substituted examples. It is interesting that this

CANADIAN JOURNAL OF CHEMISTRY. VOL. 43, 1965

TABLE VIII

¹³C chemical shifts of certain nuclei in some ortho-alkyl acetophenones (p.p.m. from CS₂)

	C-4		CH ₃ C==0	C==	00
Substituent(s)	Obsd.	Corr.	Obsd.	Obsd.	Corr.
H 2-CH ₃ 2,3-(CH ₃) ₂ 2,4-(CH ₃) ₂ 2,5-(CH ₃) ₂ 2,4,5-(CH ₃) ₃ 2,6-(CH ₃) ₂ 2,4,6-(CH ₃) ₂ 2,4,6-(CH ₃) ₂ 2,6-(CH ₃) ₂ 2,6-(CH ₃) ₂ 2,6-(CH ₃) ₄ 2,3,4,6-(CH ₃) ₄ 2,3,4,6-(CH ₃) ₄ 2,3,4,5,6-(CH ₃) ₄ 2,3,4,5,6-(CH ₃) ₄ 2,3,4,5,6-(CH ₃) ₄ 2,6-(C ₂ H ₅) ₂ 2- <i>i</i> -C ₃ H ₇ 2,6-(<i>i</i> -C ₃ H ₇) ₂ [*] 2,6-(<i>i</i> -C ₄ H ₇) ₃ [†] 2,5-(<i>i</i> -C ₄ H ₇) ₃ [†]	$\begin{array}{c} 61.2\\ 62.4\\ 61.2\\ 55.2\\ 64.2\\ 53.9\\ 65.6\\ 55.6\\ 52.3\\ 60.8\\ 50.4\\ 62.5\\ 64.4\\ 63.0\\ 63.3\\ 43.9\\ \hline \end{array}$	$\begin{array}{c} 61.2\\ 62.7\\ 61.8\\ 64.6\\ 64.8\\ 63.6\\ 65.0\\ 64.4\\ 62.3\\ 62.0\\ 60.7\\ 62.6\\ 64.6\\ 62.7\\ 62.7\\ 63.2 \end{array}$	$\begin{array}{c} 167.9\\ 164.2\\ 163.7\\ 164.9\\ 164.4\\ 164.7\\ 162.0\\ 161.7\\ 160.0\\ 161.0\\ 159.4\\ 158.1\\ 164.3\\ 161.5\\ 164.3\\ 160.8\\ 160.8\\ 160.8\\ 161.6\end{array}$	$\begin{array}{r} -3.2 \\ -6.5 \\ -7.8 \\ -5.8 \\ -5.7 \\ -5.5 \\ -12.9 \\ -13.4 \\ -13.3 \\ -13.5 \\ -14.2 \\ -14.1 \\ -6.9 \\ -13.0 \\ -8.0 \\ -13.5 \\ -13.8 \\ -15.3 \end{array}$	$\begin{array}{r} -3.2\\ -7.5\\ -8.8\\ -6.7\\ -6.5\\ -14.9\\ -15.4\\ -15.3\\ -15.5\\ -16.2\\ -16.1\\ -7.9\\ -15.0\\ -9.0\\ -15.5\\ -15.8\end{array}$
2-C ₆ H ₅			163.0	-9.6	

*Saturated solution in CS2. †Saturated solution in 1,4-dioxane. ‡In CHCl3.

