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The Proton Resonance Spectra of the Methoxybenzenes¹

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The proton magnetic resonance spectra of the methoxybenzenes have been obtained. The chemical shifts relative to tetramethylsilane (τ -values) were measured at equal molar concentrations. Hückel molecular orbital calculations were made on the methoxybenzenes with hetero atom parameters $\alpha_o = \alpha_c + 2\beta_{oc}$ and $\beta_{oo} = 0.8\beta_{oc}$. The ring proton shifts were found to be approximately proportional to the calculated charge densities on the attached ring-carbon sites. A least mean squares treatment of the chemical shifts of the 19 nonequivalent aromatic protons in the set of compounds suggests that a chemical shift of 9.95 p.p.m. per unit of π -electron density occurs.

Introduction

The chemical shift of the nuclear magnetic resonance absorption of aromatic protons has long been thought to be partially due to variation of charge density on the bonded ring carbon atom.² In the isoelectronic series $C_6H_5^-$, C_6H_6 , $C_7H_7^+$, where the π -electron densities are known because of the symmetry of the molecules, the relationship of charge density to chemical shift has been found to be good,³⁻⁵ and a proportionality constant, Q_H , of ~ 10 p.p.m./electron has been proposed⁴ for an expression in the form of eq. 1

$$\delta_H = Q_H \rho_C \quad (1)$$

where δ_H is the proton chemical shift in parts per million (p.p.m.) relative to a standard reference, and ρ_C is the calculated charge density on the bonded carbon. This equation is similar to that due to McConnell⁶ which relates the aromatic proton hyperfine coupling constant to the unpaired electron density, and is presumably due to the same type of configuration interaction of the C-H σ -bond with the π -system. However, there has been more uncertainty as to the reliability of eq. 1, and few tests of its accuracy.⁷ This has been due primarily to the early recognition of the contribution of the intramolecular ring current to the aromatic proton chemical shift.² Because the ring current contribution varies considerably in the catacondensed alternant aromatic hydrocarbon series and because the π -electron charge densities vary only slightly (not at all by Hückel calculations), it has not been possible to relate the chemical shifts to MO calculated charge densities in this series of molecules. Other effects on the proton chemical shifts also must be considered. The charge densities on neighboring but not directly bonded atoms is thought⁸ to influence the proton chemical shift. An intermolecular ring-current effect is also well recognized.⁹ This is essentially a solvent effect, however, and can be removed by extrapolating measurements to infinite dilution, or minimized by making all measurements at equal molar concentrations in the same solvent. The magnetic anisotropy of substituents frequently contributes significantly to the proton shifts,¹⁰ and finally, an electric field effect due to neighboring bond dipoles is also recognized as making an appreciable contribution.^{8,11}

(1) Part IV in a series on Cumulative Effects of Substituents on the π -System Properties of Aromatics. Part 111: A. Zweig, J. E. LehnSEN, W. G. Hodgson, and W. Jura, *J. Am. Chem. Soc.*, **85**, 3937 (1963).

(2) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959.

(3) J. R. Leto, F. A. Cotton, and J. S. Waugh, *Nature*, **180**, 978 (1957).

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(9) A. A. Bothner-by and R. E. Glick, *ibid.*, **26**, 1647 (1957).

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Nevertheless, eq. 1 remains attractive because it corresponds to the approximate additive effect which substituents have on the chemical shift of aromatic protons. Further testing of eq. 1 is therefore warranted to achieve a better understanding of the causes of aromatic proton shifts. To perform such tests, a set of compounds is needed where (a) the intramolecular ring current contribution to the chemical shifts can be regarded as nearly constant, (b) the π -electron charge densities on the ring positions should be calculable, (c) the charge densities vary enough so that the corresponding chemical shifts would be large compared to the inaccuracies of measurement, (d) the magnetic anisotropy of substituent groups is small enough to be neglected, and (e) the electric field effect is either small or capable of evaluation. Suitable compounds of this nature may be found in the sets of benzene derivatives with a single type of substituent.

