Intramolecular Hydrogen Bonding in *ortho*-Substituted Benzoic Acids

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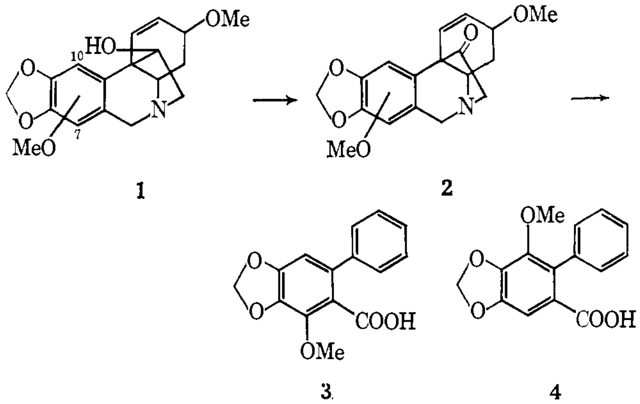
Abstract: Unbonded *meta-* and *para*-substituted benzoic acids show hydroxyl absorption between 3531 and 3545 cm^{-1} depending on the electronegativity of the substituent. *ortho*-Substituted acids where the substituent is not oxygenated also absorb at 3521–3538 cm^{-1} and show the same frequency–pK_a relationship earlier established for *meta-* and *para*-substituted acids. *o-t*-Butylbenzoic acid is anomalous. *o*-Methoxybenzoic acids are intramolecularly bonded and the frequency shift can be correlated with the position and electronegativity of the second substituent. When the second substituent flanks the methoxyl group an unusual compressive effect abnormally lowers the frequency; when the substituent flanks the carboxyl, hydrogen bonding is completely inhibited regardless of the nature of the substituent.

During an earlier investigation of the structure of ambelline (**1**) two positions, 7 and 10, were considered possible for the aromatic methoxyl group. Hofmann degradation of the corresponding ketone (**2**)[1] followed by oxidation of the product furnished a biphenyl acid which could be formulated as either **3** or **4**.



The infrared spectrum of this acid was measured in carbon tetrachloride at high dilution under the assumption that intramolecular hydrogen bonding would be observed between the carboxyl and methoxyl groups if structure **3** were correct. This seemed reasonable in view of the fact that *o*-methoxybenzoic acid (**46**, Table III) exhibits a broad absorption band at 3362 cm^{-1} [2] while 6-phenylpiperonylic acid (**45**) shows a narrow band at 3532 cm^{-1}, only slightly lower in frequency than piperonylic acid (**17**) itself (3544 cm^{-1}). Since it was found that the biphenyl acid (**3** or **4**) absorbs at 3522 cm^{-1}, structure **4** was provisionally accepted. External evidence[1] subsequently proved that the methoxyl group of ambelline is actually at position 7 and therefore the biphenyl acid possesses structure **3**.

In the following work we have sought an explanation for this apparent anomaly through a study of the infrared spectra of a series of related *o*-alkoxybenzoic acids. It soon became apparent that both steric and electronic factors affect the OH-stretching frequencies in *ortho*-substituted acids.[3] Therefore it was necessary to study a series of *meta-* and *para*-substituted acids to determine the "normal" OH frequency. The values obtained were also compared to that of a similar series of acids substituted in the *ortho* position with groups not containing oxygen in an effort to estimate the magnitude of the frequency shift due to steric factors alone.

Experimental Section

The acids were recrystallized several times to literature melting points, dried at 76° under vacuum, and dissolved in carbon tetrachloride. In general, the samples were run initially in a 1-cm quartz "infrasil" cell,[4a] then diluted to half the initial concentration and measured again in a 2-cm cell in order to distinguish inter- from intramolecular bonding. Only the intramolecular bonds are reported here.

A Beckman IR-7 was employed and the spectra were scanned in absorbance *vs.* wavenumber. The spectral slit width was approximately 4 cm^{-1} and the instrument was calibrated against water vapor, in the 3-μ region using the calibration peaks described by Plyler, *et al.*[4b] The wavelengths are felt to be accurate to within ±2 cm^{-1}. Compounds not commercially available were prepared as follows.

***m*-Phenylbenzoic acid (16)**, mp 166°, by permanganate oxidation of *m*-methylbiphenyl.[5]

***o*-Phenylbenzoic acid (34)**, mp 114°, by hydrolysis of fluorenone.[6]

3-Methoxy-4,5-methylenedioxybenzoic acid (myristicic acid, **20**), mp 212°,[7] by hydrogen peroxide oxidation of the corresponding aldehyde.