TABLE IX

¹³C chemical shifts of specific nuclei in some ortho-substituted acetophenones (in p.p.m. from CS₂)

	C	-4	CH₃C==0	C=	=0
Substituent(s)	Obsd.	Corr.	Obsd.	Obsd.	Corr.
H 2-CH ₃ O 2-C ₂ H ₅ O* 2,4-(CH ₃ O) ₂ * 2,5-(CH ₃ O) ₂ * 2,6-(CH ₃ O) ₂ † 2-Cl 2,4-Cl ₂ 2,6-Cl ₂ ‡ 2-Br 2,4,6-Br ₃ * 2-I*	$\begin{array}{c} 61.2\\ 59.7\\ 59.2\\ 29.2\\ 74.1\\ 61.4\\ 62.6\\ 56.8\\ 62.7\\ 61.0\\ 69.2\\ 61.1 \end{array}$	$\begin{array}{c} 61.2\\ 60.0\\ 60.3\\ 60.3\\ 63.2\\ 63.6\\ 64.2\\ 64.2\\ 64.7\\ 63.2\\ 67.2\\ 67.2\\ 63.7\end{array}$	$\begin{array}{c} 167.9\\ 161.8\\ 160.9\\ 161.8\\ 162.2\\ 161.2\\ 163.3\\ 162.9\\ 162.6\\ 163.1\\ 162.4\\ 163.8 \end{array}$	$\begin{array}{r} -3.2 \\ -5.0 \\ -5.9 \\ -2.8 \\ -4.5 \\ -6.8 \\ -5.9 \\ -3.9 \\ -5.2 \\ -6.5 \\ -7.2 \\ -8.0 \end{array}$	$\begin{array}{r} -3.2 \\ -9.8 \\ -10.7 \\ -7.6 \\ -9.3 \\ -11.6 \\ -7.1 \\ -5.1 \\ -7.6 \\ -5.8 \\ -5.8 \\ -5.8 \end{array}$
2-NO2	62.7	63.5	164.4	-5.5	-6.4

*Saturated solution in CHCla. †Saturated solution in CS2. ‡Saturated solution in 1,4-dioxane.

analysis of the data for the 2-methoxyl derivatives indicates no steric interference between the acetyl and methoxyl groups, but there is an indication of crowding for the 2,6-dimethoxyl case. Another feature is that the "corrected" para-carbon shielding is similar for each of the three mono-halo derivatives (Cl, Br, I), but the "corrections" for two of these cases are relatively large (i.e., 2.2 p.p.m. for Br, 2.6 p.p.m. for I) and these could be in error, although there is no obvious way to check this point. A further disadvantage to the use of the para-carbon shifts for estimating the extent of steric hindrance in these systems is the relatively small range of 4 p.p.m. over which one can expect to observe

492

changes. This consideration of para-carbon shieldings, however, does show that the general trends are consistent with those expected for steric inhibition of conjugation and that the observed shifts might be used to support evidence from other spectral features.

The observed shifts for the acetyl methyl carbons have been included in Tables VIII and IX to show more clearly the regular reduction in shielding with increasing bulk and number of ortho-groups mentioned above (see Fig. 4). While this trend to lower field is qualitatively reasonable, the maximum change observed is larger than expected, if the extent of conjugation of the carbonyl group with the aromatic ring were the dominant factor, indicating that longer range substituent effects contribute to these shieldings as well. Approximate estimates of the ring anisotropic effects indicate a maximum difference of 0.2 p.p.m. between the planar and perpendicular orientation of an acetyl methyl carbon with the ring, following the method of Johnson and Bovey (41) and, of course, this change is in the opposite direction to that observed.

Qualitatively, however, the observed variation of the acetyl methyl shieldings appears to indicate the extent of steric interference of the ortho-substituents with the acetyl group. In contrast to the para-carbon shieldings, these data indicate appreciable steric hindrance by *one* ortho-methoxyl group which is only slightly increased by the introduction of a second ortho-methoxyl.

While a full discussion of the probable significance of the carbonyl shieldings has been presented (2), further evidence in support of these ideas is given by the data in Tables VIII and IX for 30 examples and which are completely consistent with our original interpretation. The empirical expression, $\cos^2 \theta = (\delta_C^{x} + 23.2)/20$ (where θ is the angle of twist for the acetophenone bearing the X substituent and δ_C^{x} is its ¹³C carbonyl chemical shift), which was developed previously, permits one to estimate the dihedral angle between the planes of the carbonyl group and the aromatic ring and the calculated angles for the examples included in this study are given in Table X.

