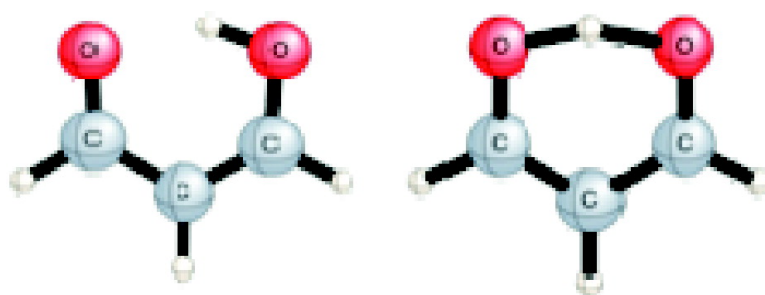


Short Intramolecular Hydrogen Bonds: Derivatives of Malonaldehyde with Symmetrical Substituents

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Short Intramolecular Hydrogen Bonds: Derivatives of Malonaldehyde with Symmetrical Substituents

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Abstract: A systematic study of various derivatives of malonaldehyde has been carried out to explore very short hydrogen bonds ($r_{\text{OO}} < 2.450 \text{ \AA}$). Various electron-withdrawing groups, including CN, NO_2 , and BH_2 , have been attached to the central carbon atom, C_2 . To C_1 and C_3 , strong electron donors and/or sterically hindered substituents were used to strengthen the intramolecular hydrogen bond, including but not limited to NH_2 , $\text{N}(\text{CH}_3)_2$, and $\text{C}(\text{CH}_3)_3$. Seven molecules (Figure 2) were found to have extremely short intramolecular hydrogen bonds. The chemical systems investigated are intriguing due to their low energetic barriers for the intramolecular hydrogen atom transfers. Classical barriers were predicted using correlated methods including second-order perturbation theory and coupled cluster theory in conjunction with the Dunning hierarchy of correlation consistent basis sets, cc-pVXZ ($X = \text{D}, \text{T}, \text{Q}, 5$). Focal point analyses allowed for the barriers to be evaluated at the CBS limit including core correlation and zero-point vibrational energy corrections. B3LYP energies are benchmarked against highly accurate correlated energies for intramolecular hydrogen bonded systems. The focal point extrapolated method, including coupled cluster full triple excitation contributions, gives a hydrogen transfer barrier for malonaldehyde of $\sim 4 \text{ kcal mol}^{-1}$. We describe two compounds with extremely low classical barriers, nitromalonamide ($0.43 \text{ kcal mol}^{-1}$) and 2-borylmalonamide ($0.60 \text{ kcal mol}^{-1}$). An empirical relationship was drawn between the B3LYP energetic barriers and the predicted coupled cluster barriers at the CBS limit. By relating these two quantities, barrier heights may be estimated for systems too large to presently use highly correlated electronic structure methods.

Introduction

Intramolecular hydrogen bonding interactions are essential in biochemical reactions and enzymatic processes.^{1,2} Malonaldehyde (MA) has been studied extensively not only because of the system's biological connections, but additionally because it is the prototypical model for intramolecular hydrogen bonding. Malonaldehyde has a symmetrical double well potential energy surface, with two equivalent C_s minima and a C_{2v} transition state (See Figure 1 for atom numbering in MA).^{3–17} Specifically, intramolecular hydrogen bonding is displayed between

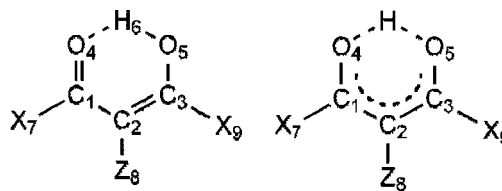


Figure 1. (Left) Malonaldehyde parent structure at its C_s equilibrium geometry. (Right) C_{2v} transition state.

the two electronegative atoms, which are designated proton donors and proton acceptors.¹ The 2,4-diketones and *cis*-enoicacids are two classes of molecules where some of the shortest intramolecular hydrogen bonding distances occur.¹⁸ The low energy barrier for proton transfer in enolized 2,4-diketones, including malonaldehyde, is usually explained by π delocal-

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ization and hydrogen bond shortening.^{19–21} In fact, when hydrogen atom transfer occurs from an equilibrium geometry to a transition state, there is significant π delocalization over the six-membered cyclic transition state geometry.²² The addition of electron-withdrawing and/or electron-donating substituents on the 2,4-diketone affects the delocalized π system, hence lowering or raising the barrier height of the symmetric double well energy potential.

Malonaldehyde and its derivatives have been the focus of numerous experimental^{7,13–15,23–33} and theoretical investigations.^{22,34–38} In 1985, Frisch et al.⁸ performed the first modern theoretical computations on malonaldehyde. At the SCF level of theory using a 6–31G** basis set, the hydrogen bonded distance H \cdots O for MA was much too large, 1.88 Å, compared to E.B. Wilson's definitive experimental result⁷ of 1.68 Å for the deuterated compound. With the MP2 method using a 6–31G** basis set, a hydrogen bond distance comparable to experiment (1.694 Å) was predicted.^{8–10} In 2003, Mil'nikov and co-workers computed the energy barrier at the CCSD(T)/aug-cc-pVTZ level to be 3.8 kcal mol⁻¹, for a time the best *ab initio* value available.¹¹ Recently, Wang, Braams, Bowman, Carter, and Tew determined an *ab initio* potential energy surface of malonaldehyde at the basis set limit using CCSD(T) electronic energies. They computed the barrier to be 4.1 kcal mol⁻¹, the most reliable result to date.¹⁶ However, the most remarkable feature of the pioneering work of Bowman and co-workers is their full-dimensional quantum mechanical treatment of the malonaldehyde tunneling splittings.

