Calculated pK_{Enol} Values for Enols of Carboxylic Acid Derivatives HC═C(OH)X (X = OH, NH_2, NMe_2, OMe, OCHO, F, Cl, Br)

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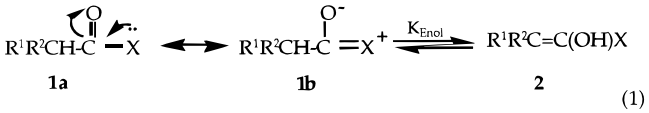
Abstract: The energies of acetic acid and its $CH_3C(═O)X$ derivatives and of the corresponding enols $H_2C═C(OH)X$, for X = OH, NH_2, NMe_2, OMe, OCHO, F, Cl, and Br, were calculated by the MO ab initio method MP2(full)/6-31G**, by single-point CCSD(T)(full)/6-311G**/MP2(full)/6-31G**), and by the hybrid density functional method B3LYP/6-31G**. The calculated pK_{Enol} = −log K_{Enol} values for the "keto"/enol equilibria are all high (17.5−24.0) and follow the order for X:H < alkyl < OCHO < Br∼Cl < F < NH_2 < NMe_2 < OH, OMe. By using the appropriate isodesmic reactions, it was shown that all substituents stabilize more the acid species than its enol (where Br and Cl are slightly destabilizing). All the computational methods display a similar trend. The structures and energies of the various conformations of both species are given. Comparison with the scarce experimental pK_{Enol} data shows a reasonable agreement with the calculations.

Introduction

Whereas the equilibria and tautomerization kinetics of the keto/enol system was extensively investigated,[1] little is known about the enols of carboxylic acid derivatives, R^1R^2CHCOX, X = OH, OR′, OCOR″, NR_2‴, Halogen, and quantitative data about their stability are scarce.[2] Qualitatively it is believed that in these acid derivatives the "keto" form **1a** is stabilized by resonative electron donation from the heteroatom X (cf. **1b**) so that the equilibrium with the enol form **2** is shifted strongly toward **1**, in comparison with aldehydes (X = H) and ketones (X = alkyl). This is reflected in low equilibrium constants K_{Enol} (pK_{Enol} = −log K_{Enol}) values (eq 1).



(1)

Enols **2** were suggested as short-lived intermediates. Enols of acids were suggested as intermediates in the decarboxylation of a dicarboxylic acid,[3a] in the reductive debromination of a carboxylic acid,[3b] in the nitrosation of malonic acids,[3c] and in the Hell−Volhard−Zelinskii bromination of acids.[3d] Enols of esters, acyl halides, and amides were suggested as intermediates in nitrosation of XCH_2CO_2Et (X = H, CN)[4a] and addition of alcohols[4b] or H−Hal[4c] to ketenes, water addition to ketenimines,[4d] and electrophilic substitution of malonamide,[4e] respectively. A conjugated enol amide was observed by UV in a low-temperature photolysis of a dienone in the presene of an amine.[4f] An anhydride enol was suggested in the addition of Ph_3C^+ to Ac_2O.[4g] There are X-ray data for enols of amides which are apparently stabilized by hydrogen bonding.[5] Enols of acids were generated recently by hydration of ketenes.[6,7] Kresge's and Wirz's groups measured pK_{Enol} values (given in parentheses) for cyclopentadiene-1-carboxylic acid[2b,6a] (8.4), its monobenzo (9.3)[6b] and dibenzo (9.5)[6c] derivatives, and PhC(Y)═$C(OH)_2$, where Y = OH (15.4),[6d] Y = CN (7.22).[6e] Hegarty's and Rappoport's groups generated $Ar_2C═C(OH)_2$, where Ar =

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mesityl,[7a] pentamethylphenyl,[7a] and tipyl.[7b] Enols of bulky amides were also "observed" by addition of amines to ketenes.[8] All available data show that enols of acids and derivatives have pK_{Enol} values much higher than those of aldehydes and ketones, in agreement with the qualitative resonance argument presented above

The pK_{Enol} values for the parent $CH_3COOH/CH_2{=}C(OH)_2$ pair were calculated, at several theoretical levels, giving values of 26 (6-31G*//3-21G),[9a] 20.5,[2a] 18.8,[9b] 20.4 (at CASSCF/6-31G*),[9c] and 19.3 (MP2/aug-cc-pVTZ/6-311+G(d,p)).[9d] Experimental estimates range between 18.2 and 21.2.[9e−g] Calculated pK_{Enol} values for other carboxylic acids are 28.3 for 1-cyclopropanecarboxylic acid and 30.2 for 3-cyclopropenecarboxylic acid (at 3-21G).[9b] Calculated pK_{Enol} values for acetamide and acetyl fluoride are (6-31G*//3-21G) 24.4 and 23.1, respectively.[9a,h]

In this paper, we report high-level MO calculations of the structures and energies of the $CH_3C(=O)X/CH_2{=}C(OH)X$ pairs, for X = OH, NH_2, NMe_2, OMe, OCHO, F, Cl, and Br, to provide the first extensive systematic and reliable set of pK_{Enol} values for these fundamentally important molecules.

