Substituent Effects in the Benzofuran System. I. Proton and Carbon-13 Chemical Shifts

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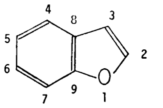
PMR and CMR spectra of benzofuran and its derivatives (2-CH_3, 3-CH_3, 5-CH_3, 6-CH_3, 5-CH_3O, 6-CH_3O, and 5-Cl) have been measured. The chemical shifts of 2-H and 2-C of 5- and 6-substituted derivatives obeyed a modified Hammett equation, $\delta = \rho_1\sigma_1 + \rho_2\sigma_2 + \delta_0$. Electronic effects were found to be transmitted mainly through the bond 8—3. It was concluded that the ground-state electronic structure is similar to that of styrene rather than phenyl vinyl ether.

A great number of reaction rates and ground-state properties of benzene derivatives have been treated in terms of the Hammett $\rho\sigma$ relationship.[1] Much less is known of its application to fused ring systems which have two transmission paths of substituent effects. Such an application was first undertaken by Jaffé[2a] with the use of a modified Hammett equation.

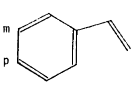
$$\log(k/k_0) = \rho_1\sigma_1 + \rho_2\sigma_2 \qquad (1)$$

The treatment has successfully been applied to the phthalide system.[2a] These treatments on heteroaromatic fused rings have been summarized in a review.[2b] Some examples of the benzofuran system are included but full accounts are not available. Noyce and Nichols[3] have recently treated the solvolysis rates of 2- and 3-benzofuryl derivatives in terms of the σ_{ij} constants with the modified Dewar-Grisdale equation.[4]

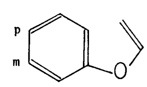
Because of our continuing interest in the chemical properties of aromatic olefins as well as enol ethers, we have studied the substituent effects observable in the benzofuran system. Benzofuran (BF) is structurally analogous to both styrene (ST) and phenyl vinyl ether (PVE).



BF



ST



PVE

Accordingly, its chemical behavior should be dual in its character. First, in the present communication, we will analyze the ground-state electronic structure of BF on the basis of ^1H and ^{13}C NMR observations. In the following two papers, the chemical reactivities will be treated for the bromination[5a] and the cationic polymerization.[5b]

Results

PMR Spectra. The proton magnetic resonance (PMR) spectra of BF and its derivatives have been recorded at a frequency of 100 MHz with a 10% solution in carbon tetrachloride using tetramethylsilane as internal standard. Measurements are accurate within 0.05 Hz. Assignment of signals has been made based on their coupling mode. Spectral feature of unsubstituted phenylene ring is too complicated for simple analysis and was not subjected to further attempts of analysis. Chemical shifts and coupling constants are summarized in Table 1.

CMR Spectra. The ^{13}C NMR spectra of BF derivatives have been obtained usually with a 50% solution in carbon disulfide. The complete proton noise decoupled spectrum of BF gave eight sharp singlets. The signals responsible for quaternary carbon atoms are easily characterized by a partial proton decoupling technique, remaining as singlet. All the signals have been assigned empirically by using the additivity rule.[6] The 6-methoxy derivative, proton spectrum of which is well separated, was subjected to single-frequency decoupling to aid the assignment. The chemical shifts are given in Table 2 as expressed in ppm downfield from TMS. For closely-spaced signals, however, some uncertainties were inevitable and such chemical shifts are presented with parentheses in Table 2.

Table 1. The chemical shifts and coupling constants for the PMR spectra of substituted benzofurans[a)]

Substituent	Chemical shift, ppm						Coupling constant, Hz					
	H-2	H-3	H-4	H-5	H-6	H-7	J_{23}	J_{37}	J_{45}	J_{67}	J_{57}	J_{46}
H	7.507	6.623					2.3	1.0				
2-CH_3	(2.39)	6.21					(1.0)	1.0				
3-CH_3	7.291	(2.20)					(1.1)					
5-CH_3	7.463	6.532	7.24	(2.425)	7.28	6.96	2.2	0.8		8.4		
6-CH_3	7.439	6.564	7.343	6.93	(2.42)	7.209	2.2	0.9	8.1			
5-CH_3O	7.476	6.544	6.888	(3.745)	6.566	7.280	2.3	0.9		8.9		2.6
6-CH_3O	7.423	6.562	7.324	6.754	(3.747)	6.92	2.2	0.9	8.4		2.2	
5-Cl	7.544	6.586	7.476	—	7.158	7.343		0.9		9.0		2.0

a) The values in parentheses show those concerning methyl protons.

