Electron Reorganization induced by Intramolecular Hydrogen Bonding in Phenol Derivatives: Relationship between Proton Chemical Shifts and the Hydroxylic Electron Populations

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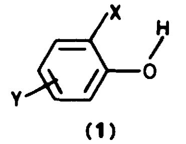
Intramolecular hydrogen-bonding effects in *ortho*-substituted phenols have been studied by ^1H n.m.r. and i.r. spectroscopy and CNDO/2 calculations. Full geometry optimization using the CNDO/2 method indicates definite variations of the OH bond length in intramolecular hydrogen-bonded phenols whereas these lengths remain nearly constant in *para*- or *meta*-substituted derivatives. There is a good linear relationship between the OH bond length and the i.r. ν_{OH} frequency shift, considered as reflecting the intramolecular association strength. Comparison of *ortho*- and *para*-substituted phenols shows that intramolecular hydrogen-bond formation induces important σ electron transfer from the substituent X to the hydroxylic oxygen *via* the bonded hydrogen atom whereas the electron population of this hydrogen atom decreases. This transfer results in π-electron reorganization of the X–C(1)–C(2)–OH fragment, and thereby increases the electron-releasing character of the OH group and the electron-withdrawing power of acceptor X groups, but the remaining atoms of the ring are little affected. With such an unusual electron reorganization, the chemical shifts of the phenolic hydrogen in *ortho*-, *meta*-, and *para*-substituted phenols can be simultaneously correlated with the electron population only if we consider both the proton investigated and the oxygen atom bearing it. The correlation $\Delta\delta = -31.6\Delta q_H + 16.1\Delta Q_O^{\sigma} + 0.08$ satisfactorily reflects the proton shifts for the 22 compounds investigated.

On account of its prime importance in chemistry and biology, *e.g.* anaesthetic potency[1] or antibacterial activity,[2] association by hydrogen bonding is the subject of increasing interest. We are currently investigating such associations by i.r. spectroscopy and semi-empirical CNDO/2 calculations in order to relate changes in the association strength to corresponding variations in the molecular structure.[3] In this work, two complementary approaches are used, ^1H n.m.r. and CNDO/2 calculations. Indeed, for evaluating the influence on screening constants of electron population variations induced by complexation, we need to know the sensitivity of the chemical shifts to these charge distributions.

Linear correlations between ^1H chemical shifts and the electron populations of the hydrogen atom, or on the atom bearing it, were observed for aromatic amines[4] and alkenes.[5] Similarly, in a previous paper[6] we have characterized, for *meta*- and *para*-substituted phenols, the sensitivity of the hydroxylic hydrogen chemical shift to the electron populations on the hydrogen or oxygen atom. The validity of such a δ–q relationship for strongly perturbated systems, such as *ortho*-substituted phenols (**1**), are examined herein. All X groups having a lone pair of electrons or π-electrons can form intramolecular hydrogen bonds.



(**1**)

After determining the hydroxylic proton chemical shifts, the importance of the proximity effects of X are examined. Owing to the large perturbations induced by an intramolecular hydrogen bond between OH and X groups, it is essential to evaluate electron populations on optimized geometries. As we plan to extend this work to intermolecular complexes between medium- or large-size molecules, we must use a semi-empirical CNDO/2 method rather than an *ab initio* approach, owing to computer time constraints.

Experimental

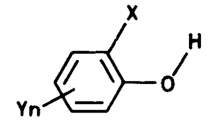
N.m.r. spectra were recorded on a Bruker WP 80 spectrometer at 80 MHz using tetramethylsilane as an internal standard. The magnetic field was locked with the ^2H signal of [$^2H_{12}$]cyclohexane (capillary inserted in the sample tube). The magnet gap temperature is 30 °C. The spectrum width is 1 000 Hz sampled on an 8K memory block (digital resolution of 0.25 Hz). I.r. spectra were run on a Perkin-Elmer 281 spectrometer operating in the double-beam, high-resolution mode. For weak concentrations, 1 cm optical length quartz cells with NaCl windows were used. The temperature of the solutions was 30 °C. Frequency calibration was performed by use of the indene bands. The uncertainty in ν(OH) is ± 1 cm^{-1}.

Results and Discussion

Chemical Shifts.—The chemical shifts of the hydroxylic proton of derivatives (**1**) have been measured for CCl_4 solutions for concentrations <0.1M (Table 1). We have checked that these chemical shifts remain constant, within experimental uncertainty, for solutions <0.1M and increase with concentration >0.1M.