Relatively few such sets are known where the entire 12 members are either available or readily prepared. This practical consideration is important since the complete set obviously enables one to obtain the maximum amount of experimental information with which to compare theoretical parameters. Unfortunately, most of the highly substituted members of the sets of such interesting benzene substituents as nitro, cyano, amino, mercapto, vinyl, etc., are not known. Other complete sets of substituted benzene derivatives that are available or known are the methylbenzenes and the halobenzenes, particularly the chlorobenzenes. In the methylbenzene set most of the n.m.r. spectra show only a single aromatic proton line, and when splitting due to nonequivalent ring protons is observed the total spread in the chemical shifts is very small, and the effects of substitution are not readily interpreted. Essentially the same thing is true with the chlorobenzenes, although somewhat larger splittings are observed with these compounds.² The methoxybenzenes, however, constitute a complete set of substituted benzenes with strong π -orbital interaction of ring and substituent. These compounds are all available and well characterized.¹² Their ring currents can be regarded as constant,² and there appears to be no appreciable contribution of the magnetic anisotropy of the methoxy group to proton chemical shifts.¹⁰ The electric field effect of the methoxy group on the chemical shift might be corrected for, since the moments of the dipoles involved are well established.¹³ The charge distribution in these compounds can be estimated readily by the Hückel LCAO approximation.¹⁴

Results

Nuclear Magnetic Resonance.—The proton magnetic resonance spectra of the methoxybenzenes were

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TABLE I
CHEMICAL SHIFTS (τ) OF AROMATIC PROTONS AND π -CHARGE DENSITIES AT THE ATTACHED RING SITES IN THE METHOXYBENZENES

Compound	Positions	No. in shifts, Fig. 1	Chemical shift, τ^a	π -charge density
Methoxybenzene	2, 6	1	3.26	1.040
	3, 5	2	2.80	0.998
	4	3	3.26 ^b	1.030
1,2-Dimethoxybenzene	3, 6	4	3.25	1.040
	4, 5	5	3.25	1.026
1,3-Dimethoxybenzene	2	6	3.72	1.082
	4, 6	7	3.61	1.068
	5	8	2.95	0.996
1,4-Dimethoxybenzene	2, 3, 5, 6	9	3.31	1.037
1,2,3-Trimethoxybenzene	4, 6	10	3.56	1.066
	5	11	3.18	1.024
1,2,4-Trimethoxybenzene	3	12	3.65	1.079
	5	13	3.78	1.066
	6	14	3.36	1.037
	6	14	3.36	1.037
1,3,5-Trimethoxybenzene	2, 4, 6	15	4.09	1.109
1,2,3,4-Tetramethoxybenzene	5, 6	16	3.58	1.064
1,2,3,5-Tetramethoxybenzene	4, 6	17	4.05	1.106
1,2,4,5-Tetramethoxybenzene	3, 6	18	3.57 ^c	1.078
Pentamethoxybenzene	6	19	3.83	1.104
Benzene		B	2.72	1.000

^a 5 moles/l. in CCl₄. ^b Estimated by comparison of *p*-deuterioanisole and undeuterated anisole. ^c Obtained at a concentration of 1.25 moles/l. in CCl₄.

TABLE II
CHEMICAL SHIFTS OF METHYL PROTONS AND π -CHARGE DENSITIES ON OXYGEN AND OXYGEN-ATTACHED RING SITES IN THE METHOXYBENZENES

