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Hydrogen Bonds in Carboxylic Acid–Carboxylate Systems in Solution. 1. In Anhydrous, Aprotic Media

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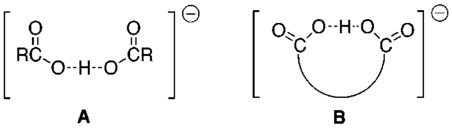
ABSTRACT



Preliminary NMR studies on hydrogen bonding of carboxylic acid–carboxylate systems in an anhydrous, aprotic solvent are presented. In all cases, a low-field resonance (16–20 ppm) indicative of strong hydrogen bonding was observed. From these results, it seems probable that this characteristic downfield shift should be exhibited by all carboxylic acid–carboxylate systems in *anhydrous*, aprotic media.

We have initiated a study of hydrogen bonds in carboxylic acid−carboxylate systems. McAllister has calculated a number of characteristics for the parent system, formic acid−formate.[1] In this system, the optimized gas-phase structure had an energy of about 27 kcal/mol and contained a linear O−H−O unit with an O···O distance of about 2.5 Å. Inclusion of the formic acid−formate unit (**A**) in a polarized cavity reduces the energy to about 12 kcal/mol, which is still well above a normal (weak) hydrogen bond. The extension, compression, and/or bending of the O−H−O moiety all result in lower energy. The degree to which the energy is reduced by this extension or compression suggested considerable covalent character in the bond. Because of the energetics, this bond is considered to belong in the low-barrier hydrogen bond (LBHB) category. LBHBs have been identified and characterized most commonly by means of a low-field NMR peak usually located in a range of 16−22 ppm.[2] This paper presents NMR observations of carboxylic acid−carboxylate systems present in a non-hydrogen-bonding solvent, CD_2Cl_2.

On the basis of McAllister's calculations, it seemed quite reasonable that all monocaboxylic acid−monocarboxylate systems should exhibit strong O−H−O bonds.[3] Initial attempts to observe these signals by NMR were unsuccessful until it was found that trace amounts of water compete with the hydrogen bond. Careful drying resulted in characteristic resonances for benzoic acid−benzoate and substituted benzoic acids−benzoates of approximately 18 ppm with small line widths ($W_{1/2}$ is the width at half-height). Some examples containing an sp^2-hybridized carbon framework are shown in Table 1. It should be noted that there is no hindrance or any other geometric constraint to hydrogen bond formation. The resulting hydrogen bonds should correspond simply to the most stable arrangement, analogous to the formic acid−formate system (**A**).

With the understanding that the carboxyl−carboxylate hydrogen bond is in competition with water, it seemed reasonable that elimination of trace water would allow the observation of hydrogen bonds in *any* carboxylic acid−carboxylate system. Thus, with a number of half-neutralized

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[1] (a) Smallwood, C. J.; McAllister, M. A. *J. Am. Chem. Soc.* **1997**, *119*, 11277−11281. (b) Pan, Y.; McAllister, M. A. *J. Am. Chem. Soc.* **1998**, *120*, 166−169.

[2] Hibbert, F.; Emsley, J. *Adv. Phys. Org. Chem.* **1990**, *26*, 255−379.

[3] The monocarboxylate monosolvates were prepared by addition of 0.5 equiv of tetrabutylammonium hydroxide (1.0 M in methanol) to the carboxylic acid in methanol or tetrahydrofuran. The acid salts of the diacids were prepared by adding 1 equiv of tetrabutylammonium hydroxide (1.0 M in methanol) to a solution of the diacid in tetrahydrofuran. The reagents were left to react for 30 min at room temperature, after which the solvents were removed in vacuo. The resulting salts were dried for 14 h under vacuum at 70 °C. After the acids were converted into their corresponding hemisalts, their NMR spectra were recorded in anhydrous CD_2Cl_2 (0.15 M in 0.5 mL CD_2Cl_2).

