

Conformational Analysis and Near-Infrared-Induced Rotamerization of Malonic Acid in an Argon Matrix

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Relative energies and vibrational spectra of the conformational states of a malonic acid monomer (HOOCCH₂COOH) were calculated using various levels of approximation [Hartree–Fock (HF), Møller–Plesset to second order (MP2), and B3LYP density functional theory (DFT)]. The calculations predict the existence of six different conformers according to skeletal C–C bond and O–H bond rotation. Three conformers are found with energies close enough to enable their spectroscopic observation. The lowest-energy conformer (**I**) shows a nearly planar structure with an OH···O=C intramolecular hydrogen bond closing a six-membered $\overline{\text{O}=\text{C}-\text{CH}_2-\text{C}-\text{O}-\text{H}}$ ring. The second- and third-lower energy conformers (**II** and **III**) differ from the conformational ground state by less than 5 kJ mol⁻¹. Conformers **II** and **III** adopt a cis arrangement around the C–O bonds: conformer **II** exhibits the two carbonyl bonds in a nearly orthogonal arrangement, with one carboxylic group in the plane containing the carbon atoms, whereas in conformer **III** (C₂ symmetry), the carbonyl bonds make a dihedral angle of ca. 120°, and both carboxylic groups are placed out of the plane containing the skeletal carbons. Their relative energy is predicted by the highest-level calculations to be ca. 1 kJ mol⁻¹. The theoretical predictions agree with the analysis of the infrared spectra of monomeric malonic acid isolated in a solid argon matrix, where the presence of the three above-mentioned conformers was unequivocally identified. Narrowband tunable irradiation in the near-infrared region was found to promote efficiently the interconversion between the experimentally observed conformers.

Introduction

Malonic acid based compounds have been studied as inhibitors of matrix metalloproteinases involved in tissue remodeling and thus in various disease processes, including tumor invasion and joint destruction.¹ Malonic acid based inhibitors were found to bind in a unique way to the enzymes, leading to a 500–1000-fold improvement in inhibitory potency when compared with more conventional inhibitors.¹ The discovery of the specific binding of this new class of inhibitors was tentatively correlated with the molecular conformation of the malonic acid fragment at the inhibitor interaction sites. The selective conformer activity opens new perspectives in the design of more efficient drugs. However, the information available on the conformational properties of malonic acid is relatively scarce and concerns mainly the structure of its crystalline phases.^{2–9}

Malonic acid was found to exist in three distinct crystalline varieties, depending on the temperature: phase γ is stable below 48 K;² phase β is stable between 48 and 360 K;^{3,5} and phase α , which is the high-temperature phase, is stable above 360 K.^{3,6} The room-temperature phase is a centrosymmetric triclinic crystal with two molecules per unit cell. Molecules are arranged in zigzag chains, with the hydrogen-bonded carboxyl groups forming two crystallographically and spectroscopically different rings, which are nearly orthogonal.⁵ The conformation of the

individual molecules in this crystal is characterized by a nearly orthogonal arrangement of the two carboxylic groups (both in a cis configuration around the C–O bond), with one carboxyl group being coplanar with the carbon skeleton (see Figure 1).⁷ Phase α is orthorhombic, with four molecules in the unit cell, and is characterized by hydrogen-bonded dimeric units linked through symmetry-equivalent carboxyl groups. As in phase β , the molecules form zigzag chains, but the carboxylic groups are related by a 2-fold symmetry axis.^{3,6} The individual molecules belong to the C₂ symmetry point group, with both carboxylic groups out of the plane of the carbon atoms adopting the cis arrangement around the C–O bond (Figure 1).⁷

Monomeric malonic acid and its monoanion have been studied previously by Hartree–Fock ab initio self-consistent field (SCF)-molecular orbital (MO) calculations using small-size basis sets (STO-3G and 4-21G) in order to explain the large dissociation constant ratio k_1/k_2 . This ratio is usually exhibited by dicarboxylic acids where the monoanion can be stabilized by intramolecular hydrogen bonding.⁸ In this earlier study, it was suggested that nonplanar conformations of malonic acid are generally favored over the planar forms, stressing the importance of the steric repulsion between the two carboxylic groups. Nevertheless, the intramolecularly hydrogen-bonded planar structure was found to be the most stable conformer in the case of the monoanion.⁸ In a more recent paper, the HF/6-31G(d,p) calculated vibrational frequencies of monomeric

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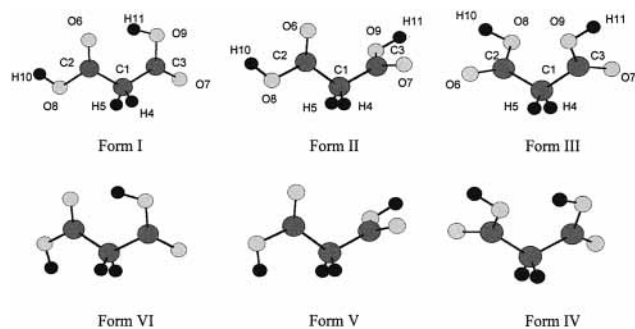


Figure 1. Malonic acid predicted conformers according to HF/6-31G(d) calculations. In crystalline phases α and β , individual molecules assume conformations similar to forms II and III, respectively. Relative energies (kJ mol^{-1}) and populations (%) are as follows: (I, 9.05, 1.1); (II, 0.00, 65.9); (III, 1.65, 33.0); (IV, 24.21, 6.0×10^{-3}); (V, 31.14, $<1.0 \times 10^{-3}$); and (VI, 37.67, $<1.0 \times 10^{-3}$). The total energy of conformer II, accounting for the zero-point vibrational energy correction, is $-1090466.35 \text{ kJ mol}^{-1}$.

malonic acid and larger dicarboxylic acids were used to test the possibility of developing a unified force field with a reasonable set of force constants for predicting solid-state spectra of these compounds.⁹ To the best of our knowledge, no further systematic structural or vibrational studies have been reported on malonic acid.

In this article, we present a detailed study of the conformational space of monomeric malonic acid. This study was undertaken with the use of high-level *ab initio* and density functional theory (DFT) calculations and matrix-isolation vibrational spectroscopy connected with selective near-infrared-induced rotamerization. In particular, the main factors that determine the stability of the different conformations and the photochemically induced interconversion processes between the lowest-energy species are analyzed.