Many other studies have examined acetyl acetone, which is malonaldehyde with methyl groups substituted on C₁ and C₃ (see Figure 1 for atom labels), over the years via *ab initio* and experimental methods.^{23,24,32,33,36,37,39–43} There have been controversial discussions about the ground-state of acetylacetone, whether or not it is a single- or double-well potential. For example, Dannenberg and Rios reported results on the various

conformations of acetyl acetone in 1994.²² They performed computations at the HF and MP2 levels of theory using basis sets up to D95++**. Dannenberg and Rios conclude in their study that the conjugated enol of acetyl acetone has a double well potential with respect to the hydrogen atom.²² Zewail and co-workers²³ used ultrafast electron diffraction and concluded that the double well potential exists. However, other work including that of Lowrey, George, D'Antonio and Karle,²⁴ as well as Caminati and Grabow,³² disagrees saying that the ground-state has a symmetrical C_{2v} structure.

Various symmetrically substituted derivatives of malonaldehyde have been investigated.^{18,40,44–48} The halogenated, amino, and nitro-substituted derivatives examined by Buemi and Zuccarello^{44,45} gave rise to several conclusions reexamined in this research. Electron-withdrawing groups substituted on the central atom C₂ shortened the intramolecular hydrogen bond. When electron-withdrawing groups, including halogens, are substituted on the symmetrical carbons, C₁ and C₃, the intramolecular hydrogen bond is lengthened. Electron-donating groups substituted on the symmetrical carbons also contribute to the shortening of the intramolecular hydrogen bond. Because hydrogen bonds cannot be straightforwardly examined by X-ray crystallography, these bonds are typically characterized the distance between O₄ and O₅. Gas phase and crystallographic evidence differs. While gas phase evidence requires reasonably strong intermolecular interactions between monomeric free molecules, crystallographic evidence takes place in an asymmetric field where the space group and unit cell are necessary to understand the environments of individual molecules. One of the shortest intramolecular hydrogen bonds known to date is that for nitromalonamide, where C₁ and C₃ are substituted with amino groups and C₂ is substituted with a nitro group. For nitromalonamide the O \cdots O separation is predicted to be 2.394 Å using the B3LYP method with the cc-pVTZ basis set.⁴⁷

In this study we initially apply the density functional theory (DFT) to examine several symmetrical derivatives of MA and characterize the intramolecular hydrogen bond by the distance between the oxygen atoms. We also applied DFT to study the classical barrier heights for hydrogen transfer. Highly correlated electronic structure methods are then used for focal point extrapolations nailing down accurate barrier heights of the intramolecular proton transfers for the eight simplest systems. An empirical scheme was developed to approximate the barrier heights at highly correlated levels using only DFT energy barriers, which are predicted to be too low. We investigate whether or not it is possible to have a substituted malonaldehyde system without a barrier.

Theoretical Methods

Energies, optimized structures, transition state structures, and vibrational frequencies were initially determined using the B3LYP

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generalized gradient approximation (GGA) exchange correlation functional. B3LYP is a combination of Becke's exchange functional, the 3-parameter HF/DFT hybrid exchange function (B3),⁴⁹ and the dynamical correlation functional of Lee, Yang, and Parr (LYP).⁵⁰ All computations were performed using double- ζ -quality basis sets with polarization and diffuse functions, designated DZP++.

The DZP++ basis sets were constructed by augmenting the Huzinaga–Dunning^{51,52} sets of of contracted double- ζ Gaussian functions with one set of p -type polarization functions for each H atom and one set of five d -type polarization functions for each B, C, N, and O atom [$\alpha_p(\text{H}) = 1.0$, $\alpha_d(\text{C}) = 0.75$, $\alpha_d(\text{O}) = 0.85$, $\alpha_d(\text{N}) = 0.80$, $\alpha_d(\text{B}) = 0.70$]. To complete the DZP++ basis, even-tempered s and p diffuse functions were centered on each heavy atom. The even-tempered orbital exponents were determined according to the prescription of Lee.⁵³

The final DZP++ set contains six functions per H atom ($5s1p/3s1p$) and 19 functions per B, C, N, or O atom ($10s6p1d/5s3p1d$), yielding a total of 119 contracted functions for the parent molecule, malonaldehyde. DFT numerical integrations were performed using Q-Chem 3.1⁵⁴ with a grid consisting of 75 radial shells and 302 angular points. All structures were optimized using analytic gradients with tight convergence criteria. Vibrational frequency evaluations were done on all structures, and no scaling factors were applied.

