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The Conformations of 1,4-Butanedioic Acid as a Function of Solvent Polarity in a Series of Alcohols as Determined by NMR Spectroscopy[†]

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Vicinal proton−proton NMR couplings have been employed to estimate the differences in conformational equilibria for 1,4-butanedioic-2,3-$^{13}C_2$ acid in the progression of its diprotic to monoprotic to di-ionized forms as a function of solvent in water and in a series of alcohols ranging from methanol to *tert*-butyl alcohol. Except for water, the percentage of gauche increases from diacid to monoanion and then decreases from monoanion to dianion. The substantial gauche preference for the monoanion species in the less-polar alcohols is clearly the result of intramolecular hydrogen bonding.

Introduction

1,4-Butanedioic acid and its salts normally exist in gauche and trans conformations that ideally would have rotational dihedral angles (θ_g and θ_t) between their carboxyl substituents of 60° and 180°, respectively. In this research, we report the positions of conformational equilibria between these conformations for 1,4-butanedioic acid, its monoanion, and its dianion in the solvent series water, methanol, ethanol, isopropyl alcohol, and *tert*-butyl alcohol with the aid of the proton NMR coupling constants [J_{13} and J_{14}, where J_{13} ($=J_{24}$) is taken as the smaller gauche coupling and J_{14} ($=J_{23}$) is the larger trans coupling, both for the same trans conformation], as used previously for 1,4-butanedioic acid-2,3-$^{13}C_2$ species.[1−3]

Other studies[2,3] have shown that monohydrogen 1,4-butanedioate assumes the gauche conformation exclusively in *aprotic* solvents such as tetrahydrofuran (THF) and dimethyl sulfoxide (DMSO) as a result of strong intramolecular bonding. However, the conformational preference for the dianion in the same solvents is somewhat ambiguous, although the proton−proton couplings indicate clearly that there is a large fraction of the gauche conformation. Our purpose here is to investigate the conformation changes that occur with a reasonably graded series of similar *protic* solvents with different degrees of polarity and hydrogen-bonding powers.

Experimental Section

Sample Preparation. The samples used for the NMR spectral determinations had constant 0.05 M concentrations of the 1,4-butanedioic species and were prepared by mixing a stock solution of 0.05 M dilabeled 1,4-butanedioic acid with 0, 0.5, 1.0, 1.5, and 2.0 equiv of a stock solution of 0.05 M dilabeled 1,4-butanedioic acid and 0.1 M tetrabutylammonium cyanide as the base. To ensure that the reaction went to completion, the acid and cyanide salt were first dissolved in methanol and evaporated to dryness under reduced pressure to remove the methanol and the resulting hydrogen cyanide. Orienting experiments showed that this mode of preparation was indeed required for nonaqueous solvents.

NMR Spectra. The NMR spectra were recorded at ambient temperature with GE QE 300-MHz proton NMR spectrometers. The ^1H NMR peaks were referenced to known chemical shift positions of the alcohols and/or TMS. The degree of ionization was checked by measuring the ^{13}C shifts of the labeled methylene groups directly after the ^1H spectra were recorded.[2]

Coupling Constant Calculations. The coupling constants were extracted from the NMR peak positions with the aid of a True BASIC version of the iterative program LCN3.[4] The couplings are summarized in Table 1. The positions of conformational equilibria were estimated from the coupling constants through comparisons with theoretical coupling constants calculated by the Altona−Haasnoot procedure.[5−7] Each of the individual vicinal couplings, J_{13} and J_{14}, gives an independent value of the position of the conformational equilibrium for a given system, and these values are reported in Table 1.

Results and Discussion

In this study of 1,4-butanedioic acid and its salts, it was important to take into consideration the extent of formation of the monoanion in the equilibrium between the diacid and the dianion, which is determined by K_1/K_2. If K_1/K_2 is relatively small, as it is for water (28), then the maximum extent of formation of the monoanion is only 73% of the total acid present. The experimental coupling constants at the maximum concentration of the monoanion (the pH at the first equivalence point) are the weighted averages of couplings of the diacid, dianion, and monanion. The J_{13} or J_{14} couplings of the monoanion in water can be extracted from the weighted average by eq 1, where the coefficients are those calculated for K_1/K_2 = 28.

$$J_{1n}(\text{expt}) = 0.135J_{1n}(\text{diacid}) + 0.135J_{1n}(\text{dianion}) + 0.73J_{1n}(\text{monoanion}) \quad (1)$$

Here, J_{1n}(diacid) and J_{1n}(dianion) are the separately measured values at low and high enough pH values to ensure that these are the only 1,4-butanedioate species present.[1] To proceed further, we need to address the issue of the value of *J* for each of these species in water solution, which, when the estimated coupling constants for the gauche and trans conformations are obtained by the Altona [6,7] procedure, correspond to an average of 67% gauche, which is about the same as when the couplings are obtained by a different procedure[1] and recalculated per