The chemical shift concentration dependence is attributed to dimer formation[10] as proved by i.r. spectroscopy: indeed, for *o*-chlorophenol, a broad band appears at *ca.* 3 500 cm^{-1} for 0.4M

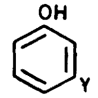
Table 1. ^1H Chemical shifts of the hydroxylic proton and ν_{OH} stretching frequencies for *ortho*-, *meta*-, and *para*-substituted phenols



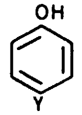
X	Y_n	δ_{OH} *	ν_{OH} †
H	4-CH_3O	3.97^a	3 617.5^h
H	4-CH_3	4.10^a	3 614.0^h
H	3-CH_3	4.18^a	3 612.0^h
H	H	4.29^a	3 612.0^h
H	4-Cl	4.33^a	3 610.0^h
H	4-F	4.20^a	3 615.0^h
H	3-Cl	4.47^a	3 608.0^h
H	4-NO_2	5.16^a	3 595.0^h
H	3-NO_2	4.95^a	3 600.0^h
H	3-CF_3	4.68^a	3 606.0^h
H	4-CN	5.09^a	3 597.0^h
H	3-CN	4.85^a	3 602.5^h
Cl	H	5.35^b	3 547.0
OH	H	4.76^c	3 567.0
CH_3O	H	5.29^d	3.558.0^i
NO_2	H	10.60^e	3.237.0^j
CN	H	5.82	3 560.0
CH_2OH	H	7.02	3 443.0^k
$COCH_3$	H	12.05^f	3 046.0^l
Cl	3,4,5,6-Cl_4	5.94	3 525.5^m
F	3,4,5,6-F_4	4.96^g	3 573.5
Cl	6-Cl	5.65	3 538.0^n

* Solvent CCl_4, downfield from internal Me_4Si. † In cm^{-1}. ^{a} Taken from ref. 6. ^{b} lit.,[7] 5.30. ^{c} lit.,[7] 4.31. ^{d} lit.,[7,8] 5.41. ^{e} lit.,[7] 10.54; lit.,[9] 10.51. ^{f} lit.,[7] 9.50. ^{g} lit.,[10] 4.85. ^{h} In agreement with refs. 11—13. ^{i} lit.,[14] 3 544; lit.,[9] 3 558. ^{j} lit.,[14] 3 258; lit.,[9] 3 231; lit.,[16] 3 240; lit.,[17] 324. ^{k} lit.,[9] 3 440; ^{l} lit.,[15] 3 040. ^{m} lit.,[14] 3 523. ^{n} lit.,[13] 3 537.

solutions, and its intensity increases with concentration. This absorption is ascribed to a phenolic dimer by comparison with the band observed at 3 482 cm^{-1} in the dimerization of unsubstituted phenol.[18] Similar behaviour is also observed for *o*-methoxyphenol. For derivatives (**1**), the constancy of the chemical shift for concentrations <0.1M is characteristic of a monomeric species. Baker *et al.*[14] have determined that the *cis*- and *trans*-conformations for *o*-chlorophenol are in a 56:1 ratio. Similarly, a recent study [18] of *o*-nitrophenol established that, for concentrations <0.2M, only an intramolecularly bonded species is observed. Because only one OH band is observed at this concentration, the chemical shifts measured are attributed to the intramolecularly hydrogen-bonded form. Table 1 also gives the chemical shifts for *meta*- and *para*-substituted phenols (**2**) and (**3**) derivatives at concentrations <0.009M, a range where



(**2**)



(**3**)

the chemical shift is not concentration-dependent. These latter data are taken from our previous work.[6]

Optimized Molecular Geometry.—For derivatives (**2**) and (**3**), the structures of maximum stability were determined by complete optimization of geometrical parameters with the Pople and Beveridge CNDO/2 method and the Rinaldi GEOMO optimization program.[19–21] For these compounds, the maximum stability corresponds to planar structures and this observation is consistent with the experimental data.[22] Optimized values of bond lengths and angles for the OH group and the aromatic ring are given in Table 2. The OH bond length of phenol (1.03 Å) is greater than the value obtained by *ab initio* STO-3G (0.99 Å)[23] or MINDO-3 calculations (0.95 Å).[24] This overestimate of the OH bond length is generally observed with CNDO/2 calculations.[25] The other lengths and angles thereby determined are in agreement with the values derived from other quantum calculations[23,24] or experimental determinations.[22] *meta*- And *para*-substitution on the aromatic ring induces variations $<2 \times 10^{-4}$ and 5×10^{-3} Å for d_{O-H} and d_{C-OH}, respectively, and the COH angles change only within *ca.* 0.7°. This behaviour is observed for interatomic bonds and angles in the ring.

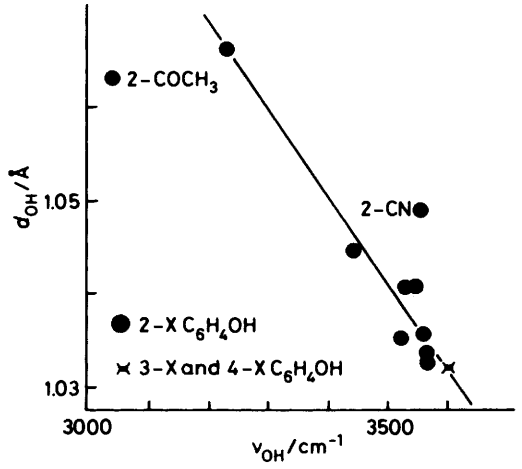


Figure 1. Correlation between the calculated OH bond length and the ν_{OH} frequencies for *meta*-, *para*-, and *ortho*-substituted phenols

The optimized geometrical parameters for derivatives (**1**) are gathered in Table 3. For various X substituents, aromatic C–C bond lengths and C–C–C angles exhibit very minute changes, with maximum variations of 0.02 Å and 10°, respectively. Our calculations show that, for the intramolecularly hydrogen-bonded derivatives (**1**), changes of *ca.* 0.03 Å occur for the OH bond whereas practically no change is observed for derivatives (**2**) and (**3**) (variations of *ca.* 10^{-4} Å). Moreover these variations in derivatives (**1**) are larger for X groups able to form strong hydrogen bonds in six-membered chelates (NO_2 and $COCH_3$).