6-Nitroveratric acid (40), mp 192°, by nitration of veratric acid.[8]

6-Nitropiperonylic acid (42), mp 172°, by nitration of piperonylic acid.[9]

6-Bromoveratric acid (43), mp 185–186°, by bromination of veratric acid.[10]

6-Bromopiperonylic acid (44), mp 204–205°, by bromination of piperonylic acid.[11,12]

2-Nitro-3,4,5-trimethoxybenzoic acid (41), mp 165°, by nitration and subsequent hydrolysis of methyl 3,4,5-trimethoxybenzoate.[13]

6-Phenylpiperonylic acid (45), mp 213°, by degradation of tazettine.[12]

6-Methoxypiperonylic acid (49), mp 148°,[14] obtained as a by-

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[1] P. Naegeli, E. W. Warnhoff, H. M. Fales, R. E. Lyle, and W. C. Wildman, *J. Org. Chem.*, **28**, 206 (1963).

[2] J. J. Fox and A. E. Martin, *Nature*, **143**, 199 (1939).

[3] J. D. S. Goulden, *Spectrochim. Acta*, **6**, 129 (1954).

[4] (a) Available from Quaracell Products, Inc., New York, N. Y. (b) E. K. Plyler, A. Danti, L. R. Blaine, and E. D. Tidwell, *J. Res. Natl. Bur. Std.*, **64**, 29 (1960).

[5] P. Jacobson, *Ber.*, **28**, 2547 (1895).

[6] M. Weger and K. Döring, *ibid.*, **36**, 878 (1903).

[7] F. W. Semmler, *ibid.*, **24**, 3820 (1891).

[8] F. Tiemann and K. U. Matsmoto, *ibid.*, **9**, 938 (1876).

[9] J. Jobst and O. Hesse, *Ann.*, **199**, 70 (1879).

[10] K. U. Matsmoto, *Ber.*, **11**, 136 (1878).

[11] R. Fittig and W. H. Mielck, *Ann.*, 172, 158 (1874).

[12] H. Kondo, T. Ikeda, J. Taga, *Ann. Rept. Itsuu Lab.*, **3**, 65 (1952).

[13] J. Pollak and H. Feldscharek, *Monatsh.*, **29**, 146 (1908).

[14] K. C. Campbell, P. F. Hopper, and B. K. Campbell, *J. Org. Chem.*, **16**, 1736 (1951).

product in the copper-catalyzed reaction of 6-bromopiperonylic acid and dimedone.[15]

6-Methoxyveratric acid (asaronic acid, **50**), mp 144°,[16] by similar treatment of 6-bromoveratric acid.[15]

2-Methoxy-3,4-methylenedioxybenzoic acid (croweacic acid, **53**), mp 153°,[17] by alkaline peroxide oxidation of the corresponding aldehyde.

2-Methoxy-3-methylbenzoic acid (**54**), mp 85°,[18] by methylation with diazomethane and subsequent alkaline hydrolysis of 3-methylsalicylic acid.

2,5-Dimethoxy-3,4-methylenedioxybenzoic acid (apiolic acid, **55**), mp 175°, by alkaline peroxide oxidation of apiol.[19]

2-Methoxy-5-nitrobenzoic acid (**56**), mp 160–161°, from nitration of *o*-methoxybenzoic acid.[20]

2-Methoxy-3-nitrobenzoic acid (**57**), mp 194°, as a by-product of the above reaction.[20]

2-Nitro-4,5,6-trimethoxybenzoic acid (**61**), mp 154–155°, from the nitration of the corresponding acid.[21]

3,4-Dimethoxyphthalic acid 1-methyl ester (**62**), mp 138°, from methanolysis of hemipinic anhydride.[22]

2-Methoxy-3,4-methylenedioxy-6-nitrobenzoic acid (**63**), mp 190–192°, by nitration of croweacic acid.[23]

Methyl 2,6-dihydroxybenzoate (**67**), mp 67–68°,[24] by brief treatment of 2,6-dihydroxybenzoic acid with diazomethane.

Methyl 2,4-dihydroxybenzoate (**70**), mp 119°,[25] by similar treatment of 2,4-dihydroxybenzoic acid.

Methyl 2-hydroxy-6-methoxybenzoate (**68**), mp 51–52°, by the prolonged treatment of 2,4-dihydroxybenzoic acid with diazomethane, colorless needles from petroleum ether, mol wt 158 by mass spectrometry. *Anal.* Calcd for $C_9H_{10}O_4$: C, 59.33; H, 5.53. Found: C, 59.76; H, 5.66.

2-Hydroxy-6-methoxybenzoic acid (**69**), mp 135°, by alkaline hydrolysis of the above ester.[24]

***o*-*t*-Butylbenzoic acid** (**33**), mp 81°, by the permanganate oxidation of *o*-*t*-butyltoluene.[26] An interesting by-product isolated in low yield from this reaction was α,α-dimethylhomophthalic anhydride, mp 81–83°,[27] identified by its characteristic infrared and nmr spectra and reaction with methylamine to give N,α,α-trimethylhomophthalimide, mp 100–102°.[27]

2,3,4-Trimethoxybenzoic acid (**52**), mp 99–100°,[28] was prepared in low yield from the carbonation of the lithium derivative of 1,2,3-trimethoxybenzene. The latter was prepared from the metalation of the ether with *n*-butyllithium.