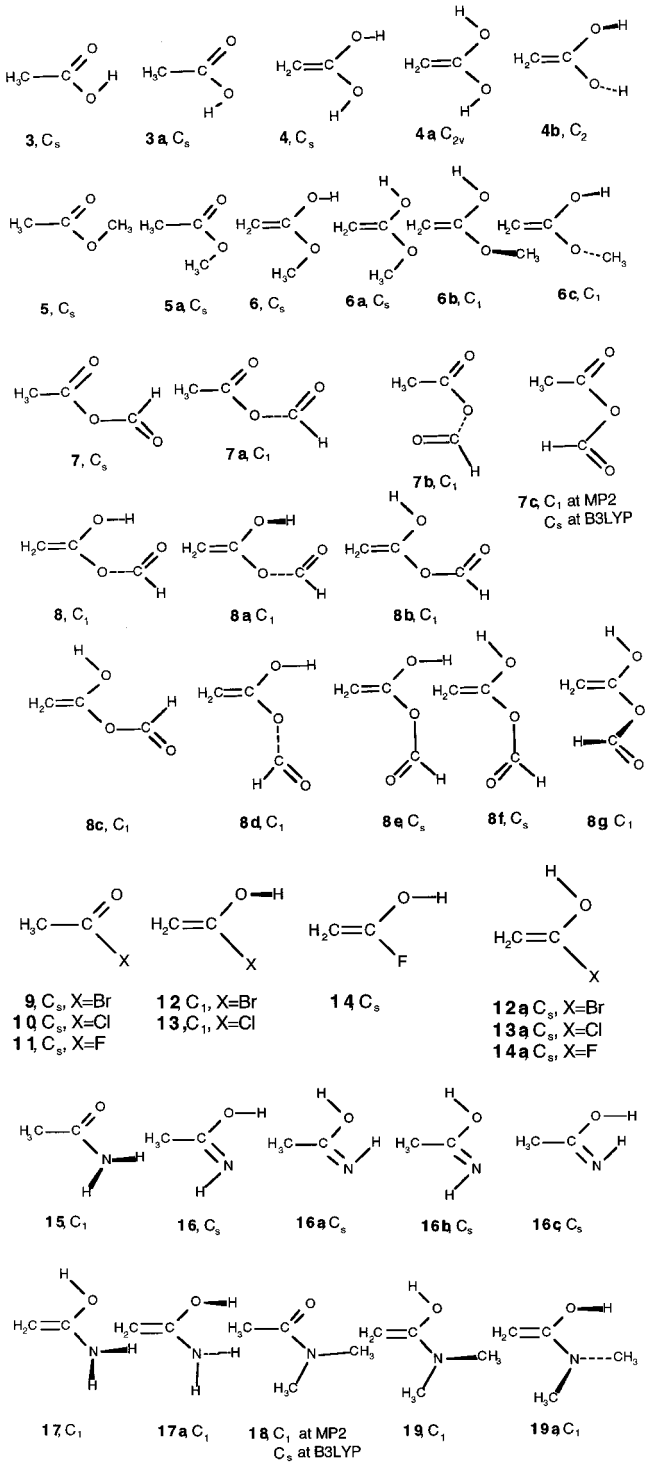
Computational Methods

All calculations were carried out by using the Gaussian 94 series of programs.[10] The geometries of all species were fully optimized at two levels: (a) using the hybrid density functional method B3LYP/6-31G** (hereafter designed B3LYP) and (b) using second-order Moller−Plesset theory MP2(full)/6-31G** (hereafter designated MP2). Minima were characterized by calculating their Hessian matrices. Single-point energies were also calculated at CCSD(T)(full)/6-311G**//MP2(full)/6-31G** (hereafter designated CCSD(T)), to improve the treatment of electron correlation. B3LYP/6-31G** and MP2(full)/6-31G** vibrational frequencies were calculated for all species. The calculated absolute energies (Table S1), zero point energies (Table S2), and the Gibbs free energies (Table S3) are given in the Supporting Information.

Results and Discussion

Most of the species showed more than one minimum, and these structures are shown in Chart 1. Selected geometrical parameters for the most stable conformation of the enols **2** and of the carboxylic acid derivative species **1** are given in Tables 1 and 2. The relative energies of the various conformers compared with the most stable one are given in Table 3.

