

## Preferred Conformers and Photochemical ( $\lambda > 200$ nm) Reactivity of Serine and 3,3-Dideutero-Serine In the Neutral Form

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A systematic investigation of the conformational potential energy surface of neutral serine [HOCH<sub>2</sub>CHNH<sub>2</sub>COOH] and 3,3-dideutero-serine [HOCD<sub>2</sub>CHNH<sub>2</sub>COOH] was undertaken, revealing the existence of 61 different minima. The structures and vibrational spectra of the most stable conformers, which were estimated to have relative energies within 7 kJ mol<sup>-1</sup> and account for ca. 93% of the total conformational population at room temperature, were calculated at both the MP2 and DFT/BLYP levels of theory with the 6-311++G-(d,p) basis-set and used to interpret the spectroscopic data obtained for the compounds isolated in low-temperature inert matrixes. The assignment of the main spectral infrared features observed in the range 4000–400 cm<sup>-1</sup> to the most stable conformers of serine was undertaken. In addition, UV irradiation ( $\lambda > 200$  nm) of the matrix-isolated compounds was also performed, leading to decarboxylation, which was found to be strongly dependent on the conformation assumed by the reactant molecule.

### Introduction

Organic compounds observed in the interstellar medium and in solar system bodies are of particular importance for revealing the chemistry that may have led to life's origin and evolution.<sup>1–5</sup> Among these compounds, amino acids may have a crucial importance, since they are the basic components of proteins, which are the essential constituents of all organisms. Understanding the details of the structure of amino acids, under different experimental conditions, is then a fundamental problem in chemistry. On the other hand, the knowledge of the fundamental photochemical behavior of this type of compounds does also appear relevant to biochemistry and prebiotic chemistry.

Amino acids are well-known to exist in the zwitterionic form in the liquid or solid phases. Only very recently the neutral form of simple amino acids [glycine, sarcosine and *N,N*-dimethylglycine (DMG)] could be observed for the pure solid compounds, as a metastable species resulting from fast deposition of the gaseous compound onto a suitable substrate cooled at ca. 10 K.<sup>6</sup> The stabilization of the zwitterionic form in the condensed phases is essentially due to dipolar interactions and intermolecular H-bonds. On the contrary, in the gaseous phase, as well as for the compound isolated in low-temperature inert matrixes, amino acids exist in the neutral form. This has been confirmed for several amino acids, such as glycine,  $\alpha$ - and  $\beta$ -alanine, proline, sarcosine, DMG, and  $\gamma$ -aminobutyric acid (GABA), by experimental studies based on microwave spectroscopy, electron diffraction and matrix-isolation infrared spectroscopy techniques.<sup>6–14</sup> In fact, for the isolated molecule situation, the zwitterionic species of simple amino acids have been shown not to constitute minimum energy structures, as revealed by high-level computational studies.<sup>15,16</sup>

The main obstacle to investigation of the neutral forms of amino acids is due to the difficulty of promoting sublimation of this kind of compound without significant decomposition. This results from the low vapor pressure shown by most of the amino acids at room temperature, due to the presence of very strong intermolecular H-bonds in the solid phase.

Serine is, among the simplest amino acids, one of those exhibiting lower vapor pressure and it decomposes extensively below its melting point, at normal pressure. Such behavior justifies the absence of any experimental study dealing with this amino acid in the gaseous phase. On the other hand, serine in the neutral form is a very interesting and challenging molecular system for structural research, because it contains a variety of intramolecular interactions. In particular, different types of H-bonds can be established between the various substituents in the molecule, leading to a large number of low energy conformers, stabilized by different intramolecular interactions.

Despite the relative complexity of serine, which is a conformationally flexible molecule with five internal rotation axes, several computational studies on this molecule have been reported previously.<sup>17–29</sup> However, with a single exception,<sup>30</sup> all studies have only considered a small subset of possible conformers.

Experimentally, amino acids have been extensively studied in their easily accessible zwitterionic form, but as mentioned above, they have been considerably less studied as neutral species. For instance, the photo- and thermal-decomposition behavior of neutral amino acid forms is a relatively recent topic of research.<sup>31–33</sup> In the case of serine, Zubavichus et al.<sup>34</sup> focused their attention on photodecomposition of the compound, as a solid layer adsorbed over indium, upon X-ray irradiation in ultrahigh vacuum. The experimental results indicated that the molecule decomposes by several pathways, such as dehydration, decarboxylation, decarbonylation, and deamination. On the other hand, Sato et al.<sup>35</sup> investigated the thermal decomposition of zwitterionic serine in water solution at high temperature (200–340 °C) and high pressure (MPa), concluding that the general

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reaction network of amino acids under hydrothermal conditions takes two main paths: deamination to produce ammonia and organic acids and decarboxylation to produce carbonic acid and amines.

Neutral serine was for the first time successfully isolated in a low-temperature matrix in our laboratory, and preliminary results on the conformational preferences of this species were reported.<sup>36,37</sup> To sublimate efficiently the necessary amount of the compound without appreciable decomposition, we took advantage of the capabilities of the specially designed internal minifurnace developed in our laboratories for preparation of cryogenic matrixes of thermolabile low-vapor-pressure compounds.<sup>38</sup> Our experimental approach has been used later on by Lambie et al.,<sup>29</sup> to investigate the infrared spectrum of neutral serine isolated in solid argon. In that study, an assignment of the observed spectrum was proposed, which assumed significant contributions to the observed spectral features from the four conformers we had previously identified experimentally (Figure 1).<sup>36,37</sup> However, to undertake the band assignments, Lambie et al. relied only on the comparison between the experimental data and theoretical predictions of the vibrational spectra of the four conformers obtained at the DFT/B3LYP/6-31++G(d,p) level, not attempting to use any further information, such as, for example, those obtained by annealing or in situ irradiation of the matrix. These procedures can be expected to change the relative conformational populations and then enable a more reliable identification of bands due to each experimentally observable conformer. Furthermore, the possibility of contribution to the observed spectra of more than 4 conformers was not taken into consideration in that study.<sup>29</sup> As it will be shown in the present paper, this last assumption is in fact not supported by the experimental data.

In this work, the conformational preferences of neutral serine were studied, starting by a full systematic investigation of its potential energy surface. The optimized geometries and vibrational spectra of the 61 different conformers of serine and its 3,3-dideutero isotopologue were calculated, indicating that 9 conformers lay within 7 kJ mol<sup>-1</sup> and account for ca. 93% of the total conformational population at room temperature. Theoretical calculations, undertaken at both the MP2 and DFT/B3LYP levels of theory with the 6-311++G(d,p) basis-set, together with temperature variation studies and in situ irradiation experiments were then used to interpret the spectroscopic data obtained for the compounds isolated in low-temperature inert matrixes. The assignment of the main spectral infrared features observed in the range 4000–400 cm<sup>-1</sup> to the most stable conformers of serine was undertaken and the photochemical decarboxylation of both serine isotopologues, resulting from in situ UV irradiation ( $\lambda > 200$  nm) of the matrixes, was also investigated.

## Materials and Methods

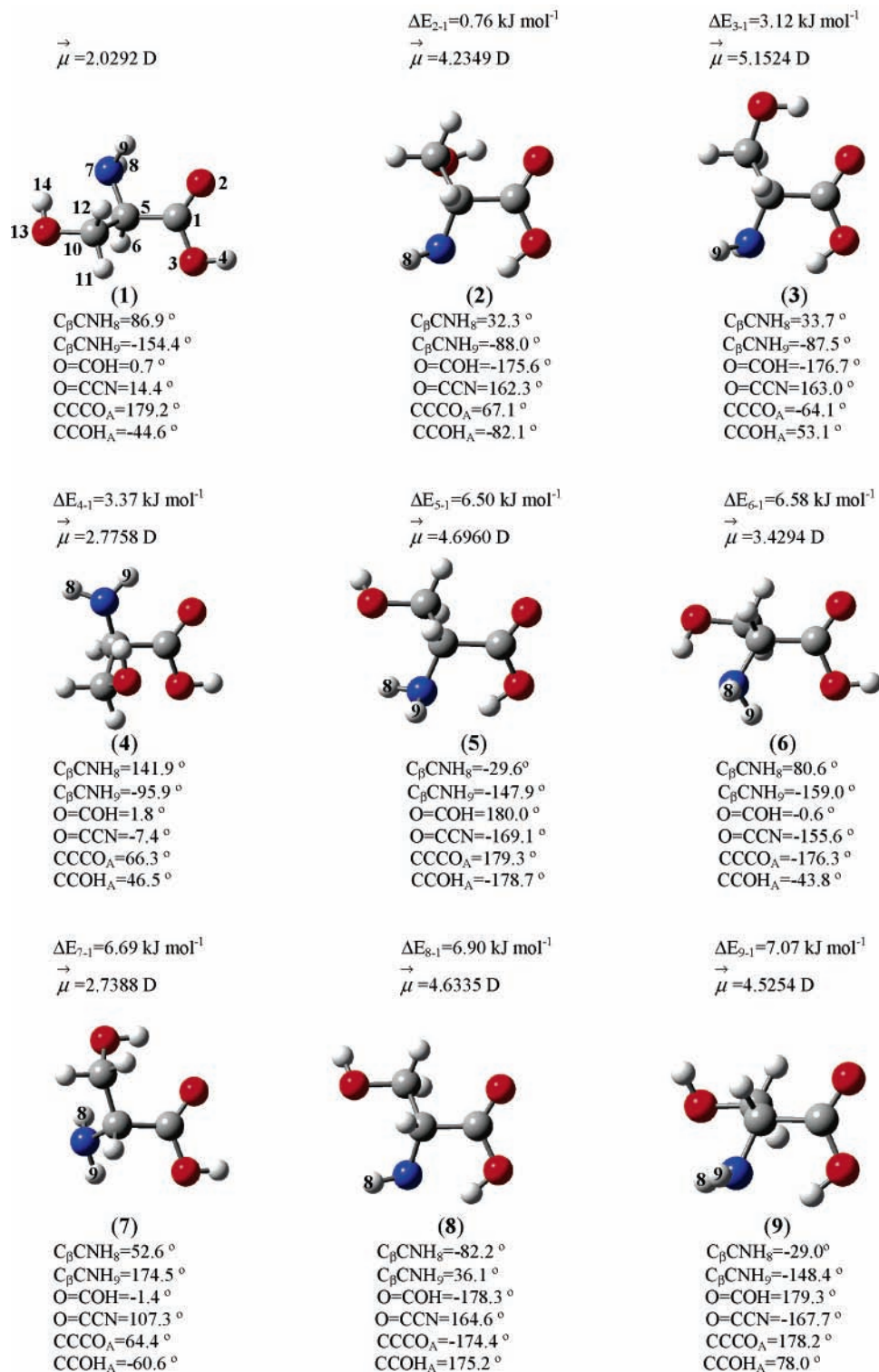
**Computational Details.** The theoretical calculations on serine and 3,3-dideutero-serine were performed with the Gaussian98 program package<sup>39</sup> at Hartree–Fock (HF), density functional theory (DFT), and second-order Møller–Plesset (MP2) levels of theory, with the standard split-valence 3-21G(d)<sup>40–42</sup> and extended 6-311++G(d,p)<sup>43</sup> basis sets. The DFT calculations were carried out with the three-parameter density functional abbreviated as B3LYP, which includes Becke's gradient exchange correction<sup>44</sup> and the Lee, Yang, and Parr correlation functional.<sup>45</sup> All structures were subjected to optimization without any geometrical constraints, and the resulting optimized

geometries were characterized by inspection of the corresponding Hessian matrixes. Optimizations were followed by frequency calculations, performed at the same level of theory. The calculated frequencies were used to assist the analysis of the experimental spectra and to account for the zero-point vibrational energy (ZPVE) corrections. Due to the general good correspondence between the experimentally observed and the DFT/B3LYP/6-311++G(d,p) predicted spectra, these calculations were preferentially used both to assign the main features observed in the spectra of matrix-isolated monomers and to calculate energy barriers between the experimentally relevant conformers of serine. The DFT/B3LYP/6-311++G(d,p) harmonic frequencies and ZPVE were scaled using a single factor of 0.978,<sup>46–48</sup> except for  $\nu$ OH stretching modes, which were found to require the use of different scaling factors to describe properly the experimental spectra. For these vibrations, two scaling factors were used (0.953 or 0.913) depending on the strength of the H-bond interactions in which the corresponding hydroxyl group is involved.