To confirm that the evolution of the OH bond length is depending on the substituent for all derivatives, we have established that these d_{OH} values are linearly related to the ν_{OH} stretching frequency (Figure 1), except for *o*-cyano- and *o*-acetylphenol.* This linear correlation indicating that, if the CNDO/2 method overestimates the OH bond lengths, it gives, for most cases, a *consistent picture* of the variations of these OH distances induced by the X substituents and leading to large variations of ν_{OH} of *ca.* 400 cm^{-1}. The use of this CNDO/2 method for investigating the complexation processes of medium-size molecules appears to be quite justified.

Electron Population Reorganization.—From the optimized geometries determined for the 22 phenolic derivatives, we have

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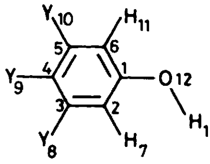
* Various factors may be responsible for these deviations. It may be difficult to estimate $\nu_{max.}$ for the associated OH band in *o*-acetylphenol and there may be poor calculations of CN substituent effects with CNDO/2 parameterization and a change in the nature of the association involving the π-electrons on the CN group.

Table 2. CNDO/2 Optimized structural parameters for *meta*- and *para*-substituted phenols

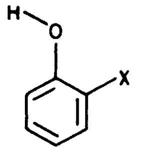


	4-CH$_3$O^a	4-CH$_3$^{b}	3-CH$_3$^{c}	H	4-Cl	4-F	3-Cl	4-NO$_2$^{d}	3-NO$_2$^{e}	3-CF$_3$^{f}	4-CN^g	3-CN^h
Bond lengths (Å)												
C(1)–C(2)	1.3914	1.3905	1.3918	1.3915	1.3930	1.3914	1.3929	1.3931	1.3920	1.3918	1.3921	1.3908
C(2)–C(3)	1.3816	1.3832	1.3827	1.3835	1.3827	1.3830	1.3845	1.3802	1.3834	1.3828	1.3825	1.3934
C(3)–C(4)	1.3940	1.3945	1.3839	1.3844	1.3832	1.3877	1.3843	1.3939	1.3831	1.3843	1.3950	1.3948
C(4)–C(5)	1.3924	1.3968	1.3956	1.3851	1.3845	1.3886	1.3832	1.3946	1.3929	1.3926	1.3959	1.3850
C(5)–C(6)	1.3836	1.3811	1.3946	1.3828	1.3817	1.3820	1.3814	1.3796	1.3912	1.3917	1.3824	1.3837
C(6)–C(1)	1.3915	1.3929	1.3914	1.3928	1.3947	1.3930	1.3929	1.3940	1.3910	1.3921	1.3936	1.3932
C(2)–H(7)	1.1173	1.1170	1.1167	1.1170	1.1171	1.1172	1.1169	1.1162	1.1168	1.1169	1.1168	1.1168
C(3)–Y(8)	1.1169	1.1191	1.1175	1.1175	1.1159	1.1153	1.1177	1.1165	1.1168	1.1168	1.1167	1.4172
C(4)–Y(9)	1.3746	1.4581	1.1182	1.1166	1.6812	1.3504	1.1149	1.4203	1.1157	1.1168	1.4171	1.1163
C(5)–Y(10)	1.1169	1.1192	1.4580	1.1176	1.1160	1.1154	1.6832	1.1165	1.4231	1.4665	1.1168	1.1168
C(6)–H(11)	1.1167	1.1162	1.1179	1.1163	1.1164	1.1165	1.1148	1.1156	1.1156	1.1167	1.1162	1.1162
C(1)–O(12)	1.3697	1.3688	1.3685	1.3687	1.3675	1.3692	1.3681	1.3652	1.3678	1.3677	1.3668	1.3673
O(12)–H(13)	1.0323	1.0323	1.0323	1.0323	1.0323	1.0322	1.0323	1.0323	1.0322	1.0322	1.0321	1.0321
Bond angles (°)												
C(1)–C(2)–C(3)	120.37	120.03	119.09	119.94	120.26	120.70	120.70	119.99	120.28	120.28	120.46	120.91
C(3)–C(3)–C(4)	121.14	122.87	120.63	120.57	117.89	118.88	121.05	120.49	120.60	120.42	120.54	119.38
C(3)–C(4)–C(5)	118.34	115.50	121.69	119.37	123.34	121.43	116.38	119.24	119.27	120.36	118.75	119.89
C(4)–C(5)–C(6)	120.54	123.03	116.79	120.68	118.03	118.96	124.93	120.51	120.48	119.10	120.80	120.54
C(5)–C(6)–C(1)	120.94	119.96	122.17	119.85	120.12	120.63	116.98	119.93	119.41	120.79	120.13	120.20
C(6)–C(1)–C(2)	118.67	118.61	119.63	119.59	120.36	119.40	119.96	119.84	120.02	120.35	119.32	119.25
C(1)–C(2)–H(7)	119.70	119.82	120.12	119.72	119.45	119.57	119.33	119.86	119.56	119.65	119.53	119.20
C(2)–C(3)–Y(8)	119.63	118.05	119.59	119.50	120.90	120.66	119.14	120.23	119.69	119.72	120.54	120.49
C(3)–C(4)–Y(9)	116.38	122.65	118.89	120.27	118.82	119.29	121.90	120.21	120.90	119.99	121.16	120.07
C(4)–C(5)–Y(10)	121.16	118.84	122.13	119.85	121.02	120.32	118.39	119.37	119.92	121.75	119.47	119.75
C(5)–C(6)–H(11)	119.51	120.23	119.47	120.44	120.44	119.84	121.64	120.29	119.84	119.86	120.12	121.64
C(2)–C(1)–O(12)	123.25	123.24	122.87	122.82	122.52	122.94	122.70	122.70	123.03	123.08	122.60	122.59
C(1)–O(12)–H(13)	108.09	108.17	108.27	108.38	108.58	108.24	108.51	108.60	108.27	108.37	108.68	108.66