8-Methoxy-1-naphthoic acid (**60**), mp 161–162°, was prepared by a similar metalation and carbonation of 1-methoxynaphthalene.[29]

3-Methoxy-4,5-methylenedioxy-2-biphenylcarboxylic acid (ambelline acid, **3**) was prepared by treating 200 mg of oxoambelline with methyl iodide and allowing the resulting methiodide to undergo conversion to the corresponding sarcosine derivative in 10% sodium hydroxide. The resulting sodium salt was removed by filtration, redissolved in water, and treated with permanganate until a color persisted. An oil, consisting of the corresponding biphenylaldehyde (infrared) and the N-methylbenzylamine (infrared, nmr), was extracted with chloroform. Partition between acid and benzene gave the neutral aldehyde which was then oxidized to the acid in ethanol with a large excess of alkaline hydrogen peroxide. The free acid precipitated on acidification and was purified by recrystallization from ethanol, mp 240–241°, yield 20 mg, λ_{max}^{EtOH} 262 mμ (ϵ 7820). *Anal.* Calcd for $C_{15}H_{12}O_6$: C, 66.17; H, 4.44; neut equiv, 272. Found: C, 65.96; H, 4.65; neut equiv, 279.

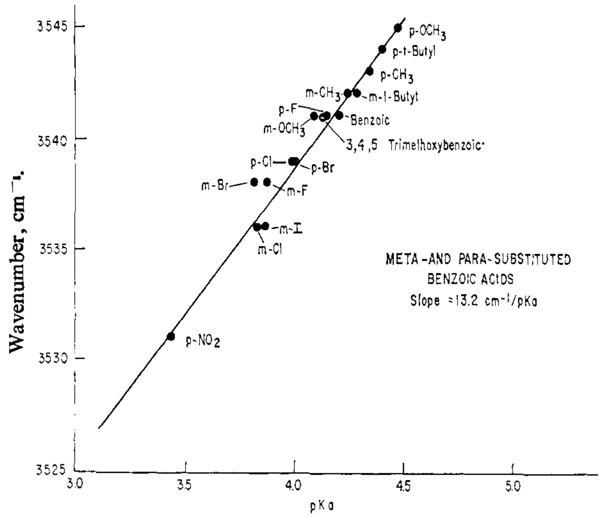

Figure 1. Hydroxyl-stretching frequency–pK_a relationship of *meta*- and *para*-substituted benzoic acids.

Discussion of Results

I. Nonbonded Benzoic Acids. Table I lists a series of simple *meta*- and *para*-substituted benzoic acids and their OH-stretching frequencies along with the half-intensity bandwidths. Formic and acetic acids are included for comparison. The infrared maxima all lie within the rather narrow range of 3531–3545 cm^{-1} and exhibit bandwidths of 26–34 cm^{-1}. The small but significant variations in frequency are paralleled by corresponding changes in pK_a (Figure 1) as Goulden,[3] Fox and Martin,[30] Davies and Sutherland,[31] and Flett[32] have already shown in a series which included aliphatic acids.

At first glance it seems surprising[31] that a correlation should exist between the unbonded OH-stretching frequency of an acid dissolved in carbon tetrachloride and its pK_a value, as determined in water. In carbon tetrachloride solvation is minimal and only the undissociated acid is observed. In water on the other hand, both species present, acid and anion, are extensively solvated and to a different degree. The existence of this correlation shows that solvation of the anion relative to that of the acid is constant throughout the series. It also emphasizes that electronic accession to (or withdrawal from) the O–H linkage affects the partial separation of the proton from the oxygen as observed in the stretching frequency in a manner directly proportional to its complete removal as expressed by pK_a.

The frequency shifts of the acids of unknown pK_a are in line with the electron-withdrawing characteristics of their substituents and rough pK_a values may be estimated from their frequencies.

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(15) H. M. Fales, E. W. Warnhoff, and W. C. Wildman, *J. Am. Chem. Soc.*, **77**, 5889 (1955).

(16) B. Dunston, W. Luff, W. H. Perkin, and R. Robinson, *J. Chem. Soc.*, **97**, 1131 (1910).

(17) A. R. Penfold, G. R. Ramage, and J. L. Simonsen, *ibid.*, 756 (1938).

(18) C. Schall, *Ber.*, **12**, 823 (1879).

(19) W. Baker and R. I. Savage, *J. Chem. Soc.*, 1606 (1938).

(20) J. L. Simonsen and M. G. Rau, *ibid.*, **111**, 224 (1917).

(21) V. J. Harding, *ibid.*, **99**, 1597 (1911).

(22) I. Heilbron, Ed., "Dictionary of Organic Compounds," Vol. 2, Eyre and Spottiswoode, Ltd., London, 1965, p 1133; but V. M. Rodinov and A. M. Fedorova, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 139 (1943), report both melting points as 149–150°; *cf. Chem. Abstr.*, **38**, 4260^5 (1944).