**Experimental Details.** Both D,L-serine and its 3,3-dideutero (>98% D) isotopologue used in this study were commercial products obtained from Aldrich and Icon Stable Isotopes, respectively. Matrixes were prepared by deposition of the vapor of the compounds onto a cold CsI (10 K) window directly assembled to the cold tip of a continuous flow liquid helium cryostat. The compounds were sublimated by electrical heating (470 K) in a specially designed minifurnace,<sup>38</sup> placed inside the vacuum chamber of the cryostat. The vapors of the compounds were deposited during ca. 70 min, together with a large excess of argon by Linde AG. T. These experimental conditions allowed minimization of trace amounts of thermal decomposition of the compound during sublimation. Argon of spectral purity (6.0) was supplied by Linde AG. The infrared spectra were recorded in the range 4000–400 cm<sup>-1</sup>, with 0.5 cm<sup>-1</sup> resolution and 600 scans, using a Thermo Nicolet Nexus 670 FTIR spectrometer equipped with KBr beam splitter and DTGS detector. Integral intensities of the IR absorption bands were measured by numerical integration. The matrixes were irradiated through the outer quartz window of the cryostat, using a high-pressure mercury lamp (HBO200) fitted with a water filter and a cutoff filter transmitting light with  $\lambda > 200$  nm. The time of irradiation was 30 min. After UV irradiation, the matrixes were annealed to 30 K.

## Results and Discussion

**Computational Results (Structures and Relative Conformational Energies).** To truly characterize the conformations of serine, the full ensemble of possible conformations was considered. Preliminary calculations were undertaken at the less expensive HF level of theory, using the split-valence 3-21G(d) basis set. The starting set of serine conformations was chosen by allowing all possible combinations of single-bond putative rotamers (see Figure 2). There are five different internal rotation axes in serine that can give rise to conformational isomers. For the carboxyl group, internal rotation around the C(1)–O(3) bond leads to two possible minimum-energy arrangements: syn ( $\tau(\text{O}(2)=\text{C}(1)\text{O}(3)\text{H}(4)) = 0^\circ$ ) and trans ( $\tau(\text{O}(2)=\text{C}(1)\text{O}(3)\text{H}(4)) = 180^\circ$ ). The orientation of the  $\alpha$ -carbon substituents (NH<sub>2</sub> and CH<sub>2</sub>OH) relative to the COOH group (internal rotation around the C <sub>$\alpha$</sub> –C(1) bond) can lead to six possible minimum-energy structures (corresponding to 3 staggered and 3 eclipsed geometries relative to the C=O bond). Both the NH<sub>2</sub> and CH<sub>2</sub>–OH groups may adopt three different staggered arrangements (defined by the C <sub>$\alpha$</sub> –N and C <sub>$\alpha$</sub> –C <sub>$\beta$</sub>  internal rotations). Finally,



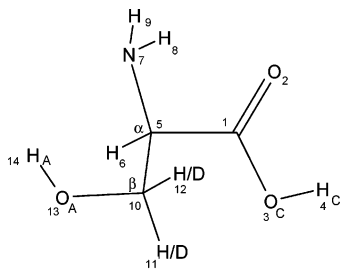
**Figure 1.** Nine most stable conformers of serine. Dihedral angles, dipole moments and energies presented in the Figure were obtained at the DFT/B3LYP/6-311++G(d,p) level. MP2/6-311++G(d,p) results are provided in the Supporting Information Table S1. Experimental observation of conformers 1–4 have been reported first in refs 33 and 34. In Figure S1 (Supporting Information), the nine conformers are represented in three alternative perspectives, for better viewing of some of the intramolecular interactions discussed in the text.

the  $C_{\beta}$ –O(13) bond represents a 3-fold rotor (Figure 2), defining the possible conformations of the  $OH_A$  group (throughout this article, in references to the OH groups, the subscript A stands for alcohol, whereas the subscript C stands for carboxylic group). All possible rotations around the axes described above lead to a total of 324 trial structures for the conformational states of serine, which were submitted to optimization. From the HF/3-21G(d) optimizations, 71 unique conformers were identified.

These structures were afterward submitted to reoptimization at the DFT/B3LYP/6-311++G(d,p) level of theory.

At the DFT/B3LYP/6-311++G(d,p) level of theory, only 61 unique conformations were located, with energies varying by  $\approx 47 \text{ kJ mol}^{-1}$  (Table 1). Ten structures predicted at the HF/3-21G(d) level as minimum-energy conformations by the lower-level theory used were found to converge to other forms.





**Figure 2.** Atom numbering of serine/3,3-dideutero-serine. Internal rotation axes leading to possible rotamers: 2-fold, C(1)–C(3); 6-fold, C(1)–C(5); 3-fold, C(5)–N(7), C(5)–C(10), and C(5)–C(10). Subscripts A and C mean for “alcoholic” and “carboxylic”.

Due to the very small differences in the relative conformational energies obtained at the DFT level, the energies of all conformers of serine predicted at this level of theory with energies within 7 kJ mol<sup>-1</sup> were recalculated at the MP2/6-311++G(d,p) level of approximation (Table S1, Supporting Information), which usually estimates better this property than the DFT/B3LYP method with the same basis set.<sup>49,50</sup> The main difference between the results obtained with the two levels of theory relates to the relative energy of conformer **4** (see Figure 1 and Tables 1 and S1), which is predicted by the MP2 as lower than that obtained by the DFT calculations.

The relative energies shown in both Tables 1 and S1 suggest that the equilibrium mixture should contain significant contributions from several conformers, with the first nine (see Figure 1) playing the most important role. The relative populations of the nine most stable conformers, at  $T = 470$  K (the temperature of the vapor immediately before deposition used in the matrix isolation experiments reported in this study), were predicted by the DFT calculations to be 1.00:0.74:0.28:0.26:0.07:0.07:0.07:0.06:0.06 [corresponding as a whole to 75% (21:17:9:9:4:4:4:4:3%) of the total conformational population]. [The relative populations predicted at the MP2 level are 1.00:0.63:0.09:0.55:0.07:0.08:0.06:0.03:0.04. Since at this level of theory only the energies of these nine conformers were calculated, no percent absolute populations can be given.]

As already mentioned, the presence of three H-bond donor and four H-bond acceptor groups in serine allows for a wide range of intramolecular interactions and, consequently, for a large number of stable conformations. For the purpose of systematically analyzing the large conformational data set studied, conformations were characterized by the H-bonds they exhibit. A distance of 2.7 Å was here used as a cutoff distance for H-bond interactions. This distance is consistent with typically values found in analogous systems with weak intramolecular H-bond interactions.<sup>51</sup> Although this approach is somewhat simplistic, it appears to be considerably more useful than a mere list of dihedral angles for illustrating the complex interactions found in the studied amino acid. It is worth mentioning the marked nonlinearity of intramolecular H-bonds, which leads to weakening of these interactions in serine.

The possible H-bonding schemes for serine are depicted schematically in Figure 3: **A**, COOH group in the cis conformation; OH<sub>A</sub> group acting as proton-donor to the nitrogen atom. **B**, COOH group in the trans conformation; OH<sub>C</sub> group acting as proton-donor to the nitrogen atom. **C**, COOH group in the cis conformation; OH<sub>A</sub> group acting as proton-donor to the carbonyl oxygen. **D**, COOH group in the cis conformation; OH<sub>A</sub> group acting as proton-donor to the O<sub>C</sub> atom. **E**, COOH group in the cis conformation; NH<sub>2</sub> group acting as proton-donor to the carbonyl oxygen atom. **F**, COOH group in the cis conformation; NH<sub>2</sub> group acting as proton-donor to the O<sub>A</sub> atom.

**G**, COOH group in the cis conformation; NH<sub>2</sub> group acting as proton-donor to the O<sub>C</sub> atom. **H**, COOH group in the trans conformation; OH<sub>C</sub> group acting as proton-donor to the O<sub>A</sub> atom. **I**, COOH group in the trans conformation; OH<sub>A</sub> group acting as proton-donor to the carbonyl oxygen. **J**, COOH group in the trans conformation; OH<sub>A</sub> group acting as proton-donor to the nitrogen atom. **K**, COOH group in the trans conformation; NH<sub>2</sub> group acting as proton-donor to the O<sub>A</sub> atom. **L**, COOH group in the trans conformation; NH<sub>2</sub> group acting as proton-donor to the carbonyl oxygen atom. The H-bonding schemes appearing in each conformer of serine are given in Table 1. Note that associated with some of the H-bonding schemes there might also be a prevalence for occurrence of important steric repulsions, which may considerably destabilize the structures (e.g., in scheme **L**, the repulsion between OH<sub>C</sub> and the hydrogen atoms of the methylene group; see Figure 3).

As a way of analyzing the general stability of the H-bonding schemes of serine, the average energies of the conformers within each scheme are compared with the overall mean energy in Table 2. The average energy of all conformers where the conformation of the carboxylic group is cis (37 conformers; see Table 1) was found to be 3.68 kJ mol<sup>-1</sup> lower than the overall mean energy, whereas the corresponding value for the 24 conformers exhibiting a trans carboxylic group is larger than the global energy mean by 5.66 kJ mol<sup>-1</sup>. These results show the general preference for the cis arrangement around the C–O<sub>C</sub> bond, as it is commonly found for unsubstituted carboxylic acids.<sup>52–55</sup> From the data shown in Table 2, it can also be concluded that in bonding schemes **A–H** the intramolecular attractive interactions are dominant, whereas in bonding schemes **I–L**, the repulsive interactions dominate.

As could be realized, serine can find stabilization via a variety of different combinations of the above considered H-bonding schemes. The nine most stable conformers differ in energy by less than ca. 7 kJ mol<sup>-1</sup> and contain representatives of bonding schemes **A–C**. The first 44 conformers span less than 20 kJ mol<sup>-1</sup>, and contain the entire characteristic set of bonding schemes (**A–L**).

Bonding scheme **A** (COOH group in the cis conformation; OH<sub>A</sub>···N H-bond) is clearly more favorable than all of the remaining, justifying in large amount the greatest stability of conformer **1** and contributing also to the stabilization of conformers **4** and **6**.

The bonding scheme **B** is dominant in conformers **2**, **3**, **5**, **8**, and **9** which are stabilized by a strong OH<sub>C</sub>···N hydrogen bonding interaction. In conformer **2**, the calculated OH<sub>C</sub>···N distance is as short as 1.916 Å. On the other hand, to establish this H-bond, the conformation adopted by the carboxylic group in these conformers must be the less stable trans configuration.<sup>52–55</sup> However, the increase in energy due to the less stable geometry adopted by the carboxylic group is compensated by the establishment of a considerably strong H-bond, where the combination of donor and acceptor groups is the most favorable possible in serine.

Finally, conformer **7** reveals three different types of H-bonding schemes (**C**, **F** and **G**), with two of them (**C**, which is the dominant interaction, and **F**) existing only in this form (among the nine lowest energy conformers under analysis). Like in conformers **1**, **4** and **6**, the carboxylic group in this conformer adopts a cis conformation, but, instead of having the OH<sub>A</sub> group acting as proton-donor to the nitrogen atom, this group establishes an H-bond with the carbonyl oxygen atom [scheme **C**;  $d(\text{OH}_A \cdots \text{O}=\text{C}) = 2.194$  Å]. In addition, this conformer is also stabilized by two weaker H-bonds where the NH<sub>2</sub> group acts

