Supplementary Materials

Structural Analysis of 3,5-Bistrifluoromethylhydrocinnamic Acid

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Table S1. Geometric and energetic parameters for the conformers of the unsubstituted hydrocinnamic acid and 3,5-bis-trifluoromethylhydrocinnamic acid (B3LYP/aug-cc-pvDZ level, gas-phase, with Grimme D3 correction for dispersion).

hydrocinnamic acid						3,5-bistrifluoromethylhydrocinnamic acid					
			Side-chain dihedral angles						Side-chain dihedral angles		
		ΔG [kJ/mol]	θ_1	θ_2	θ_3			ΔG [kJ/mol]	θ_1	θ_2	θ_3
1	trans-1 *(c,ap,sp)*	0.0	-89	180	0	1	trans-1 *(c,ap,sp)*	0.0	-89	180	-47
2	gauche-1 *(c,sc,sp)*	2.5	-87	-73	-24	4	gauche-1 *(c,sc,sp)*	3.1	-86	-72	-64
3	trans-2 *(c,ap,c)*	3.2	-90	-179	99	3	trans-2 *(c,ap,c)*	3.9	-91	-179	104
4	trans-flat *(sp,ap,sp)*	5.8	180	180	0	2	trans-flat *(sp,ap,sp)*	7.6	180	180	-47
5	gauche-2 *(c,sc,ac)*	5.8	-81	-62	131	5	gauche-2 *(c,sc,ac)*	7.6	-82	-60	132

A comment on GD3-corrected calculations:

When Grimme D3 correction for dispersion correction is applied to the calculations in the gas phase, the order of conformers of the hydrocinnamic acid changes. The ΔG between **gauche-1** and **trans-flat** is 3.4 kJ/mol.

In 3,5-bistrifluoromethylhydrocinnamic acid, the order of conformers with the D3 correction applied is just like in the calculations without this correction. ΔG between **gauche-1** and **trans-flat** is 4.4 kJ/mol. This is qualitatively consistent with the gas-phase, uncorrected calculations – **gauche-1** stabilization increases with 3,5-CF_3-substitution.

Table S2. Geometric and energetic parameters for the conformers of the unsubstituted hydrocinnamic acid and 3,5-bis-trifluoromethylhydrocinnamic acid (B3LYP/aug-cc-pvDZ level, with PCM solvent [water] model).

hydrocinnamic acid						3,5-bistrifluoromethylhydrocinnamic acid					
			Side-chain dihedral angles						Side-chain dihedral angles		
		ΔG [kJ/mol]	θ_1	θ_2	θ_3			ΔG [kJ/mol]	θ_1	θ_2	θ_3
1	trans-1 *(c,ap,sp)*	0.0	-89	180	0	1	trans-1 *(c,ap,sp)*	0.0	-89	180	-47
2	trans-2 *(c,ap,c)*	3.4	-90	-179	98	2	trans-2 *(c,ap,c)*	1.9	-90	-179	107
3	gauche-1 *(c,sc,sp)*	4.3	-87	-73	-24	3	gauche-1 *(c,sc,sp)*	3.8	-76	-71	-64
4	trans-flat *(sp,ap,sp)*	4.5	180	180	0	4	trans-flat *(sp,ap,sp)*	5.6	180	180	-48
5	gauche-2 *(c,sc,ac)*	5.8	-79	-63	121	5	gauche-2 *(c,sc,ac)*	6.6	-76	-62	131

A comment on calculations in water (with PCM solvent model).

First of all, it is to be noted, that the calculations were done on unionized acids, while pKa's for these analogues are to be expected at around 4.5-5. Therefore, they are applicable to low pH situation.

In the unsubstituted hydrocinnamic acid, the order of conformers is changed compared to the gas phase calculations. The **gauche-1** and **trans-flat** confomers are almost equinenergetic (ΔG=0.2 kJ/mol).

In the substituted analogue, again the order of conformers is different than in the gas phase. The ΔG between **gauche-1** and **trans-flat** significantly increases (ΔG = 2.3 kJ/mol).

This is analogous to the gas phase results, in which 3,5-bisCF_3 substitution increases the population of **gauche-1** conformers.