TABLE 2. THE ^{13}C CHEMICAL SHIFTSa) OF SUBSTITUTED BENZOFURANS

Subst.	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	CH_3
H	145.1	106.9	121.6	123.2	124.6	111.8	127.9	155.5	—
2-CH_3	(155.9)	104.0	121.2	123.5	124.2	111.7	130.2	(155.7)	14.7
3-CH_3b)	141.6	116.0	119.8	122.7	124.5	111.7	129.4	155.8	7.4
5-CH_3	145.4	107.1	121.9	132.5	126.4	111.7	128.4	154.1	22.0
6-CH_3	144.8	107.2	121.5	125.1	134.8	112.5	125.6	156.0	22.7
5-CH_3O	146.2	107.6	104.2	156.8	112.6	114.1	128.8	150.6	55.9
6-CH_3O	144.4	106.9	121.7	112.6	158.7	95.8	121.2	156.6	55.1
5-Cl	146.8	107.1	121.7	(129.7)	125.4	110.9	(129.4)	154.0	—

a) In ppm downfield from TMS. Measured with a 50% solution in CS_2. b) Measured with a neat sample.

Discussion

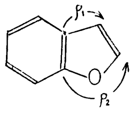
Spectral Characterization. PMR spectra of various methyl-substituted BF's have previously been measured, and the results on the 2- and 3-protons reported.7) The present results on these derivatives coincide satisfactorily with those reported data.7) A long-range coupling between the 3- and 7-protons of *ca.* 1 Hz observed here conforms also to the earlier results.7)

The CMR spectrum of BF has recently been measured.8) Assignment of signals has been made in analogy to that for indoles.9) The assignment of C-4, C-5, and C-6 reported contradicts that presented in Table 2. Although the signals responsible for these carbons are very close, a comparison of these signals among various 5- and 6-substituted BF's coupled with the empirical additivity rule6) permits us to assign them with confidence. Since *ortho*-methyl substitution usually effects a small downfield shift,6) a signal at 121.6 ppm of BF should be assigned to C-4. It is noticeable by comparing the results on a pair of 5- and 6-substituted derivatives that the chemical shift of C-6 is greater than that of C-5 for both the methyl and methoxy derivatives. Hence, it might be reasonable that the signals at 123.2 and 124.6 ppm should be assigned to C-5 and C-6 of BF, respectively. These assignments are consistent for all the derivatives from the viewpoint of the additivity rule.

Substituent Effects on the Chemical Shifts. A variety of proton and carbon chemical shifts (δ_H and δ_C) of benzene derivatives have been treated in terms of a Hammett-type equation.1b) They reflect the ground-state electronic structure. The effects of 5- and 6-substituents on δ_H and δ_C at the 2- and 3-positions of BF may be treated in a similar way. Because of two transmitting paths of electronic effects, they should be expressed by an equation similar to Eq. (1):

$$\delta = \rho_1\sigma_1 + \rho_2\sigma_2 + \delta_0 \tag{2}$$

where ρ_1 and ρ_2 are defined as sensitivity constants through the bonds 8–3 and 9–1–2, respectively.



The constants σ_1 and σ_2 refer correspondingly to the Hammett σ values of substituent relative to carbons 8 and 9, respectively. The value δ_0 is the chemical shift for the parent BF.

TABLE 3. SENSITIVITY CONSTANTS FOR THE EFFECTS OF 5- AND 6-SUBSTITUENTS ON THE PROTON AND CARBON CHEMICAL SHIFTS OF BENZOFURAN

	H-2	H-3	C-2	C-3
ρ_1	0.175	0.017	4.08	0.53
$S_{\rho 1}$	0.041	0.070	0.41	0.33
ρ_2	0.036	0.094	−0.88	−1.04
$S_{\rho 2}$	0.051	0.087	0.51	0.42
δ_0	7.477	6.571	145.43	107.11
$S_{\delta 0}$	0.008	0.014	0.08	0.07
S_δ	0.020	0.035	0.20	0.16

The values ρ_1, ρ_2, and δ_0 were calculated by the least-squares method and are given in Table 3. Noticeable in Table 3 is that both δ_H and δ_C at the 3-position receive virtually no effect or at least no simple electronic effect (with a large standard deviation) by substitution. By contrast, δ_H and δ_C at the 2-position reflect normal electronic effects of ring substituents. Linearities between the calculated values (Eq. (2)) and the observed δ_H and δ_C are illustrated in Figs. 1 and 2. The greater magnitude of ρ_1 as compared with ρ_2 for the 2-position indicates that the electronic effects of substituents are transmitted to C-2 mainly through the bond 8–3, ST-type. A similar tendency was previously observed for the acid dissociation of coumarilic acid.2b)

As a whole, the electronic structure of the 2–3 double bond of BF system seems to be similar to that of the

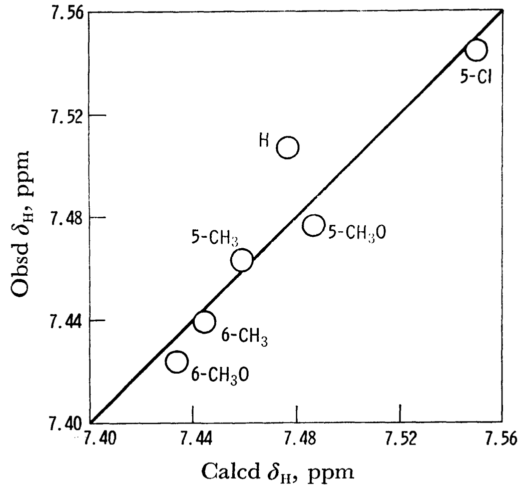


Fig. 1. Plots of the calculated and the observed chemical shifts of H-2 of substituted benzofurans.