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(24) F. Mauthner, *J. Prakt. Chem.*, [2] **124**, 319 (1930); see also I. Heilbron, Ed., "Dictionary of Organic Compounds," Vol. 2, Eyre and Spottiswood, Ltd., London, 1965, p 1056.

(25) J. B. Shoesmith and J. Haldane, *J. Chem. Soc.*, **125**, 113 (1924).

(26) K. T. Serijan, H. F. Hipsher, and L. C. Gibbons, *J. Am. Chem. Soc.*, **71**, 873 (1949).

(27) S. Gabriel, *Ber.*, **19**, 2364 (1886); **20**, 1199 (1887).

(28) W. Will, *ibid.*, **21**, 2020 (1888).

(29) R. A. Barnes and L. Nehmsmann, *J. Org. Chem.*, **27**, 1939 (1962).

(30) J. J. Fox and A. E. Martin, *Proc. Roy. Soc.* (London), **A162**, 419 (1937), were perhaps the first to note the relationship.

(31) M. M. Davies and G. B. B. M. Sutherland, *J. Chem. Phys.*, **6**, 755 (1938), also noted the difference in frequency between acetic and trichloroacetic acids but doubted that a quantitative relationship would exist; see p 761.

(32) M. St. C. Flett, *Trans. Faraday Soc.*, **44**, 767 (1948).

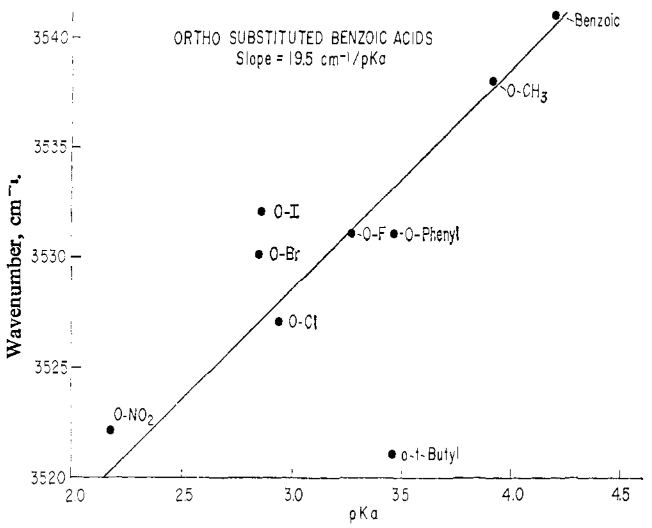
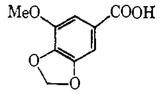
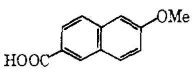


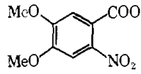
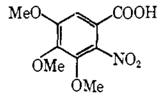
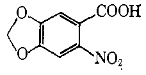
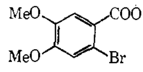
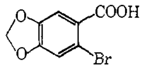
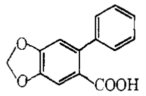
Figure 2. Hydroxyl-stretching frequency–pK_a relationship of *ortho*-substituted benzoic acids.

Table I. Infrared Hydroxyl-Stretching Frequencies of Aliphatic and Simple *meta*- and *para*-Substituted Aromatic Acids

	Acid	Frequency, cm^{-1} (half-intensity bandwidth)	pK_a
6	Formic	3516 (30)	3.77[a]
7	Acetic	3537 (23) [lit. 3533,[b] 3546[c]]	4.76[d]
8	Benzoic	3541 (28) [lit. 3536,[b] 3551[e]]	4.20[d]
9	*p*-Toluic	3543 (26) [lit. 3556[d]]	4.34[a]
10	*m*-Toluic	3542 (26)	4.24[a]
11	*p*-*t*-Butylbenzoic	3544 (26)	4.40[a]
12	*m*-*t*-Butylbenzoic	3542 (27)	4.28[a]
13	*p*-Methoxybenzoic (anisic)	3545 (27) [lit. 3541,[b] 3560[e]]	4.47[d]
14	*m*-Methoxybenzoic	3542 (28)	4.09[a]
15	*p*-Phenylbenzoic	3542 (28)	
16	*m*-Phenylbenzoic	3542 (29)	
17	3,4-Methylenedioxybenzoic (piperonylic)	3544 (27)	
18	3,5-Dimethoxybenzoic (veratric)	3540 (30) [lit. 3540[b]]	
19	3,4,5-Trimethoxybenzoic	3541 (32)	4.13[c]
20		3542 (30)	
21	*p*-Fluorobenzoic	3542 (29)	4.14[a]
22	*m*-Fluorobenzoic	3538 (29)	3.87[a]
23	*p*-Chlorobenzoic	3539 (29) [lit. 3535,[b] 3551[2]]	3.98[d]
24	*m*-Chlorobenzoic	3536 (31) [lit. 3532[b]]	3.83[d]
25	*p*-Bromobenzoic	3539 (30)	4.00[a]
26	*m*-Bromobenzoic	3538 (30)	3.81[a]
27	*p*-Iodobenzoic	3536 (30)	
28	*m*-Iodobenzoic	3536 (30)	3.86[a]
29		3543 (27)	
30	*p*-Nitrobenzoic	3531 (32) [lit. 3527,[b] 3541[e]]	3.44[a]
31	*m*-Nitrobenzoic	3531 (34) [lit. 3528,[b] 3548[e]]	3.45[a]