Compound	Positions	Chemical shift, τ	Oxygen π -charge density	Oxygen-attached ring charge density
Methoxybenzene	1	6.26	1.940	0.954
1,2-Dimethoxybenzene	1, 2	6.23	1.944	.990
1,3-Dimethoxybenzene	1, 3	6.28	1.940	.954
1,4-Dimethoxybenzene	1, 4	6.32	1.943	.982
1,2,3-Trimethoxybenzene	1, 3	6.22	1.944	.990
	2	6.28	1.946	1.029
1,2,4-Trimethoxybenzene	1	6.32 ^a	1.946	1.017
	2	6.28 ^a	1.943	0.988
	4	6.24 ^a	1.943	.980
1,3,5-Trimethoxybenzene	1, 3, 5	6.30	1.940	.951
1,2,3,4-Tetramethoxybenzene	1, 4	6.22 ^a	1.946	1.016
	2, 3	6.26 ^a	1.946	1.028
1,2,3,5-Tetramethoxybenzene	1, 3	6.23	1.944	0.988
	2	6.36 ^a	1.948	1.056
	5	6.32 ^a	1.942	0.978
1,2,4,5-Tetramethoxybenzene	1, 2, 4, 5	6.27	1.946	1.016
	2, 4	6.30	1.950	1.054
Pentamethoxybenzene	1, 5	6.23	1.946	1.014
	3	6.18	1.946	1.026
Hexamethoxybenzene	1-6	6.21	1.949	1.051

^a Position assignments are tentative.

obtained on a standard Varian Model DP60 spectrometer at 56.4 Mc./sec. The compounds were measured at a concentration of 5 moles/l. in carbon tetrachloride containing a small amount of tetramethylsilane (TMS) as an internal standard. The chemical shifts relative to TMS were measured by the method of audio side-band modulation using a Hewlett-Packard frequency counter. Actual oscilloscope observation of a zero beat from the sideband peak and the peak being measured was used when feasible; for the complex aromatic proton patterns, interpolations using several sweeps were made with the side-band position set just above and below the

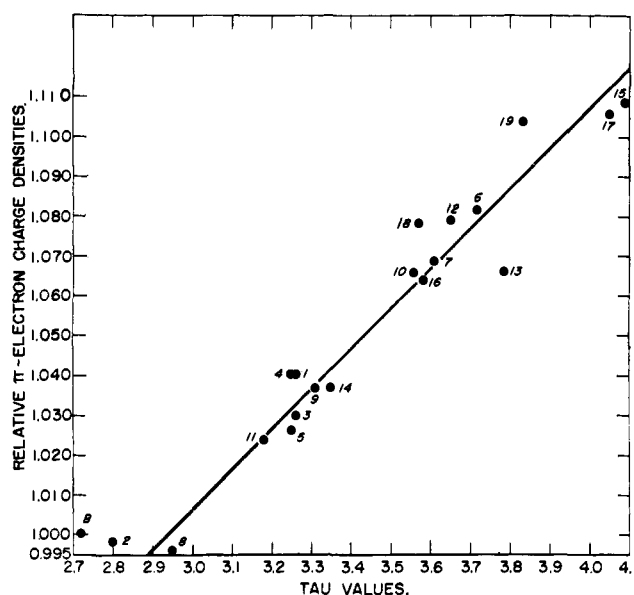


Fig. 1.—Plot of aromatic proton τ -values against calculated charge densities at attached ring positions in methoxybenzenes.

pattern. The chemical shifts are thus believed to be accurate to better than ± 0.01 p.p.m. Extrapolations to infinite dilution were made on several of the compounds, but no significant changes in the chemical shifts were observed.

The aromatic proton coupling patterns for all the methoxybenzenes except anisole were readily evaluated by standard treatment. The assignments were made on the basis of the known values of *o*-, *m*-, and *p*-proton coupling constants in aromatic molecules.² Evaluation of the *o*- and *m*-proton shifts in anisole was made with the aid of *p*-deuterioanisole, and the *p*-proton shift was then estimated. The eleven methoxybenzenes from anisole to pentamethoxybenzene contain 19 nonequivalent aromatic protons. Their chemical shifts related to TMS are reported in Table I, and extend from 2.80 to 4.09 τ . For comparison, the proton chemical shift of benzene at 5 moles/l. in carbon tetrachloride is 2.72 τ . In Table II are reported the methyl group τ -values for the 12 methoxybenzenes, measured under the same conditions. As can be seen, the chemical shifts here are all nearly the same, ranging over less than 0.2 τ unit.