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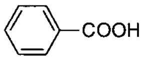
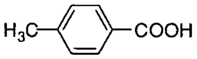
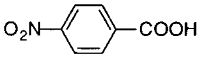
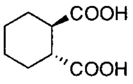
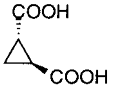
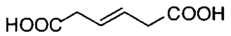
Table 1. Summary of the NMR Data for the Hydrogen-Bonded Proton in $NBu_4[RCOOH·RCOO]$ (ambient temperature, CD_2Cl_2)

Carboxylic Acid		δ (^{1}H) (ppm)	$W_{1/2}$ (Hz)
	**1**	18.27	9
	**2**	18.02	12
	**3**	18.05	9
	**4**	16.96	320
	**5**	16.90	32
	**6**	16.60	27

trans-1,2-diacids, characteristic NMR shifts in the region of 16−17 ppm with varied $W_{1/2}$ were observed. Several salts of *trans*-1,2-dicarboxylic acids containing an sp^3-hybridized carbon framework are shown in Table 1. In these compounds, it is impossible for intramolecular hydrogen bonding to occur due to steric constraints. It should be noted that the hydrogen dicarboxylate of **4** has been reported as not showing any signal downfield between 16 and 22 ppm in a non-hydrogen-bonding solvent.[4] The intermolecular hydrogen bond in this series of compounds exhibits a resonance upfield with a broader $W_{1/2}$ than in our previous examples. This is due to differences in the carbon framework (sp^2- vs sp^3-hybridized carbons) and the number of carboxyl groups. The hybridization of the carbons exhibits an electronic effect on the position of the chemical shift. Furthermore, the proton resonance is a time-averaged signal for all of the carboxylic protons, whether they are hydrogen-bonded or not. There is no possibility for both the carboxylic acid−carboxylate groups in one molecule to be aligned perfectly to form two intermolecular hydrogen bonds with the other carboxylate−carboxylic acid portion of another molecule. Therefore, these resonances appear upfield and broadened with respect to the salts of compounds **1**−**3**. These signals are also concentration dependent. With increasing concentrations, the signals shift further downfield due to aggregation effects (higher order oligomers). In any case, no hindrance to intermolecular hydrogen bond formation is present in the salts of compounds **4**−**6**. The hydrogen bonds formed should be analogous to the formic acid−formate system, i.e., bimolecular but also of LBHB-type (**A**).

In the case of acid salts of *cis*-1,2-diacids and malonic acids, a somewhat different situation exists. To form an intramolecular hydrogen bond, the hydrogen bond must be bent, and the carboxyl groups, and correspondingly the O···O distance, will be compressed by the framework to which they are attached or their attaching bonds will be bent, or both factors will occur. The result is strain not present in the intermolecular cases and absent in the previous systems. Several examples of the hydrogen *cis*-1,2-dicarboxylates, some of which have been reported previously, are shown in Table 2 (**B**).[5] All of these compounds exhibit a downfield resonance in the range of approximately 18−20 ppm.

In aqueous systems for a set of *cis*-diacids with intramolecular hydrogen bonding present in their acid salts, it is assumed that as pK_{a1} decreases, pK_{a2} increases, and, therefore, ΔpK_a increases. Assuming that no special conditions affect pK_{a1} and pK_{a2} separately, the increase in ΔpK_a represents an increase in the strength of the intramolecular hydrogen bond.[6,7] From the reported values in Table 2, no obvious relationship between ΔpK_a and the extent of the shift downfield is apparent.