A focal point analysis using the HF, MP2, CCSD, CCSD(T), and CCSDT levels of theory was performed using the correlation consistent basis sets of Dunning⁵⁵ (cc-pVXZ, $X = \text{D, T, Q, 5}$) to yield values extrapolated to the basis set limit. Geometries used for the focal point analysis were generally computed using the aforementioned DFT method. However, for malonaldehyde and its transition state geometries were computed at the far more complete CCSD(T)/cc-pVQZ level of theory to compare the two methods. For nitromalonamide the CCSD(T)/cc-pVQZ computations include 700 basis functions. For the core correlation corrections the correlation-consistent, core-valence polarized, triple- ζ (cc-pCVTZ) basis set of Woon and Dunning was used.⁵⁶ The total electronic energy extrapolation, was partitioned in two terms. The first term corresponds to the total SCF energy and was fitted to the functional form⁵⁷

$$E_{\text{SCF}}(X) = A + Be^{-CX}$$

where X is the cardinal number corresponding to the maximum angular momentum of the basis set. The correlation energy was extrapolated using the formula⁵⁸

$$E_{\text{CORR}}(X) - E_{\text{SCF}}(X) = A + BX^{-3}$$

Molpro^{59–64} version 2006.1 was used for all energies computed in the focal point analyses. For the malonaldehyde transition state,

the geometry was optimized using PSI3.⁶⁵ The single point energy for malonaldehyde at the CCSDT level was computed using Aces II.⁶⁶

Results and Discussion

Geometries. In the present research we explore a substantial range of malonaldehyde derivatives targeting the shortest symmetrical intramolecular hydrogen bond. These hydrogen bonds are characterized by their $\text{O}\cdots\text{O}$ distances, where short and very short $\text{O}\cdots\text{O}$ connections are considered⁶⁷ ≤ 2.500 and ≤ 2.450 Å, respectively. X-ray diffraction experiments⁶⁸ have shown that one of the derivatives of MA with the shortest hydrogen bond is nitromalonamide (Figure 2, VII), where amino groups are substituted on C_1 and C_3 and a nitro group attached to C_2 . In this work we predict the $\text{O}_4\cdots\text{O}_5$ distance in nitromalonamide to be 2.380 Å, which is the shortest $\text{O}_4\cdots\text{O}_5$ distance found here. In the exploration we used nitromalonamide as a model for short intramolecular hydrogen bonds where one substituent, X , was placed on C_1 and C_3 (see Figure 1), and a second substituent, Z , was placed on C_2 . In this research, the unique structures I–VI are found to have the shortest $\text{O}_4\cdots\text{O}_5$ distances following nitromalonamide.

Let us first consider the effect of substituents bonded to the central carbon atom C_2 . B3LYP/DZP++ predicts that the parent reference structure MA has an $\text{O}\cdots\text{O}$ distance of 2.546 Å. When an electron-withdrawing group is attached to C_2 the hydrogen bond is shortened. A cyano group was substituted in this position, and an $\text{O}\cdots\text{O}$ distance of 2.526 Å was predicted. The nitro substituted molecule also has a shortened hydrogen bond, with an $\text{O}\cdots\text{O}$ distance of 2.521 Å. When a BH_2 group is substituted on C_2 , the shortest hydrogen bond of this series is obtained, with an $\text{O}\cdots\text{O}$ distance of 2.499 Å.

There are several trends to consider when substituents X_7 and X_9 replace the malonaldehyde H atoms bound to C_1 and C_3 , while the atom Z_8 bonded to C_2 remains hydrogen. The most significant factors playing a role in the hydrogen bond distances are the electron-donating properties of substituents and steric hindrance. Previous results show that upon placing electron-withdrawing groups on C_1 and C_3 , the $\text{O}\cdots\text{O}$ distance increases with respect to the parent MA.⁴⁴ Electron-donating groups attached to C_1 and C_3 have the desired effect of decreasing the $\text{O}\cdots\text{O}$ distances. When electron donors are connected to these positions the $\text{O}\cdots\text{O}$ distances decrease. The hydrogen bond distance decreases as the strength of the electron donor increases. With methoxy groups bonded to C_1 and C_3 , the distance of the hydrogen bond decreases, with $\text{O}\cdots\text{O} = 2.498$ Å, while an amino group further decreases the $\text{O}\cdots\text{O}$ distance to 2.474 Å.

To examine the chemical consequences of steric hindrance, we substituted C_1 and C_3 with methyl, isopropyl, and tert-butyl groups. The methyl substituted structure has an $\text{O}\cdots\text{O}$ distance of 2.511 Å. This is a shorter hydrogen bond than MA (2.546 Å), and can be explained considering the steric hindrance of the methyl group. As the size of the substituent continues to increase to isopropyl and tert-butyl, the $\text{O}\cdots\text{O}$ distance decreases to 2.491 and 2.466 Å, respectively. This series of molecules exemplifies the importance the bulk of the substituent on the hydrogen bond distance.