[a] Reference 33, p 588. [b] Reference 3. [c] G. B. Barlin and D. D. Perrin, *Quart. Rev.* (London), **20**, 75 (1966). [d] J. F. J. Dippy, *Chem. Rev.*, **25**, 151 (1939). [e] Reference 32.

Table II. Infrared Hydroxyl-Stretching Frequencies of Nonbonded *ortho*-Substituted Aromatic Acids

	Acid	Frequency, cm^{-1} (half-intensity bandwidth)	pK_a
32	*o*-Toluic	3538 (30)	3.91[a]
33	*o*-*t*-Butylbenzoic	3521 (28)	3.46[a]
34	*o*-Phenylbenzoic	3531 (32)	3.46[a]
35	*o*-Nitrobenzoic	3522 (36)	2.17[a]
36	*o*-Fluorobenzoic	3531 (30)	3.27[a]
37	*o*-Chlorobenzoic	3527 (37)	2.94[a]
38	*o*-Bromobenzoic	3530 (36)	2.85[a]
39	*o*-Iodobenzoic	3532 (37)	2.86[a]
40		3528 (36)	
41		3530 (36)	
42		3524 (38)	
43		3531 (38)	
44		3531 (37)	
45		3532 (27)	

[a] Reference 33, p 588.

The *ortho*-substituted acids listed in Table II are at slightly lower frequencies, ranging between 3521 and 3538 cm^{-1}. Although Goulden[3] did not consider these acids, it is interesting to note that they also show a similar correlation of OH-stretching frequency and pK_a (Figure 2), in spite of the fact that they are much more acidic than the corresponding *meta* and *para* isomers. Brown[33] has considered that the increased acidity is caused by the insulation of the carboxyl group from electron accession from the ring. This is presumably due to unfavorable π-orbital overlap of the carboxyl and ring carbon atoms since the carboxyl group may not lie in the plane of the ring because of the bulky *ortho* substituent. Figure 2 implies that the relative solvation of the two species, acid and anion, is also constant in this series. However, *o*-*t*-butylbenzoic acid (**33**) does not lie on the curve and it might be concluded that such a bulky group has seriously perturbed the OH-stretching frequency, shifting it about 13 cm^{-1} toward lower frequencies than expected. However this shift is in the opposite direction to that expected from steric compression and consequent shortening of the O–H linkage. The anomaly might be explained as an abnormally low acidity. The carboxylate anion, due to its charge, is inherently more heavily solvated than the free acid so that the loss of solvation due to steric factors might be expected to destabilize this species.

The *o*-halobenzoic acids present a special problem since they are formally capable of hydrogen bonding. Although the *o*-fluoro and *o*-chloro derivatives fall on the pK_a–frequency curve (Figure 2), the more bulky *o*-bromo and *o*-iodo acids are displaced in a direction

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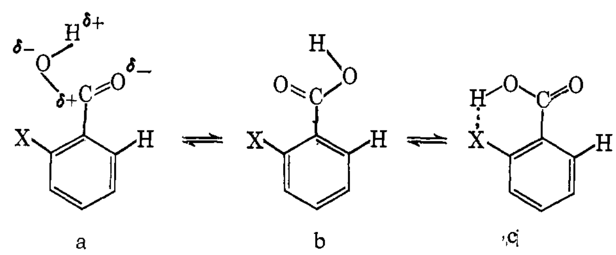
[33] H. C. Brown, D. H. McDaniel, and O. Häflinger in "Determination of Organic Compounds by Physical Methods," Vol. I, E. A. Braude and F. C. Nachod, Ed., Academic Press Inc., New York, N. Y., 1955, p 604.

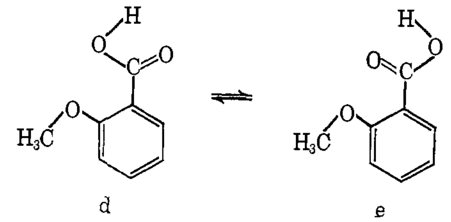
opposite to that noted in the case of *o-t*-butylbenzoic acid. Still, as a group, the frequency shifts of these acids relative to their *meta* and *para* isomers are well accounted for by the corresponding pK_a values and we conclude that they are not intramolecularly bonded to any great degree. The intramolecularly bonded *o*-halophenols[34] show a wide difference in frequency, unlike anything observed here, on passing from the *o*-fluoro to the *o*-iodo substituent. Considerable energy would be required to convert the normally *cis* polar orientation[35,36] of the carboxyl group (a or b) to the *trans* configuration (c) necessary for intramolecular hydrogen bonding. If a bond of such strength did exist it might be expected to cause a much more distinctive frequency shift than is actually observed.