Experimental and Computational Details

The matrix samples were prepared by continuously flushing a copper tube containing malonic acid (Aldrich, 99+%), heated to 323 K, with high-purity argon (99.9999%). The gaseous mixture was deposited onto a cooled CsI window in a close-cycle helium cryostat (APD, DE202A) at 7.5 K. The IR spectra ($4000\text{--}450 \text{ cm}^{-1}$) were measured using a Nicolet SX-60 FTIR spectrometer equipped with a liquid nitrogen cooled MCT detector and a KBr beam splitter, with spectral resolutions of 0.25 or 1.0 cm^{-1} . Typically 200 interferograms were coadded. In our samples, monomeric species were formed almost exclusively, this was achieved by choosing an appropriate temperature for the substance container and optimizing the matrix-gas flow rate.

To promote conformational interconversions, tunable pulsed near-infrared (NIR) irradiation was used, as provided by the idler beam of an optical parametric oscillator (OPO Sunlite, Continuum). The pulse duration of the NIR irradiation was ca. 5 ns, with a line width of $\sim 0.1 \text{ cm}^{-1}$. The frequency of the NIR radiation was established with an accuracy better than 1 cm^{-1} by a Burleigh WA-4500 wavemeter used to control the OPO signal radiation wavelength.

Ab initio and DFT calculations^{10–12} were performed with GAUSSIAN 92/DFT or 94,¹³ on a DEC ALPHA 7000 computer at the Center of Informatics of the University of Coimbra (CIUC) and on an SGI Origin 2000 at the Center for Scientific Computing Ltd. (CSC, Espoo, Finland).

Optimized geometries and vibrational frequencies were calculated at three different levels of theory [Hartree–Fock

(HF), Møller–Plesset to second order (MP2), and density functional theory (DFT/B3LYP)]. Several basis sets with increasing degrees of flexibility were used, ranging from the moderate size 6-31G(d) to the extended 6-311++G(3dp,3df) basis set.^{14,15}

The force constants (symmetry internal coordinates) to be used in the normal coordinate analysis were obtained from the DFT Cartesian harmonic force constants [B3LYP/6-31G(d,p)] using the program TRANSFORMER.¹⁶ This program was also used to prepare the input data for the normal coordinate-analysis programs used in this study (BUILD-G and VIBRAT).¹⁷ The calculated frequencies (B3LYP) were then scaled with the use of a single scale factor (0.9614).¹⁸

Results and Discussion

Molecular Geometries and Energetics. To find the stable conformations of malonic acid, we performed a systematic search on the HF/6-31G(d) potential energy surface (PES). These calculations are relatively inexpensive in computational terms and have been proven to yield reasonable structural data for similar compounds.^{8,18} We then used the HF/6-31G(d) calculations as a first estimate to the higher-level MP2 and DFT calculations.

In these preliminary calculations, the $\text{O}=\text{C}-\text{C}$ dihedrals of the initial structures submitted to geometry optimization were varied by 60° within the range $0\text{--}360^\circ$, and the initial $\text{O}=\text{C}-\text{O}-\text{H}$ dihedrals were made equal to 0° or 180° (all nonequivalent-by-symmetry combinations of the dihedrals were considered). The HF/6-31G(d) calculations predict the existence of six distinct conformers with nonplanar skeletons (see Figure 1). The three lowest-energy conformers (I, II, and III in Figure 1) are predicted to have relative energies differing by less than 10 kJ mol^{-1} , whereas the remaining conformers correspond to high-energy forms.

Conformer II is predicted by the HF/6-31G(d) calculations to be the lowest-energy form. It has two carboxylic groups in a nearly orthogonal arrangement; one of these groups is coplanar with the carbon atom backbone. In conformer III (belonging to the C_2 symmetry point group), the carbonyl bonds make a dihedral angle of ca. 120° , and both carboxylic groups are placed out of the plane containing the carbons. Conformers II and III adopt a *cis* arrangement around the $\text{C}-\text{O}$ bonds. Both of these structures have been described previously by low-level HF calculations.⁸ Conformer I is predicted to have an energy higher than that of conformer II or III, and it shows a nearly planar structure, with an $\text{OH}\cdots\text{O}=\text{C}$ intramolecular hydrogen bond closing a six-member $\text{O}=\text{C}-\text{CH}_2-\text{C}-\text{O}-\text{H}$ ring.

Figure 1 also gives the calculated relative populations of the various conformers at 323 K, which is the temperature used to prepare the gas-phase samples deposited onto the matrix window for IR data collection. The HF/6-31G(d) calculated relative energies were taken into account and a Boltzmann distribution was assumed. Because the relative populations of the three less-stable conformers of malonic acid are too low to enable their spectroscopic observation under the experimental conditions used in this study, the highest-level calculations (MP2 and DFT/B3LYP) were undertaken only for the three most stable conformers.

The MP2 and B3LYP relative energies, calculated using different basis sets, are presented in Table 1. Table 2 shows the optimized MP2 geometries for conformers I, II, and III, calculated using the largest 6-311++G(3df,3pd) basis set considered in this study.

The B3LYP results are not significantly affected by changing the basis set. Conformer I is always predicted to be the most

TABLE 1: B3LYP and MP2 Relative Energies (kJ mol⁻¹) of the Three Most Stable Conformers of Malonic Acid

conformer	6-31G(d,p)	6-311++G(2d,2p)	6-311++G(3df,3pd)
DFT/B3LYP			
I	0.00	0.00	0.00
II ^a	5.29	3.40	3.83
III	5.35	4.35	4.81
MP2			
I	3.58	0.33	0.00
II ^a	0.00	0.00	0.28
III	0.31	0.65	1.09

^a Doubly degenerated conformer.