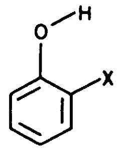
Geometrical parameters of substituents. [a] C(9)C = 1.3688, CH = 1.1215 Å, C(1)O(9)C = 109.19° Å. [b] C(9)H = 1.1201 Å. [c] C(10)H = 1.1201 Å. [d] H(9)O = 1.2251 Å, C(4)N(9)O = 119.42°. [e] N(10)O = 1.2246 Å, C(5)NO = 119.92°. [f] C(10)F = 1.3513 Å. [g] C(9)N = 1.1917 Å, C(6)C(9)N = 179.97°. [h] C(8)N = 1.1918 Å, C(3)C(8)N = 179.94°.

calculated the total electron populations (e.p.) on the hydroxylic oxygen and hydrogen atoms (q^{t}_{O} and q_H) and the e.p. localized along an axis perpendicular to the molecular plane, and characterizing the π charge on the oxygen atom. These values are collected in Table 4. For derivatives (**2**) and (**3**), q_H varies over *ca.* 0.01 e in accord with the usual direction of inductive and resonance effects. With derivatives (**1**), the range of variations in q_H is far larger. So, the introduction of an *o*-nitro group decreases the value of q_H by 0.11 e.

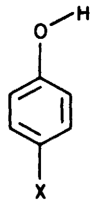
To get some insight into the electron population reorganization involved in intramolecular hydrogen bonding, we have examined CNDO/2 results for some derivatives (**1**) in conformations (**1b** and **f**), used as models for these calculations, and for the corresponding derivatives (**3**) (Table 5).



(**1f**)



(**1b**)

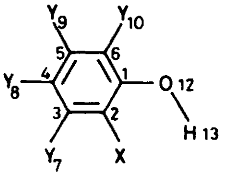


(**3**)

The values of e.p. show that both electron-withdrawing and -releasing X groups exert a similar effect on q_H and q^{t}_{O} in (**1f**) and in the corresponding derivatives (**3**). We can also observe in this comparison that the sum of π e.p. on the aromatic ring remains practically constant. By contrast, q^{σ}_{O} is largely modified according to the position of the X group. For instance, the q^{σ}_{O} values are 4.3243 and 4.2941 e for *p*- and *o*-acetylphenol, respectively. The decrease of e.p. in conformation (**1f**) can be attributed to a spatial electron repulsion between the lone pairs of electrons on the hydroxylic oxygen and both the *n* and π orbitals of the carbonyl group. An additional field effect, not easily distinguished from the former, may intervene in the same way. However, in all examples investigated, the resultant effect is definitely smaller than the variations induced by hydrogen-bond formation [compare for instance q_H and q^{t}_{O} for isomers (**1f**), (**1b**), and (**3**) in Table 5].

As expected, formation of the intramolecular hydrogen bond always induces increased acidic character of the hydrogen [for instance, for the nitrophenol, q_H 0.7529 e in (**1b**) and 0.8579 e in (**3**)]. Since, in conformation (**1f**), a spatial electron repulsion effect modifies the σ e.p. on the oxygen hydroxylic atom, in order to determine the specific effect of hydrogen-bond formation we prefer to compare the electron reorganization in (**1b**) and (**3**). The validity of this comparison lies in the observation that the rotation of the hydroxy group in the