The half-intensity bandwidths of the *ortho*-substituted acids are slightly larger than in the *meta* and *para* acids, but since this effect is also noted with *o*-methylbenzoic (**32**) as well as *o*-chlorobenzoic (**37**) it obviously does not reflect hydrogen bonding.

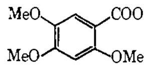
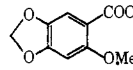
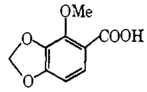
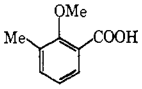
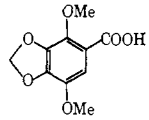
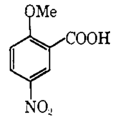
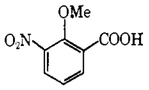
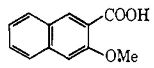
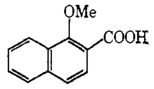
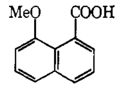
It is therefore concluded that the unbonded benzoic acid OH-stretching frequency lies in the narrow range of 3520–3545 cm^{-1} and that it is only slightly affected by steric or electronic factors.

II. Bonded and Hindered Methoxybenzoic Acids. The *o*-methoxybenzoic and -naphthoic acids listed in Table III contain the much more potent hydrogen bond accepting methoxyl groups and they all show an intramolecularly bonded hydroxyl absorption band at 3267–3386 cm^{-1}. They are further characterized by half-intensity bandwidths which are roughly twice that of the unbonded isomers. In these cases, some unbonded rotamer (d or e) is invariably present and a much less intense band is observed near the usual free hydroxyl frequency of 3530 cm^{-1}. These acids exhibit intramolecularly bonded OH-stretching frequencies which depend much more strongly on the nature of other substituents than in the case of the unbonded acids. The basicity of the methoxyl group as well as the acidity of the carboxyl group affect the observed bond in a predictable manner. Thus, an additional methoxyl oriented *para* to the existing *o*-methoxy group as in 2,5-dimethoxybenzoic acid (**47**) lowers the bonded frequency by 26 cm^{-1} since its main effect is to increase the basicity of the 2-methoxy substituent and improve the bond. On the other hand, when the methoxyl is placed *para* to the carboxyl group as in 2,4-dimethoxybenzoic acid (**48**), the acidity of the carboxyl is correspondingly reduced and the hydrogen bond is shifted 20 cm^{-1} toward higher frequencies. The two effects nearly cancel each other in the case of 2,4,5-trimethoxybenzoic acid (**49**) and 2-methoxy-4,5-methylenedioxybenzoic acid (**50**). The slight shift observed relative to *o*-methoxybenzoic acid (*ca.* 4 cm^{-1}) can be calculated almost exactly by adding the opposing effects.



Placement of the additional methoxyl group adjacent to the existing *o*-methoxy as in 2,3-dimethoxybenzoic acid (**51**) also strengthens the hydrogen bond by in-

Table III. Infrared Hydroxyl-Stretching Frequencies of *o*-Alkoxy Aromatic Acids

	Acid	Frequency, cm^{-1} (half-intensity bandwidth) Free	Bonded	Intensity ratio, bonded/free
46	2-Methoxybenzoic	3533 (31) [lit. 3523[2]]	3366 (75) [lit. 3362[2]]	15
47	2,5-Dimethoxybenzoic	3535 (30)	3340 (80)	23
48	2,4-Dimethoxybenzoic	3539 (35)	3386 (60)	12
49		3530 (30)	3364 (77)	13
50		3530 (35)	3362 (75)	12
51	2,3-Dimethoxybenzoic	3530 (25)	3267 (82)	12
52	2,3,4-Trimethoxybenzoic	3537 (30)	3285 (77)	10
53		3534 (32)	3342 (80)	7
54		3535 (33)	3278 (78)	2.5
55		3532 (30)	3313 (92)	6
56		3532 (39)	3404 (42)	1.1
57		3527 (38)	3340 (60)	0.2
58		3531 (30)	3359 (70)	11
59		3533 (32)	3296 (82)	1.4
60		3529 (24)		

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(34) P. R. Wulf, U. Liddel, and S. B. Hendricks, *J. Am. Chem. Soc.*, 58, 2287 (1936).

(35) S. H. Bauer and R. M. Badger, *J. Chem. Phys.*, 5, 839, 852 (1937).