TABLE 2: Geometric Parameters of Malonic Acid Conformers Obtained at the MP2/6-311++G(3df,3pd) Level of Theory

geometric parameters	conformers		
	I	II	III
Bond (Å)			
C ₁ –C ₂	1.501	1.509	1.509
C ₂ =O ₆	1.216 ^a	1.204	1.204
C ₂ –O ₈	1.336	1.349	1.349
O ₈ –H ₁₀	0.968	0.968	0.967
C ₁ –C ₃	1.527	1.504	1.509
C ₃ =O ₇	1.203	1.205	1.204
C ₃ –O ₉	1.334	1.347	1.349
O ₉ –H ₁₁	0.978 ^a	0.967	0.967
C ₁ –H ₄	1.086	1.088	1.087
C ₁ –H ₅	1.092	1.087	1.087
Angle (deg)			
C ₂ C ₁ C ₃	117.52	110.15	111.99
C ₁ C ₂ O ₆	125.53	125.80	125.72
O ₆ C ₂ O ₈	122.60	123.73	123.67
C ₂ O ₈ H ₁₀	106.78	106.08	106.33
C ₁ C ₃ O ₇	120.18	125.08	125.72
O ₇ C ₃ O ₉	122.52	123.90	123.67
C ₃ O ₉ H ₁₁	108.50	106.23	106.33
Dihedral Angle (deg)			
O ₆ =C ₂ –O ₈ H ₁₀	–0.6	–0.3	1.1
O ₆ =C ₂ C ₁ C ₃	–19.9	–3.1	–127.5
O ₇ =C ₃ –O ₉ H ₁₁	176.4	–3.0	1.1
O ₇ =C ₃ C ₁ C ₂	164.1	98.3	–127.5
H ₄ C ₁ C ₃ C ₇	–38.3	–141.3	–6.9
H ₅ C ₁ C ₂ C ₆	100.0	116.6	–6.9
O ₆ ···H ₁₁	1.756		

^a C₂=O₆ and O₉–H₁₁ bond lengths in form I clearly show the intermolecular O₉–H₁₁···O₆=C₂ hydrogen bond in this conformer, as they are clearly longer than in the free O–H and C=O bonds in the other conformers.

stable conformer, followed by conformers **II** and **III**. These two structures are predicted to be ca. 5 kJ mol⁻¹ higher in energy, being of almost similar energy when compared with each other. On the other hand, the MP2 results show an interesting dependence on the basis set. In particular, increasing the flexibility of the basis set leads to a stabilization of conformer **I** relative to conformers **II** and **III**. Indeed, when the largest basis set is used, the MP2 calculated relative energies follow the same trend as those resulting from DFT calculations, with conformer **I** predicted as the lowest-energy conformer, followed by conformers **II** and **III**. The smaller basis sets at the MP2 level predict conformer **II** to be slightly lower in energy than conformer **I**. These results are a direct consequence of the better description of the intramolecular hydrogen bond when the basis set is enlarged. Indeed, the C=O···H hydrogen-bond distance becomes shorter with the increase of the basis set [6-31G(d,p), 183.1 pm; 6-311++G(2d,2p), 178.5 pm; 6-311++G(3df,3pd),

175.6 pm], indicating that this bond becomes stronger when the flexibility of the basis set is increased to describe the outer electrons.

It is interesting to note that the description of the intramolecular hydrogen bond in malonic acid from the B3LYP calculations seems to be rather insensitive to basis set. This observation can be correlated with the above-mentioned quasi-invariance of the B3LYP relative conformational energies with basis set. It is also reflected in the fact that the B3LYP-calculated C=O···H hydrogen-bond distance in conformer **I** does not differ significantly with basis set [6-31G(d,p), 177.3 pm; 6-311++G(2d,2p), 177.8 pm; 6-311++G(3df,3pd), 177.1 pm]. Because the hydrogen-bond distances predicted by B3LYP calculations are close to the highest-level MP2/6-311++G(3df,3pd) calculations, it seems the DFT method provides a relatively good description of the intramolecular hydrogen bond in conformer **I** even when the relatively modest 6-31G(d,p) basis set is used. Moreover, for studies of larger dicarboxylic acids in progress in our laboratories, the B3LYP/6-31G(d,p) calculations can be favored over extensive MP2 calculations to obtain acceptable data on the conformer properties.

Near-Infrared-Induced Conformational Interconversions.

Selective irradiation of the OH stretching fundamental vibrations has been found to be an elegant way to promote conformational isomerization processes in carboxylic compounds,^{19,20} although the elementary mechanism of IR-induced rotamerization is far from being completely understood. Recently, we have used an approach that is based on selective irradiation at a frequency matching that of the first overtone of the ν OH vibration.^{18,21} This approach proved to be considerably more efficient in promoting conformational isomerization of matrix-isolated oxalic acid than irradiating one of the fundamental modes. Thus, it also appears to be a very promising technique for characterization of the conformational distribution of matrix-isolated malonic acid.

On the basis of previous NIR irradiation experiments performed in similar compounds,^{18,21} we expected the first overtones of the OH stretching vibrations of matrix-isolated malonic acid to occur in the 7000–6200 cm⁻¹ region. Because the overtone bands are expected to be extremely weak, to tune the laser on the desired frequency, we began a systematic scanning within this spectral region, using a narrowband tunable laser source until changes were observed in the vibrational spectra. This approach has already been used successfully in previous studies.^{18,21} It constitutes a new method of finding overtones even when they cannot be recorded directly.

The IR spectrum of matrix-isolated malonic acid (nonirradiated sample) is shown in Figure 2 (3700–3200 cm⁻¹ and 1900–1700 cm⁻¹ regions). In the OH stretching region, the spectrum shows bands at 3570–3560 cm⁻¹ and at 3550–3540 cm⁻¹, which are typical values for an O–H group not involved in hydrogen bonding, and a broad band at \approx 3250 cm⁻¹, which can be assigned to an O–H group participating in a strong intramolecular hydrogen bond. In the C=O stretching region, a complex multiplet of bands appears in the 1815–1770 cm⁻¹ region, typical of unperturbed carbonyl groups, beside the band at 1740 cm⁻¹, which appears redshifted as a result of hydrogen bonding. The presence of these groups of bands clearly reveals the coexistence of more than one conformer in the matrix. One of the conformers exhibits an intramolecular hydrogen bond, and, taking into consideration the theoretical predictions, it corresponds to conformer **I**.