**TABLE 1: DFT/B3LYP/6-311++G(d,p) Calculated Dihedral Angles, Relative Energies  $\Delta E^{ZPVE}$  [with Correction of Non-Scaled ZPVE] and Relative Populations at 298 and 470 K<sup>a</sup> of the Conformers of Serine**

conformer	$C_{\beta}CNH_3^b$ (°)	$C_{\beta}CNH_0$ (°)	O=COH (°)	O=CCN (°)	CCCO <sub>A</sub> (°)	CCOH <sub>A</sub> (°)	<i>E</i> (kJ mol <sup>-1</sup> )	ZPVE (kJ mol <sup>-1</sup> )	<i>E</i> <sup>ZPVE</sup> (kJ mol <sup>-1</sup> )	$\Delta E^{ZPVE}$ (kJ mol <sup>-1</sup> ) <sup>c</sup>	population (%)		H-bonding schemes <sup>d</sup>
											298 K	470 K	
1	86.9	-154.4	0.7	14.4	179.2	-44.6	-1047831.551	297.6457	-1047533.906	0.00	36.1	20.5	A/E
2	32.3	-88.0	-175.6	162.3	67.1	-82.1	-1047831.691	298.5456	-1047533.145	0.76	26.4	16.9	B/K
3	33.7	-87.5	-176.7	163.0	-64.1	53.1	-1047830.085	299.2947	-1047530.790	3.12	9.9	9.2	B/I
4	141.9	-95.9	1.8	-7.4	66.3	46.5	-1047828.035	297.4995	-1047530.535	3.37	8.9	8.7	A/E
5	-29.6	-147.9	180.0	-169.1	179.3	-178.7	-1047825.352	297.9462	-1047527.406	6.50	2.4	3.9	B/K
6	80.6	-159.0	-0.6	-155.6	-176.3	-43.8	-1047824.967	297.6457	-1047527.322	6.58	2.4	3.8	A/G
7	52.6	174.5	-1.4	107.3	64.4	-60.6	-1047825.222	298.0013	-1047527.220	6.69	2.3	3.7	C/F/G
8	-82.2	36.1	-178.3	164.6	-174.4	175.2	-1047824.449	297.4478	-1047527.001	6.90	2.1	3.5	B
9	-29.0	-148.4	179.3	-167.7	178.2	78.0	-1047825.105	298.2742	-1047526.831	7.07	1.9	3.4	B/K
10	56.7	173.9	1.4	-3.2	63.1	173.8	-1047821.437	296.1441	-1047525.293	8.61	1.0	2.3	E/F
11	66.4	-172.9	0.1	120.1	-57.9	69.9	-1047822.424	297.3426	-1047525.082	8.82	0.9	2.1	G
12	-88.9	29.7	-179.6	169.1	-175.3	87.4	-1047821.344	296.8667	-1047524.478	9.43	0.7	1.8	B/K
13	51.8	169.4	-2.2	-16.1	62.3	-83.9	-1047820.846	296.5127	-1047524.333	9.57	0.7	1.8	D/E
14	171.8	-68.2	-0.8	142.5	-66.4	65.5	-1047820.736	297.1945	-1047523.541	10.36	0.5	1.4	C/G
15	152.7	-85.4	-1.3	174.5	69.9	44.6	-1047820.151	297.1617	-1047522.989	10.92	0.4	1.3	A/G
16	72.5	-170.0	0.0	2.2	-72.2	56.8	-1047819.435	296.4588	-1047522.976	10.93	0.4	1.3	D/E
17	152.0	-86.1	-0.1	-16.7	-74.8	63.4	-1047819.549	296.6436	-1047522.906	11.00	0.4	1.2	D/E
18	-175.9	-56.5	-1.8	134.2	-174.4	-171.3	-1047818.575	295.9719	-1047522.603	11.30	0.3	1.1	F/G
19	-83.1	36.1	-3.3	91.5	67.9	-62.4	-1047820.137	297.7695	-1047522.368	11.54	0.3	1.1	C/F
20	57.0	176.1	-1.4	-179.4	68.3	179.9	-1047817.893	296.3459	-1047521.547	12.36	0.2	0.9	F/G
21	137.2	-102.3	174.9	-14.3	-64.7	172.7	-1047818.496	297.2282	-1047521.267	12.64	0.2	0.8	H/L
22	-42.3	78.4	0.4	26.1	-179.0	-173.1	-1047816.962	295.7810	-1047521.181	12.72	0.2	0.8	E/F
23	-35.6	84.7	0.5	24.7	177.8	75.8	-1047817.396	296.4014	-1047520.994	12.91	0.2	0.8	E/F
24	170.0	-68.0	-0.6	-20.3	-173.6	-167.2	-1047816.336	295.534	-1047520.802	13.10	0.2	0.7	E/F
25	35.6	-87.7	-179.1	166.2	-169.8	-76.5	-1047817.714	297.1392	-1047520.575	13.33	0.1	0.7	B
26	52.8	176.1	0.6	-97.8	72.1	-65.0	-1047818.241	297.7322	-1047520.508	13.40	0.1	0.7	D/F
27	74.8	-166.5	3.5	-140.3	-51.6	-66.0	-1047816.547	296.3509	-1047520.196	13.71	0.1	0.6	E
28	74.9	-165.7	2.6	54.2	-58.0	169.8	-1047815.802	295.9148	-1047519.887	14.02	0.1	0.6	E
29	-40.4	83.1	-0.4	15.3	-74.4	53.7	-1047815.381	296.0383	-1047519.343	14.56	0.1	0.5	D/E
30	139.9	-99.3	174.5	-17.4	-61.1	-85.9	-1047815.501	297.2116	-1047518.289	15.62	0.1	0.4	H/L
31	-54.3	67.5	0.5	-179.5	-67.5	51.7	-1047815.022	296.8826	-1047518.140	15.77	0.1	0.4	C/G
32	173.7	-63.0	-0.2	-17.0	-176.1	81.5	-1047813.311	295.4638	-1047517.847	16.06	0.0	0.3	E/F
33	70.5	-169.1	-1.9	-121.8	-48.8	-66.5	-1047814.021	296.2316	-1047517.789	16.12	0.0	0.3	G
34	-173.4	-52.7	-2.0	136.6	-176.5	80.9	-1047813.096	295.6976	-1047517.399	16.51	0.0	0.3	F/G
35	-52.0	67.1	1.9	-146.2	-174.8	-176.0	-1047812.592	295.6610	-1047516.931	16.97	0.0	0.3	F/G
36	-47.0	71.6	1.6	-148.4	-177.0	78.7	-1047812.975	296.1574	-1047516.818	17.09	0.0	0.3	F/G
37	71.9	-167.5	-1.3	-107.9	-55.2	173.0	-1047812.601	295.8302	-1047516.771	17.13	0.0	0.3	G
38	164.0	-77.8	176.0	-86.7	62.0	52.7	-1047815.990	299.3557	-1047516.635	17.27	0.0	0.2	H/J/L
39	-42.9	77.0	1.5	14.3	60.6	-179.2	-1047811.444	294.9948	-1047516.449	17.46	0.0	0.2	E/F
40	-50.0	70.9	2.4	44.1	-57.3	-61.6	-1047811.609	295.9102	-1047515.699	18.21	0.0	0.2	E
41	-60.6	60.7	0.8	61.1	-63.2	167.0	-1047810.846	295.4981	-1047515.348	18.56	0.0	0.2	E
42	-58.6	60.4	-1.0	-167.5	67.5	-173.5	-1047810.148	295.6005	-1047514.548	19.36	0.0	0.1	F
43	-163.6	-44.7	-178.5	-162.5	60.0	59.3	-1047812.077	297.6456	-1047514.431	19.47	0.0	0.1	B/J
44	-64.2	59.7	1.9	-143.6	-176.1	-77.7	-1047809.706	295.3557	-1047514.350	19.56	0.0	0.1	e
45	-61.8	59.2	0.2	-126.3	-51.7	-60.2	-1047808.461	295.5457	-1047512.916	20.99	0.0	0.1	G
46	86.7	-155.4	-178.1	16.8	-179.5	-46.0	-1047807.716	296.4969	-1047511.219	22.69	0.0	0.1	J/L
47	-67.0	54.6	0.8	-115.1	-58.3	171.6	-1047805.625	295.0778	-1047510.547	23.36	0.0	0.1	G
48	-90.0	148.5	172.8	-19.1	62.1	46.3	-1047803.188	296.5185	-1047506.670	27.24	0.0	0.1	J/L
49	-176.2	-57.3	-0.9	-109.3	-57.9	-65.3	-1047801.585	295.5773	-1047506.007	27.90	0.0	0.0	e
50	179.2	-61.5	-1.2	107.5	-72.6	-70.1	-1047800.876	295.4302	-1047505.446	28.46	0.0	0.0	G
51	-78.1	43.1	-171.4	-103.2	67.7	-175.0	-1047800.389	296.3958	-1047503.994	29.91	0.0	0.0	K
52	49.3	170.8	175.8	91.3	66.0	-63.1	-1047799.607	297.2640	-1047502.343	31.56	0.0	0.0	I/K
53	43.7	-77.2	-174.4	156.0	-75.7	-67.0	-1047797.804	296.4284	-1047501.376	32.53	0.0	0.0	B
54	-42.3	78.0	-174.6	38.0	-177.6	-169.0	-1047794.188	294.9467	-1047499.241	34.66	0.0	0.0	K/L
55	59.2	175.4	176.6	-7.0	60.1	165.1	-1047794.171	294.9798	-1047499.192	34.71	0.0	0.0	K/L
56	77.4	-161.8	-175.6	-93.6	-177.0	-41.6	-1047793.509	296.7026	-1047496.806	37.10	0.0	0.0	J
57	-34.8	85.1	-174.1	33.8	176.4	76.3	-1047791.608	295.1318	-1047496.476	37.43	0.0	0.0	K/L
58	160.5	-75.9	-178.4	-8.7	-171.8	-157.1	-1047790.114	293.9490	-1047496.165	37.74	0.0	0.0	K/L
59	167.5	-67.5	179.4	-13.4	-176.7	74.7	-1047784.412	294.0524	-1047490.359	43.55	0.0	0.0	K/L
60	-29.5	90.9	-176.4	16.6	59.4	177.4	-1047783.446	293.3753	-1047490.071	43.83	0.0	0.0	L
61	68.3	-170.1	179.0	-100.7	-57.3	67.4	-1047781.707	294.6814	-1047487.025	46.88	0.0	0.0	e

<sup>a</sup> 470 K, sublimation temperature used during the deposition process in the matrix isolation experiments. <sup>b</sup> See Figure 2 for atom numbering. <sup>c</sup> For the nine most stable conformers,  $\Delta E^{ZPVE}$  values calculated at the MP2/6-311++G(d,p) level are 0.00, 1.13, 5.88, 1.46, 6.47, 6.13, 7.03, 8.43, and 7.98 kJ mol<sup>-1</sup> (see also Table S1). <sup>d</sup> In the last column the H-bonding schemes for the corresponding conformer are indicated (see text). See Figure 3 for H-bonding schemes labeling. <sup>e</sup> Conformers **61**, **44**, and **49** of serine do not show any intramolecular hydrogen bond.

as proton-donor: NH<sub>(8)</sub>···O<sub>A</sub> (scheme **F**) and NH<sub>(9)</sub>···O<sub>C</sub> (bonding scheme **G**).

As general conclusions, from the data shown in Table 2 (and also in Table 1), the following can be stated:

(a) The cis arrangement of the carboxylic group is preferred over the trans configuration (with a single exception, **B**, all preferred bonding schemes have the carboxylic group in the cis conformation).

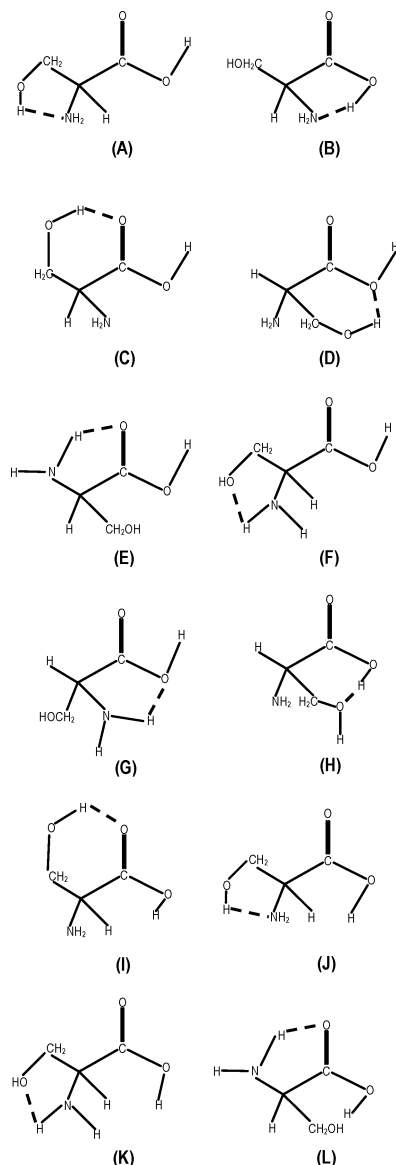


Figure 3. H-bonding schemes for serine.

TABLE 2: Average Energy ( $AE_T$ ) of the Conformers of Serine with H-Bonding Scheme  $\Gamma^a$

H-bond schemes ( $\Gamma$ )	$AE_T^b$ (kJ mol <sup>-1</sup> )	$AE_T - AE_A$ (kJ mol <sup>-1</sup> )	$\overline{AE_T - AE}$ (kJ mol <sup>-1</sup> )
A	-1047528.7	0.0	-10.8
B	-1047522.9	5.8	-5.0
C	-1047522.8	5.9	-4.9
D	-1047522.0	6.7	-4.1
E	-1047521.7	7.0	-3.8
F	-1047520.2	8.5	-2.3
G	-1047518.9	9.8	-1.0
H	-1047518.7	10.0	-0.8
I	-1047516.6	12.1	1.3
J	-1047509.2	19.5	8.7
K	-1047508.5	20.2	9.4
L	-1047504.1	24.5	13.8

<sup>a</sup>  $AE_A$  is the average energy of serine conformers with H-bonding scheme A.  $AE$  is the average energy of all conformers of serine. <sup>b</sup> All energies were calculated at DFT/B3LYP/6-311++G(d,p) level, with ZPVE correction taken into account.