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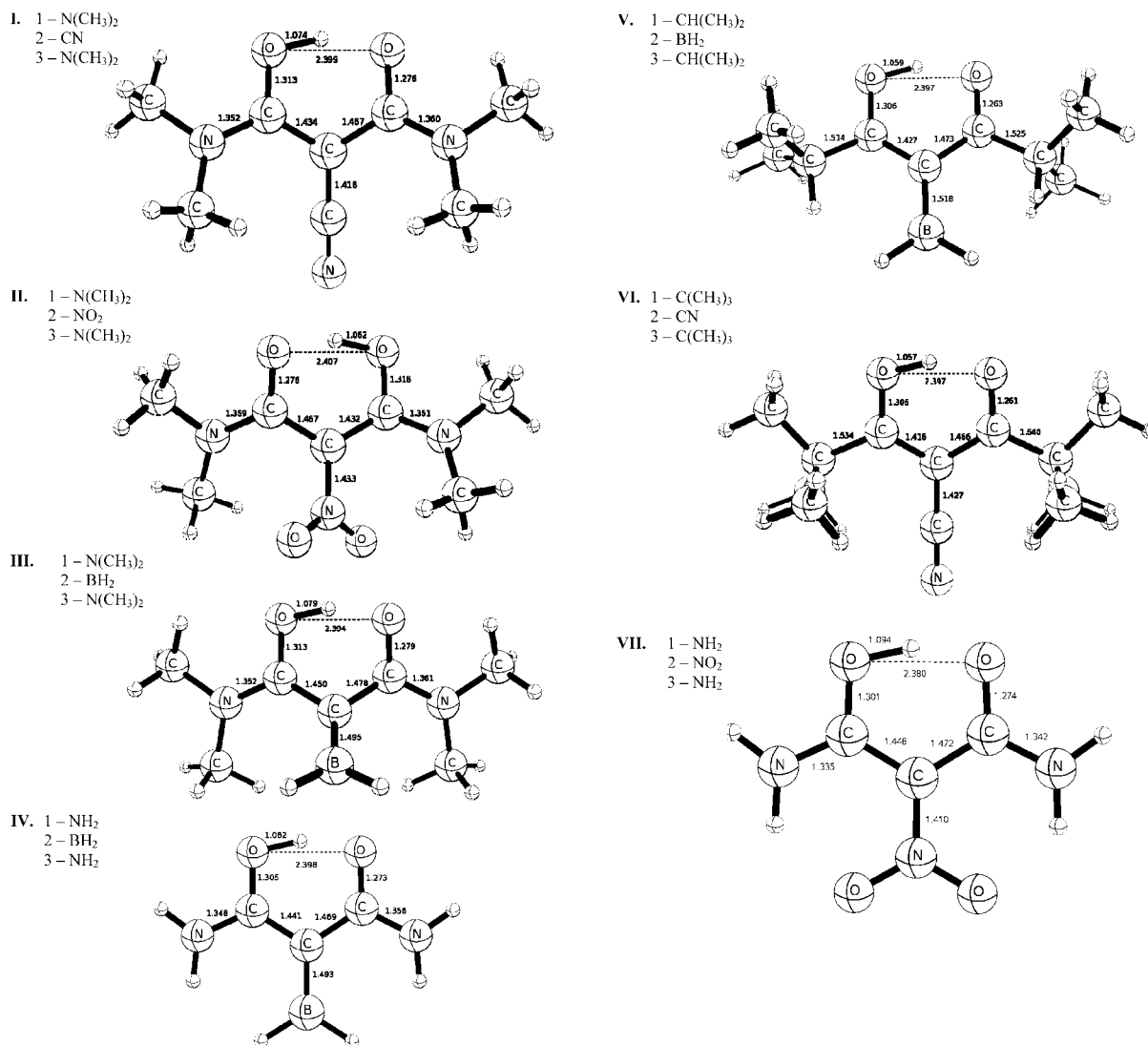


Figure 2. Seven structures with very short intramolecular hydrogen bonds. Bond distances are reported in Å. The six compounds are named by their substituents. See atom numbering in Figure 1.

Table 1. Distance (Å) between Atoms O₄ and O₅ and |Q| Value^a

Unique Carbon Substituents	Substituents on the Symmetrical Carbons									
	H	NH ₂	N(CH ₃) ₂	CH ₃	CH(CH ₃) ₂	C(CH ₃) ₃	OCH ₃	OCH(CH ₃) ₂	OC(CH ₃) ₃	
H	2.546	2.474	2.434	2.511	2.491	2.466	2.498	2.487	2.485	
	0.136	0.104	0.082	0.136	0.122	0.117	0.114	0.111	0.110	
CN	2.526	2.448	2.399	2.471	2.456	2.397	2.464	–	–	I
	0.134	0.087	0.069	0.125	0.118	0.091	0.102	–	–	
NO ₂	2.521	2.380	2.407	2.423	2.425	–	2.442	–	–	VII
	0.124	0.051	0.079	0.101	0.109	–	0.095	–	–	II
BH ₂	2.499	2.398	2.394	2.419	2.397	–	2.421	–	–	III
	0.114	0.061	0.063	0.099	0.089	V	0.080	–	–	

^a The upper result (in each pair of rows) is the distance (Å) between atoms O₄ and O₅ (see Figure 1), shown for molecules with varying substituents. This method is useful for characterizing the intramolecular hydrogen bond, because the results may be directly compared to the few available crystal structures, where the precise positions of the H atoms are not known. The lower result is the |Q| value,²¹ which helps to understand the amount of π delocalization present in the system.

When considering the shortest, symmetrical, intramolecular hydrogen bond one should attempt to determine the more important factor affecting the distance of the hydrogen bond, namely electron donation or steric hindrance. Here substituents of similar size were compared, one being an electron donor and the other having more steric hindrance surrounding the oxygens of the parent compound. These results are summarized in Table 1. Methyl and methoxy C₁ and C₃ substituted molecules have

similar hydrogen bonding characteristics, with O \cdots O distances of 2.511 and 2.498 Å, respectively. When comparing the isopropyl and isopropoxide substituted molecules, a trend still is not clear. However, when increasing the size of the substituent to tert-butyl and tert-butoxide there is a clear discrimination. The tert-butyl group with more steric hindrance has a shorter hydrogen bond than the tert-butoxide substituted compound, the O \cdots O distances being 2.466 and 2.485 Å, respectively.