		θ			θ
Substituent(s)	-	Corr.	Substituent(s)		Corr.
2-СН3	24	28	2-C ₆ H ₅	34	
$2.3 - (CH_3)_2$	29	32			
$2, 4 - (CH_3)_2$	21	25	2-CH₃O	17	35
$2.5 - (CH_3)_2$	21	25	$2-C_2H_5O$	22	38
$2.4.5 \cdot (CH_3)_3$	20	24	$2.4-(CH_{3}O)_{2}$	0	28
			$2,5-(CH_{3}O)_{2}$	15	34
$2.6-(CH_3)_2$	44	50			
$2,4,6-(CH_3)_3$	46	51	$2,6-(CH_{3}O)_{2}$	25	40
$2.6 - (CH_3)_2 - 4 - (t - C_4H_9)$	45	51			
2.3.4.6-(CH ₃) ₄	46	52	2-C1	22	26
$3.5.6 - (CH_3)_4$	48	54	2,4-Cl ₂	11	18
2.3.4.5.6-(CH ₃) ₅	48	53			
, , , , , , , , , , , , , , , , , , , ,			2,6-Cl ₃	18	28
2-C ₉ H ₅	25	29			
			2-Br	24	21
$2.6 - (C_2 H_5)_2$	44	50	U		
, - (2,4,6-Br ₃	27	21
$2-i-C_3H_7$	29	33			
· · • •			2-I	29	
$2.6 - (i - C_3 H_7)_2$	46	52	11		
$2.4.6 - (i - C_3 H_7)_3$	47	53	2-NO2	20	24
$2.5 - (t - C_4 H_9)$	51				
			n		

TABLE X

Estimated angles o	f twist, θ,	for some orth	10-substituted	l acetophenones	(in e	degrees)
--------------------	-------------	---------------	----------------	-----------------	-------	----------

CANADIAN JOURNAL OF CHEMISTRY. VOL. 43, 1965

On the basis of Lauterbur's results for several aromatic series, there seems little doubt that closely neighboring groups can exert certain "ortho" effects on the shielding of the carbonyl nuclei which are independent of, and simultaneously operative with, any effects whose origins are steric in nature. The cause or causes of this mysterious effect are obscure. Although the most popular interpretation attributes these "ortho" effects to neighboranisotropy phenomena, it appears unlikely that this is the sole, or even the most important, factor for all cases. The problem has been discussed for particular cases, e.g. I (3c). The estimation of the magnitude of the non-steric "ortho" effect presents a difficult problem but, as a first approximation, we have examined the possibility of using estimates based on the data for various substituted toluenes (42, 43). At first, this approach seemed a reasonable one since the variation of the ¹³C methyl shift with polar substitution is very small for meta- and para-substituted toluenes but there are significant changes from these in the ortho-derivatives. We assumed that this change is primarily due to a non-steric "ortho" effect of uncertain origin. By taking the difference between the observed methyl carbon shift for an ortho-substituted toluene and the averaged methyl shift for the corresponding meta- and para-substituted toluenes, we calculated "correction" factors for the various substituents. Applying these factors to the observed carbonyl carbon shielding data, we obtained "corrected" shielding values which are listed in the last column of Tables VIII and IX. Because of the unavailability of the required ethyl-, isopropyl-, and t-butyltoluenes, the "correction" factor for methyl carbons, found from the xylene data, were used for the first two cases since both can adopt conformations which would tend to minimize steric interactions and which would be approximately similar to those for methyl substitution. A factor for the *t*-butyl group, however, is more difficult to estimate and we hesitate to hazard a guess as to its magnitude. For the same reasons, "correction" factors for the ortho-phenyl and iodine nuclei have been omitted. For the tables, the following "correction" factors were employed: CH₃, -1 p.p.m., Cl, -1.2 p.p.m., Br, +0.7 p.p.m., NO₂, -0.9 p.p.m., and CH₃O, -4.8 p.p.m. Two immediate surprises in these figures appear to be the value for the methoxyl group and the opposite signs of the factors for chlorine and bromine. Substitution of the "corrected" carbonyl shieldings in the expression given above yielded the angles of twist, θ , listed in Table X and termed "corr." For most cases, the "corrected" angles are only slightly different from the original values. These estimates seem to be satisfactory for the alkyl groups, but some of the results for the polar groups are dubious.

