Stereoelectronic substituent effects on intramolecular H-bonding in crowded *o*-anisic acids †

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The minimum energy geometries, OH stretching frequencies, and fractional distributions of the free and intramolecularly hydrogen-bonded conformers of eleven substituted *o*-anisic acids were determined by density functional theory. The structural changes that are associated with formation of the intramolecular H-bond are discussed. Intensities and areas of pertinent peaks in the measured infrared spectra were used to obtain the mol fractions of the intramolecularly H-bonded conformer, in equilibrium with the intermolecularly H-bonded dimers in chloroform solution. These mol fractions follow the same order as the theoretically determined "gas phase" values. They also correlate linearly with the change in the time-averaged ^{13}C NMR shift of the carboxyl group that is produced by a change of solvent from DMSO to CDCl$_3$. The same solvent change leads to an increase in the size of the one-bond C–H coupling constant of the methoxy group because of the greater polarization of the its H–C bonds in the intramolecular H-bonded conformer. The solvent-induced changes in the CH$_3$O coupling constant correlate with those of the *ipso* **C2**-OMe shift. The latter shift changes involve opposing effects of *intra*- and *inter*molecular H-bonding of the *o*-anisic acids.

Intramolecular H-bonding plays a pivotal role in numerous chemical and biochemical processes. It is often the dominant force that stabilizes the secondary structures of many bio-molecules, that maintains the conformations necessary for the chemical functionality of flexible macromolecules, and that determines the shapes of crystalline substances. The formation of an intramolecular H-bond in any given molecule may involve a careful balance between the effects of steric crowding, dipole–dipole interactions, electron pair repulsions, and sometimes resonance. This paper evaluates the relative importance of these factors in the intramolecular H-bonding of crowded *o*-methoxybenzoic acids. These molecules are of interest because of the limited flexibility and particular disposition of their proton donor/acceptor pair which especially favor the formation of a stable 6-atom chelate ring.

The present work shows how substituents of varying steric and electronic requirements influence the molecular geometry, conformer distribution, and intramolecular H-bonding of the substituted 2-methoxybenzoic acids **1**, **2**, and **3**. Although an IR spectroscopic study[1] of these acids appeared in 1966, and a scattered few of them have been the subject of NMR[2a–c] or X-ray analyses,[3] this investigation provides a more focused analysis of this series by the combined use of IR and ^{13}C NMR spectroscopy and molecular orbital calculations.

A recent theoretical study,[4] involving a variety of computational methods, gives geometries and conformational preferences of several of the anisic acids investigated here. A comparison with the extant IR data shows these calculations to either grossly overestimate, or underestimate, the propensity of the anisic acids to undergo intramolecular H-bond form-
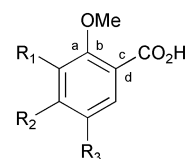
1a, R$_1$ = R$_2$ = R$_3$ = H
  b, R$_1$ = R$_2$ = H, R$_3$ = OMe
  c, R$_1$ = R$_3$ = H, R$_2$ = OMe
  d, R$_1$ = R$_2$ = H, R$_3$ = NO$_2$

2a, R$_1$ = *t*-Bu, R$_2$ = H, R$_3$ = Me
  b, R$_1$ = Me, R$_2$ = R$_3$ = H
  c, R$_1$ = NO$_2$, R$_2$ = R$_3$ = H
  d, 1-methoxy-2-naphthoic acid

3a, R$_1$ = OMe, R$_2$ = R$_3$ = H
  b, R$_1$ = R$_2$ =OMe, R$_3$ = H
  c, R$_1$ - R$_2$ = O-CH$_2$-O, R$_3$ = H

ation. In the present work, use of density functional theory in conjunction with a higher basis set gives results that are much more in line with the experimental findings.