Chart 1



For the keto ⇌ enol equilibria, both ΔH and ΔG values were calculated. Except for a single case they differ by less than 1 kcal mol^{-1}, and the results are summarized in Table 4. The following discussion is in terms of ΔG except for eqs 2−7, which are discussed in terms of ΔH. The following designations are used: (a) all values without parentheses are at B3LYP, (b) values in round parentheses ( ) are at MP2, and (c) values in square brackets [ ] are at CCSD(T).

(a) pK_{Enol} Values and Structures. AcOH is calculated to be 30.0 (32.7) [29.2] kcal mol^{-1} more stable than its enol, 1,1-ethenediol, the derived pK_{Enol} values being 22.0 (24.0) [21.5] at 298 K. The most stable conformer of the acid is **3** having syn OH and C=O groups.[11a] The acid enol **4** can exist in three

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Table 1. Selected Geometrical Parameters at B3LYP/6-31G** and MP2(full)/6-31G** (in Parentheses) of the Most Stable Enol Species[a]

compd	sym	conf[b]	*r*(C−O)	*r*(C−X)	*r*(C═C)	∠(C−O−H)	∠(C═C−O−H)
4	C_s	A,S	135.2 (135.4)	136.6 (136.7)	133.7 (133.6)	107.6, 109.1 (107.0, 108.6)	0.0 and 180.0 (0.0 and 180.0)
6	C_s	A	135.6 (135.8)	136.2 (136.2)	133.8 (133.8)	107.1 (106.5)	180.0 (180.0)
8	C_1	G	134.0 (134.9)	141.6 (141.6)	133.1 (133.0)	108.3 (107.1)	−152.0 (−138.1)
12	C_1	G	135.0 (135.6)	193.1 (191.2)	132.9 (133.2)	109.7 (109.1)	160.8 (160.5)
13	C_1	G	135.1 (135.8)	177.2 (174.3)	132.9 (133.2)	109.9 (109.2)	157.5 (157.3)
14	C_s	A	134.7 (134.8)	135.0 (135.3)	132.7 (132.8)	108.0 (107.6)	180.0 (180.0)
16	C_s	A	135.7 (135.9)	127.2[c](127.7[c])	150.6[d](149.8[d])	105.5 (105.0)	180.0 (180.0)
17	C_1	S	136.8 (136.9)	139.0 (139.1)	134.4 (134.2)	108.0 (107.7)	−2.6 (−2.8)
19	C_1	S	137.3 (137.5)	138.8 (138.8)	134.8 (134.7)	107.4 (107.1)	12.2 (11.3)

[a] Bond lengths are in picometers and bond (dihedral) angles in degrees. [b] Orientation of the OH group relative to the C═C bond; S = syn, G = gauche, A = anti. [c] *r*(C═N). [d] *r*(C−C).

Table 2. Selected Bond Lengths (pm) of the Most Stable "Keto" Form of the Acid Derivative Calculated at B3LYP/6-31G** and MP2(full)/6-31G**

compd	sym	*r*(C−X)	*r*(C−C)
3	C_s	135.8 (136.0)	150.7 (150.0)
5	C_s	135.5 (135.7)	151.0 (150.2)
7	C_s	139.2 (139.4)	150.2 (149.6)
9	C_s	201.2 (200.0)	150.2 (149.7)
10	C_s	183.5 (179.7)	150.3 (149.8)
11	C_s	136.3 (136.7)	149.9 (149.4)
15	C_1	136.8 (137.1)	152.3 (151.3)
18	C_s	137.8 (137.4[a])	152.5 (151.5[a])

[a] C_1 at MP2(full)/6-31G**.

Table 3. Relative Energies (kcal mol^{-1}) of All the Calculated Conformers of Acid Derivatives and Their Enols

	MP2[a]	B3LYP[b]	CCSD(T)[c]		MP2[a]	B3LYP[b]	CCSD(T)[c]
3	0.00	0.00	0.00	**8d**	3.15	3.60	2.94
3a	6.52	5.93	5.97	**8e**	2.72	3.40	2.66
4	0.00	0.00	0.00	**8f**	3.43	4.24	3.48
4a	1.41	1.44	1.26	**8g**	4.30	4.83	4.01
4b	2.92	3.01	2.28	**12**	0.00	0.00	0.00
5	0.00	0.00	0.00	**12a**	1.31	1.73	0.81
5a	8.57	7.66	8.36	**13**	0.00	0.00	0.00
6	0.00	0.00	0.00	**13a**	0.45	1.02	0.69
6a	1.63	1.63	1.62	**14**	0.00	0.00	0.00
6b	2.72	2.53	2.63	**14a**	1.00	0.96	0.73
6c	3.58	3.71	3.18	**16**	0.00	0.00	0.00
7	0.00	0.00	0.00	**16a**	3.67	3.51	3.30
7a	2.41	3.24	2.61	**16b**	7.56	7.11	6.97
7b	3.11	3.40	2.85	**16c**	2.57	2.72	2.50
7c	7.79	7.17	7.60	**17**	0.00	0.00	0.00
8	0.00	0.00	0.00	**17a**	1.05	1.13	0.70
8a	3.06	4.40	2.53	**19**	0.00	0.00	
8b	2.33	3.82	1.89	**19a**	0.38	0.85	
8c	4.27	4.75	3.68				