Table 3. CNDO/2 optimized structural parameters for *ortho*-substituted phenols



	2-Cl	2-OH[a]	2-CH$_3$O[b]	2-NO$_2$[c]	2-CN[d]	2-CH$_2$OH[e]	2-COCH$_3$[f]	Cl$_5$	F$_5$	2,6-Cl$_2$
Bond lengths (Å)										
C(1)–C(2)	1.3926	1.3956	1.4019	1.4045	1.4058	1.4030	1.4039	1.4020	1.3939	1.3926
C(2)–C(3)	1.3795	1.3892	1.3885	1.3957	1.3889	1.3954	1.3988	1.3762	1.3908	1.3801
C(3)–C(4)	1.3840	1.3853	1.3867	1.3786	1.3837	1.3826	1.3783	1.3736	1.3918	1.3860
C(4)–C(5)	1.3876	1.3857	1.3885	1.3899	1.3866	1.3856	1.3898	1.3805	1.3919	1.3860
C(5)–C(6)	1.3840	1.3864	1.3850	1.3795	1.3839	1.3802	1.3796	1.3796	1.3916	1.3840
C(6)–C(1)	1.3918	1.3897	1.3879	1.3995	1.3902	1.3928	1.3962	1.4000	1.3940	1.3898
C(2)–X	1.6779	1.3707	1.3756	1.4180	1.4159	1.4664	1.4465	1.6746	1.3483	1.6786
C(3)–Y(7)	1.1152	1.1156	1.1163	1.1165	1.1171	1.1292	1.1194	1.6744	1.3453	1.1149
C(4)–Y(8)	1.1170	1.1159	1.1171	1.1160	1.1165	1.1172	1.1162	1.6745	1.3462	1.1168
C(5)–Y(9)	1.1177	1.1166	1.1170	1.1177	1.1178	1.1177	1.1181	1.6722	1.3453	1.1161
C(6)–Y(10)	1.1162	1.1155	1.1160	1.1158	1.1157	1.1167	1.1160	1.6744	1.3470	1.6809
C(1)–O(12)	1.3642	1.3680	1.3694	1.3569	1.3369	1.3664	1.3587	1.3619	1.3651	1.3613
O(12)–H(13)	1.0407	1.0331	1.0356	1.0663	1.0488	1.0447	1.0629	1.0354	1.0329	1.0409
Bond angles (°)										
C(1)–C(2)–C(3)	127.27	120.43	119.58	120.69	120.01	116.77	117.33	127.36	121.75	125.85
C(2)–C(3)–C(4)	116.33	119.67	119.40	120.98	119.60	122.36	122.28	119.85	119.37	117.02
C(3)–C(4)–C(5)	120.30	120.16	120.87	119.35	119.91	119.56	118.98	117.06	119.78	120.43
C(4)–C(5)–C(6)	122.05	120.42	120.30	121.52	121.58	119.56	120.97	120.15	120.10	119.56
C(5)–C(6)–C(1)	119.19	119.94	119.25	199.95	118.59	120.05	126.77	126.77	120.98	123.13
C(6)–C(1)–C(2)	116.86	119.38	120.60	118.43	120.31	121.70	120.81	108.81	118.02	114.01
C(1)–C(2)–X	106.41	116.62	113.42	118.15	106.42	123.38	118.43	115.59	118.08	106.14
C(2)–C(3)–Y(7)	121.76	119.94	121.39	119.25	120.07	119.12	119.03	119.20	120.44	121.20
C(3)–C(4)–Y(8)	120.00	119.76	119.21	120.21	120.09	120.02	120.54	123.57	120.19	119.81
C(4)–C(5)–Y(9)	119.01	119.82	120.00	119.21	119.26	120.14	119.41	123.70	199.88	120.57
C(5)–C(6)–Y(10)	120.40	120.30	120.69	120.56	120.74	120.28	120.58	104.64	119.35	118.25
C(2)–C(1)–O(12)	121.46	120.70	119.03	120.69	118.38	120.90	120.44	129.74	122.18	122.70
C(1)–O(12)–H(13)	107.47	107.90	105.35	104.19	104.42	107.29	104.78	107.84	107.86	106.86

Geometrical parameters of substituents: [a] OH = 1.0318 Å, C(2)OH = 108.56°. [b] CC = 1.3691, CH = 1.206 Å, C(2)OC = 108.02°. [c] NO(1) bonded = 1.2374; NO(2) = 1.2182 Å, C(2)NO(1) = 119.38 C(2)NO(2) = 120.82°. [d] CN = 1.1853 Å, C(2)CN = 172.73°. [e] CH = 1.1277, CO = 1.3774, OH = 1.0329 Å, C(2)CO = 112.00, COH = 107.51, OCH = 109.00°. [f] CO = 1.2870, CC = 1.4536, CH = 1.1193 Å, C(2)CO = 118.89, C(2)CC = 123.92, OCH = 111.64°.

bonded form practically suppresses the repulsion effect between the lone pairs of the oxygen atom and those of the X group. Furthermore, the π e.p.s are nearly invariant between (**1f**) and (**3**). In the form (**1b**), the total e.p. on the oxygen atom is much greater than that in the corresponding isomer (**3**). This overall difference on e.p. results from the balance of the large increase of q^{σ}_{O} (+0.1094 e) and a small decrease of q^{π}_{O} (−0.0267 e) between nitrophenols (**3**) and (**1b**) induced by hydrogen-bond formation. An analogous decrease of the π e.p. is observed for C(1). In contrast, the π e.p. for C(2) and for the bonded oxygen of the nitro group are increased. This new electron distribution is attributed mainly to an electron transfer in the fragment X–C(2)–C(1)–OH, from X to the hydroxy oxygen *via* the bonded hydrogen whose e.p. is also decreased. The resulting electron reorganization concerns mainly the two groups X and OH and C(1), C(2) bearing them, whereas the other aromatic carbons as well as the total e.p. on the ring are nearly unmodified.