Results and discussion

Computational studies

The lowest energy conformations of anisic acids **1–3** were found to be the intramolecularly hydrogen-bonded form **A** and the non-bonded conformers **B** and **C**. Their geometries were determined by using density functional theory (B3-LYP) with the 6-31g(d, p) basis set. Pertinent structural parameters are summarized in Tables 1 and S1 (see Electronic supplementary information (ESI)†). Each of the three conformations of sterically unhindered anisic acids **1** exhibit approximately all-planar geometries. However, substituting R for H at C3 (**1** → **2**, **3**) forces the Me–O bond to rotate out from the molecular

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Table 1 Selected geometric parameters and conformer distributions of anisic acids **1**–**3**

Compound, conformer	Mol fraction (298.15 K)	ΔE/kcal	∠C1–C2–O–Me (a)	∠C2–C1–C–OH	d(MeO···HO,OH,O=C)
1a, A	0.8875	0.00	180.0	0.0	1.7492
1a, B	0.0644	1.55	180.0	0.0	2.5967
1a, C	0.0481	1.73	180.0	180.0	2.6828
1a, X-ray			174.9	174.8	2.927
1b, Aa	0.8171	0.00	−180.0	0.0	1.7425
1b, Ba	0.0223	2.13	180.0	0.0	2.5999
1b, Ca	0.0086	2.70	180.0	−180.0	2.6835
1b, As	0.1437	1.03	−180.0	0.0	1.7423
1b, Bs	0.0048	3.04	180.0	180.0	2.5992
1b, Cs	0.0036	3.22	180.0	0.0	2.6856
1c, Aa	0.6848	0.00	180.0	0.0	1.7601
1c, Ba	0.0625	1.42	180.0	180.0	2.6068
1c, Ca	0.0431	1.64	180.0	180.0	2.6946
1c, As	0.1652	0.84	179.0	0.0	1.7619
1c, Bs	0.0246	1.97	−180.0	0.0	2.6025
1c, Cs	0.0197	2.10	−180.0	180.0	2.6946
1d, A	0.3799	0.00	180.0	−0.1	1.7683
1d, B	0.2596	0.23	180.0	−0.1	2.5965
1d, C	0.3605	0.03	180.0	−180.0	2.6778
2a, A	0.1462	0.93	−76.5	−16.3	1.8299
2a, B	0.1554	0.89	−65.4	−20.1	2.7418
2a, X-ray			59.6	166.7	2.795
2b, A	0.6488	0.00	96.2	11.0	1.7663
2b, B	0.0902	1.17	87.3	−2.5	2.6844
2b, C	0.2610	0.54	87.4	161.9	2.8237
2c, A	0.3646	0.06	−93.3	−13.9	1.7876
2c, B	0.2339	0.32	−86.1	−2.4	2.6788
2c, C	0.4015	0.00	−88.2	−161.9	2.8135
2d, A	0.6100	0.00	−95.2	−10.5	1.7783
2d, B	0.1315	0.91	−87.1	3.4	2.6808
2d, C	0.2585	0.51	−84.2	−165.4	2.8086
2d, X-ray			−90.1	−175.8	2.728
3a, A	0.9054	0.00	−111.0	−7.9	1.7373
3a, B	0.0363	1.91	−106.2	19.4	2.6845
3a, C	0.0551	1.66	101.5	155.7	2.8159
3a, X-ray			108.2	−36.7	2.797
3b, A	0.8886	0.00	112.1	6.0	1.7486
3b, B	0.0497	1.71	104.3	−13.0	2.6875
3b, C	0.0617	1.58	98.2	161.9	2.8152
3c, A	0.8458	0.00	−131.9	−3.8	1.7508
3c, B	0.0724	1.46	−119.8	15.4	2.6759
3c, C	0.0818	1.38	93.7	162.0	2.8255
2a, C	0.6984	0.00	47.6	−163.4	2.8981

plane. The degree of rotation, *a*, varies with R and the particular conformation. Most of the 3-substituted anisic acids **2** and **3** have Me–O–Ar and benzene planes that are *ca.* mutually perpendicular (*a* ≈ 90°, within 6°). Only in **2d** and **3a**–**c** is the methoxy plane significantly tilted in the direction of the less spatially demanding, proximate substituent (**2d**, *a* = 48–77°; **3a**–**c**, up to 131°). The carboxyl moiety adjacent to the out-of-plane methoxy substituent of **2** and **3** also deviates somewhat from coplanarity with the benzene ring, especially in the non-cyclic structures **B** and **C** (Table 1).