[a] MP2(full)/6-31G**//MP2(full)/6-31G**. [b] B3LYP/6-31G**//B3LYP/6-31G**. [c] CCSD(T)/6-311G**//MP2(full)/6-31G**.

distinct conformations:[11b] anti−syn **4**, syn−syn **4a**, and gauche−gauche **4b**. The anti−anti C_{2v} species is a high-lying stationary point on the potential energy surface (PES) having two imaginary frequencies at both the B3LYP and MP2 levels. The most stable conformer is **4** with an anti orientation of one hydroxyl group and a syn orientation of the second OH group relative to the C═C bond. Conformer **4a** with two syn OH groups is less stable than **4** by 1.4 (1.4) [1.3] kcal mol^{-1}. Conformer **4b** with two identical gauche OH groups (the HOCC dihedral angles being 137.0° (136.2°)) is the least stable conformer of the acid enol, lying 3.0 (2.9) [2.3] kcal mol^{-1} above **4**, indicating the importance of conjugation between the oxygen 2p lone pair and the C═C bond in **4**. These computational results agree with those of Rodler,[11a] Csizmadia,[9b] Nguyen,[11b] Hegarty,[11c] and others,[9c,g,11d] who found that **4** is the most stable conformer, but these authors considered only the two conformers **4** and **4a.**

Methylation of the hydroxy group has a small effect on pK_{Enol}. The ester is by 30.3 (32.7) [29.2] kcal mol^{-1} more stable than the hemiacetal **6**. The corresponding pK_{Enol} values at 298 K are 22.3 (24.0) [21.4]. Experimentally estimated pK_{Enol} values are 19.4 for AcOMe[9g] and 18.6 for AcOEt.[11e] The stability order of the conformers of the hemiacetal **6** is the same as that of the acid enol **4**. The most stable conformation is **6,** which has anti (OH) and syn (OCH_3) arrangements relative to the C═C bond. **6a** with syn OH and OCH_3 groups is less stable than **6** by 1.6 (1.6) [1.6] kcal mol^{-1}. The syn (OH) and gauche (OCH_3) conformer **6b** is less stable than **6** by 2.5 (2.7) [2.6] kcal mol^{-1}, and the least stable species is **6c**, having gauche orientations of both groups, which lies higher than **6** by 3.7 (3.6) [3.2] kcal mol^{-1}.

The keto−enol energy differences are lower for the anhydride. The mixed formic−acetic anhydride **7** is 23.9 (27.1) [24.1] kcal mol^{-1} more stable than enol **8**, giving pK_{Enol} values of 17.6 (19.9) [17.7]. For the "keto" form of the acid **3**, the ester **5** and the mixed formic−acetic anhydride species **7**, the most stable arrangement of the substituents (OH, OCH_3, and OCHO, respectively) is the syn relative to the C═O bond (i.e., **3**, **5**, and **7**). The enol form of the mixed formic−acetic anhydride **8** can exist as eight distinct conformers **8**−**8g**. The most stable one is **8**, having gauche orientations of both the hydroxyl group and the anhydridic C−O bond with respect to the C═C bond (∠CCOH −152.0° (−138.1°); ∠CCOC 156.9° (142.1°)) and a syn arrangement of the C═O bond relative to the C−O bond (∠COCO −0.6° (0.8°)). All other conformers lie higher by 3.4−4.8 (2.3−4.3) [1.9−4.0] kcal mol^{-1}.

For acyl halides, the enol is less stable than the "keto" forms **9**−**11** by 26.9 (29.9) [26.8] kcal mol^{-1} for X = F, by 25.4 (26.7) [24.2] kcal mol^{-1} for X = Br, and by 25.3 (26.3) [23.8] kcal mol^{-1} for X = Cl. The pK_{Enol} values for acetyl bromide, chloride, and fluoride are 18.7 (19.6) [17.8], 18.6 (19.3) [17.5], and 19.8 (22.0) [19.7], respectively. There are three distinct conformations of the corresponding enols with either syn OH, gauche OH, or anti OH. The gauche conformations are the most stable for **12** (X = Br) and **13** (X = Cl), while for **14** (X = F), the anti conformation is the most stable. For X = Br, Cl, and F, the syn conformations **12a**, **13a,** and **14a** are slightly less stable (by 0.5−1.7 kcal mol^{-1} depending on the level of calculation) than conformations **12**, **13**, and **14**.