Table 2. This Focal Point Analysis Shows the Classical Barrier Height for Proton Transfer between the Two Oxygen Atoms in Malonaldehyde^a

basis set	ΔE_b [RHF]	$+\delta$ [MP2]	$+\delta$ [CCSD]	$+\delta$ [CCSD(T)]	$+\delta$ [CCSDT]	ΔE_b [CCSDT]
[a]						
cc-pVDZ	+8.03	-5.12	+1.87	-0.96	+0.04	+3.86
cc-pVTZ	+8.11	-5.34	+2.00	-1.08	[+0.04]	[+3.73]
cc-pVQZ	+8.21	-5.31	+2.06	-1.10	[+0.04]	[+3.90]
cc-pV5Z	+8.21	-5.31	+2.08	[-1.10]	[+0.04]	[+3.92]
CBS limit	[+8.21]	[-5.32]	[+2.10]	[-1.10]	[+0.04]	[+3.93]
$\Delta E_b(\text{final}) = \Delta E_c[\text{CBS CCSDT}] + \Delta_{\text{core}}[\text{MP2/cc-pCVTZ}] = 3.93 - 0.01 = \mathbf{3.92} \text{ kcal mol}^{-1}$						
$\Delta E_{b,0}(\text{final}) = \Delta E_c[\text{CBS CCSDT}] + \Delta_{\text{ZPVE}}[\text{B3LYP/DZP++}] + \Delta_{\text{core}}[\text{MP2/cc-pCVTZ}] = 3.93 - 2.38 - 0.01 = \mathbf{1.54} \text{ kcal mol}^{-1}$						
Fit	$a+be^{-cX}$	$a+bX^{-3}$	$a+bX^{-3}$	$a+bX^{-3}$	additive	
Points (X)	3,4,5	4,5	4,5	3,4		
[b]						
cc-pVDZ	+9.17	-6.39	+2.34	-1.18	+0.05	+3.99
cc-pVTZ	+9.31	-6.63	+2.49	-1.32	[+0.05]	[+3.90]
cc-pVQZ	+9.44	-6.60	+2.56	-1.33	[+0.05]	[+4.12]
cc-pV5Z	+9.43	-6.60	+2.58	[-1.33]	[+0.05]	[+4.13]
CBS limit	[+9.43]	[-6.60]	[+2.58]	[-1.33]	[+0.05]	[+4.13]
$\Delta E_b(\text{final}) = \Delta E_c[\text{CBS CCSDT}] + \Delta_{\text{core}}[\text{MP2/cc-pCVTZ}] = 4.13 - 0.06 = \mathbf{4.07} \text{ kcal mol}^{-1}$						
$\Delta E_{b,0}(\text{final}) = \Delta E_c[\text{CBS CCSDT}] + \Delta_{\text{ZPVE}}[\text{B3LYP/DZP++}] + \Delta_{\text{core}}[\text{MP2/cc-pCVTZ}] = 4.13 - 2.50 - 0.06 = \mathbf{1.57} \text{ kcal mol}^{-1}$						
Fit	$a+be^{-cX}$	$a+bX^{-3}$	$a+bX^{-3}$	$a+bX^{-3}$	additive	
Points (X)	3,4,5	4,5	4,5	3,4		

^a MA is optimized at B3LYP/DZP++ in [a] and CCSD(T)/cc-pVQZ in [b]. For the correlated methods, the symbol δ denotes the increment in the relative energies between the preceding level of theory in the hierarchy. The square brackets signify the values extrapolated from the basis sets, where all other entries are computed values. The final predictions are in bold print.

When combining the two factors of steric hindrance and electron donation, the best hydrogen bond shortening substituent for C₁ and C₃ is an excellent electron-donating group with significant steric hindrance to surround the oxygen atoms. When considering only substituents on C₁ and C₃, dimethylamino gives the shortest hydrogen bond of this series with an O...O distance of 2.434 Å. This appears to be caused by electron donation to the π orbitals of MA and the steric hindrance of the methyl groups.

By means of the systematic examination we have found that particular combinations of substituents attached to all three carbons in the parent malonaldehyde structure result in some very short symmetrical intramolecular hydrogen bonds. Besides the amino and nitro derivatives of MA, including nitromalonamide, we present several other structures with short hydrogen bonds. A fascinating molecule examined during this inquiry has BH₂ attached to C₂ and NH₂ bonded to C₁ and C₃. This structure, **IV**, (Figure 2) has an O...O distance of 2.398 Å. In this respect structure **IV** is similar to nitromalonamide in structure, with a comparable hydrogen bond distance.

Dimethylamino substituted MA leads to the series with some of the shortest intramolecular hydrogen bonds among those considered here. The C₂ cyano derivative (structure **I**) displays a short hydrogen bond, with an O...O distance of 2.399 Å. The nitro derivative (structure **II**) has an O...O distance of 2.407 Å, larger than that for structure **I** because the substituent does not lie in the molecular plane due to the steric effects of the substituents attached to C₁ and C₃. With BH₂ substituted on the unique carbon (structure **III**) the O...O distance shortens to 2.394 Å. It is seen that the BH₂ group usually has a more significant electron-withdrawing effect compared to the nitro and cyano groups.