A **B** **C**

A *a*,**B**a,**C**a(*anti*)   **As**,**Bs**,**Cs**(*syn*)
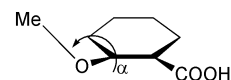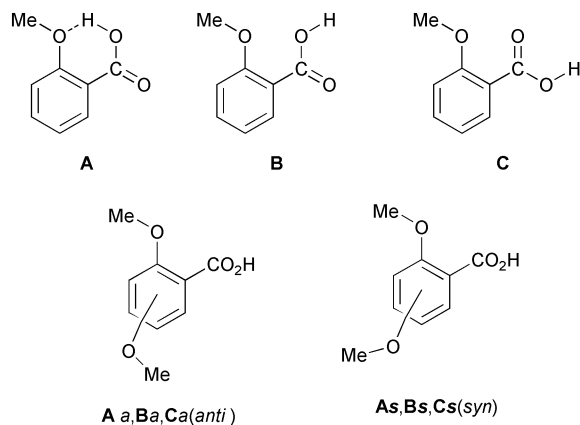
In the case of the planar dimethoxy-substituted acids **1b** and **1c** there are six minimum energy conformations because conformers **A**, **B**, and **C** can each have two possible orientations of their methoxyl methyl groups—either *syn* or *anti* with respects the line joining their oxygens. Recent NMR NOE experiments [2a] suggest a net *anti:syn* ratio of 3:1 for the sum of all conformers of **1b** in chloroform solution. The data for **1c** were ambiguous. The corresponding theoretical ratios, calculated here from the energy distributions of all *syn* and *anti* forms of **A**–**C** (Table 1), are 5.6:1 for **1b** and 3.8:1 for **1c**.

Non-H-bonded conformers **B** and **C** of **1**–**3** differ mainly in the separation between their methoxyl– and nearest carboxyl–oxygen (O=C or OH; See Table 1), which is shorter in **B** than it is in **C**, and in the C2–C1–CO2H angle *c*, which in **B** is splayed by 4–6° beyond 120°, but by only 1–2° in **C** (Table S1 †). As a consequence there must be greater O···O electron pair repulsion and angle strain in **B** and, indeed, it is this conformer of **2** and **3** which turns out to be the higher energy structure. In planar anisic acids **1**, the O···O distances of **B** and **C** are more nearly identical and *ca.* 0.1 Å shorter than they are in **2** and **3**, because of steric strain between the in-plane methoxyl methyl group and nearest *ortho* hydrogen. Here theory predicts **B** to be the more stable form. The dipole moments of conformers **B** are

consistently larger than those of conformers **C** for anisic acids having non-polar substituents, but they are much smaller than the value for the intramolecularly H-bonded form **A**. It is interesting that the X-ray structures reported for **1a**,[3a,b] **2a**,[3c] **2d**,[3d,e] and **3a**[3f] are all **C** conformers, intermolecularly H-bonded, as is usual for carboxylic acids in the solid state, with C2–C1–CO$_2$H angles that are within 0.5–2° of those calculated here.

Intramolecular H-bonding—**B**, **C** → **A**—slightly elongates the carboxyl H–O bond (d_{OH} in Table S1 †) in accord with observations on intermolecularly H-bonded carboxylic acids.[5] In addition, the exocyclic bonds to the COOH and CH$_3$O groups lengthen by *ca.* 0.02 Å (Table S1 †). This helps to reduce potential strain within the 6-membered chelate ring and also suggests that there may be a decrease in methoxy → aryl and aryl → carboxyl resonance. Such a curtailment of resonance should enhance the acid–base properties of the proton donor–acceptor pair and lead to a stronger H-bond. In contrast, the Ar–OMe bond lengths of additional methoxy groups, as in **1b**, **1c**, **3a**, and **3b**, are not altered in the process of H-bonding.

Only when R = ᵗbutyl (**2a**) or alkoxy (**3a–c**) does formation of the H-bond alter the orientation of the proton accepting methoxy group. In these cases the methoxyl plane tilts further away from the COOH group (larger value of *a*), becoming more nearly perpendicular to the aromatic ring in **2a**, but more coplanar in **3**. These rotational changes, which are of the order of 10–40°, help to better position the oxygen electronic charge in the direction of the carboxyl proton donor. The COOH group of alkoxy-substituted anisic acids **3** also rotates by 10–15° toward coplanarity with the aromatic ring (∠C2–C1–C–OH of Table 1), thereby reducing the distance between the methoxy oxygen and the COOH hydrogen on the distal side of the methoxyl methyl group.