With primary and secondary amides, tautomerization of the CH or the NH proton can give either the amide enol or the

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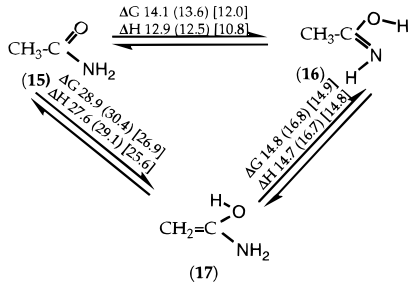
Table 4. Calculated Energy Differences ΔH and ΔG (kcal mol^{-1}) between the Acid Derivative $CH_3C(=O)X$ and the Enol Form $H_2C=C(OH)X$[a] and as pK_{Enol} Values, at B3LYP/6-31G**//B3LYP/6-31G** (No Parentheses), MP2(full)/6-31G**//MP2(full)//6-31G** (Round Parentheses), and CCSD(T)/6-311G**//MP2(full)//6-31G** [Square Parentheses]

X	ΔH[a]	ΔG[b]	pK_{Enol}	pK_{Enol}(exp)
H	13.1 (14.8) [12.5]	13.4 (15.1) [12.8]	9.9 (11.2) [9.5]	9.9, 11.2,[c] 6.23[d]
Me	14.9 (16.2) [14.0]	15.6 (16.6) [14.4]	11.5 (12.2) [10.7]	13.9,[c] 8.33[d]
OH	29.9 (32.7) [29.2]	30.0 (32.7) [29.2]	22.0 (24.0) [21.5]	21.2[9f]
OMe	29.6 (32.3) [28.7]	30.3 (32.7) [29.2]	22.3 (24.0) [21.4]	19.4[9g]
OCHO	23.2 (26.4) [23.4]	23.9 (27.1) [24.1]	17.6 (19.9) [17.7]	
NH_2	27.6 (29.1) [25.6][f]	28.9 (30.4) [26.9]	21.3 (22.4) [19.8]	
NMe_2	28.1 (29.3) —	28.8 (30.0) —	21.2 (22.1) —	
F	27.0 (30.2) [27.0]	26.9 (29.9) [26.8]	19.8 (22.0) [19.7]	
Cl	25.0 (26.1) [23.6]	25.3 (26.3) [23.8]	18.6 (19.3) [17.5]	
Br	25.2 (26.6) [24.0]	25.4 (26.7) [24.2]	18.7 (19.6) [17.8]	

[a] Including zero-point energies between the most stable conformers of both species: ZPE were calculated at MP2 for the MP2 and CCSD(T) levels and at B3LYP for the B3LYP level. [b] Including the entropy contribution. ΔG (at CCSD(T)) = ΔH (at CCSD(T)) + ΔG (at MP2) − ΔH (at MP2). [c] Gas-phase data from ref 18. [d] In water (Keefe, J. R.; Kresge, A. J.; Schepp, N. P. *J. Am. Chem. Soc.* **1988**, *110*, 1993). [e] Estimated experimental values in water. [f] Recent values:[9h] 31.8 (HF/6-31G*), 31.7 (MP2/6-31G*), 27.5 (MP2/6-31+G**), 28.7 (MP3/6-31G*), 32.0 (MP4(sdtq)/6-31G*).

Scheme 1



imine. The results of the calculations (in kcal mol^{-1}) at the three computational levels, for acetamide (**15**), 1-aminoenol (**17**), and 2-hydroxyethylimine (**16**) are shown in Scheme 1. Enol (**17**) is 28.9 (30.4) [26.9] kcal mol^{-1} less stable than acetamide **15**, giving a pK_{Enol} of 21.3 (22.4) [19.8]. However, the corresponding imine (**16**) is much more stable than the enol (**17**), **15** being 14.1 (13.6) [12.0] kcal mol^{-1} more stable than **16**.[12] *N*,*N*-Dimethylation of the amide excludes the imine form and dimethylacetamide is 28.8 (30.0) kcal mol^{-1} more stable than its enol (pK_{Enol} = 21.2 (22.1)).