(b) The interaction of the carboxyl proton with the hydroxyl side chain (bonding scheme H) is less favorable than those with nitrogen (bonding scheme B).

(c) When acting as donor group, the alcohol group ( $OH_A$ ) prefers to take part in H-bonding interactions with the nitrogen atom (scheme A) or with the carbonyl oxygen atom (scheme C) than with  $O_C$  (scheme D). This trend correlates well with the increase in the basicity of the acceptor group along the series  $O_C$ ,  $O=$ ,  $N$ .

(d) In general, the H-bonding schemes where either the  $OH_C$  or  $OH_A$  groups act as the donating group are preferred over those where the  $NH_2$  group takes this role (thus, schemes A, C and D are preferred over E, F and G, and schemes H, I and J are preferred over K and L).

(e) The conjugation of better donating ( $OH_C$ ) and acceptor (N) moieties occurs in scheme B, justifying the exceptional character of the position occupied by this bonding scheme (which is associated with the higher-energy trans arrangement of the carboxylic group, but corresponds to the second preferred structural arrangement) in the energy scale.

(f) taking into consideration the dominant intramolecular interactions in the nine most stable conformers of serine, they can be grouped in 3 classes: 1, 4 and 6, where bonding scheme A dominates; 2, 3, 5, 8 and 9, where bonding scheme B is prevalent and 7, where the most relevant interaction is C.

It is also worth noting that the different types of structures exhibited by the nine most stable conformers of serine are reflected in their geometrical parameters (see Table S2, provided as Supporting Information). For instance, the  $C=O$  and  $C-O_C$  bonds are systematically longer (by  $\sim 0.003$  and  $\sim 0.02$  Å, respectively) and the  $C-C_\alpha$  and  $C_\alpha-N$  bonds are shorter (by  $0.01-0.02$  Å) in conformers where the carboxyl group adopts the cis conformation, relative to those where the same group assumes the trans orientation. On the other hand, the involvement of the carbonyl oxygen in the  $OH_A \cdots O=$  hydrogen bond in both forms 3 and 7 can easily be correlated with the longer  $C=O$  distances observed for these two conformers (indeed, regarding the  $C=O$  bond length, conformer 3, which has a trans carboxylic group is the exception relative to the above-mentioned trend which states that this bond length should be longer for conformers with cis carboxylic groups than for those with a trans carboxylic group). Furthermore, accordingly to the involvement in the strong  $OH_C \cdots N$  hydrogen bond, the  $OH_C$  bond attains its maximum length in conformers 2, 3, 5, 8, and 9 (longer by ca.  $0.14$  Å than in the other conformers), whereas the  $OH_A$  bond is consistently longer in the conformers where this group acts as H-bond donor (1, 3, 4, 6, and 7) than in the remaining conformers.

The distinction between the cis and trans carboxylic conformers of serine can also be clearly noticed in the calculated dipole moments (see Figure 1). The trans conformers (2, 3, 5, 8, and 9) exhibit a systematically higher dipole moment (ca.  $4-5$  D) than the cis forms (ca.  $2-3$  D).

#### Spectroscopic Results (Supported by Calculated IR Spectra and Energy Barriers to Conformational Isomerization).

As discussed in detail above, the calculated relative energies (see Table 1) suggest that in the gas-phase-equilibrium the conformational mixture shall contain relevant contributions from the nine most stable conformers of serine. Assuming that the relative populations of serine conformers frozen into a low-temperature matrix should correspond to gas-phase equilibrium, the matrix-isolation infrared (MI-IR) spectroscopy technique could provide a suitable way to experimentally test the theoretical predictions, since the different conformers of serine shall give rise to distinguishable MI-IR spectra (see Tables S3-S21, provided as Supporting Information).



As already mentioned, the set of nine most stable conformers of serine can be divided into three groups (group **A**, conformers **1**, **4**, and **6**; group **B**, **2**, **3**, **5**, **8**, and **9**; and group **C**, **7**). In each of these groups, there are common structural characteristics that can be expected to be relevant in determining the vibrational signature of its elements, in particular in the spectral regions corresponding to vibrations that can be expected to be most affected by H-bond interactions. To facilitate discussion of the assignment of the infrared spectra of D,L-serine and D,L-3,3-dideutero-serine, the analysis will be performed by dividing the spectra into different regions. Only the most representative spectral regions will be discussed in detail in the forthcoming sections. Tables 3 and 4 summarize the proposed assignments for these two molecules and compare the experimentally observed frequencies with those obtained theoretically at the DFT/B3LYP/6-311++G(d,p) level for the relevant conformers.

*$\nu\text{OH}$  and  $\nu\text{NH}_2$  Stretching Region (3700–3100  $\text{cm}^{-1}$ ).* In this spectral region, the theoretical calculations predict that all conformers of practical relevance should give rise to bands due to  $\nu\text{NH}_2$  stretching modes (both symmetric and antisymmetric). These bands are of low intensity and lie at nearly the same position ( $\nu\text{NH}_2$  asym: 3498–3528  $\text{cm}^{-1}$ ;  $\nu\text{NH}_2$  sym: 3418–3440  $\text{cm}^{-1}$ ; see Tables 3 and 4 and Figure 4). Experimentally, the features ascribable to the antisymmetric mode are observed between 3500 and 3540  $\text{cm}^{-1}$  and those due to the symmetric mode between 3390 and 3440  $\text{cm}^{-1}$ , in good agreement with the theory. On the other hand, the bands due to  $\nu\text{OH}$  stretching vibrations were predicted to appear at considerably different frequencies in the three groups of conformers (see Figure 4). In conformers belonging to group **A**, the  $\nu\text{OH}_\text{C}$  bands are predicted to occur at slightly higher frequencies than  $\nu\text{OH}_\text{A}$ , since in these conformers the alcohol group is H-bonded to the amine group. The predicted frequency for  $\nu\text{OH}_\text{C}$  is typical of a free cis carboxylic group and is considerably lower than those of the free alcohol groups in all conformers of group **B** but conformer **3** (where  $\text{OH}_\text{A}$  is H-bonded to the carbonyl oxygen; see Figure 1). In conformer **7** (group **C**), the predicted order of frequencies for the  $\nu\text{OH}_\text{C}$  and  $\nu\text{OH}_\text{A}$  modes is reversed, since in this case the H-bond involving the alcohol group is established with the carbonyl oxygen atom, which is a weaker H-bond acceptor than the amine nitrogen. Despite the change in the order of the two  $\nu\text{OH}$  stretching modes in groups **A** and **C**, the general pattern of the spectra for all conformers belonging to these two groups is predicted to be identical (see Figure 4). In conformers belonging to group **B**, where the alcohol group is free,  $\nu\text{OH}_\text{A}$  is predicted at frequencies above 3600  $\text{cm}^{-1}$  (scaled values; the exception is conformer **3** where, as mentioned above, the  $\text{OH}_\text{A}$  group is H-bonded to the carbonyl oxygen and then gives rise to a  $\nu\text{OH}_\text{A}$  vibration with a frequency similar to those found in groups **A** and **C**), whereas  $\nu\text{OH}_\text{C}$  is predicted at considerably lower frequencies, due to the involvement of the carboxylic group in the strong  $\text{OH}_\text{C}\cdots\text{NH}_2$  hydrogen bond (see Figure 4). In consonance with these predictions, in the spectra of D,L-serine and D,L-3,3-dideutero-serine in an argon matrix the “free”  $\nu\text{OH}_\text{A}$  bands of **B** conformers **2**, **9**, **5**, and **8** are observed at 3629, 3637, 3660, and 3664  $\text{cm}^{-1}$ , respectively, whereas those corresponding to the H-bonded  $\text{OH}_\text{A}$  group in **C** and **A** conformers appear at 3610  $\text{cm}^{-1}$  and in the 3560–3550  $\text{cm}^{-1}$  region, respectively (the  $\nu\text{OH}_\text{A}$  band of conformer **3** is observed at 3543  $\text{cm}^{-1}$ ). In turn, the “free”  $\nu\text{OH}_\text{C}$  vibrations in conformers belonging to groups **A** and **C** give rise to the bands observed at 3592 (form **4**), 3585 (**6**), 3567 (**1**), and 3564 (**7**)  $\text{cm}^{-1}$ , whereas

those originated in the strongly H-bonded carboxylic group of **B** conformers can be ascribed to the broad band centered around 3170  $\text{cm}^{-1}$ .

It is important to note that it was possible to identify bands in this spectral region ascribable to each one of the nine conformers of serine that are predicted by the theory to contribute in significant amounts to the conformational equilibrium at the temperature used for evaporation of serine during deposition of low-temperature matrixes.

To change the relative populations of the conformers trapped in the matrix and allow for a more clear assignment of the bands to the different conformers, UV irradiation ( $\lambda > 200$  nm) of the sample followed by annealing up to 30 K was undertaken. The following processes were observed to occur:

(i) Upon UV irradiation of the matrixes, decarboxylation of serine was observed, as easily noticed by the appearance of features due to matrix isolated  $\text{CO}_2$ , around 2340  $\text{cm}^{-1}$  (antisymmetric stretching) and 668  $\text{cm}^{-1}$  (bending). The photoproducts of serine decarboxylation ( $\text{CO}_2$  and other photogenerated species) are confined in the same matrix cage. The interaction between these photoproducts is revealed by the broad profile of the antisymmetric stretching band, which differs considerably from that characteristic of monomeric  $\text{CO}_2$  in an argon matrix<sup>56</sup> (Figure 5).

(ii) With all probability, ethanolamine is produced together with  $\text{CO}_2$ . However, the complexity of the spectra, together with the low intensity of the bands of ethanolamine comparatively to those of serine (the most intense band of ethanolamine lying in the accessible spectral region was predicted at the DFT-(B3LYP)/6-311++G(d,p) level of theory to have an IR intensity of only ca. 100  $\text{km mol}^{-1}$ , whereas the most intense bands of serine have IR intensities over 300  $\text{km mol}^{-1}$ ), the possibility of photoproduction of different conformers of ethanolamine (absorbing at slightly different frequencies), and the relatively low efficiency of the photoprocess, preclude a clear identification of this compound in the spectra of the irradiated matrixes. In the high frequency ( $\nu\text{OH}$  stretching) region of the IR spectrum, the most stable conformer of ethanolamine isolated in an Ar matrix absorbs at 3555  $\text{cm}^{-1}$ ,<sup>57</sup> which coincides exactly with the frequency of the most intense group of bands observed in this spectral region for serine. A band, appearing in the high-frequency range of the IR spectrum upon UV irradiation of the matrix, is observed at 3624  $\text{cm}^{-1}$  (at the same frequency in the spectra of irradiated serine and irradiated deuterated serine). This band might correspond to ethanolamine complexed with  $\text{CO}_2$ , but this assignment must be considered as tentative. In addition, there are also new bands at 3726 and 3701  $\text{cm}^{-1}$ . These bands might be ascribed to water appearing after irradiation. Water can be formed together with carbon monoxide and acetamide. Identification of a small amount of CO could be easily done, since its characteristic band at 2138  $\text{cm}^{-1}$  was also observed in the spectrum of the irradiated sample. On the other hand, no conclusive identification of acetamide could be made, because this molecule absorbs in spectral regions where intense bands due to serine appear and, as inferred by the intensity of the bands at 3726 and 3701  $\text{cm}^{-1}$  as well as that ascribed to CO, the dehydration reaction was of minor importance.