Irradiation of the matrix at 6964 cm⁻¹ led to an increase in the intensity of the bands that could be ascribed to the hydrogen-

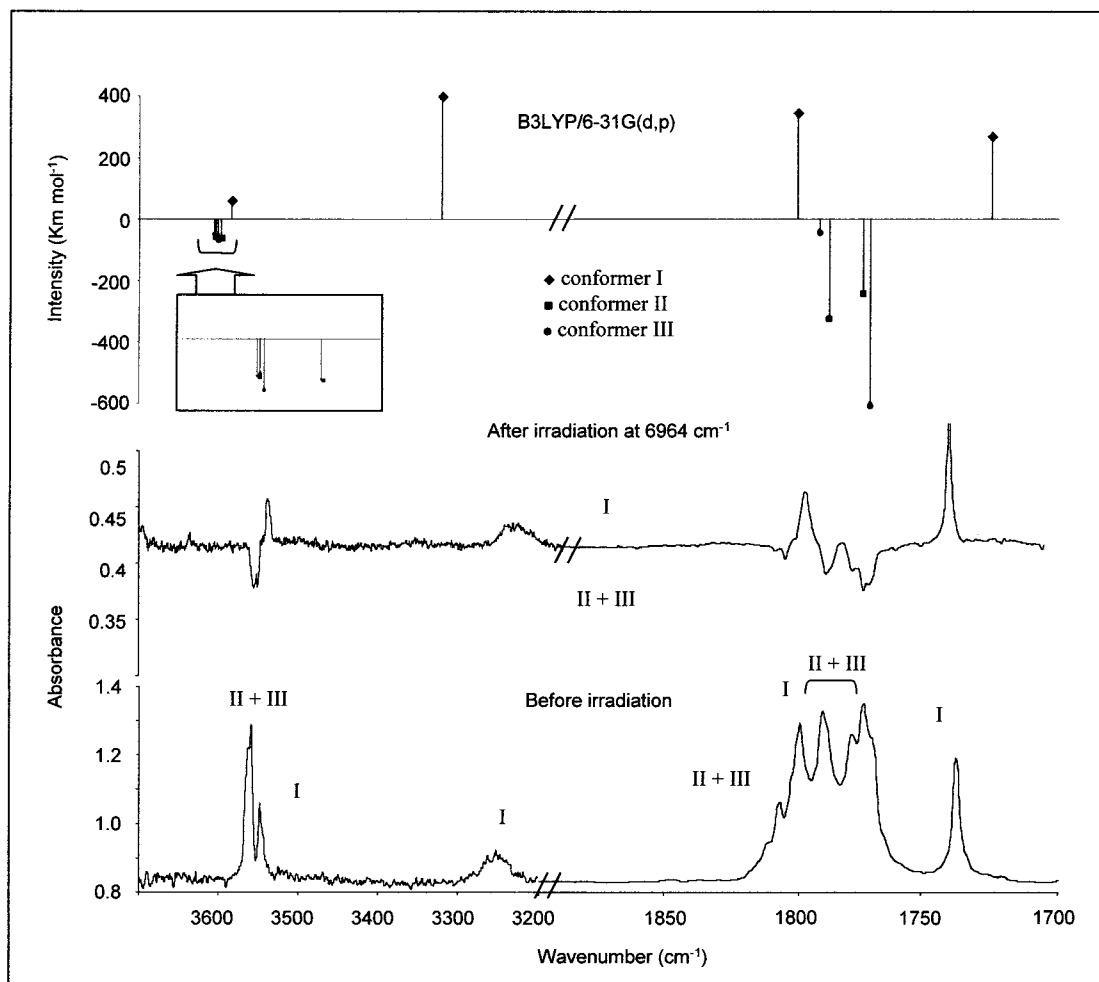


Figure 2. Infrared spectrum (3700–3200 cm^{-1} and 1900–1700 cm^{-1} regions) of malonic acid in an argon matrix at 7.5 K: difference spectrum (irradiated sample at 6964 cm^{-1} – nonirradiated sample), and B3LYP/6-31G(d,p) spectra of the three most stable conformers.

bonded conformer **I** (see Figure 2). Considering the theoretical results (relative conformational energies and vibrational spectra—see Table 1 and Figure 2), conformers **II** and **III** should correspond to the reactant species and give rise to the decreasing bands in the difference spectrum shown in Figure 2. Because the bands assigned to the OH stretching fundamentals of these two conformers differ by less than 3 cm^{-1} , the corresponding overtones are expected to overlap considerably, and thus conformers **II** and **III** are being simultaneously pumped during irradiation at this wavenumber.

The bands at $3550\text{--}3540 \text{ cm}^{-1}$ and $\approx 3250 \text{ cm}^{-1}$, which increase during irradiation, are the OH stretching modes of the free and hydrogen-bonded OH groups of conformer **I**, respectively. The decreasing bands are due to conformers **II** and **III**, which, accordingly to the calculations, give rise to bands at nearly the same frequency.

In the C=O stretching region, the band at 1740 cm^{-1} corresponds to the stretching mode of the intramolecularly hydrogen-bonded carbonyl group of conformer **I**, while the component of the multiplet appearing near 1800 cm^{-1} , which also increases in intensity upon irradiation, can be ascribed to the free carbonyl group of the same conformer. The remaining bands appearing in this spectral region are assigned to conformers **II** and **III**, as shown in Figure 2.

In a second series of experiments, the matrix was irradiated at 6920 or 6365 cm^{-1} , pumping the first overtone of the OH stretching mode of the free or hydrogen-bonded O–H groups of conformer **I**, respectively. Thus, once the population of

conformer **I** was increased by irradiation at 6964 cm^{-1} , back-conversion of this conformer to **II** and **III** could be achieved. As shown in Figure 3, where we present the difference spectra, bands due to conformer **I** decrease whereas bands due to conformers **II** and **III** increase in intensity upon photolysis. The results obtained from irradiation at 6365 cm^{-1} were similar, but the process of conversion of conformer **I** into conformers **II** and **III** was found to be much less efficient than when irradiation at 6920 cm^{-1} was used. This possibly is due to the higher dispersion of the vibrational energy levels associated with the vibration being pumped ($\nu\text{O-H}$ of the intramolecularly H-bonded hydroxyl group) because of hydrogen bonding. The intramolecular interaction is also clearly manifested by the broadness of the vibrational band typically found for hydrogen-bonded species.²²

The irradiation experiments unequivocally confirmed the predictions made theoretically with respect to the nature of the most stable conformers of malonic acid. In particular, they allowed us to clearly identify the presence of conformer **I** in the matrixes, which is predicted by the highest-level calculations to be the lowest-energy conformer of malonic acid. Conformers **II** and **III** could also be identified from the detailed analysis of the spectra, although irradiation experiments alone were not enough to enable a positive discrimination between these two conformers.