Intramolecular H-bonding in **1**, **2**, and **3** lowers the calculated frequency of the carboxyl OH stretching vibration in accord with the experimental findings. Such a shift in frequency is often cited as an index of the H-bond strength. Fig. 1a (and Table S1 †) shows that there is an inverse linear relationship between the calculated frequencies of H-bonded conformer **A** and the computed length of its covalent H–O bond. For comparison, the experimentally measured frequencies of **1**–**3** in CCl$_4$[1] and in CHCl$_3$ (this study) are also plotted. The slopes of the theoretical and experimental frequency data are similar, and the sequence of correlation lines along the *y*-axis—γ_{OH}:calculated ("free") > gaseous phase > CCl$_4$ > CHCl$_3$—follows the partial order previously reported for the solvation of H-bonded alcohol–ether pairs.[6] However, for **1**–**3** in each of the two solvents, plotting the experimentally measured frequencies *versus* the theoretically determined ones (Fig. 1b) produces *two* correlation lines, with a much improved fit of the data. The line at the higher experimental frequencies involves anisic acids having a polar (NO$_2$ or RO) substituent *ortho* to the methoxyl proton acceptor. The other is that of the remaining acids, those having a non-polar substituent at C3, or with polar groups elsewhere in the molecule. This splitting of the frequency data may be due to the influence that specific solvation of a proximate polar substituent has on the strength of the H-bond, and/or density functional theory is unable to adequately model through-space electrical interactions between neighboring groups.

Fig. 2 is a plot of γ_{OH} *versus* the H-bond length, d(MeO···HO), which clearly shows that the OH stretching frequencies of conformers **A** are 50–150 cm^{-1} higher for anisic acids **1** than for **2** or **3** with comparable MeO···HO separations. Evidently, anisic acids with in-plane methoxyl groups form weaker intramolecular H-bonds than those having the proton acceptor rotated out from the aromatic plane. The data point for H-bonded **3c** lies between the correlation lines of
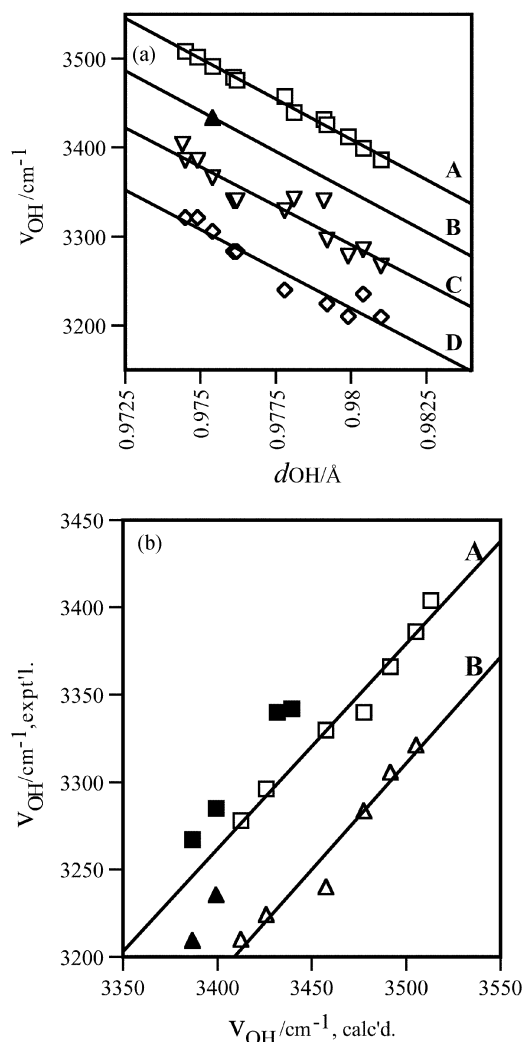

Fig. 1 (a) Calculated OH stretching frequency *vs.* length of the carboxyl OH bond: (A) calculated, (B) gas phase, (C) CCl$_4$, (D) CHCl$_3$. (b) Experimental *vs.* calculated OH stretching frequencies of **1**–**3**: A: CCl$_4$; B: CHCl$_3$.
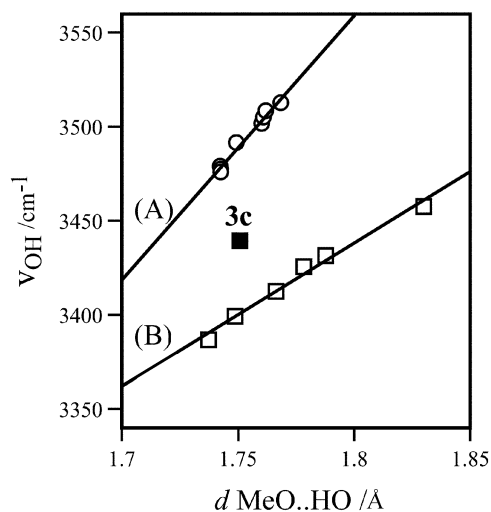