Table 4. Boiling points and elemental analysis data of substituted benzofuran

Substuent	Mp[a] (°C)	Bp (°C/mmHg(lit.))	Calcd(%) C	Calcd(%) H	Found(%) C	Found(%) H
H	191.5	54.0/13(66.5/22)[b]	81.33	5.11	81.06	5.08
2-CH_3	—	87—88/20(81/14)[c]	81.78	6.11	81.84	6.14
3-CH_3	192—193	75.2/15(90/23)[c]	81.78	6.11	81.69	6.12
5-CH_3	234.8	88.0/18(86/20)[c]	81.78	6.11	81.64	6.04
6-CH_3	200	80.0/22(88/23)[c]	81.78	6.11	81.67	6.17
5-CH_3O[d]	211	123/30(119—120/25)[e]	72.95	5.44	73.08	5.48
6-CH_3O	211—213	103—104/10(99—100/10)[f]	72.95	5.44	73.05	5.51
5-Cl[g]	190—193	91.5/20(56/2)[h]	62.97	3.31	63.00	3.29

a) Mp of coumarilic acid. b) Ref. 13a. c) Ref.7. d) Mp of BF was 32—33 °C (lit,[e] 33—34.5 °C). e) S. D. Darling and K. D. Wills, *J. Org. Chem.*, **32**, 2794 (1967). f) R. L. Shriner and J. Anderson, *J. Amer. Chem. Soc.*, **60**, 1418 (1938). g) Cl: Calcd, 23.23; Found, 23.28%. h) E. N. Givens, L. G. Alexakos, and P. B. Venuto, *Tetrahedron,* **25**, 2407 (1969).

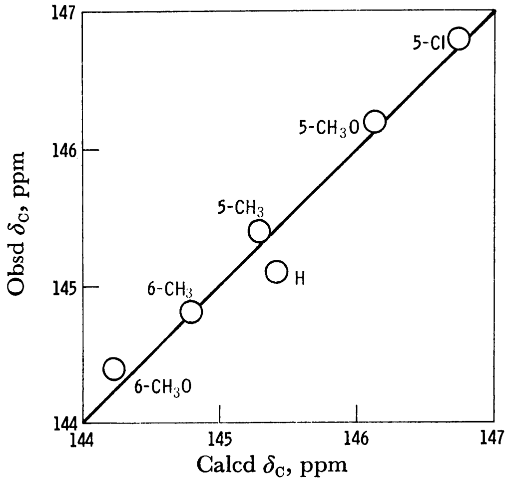


Fig. 2. Plots of the calculated and the observed chemical shifts of C-2 of substituted benzofurans.

extracyclic double bond of ST rather than PVE. However, the ρ_1 values are relatively small (markedly for δ_H) as compared with the ρ values for the terminal chemical shifts of styrene, 0.325 (δ_H)[10] and 4.73 (δ_C)[11] ppm/σ. This may probably be due to the substantial difference in the structure; the 2–3 bond is a part of aromatic ring of BF.

Experimental

Materials. Benzofuran (BF) and its 5- and 6-substituted derivatives were prepared from an appropriate salicylaldehyde and diethyl bromomalonate[12] *via* coumarilic acid according to the procedure of Nakazaki.[13] Methyl- and methoxysalicylaldehydes were obtained by the Reimer-Tiemann reaction.[14] 5-Chlorosalicylaldehyde was prepared by the chlorination of salicylaldehyde.[15] Treatments of a salicylaldehyde and bromomalonate by Nakazaki's procedure gave 50—30% of a coumarilic acid which was decarboxylated to give a benzofuran. Bp and elemental analysis data are given in Table 4.

2- and 3-Methylbenzofurans were prepared according to the literature.[16,17] Boiling points and analysis data are included in Table 4.

NMR Measurements. The PMR spectra were obtained on a JNM-4H-100 spectrometer operating at a frequency of 100 MHz at room temperature (*ca.* 22 °C). A 10% solution of a sample in CCl_4 was applied to the measurement and the chemical shifts did not vary within the experimental error of 0.05 Hz by dilution. TMS was used as an internal standard.

The CMR spectra were recorded at *ca.* 24 °C on a JEOL C-60HL spectrometer with a 15.09 MHz RF unit. Samples of neat liquid or 50% solution in CS_2 were used. The signal-to-noise ratio of the spectra was enhanced by the ^{13}C–H noise decoupling. The chemical shift measurements were performed with a nuclear-resonance single-side-band technique, being accurate within 0.2 ppm. CS_2 was used as an external standard. The chemical shifts are given in PPM downfield from TMS by using the chemical shift of CS_2 of 192.8 ppm.

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