Because the calculations predict very small energy differences among the three observed conformers (the highest-level MP2 calculated values are $<1.5 \text{ kJ mol}^{-1}$; see Table 1), we tried to

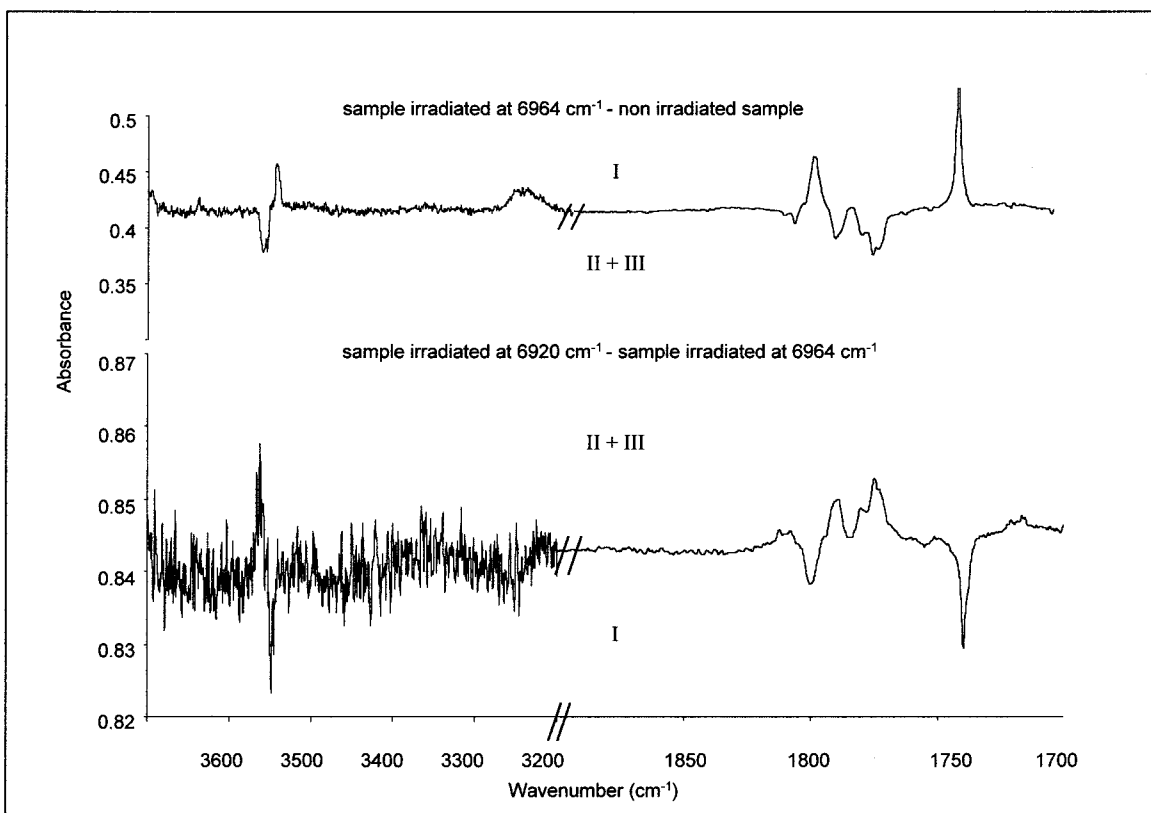


Figure 3. Infrared difference spectrum (3700–3200 cm^{-1} and 1900–1700 cm^{-1} regions) of malonic acid isolated in an argon matrix at 7.5 K: irradiated sample at 6964 cm^{-1} minus nonirradiated sample (top) and irradiated sample at 6920 cm^{-1} minus irradiated sample at 6964 cm^{-1} (bottom).

promote thermally induced conformational isomerization by annealing a freshly prepared matrix to verify the theoretical predictions. This effort would require that energy barriers separating the various conformers be low enough to be overcome at experimentally accessible temperatures. However, annealing of the matrix up to 35 K led to no observable changes in the spectrum that would indicate conformational interconversions; thus we were unable to draw any definitive conclusion from the use of this method. On the other hand, these findings enable us to conclude that the energy barriers associated with the rotamerization reactions in an argon matrix are higher than 12 kJ mol^{-1} .²³

Vibrational Assignments. The different behavior exhibited by the bands that could be ascribed to the conformers upon irradiation, as well as a comparison between the calculated and experimental spectra, enabled us to assign the IR spectrum of malonic acid. Table 3 presents the symmetry coordinates used to perform the normal coordinate analysis. Table 4 shows the experimental and calculated wavenumbers and potential energy distributions (PEDs).

The assignment of bands due to conformer **I**, based on the calculations and NIR irradiation experiments, is rather straightforward. On the other hand, because bands due to conformers **II** and **III** follow the same pattern of changes upon irradiation, the NIR experiments alone did not allow us to distinguish the bands due to each one of these forms. However, some evidence in the spectra supports the simultaneous presence of conformers **II** and **III** in the matrixes, as is pointed out below.

In the C=O stretching region, at least six bands are observed between 1812 and 1771 cm^{-1} that are not due to conformer **I**. These bands cannot be attributed to site effects alone because they spread over a relatively wide region. Therefore, the bands at 1790 and 1780 cm^{-1} were ascribed to the two C=O stretching modes of conformer **II** (which were predicted at 1794 and 1781

cm^{-1} , respectively), and the doublets appearing at 1812, 1808 cm^{-1} and 1775, 1771 cm^{-1} were assigned to the vibrations of conformer **III** (calculated values: 1799 and 1778 cm^{-1}), split as a result of matrix site effects.