Fig. 2 Calculated HO frequency *vs.* length of the intramolecular H-bond of anisic acids **1** (A), **2** and **3a**–**b** (B).

anisic acids with in- and out-of-plane methoxyl groups. The H-bond length of **3c** is like that of **1a** and **3b** (1.75 Å), and the through-bond substituent effects on the acid–base strengths of its donor–acceptor pair cancel, as they do in **3b**.[1] If the differences in the values of γ_{OH} for **1a**, **3b**, and **3c** are mainly due to

variations in the extent of methoxy–aryl resonance,‡ then γ_{OH} for a given H-bond length will correlate with $\cos^2 a$.[3c] By using the values of γOH of **1a**, **3b**, and **3c**, together with the angles a of **1a** and **3c** obtained from their computed geometries, one derives§ an angle a of 44° for conformer **A** of **3c**. This value is in excellent agreement with the 48°—figure obtained directly through geometry optimization.

The theoretical treatment predicts higher carbonyl stretching frequencies for conformers **C** than for **B**, as found experimentally,[8] but, unlike experimental observations, the values for intramolecularly H-bonded **A** are the highest of all (Table S1†). The CO extinction coefficients of **A**, **B**, and **C** are nearly identical, in accord with the data on simple carboxylic acids.[9,10] However, there is a modest 2-to-4-fold increase in the intensity of the OH stretching vibration on H-bond formation. This factor is much smaller than the 10–35-fold increase reported for *inter*molecular H-bonding of carboxylic acids,[11] and accords with trends observed for other intra- *vs.* intermolecularly H-bonded systems.[12]

The fractional distribution of conformers **A**–**C** of **1**–**3** at 25 °C (Table 1) was derived from the computed single-point energies, obtained by using a higher basis set and the previously determined geometries (B3-LYP/6–311+G(2df,p)//B3-LYP/6-31G(d,p) + ZPVE). A plot of γ_{OH} of H-bonded **A** *versus* its computed mol fraction f_A (Fig. 3) shows separate inverse linear
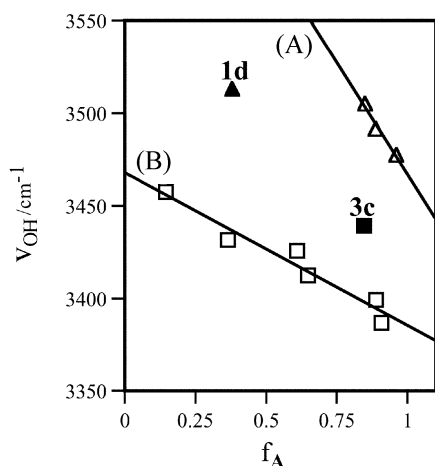

Fig. 3 HO stretching frequency of conformer **A** *vs.* mol fraction of **A**. (A): **1**; (B): **2**, **3**.

relationships for the planar and non-planar acids, **1** and **2**–**3**. Thus, within each set, the preference for the intramolecularly H-bonded form **A**, in equilibrium with **B** and **C**, depends directly on the strength of its H-bond. Again, the point for **3c** deviates from the correlation lines, as does that of the *p*-nitro-substituted anisic acid **1d** (*vide infra*).

Evident in Fig. 3 is the unexpectedly high preference on the part of planar anisic acids **1** for conformer **A** over **B** and **C**. This is, at first, surprising, given that the intramolecular H-bond of in-plane methoxy groups was found to be weaker than that of groups rotated out from the molecular plane. The particularly unfavorable geometries of conformers **B** and **C** of **1** may be the reason. Here the MeO···O (–H, =C) separations are *ca.* 0.1–0.2 Å shorter than they are in the corresponding open forms of anisic acids **2** and **3** (Table 1). Consequently, the

‡ In simple anisoles, a 90° rotation of the methoxy group reduces CH₃O ⟶ Ar resonance by *ca.* 40%, which causes a four-fold increase in the value of the equilibrium constant for intermolecular H-bonding with TFA.[3b,7]
§ The linear relationship, $\gamma_{OH}(r = 1.75 \text{ Å})/\text{cm}^{-1} = 107.6\cos^2 a + 3384$, is derived from the calculated values: 3491.6 cm⁻¹; 180° and 3399.3 cm⁻¹; 112.1° for $\gamma_{OH}(r = 1.75 \text{ Å})/\text{cm}^{-1}$; a of **1a** and **1c**. Substituting = 3439.3 cm⁻¹, the calculated value for **3c**, gives 44° for a of **3c**.