This σ transfer induces a new π-electron distribution leading to an increase of both the π-electron-releasing power of the hydroxy group and of the π-electron-withdrawing character of the nitro group. This results in an increased π e.p. on C(2) (bearing the NO$_2$ group) whereas the π e.p. on C(1) decreases. Behaviour such as the interaction between the π and σ e.p. distribution is quite consistent with previous results (and our own data) on polysubstituted aromatic compounds.[26,27] Similar behaviour is observed for all derivatives, here investigated, including donor and attractor X groups.

Charge–Chemical Shift Relationship.—For derivatives (**2**) and (**3**), the chemical shifts reflect the expected field and resonance effects. So, data analysis using a dual substituent parameter equation yields correlations (1) and (2) of fairly good

For *para*-substituted phenols

$$\delta = 0.89\sigma_i + 1.69\sigma_R^O + 4.33 \quad (1)$$

$$\text{mean deviation (m.d.)} = 0.66\ \text{p.p.m.};\ r = 0.98$$

For *meta*-substituted phenols

$$\delta = 0.76\sigma_i + 0.96\sigma_R^O + 4.3 \quad (2)$$

$$\text{m.d.} = 0.02\ \text{p.p.m.};\ r = 0.996$$

precision. Such relationship cannot be established for *ortho*-substituted derivatives, where both substituent donors and acceptors induce downfield OH shifts.

Since the screening constants do not depend only on the electron densities, it is necessary to check that the influence of

Table 4. Electron populations on hydroxylic hydrogen and oxygen atom for substituted phenol derivatives

Substituent	q_H	q_O^t	q_O^π
4-CH_3O	0.8705	6.2376	1.9403
4-CH_3	0.8702	6.2383	1.9369
3-CH_3	0.8701	6.2384	1.9361
H	0.8696	6.2386	1.9366
4-Cl	0.8646	6.2346	1.9329
4-F	0.8678	6.2358	1.9389
3-Cl	0.8649	6.2354	1.9349
4-NO_2	0.8579	6.2302	1.9260
3-NO_2	0.8605	6.2311	1.9350
3-CF_3	0.8624	6.2323	1.9350
4-CN	0.8647	6.2351	1.9323
3-CN	0.8653	6.2354	1.9354
2-Cl	0.8314	6.2410	1.9276
2-OH[a]	0.8554	6.2387	1.9398
2-CH_3O	0.8549	6.2395	1.9389
2-NO_2	0.7529	6.3129	1.8993
2-CN	0.8271	6.2680	1.9267
2-CH_2OH	0.8158	6.2861	1.9286
2-$COCH_3$	0.7636	6.3212	1.8996
Cl_5	0.8110	6.2813	1.9351
F_5	0.8363	6.2045	1.9355
2,6-Cl_2	0.8262	6.2244	1.9222

[a] $q_H = 0.8657$, $q_O^t = 6.2402$, $q_O^\pi = 1.9433$ for the hydroxy group X. All *ortho*-substituted phenols are described in the bonded conformation.

Table 5. Electron population for *ortho*-substituted phenols for which the OH vibrator is free (**1f**) or bonded (**1b**) and for the corresponding *para*-phenol (**3**)

	X = $COCH_3$			X = NO_2			X = CN			X = OH		
	(**1b**)	(**1f**)	(**3**)	(**1b**)	(**1f**)	(**3**)	(**1b**)	(**1f**)	(**3**)	(**1b**)	(**1f**)	(**3**)
q_H	0.7636	0.8713	0.8643	0.7529	0.8592	0.8579	0.8271	0.8641	0.8652	0.8554	0.8704	0.8711
q_O^π	1.8996	1.9239	1.9292	1.8993	1.9220	1.9260	1.9267	1.9322	1.9323	1.9398	1.9407	1.9412
q_O^σ	4.4216	4.2941	4.3243	4.4136	4.2844	4.3042	4.3414	4.3012	4.3028	4.2989	4.2870	4.2969
$\Sigma_{i=1}^{6}\, q_c^\pi$ (cycle)	6.0044	6.0229	6.0181	6.0438	6.0402	6.0378	6.0395	6.0427	6.0423	6.1164	6.1185	6.1178
$\Sigma_{i=1}^{6}\, q_c^\sigma$ (cycle)	17.8652	17.8381	17.8426	17.7599	17.7489	17.7559	17.7809	17.7719	17.7758	17.6705	17.6653	17.6714
$q_{C(1)}^\pi$ *ipso* OH	0.8680	0.9177	0.9188	0.8733	0.9135	0.9076	0.9315	0.9462	0.9361	0.9982	1.0026	0.9864
$q_{C(1)}^\sigma$ *ipso* OH	2.9089	2.8803	2.8799	2.9087	2.8819	2.8837	2.8724	2.8636	2.8730	2.8658	2.8625	2.8561
$q_{C(2)}^\pi$ *ipso* X	1.1239	1.0769	1.0609	1.1761	1.1311	1.1138	1.0752	1.0588	1.0427	1.0133	1.0026	0.9864
$q_{C(2)}^\sigma$ *ipso* X	2.9818	2.9894	2.9835	2.8769	2.8899	2.8831	2.9559	2.9509	2.9447	2.8655	2.8625	2.8561
q_x^π	3.1470	3.0780	3.0768	4.0569	4.0380	4.0364	2.0337	2.0250	2.0254	1.9437	1.9407	1.9412
q_x^σ	13.8768	13.9502	13.9626	13.1159	13.1526	13.1663	7.0501	7.0552	7.0651	5.1619	5.1574	5.1680