In the C–O stretching region, comparison with the computational predictions clearly indicates that the four observed bands not ascribable to conformer **I** must correspond to those expected in the presence of conformers **II** and **III**. Thus, the bands at 1379 and 1340 cm^{-1} are ascribed to conformer **II**, and those appearing at 1355 and 1334 cm^{-1} are assigned to conformer **III**. Note that the observed differences in frequencies between the two C–O stretching modes belonging to the same conformer are in excellent agreement with the calculations, as follows: conformer **II**, exptl 35 cm^{-1} /calcd 25 cm^{-1} ; conformer **III**, exptl 21 cm^{-1} /calcd 22 cm^{-1} (see Table 4).

The analysis of other spectral regions also clearly indicates that both conformers **II** and **III** contribute to the spectrum. A complete assignment of bands to these forms, based essentially on the comparison between the observed and the calculated spectra (both frequencies and intensities were used), is given in Table 4, although some of the assignments should be considered tentative.

Some additional comments should be made concerning (1) the results of the PED calculations (see also Table 4) and (2) spectral evidence of the relative strength of the intramolecular hydrogen bond in malonic acid (conformer **I**) and in other relevant compounds.

(1) As is usual in this type of compound, the C–O and C–C stretching modes and the COH and OCO in-plane bending vibrations were found to be strongly coupled. This behavior is particularly evident in the case of the C–O stretching mode of conformer **I** (calcd, 1362 cm^{-1} ; exptl, 1376 cm^{-1}), where the C–O stretching coordinate is not the calculated main contribution to the normal coordinate. However, the assignment made

TABLE 3: Definition of the Internal Symmetry Coordinates Used in the Normal-Coordinate Analysis

coord- inate	sym- metry ^a	approximate description		definition ^b		
		conformer I and conformer II	conformer III	conformer I and conformer II	conformer III	
S1	B	ν C=O	ν C=O as	ν C ₂ =O ₆	ν C ₂ =O ₆ - ν C ₃ =O ₇	
S2	A	ν C=O'	ν C=O s	ν C ₃ =O ₇	ν C ₂ =O ₆ + ν C ₃ =O ₇	
S3	B	ν C-O	ν C-O as	ν C ₂ -O ₈	ν C ₂ -O ₈ - ν C ₃ -O ₉	
S4	A	ν C-O'	ν C-O s	ν C ₃ -O ₉	ν C ₂ -O ₈ + ν C ₃ -O ₉	
S5	B	ν O-H	ν O-H as	ν O ₈ -H ₁₀	ν O ₈ -H ₁₀ - ν O ₉ -H ₁₁	
S6	A	ν O-H'	ν O-H s	ν O ₉ -H ₁₁	ν O ₈ -H ₁₀ + ν O ₉ -H ₁₁	
S7	B	ν C-C	ν C-C as	ν C ₁ -C ₂	ν C ₁ -C ₂ - ν C ₁ -C ₃	
S8	A	ν C-C'	ν C-C s	ν C ₁ -C ₃	ν C ₁ -C ₂ + ν C ₁ -C ₃	
S9	B	ν CH	ν CH ₂ as	ν C ₁ -H ₄	ν C ₁ -H ₄ - ν C ₁ -H ₅	
S10	A	ν CH'	ν CH ₂ s	ν C ₁ -H ₅	ν C ₁ -H ₄ + ν C ₁ -H ₅	
S11	B	δ COH	δ COH as	δ C ₂ O ₈ H ₁₀	δ C ₂ O ₈ H ₁₀ - δ C ₃ O ₉ H ₁₁	
S12	A	δ COH'	δ COH s	δ C ₃ O ₉ H ₁₁	δ C ₂ O ₈ H ₁₀ + δ C ₃ O ₉ H ₁₁	
S13	B	δ OCO	δ OCO as	2δ O ₆ C ₂ O ₈ - δ O ₆ C ₂ C ₁ - δ O ₈ C ₂ C ₁	2δ O ₆ C ₂ O ₈ - δ O ₆ C ₂ C ₁ - δ O ₈ C ₂ C ₁ - 2δ O ₇ C ₃ O ₉ + δ O ₇ C ₃ C ₁ + δ O ₉ C ₃ C ₁	
S14	A	δ OCO'	δ OCO s	2δ O ₇ C ₃ O ₉ - δ O ₇ C ₃ C ₁ - δ O ₉ C ₃ C ₁	2δ O ₆ C ₂ O ₈ - δ O ₆ C ₂ C ₁ - δ O ₈ C ₂ C ₁ + 2δ O ₇ C ₃ O ₉ - δ O ₇ C ₃ C ₁ - δ O ₉ C ₃ C ₁	
S15	B	δ CC=O	δ CC=O as	δ O ₆ C ₂ C ₁ - δ O ₈ C ₂ C ₁	δ O ₆ C ₂ C ₁ - δ O ₈ C ₂ C ₁ - δ O ₇ C ₃ C ₁ + δ O ₉ C ₃ C ₁	
S16	A	δ CC=O'	δ CC=O s	δ O ₇ C ₃ C ₁ - δ O ₉ C ₃ C ₁	δ O ₆ C ₂ C ₁ - δ O ₈ C ₂ C ₁ + δ O ₇ C ₃ C ₁ - δ O ₉ C ₃ C ₁	
S17	A	δ CH ₂	δ CH ₂	5δ H ₄ C ₁ H ₅ - δ C ₂ C ₁ H ₄ - δ C ₂ C ₁ H ₅ - δ C ₃ C ₁ H ₄ - δ C ₃ C ₁ H ₅ - δ C ₂ C ₁ C ₃	<i>c</i>	
S18	A	δ CCC	δ CCC	4δ C ₂ C ₁ C ₃ - δ C ₂ C ₁ H ₄ - δ C ₂ C ₁ H ₅ - δ C ₃ C ₁ H ₄ - δ C ₃ C ₁ H ₅	<i>c</i>	
S19	B	ω CH ₂	ω CH ₂	δ C ₂ C ₁ H ₄ + δ C ₂ C ₁ H ₅ - δ C ₃ C ₁ H ₄ - δ C ₃ C ₁ H ₅	<i>c</i>	
S20	B	τ CH ₂	τ CH ₂	δ C ₂ C ₁ H ₄ - δ C ₂ C ₁ H ₅ - δ C ₃ C ₁ H ₅ + δ C ₃ C ₁ H ₄	<i>c</i>	
S21	A	γ CH ₂	γ CH ₂	δ C ₂ C ₁ H ₄ - δ C ₂ C ₁ H ₅ + δ C ₃ C ₁ H ₅ - δ C ₃ C ₁ H ₄	<i>c</i>	
S22	B	γ C=O	γ C=O as	γ C ₂ =O ₆	γ C ₂ =O ₆ - γ C ₃ =O ₇	
S23	A	γ C=O'	γ C=O s	γ C ₃ =O ₇	γ C ₂ =O ₆ + γ C ₃ =O ₇	
S24	B	τ C-O	τ C-O as	τ C ₂ -O ₈	τ C ₂ -O ₈ - τ C ₃ -O ₉	
S25	A	τ C-O'	τ C-O s	τ C ₃ -O ₉	τ C ₂ -O ₈ + τ C ₃ -O ₉	
S26	B	τ C-C	τ C-C as	τ C ₁ -C ₂	τ C ₁ -C ₂ - τ C ₁ -C ₃	
S27	A	τ C-C'	τ C-C s	τ C ₁ -C ₃	τ C ₁ -C ₂ + τ C ₁ -C ₃	