destabilizing repulsive O···O interactions in **B** and **C** of planar anisic acids **1** must be more severe than in the case of **2** and **3**, so that conformer **A** becomes, by default, the favored equilibrium structure of **1**. The unusually low value of f_A for *p*-nitro-anisic acid **1d** accords with this interpretation, 0.380 instead of 0.819, as predicted from the correlation line of series **1** in Fig. 3. In this molecule, extensive mesomeric electron withdrawal from the methoxy oxygen by the conjugated NO₂ group reduces the size of the O···O repulsions in conformers **B** and **C**, thereby shifting the equilibrium in their favor.

IR measurements

The equilibrium distributions of H-bonded **A**, free monomer, and acid dimer in 0.002–0.2 M chloroform solutions of **1**–**3** were estimated by using the measured ratios of the monomer:dimer carbonyl peak areas and OH intensities, A_r^{CO} and I_r^{OH}, of the IR spectra, and the corresponding ε_r^{OH} ratios furnished by the *ab initio* calculation. Assuming identical carbonyl extinction coefficients for all species in solution, one obtains f_{HB}, the fraction of intramolecularly H-bonded conformer **A** at a given concentration:

$$f_{HB} = A_r^{CO} I_r^{OH} (\varepsilon_r^{OH})^{-1} / (1 + I_r^{OH}(\varepsilon_r^{OH})^{-1})(1 + A_r^{CO}) \quad (1)$$

By extrapolating plots of f_{HB} *versus* the stoichiometric concentration of the anisic acid, one derives approximate values for f_A(exp), the mol fraction of H-bonded **A** of **1**–**3** at the 0.5 M concentration at which ¹³C NMR measurements were subsequently made. At this concentration the primary species in solution are H-bonded **A** plus the *inter*molecularly H-bonded cyclic dimers of **B** and/or **C**. As seen in Table 2, these estimates follow the same sequence as the computed f_A values derived from the Boltzman distributions of the equilibrium between **A** and monomeric forms **B** and **C**.

NMR measurements

Tables 2 and S2† summarize pertinent ¹³C NMR shift data and one bond C–H(OMe) coupling constants for 0.5 M solutions of **1**–**3** in DMSO and CDCl₃. In DMSO all anisic acids are apparently in the form of monomers **B** or **C**, intermolecularly H-bonded with the solvent; their ¹³C chemical shifts are unaffected by a decrease in concentration and their methoxyl shifts differ by less than 0.2 ppm from those of some corresponding methyl esters in CDCl₃. In chloroform all shifts become concentration dependent because now each is the weighted average of the shifts of conformer **A** and of the corresponding intermolecularly H-bonded acid dimer, in rapid equilibrium with each other. As seen in Fig. 4, the changes
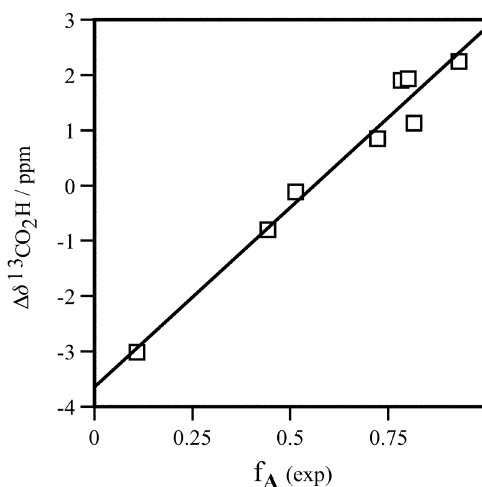

Fig. 4 Change in the ¹³C NMR shift of COOH of **1**–**3** *vs.* the experimental mol fraction of **A**.