The downfield resonance of the carboxyl proton in the salt of compound **10** was found to be concentration dependent. The signal assigned to the H-bond shifted further downfield with increasing concentration, which is indicative of the presence of intermolecular hydrogen bonds. There is most probably an equilibrium between intra- and intermolecular hydrogen-bonded species. A small ΔpK_a value for the diacid supports the assumption that the formation of an intramolecular hydrogen bond is unfavorable. The steric compression of the methyl groups makes the formation of an intramolecular hydrogen bond unfavorable in this compound.[7]

From our present work, we have found that a strongly downfield-shifted signal was observed in all cases inde-

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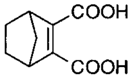
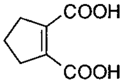
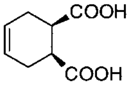
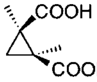
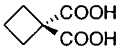
(4) Cassidy, C. S.; Lin, J.; Tobin, J. B.; Frey, P. A. *Bioorg. Chem.* **1998**, *26*, 213−219.

(5) (a) Perrin, C. L.; Nielson, J. B. *J. Am. Chem. Soc.* **1997**, *119*, 12734−12741. (b) Perrin, C. L.; Nielson, J. B.; Kim, Y. J. *Ber. Bunsen Ges.* **1998**, *102*, 403−409. (c) Perrin, C. L.; Nielson, J. B. *Annu. Rev. Phys. Chem.* **1998**, *102*, 511−544.

(6) (a) Westheimer, F. H.; Benfey, O. T. *J. Am. Chem. Soc.* **1956**, *78*, 5309−5311. (b) Eberson, L.; Wadsö, I. *Acta Chem. Scand.* **1963**, *17*, 1552−1562. (c) McCoy, L. L. *J. Am. Chem. Soc.* **1967**, *89*, 1673−1677.

(7) McCoy, L. L.; Nachtigall, G. *J. Am. Chem. Soc.* **1963**, *85*, 1321−1324.

Table 2. Summary of the NMR Data for the Hydrogen-Bonded Proton in $NBu_4[R(COOH)COO^-]$ (ambient temperature, CD_2Cl_2)

Carboxylic Acid		δ (^{1}H) (ppm)	$W_{1/2}$ (Hz)	ΔpK_a[a,b]
	**7**	19.99	8	6.68
	**8**	20.35	7	5.63
	**9**	19.75	12	3.02
	**10**	18.31	25	2.50
	**11**	18.91	25	2.36

[a] $\Delta pK_a = pK_{a2} - pK_{a1}$, where K_{a1} and K_{a2} are the first and second acid dissociation constants, respectively. [b] *Dictionary of Organic Compounds*, 6th ed.; Chapman and Hall: London, 1996.

pendent of bonding type (intramolecular/intermolecular). Therefore, all carboxylic acid–carboxylate systems arising from either mono- or diacids should exhibit a downfield resonance in the range of 16–22 ppm indicative of "strong" hydrogen bonding in anhydrous, aprotic solvents. The presence of a low-field ^{1}H NMR signal in carboxylic acid–carboxylate systems linked to intermolecular hydrogen bonding has been reported in only a few cases, mainly in complexes involving trifluoroacetic acid.[8] Even though these hydrogen bonds, especially the intermolecular hydrogen bonds in compounds **1**–**6**, are observed in a region considered to be of LBHB type, they are extremely sensitive to trace amounts of water. Finally, the extent to which the resonance is shifted downfield is also dependent on the environment of the hydrogen bond. Even though a resonance of 18 ppm is observed for the benzoic acid–benzoate systems and can be attributed to the "ideal" hydrogen bond, other intramolecularly hydrogen-bonded hemisalts of diacids exhibit a resonance further downfield. We are expanding our H-bonding studies to include temperature, geometric/structural factors, and influence of water to determine, if possible, the features that affect the characteristics of the NMR peak for these hydrogen-bonded systems.

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Supporting Information Available: General experimental details and ^{13}C NMR spectra for all of the salts. This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) (a) Clark, J. H.; Emsley, J. *J. Chem. Soc., Dalton Trans.* **1974**, 1125–1129. (b) Jones, R. G.; Dyer, J. R. *J. Am. Chem. Soc.* **1973**, *95*, 2465–2470.