Table 6. Chemical-shift variations (p.p.m.) induced by magnetic anisotropy and electric field effects of the X group in some derivatives (**1**)

X	$-M$	E
CH_3CO	3.00	0.50
NO_2	0.50	0.45
Cl	0.30	0.70

Positive values correspond to upfield shifts. Magnetic susceptibilities and dipolar moments are taken from literature data[30–33] for non-hydrogen-bonded structures. The same is true for the point of localization of the dipole.

the other factors acting on δ is negligible or remains constant. In a pioneering work on various chelated phenols in solution in $CDCl_3$, Matsui *et al.*[9] have shown that δ is linearly related to ν_{OH}, the slope of this relationship being -0.012. Similar behaviour is observed from our own results in CCl_4 solutions. So for the whole set of *ortho*-substituted phenols, except *o*-acetylphenol, we obtain a linear correlation (3).

$$\Delta\delta = -0.016\Delta\nu_{OH} + 0.18 \qquad (3)$$
$$r = 0.993;\ \text{m.d.} = 0.14\ \text{p.p.m.}$$

Δδ Is the difference in chemical shift between *o*-substituted phenol and phenol and similarly $\Delta\nu_{OH} = \nu_{OH}$ (2-X-phenol) $- \nu_{OH}$ (phenol). This relationship suggests that the variation of Δδ and $\Delta\nu_{OH}$ may result from the same electronic factors. To test this hypothesis, we have calculated for *o*-acetyl-, *o*-nitro-, and *o*-chloro-phenols, considered as significant examples, the direct influence of the X substituent on the electronic field or magnetic anisotropy effects using Buckingham[28] and MacConnell–Robertson[29] equations. Although the distances between the hydroxy hydrogen and the points of localization of the electric or magnetic dipoles are not very large, we think that these models give at least a rough estimate of the magnitude of these effects. The corresponding values are reported in Table 6.

It can be seen that the total electron density on the six aromatic carbons is 6.0667 e for phenol and varies by only 0.12 e between *o*-acetyl- and *o*-methoxy-phenol. Using Johnson and Bovey's model, and assuming that the anisotropy effect is proportional to the number of π-electrons, ring-current effects account for 0.8 p.p.m. in the δ value observed for phenol, but this value changes little, within experimental uncertainty, for the substituted phenols investigated here. It may thus be concluded that the various proximity effects arising from 2-X substituents and from the aromatic ring remain weak compared with the overall variations of the chemical shifts, except for *o*-acetylphenol. Therefore, subsequent discussion is largely focused on electronic charge effects. In accord with the preceding observations, *o*-acetylphenol will be also considered in the discussion, after a -2.5 p.p.m. correction for proximity effects ($\delta_{corr.} = 9.55$).

In a previous paper,[6] we established a good linear relationship (δ–q_H) for *meta*- and *para*-substituted phenols. This is shown in Figure 2 where the chemical shifts for the hydroxylic proton are plotted *versus* the corresponding electronic charges. For derivatives (**1**), the sensitivity of chemical shifts to electronic charges is smaller than that observed with derivatives (**2**) and (**3**). This behaviour cannot be attributed to variations in substituent effects caused by geometrical modifications, since for compounds (**1**)—(**3**) both experimental and theoretical results favoured the planar conformation. This implies that the e.p. of the hydroxy hydrogen cannot be used alone to explain the modifications of the chemical shift for all derivatives.

Indeed, it is noteworthy that series (**2**) and (**3**) have quite different behaviour compared with derivatives (**1**). For the former (monomeric, free OH), an electron-withdrawing group decreases both q_H and q_O^t; for the latter (intramolecular, bonded

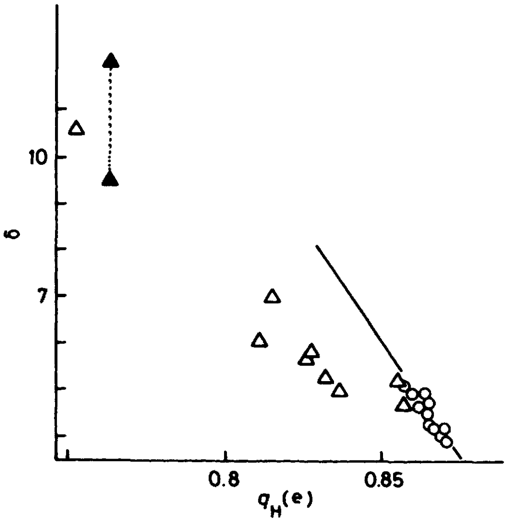


Figure 2. Correlation between the chemical shift and the charge of the hydroxy proton of phenol derivatives: ○, *meta*- and *para*-derivatives; △, chelated phenols; ▲, 2-acetylphenol. For *o*-hydroxyphenol the values for δ and q_H correspond to the mean for the two OH groups