Table 2 Fraction of intramolecularly H-bonded conformer **A**, values of ΔJ_{MeO}/Hz[a], and $\Delta\delta^{13}$Ci/ppm,[b] **1–3**

Compound	f_A,calc	f_A(exp)	ΔJ_{MeO}/Hz	$\Delta\delta^{13}$COOH	$\Delta\delta^{13}$CH$_3$O	$\Delta\delta^{13}$C2$_{(MeO)}$	$\Delta\delta^{13}$C1$_{(COOH)}$
1a	0.8875	0.800	1.81	−1.934	0.402	−0.410	−4.325
1b	0.9608 (*syn* plus *anti*)	0.926	2.10	−2.248	0.324	−0.420	−4.415
1c	0.8501 (*syn* plus *anti*)	0.815	1.66	−1.123	0.317	−1.436	−2.874
2a	0.1462	0.108	0.58	3.019	1.086	1.326	−3.228
2b	0.6488	0.515	1.38	0.118	0.478	0.032	−4.124
2d	0.6100	0.443	0.99	0.806	0.558	1.067	−3.128
3a	0.9086	0.783	2.48	−1.903	0.819	−1.393	−5.581
3b	0.8886	0.722	2.42	−0.845	0.482	−1.021	−4.417

[a] $\Delta J_{MeO} = (J_{MeO}, 0.5$ M CDCl$_3) - (J_{MeO}, 0.5$ M DMSO). [b] $\Delta\delta^{13}$Ci $= \delta^{13}$Ci (0.5 M CDCl$_3) - \delta^{13}$Ci (0.5 M DMSO).

in the carboxyl carbon shifts of **1–3** in 0.5 M solutions—$\Delta\delta^{13}$COOH (= δ^{13}COOH (CDCl$_3$) − δ^{13}COOH (DMSO))—correlate linearly with the mol fractions f_A(exp), obtained from the IR measurements for H-bonded **A** in 0.5 M CHCl$_3$. The fit of the data is surprisingly good, given the errors inherent in extrapolating the IR data to higher concentrations and the difficulty of accurately determining areas and intensities of IR peaks. Because all anisic acids—both planar and non-planar—obey the correlation, the $\Delta\delta^{13}$COOH values must be sensitive essentially only to the change in environment of the carboxyl group—from the DMSO-solvated monomer to the *intra-* and/or *inter*molecularly H-bonded structures. The intercept of Fig. 4 is 3.642 ppm and represents the downfield movement of the carboxyl resonance on full conversion of the DMSO-solvated monomers of **B** and/or **C** to their *inter*molecularly H-bonded dimers. This value is satisfactorily close to the 3.86 ppm figure that one obtains for the corresponding shift change of *p*-anisic acid. The slope of Fig. 4 (6.498 ppm) is the size of the upfield shift of the COOH resonance of the *intra*molecularly H-bonded conformer **A** from that of the **B**, **C** dimers in chloroform solution.

H-bonding of methoxyl oxygens increases the polarization of the C–H and C–O bonds, causing the CH$_3$O carbon resonance to move downfield, as observed in the complexing of anisoles with TFA.[7] For **1–3**, a change of solvent from DMSO to CDCl$_3$ likewise causes deshielding of the OMe group, by 0.3–1.1 ppm, due to the presence of the intramolecularly H-bonded conformer **A** in chloroform solutions. At the same time the *ca.* 144 Hz one-bond C–H coupling constant of the chelating CH$_3$O group increases by 0.6–2.5 Hz. In contrast, the solvent-induced changes in δCH$_3$O and J_{OMe} of methoxy substituents, located elsewhere in the molecule and, thus, not involved in intramolecular H-bonding, are much like those of simple anisoles—small (0–0.2 ppm; <0.2 Hz) and generally negative. A small, but consistent increase in the calculated value of the symmetrical methoxyl C–H stretching frequency for the conversion of **B**, **C** to **A** (γ_{H-C-O} of Table S1 †) accords with the higher dipolar character predicted for the C–H bond in H-bonded **A**.