(iii) During UV irradiation, the decrease of intensity of the bands ascribed to the different conformers of serine occurs at different rates. Among the nine conformers experimentally observed, conformer **7** (**C** conformer) is the one that reacts faster, followed by **A**-type conformers (conformers **1**, **4**, and **6**). This means that the photodecarboxylation is strongly influenced by the conformation of the reactant molecule,







TABLE 3 (Continued)

approx. descript. <sup>a</sup>	1		2		3		4		5		6		7		8		9		exptl				
	freq. <sub>scal</sub> <sup>b</sup> (cm <sup>-1</sup> )	int.	freq. <sub>scal</sub> <sup>b</sup> (cm <sup>-1</sup> )	int.	freq. <sub>scal</sub> <sup>b</sup> (cm <sup>-1</sup> )	int.	freq. <sub>scal</sub> <sup>b</sup> (cm <sup>-1</sup> )	int.	freq. <sub>scal</sub> <sup>b</sup> (cm <sup>-1</sup> )	int.	freq. <sub>scal</sub> <sup>b</sup> (cm <sup>-1</sup> )	int.	freq. <sub>scal</sub> <sup>b</sup> (cm <sup>-1</sup> )	int.	freq. <sub>scal</sub> <sup>b</sup> (cm <sup>-1</sup> )	int.	freq. <sub>scal</sub> <sup>b</sup> (cm <sup>-1</sup> )	int.	freq. (cm <sup>-1</sup> )	int. <sup>c</sup>			
$\nu_{\text{COO}}$									713.4	15										732; sh; 727; sh; 721 m			
$\delta_{\text{C}_\alpha\text{C}_\beta\text{O}}$													693.3	20									
$\delta_{\text{C-O}_\text{C}}$																	643.3	5					
$\delta_{\text{C=O}}$	640.6	17																			645 m		
$\delta_{\text{C-O}_\text{C}}$									638.4	11													
$\delta_{\text{C=O}}$											627.0	49										633 w	
$\tau_{\text{C-O}_\text{C}}$								625.0	80													617 m	
$\delta_{\text{C=O}}$								588.6	121								598.1	22				587 m	
$\tau_{\text{C-O}_\text{C}}$														593.8	120							579 m	
$\tau_{\text{C-O}_\text{A}}$					589.9	64																	
$\tau_{\text{C-O}_\text{C}}$											585.6	117											
$\delta_{\text{C}_\alpha\text{C}_\beta\text{O}}$			584.3	6																		568 s	
$\tau_{\text{C-O}_\text{C}}$	582.4	111																					
$\delta_{\text{C-O}_\text{C}}$					571.4	75																	
$\tau_{\text{C-O}_\text{A}}$	554.4	133					556.1	55															
$\delta_{\text{C=O}}$										548.6	9							550.9	7			566 s	
$\delta_{\text{C=O}}$																						561 m	
$\tau_{\text{C-O}_\text{A}}$													546.0	95								546 vw	
$\nu_{\text{C}_\alpha\text{C}}$			537.2	7																		531 sh	
$\delta_{\text{C=O}}$					533.5	5																	
$\delta_{\text{CC(C)N}}$													528.7	42								526 sh	
$\rho_{\text{C}_\beta\text{C}_\alpha\text{C}}$							515.9	27															
$\tau_{\text{C-O}_\text{A}}$																							
$\delta_{\text{C-O}_\text{C}}$	514.4	9																				521; m; 518 m	
$\delta_{\text{C-O}_\text{C}}$			506.9	3																			
$\delta_{\text{C-O}_\text{C}}$							470.6	33														494 m	
$\delta_{\text{C}_\alpha\text{C}_\beta\text{O}}$																							
$\delta_{\text{NC}_\alpha\text{C}}$									413.1	7								416.0	10				
$\delta_{\text{C}_\alpha\text{C}_\beta\text{O}}$					407.3	3																	
$\delta_{\text{NC}_\alpha\text{C}}$													401.5	14									
$\tau_{\text{C-O}_\text{A}}$			399.7	93																			
$\delta_{\text{NC}_\alpha\text{C}}$	397.8	28																				408 w	
$\delta_{\text{C-O}_\text{C}}$																							
$\delta_{\text{CC(C)N}}$														371.2	6								
$\delta_{\text{NC}_\alpha\text{C}}$			359.3	20			357.7	3															

<sup>a</sup> See Table S3 for definition of coordinates. <sup>b</sup> The scale factor used for all modes was 0.978, except for the two  $\nu_{\text{OH}_{\text{A/C}}}$ . The scale factor used for  $\nu_{\text{OH}_{\text{A}}}$  in all conformers and for  $\nu_{\text{OH}_{\text{C}}}$  in **A** and **C** conformers was 0.953; the factor 0.913 was used to scale  $\nu_{\text{OH}_{\text{C}}}$  modes of **B** conformers (see Experimental section for details). <sup>c</sup> Experimental IR intensities are presented in a qualitative way (vw, very weak; w, weak; m, medium; s, strong; vs, very strong; sh, shoulder; vb, very broad). For the lowest intensity bands predicted by calculations lying at nearly the same frequency of more intense bands, the assignments were made as an indication that these bands should also contribute to the experimental bands as a minor species.

occurring preferentially for those conformers where the carboxylic group is not engaged in H-bond as proton donor. The reason for the observed specific preference for the **C** conformer relative to the **A** conformers can be related with the presence in the **C** conformer of the stronger  $\text{O-H}_\text{A}\cdots\text{O}=\text{O}$  bond instead of the considerably weaker  $\text{N-H}\cdots\text{O}=\text{O}$  bond present in the **A** conformers. The different rates of decarboxylation associated with the three groups of serine conformers strongly facilitated the assignment of the experimental spectra. This is clearly demonstrated in the case of the  $\nu_{\text{O-H}}$  stretching spectral region in Figure 4, but it does also apply to the other regions of the spectra, as will be stressed further below.

(iv) Besides aggregation, which can be noticed by appearance of characteristic bands of aggregates throughout the spectra, annealing of the matrixes led only to minor spectral changes, from which the most relevant is the increase of the intensity of the bands with predominant contribution from conformers **1** and **3** relative to bands due to other conformers. This is illustrated in Figure 4 by the relative increase of intensity of the bands at 3567 and 3556  $\text{cm}^{-1}$ , due to conformer **1** and at 3543  $\text{cm}^{-1}$ , ascribed to conformer **3**. When annealing of the matrix is done, conversion from the less stable conformers into an energetically accessible lower energy form shall take place. The energy barriers separating the reactant conformers from the products shall be low enough to be overcome at the low work temperature. As a rough estimate of the barriers of interconversion between the different experimentally observed conformers of

serine in the low-temperature matrixes, the DFT/B3LYP/6-311++G(d,p) barriers for the molecule in a vacuum were calculated (see Table S22 of the Supporting Information; the  $\text{COOH cis} \leftrightarrow \text{COOH trans}$  interconversion is well-known to have associated barriers of more than ca. 40  $\text{kJ mol}^{-1}$ <sup>58</sup> and was not here subjected to calculation). The calculated barriers are, in general, predicted to be relatively high. Indeed, in many cases, the simultaneous rearrangement of several groups, as well as breaking of H bonds, are required for the molecular system to undergo a transition from one conformer to other of lower energy. However, taking into account the margin of error associated with the unavoidable intrinsic errors in the theoretical estimations as well as the effects of the environment, the calculated values for the energy barriers are compatible with observation of, at least, some conformational rearrangements upon annealing of the matrixes. If we took into consideration the theoretical results just as an indicator of the relative accessibility of the various processes (by looking at the relative values of the barriers), then, in consonance with the experimental observations, for cis carboxylic conformers (**A** and **C** conformers), one could expect an increase of population of conformer **1**, particularly at expenses of both forms **4** and **7** (conformer **6** might also be converted to **1** in a two step process  $\mathbf{6} \rightarrow \mathbf{4} \rightarrow \mathbf{1}$ ; see Table S22). In the case of trans carboxylic conformers (**B** conformers), the theoretically predicted energy barriers are consistent with conversion from conformers **5**, **8**, and **9** either in conformer **2** or/and **3** (energy barriers leading to production







TABLE 4 (Continued)

approx. descript. <sup>a</sup>	1		2		3		4		5		6		7		8		9		exptl			
	freq. <sub>scal</sub> <sup>b</sup> (cm <sup>-1</sup> )	int.	freq. <sub>scal</sub> <sup>b</sup> (cm <sup>-1</sup> )	int.	freq. <sub>scal</sub> <sup>b</sup> (cm <sup>-1</sup> )	int.	freq. <sub>scal</sub> <sup>b</sup> (cm <sup>-1</sup> )	int.	freq. <sub>scal</sub> <sup>b</sup> (cm <sup>-1</sup> )	int.	freq. <sub>scal</sub> <sup>b</sup> (cm <sup>-1</sup> )	int.	freq. <sub>scal</sub> <sup>b</sup> (cm <sup>-1</sup> )	int.	freq. <sub>scal</sub> <sup>b</sup> (cm <sup>-1</sup> )	int.	freq. <sub>scal</sub> <sup>b</sup> (cm <sup>-1</sup> )	int.	freq. <sub>scal</sub> <sup>b</sup> (cm <sup>-1</sup> )	int. <sup>c</sup>		
$\gamma$ COO											714.8	30							720;	vw;		
$\delta$ C=O															712.7	12			716	sh		
$\gamma$ COO	708.1	33																	710	m		
$\gamma$ COO									702.6	14												
$\gamma$ COO																	697.6	13	695;	w;		
$\gamma$ COO					685.7	17													691	sh		
$\delta$ C <sub><math>\alpha</math></sub> C <sub><math>\beta</math></sub> O													676.5	18								
$\delta$ C-O <sub>C</sub>																	638.9	4				
$\delta$ C=O	638.5	17																	641	w		
$\delta$ C-O <sub>C</sub>									633.6	11												
$\delta$ C=O											625.8	47								631	m	
$\tau$ C-O <sub>C</sub>								622.3	81											613	m	
$\tau$ C-O <sub>C</sub>														590.9	115					583;	m	
																				581;		
																				577		
$\gamma$ COO															589.8	19				567;	sh;	
$\tau$ C <sub><math>\beta</math></sub> O					585.9	80														565	sh	
$\tau$ C-O <sub>C</sub>											579.8	100										
$\tau$ C-O <sub>A</sub>								577.5	157												563	s
$\tau$ C-O <sub>C</sub>	576.0	85																				
$\delta$ C-O <sub>C</sub>																					560;	s;
$\delta$ C <sub><math>\alpha</math></sub> C <sub><math>\beta</math></sub> O					567.5	55															558;	sh;
$\tau$ C-O <sub>A</sub>	553.3	152	563.1	5																	554;	w;
$\delta$ C=O								547.7	16												551	vw
$\tau$ C-O <sub>A</sub>											541.1	144	545.7	163							540	m
$\delta$ C=O										531.1	6							530.3	3		531	w
$\nu$ C <sub><math>\alpha</math></sub> C			530.5	7																		
$\nu$ C <sub><math>\alpha</math></sub> C;					523.3	4															525;	w;
$\delta$ C=O																					524;	w;
																					521	sh
$\delta$ C-O <sub>C</sub>											510.6	5									508;	m;
$\nu$ C <sub><math>\alpha</math></sub> C													508.7	42							506;	m;
$\gamma$ COO							506.5	26													505;	m;
$\delta$ C-O <sub>C</sub>															506.9	1					503	m
$\delta$ C-O <sub>C</sub>	493.5	10	495.9	2																	491	w
$\delta$ C-O <sub>C</sub>							465.4	30													477	m
$\delta$ C <sub><math>\alpha</math></sub> C <sub><math>\beta</math></sub> O					401.7	3			397.7	10								404.3	23			
$\tau$ C-O <sub>A</sub>			397.1	102																	402	w
$\delta$ C <sub><math>\alpha</math></sub> C <sub><math>\beta</math></sub> O															392.7	13						
$\delta$ NC <sub><math>\alpha</math></sub> C	390.3	24									391.6	12										

<sup>a</sup> See Table S3 for definition of coordinates. <sup>b</sup> The scale factor used for all modes was 0.978, except for the two nOHA/C. The scale factor used for nOHA in all conformers and for nOHC in **A** and **C** conformers was 0.953; the factor 0.913 was used to scale nOHC modes of **B** conformers (see the Experimental Section for details). <sup>c</sup> Experimental IR intensities are presented in a qualitative way (vw, very weak; w, weak; m, medium; s, strong; vs, very strong; sh, shoulder; vb, very broad). For the lowest intensity bands predicted by calculations lying at nearly the same frequency of more intense bands, the assignments were made as an indication that these bands should also contribute to the experimental bands as a minor species.