Acetamide **15** is almost planar or has a slightly pyramidal NH_2 group: ∠CCNH = −0.6° and −178.5° (17.2° and 172.4°). The most stable imine conformation **16** has the "enolic" hydrogen syn to the C=N bond and syn imino hydrogen and methyl group. The second and the third most stable conformers, **16c** and **16a**, respectively, have the imino hydrogen syn to the C−O bond and the "enolic" hydrogen anti (**16c**) and syn (**16a**), respectively, to the C−C bond. They lie higher in energy than **16** by 2.7−3.5 (2.6−3.7) [2.5−3.3] kcal mol^{-1}. **16b** has both groups in the gauche arrangement, and it is by 7.1 (7.6) [7.0] kcal mol^{-1} less stable than **16**. The most stable conformation of the amide enols **17** and **19** has a syn OH arrangement with ∠CCOH of −2.6°(−2.8°) for **17** and 12.2° (11.3) for **19** and with ∠CCNC of 18.5° and 148.0° (19.9° and 146.7°) for **17** and 2.5 and −141.8° (0.1; −136.6°) for **19**. The corresponding gauche conformers **17a** (C_1) and **19a** (C_1) are slightly less stable (<1.1 kcal mol^{-1}).

(b) Trends in pK_{Enol} Values. The effects of the substituent X (relative to X = H) on the stabilities of **1** and **2** are given by two pairs of isodesmic equations, eqs 2 and 3 and eqs 4 and 5, respectively. In eqs 2 and 3, the reference compounds are saturated (CH_3CH_3 and CH_3X), while in eqs 4 and 5, they have a C=C bond ($CH_2=CH_2$ and $H_2C=CHX$). Note that the subtraction of eq 2 from eq 3 (or of eq 4 from eq 5)

$$CH_3C(=O)X + CH_3CH_3 \rightleftharpoons CH_3C(=O)CH_3 + CH_3X \quad (2)$$

$$H_2C=C(OH)X + CH_3CH_3 \rightleftharpoons H_2C=C(OH)CH_3 + CH_3X \quad (3)$$

$$CH_3C(=O)X + H_2C=CH_2 \rightleftharpoons CH_3C(=O)H + H_2C=CHX \quad (4)$$

$$H_2C=C(OH)X + H_2C=CH_2 \rightleftharpoons H_2C=C(OH)H + H_2C=CHX \quad (5)$$

gives the difference in the pK_{Enol} values of a particular $CH_3C(=O)X/H_2C=C(OH)X$ pair and acetone (or acetaldehyde) and its enol. The results in terms of ΔH, presented in Table 5, show that all substituents X stabilize both species (except for X = Cl, Br, which slightly destabilize the enol **2**), but the "keto" form is always substantially more stabilized than the enol, i.e., by 8−16.5 kcal mol^{-1} (eqs 2 and 3) or 10−18 kcal mol^{-1} (eqs 4 and 5). The stabilization is more pronounced for strongly conjugating electron-donating substituents such as NH_2 and OH. These quantitative results reinforce the qualitative resonance argument shown in eq 1.

Examination of the computational results in Table 5 provide interesting insights into the effects of the various substituents on the thermodynamic stabilities of the "keto" and the enol forms and thus on the observed trend in the pK_{Enol} values as a function of X. First we note that the results obtained with either of the equation pairs (i.e., with eqs 2 and 3 or eqs 4 and 5) are very similar, and we therefore discuss the results in terms of eqs 2 and 3 and use in the discussion the CCSD(T) values.

In the halogen series Cl and Br behave almost identically, while F behaves differently, stabilizing both the "keto" and the enol forms significantly more strongly than Cl or Br. For the acyl halides, it is interesting to compare the calculated energies (kcal mol^{-1}) for eq 2, i.e., 5.5 (Br) < 6.9 (Cl) < 18.6 (F), with those for the corresponding XCH_2^+ cations (eq 6), i.e., 34.2 (Br) > 31.9 (Cl) > 25.0 (F) at the CCSD(T) level.

$$CH_2X^+ + CH_4 \rightleftharpoons CH_3X + CH_3^+ \quad (6)$$

A not much different order of values was obtained by Frenking

(12) These results might be relevant to the mechanism of peptide racemization.

Table 5. Calculated Energies (ΔH in kcal mol^{-1}) of Eqs 2−7 at B3LYP (No Parentheses), MP2 (Round Parentheses), and CCSD(T) [Square Parentheses][a]

eq	NH_2	OH	OMe	OCHO	F	Cl	Br
2	21.2 (20.8) [19.2]	25.3 (26.3) [24.7]	23.3 (25.0) [23.3]	11.4 (12.4) [11.3]	19.9 (20.8) [18.6]	7.2 (8.1) [6.9]	7.1 (7.6) [5.5]
3	8.5 (7.9) [7.6]	10.3 (9.8) [9.5]	8.7 (8.9) [8.5]	3.2 (2.2) [1.8]	7.8 (6.8) [5.6]	−2.9 (−1.9) [−2.7]	−3.2 (−2.9) [−4.6]
4	17.0 (18.1) [17.0]	20.5 (22.6) [21.5]	20.1 (22.2) [21.1]	12.4 (14.4) [13.8]	18.5 (20.8) [19.3]	11.2 (11.4) [10.8]	11.9 (12.2) [10.7]
5	2.5 (3.7) [3.9]	3.8 (4.8) [4.8]	3.6 (4.7) [4.9]	2.3 (2.8) [2.9]	4.6 (5.5) [4.8]	−0.7 (0.1) [−0.3]	−0.2 (0.3) [−0.9]
6[b]	97.6 (98.2) [96.4]	64.9 (64.9) [64.9]	77.3 (76.9) [76.6]	53.8 (55.7) [56.1]	26.2 (25.3) [25.0]	29.1 (29.9) [31.9]	32.9 (29.8) [34.2]
7	13.1 (13.8) [13.7]	16.5 (17.4) [17.1]	15.0 (16.5) [15.9]	14.2 (15.5) [15.0]	16.3 (17.1) [16.3]	9.3 (9.2) [8.9]	9.1 (8.8) [7.7]