There are two other molecules with theoretical O...O distances ≤ 2.400 Å. The first molecule has a tert-butyl group substituted on C₁ and C₃ and a cyano group substituted on C₂

(structure **VI**). Structure **VI** has been studied by neutron diffraction crystallography and determined to have O...O distance of 2.393 Å.¹⁸ Here B3LYP with the DZP++ basis set predicts a distance of 2.398 Å. This agrees very well with experiment and confirms the strength of the intramolecular hydrogen bond of **IV**. Another system (structure **V**) with a very short hydrogen bond has isopropyl as the C₁ and C₃ substituents and BH₂ as the C₂ substituent. This structure has an O...O distance of 2.398 Å, presumably due to the steric hindrance of the isopropyl group and the strength of the BH₂ group.

Energy Barrier Studies. Another way to characterize substituted malonaldehyde hydrogen bonds is the classical energy barrier (ΔE_b , Table 2) occurring between the two equivalent minima. B3LYP energy barriers have been established to be underestimated for such systems.⁶⁹ However, the study of larger chemical systems at higher levels of theory may be impractical. We determined the energy barrier for intramolecular proton transfer for several derivatives of MA using the B3LYP method with the DZP++ basis set. The B3LYP energies show the correct qualitative trend based upon the O...O distance; however the DFT energies are underestimated. For example, the best estimate of the barrier from the literature¹⁶ is 4.09 kcal mol⁻¹, while B3LYP predicts a barrier of only 2.1 kcal mol⁻¹. To benchmark the B3LYP energy barriers we performed high level focal point analyses of MA and seven of its derivatives.

In addition, to help verify the method used in this work, the geometry for MA was optimized at the CCSD(T) level using a cc-pVQZ basis set. The energy barrier at this level of theory is 4.06 kcal mol⁻¹. A focal point analysis was performed using this geometry, and the energy barrier is computed to be 4.07 kcal mol⁻¹. A comparison can be drawn between this value, 4.07 kcal mol⁻¹, and 3.92 kcal mol⁻¹, the number computed

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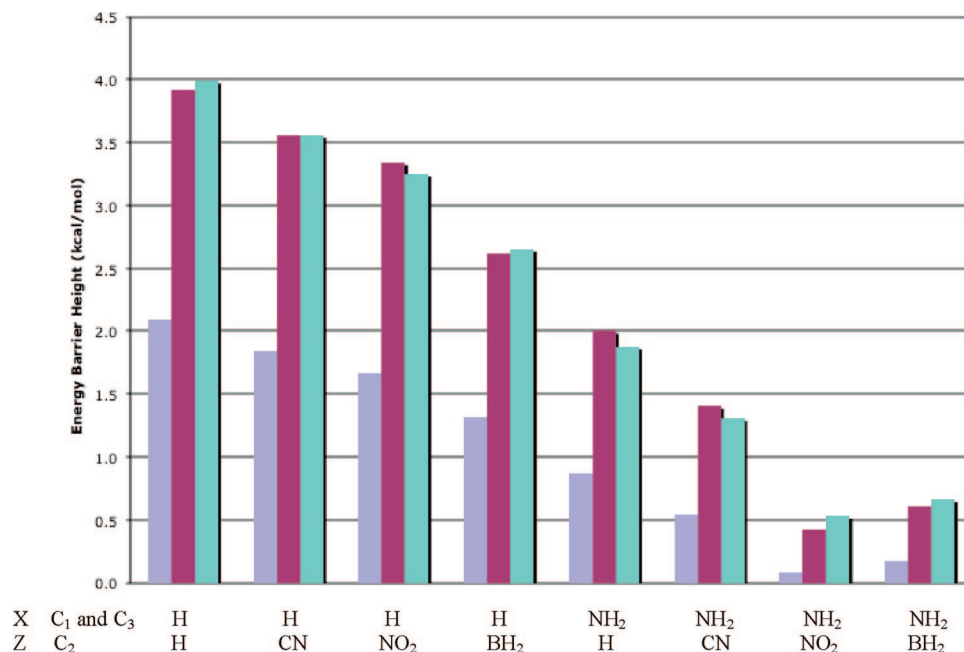


Figure 3. For molecular systems 1–8, this figure draws a comparison between the barrier heights between the DFT (left column), the extrapolated focal point energy (middle column), and the energy predicted using the linear fit (right column).

from the focal point analysis with the B3LYP/DZP++ geometry. The difference between these two methods is 0.15 kcal mol⁻¹, which is a satisfactorily accurate prediction obtained without performing rigorous coupled cluster geometry optimizations.

The focal point analysis for MA is reported in Table 2. Our complete basis set extrapolated energy barrier is 3.92 kcal mol⁻¹. We find excellent convergence with respect to correlation and basis set treatments; the CCSD(T)/cc-pVDZ and CCSDT/cc-pVDZ energies are separated by only 0.04 kcal mol⁻¹, while the CCSD(T) cc-pVQZ and the CCSD(T) cc-pVTZ are separated by only 0.02 kcal mol⁻¹. Core-correlation is estimated to lower the barrier by 0.01 kcal mol⁻¹.