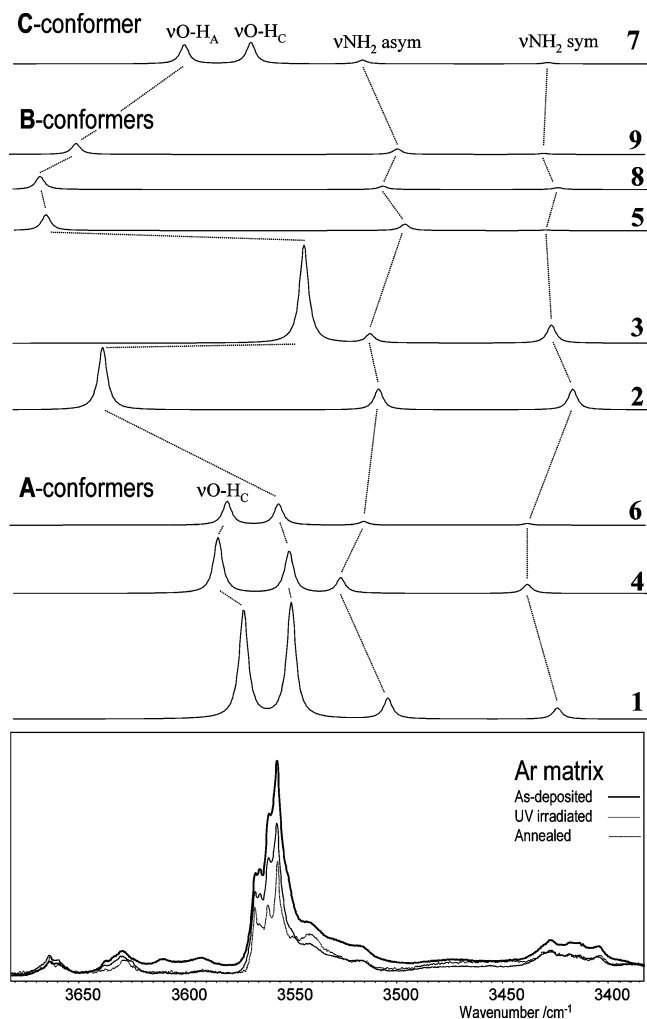
of **2** and **3** from **5**, **8**, and **9** are of the same order of magnitude). However, accordingly with the experimental observations, pathways leading to production of conformer **3** appear to be favored.

A final note shall be made regarding the assignments now proposed for the  $\nu$ OH and  $\nu$ NH<sub>2</sub> stretching region (3700–3100 cm<sup>-1</sup>) in comparison with those previously made by Lambie et al.,<sup>29</sup> which in some cases differ considerably from ours. The present assignments are supported by a complete theoretical analysis of the conformational space of the molecule and calculation of the IR spectra of all relevant conformers, which indeed were found to be nine instead of the four previously considered. The assignments were also supported by the irradiation and annealing experiments, which promoted changes in the relative populations of the conformers, facilitating identification of the bands due to individual conformers. Finally, use of deuterated species provides additional data for further validation of the assignments now presented. As it will be shown in the next sections, the same can be stated for the interpretation of the other spectral regions.

$\nu$ C <sub>$\beta$</sub> (H/D)<sub>2</sub> and  $\nu$ C <sub>$\alpha$</sub> H Stretching Regions (3100–2800 and 2260–2000 cm<sup>-1</sup>). The  $\nu$ C <sub>$\alpha$</sub> -H/D vibrations have been recently shown to provide information about the involvement of a hydroxyl group attached in the  $\alpha$  position in hydrogen bonding

interactions.<sup>59</sup> For the model compound *n*-[1-D]propanol, the  $\nu$ C <sub>$\alpha$</sub> -H/D frequency could be successfully correlated with the H-bond strength in a series of different experimental conditions, which included the matrix isolated compound (argon), pure liquid and low temperature glassy states, and solution in different solvents. However, it was found that such correlation can only be established when the OH group is not acting simultaneously as proton donor and acceptor.<sup>59</sup> In serine conformers, with a few exceptions (see Figure 1), this last condition is not fulfilled. Hence, it is not expected that the analysis of this spectral region could provide any information that can be considered particularly significant regarding H-bonding in the studied compound. Nevertheless, some useful information could still be extracted from an analysis.

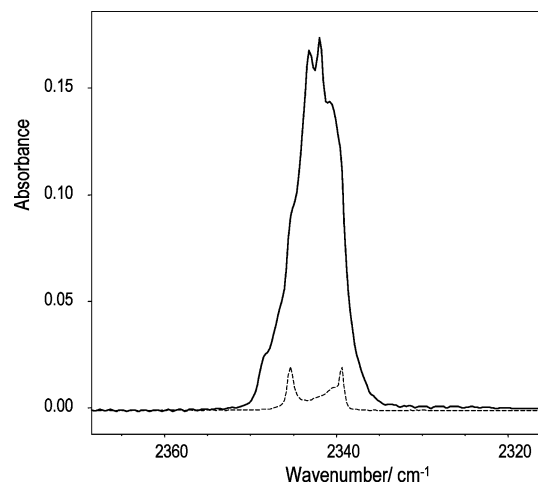
First, upon UV irradiation of the matrixes, intensity changes in the complex profiles of the  $\nu$ CH/D stretching bands were found to be consistent with the appearance of new bands at frequencies expected for  $\nu$ CH/D stretching vibrations in ethanolamine. In the case of the nondeuterated compound, an increase of intensity was noticed at ca. 2866 cm<sup>-1</sup>, that is at a frequency similar to those corresponding to the ethanolamine  $\nu$ CH<sub>2</sub> symmetric stretching modes (2882 and 2861 cm<sup>-1</sup>).<sup>60,61</sup> The bands due to antisymmetric vibrations have been observed previously at ca. 2950 cm<sup>-1</sup>,<sup>60,61</sup> but could not be detected in



**Figure 4.**  $\nu\text{O-H}$  and  $\nu\text{NH}_2$  stretching region (above  $3350\text{ cm}^{-1}$ ) of the IR spectrum of matrix-isolated serine (Ar matrix) and spectra calculated at the DFT/B3LYP/6-311++G(d,p) level (wavenumbers were scaled: positions of the bands due to  $\nu\text{NH}_2$  by a factor of 0.978, of the bands due to  $\nu\text{OH}$  in the spectra of forms **1**, **3**, **4**, and **6** by a factor of 0.913, and of the bands due to  $\nu\text{OH}$  in the spectra of forms **2**, **5**, **7**, **8**, and **9** by a factor of 0.953) for the nine experimentally relevant conformers. In the calculated spectra, intensities are multiplied by the estimated relative populations. As mentioned in the text,  $\nu\text{O-H}_C$  of the H-bonded B-type conformers are observed as a broad band centered around  $3170\text{ cm}^{-1}$ .

the present study since they fall in a more congested spectral region. However, in the spectrum of 3,3-dideutero-serine, the four bands expected for the photoproduct deuterated ethanolamine (symmetric and antisymmetric  $\nu\text{CH}_2$  and  $\nu\text{CD}_2$  stretching modes) can be assigned to the bands emerging at  $2950\text{--}2903$ ,  $2870$ ,  $2214$ , and  $2100\text{ cm}^{-1}$ . As expected, the  $\nu\text{CH}_2$  bands were then observed at similar frequencies in both deuterated and nondeuterated molecules, whereas the  $\nu\text{CD}_2$  bands were observed at frequencies closely matching those predicted by the DFT(B3LYP)/6-311++G(d,p) calculations:  $2223$  and  $2112\text{ cm}^{-1}$ . Hence, these observations strongly support the idea that ethanolamine, together with  $\text{CO}_2$ , is the major photoproduct species.

An additional band appearing in this region upon UV irradiation is observed at  $2276\text{ cm}^{-1}$ . The origin of this band is uncertain, but it might be tentatively assigned to methyl isocyanate ( $\text{CH}_3\text{NCO}$ ), which can result from photolysis of acetamide ( $\text{CH}_3\text{NCO}$  would be formed together with  $\text{H}_2$ ). Note that  $\text{CH}_3\text{NCO}$  should also absorb around  $776\text{ cm}^{-1}$ , and in fact,



**Figure 5.**  $\text{CO}_2$  asymmetric stretching spectral region of the serine irradiated matrix (solid line) and of free  $\text{CO}_2$  isolated in argon (dashed line).

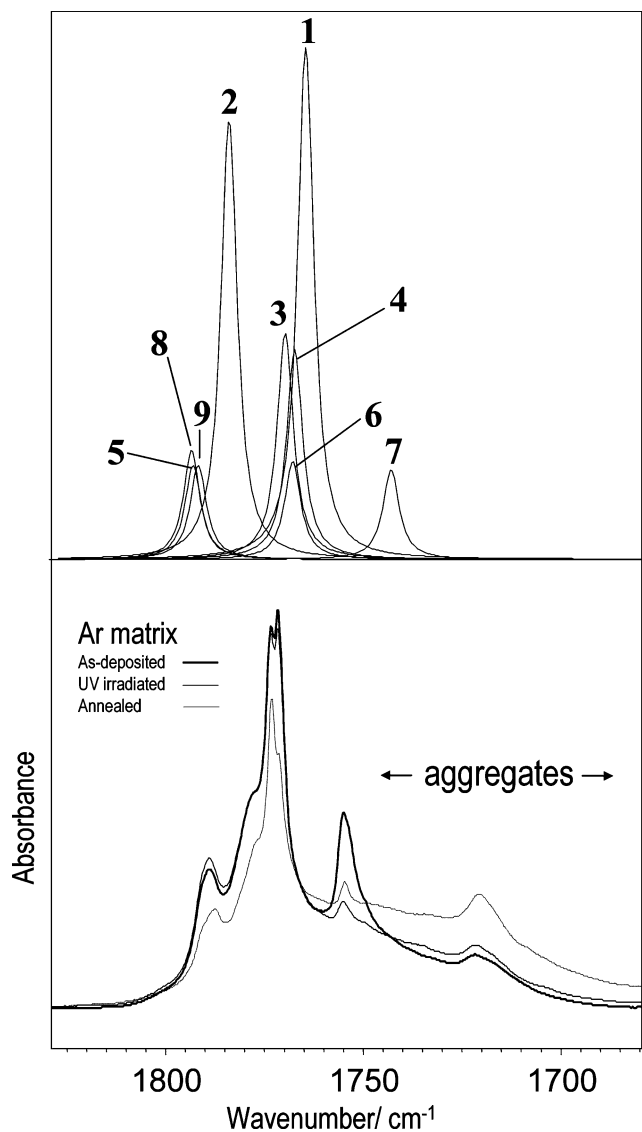
the spectral intensity in the  $780\text{--}765\text{ cm}^{-1}$  region increases after irradiation, thus supporting the assignment of the  $2276\text{ cm}^{-1}$  band to  $\text{CH}_3\text{NCO}$ .

Finally, the annealing experiments reveal that the low-frequency region of the feature assigned to the  $\nu\text{CH}_2$  symmetric stretching vibration increases in intensity relative to all other features observed in the  $3100\text{--}2800\text{ cm}^{-1}$  spectral range. Very interestingly, the calculations predicted that the conformers of serine where  $\nu\text{CH}_2$  symmetric stretching should occur at lowest frequency were conformers **1** and **3** (see Table 3). Hence, the analysis of this spectral region is also consistent with an increase of population of these two conformers upon annealing of the matrix, reinforcing the conclusions extracted from the analysis of the  $\nu\text{OH}$  stretching region.

**$\nu\text{C=O}$  Stretching Region ( $1850\text{--}1700\text{ cm}^{-1}$ ).** In this spectral region, the spectra of both isotopologues of serine are very similar to each other. Six main bands due to monomeric serine are observed between  $1850$  and  $1740\text{ cm}^{-1}$  (Figure 6). The absorptions with maximum at ca.  $1720\text{ cm}^{-1}$ , that increased considerably upon annealing are originated in aggregates, appearing at similar frequencies observed for aggregates of analogous compounds.<sup>62</sup> According to the calculations, **B** conformers should give rise to  $\nu\text{C=O}$  bands appearing at higher frequencies than **A** conformers, whereas conformer **7** (of the **C**-type) should absorb at a considerably lower frequency than all of the other forms (see Figure 6). Conformer **3** (**B**-type) is once again an exception to the regularities found for other **B**-type conformers. The reason for that could be the presence in this form of the relatively stronger  $\text{OH}_A\cdots\text{O}=\text{H}$  bond that reduces the frequency of the carbonyl stretching mode and makes the experimental frequency of the  $\nu\text{C=O}$  band in **C** similar to the corresponding values in **A** group of conformers.

In consonance with the theoretical predictions, the  $\nu\text{C=O}$  modes of conformers **5**, **8**, and **9** are assigned to the two overlapping higher frequency bands observed in this region at  $1790$  and  $1788\text{ cm}^{-1}$ , whereas conformer **2** gives rise to the band at  $1778\text{ cm}^{-1}$ . In conformers **5**, **8**, and **9**, the carbonyl group is not participating in any H bond. The two intense bands at  $1773$  and  $1771\text{ cm}^{-1}$  are due to **A**-type conformers and conformer **3**. Upon irradiation of the matrix, the band at  $1771\text{ cm}^{-1}$  decreases considerably in intensity, whereas the band at  $1773\text{ cm}^{-1}$  does not change very much. This result indicates that the lowest-frequency band is essentially due to **A**-type conformers, whereas conformer **3** shall contribute to the highest frequency band. On the other hand, upon annealing (after





**Figure 6.** Carbonyl stretching region of the IR spectrum of matrix-isolated serine (Ar matrix) and Simulated DFT/B3LYP/6-311++G(d,p) spectra (scaled; see Materials and Methods section for details) for the nine experimentally relevant conformers. In the calculated spectra, intensities are multiplied by the estimated relative populations.