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TABLE 1: Calculated and Measured J_{HH} Coupling Constants of 1,4-Butanedioic-2,3-^{13}C Acid and Its Mono- and Ditetrabutylammonium Salts in Water and Alcohols and Their Derived Conformational Preferences

solvent	base added (equiv)	J_{13}/J_{14} Altona-calcd[a]	J_{13}/J_{14} obsvd	calcd % gauche using $\theta_g = 60°/70°$[b]	^{13}C methylene shift (ppm)
H_2O	0.0	8.77/3.62 3.90/14.21	8.00/5.15[c]	84/74[c]	–
	0.5	8.95/3.65 3.88/14.37	7.65/5.65	77/66[c]	–
	1.0	9.01/3.67 3.87/14.54	7.36/7.25[c,d]	66/67[c,d]	–
	1.5	9.14/3.70 3.84/14.71	6.83/8.40	59/43[c]	–
	2.0	9.25/3.73 3.83/14.88	6.30/10.10[c]	43/39[c]	–
MeOH	0.0	*a*	7.77/5.59	78/68	29.985
	0.5		7.97/5.78	81/70	31.655
	1.0		7.81/6.14	78/68	32.962
	1.5		6.90/8.00	60/52	–
	2.0		5.66/11.00	34/29	35.677
EtOH	0.0	*a*	7.46/6.42	73/65	29.698
	0.5		8.21/5.38	84/74	–
	1.0		8.30/4.90	87/76	33.044
	1.5		7.40/7.40	67/58	34.532
	2.0		5.16/12.01	26/22	36.484
i-PrOH	0.0	*a*	7.20/6.81	68/60	29.315
	0.5		8.20/4.80	87/76	31.066
	1.0		9.12/3.24	>100/90	32.996
	1.5		6.54/8.83	52/46	35.354
	2.0		4.84/12.87	18/16	36.596
t-BuOH	0.0	*a*	7.15/7.15	67/58	29.477
	0.5		8.76/4.27	97/83	31.676
	1.0		9.67/2.40	>100/99	33.252
	1.5		8.06/6.29	77/68	34.831
	2.0		4.70/13.00	16/14	37.275

[a] The pairs of *J* values, first gauche and second trans, shown in this column were calculated by the Altona–Haasnoot procedure[6,7] with λ values of 0.47 for $-CO_2H$ and 0.29 for $-CO_2^-$ and with θ_g taken to be 60° and θ_t taken to be 180°. We have seen, at most, only small variations of λ with solvent, so the values listed were assumed to be solvent-independent and were used for the alcohols as solvents, when θ_g was taken to be 60°. [b] Respective values for θ_g used to calculate the % gauche by the Altona–Haasnoot method with $\theta_t = 180°$. [c] *J* values given here for water are those reported earlier,[1] but the % gauche has been recalculated with λ values instead of Huggins electronegativities.[6,7] [d] The values of 7.30/7.35 have been corrected for the proportion of monoanion in the mixture by eq 1.

Altona[6,7] rather than the older procedure of Haasnoot.[5] The use of eq 1 leads to $J_{13} = 7.36$ Hz and $J_{14} = 7.25$ Hz, which then results in a correction of about +1% in the proportion of gauche over what would be calculated (66%) by taking the coupling constants of the equivalence solution and assuming that only the monoanion is present.

In methanol, K_1/K_2 for 1,4-butanedioic acid is about 250,[8] and in ethanol, it is about 340, more than 13 times larger than in water.[9] These K_1/K_2 values correspond at the first equivalence point to 89 and 90% monoanion in methanol and ethanol, respectively. The same procedure used for water leads to corrected values of J_{13} and J_{14} for the monoanion of 7.59 and 5.87 Hz in methanol and 8.52 and 4.43 Hz in ethanol. These results can be compared to the corresponding values of 7.81 and 6.14 Hz and 8.30 and 4.90 Hz for the respective alcohols determined from the solutions at the equivalence point. These changes amount to a 4% increase in gauche for ethanol, if we assume a 70° dihedral angle for the gauche rotamer (θ_g) of the monoanion, a matter to be discussed in more detail shortly. In methanol, proceeding as with ethanol, the corrected value for the percent of gauche for the monoanion is 3% higher, from increasing 68 to 71% gauche. With *tert*-butyl and isopropyl alcohols as solvents, it seems safe to assume that the K_1/K_2 values will be greater than that for ethanol because these solvents have lower dielectric constants and less hydrogen-bonding capability for stabilizing the dianion.[8] Thus, adjusting the coupling constants with eq 1 for these solvents is not expected to make a significant difference in the percent of gauche calculated for the monoanion.