Support for the inclusion of the "correction" factor for methyl groups in the orthoposition(s) was noted in our earlier report, based on the results for substituted benzaldehydes. In the present series, the results give no reason to change this conclusion for the alkyl groups. No supporting evidence, however, can be put forward for the other substituents. In fact, in view of the apparent discrepancies in the results obtained using the "corrected" carbonyl data, it would seem more desirable to accept the uncorrected figures as a better indication of the geometry of the molecules. Clearly more information on the nature of the indirect effects of these polar groups on the shielding of carbon nuclei is required to allow a full understanding of the present results. The main difficulty which must be overcome is by no means trivial and clear approaches to its resolution are difficult to suggest. This problem is the estimation of the contribution to the observed effect of that portion which is operative through space, the so-called field effect. The usual approach employed is an application of the point dipole model (44) to evaluate the so-called neighbor-anisotropy contribution (44, 45) due to the field induced circulation of electrons on the X atom. Several examples, however, are known for which inclusion of the neighboranisotropy effect is insufficient to rationalize the observed data, the case of iodine, for

Can. J. Chem. Downloaded from www.nrcresearchpress.com by Scientific Library of Lomonosov Moscow State Univ on 11/20/13 For personal use only.

494

495





Can. J. Chem. Downloaded from www.nrcresearchpress.com by Scientific Library of Lomonosov Moscow State Univ on 11/20/13 For personal use only.

example (3c). With the present state of knowledge, we would favor neglecting these "correction" factors until a more rational method for their estimation is suggested.

A weakness of this overall approach to θ values may appear to be the estimation of the shielding of the carbonyl carbon nucleus for the 90° case. To show that an estimated value of 17 p.p.m. for the conjugative shielding effect of the phenyl group is not extremely critical, we have plotted the variation of θ with $\delta_{\rm C}^{\rm X}$, the difference between the carbonyl shielding in acetophenone and that for an X-substituted compound, for other values of the phenyl conjugative effect, viz. 15 and 19 p.p.m. (see Fig. 5). Only for the highly hindered cases is there an appreciable change in θ , although < 8° at 50°. Hence, we feel that this weakness is not a strong objection to the proposed approach to estimates of angles of twist.

An examination of the data in Table X indicates that the estimates of θ based on the observed shieldings are in substantial agreement with simple stereochemical considerations. In general, these estimates tend to be somewhat smaller than those obtained from analyses of ultraviolet spectral data or dipole moments (22, 46), comparisons with which were given previously (2). Estimates of θ for the 2,4,6-trimethyl- and 2,3,5,6-tetramethyl-acetophenones have recently appeared derived from determinations of the Kerr constants (47) and are found to be 90° for each of these cases. Clearly, these values are greatly different from any of the previous estimates and seem to be much too large.

An additional example of the buttressing effect of a second methyl group has been found

CANADIAN JOURNAL OF CHEMISTRY. VOL. 43, 1965

(2.3-dimethylacetophenone) and the observed change in θ by ca. 4° is comparable to that found for acetyldurene. No additional hindrance appears to be associated with the introduction of a fifth methyl group in the latter case.