Hückel Molecular Orbital Calculations.—The π -electron charge densities were calculated by the Hückel molecular orbital theory (without overlap). The π -system was regarded as being made up from atomic orbitals on the benzene ring carbon atoms and the oxygen atoms, with the carbon atoms contributing one electron and the oxygen atoms contributing two to the molecular orbitals. The C-O resonance integral (β_{co}) was taken as 0.8 of the C-C resonance integral (β_{cc}), and the oxygen coulomb integral (α_o) was taken as equal to $\alpha_c + 2\beta_{cc}$ as recommended by Streitwieser.¹⁴ The charge densities so obtained are reported in Table I (ring positions bearing protons), and in Table II (oxygen and oxygen bearing ring positions). These calculations do not take into account the diminution of β_{co} due to steric inhibition of resonance in five of the methoxybenzenes.¹² It is known, however,¹⁴ that such changes of the resonance integral have a relatively small effect on the eigenvectors.

Discussion

A plot of the 19 aromatic proton chemical shifts of the methoxybenzenes against the calculated charge densities on the adjacent ring positions is made in Fig. 1. The least mean squares equation, with the error as-

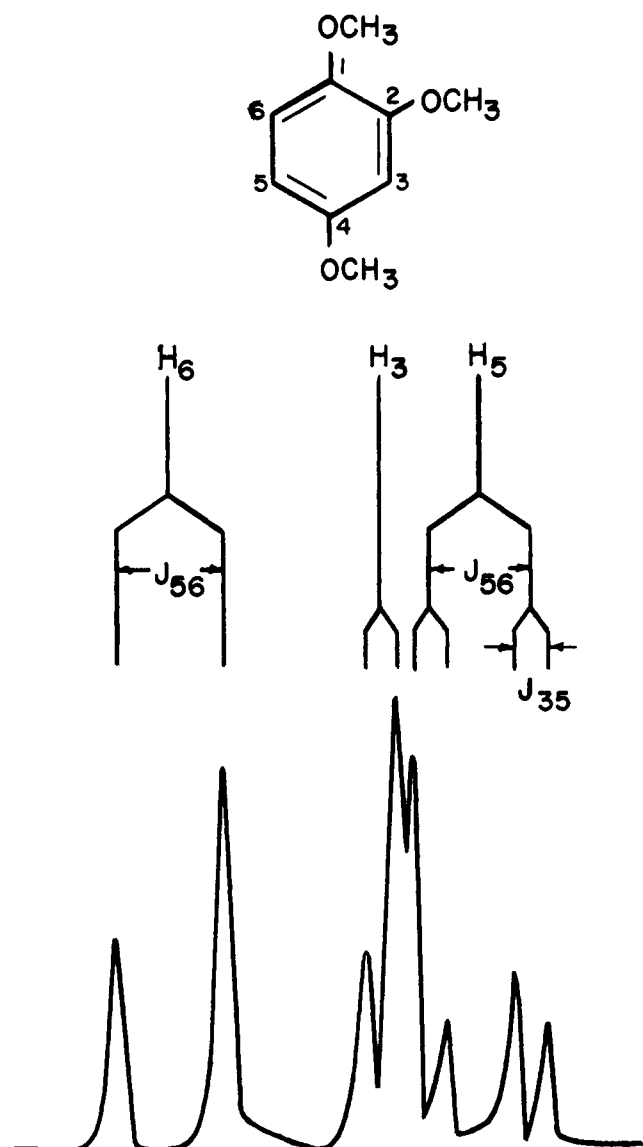


Fig. 2.—Proton spectrum of 1,2,4-trimethoxybenzene schematically indicating the assignments of the aromatic protons.

sumed to be all in the chemical shifts, is chemical shift (τ -values) = $9.95 \times \text{charge density} - 7.02$. The average deviation is $\pm 0.07 \tau$ unit.