The conformational angle θ_g presents a serious problem in the analysis of the conformational equilibria of 1,4-butanedioic acid and its salts. In our earlier studies in aqueous solutions,[1] we operated on the principle that, in the absence of information to the contrary, we should calculate the position of the conformational equilibria on the basis of perfectly staggered conformations, at least until evidence to the contrary was obtained. Such evidence was clearly obtained with tetrabutylammonium hydrogen 1,4-butanedioate in THF[2] and DMSO,[3] where the Altona procedure[6,7] suggests that, with $\theta_g = 60°$, the gauche rotamer would have to be present to the extent of ~110%. Increasing θ_g to 70° decreases the calculated fraction of gauche to close to 100% and with $\theta_g = 80°$ to 92% gauche, provided that, as seems reasonable, the trans conformation has $\theta_t = 180°$.[1] We favor $\theta_g = 70°$ on the basis that K_1/K_2 is larger by some seven powers of ten in DMSO than it is in water,[3,8,10] as a result of favorable hydrogen bonding, which would correspond to essentially complete formation of the gauche conformer. This finding raises the difficult question as to the value of θ_g to be expected in aqueous media for 1,4-butanedioic acid and its salts. Neither the vicinal coupling constants nor the small value of K_1/K_2 in water of 28 strongly suggest intramolecular hydrogen bonding with the monoanion. Further, the fact that the conformational equilibria for the diacid are only slightly different in water and THF[2] does not argue for extensive

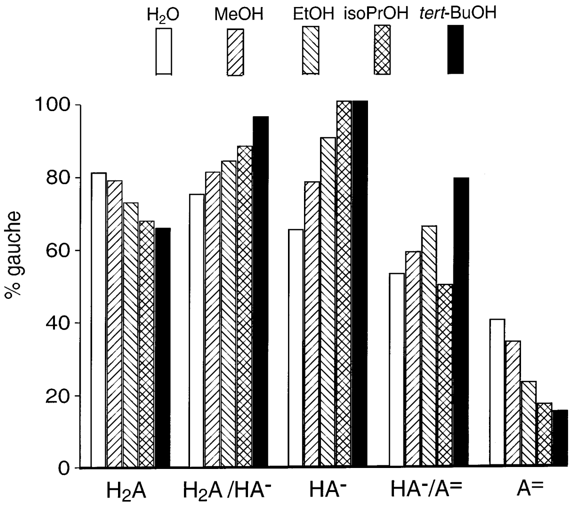

Figure 1. Trends in the conformational equilibria of 1,4-butanedioic acid and its salts with solvent from water to *tert*-butyl alcohol. The bar heights were calculated for $\theta_g = 60°$, except for isopropyl and *t*-butyl alcohols, where $\theta_g = 70°$ was used for HA^-, HA^-/A^{2-}, and A^{2-}.

intramolecular hydrogen bonding for this species either. We therefore maintain the assumption that θ_g is 60° for aqueous solutions but increases as K_1/K_2 increases in less-polar solvents as a result of intramolecular hydrogen bonding. For the calculated values in Table 1, we assume that θ_g can be 70° in methanol and ethanol, even though somewhat smaller average values are likely to be more appropriate.

The results summarized in Table 1 of the conformational calculations for 1,4-butanedioic and its salts in the various alcohol solvents are shown schematically in Figure 1. One sees a nearly linear change in the percentage of gauche going from the diacid to the monoanion across the series from methanol to *tert*-butyl alcohol, although a linear change does not, of course, correspond to a linear change in the free energies of the equilibria. As mentioned earlier, the preference for gauche with the monoanion species in the less-polar alcohols is surely the result of intramolecular hydrogen bonding.

An inverse linear change is seen for the fraction of gauche on going from the monoanion to dianion as the solvent polarity decreases. No marked trend of this kind is observed for DMSO or THF, where very substantial proportions of gauche are observed.[2,3] What causes the differences? We believe that the differences arise because THF and DMSO are *aprotic* solvents and are not able to solvate the dianion efficiently. In contrast, even though *tert*-butyl alcohol has a low polarity compared to methanol and ethanol, it should be able to hydrogen bond to the dianion and stabilize it in the electrostatically favorable trans conformation, which is normally expected in low-dielectric media. That similar behavior is observed to only a minor degree in water[1] accords with its much higher dielectric constant. As pointed out elsewhere,[11] the calculated values reported in Table 1 for the percentage of gauche conformer, especially where those values are low, as they are for isopropyl and *tert*-butyl alcohols as solvents, could well be actually even lower because of uncertainties in the accuracy of the Altona−Haasnoot relations in the regime of nearly all-trans conformations.

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