Using the focal point method one may reliably compare the barriers for some of the derivatives to MA. The C₂-cyano substituted molecule has a barrier of 3.56 kcal mol⁻¹ which is 0.36 kcal mol⁻¹ lower in energy than MA. As the strength of the electron-withdrawing substituent on C₂ increased, the barrier height is further decreased to 3.34 and 2.62 kcal mol⁻¹ for the NO₂ and BH₂ substituted molecules, respectively.

The other series of molecules examined with the focal point method include structures with amino (NH₂) groups substituted on both C₁ and C₃ and withdrawing groups substituted on C₂. For the first of the series, where an amino group is attached to C₁ and C₃ and the unique carbon is unsubstituted, the barrier height is 2.02 kcal mol⁻¹. This barrier height decreases as stronger withdrawing groups are substituted on the unique carbon. For the cyano substituted (on atom C₂) system, the barrier height decreases to 1.40 kcal mol⁻¹. The results from the focal point analyses for the systems with stronger substituents bonded to the unique carbon are 0.43 and 0.60 kcal mol⁻¹ for the NO₂ (nitromalonamide, VII), and the BH₂ (IV), substituted molecules, respectively. This relationship is exactly what is expected from the O...O distances computed in the more qualitative DFT studies. Recall that nitromalonamide is thought⁴⁷ to possess one of the smallest intramolecular proton transfer barriers, theoretically estimated to be 0.6 and 1.2 kcal mol⁻¹ using MP2/cc-pVTZ and B3LYP/cc-pVTZ, respectively. In this work, the barrier for nitromalonamide is predicted to be

0.43 kcal mol⁻¹ using the focal point method, the lowest barrier we find. This value should be the most reliable barrier reported to date for nitromalonamide, obtained with the aid of the high level focal point analysis. It appears that changing the amino substituent to dimethylamino lowers the barrier when smaller substituents are on C₂, such as cyano. However, as the size of the substituent increases to the NO₂ or BH₂ group, steric hindrance occurs between the C₂ substituents and the dimethylamino groups on C₁ and C₃. When the C₂ substituents are forced to break the plane of the MA system due to steric reasons, they have less of a strengthening affect.

The present study also investigates the relationship between the systematically underestimated B3LYP barriers and the more accurate extrapolated energies computed from the focal point method. The B3LYP energies were plotted versus the extrapolated energies for the eight chemical systems examined in the focal point extrapolations. A linear fit was performed on this plot to determine the relationship between the energies computed using the two very different methods. We apply the linear equation obtained (in kcal mol⁻¹),

$$\Delta E_b^{\text{FP}} = 1.73\Delta E_b^{\text{B3LYP}} + 0.38$$

to our chemical systems. In the above equation, $\Delta E_b^{\text{B3LYP}}$ is the barrier height computed using B3LYP, while ΔE_b^{FP} is the barrier height that is extrapolated using the focal point method. In Figure 3 and Table 3, one can see how the projected energy values have good agreement with the extrapolated values. The R^2 value for this linear equation is 0.995.

The above empirical method is now applied to interesting systems that possess very short intramolecular hydrogen bonds that may be too large to study by highly correlated methods such as the focal point analysis. Structure VI has a tert-butyl group substituted on C₁ and C₃ and a cyano group attached to the unique carbon. B3LYP predicts the energy of this barrier to be 0.38 kcal mol⁻¹. The projection method is applied to predict the energy barrier to be 1.02 kcal mol⁻¹. Structure I is probably too large to study presently by the focal point method, due to the dimethylamino substituents on C₁ and C₃ and the

Table 3. Hydrogen Atom Transfer Barrier Heights (ΔE_b) (kcal mol⁻¹) for Three Different Approaches Applied in This Research^a

C ₁ and C ₃	H				NH ₂				
	C ₂	B3LYP/ DZP++	focal point energy	linear fit	ZPVE corrected	B3LYP/ DZP++	focal point energy	linear fit	ZPVE corrected
H		2.10	3.92	4.00	1.54	0.87	2.02	1.88	-0.06
CN		1.85	3.56	3.56	1.24	0.54	1.40	1.31	-0.44
NO ₂		1.67	3.34	3.25	1.04	0.09	0.43	0.53	-0.78
BH ₂		1.32	2.62	2.66	0.40	0.17	0.60	0.67	-0.51

^a These results are shown visually in Figure 3.

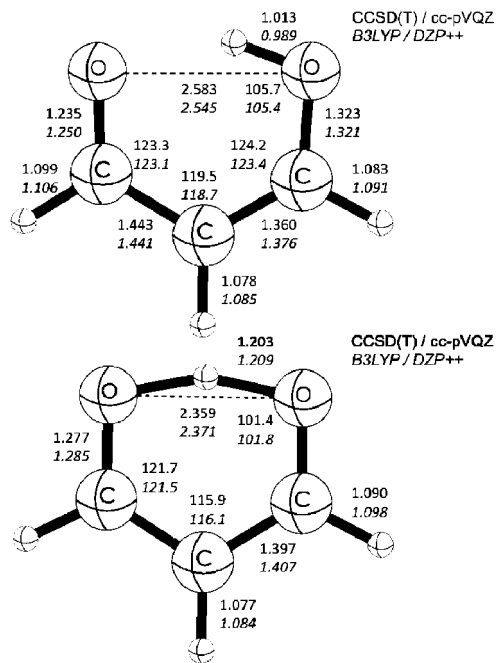


Figure 4. Optimized geometries for malonaldehyde using two levels of theory, CCSD(T)/cc-pVQZ and B3LYP/DZP++. This figure illustrates that B3LYP does a satisfactory job of reproducing the geometries computed at higher levels of theory. The B3LYP/DZP++ geometries are in italics. (Top) C_s ground-state geometry comparison and (bottom) C_{2v} transition state geometry comparison.

cyano group substituted on the unique carbon. The barrier height for the hydrogen atom transfer is predicted by B3LYP to be 0.20 kcal mol⁻¹ and when the projection method is applied the barrier height becomes 0.73 kcal mol⁻¹. This approximation corrects the underestimation that occurs with energies computed by B3LYP.