The **C1**(COOH) resonance of anisic acids **1–3** moves 2.9–5.5 ppm upfield on changing the solvent from DMSO to CDCl$_3$ (Table 2). Shielding of this *ipso* carbon is an expected consequence of the participation of the COOH group in both *inter-* or *intra*molecular H-bonding as it involves loss of negative charge from the carboxyl carbon.[13,14] In contrast, the solvent-induced shift changes of the **C2**–OMe *ipso* carbon of **1–3** range over ±1.5 ppm. In the dimerization of simple benzoic acids (with a change of solvent, DMSO → CDCl$_3$) and the hydrogen bonding of anisoles with TFA, the respective *ipso* carbon resonances uniformly experience shielding while the remaining aromatic carbon resonances move downfield. Thus for the bifunctional *o*-anisic acids **1–3**, the solvent-induced changes $\Delta\delta$C1 and $\Delta\delta$C2 must involve the opposing influences of *intramolecular* H-bonding of the methoxy and carboxyl groups in conformer **A**, plus the effects of carboxyl group dimerization, each weighted according to the relative abundance of **A** and dimerized **B** and/or **C** in the equilibrium mixtures.
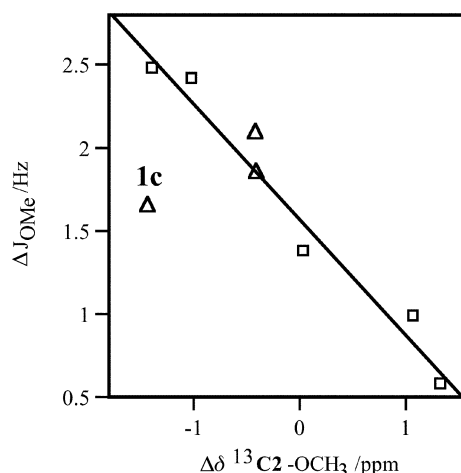

Fig. 5 Change in the one-bond C–H coupling constant, ΔJ_{OMe}, *vs.* the ^{13}C NMR shift change, $\Delta\delta^{13}$C2-OMe, of **1–3** with a change of solvent, from DMSO to CDCl$_3$. (△) **1**; (□) **2**, **3**.

Fig. 5 demonstrates a fairly good linear relationship between $\Delta^1 J_{MeO}$ and $\Delta\delta$C2(OMe) of **1–3**. Here the larger values of $\Delta^1 J_{MeO}$, and more negative values of $\Delta\delta$C2(OMe), reflect higher proportions of conformer **A** in the equilibrium mixture. Conversely, large downfield shifts of C2 in conjunction with small values of $\Delta^1 J_{C-H}$ signify a preponderance of the acid dimer. It is not clear why the point for 2,4-dimethylbenzoic acid **1c** deviates from the correlation line of Fig. 5. Or, rather, it is surprising that the data for **1a** and **1b** follow so well the correlation of non-planar structures **2** and **3**, given that the strength and the geometry of the H-bond are so different for these two series of *o*-anisic acids.

Experimental

Anisic acids **1a–1c**, **2a,b,d**, and **3a,b** were either prepared by standard methods or were commercial materials used without further purification.

^{13}C NMR spectra of the anisic acids in deuteriochloroform and in DMSO were obtained at an ambient temperature of *ca.* 27 °C by using a General Electric QE300 NMR spectrometer with a Techmac acquisition computer and operating at 75.48 MHz. For measurements in both solvents the peaks were referenced to internal cyclohexane, set at 26.92 ppm, the shift of C$_6$H$_{12}$ in CDCl$_3$ relative to internal TMS¶ Peak assignments were based on the magnitudes of the one- and three-bond coupling constants in the proton-coupled spectra and on the known effects of substituents on the ^{13}C chemical shifts of aromatic systems. The value of the C–H coupling constant, J_{MeO}, of the methoxy substituents was obtained from the proton-coupled spectrum by averaging the three intervals of the quartet. The deviation from this average was ±0.02 Hz or less.

¶ The shifts relative to C$_6$H$_{12}$ of **1–3** in DMSO solution can be converted to the TMS scale by subtracting 0.592 ppm.

Infrared spectra of 0.002–0.2 M solutions in CHCl$_3$ were recorded using a Nicolet Impact 400 Fourier transform instrument equipped with a DTGS detector. Spectra were recorded at 4 cm^{-1} resolution with a zero filling factor of two, boxcar apodization, and averaging between 16 and 640 interferometer scans (16, 32, 64, 160, 640), the number depending on the particular conformer distribution and sample concentration. Cells of 0.05 and 0.5 mm path length were used, as appropriate.

Density functional calculations were carried out using the Gaussian 98 set of programs.[15] Optimized geometries were obtained using the B3-LYP function in conjunction with the 6-31G(d,p) basis set. Harmonic vibrational frequencies and zero point vibrational energy corrections were calculated at this level of theory. These were scaled [16] by factors of 0.9613 and 0.9804, respectively. Relative energies were obtained from single point energy calculations at the B3-LYP/6–311+G(2df,p) level, using the minimized geometries and applying the appropriate zero point energy corrections.

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