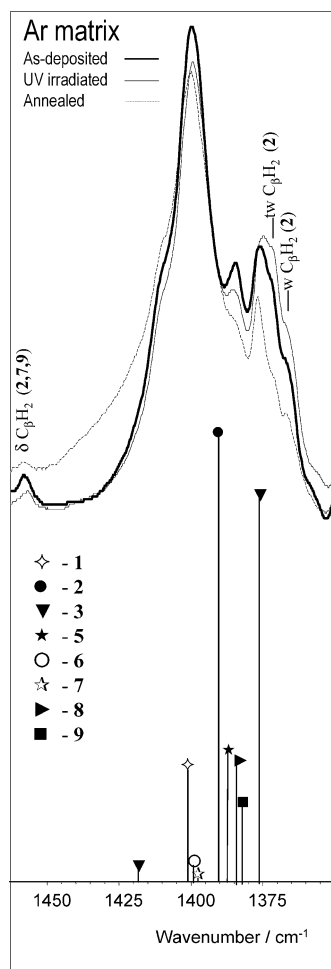
irradiation), the band at  $1771\text{ cm}^{-1}$  decreases in intensity, whereas the  $1773\text{ cm}^{-1}$  band increases. Since bands due to conformers **1** and **3** are expected to increase in intensity upon annealing and those due to other conformers are expected to decrease, the results of the annealing experiments seem to indicate that conformer **1** shall also contribute to the  $1773\text{ cm}^{-1}$  band. Thus, on the whole, the experimental results indicate that conformer **1** shall contribute to both the  $1773$  and  $1771\text{ cm}^{-1}$  bands, whereas conformer **3** and other **A** conformers (forms **4** and **6**) should contribute only to the high-frequency and low-frequency bands, respectively.

The calculations predict also that the lowest-frequency  $\nu\text{C}=\text{O}$  band ascribable to monomeric serine ( $1755\text{ cm}^{-1}$ ; with a shoulder at lower frequency in the case of the deuterated compound) is due to the **C**-type conformer **7**. This assignment is unequivocal, in particular due to the behavior exhibited by this band upon UV irradiation: as expected, it is, among all bands in this spectral region, the one showing a larger intensity reduction (see Figure 6).

**$\delta\text{COH}$  Bending Region ( $1420\text{--}1200\text{ cm}^{-1}$ ).** The  $\delta\text{COH}$  vibrations in the different serine conformers are predicted by

the calculations to give rise to IR bands appearing in a relatively broad spectral range extending over ca.  $220\text{ cm}^{-1}$  (see Tables 3 and 4 and also S4–S21). The frequencies of the  $\delta\text{COH}$  vibrations obey the general rule that the stronger a H-bond is, the higher the frequency of the  $\delta\text{COH}$  vibration should be. This rule should be valid for both alcohol and carboxylic OH groups. The  $\delta\text{COH}_\text{C}$  modes in the **A** and **C** conformers (which have their  $\text{OH}_\text{C}$  group “free”) are predicted by the calculations to give rise to low-intensity IR bands ( $5\text{--}50\text{ km mol}^{-1}$ ) in the  $1310\text{--}1274\text{ cm}^{-1}$  region, whereas for the H-bonded **B** conformers, the  $\delta\text{COH}$  vibrations shall give rise to intense ( $220\text{--}470\text{ km mol}^{-1}$ ) bands at  $1400\text{--}1375\text{ cm}^{-1}$ . On the other hand,  $\delta\text{COH}_\text{A}$  bands are predicted to have significantly lower intensities ( $<70\text{ km mol}^{-1}$ ). For all **B** conformers with a “free”  $\text{OH}_\text{A}$  group, the IR bands due to  $\delta\text{COH}_\text{A}$  vibrations are predicted to appear in the  $1205\text{--}1211\text{ cm}^{-1}$  region. Conformers **A** and **C**, with relatively weak H bonds involving the alcohol group as a proton donor, are expected to absorb within the  $1340\text{--}1400\text{ cm}^{-1}$  spectral region. Finally, for conformer **3**, with a stronger  $\text{OH}_\text{A}\cdots\text{O}=\text{H}$  bond, the  $\delta\text{COH}_\text{A}$  band is predicted to appear at the highest frequency around  $1420\text{ cm}^{-1}$ . In summary, for conformers **A** and **C** (plus conformer **3**), the frequencies of the  $\delta\text{COH}_\text{A}$  vibrations are predicted to be higher than the frequencies of the  $\delta\text{COH}_\text{C}$  vibrations, whereas for the **B** conformers (except for **3**) the reversed order of frequencies is expected.

Since in this spectral region the bands not only due to  $\delta\text{COH}$  modes, but also due to other vibrations (e.g., C–H deformations) do also appear, the complexity of the spectra precludes a detailed assignment to the bands observed in the experimental spectra to the different conformers. However, the general pattern extracted from the analysis of the theoretical spectra reflects well in the experimental data. Figure 7 displays the region between  $1460$  and  $1350\text{ cm}^{-1}$  of the spectrum of serine and compares the experimental data with a schematic representation of the calculated spectra for the conformers absorbing in this spectral region. In this figure, only the calculated bands ascribed to  $\delta\text{COH}$  modes are represented for simplification (the most intense bands due to other vibrations appearing in this region are explicitly indicated in the experimental spectra and refer to the twisting and wagging modes of conformer **2** as well as to the band here assigned to  $\delta\text{C}_\beta\text{H}_2$  in conformers **2**, **7**, and **9**; see also Table 3). The intense bands due to the  $\delta\text{COH}_\text{C}$  vibrations of **B** conformers can be easily identified. Following the general pattern already mentioned, these bands are only slightly affected by UV irradiation. In addition, for all **B** conformers but conformer **3**, the bands substantially decrease in intensity upon annealing. In the case of the  $\delta\text{COH}_\text{C}$  band of conformer **3**, at ca.  $1376\text{ cm}^{-1}$ , the apparent decrease of intensity upon annealing results from loss of intensity of the deformation bands originated in conformer **2** (and also the  $\delta\text{COH}_\text{C}$  bands of conformers **5**, **8**, and **9**, assigned to the feature around  $1384\text{ cm}^{-1}$ ) that extensively overlap with this band. However, it is clear that the  $1376\text{ cm}^{-1}$  band gains in relative intensity compared with the neighboring bands. As expected, the  $\delta\text{COH}_\text{A}$  band due to **A** and **C** conformers (mainly conformer **1**), observed as a shoulder at  $1410\text{ cm}^{-1}$ , slightly increases upon annealing. With all probability, the  $\delta\text{COH}_\text{A}$  band of conformer **3** is also contributing to the total intensity of the shoulder due to **A** and **C** conformers. The broad band emerging at frequencies between  $1450$  and  $1420\text{ cm}^{-1}$  upon annealing is due to aggregated forms, where the hydroxyl groups can be expected to participate in considerably strong intermolecular H bonds, hence, giving rise to  $\delta\text{COH}$  modes absorbing at high frequencies.



**Figure 7.**  $\delta\text{COH}$  bending spectral region of D,L-serine in argon matrix and Simulated DFT/B3LYP/6-311++G(d,p) spectra (scaled; see Materials and Methods section for details) for the nine experimentally relevant conformers in the  $1460\text{--}1350\text{ cm}^{-1}$  spectral region. In the calculated spectra, intensities are multiplied by the estimated relative populations. In the figure, only the calculated bands ascribed to  $\delta\text{COH}$  modes are represented for simplification (the most intense bands due to other vibrations appearing in this region are explicitly indicated in the experimental spectra and refer to the twisting and wagging modes of conformer **2** as well as to the band here assigned to  $\delta\text{C}\beta\text{H}_2$  in conformers **2**, **7**, and **9**; see also Table 3).

The IR bands observed in the region  $1350\text{--}1200\text{ cm}^{-1}$  are characterized by a relative low intensity. In this spectral range, band overlap is extensive, hindering the assignment of the bands due to  $\delta\text{COH}$  modes originated in “free” OH groups. Interestingly, in this region, UV irradiation leads to emergence of a band around  $1230\text{ cm}^{-1}$  that appears at nearly the same frequency of one of the  $\text{twCH}_2$  vibrations of ethanolamine.<sup>57</sup> Note that ethanolamine has also two bands at  $1385$  and  $1375\text{ cm}^{-1}$  ( $\omega\text{CH}_2$ <sup>57</sup>), which are probably very responsible for the small increase of intensity of the bands at nearly these frequencies ascribed to the twisting and wagging modes of conformer **2** of serine upon irradiation (see Figure 7).

**$\nu\text{C}\text{--}\text{O}$  and  $\nu\text{N}\text{--}\text{C}$  Stretching Region ( $1200\text{--}950\text{ cm}^{-1}$ ).** The  $\nu\text{C}\text{--}\text{O}$  ( $\nu\text{C}\text{--}\text{O}_\text{C}$  and  $\nu\text{C}\text{--}\text{O}_\text{A}$ ) and  $\nu\text{N}\text{--}\text{C}$  stretching modes are predicted by the calculations to give rise to bands in the  $1200\text{--}950\text{ cm}^{-1}$  region. Both  $\nu\text{C}\text{--}\text{O}_\text{C}$  and  $\nu\text{N}\text{--}\text{C}$  frequencies were shown not to be greatly affected by deuteration at the  $\text{C}\beta$  atom, and the expected pattern of variation with conformation was found to be identical in the two isotopologues studied. On the other hand,  $\nu\text{C}\text{--}\text{O}_\text{A}$  vibration was predicted to be strongly affected by deuteration, since in the deuterated compound it

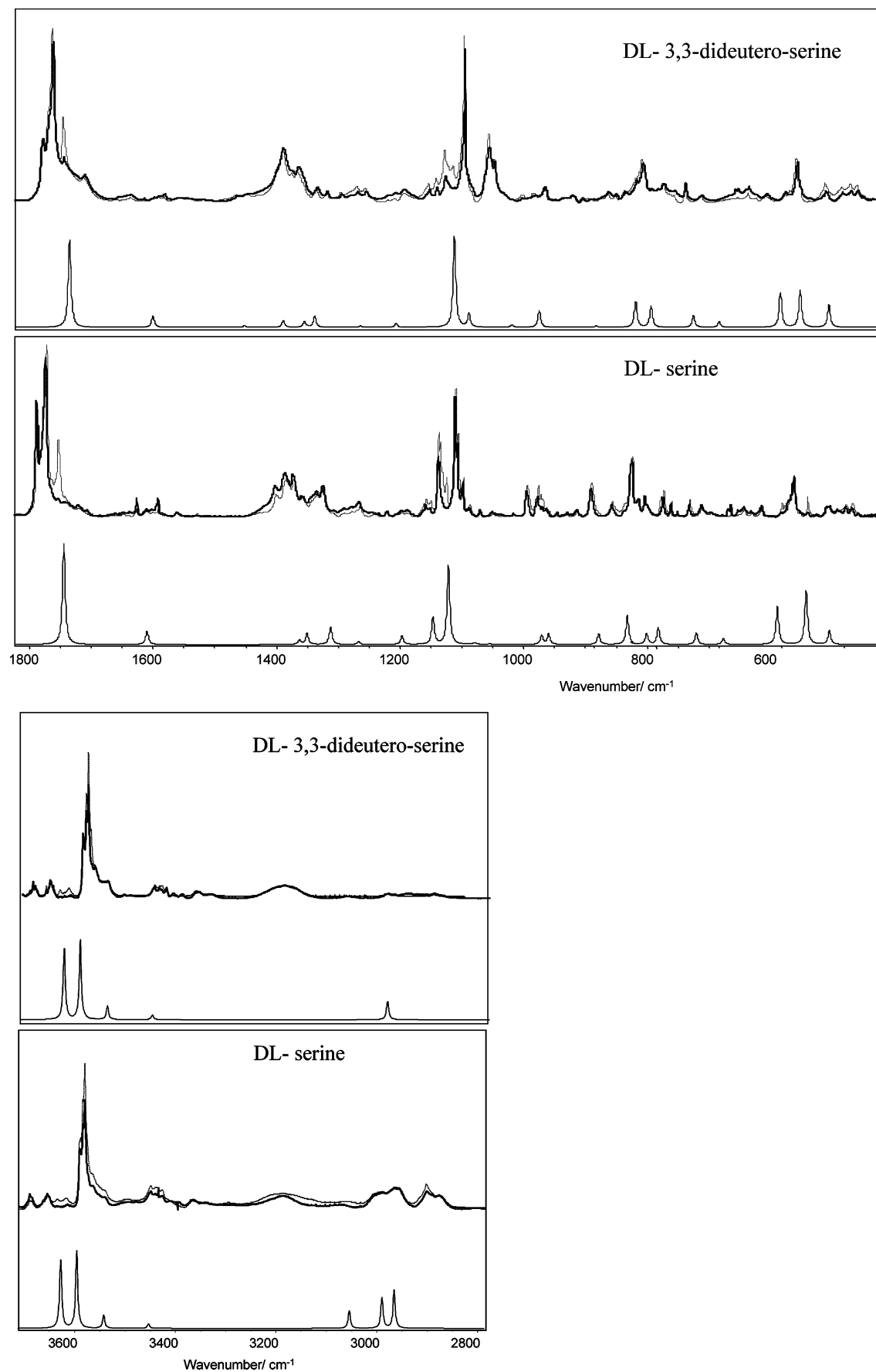
was found to couple extensively with the  $\omega\text{CD}_2$  wagging oscillation (see Tables S13–S21). For each conformer of serine, besides  $\nu\text{C}\text{--}\text{O}$  and  $\nu\text{N}\text{--}\text{C}$  stretching modes many other vibrations were predicted to give rise to bands in the  $1200\text{--}950\text{ cm}^{-1}$  spectral range. However, calculations also indicated that most of those vibrations should give rise to bands of low relative intensity.