^a Symmetry species refers to the higher-symmetry conformer (C₂). ^b For atom numbering, see Figure 1 ν , stretching; δ , bending; γ , rocking; τ , torsion. ^c Same definition as for conformers I and II.

here is unequivocal, because the dominant contribution is due to the δ CH₂ scissoring coordinate, which is by far the major component of the normal mode corresponding to the 1387 cm⁻¹ calculated frequency (obsd, 1402–1392 cm⁻¹; site split band).

(2) In oxalic acid [(C(=O)OH)₂], the smallest dicarboxylic acid], the redshift observed in the O–H stretching vibration upon intramolecular hydrogen-bond formation, $\Delta\nu$ OH, is 70 cm⁻¹.¹⁸ In malonic acid this shift is much larger (\cong 295 cm⁻¹). Therefore, the intramolecular hydrogen bond in this compound is much stronger than in oxalic acid; this is due mostly to the greater conformational flexibility of malonic acid, which allows a better interaction geometry. The intramolecular hydrogen bond in malonic acid is even stronger than in glycolic acid ($\Delta\nu$ OH = 80 cm⁻¹).²⁴

Observed versus Calculated Population of Conformational States. The relative populations of the three observed conformers can be estimated from the experimental IR band intensities recorded immediately after deposition, taking into account the calculated intensities and assuming that no conformational isomerization takes place during the deposition process.

To perform these calculations, we first corrected the predicted intensities [B3LYP/6-31G(d,p)] of selected bands ascribable to conformer I or conformers II and III so that their intensity ratios to the corresponding C=O stretching bands were equal to those observed in the IR difference spectra (irradiated sample minus nonirradiated sample). Calculations took into account the different degeneracies of the conformational states. The following equation was used:

$$I_i^{\text{corr}} = \frac{\Delta I_i^{\text{exp}}}{\Delta I^{\text{exp}(\nu\text{C=O})}} I_i^{\text{calc}(\nu\text{C=O})}$$

where I stands for integrated intensity, i refers to a given vibrational mode, and ΔI is an observed intensity in the difference spectrum. Bands that originated in the C=O and O–H stretching modes were selected for use in estimating relative populations because they appear in relatively clear spectral regions.

The (conformer II + conformer III):conformer I population ratio at 323 K calculated in this way is 77:23%, a value that is in agreement with the results of the [MP2/6-311++G(3df,3pd)] calculations (71:29%), suggesting the absence of conformational relaxation during deposition. Note that conformer II is a doubly degenerated species.

It is important to note that the agreement between the experimental and calculated relative populations is achieved only when the extended 6-311++G(3df,3pd) basis set and the MP2 level of theory are used. When relative conformational energies resulting from the DFT calculations are used, the population of conformer I is predicted to be considerably higher than the experimentally determined value (higher than 60%), indicating that the DFT calculations systematically overestimate the relative energy differences between conformers II and III and the conformational ground state (I). On the other hand, the good agreement obtained at the highest level of theory [MP2/6-311++G(3df,3pd)] strongly supports these theoretical results concerning relative conformational energies.

TABLE 4: Observed and Calculated (Scaled^a) B3LYP/6-31G(d,p) Frequencies of the Three Most Stable Conformers of Malonic Acid Isolated in an Argon Matrix