The order observed for the three ortho-haloacetophenones using the uncorrected data also is in agreement with that expected on steric grounds but, since the observed carbonyl ¹³C shielding may be strongly affected by an "ortho" effect of iodine (3c), the internal agreement of these estimates may be fortuitous. The results for the group of compounds bearing the methoxyl group in the ortho-position(s) may also be suspect. It was pointed out above that the other trends indicating steric interference in most of the cases (the acetyl methyl and para-carbon shieldings) are in direct contradiction and, in addition, the non-steric "ortho" effect of oxygen nuclei (from the toluene data) is appreciably larger than that for the other groupings examined. The estimates using the observed carbonyl data (i.e. uncorrected) appear reasonable with the exception of the 2,4-dimethoxyderivative, but the "corrected" values seem unduly large (note especially the $2,6-(CH_{3}O)_{2}$ case). At the present time, no clear explanation of these discrepancies can be offered apart from the suggestion that a smaller angle of twist might be expected for a compound bearing a para-methoxyl group due to conjugative electron release by oxygen. The slightly reduced θ in the alkylated examples having para-methyl groups may be ascribed to a similar electron release by the methyl group.

In general, the proposed method for the estimation of angles of twist in these carbonylcontaining systems yields reasonable and, most importantly, consistent results for the alkylated examples and for a number of other polar substituents. The approach possesses distinct advantages over the method based on the intensities of electronic transitions since the observed spectral band is characteristic of the ground state of the molecule. Furthermore, this transition can be assigned unambiguously and measured accurately. In addition, confirmatory evidence is provided by measurements of two other transitions in the spectrum. The results of an extension of our study of carbonyl compounds and a consideration of this approach for the estimation of steric hindrance in a series of alkyl phenyl ketones and the results of a detailed examination of several aliphatic conjugated carbonyl compounds will be reported shortly.

ACKNOWLEDGMENTS

We gratefully acknowledge the support of the Petroleum Research Fund, administered by the American Chemical Society, in the form of operating funds and the Ontario Research Foundation for a grant to purchase the 15.1 Mc/s rf unit. We also thank Professor L. R. C. Barclay for a sample of 2,5-di-t-butylacetophenone.

REFERENCES

- 1432 (1963).
 4. R. A. FRIEDEL and H. L. RETCOFSKY. J. Am. Chem. Soc. 85, 1300 (1963).
 5. J. T. ARNOLD and M. E. PACKARD. J. Chem. Phys. 19, 1608 (1951).
 6. J. D. BALDESCHWIELER and E. W. RANDALL. Chem. Rev. 63, 81 (1963).
 7. J. B. STOTHERS and J. R. ROBINSON. Can. J. Chem. 42, 967 (1964).
 8. W. F. FORBES and W. A. MUELLER. CAN. J. Chem. 35, 488 (1957).
 9. S. F. BIRCH, R. A. DEAN, F. A. FIDLER, and R. A. LOWRY. J. Am. Chem. Soc. 71, 1362 (1949).
 10. J. D. MATLOCK, S. N. CHINAI, R. A. GUZZI, and D. W. LEVI. J. Polymer Sci. 49, 533 (1961).
 11. J. W. BAKER. J. Chem. Soc. 445 (1938).
 12. E. H. MAN and C. R. HAUSER. J. Org. Chem. 17, 397 (1952).
 13. L. WELL. MONATSH. 29, 905 (1908).