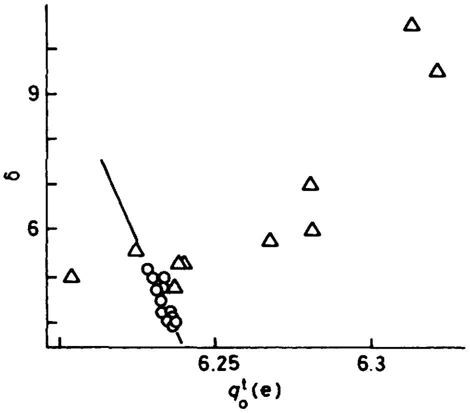


Figure 3. Correlation between the chemical shift of the hydroxy proton and the charge of the oxygen atom: ○, *meta*- and *para*-derivatives; △, chelated phenols. For *o*-hydroxyphenol the values correspond to the mean between the two OH groups

OH), all groups investigated, either electron-withdrawing or -releasing, decrease q_H but increase q_O^t. In fact, no correlation exists between δ and the total charge on the oxygen atom (q_O^t) for all substituted phenols (Figure 3). Indeed, derivatives (**2**) and (**3**) lie along a negative slope as previously observed, whereas for derivatives (**1**) the trend gives a positive slope. Relevant to this behaviour, it should be recalled that in *meta*- and *para*-substituted phenols (as in the other families already studied) q_H and q_O^t or q_O^σ remain nearly proportional, with generally small variations of q_O^π. On the other hand, in *ortho*-derivatives, the intramolecular hydrogen-bonding effect is of prime importance. Not only does q_H decrease for all groups with larger variations, but also there are important effects on the σ e.p. for the oxygen atom which undergoes nearly opposite variations in most cases. It appears that the only two points of *ortho*-substituted phenols close to the correlation (δ–q_H) previously established with (**2**) and (**3**) correspond to *o*-methoxy- and *o*-hydroxy-phenols, *i.e.* those with q_O^t or q_O^σ charges nearly equal to these of phenol. This observation suggests that the difference in sensitivity of variating δ *versus* q_H is evident for *meta*- and *para*-substituted phenols and for *ortho*-substituted phenols can reflect the changes on the oxygen electronic population.

A biparametric relationship (4) relating Δδ to both Δq_H and

$$\Delta\delta = -31.6\,\Delta q_H + 16.1\,\Delta q_O^\sigma + 0.08 \qquad (4)$$
$$n = 22 \qquad r = 0.972 \qquad \text{s.d.} = 0.42$$

Δq_O^σ for 22 compounds and including the corrected Δδ value for *o*-acetylphenol is obtained. A similar relationship (5) is observed

$$\Delta\delta = -38.8\,\Delta q_H + 12.6\,\Delta q_O^t + 0.028 \qquad (5)$$
$$n = 22 \qquad r = 0.966 \qquad \text{s.d.} = 0.46$$

by considering q_O^t charges in place of q_O^σ.

It would be interesting to define precisely the role of q_O^π, which is part of the q_O^t term; unfortunately, there is a high interdependence between q_O^π and q_H, so it would be unwise to look for a multiparametric relationship between δ and these three parameters q_H, q_O^σ, and q_O^π.

It is noteworthy that in correlations (4) and (5), the sign of the q_O^σ or q_O^t terms is positive (*i.e.* the greater q_O^σ or q_O^t, the larger the deshielding effect) and so opposite to the sign of the q_H term.* They are also opposite to the sign of the slope of the correlations previously observed in styrenes and amines between δ and the bonded atom e.p. (C or N). In fact, for compounds previously investigated for which the substituent effect is transmitted *via* the aromatic ring to the site under consideration, the electronic population q_H is proportional to the electron population on the oxygen atom. So, the perturbation produced by the change of e.p. on the neighbour atom is contained in the slope of the δ–q_H correlation. In this work, we studied compounds for which q_H and q_O^σ vary either in the same or in an inverse manner. So, it is necessary to take explicitly into account their respective variations. The contribution of q_O^t in this treatment may partly characterize modifications of anisotropic effects of this atom deriving from the variation of its electronic population. The relationships obtained here show that it is necessary to consider both the electron population of the hydrogen atom and of its neighbouring atoms when the variation chemical shifts is large.

Conclusions

The relationship proposed in this work for evaluating the hydroxy ^{1}H chemical shifts from the electronic charges within the OH group can be used either for free phenols or hydroxy groups involved in an intramolecular hydrogen bond. One of its useful functions is to characterize structural perturbations transmitted through the aromatic ring and the oxygen as well as perturbations acting directly on the hydroxy proton and transmitted to the oxygen and to the aromatic ring. The wide range of application and the nature of the mechanisms of structural interaction attest to the originality of this treatment and the difference from the chemical shift–charge correlations previously used in the literature for protons bonded to carbon or nitrogen. We are now planning the application of this model to other types of intermolecular interactions, *i.e.* association of the hydroxy proton with either a heteroatom lone pair or an aromatic system.

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* The elimination of *o*-nitro- and *o*-acetyl-phenol in this treatment, as suggested by a referee, does not change the sign of the sensitivity to the hydrogen and oxygen e.p. and weakly modifies the values of these parameters.

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