increasing bands with 6920 cm ⁻¹ excitation (II/III)					increasing bands with 6964 cm ⁻¹ excitation (I)				
ν^{obs}	I^{obs}	ν^{calc}_{II}	ν^{calc}_{III}	PED ^b	ν^{obs}	I^{obs}	ν^{calc}_I	PED ^b	
3566	m	3612		ν OH' (99)	3548	m			
3563	m		3612	ν OH (100)	3546	w	3594	ν OH (100)	
3562	m	3606		ν OH (99)	3544	w			
3559	s		3612	ν OH a (100)	3250	s, br	3353	ν OH' (100)	
n.o.			3034	ν CH a (100)	n.o.		3023	ν CH (93)	
n.o.		3020		ν CH' (64) + ν CH (36)	n.o.		2942	ν CH (94)	
n.o.			2978	ν CH (100)					
n.o.		2968		ν CH (64) + ν CH' (36)					
1812	w		1799	ν C=O (81)	1803	m	1808	ν C=O' (73)	
1808	m				1800	s			
1790	s	1794		ν C=O' (67) + ν C=O (14)					
1780	s	1781		ν C=O (67) + ν C=O' (14)					
1775	s		1778	ν C=O a (80)					
1771	s				1740	s	1728	ν C=O (72)	
					1443	w	862 + 587 ^c		
1415	w		1406	δ CH ₂ (96)	1420	w	1408	δ COH' (46) + ν C-O (10)	
1412	w	1404		δ CH ₂ (89)	1402	w			
					1396	w	1387	δ CH ₂ (55) + δ COH' (19)	
					1392	w			
1379	s	1355		ν C-O (12) + ω CH ₂ (23) + ν C-C (16) + ν C-C' (12)	1376	m	1362	ν C-O (15) + δ CH ₂ (28) + δ COH' (11) + ν CC (19)	
1355	w		1339	ν C-O (32) + δ COH (19) + δ OCO (18) + ν C-C (16)	1357	w	778 + 587 ^c		
1340	w	1330		ν C-O' (21) + δ COH' (15) + δ OCO' (11)					
1334	w		1317	ν C-O a (20) + δ COH a (28) + ν C-C a (24) + δ OCO a (13)					
1286	w		1258	ω CH ₂ (81)	1319	vw	698 + 620 ^c		
					1315	vw			
1282	w	1247		ω CH ₂ (49) + δ COH (32)					
1221	w		1202	δ COH (45) + γ CH ₂ (38)	1279	vw	1245	ω CH ₂ (53) + δ COH (29)	
				δ COH' (38) + γ CH ₂ (40) + ν C-O' (10)					
1151	w		1144	δ COH a (41) + ν C-O a (35)	1242	vw	1219	ν C-O' (43) + ν C-C' (20)	
1144	m	1128		δ COH (23) + ν C-O (31) + γ CH ₂ (12)					
1140	s				1163	w	1165	γ CH ₂ (64) + ω CH ₂ (10)	
1127	m		1106	γ CH ₂ (39) + ν C-O (24) + δ COH (19)	1137	m	1130	δ COH (25) + ν C-O (36) + γ CH ₂ (16)	
					1135	s			
1121	vs	1109		γ CH ₂ (25) + ν C-O' (15) + ν C-O (18)					
946	vw	922		τ CH ₂ (49) + γ C=O (18)					
			919	τ CH ₂ (55) + γ C=O a (14)					
903	vw	882		ν C-C' (39) + ν C-O' (26) + ν C-C (10)	950	w	932	τ CH ₂ (46) + γ C=O (20) + γ C=O' (16)	
900	vw				n.o.		895	ν C-C (45) + ν C-C' (16)	
892	w		867	ν C-C a (40) + ν CC (27) + γ C=O a (14) + δ CCC (10)	862	vw	845	ν C-C' (25) + δ CCC (21) + ν C-O' (19)	
			867	ν C-C (35) + ν C-O (27) + γ C=O (18) + ω CH ₂ (11)					
			864	ν C-C (40) + γ C=O' (19) + δ CCC (14)	778	w, br	760	τ C-O' (96)	
731	vw		716	γ C=O (31) + τ C-O (23) + δ OCO (16) + ν CC (14)					
			714	γ C=O' (28) + τ C-O' (25)	698	vw	683	δ OCO' (17) + τ C-O (27) + δ OCO (13) + δ CCC (10)	
635	m		658	τ C-O a (66) + γ C=O a (26)	696	vw			
631	m	650		τ C-O (74) + γ C=O (16)	667	vw	664	τ C-O (51)	
627	m	623		τ C-O' (64) + δ OCO (14)	662	vw			
			618	τ C-O (71) + δ OCO (18)	620	w	600	δ OCO (40) + δ OCO' (35)	
613	m		583	δ OCO a (73) + γ C=O a (10)					
611	m								
609	m								
608	m								
600	vw								
598	s	576		δ OCO' (49) + δ OCO (26)	587	m	568	γ C=O' (35) + γ C=O (25)	
596	s				584	w			
525	w		525	γ C=O a (62) + τ CH ₂ (13) + τ C-O a (14)					
521	w	515		δ OCO (21) + γ C=O' (38) + ν C-C (13)					
512	w	500		γ C=O (65) + τ CH ₂ (13)					
			489	δ OCO (37) + γ C=O (26) + ν C-C (17)					
			387	δ CC=O (65) + ν CC (12)					
			386	δ CC=O' (58) + τ CH ₂ (16)	454		γ C=O (28) + τ CH ₂ (30) + γ C=O' (16)		
			374	δ CC=O a (73) + τ CH ₂ (17)					
			352	δ CC=O (45) + δ CC=O' (16)	388		δ CC=O' (57) + ν CC (10)		
150			147	δ CCC (64) + δ CC=O (18) + γ C=O' (12)	370		δ CC=O (53) + ν CC' (12)		
			147	δ CCC (62) + γ C=O (19) + δ CC=O (15)					
			59	τ C-C' (79)	246		δ CCC (59) + δ CC=O (21)		
			50	τ C-C (97) + δ CCC (11)					
			41	τ C-C a (80)	86		τ C-C' (42) + τ C-O' (45)		
			32	τ C-C (93)	36		τ C-C (54)		

^a Scale factor 0.9614. ^b Only contributions higher than 10% are listed. ^c Tentative assignment as combination bands. ν , stretching; δ , bending; τ , torsion; γ , rocking; n.o., not observed; br, broad; vs, very strong; s, strong; m, medium; w, weak; vw, very weak.

Conclusion

The use of narrowband tunable NIR irradiation in the OH stretching first-overtone region of malonic acid allowed us to promote the interconversion between the three low-energy conformers of this molecule. These conformers were already present in the matrix before irradiation. On the other hand, thermally induced isomerization could not be observed upon annealing the matrix up to 35 K, indicating that the energy barriers associated with these isomerization processes are higher than 12 kJ mol⁻¹. Assuming that no rotamerization occurs during deposition, it was possible to characterize the conformational equilibrium of malonic acid in the gas phase at the temperature used in this study to sublime the substance (323 K). Unfortunately, it was not possible to selectively pump conformer **II** and conformer **III**, because these two forms have very similar OH stretching frequencies, although the global analysis of the vibrational data clearly indicates that these two conformers are present in the low-temperature matrix.

We could not observe any new bands in the IR spectra of the irradiated matrixes, which demonstrates that no conformational conversion into higher-energy conformers is promoted by vibrational excitation. This fact indicates that for the matrix-isolated molecules, the energy barriers associated with these processes are above the excitation energy (≈ 83 kJ mol⁻¹).

Including multiple polarization and diffuse functions in the basis set used to perform the MP2 calculations proved essential to a correct evaluation of the relative conformational energies in malonic acid. Our results support the use of these basis sets when considering relative energies of different conformers of molecules where intramolecular hydrogen bonding plays an important role. The B3LYP calculations were able to reproduce the MP2/6-311++G(3df,3pd) ordering when more modest basis sets were used, which indicates that this economical approach could be employed for larger systems of a similar nature.

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