- DHAMI AND STOTHERS: ¹⁹C N.M.R. STUDIES. PART III 497
 14. R. STEWART and K. YATES. J. Am. Chem. Soc. 80, 6355 (1958).
 15. H. RUPE and K. VON MAJEWSKI. Chem. Ber. 33, 3401 (1900).
 16. B. VAN ZANTEN and W. TH. NAUTA. Rec. Trav. Chim. 79, 1211 (1960).
 17. B. N. CAMPBELL and E. C. SPAETH. J. Am. Chem. Soc. 81, 5933 (1959).
 18. E. CAMPAIGNE and WM. B. REID. J. Am. Chem. Soc. 68, 1663 (1946).
 19. K. v. AUWERS, A. BOENNECKE, F. KROLLPFEIFFER, and G. PETERS. Ann. 408, 212 (1915).
 20. E. BESTHORN, E. BANZHAF, and G. JAEGLE. Chem. Ber. 27, 3035 (1894).
 21. (a) W. S. RAPSON and R. G. SHUTTLEWORTH. J. Chem. Soc. 487 (1941). (b) R. G. R. BACON and W. S. LINDSAY. J. Chem. Soc. 1382 (1958).
 22. E. A. BRAUDE and F. SONDHEIMER. J. Chem. Soc. 3754 (1955).
 23. E. R. SHEPARD, H. D. PORTER, J. F. NOTH, and C. K. SIMMANS. J. Org. Chem. 17, 568 (1952).
 24. L. H. SCHWARTZMAN and B. B. CORSON. J. Am. Chem. Soc. 74, 1829 (1954).
 25. W. M. SCHUBERT and H. K. LATOURETTE. J. Am. Chem. Soc. 74, 1829 (1952).
 26. E. A. BRAUDE, B. F. GOFTON, G. LOWE, and E. S. WAIGHT. J. Chem. Soc. 4054 (1956).
 27. W. F. FORBES and W. A. MUELLER. Can. J. Chem. 33, 1145 (1955).
 28. V. R. REMISCHNEIDER and B. DIEDRICH. Ann. 646, 18 (1961).
 29. R. C. FUSON, E. M. BOTTORFF, and S. B. SPECK. J. Am. Chem. Soc. 64, 1450 (1942).
 30. S. SUGASAWA. J. Chem. Soc. 1483 (1934).
 31. G. LOCK and E. BÖCK. Chem. Ber. 70, 916 (1937).
 32. R. C. FUSON, J. H. VAN CAMPEN, and D. E. WOLF. J. Am. Chem. Soc. 60, 2269 (1938).
 33. W. BAKER. J. Chem. Soc. 956 (1939).
 34. I. M. HUNSBERGER, D. LEDNICER, H. S. GUTOWSKY, D. L. BUNKER, and P. TAUSSIG. J. Am. Chem. Soc. 70, 72466 (1055).

- - 34. I. M. HUNSBERGER, D. LEDNICER, H. S. GUTOWSKY, D. L. BUNKER, and P. TAUSSIG. J. Am. Chem. Soc. 77, 2466 (1955).

 - Soc. 77, 2466 (1955).
 35. H. SPIESECKE and W. G. SCHNEIDER. J. Chem. Phys. 35, 731 (1961).
 36. P. C. LAUTERBUR. Nuclear magnetic resonance spectra of elements other than hydrogen and fluorine. In Determination of organic structures by physical methods. Edited by F. C. Nachod and W. D. Phillips. Academic Press. 1962. Chap. 7.
 37. G. B. SAVITSKY. J. Phys. Chem. 67, 2723 (1963).
 38. K. S. DHAMI and J. B. STOTHERS. Abstr. 47th Conference Chem. Inst. of Canada, Kingston. 1964. p. 60.
 39. G. E. MACIEL and G. C. RUBEN. J. Am. Chem. Soc. 85, 3903 (1963).
 40. P. C. LAUTERBUR. Tetrahedron Letters, No. 8, 274 (1961).
 41. C. E. JOHNSON and F. A. BOVEY. J. Chem. Phys. 29, 1012 (1958).
 42. P. C. LAUTERBUR. Ann. N.Y. Acad. Sci. 70, 841 (1958).
 43. K. S. DHAMI and J. B. STOTHERS. Unpublished observations.
 44. H. M. MCCONNELL. J. Chem. Phys. 27, 226 (1957).
 45. J. A. POPLE. Proc. Roy. Soc. London, Ser. A, 239, 550 (1957).
 46. W. F. FORBES. Can. J. Chem. 38, 1104 (1960).
 47. M. J. ARONEY, M. G. CORFIELD, and R. J. W. LEFEVRE. J. Chem. Soc. 648 (1964).

Can. J. Chem. Downloaded from www.nrcresearchpress.com by Scientific Library of Lomonosov Moscow State Univ on 11/20/13 For personal use only.

497