Gilli and co-workers²¹ developed a method to characterize the π delocalization. This analysis can be used to compare the trends of barrier heights versus the O...O distance. When comparing the barrier heights and the O...O distances of **IV** and **VI**, one may notice there is a difference between the two characterizations. Their O...O distances are nearly identical, but their barrier heights are 0.60 and 1.02 kcal mol⁻¹, respectively. One may compute the $|Q|$ value (Table 1) suggested by Gilli to help explain the π delocalization.

$$|Q| = d(C_3-O_5) - d(C_1-O_4) + d(C_1-C_2) - d(C_2-C_3)$$

The lower the $|Q|$ value the more π delocalization the system possesses. The $|Q|$ value is computed from the geometries and yields in the correct trends of the barrier heights (Figure 4). For **IV** and **VI** the $|Q|$ values are 0.061 and 0.091, respectively, suggesting that **IV** has much more π delocalization. This trend shows that the steric hindrance of **VI** does not lower the barrier height to the degree effected by the π delocalization that **IV** possesses.

Another feature of this research is the estimation of the hydrogen transfer barriers that include zero point vibrational energy (ZPVE) corrections ($\Delta E_{b,0}$). We have compared our ZPVE value to the “exact” malonaldehyde value determined by Bowman and co-workers.¹⁶ To match the number produced by Bowman and co-workers,¹⁴ 688.3 cm⁻¹, we would need to scale our numbers by 0.992. This is surprisingly good agreement and we expect our ZPVE corrections produced in this work to be reasonable. ZPVE energy barriers can be examined more closely in Table 3.

Conclusions

The intramolecular hydrogen bond of MA has been explored extensively as the simple molecule that shows a short intramolecular hydrogen bond for which proton transfer occurs between two oxygen atoms. In this study, a series of trends were examined to explore the effect of various substituents on the intramolecular hydrogen bonds. When placing substituents on the carbons, it was found that bulky electron donors on C₁ and C₃ and strong electron-withdrawing groups bonded to the unique carbon created the strongest intramolecular hydrogen bonds. This qualitative conclusion serves as a precursor to the precise quantitative study of the hydrogen transfer barriers.

Via a systematic study, seven compounds were predicted to have very short symmetrical intramolecular hydrogen bonds. These structures all have strong electron-withdrawing groups bonded to atom C₂. Structures **I**, **II**, and **III** have short hydrogen bonds because of the steric hindrance and electron-donating character the dimethylamino substituent provides. Structure **IV** has a short hydrogen bond due to the significant electron donation the amino substituent provides, and this structure is comparable to nitromalonamide. Structures **V** and **VI** provide much steric hindrance around the oxygen atoms, which are forced together, shortening the hydrogen bond distance.

The proton transfer energy barriers were examined using three different methodologies. B3LYP is the only level of theory applied to all the systems we have examined. However, B3LYP is known to underestimate barrier heights, and this is the case for the malonaldehyde systems. The focal point method using correlated electronic structure methods was applied to the simpler systems to accurately predict the energy required for the proton transfer. A relationship was drawn between the B3LYP energies and the high level theoretical barriers that allows for accurate predictions of the proton transfer barrier heights. This relationship utilizes B3LYP energies to accurately predict the barrier heights that might be expected from highly correlated methods.

The present study reports the first high level focal point analysis for MA and predicts a hydrogen transfer barrier of 3.92 kcal mol⁻¹. Also utilizing the focal point method we predict two substituted malonaldehyde barriers to be less than 1 kcal mol⁻¹, namely the barriers for nitromalonamide and 2-boryl-malonamide. In previous theoretical work,⁴⁷ the barrier for nitromalonamide was computed to be 0.6 kcal mol⁻¹ using the

MP2 method. The latter result may be compared to the value predicted in this work utilizing the focal point analysis, namely $0.43 \text{ kcal mol}^{-1}$. The proton transfer barrier for 2-borylmalonamide is predicted to be $0.60 \text{ kcal mol}^{-1}$. For all systems considered, this rigorous approach produces the most reliable results to date.¹⁶

A remaining goal is the identification of a substituted malonaldehyde with no barrier at all, i.e., a C_{2v} equilibrium geometry. We can speculate that increasing the size of the substituent on C_1 and C_3 may lower the proton transfer barrier for this system. It would be interesting to explore the possibility of $C[\text{C}(\text{CH}_3)_3]_3$ substituents. Another prospect would be to search for an electron-withdrawing group with a more significant effect than the substituents studied in this work.

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Supporting Information Available: Full citation for refs 54 and 59; Cartesian coordinates and electronic energies for computed structures; additional geometry and focal point tables. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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