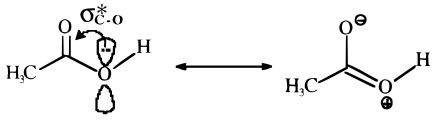
[a] Positive values indicate the substituted derivative to be more stable than the parent. [b] Values calculated by the MP2(VDZ+P) method: F 25.1; Cl 24.8; Br 29.8; I 33.5

and co-workers.[13] The contrast between the two analogous series is striking, showing that the stability of the acyl halides toward bond separation of X is not determined mainly by the π-donation ability of X, which should follow the order I > Br > Cl > F as found in the CH_2X^+ series,[13,14] but is strongly affected by σ effects and by dipolar interactions between X and the carbonyl group. These interactions are particularly strong in $CH_3C(=O)F$, as shown by the high positive energies of eqs 2 and 4. Cl and Br slightly destabilize the enol, indicating the minor energetic role of resonance structures of the type $H_2C{=}C(X){-}(OH) \leftrightarrow H_2C^-{-}C{=}X^+(OH)$. The geminal−anomeric interactions between the OH group and Cl or Br are apparently also small (see eq 5), significantly smaller than in the analogous XCH_2OH saturated series as shown by the calculated energies for the analogous isodesmic eq 7: 7.7 (X = Br), 8.9 (X = Cl), and 16.3 (X = F) at the CCSD(T) level (Table 5). Values of

$$XCH_2OH + CH_4 \rightleftharpoons CH_3X + CH_3OH \qquad (7)$$

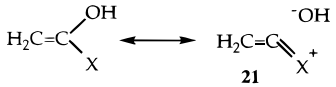
5.8 (X = Cl) and 16.2 (X = F) were calculated previously at the 3-21G*//3-21G* level.[15] Only for the highly electronegative fluorine the geminal−anomeric interactions stabilize the enol significantly (i.e., by 4.8 kcal mol^{-1}, eq 5), but also in this case, this stabilization is significantly smaller than in FCH_2OH.[15] Geminal interactions through an sp^2 carbon are apparently smaller than through an sp^3 carbon.

Another interesting comparison is between X = OH (or OMe) and NH_2. Although NH_2 is a significantly better π-donor than OH (or OCH_3),[14b] it is more costly energetically to separate the C=O and the X groups in $CH_3C(=O)OH$ and $CH_3C(=O)$-OCH_3 than in $CH_3C(=O)NH_2$. This contrasts with the stabilization order observed for the CH_2X^+ cations, i.e., 97.6 (98.2) [96.4] kcal mol^{-1} for X = NH_2 and 64.9 (64.9) [64.9] kcal mol^{-1} for X = OH, which follow their π-donation ability. This apparent anomaly again reflects the fact that although the π-type resonance shown in eq 1 is the major interaction it is not the only one operating. σ and dipolar interactions and the higher electronegativity of O relative to N also play an important role and are responsible for the fact that OH and OCH_3 stabilize the carbonyl group more effectively than NH_2, in contrast to the qualitative argument implied by eq 1. The most likely explanation for this unusual order is that, for the oxygen substituents, additional stabilization results from the geminal interaction of the second, in-plane, lone pair with the low-lying σ^*_{C-O} orbital, as shown in **20** ↔ **20a**. This type of interaction is, of course,

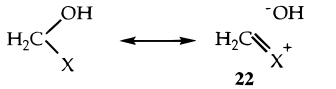


20 **20a**

not possible for NH_2, which has only one π-type lone pair. Also in the enols **2** the OH substituent is more stabilizing than NH_2, but the difference is small (i.e., 1.9 and 0.9 kcal mol^{-1} according to eqs 3 and 5, respectively). These small geminal interactions again contrast with the much larger geminal interactions in the analogous saturated XCH_2OH systems (16.5 (17.4) [17.1] and 13.1 (13.8) [13.7] for X = OH and X = NH_2, respectively). Other values are given in Table 5. In qualitative resonance terms this indicates the inefficiency of allene-type resonance forms **21** (eq 8) in comparison with the analogous vinylic forms **22** (eq 9).