(36) M. M. Davies, *Trans. Faraday Soc.*, 36, 333 (1940).

creasing the basicity of the bonded 2-methoxy group. However the shift is 73 cm^{-1} greater than expected, compared to 2,5-dimethoxybenzoic acid (**47**), and this may be due to steric compression of the hydrogen-bonded system which results in shorter internuclear distance. Even a methyl group flanking the *o*-methoxy as in 2-methoxy-3-methylbenzoic acid (**54**) shows this effect, and the acid exhibits a band at 3278 cm^{-1} compared with *o*-methoxybenzoic at 3366 cm^{-1}. In this case, the compressive influence is not accompanied by as large an increase in the basicity of the *o*-methoxy group. As a consequence, the concentration of the unbonded rotamer, which has less steric strain, is apparently increased since a band equal to half the intensity of the bonded band appears at the unbonded frequency (3535 cm^{-1}).

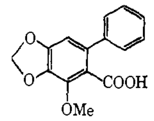
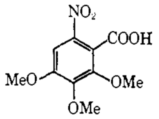
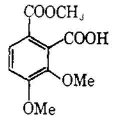
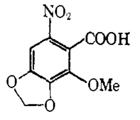
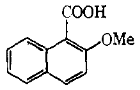
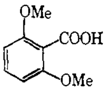
The compressive effect is not further augmented by another flanking group on the same side since 2,3,4-trimethoxybenzoic acid (**52**) absorbs at 3285 cm^{-1}, exhibiting only the 18-cm^{-1} shift to higher frequencies expected from the acid-weakening effect of the 4-methoxy group. On the other hand, when the compression is diminished by converting two of the methoxyls to a methylenedioxy system as in 2-methoxy-3,4-methylenedioxybenzoic acid (**53**), the frequency is raised to 3342 cm^{-1}, indicating relief of about one-half of the compression. Adding another methoxyl to this system as in 2,5-dimethoxy-3,4-methylenedioxybenzoic acid (**55**) increases the basicity of the 2-methoxy and lowers the frequency by 29 cm^{-1} (to 3313 cm^{-1}), just as expected from consideration of the difference between *o*-methoxybenzoic acid and 2,5-dimethoxybenzoic acid (**47**) itself.

An additional ring fused in the 4 and 5 positions as in 3-methyl-2-naphthoic acid (**58**) results in the cancellation of electronic effects as in the case of 4,5-dialkoxy-2-methoxybenzoic acids (**49** and **50**), and only a 7-cm^{-1} shift to lower frequencies relative to *o*-methoxybenzoic acid is noted. But when the new ring is fused to the 3 and 4 positions as in 1-methoxy-2-naphthoic acid (**59**) an analogous compressive influence is again observed, lowering the bonded absorption by 70 cm^{-1}. As in the above case of 3-methyl-2-methoxybenzoic acid, the band at 3533 cm^{-1} due to unbonded rotational configurations becomes appreciable, and amounts to nearly half the intensity of the bonded form. No hydrogen bond is detected in 8-methoxy-1-naphthoic acid (**60**) which has only one OH absorption band at 3529 cm^{-1}. Apparently formation of a seven-membered ring combined with unfavorable dipole orientation is not compensated by hydrogen bond formation.

The effect of nitro groups in weakening the hydrogen bond by reducing the basicity of the methoxyl group is interesting. The bonded band in 5-nitro-2-methoxybenzoic acid (**56**) is at the highest frequency (3404 cm^{-1}) encountered in this study and has the smallest bandwidth (42 cm^{-1}) in the series. This relatively poor hydrogen bonding situation is confirmed by the presence of an unbonded band of equal intensity at 3532 cm^{-1}, in spite of the absence of steric effects. When the compressive effect is also present as in 3-nitro-2-methoxybenzoic acid (**57**), the free OH band at 3527 cm^{-1} is much more intense than the bonded band. However the expected compressive shift of 64 cm^{-1} is still operating and a weak band is observed at 3340 cm^{-1}.

Substitution of the *o*-methoxybenzoic acids on the carboxyl side leads to the complete elimination of intramolecular hydrogen bonding[37,38] in every case studied (Table IV), and this observation clarified the ambiguity surrounding the ambelline acid (**3**). Even the relatively small steric requirement of an adjacent fused ring as in 2-methoxy-1-naphthoic acid (**64**) is sufficient to prevent bonding. Steric compression from the methoxy side is not effective in overcoming the inhibition to bonding, as examples **3** and **61–63** show. Most dramatic, perhaps, is the observation that the carboxyl group of 2,6-dimethoxybenzoic acid (**65**) is not bonded to either available methoxyl group. In all of these cases, it is assumed that the carboxyl group is necessarily forced out of the plane of the benzene ring and that hydrogen bonding to an adjacent methoxyl group would have to accommodate a nonplanar system with unfavorable bond angles.