This generally good agreement is achieved without a correction for the electric field effect of the methoxy groups. An approximate correction for this effect at the aromatic protons can be made by adding an approximation of the effects of individual dipoles.⁸ The effect of the dipoles on the aromatic proton chemical shift ($\Delta\sigma$) is dependent on the electric field of the dipole (E), and on the field component along the C-H bond (E_z), according to a relationship (eq. 2) derived by Buckingham.¹⁵

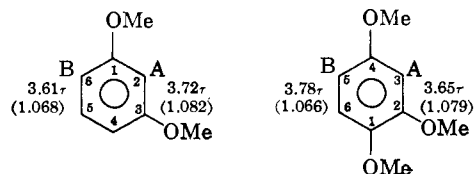
$$\Delta\sigma = -2 \times 10^{-12} E_z - 10^{-8} E^2 \quad (2)$$

Additive correction terms for the electric field effect of methoxy groups *ortho*, *meta*, and *para* to the aromatic ring positions were examined. Dipole field values could not be found which would improve the correlation when all 19 different aromatic protons were considered. This point will be amplified by a comparison of 1,3-dimethoxybenzene and 1,2,4-trimethoxybenzene (*vide infra*). If the aromatic proton chemical shifts are cor-

(15) A. D. Buckingham, *Can. J. Chem.*, **38**, 300 (1960).

rected for the effect of charge density on the two ring carbons adjacent to the attached carbon, as suggested for hydroxybenzenes,⁸ the deviations from a correlation line greatly increase.

The aromatic proton chemical shifts of 1,2,4-trimethoxybenzene are worth special mention. In this molecule, the MO calculations suggested that H-A should be at higher field than H-B. This is also indicated by a comparison of 1,2,4-trimethoxybenzene with 1,3-dimethoxybenzene. Addition of a methoxy group



to the 4-position of 1,3-dimethoxybenzene would be expected to lower slightly the charge densities at the A- and B-positions (positions *meta* to the added group). If the electric dipole effect is simply considered as additive, then the added methoxy group should affect the A- and the B-positions equally, and the resulting shifts in these positions from the disubstituted compound should be proportional. The experimental results are seen to conform neither to the relationship which neglects the electric field entirely nor to the relationship which includes an additive correction for this effect. The proton at the B position in the trisubstituted compound is found to shift 0.17 p.p.m. to *higher* field, while the proton in the A position behaves "normally," and shifts 0.07 p.p.m. to *lower* field. The assignments of the aromatic proton chemical shifts in 1,2,4-trimethoxybenzene were made by a standard analysis of the spectrum based on the known *o*-, *m*-, and *p*-proton coupling constants (Fig. 2).¹⁶ The chemical shift assignments in 1,3-dimethoxybenzene were further confirmed by examination of 2-deuterio-1,3-dimethoxybenzene.

The equilibrium geometries of the various methoxy groups in relation to the benzene ring and to each other should be considered in making accurate corrections in both the MO calculations and the electric field, particularly in the more highly substituted compounds. Since these geometries are unknown, more meaningful corrections cannot be applied to this set. Still, it is not readily apparent why such a large change occurs only at the 5-position of 1,2,4-trimethoxybenzene. Since the MO calculations suggest that the *m*-position in anisole and H-5 in 1,3-dimethoxybenzene are very slightly electron deficient compared to benzene, the electric field effect may be partly responsible for the upfield shift from benzene of the protons at these positions.¹⁷

The relative methyl proton shifts reported in Table II are small but real, since all the nonequivalent methyl groups (as many as three) can be seen in these compounds. A relationship between these chemical shifts and the charge densities on oxygen cannot be made; however, the range of the shifts is small (~ 0.2 p.p.m.), as is the calculated charge densities on the oxygens (~ 0.01 electron).

Despite the many complications, the results reported here seem to reaffirm the underlying relationship expressed by eq. 1 and a proportionality constant of ~ 10 p.p.m. per electron, for aromatic ring protons.

(16) The spectrum was analyzed as the two independent AB spectra resulting from setting J_{35} and J_{56} equal to zero separately. As a check, the line positions and intensities were calculated using the complete ABC Hamiltonian, with excellent agreement. The coupling constants used were $J_{56} = 8.5$ c.p.s., $J_{35} = 2.6$ c.p.s., and $J_{36} = 0$.

(17) H. Spiesscke and W. G. Schneider, *J. Chem. Phys.*, **35**, 731 (1961).