21 (8)



22 (9)

The OCHO substituent stabilizes both the "keto" and the enol form less than OH (or OMe), e.g., the "keto" form is stabilized by only 11.3 kcal mol^{-1} compared with 24.7 kcal mol^{-1} for OH. This can be attributed to the lower π-donation ability of the OCHO group due to the competition of two carbonyl groups for the oxygen lone pairs. Similarly, CH_3^+ is stabilized (at MP2) by 55.6 kcal mol^{-1} by OCHO substitution, less strongly than by OH substitution (64.9 kcal mol^{-1}) (Table 5).

Acid−enol differences were calculated also for cyclopentadiene-5-carboxylic acid (**23**), which is the smallest system for which an experimental K_{Enol} value for a carboxylic acid enol is available. The calculated ΔG differences for the enol **24** vs the acid **23** are 11.7 (15.3) kcal mol^{-1}, i.e., pK_{Enol} = 8.7 (11.3). The calculated B3LYP value of 8.7 is in excellent agreement with the experimental value of 8.4 in water.[2b,6a,16]

To estimate the effect of solvation on pK_{Enol} we have conducted SCRF calculations (using the SCIPCM model)[17] for the $AcOH/CH_2{=}C(OH)_2$ equilibrium using H_2O and EtOH as solvents. The calculations show a small solvent effect on ΔG, favoring the enol by 1 (at B3LYP), 1.4 (at CCSD(T), and 1.6 kcal mol^{-1} (at MP2), in agreement with Gao's Monte Carlo calculation (0.8 ± 0.4 kcal mol^{-1}) for the same system.[9d]

(13) Frenking, G.; Fau, S.; Marchand, C. M.; Grützmacher, H. *J. Am. Chem. Soc*. **1997**, *119*, 6648.

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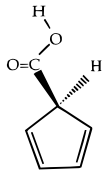
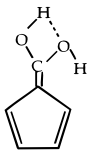
(15) Schleyer, P. v. R.; Jemmis, E. D.; Spitznagel, G. W. *J. Am. Chem. Soc*. **1985**, *107*, 6393.

(16) However, both the 1-carboxylic acid (**25**) and the 5-carboxylic acid (**23**) are formed in the ketonization (Wirz, J. Personal communication), and since the calculated ΔG difference between the more stable 1-carboxylic acid **25** and **23** is 8.7 (6.6) kcal mol^{-1}, this system is probably not ideal for calibrating the calculations.

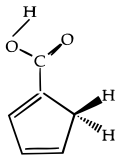
(17) Foresman, J. B.; Keith, T. A.; Wiberg, K. B.; Snoonian, J.; Frisch, M. J. *J. Phys. Chem*. **1996**, *100*, 16098.



23, C_1



24, C_s



25, C_s

Several conclusions arise from our data: (a) All the enols are much less stable than the corresponding acid derivatives. The energy differences, which are all larger than 23.8 kcal mol^{-1}, are by at least 10 kcal mol^{-1} higher than for the corresponding enols of aldehydes and ketones.[18] These large energy differences explain why only few of these species were observed. (b) The order of the calculated pK_{Enol} values for $CH_2{=}C(OH)X$ for X is H < alkyl < OCHO < Br$\sim$ Cl < F < NH_2 < NMe_2 < OH, OMe. Clearly, mesomeric electron donation from X contributes significantly to the relative stabilization of the "keto" species, but other effects are also important. For example, the pK_{Enol} value for X = OMe > X = NMe_2, although X = NMe_2 is a better π-donor. In view of the small calculated solvent effect we believe that this order will hold also in solution. (c) The experimentally estimated $pK_{Enol}(H_2O)$ value for X = OH is in good agreement with the B3LYP and CCSD(T) calculated values, but somewhat lower than the MP2 calculated value. For X = OMe the estimated $pK_{Enol}(H_2O)$ is somewhat lower than the calculated values, as was found also for X = H, Me (Table 4). However, the observed gas-phase values for X = H, Me[19] are larger than the calculated values. (d) In a search for enols of amides, an amino hydrogen should be absent in order to avoid imine formation. (e) The B3LYP, MP2, and CCSD(T) calculations display similar trends, strongly supporting the reliability of our conclusions as is the computation/experimental agreement for cyclopentadiene-5-carboxylic acid.[16] Quantitatively the calculated ΔH and ΔG values at MP2 are generally 1−3 kcal mol^{-1} higher than the B3LYP or the CCSD(T) results.

We encourage experimental testing of the computational predictions.

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Supporting Information Available: Tables of calculated absolute energies, Gibbs energies, and zero point energies (7 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

JA980354E

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