Table IV. Infrared Hydroxyl-Stretching Frequencies of Sterically Hindered *o*-Alkoxybenzoic Acids

Acid		Frequency, cm^{-1} (half-intensity bandwidth) Free
3		3522 (28)
61		3520 (32)
62		3541 (31)
63		3521 (32)
64		3521 (24)
65		3525 (27)

In an effort to define further the steric limits of inhibition to bonding as illustrated by 2,6-dimethoxybenzoic acid, the related phenolic acids and esters were investigated (Table V). As Jenkins[39] has pointed out, 2,6-dihydrobenzoic acid is 5000 times as strong as benzoic acid itself. This fact is undoubtedly due to stabilization of the anion by double hydrogen

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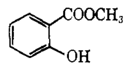
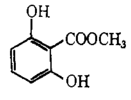
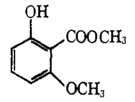
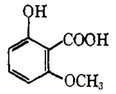
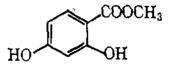
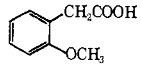
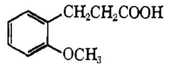
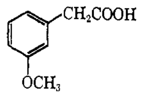
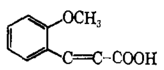
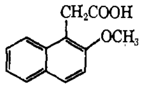
(37) A similar inhibition of bonding has been noticed in the case of 2-methyl-6-nitrophenol by V. Baliah and M. Uma, *J. Indian Chem. Soc.*, **39**, 808 (1962).

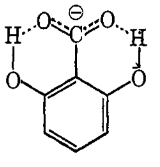
(38) For other cases of the inhibition of hydrogen bonding see L. Hunter, *Progr. Stereochem.*, **1**, 232 (1954).

(39) H. O. Jenkins, *Nature*, **151**, 561 (1943).

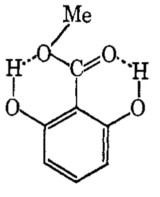
Table V. Infrared Hydroxyl-Stretching Frequencies of Phenolic Acids and Esters and Phenylacetic Acids

	Acid	Frequency, cm^1 (half-intensity bandwidth) Free	Bonded
66		...	3200 (98)
67		...	3472 (34), 3210 (~107)
68		...	3050 (~100)
69		...	3290 (~65)
70		3602 (21)	3161 (~130)
71		3537 (25)	
72		3535 (24)	
73		3533 (26)	
74		3540 (25)	
75		3535 (26)	

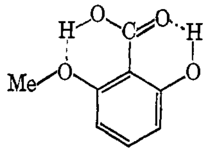
bonding as in f.[32] The methyl ester of this acid, **67**, shows two strongly bonded hydroxyls (g); the one at 3472 cm^{-1} is assigned to the OH··· OMe bond (compare the free OH bond of phenol at 3600 cm^{-1}) and the one at 3210 cm^{-1}, similar in frequency to the band at 3200 cm^{-1} in methyl salicylate (**66**), is assigned to the OH··· O=C linkage. The total steric repulsions in this phenolic ester are less than in 2,6-dimethoxybenzoic acid by one methyl group, while the bonding energy is approximately doubled by the formation of two hydrogen bonds. In the monoether, 2-hydroxy-6-methoxybenzoic acid (**69**), double hydrogen bonding is also allowed (h) since steric crowding is again reduced by one methyl group, and a broad band encompassing both hydroxyl interactions is seen at 3290 cm^{-1}. In this case, bonding from the phenol to the adjacent carbonyl of the carboxyl group has increased the acidity of the carboxyl proton improving the bond to the adjacent methoxyl and lowering its frequency. On the other hand, the OH frequency arising from the phenolic hydroxyl is raised compared with methyl salicylate since bonding is occurring to the less basic carboxyl carbonyl.



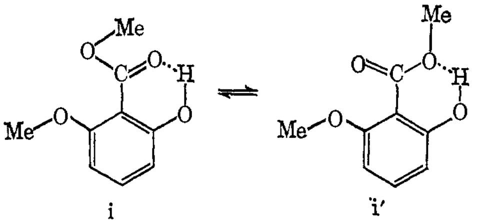
f



g



h



i ⇌ i′

Consideration of methyl 2-hydroxy-6-methoxybenzoate (**68**) allows a direct comparison, in terms of steric bulk, with 2,6-dimethoxybenzoic acid. The compound is strongly hydrogen bonded (i,i′). The band is extremely asymmetrical, but a maximum is observed at 3050 cm^{-1}, indicating a high degree of compression relative to methyl salicylate (3200 cm^{-1}). The phenolic system (**68**) has four π-bonded atoms compared to three in the related 2,6-dimethoxybenzoic acid and also has more favorable dipole orientations. Both factors are probably important in allowing the observed strong hydrogen bonding. The asymmetrical nature of the bond may be due to overlapping of bonds from rotational isomers i and i′.

Finally, a series of methoxyphenylacetic, methoxyphenylpropionic, and methoxycinnamic acids were considered (**71–75**) but no hydrogen bonding was observed. It is assumed that loss of several degrees of rotational freedom as well as an unfavorable seven- or eight-membered ring are factors in preventing bonding.