In **B** conformers,  $\nu\text{C}\text{--}\text{O}_\text{C}$  is expected to originate low-intensity bands ( $<30\text{ km mol}^{-1}$ ) at frequencies between  $1200$  and  $1160\text{ cm}^{-1}$ , whereas in both **A** and **C** conformers, this vibration shall give rise to more intense bands ( $76\text{--}320\text{ km mol}^{-1}$ ) appearing at lower frequencies ( $1135\text{--}1120\text{ cm}^{-1}$ ). Hence, these results indicate that in the studied compounds the  $\text{C}\text{--}\text{O}_\text{C}$  bond is weaker for a cis carboxylic group (as in **A** and **C** conformers) than in a trans carboxylic group (as in the **B** conformers), correlating well with the structural data presented above, which indicate that the  $\text{C}\text{--}\text{O}_\text{C}$  bond is longer in **A** and **C** conformers than in **B** forms (see also Table S2).

In various conformers, the  $\nu\text{C}\text{--}\text{O}_\text{A}$  and  $\nu\text{N}\text{--}\text{C}$  vibrations are coupled with oscillations along other coordinates. Hence, for the normal modes involving the  $\nu\text{C}\text{--}\text{O}_\text{A}$  and  $\nu\text{N}\text{--}\text{C}$  vibrations, it is difficult to extract a clear pattern of variations introduced by changes in conformational structure (see Tables S3–S21). Nevertheless, it can still be stated that in general  $\nu\text{C}\text{--}\text{O}_\text{A}$  shall correspond to a relatively intense band (ca.  $100\text{ km mol}^{-1}$  for all but the **C** conformer) appearing for nondeuterated serine between  $1060$  and  $960\text{ cm}^{-1}$ . In all conformers of deuterated serine, extensive mixing with the  $\omega\text{CD}_2$  wagging coordinate shall lead to the appearance of two bands with low intensity, at ca.  $950$  and  $1130\text{ cm}^{-1}$ , with substantial contribution from both  $\nu\text{C}\text{--}\text{O}_\text{A}$  and  $\omega\text{CD}_2$  modes. On the other hand,  $\nu\text{N}\text{--}\text{C}$  is in general predicted to give rise to a weak band at ca.  $1060\text{--}1100\text{ cm}^{-1}$  (a few exceptions can be noticed, concerning, for instance, conformers **1** and **4** in both deuterated and nondeuterated species and conformer **2** in the nondeuterated compound, where this mode is predicted to correspond to a relatively intense IR band).

In this spectral region, the experimental spectrum of the nondeuterated compound is dominated by bands due to the most stable conformer **1** at ca.  $1150$  ( $\text{twCH}_2$ ),  $1137$  ( $\nu\text{C}\text{--}\text{O}_\text{C}$ ),  $1105$  ( $\nu\text{N}\text{--}\text{C}$ ), and  $1065$  ( $\nu\text{C}\text{--}\text{O}_\text{A}$ )  $\text{cm}^{-1}$ . In consonance with the calculations, all of these bands should also overlap (or partially overlap) with bands due to other conformers, justifying the observations of a less clear pattern of variation upon irradiation and annealing. The remaining seven intense bands in this spectral region (at  $1168$ ,  $1163$ ,  $1132$ ,  $1126$ ,  $1123$ ,  $1057$ , and ca.  $975\text{ cm}^{-1}$ ) belong to the spectra of conformers other than the form **1**. The  $1168\text{ cm}^{-1}$  band is ascribable to both conformers **6** ( $\text{twCH}_2$ ) and **8** ( $\rho\text{NH}_2$ ), the  $1163\text{ cm}^{-1}$  band to conformer **5** ( $\nu\text{C}\text{--}\text{O}_\text{C}$ ),  $1132\text{ cm}^{-1}$  to **4** ( $\nu\text{C}\text{--}\text{O}_\text{C}$ ),  $1126\text{ cm}^{-1}$  to **6** ( $\nu\text{C}\text{--}\text{O}_\text{C}$ ),  $1123\text{ cm}^{-1}$  to **7** ( $\nu\text{C}\text{--}\text{O}_\text{C}$ ),  $1057\text{ cm}^{-1}$  to both **2** ( $\gamma\text{CH}_2$ ) and **4** ( $\nu\text{C}\text{--}\text{O}_\text{A}$ ), and, finally,  $975\text{ cm}^{-1}$  to **2** ( $\nu\text{C}\text{--}\text{O}_\text{A}$ ). The assignment of the band observed at  $1123\text{ cm}^{-1}$  to the most intense band predicted by the calculations for conformer **7** is particularly unambiguous, since upon irradiation this band practically disappears. As expected, all bands due to  $\nu\text{C}\text{--}\text{O}_\text{C}$  of **A** and **C** conformers (predicted to be intense) are clearly observed, whereas for **B** conformers, only the band due to conformer **5** could be experimentally identified. The relatively intense  $\nu\text{C}\text{--}\text{O}_\text{A}$  bands in **A** and **B** conformers were also observed (**1**, **3**, and **6**,  $1065\text{ cm}^{-1}$ ; **4**,  $1057\text{ cm}^{-1}$ ; **5** and **9**,  $1043\text{ cm}^{-1}$ ; **8**,  $1010\text{ cm}^{-1}$ ; and **2**,  $975\text{ cm}^{-1}$ ).

The analysis of the spectrum of deuterated serine, which in this region is somewhat less complex than that of nondeuterated serine, reinforced the general conclusions extracted from the



**Figure 8.** Experimental IR spectra of D,L-serine and D,L-3,3-dideutero-serine molecules isolated in an argon matrix [as deposited (dotted) and after UV irradiation (solid line)] versus DFT/B3LYP/6-311++G(d,p) calculated spectra for conformer **7**, the conformer which decarboxylates faster upon irradiation. (a) 1800–400  $\text{cm}^{-1}$  region; (b) 3700–2800  $\text{cm}^{-1}$  region.



analysis of the spectrum of the latter molecule. The spectrum of the deuterated isotopologue is dominated by bands due to conformer **1**. In similarity to the spectrum of the nondeuterated serine, the intense (but disappearing upon UV irradiation of the matrix) band due to  $\nu\text{C}-\text{O}_\text{C}$  vibration of conformer **7** is clearly observed at  $1124\text{ cm}^{-1}$ .

It is also interesting to note that ethanolamine was found to absorb at ca.  $1035\text{ cm}^{-1}$  ( $\nu\text{N}-\text{C}$  [57,60,61]). The DFT/B3LYP/6-311++G(d,p) calculations for deuterated ethanolamine also predicted a medium intensity IR band at this frequency. In the spectrum of nondeuterated serine, there are relatively intense bands at ca.  $1035\text{ cm}^{-1}$  and in the spectrum of the irradiated matrix no band due to photoproduct ethanolamine could be clearly observed in this region. However, in the less congested spectrum of deuterated serine, a new band around  $1035\text{ cm}^{-1}$  could be noticed, providing further evidence of photoproduction of ethanolamine during UV irradiation of serine.

**Region Below  $900\text{ cm}^{-1}$ .** The most intense bands predicted by calculations below  $900\text{ cm}^{-1}$  are due to  $\tau\text{C}-\text{O}_\text{C}$  torsional mode in all conformers and due to the  $\omega\text{NH}_2$  wagging and  $\tau\text{C}-\text{O}_\text{A}$  modes of **A** and **C** conformers. For conformers **B**, the  $\tau\text{C}-\text{O}_\text{A}$  bands are predicted at frequencies below  $400\text{ cm}^{-1}$  (out of the studied spectral region), whereas the low-intensity  $\omega\text{NH}_2$  bands should appear at ca.  $920-940\text{ cm}^{-1}$ . The exception is conformer **3**, where  $\tau\text{C}-\text{O}_\text{A}$  band was predicted to occur at  $590\text{ cm}^{-1}$  (at the highest frequency of all conformers, due to the involvement of the alcohol group in the strongest H-bond interaction among all the nine experimentally observed conformers) and where  $\omega\text{NH}_2$  vibration was predicted to give rise to absorption at  $824\text{ cm}^{-1}$ , at nearly the same frequency as in conformers **A** and **C** (see Tables S3–S21).

Accordingly to the calculations, the intense group of bands observed at ca.  $820\text{ cm}^{-1}$  for both deuterated and nondeuterated serine is ascribed mainly to the  $\omega\text{NH}_2$  wagging vibrations with predicted frequencies in this range. On the other hand, the  $\tau\text{C}-\text{O}_\text{A}$  torsions with predicted frequencies in this region, correspond to  $\text{OH}_\text{A}$  groups involved in H-bonding. Such vibrations could be expected to give rise to considerably broad bands that are difficult to be experimentally detected. Indeed, in the experimental spectra, it was not possible to clearly identify the bands due to these modes in both the deuterated and nondeuterated species. A similar situation was in fact also noticed in the case of the expected bands due to the  $\tau\text{C}-\text{O}_\text{C}$  torsion in **B** conformers, where the carboxyl group is also involved in a strong H bond, which could not be either experimentally observed. However, the bands due to this mode in **A** and **C** conformers, where the  $\text{OH}_\text{C}$  group is not taking part in H bonding, are clearly observed experimentally. For nondeuterated serine, the band at  $579\text{ cm}^{-1}$ , which almost disappears upon irradiation, is ascribed to the **C**-type conformer **7** (calculated frequency  $594\text{ cm}^{-1}$ ), whereas the **A** conformers give rise to the intense doublet at  $568/566\text{ cm}^{-1}$  (conformers **1** and **6**; predicted at  $582$  and  $586\text{ cm}^{-1}$ ) and  $617\text{ cm}^{-1}$  (conformer **4**; predicted at  $625\text{ cm}^{-1}$ ). A similar pattern was also found for DL-3,3-dideutero-serine (see Table 4).

**Conformational Selectivity of the UV Induced Decarboxylation. Its Relevance to Identification of the C Conformer.** As already mentioned, the observed photodecarboxylation of serine shows a clear dependence on the conformation of the carboxylic group. The photochemical  $\text{CO}_2$  evolution occurred preferentially for those conformers where the carboxylic group is *cis* and is not acting as proton donor. The **C** conformer reacts faster, followed by **A**-type conformers, whereas **B** conformers react considerably slower. The different rates of decarboxylation

associated with the three groups of serine conformers strongly facilitated the assignment of the experimental spectra. In particular, this photoeffect enabled an easy identification of the **C**-type conformer **7**, which had never been observed previously. The spectra of serine and deuterated serine, recorded before and after UV irradiation, are presented in Figure 8. These experimental spectra are compared with the theoretical spectra calculated for **C**-type conformers **7** of both isotopologues. As can be seen in Figure 8, the identification of the **C** conformer is particularly clear in the case of the deuterated compound, where a larger number of vibrations originated in this form appear in weakly congested spectral regions.

## Conclusions

Extensive conformational analysis has been performed for the molecule of serine. The conformers, identified on the basis of geometry optimizations carried out at the DFT/B3LYP/6-311++G(d,p) level, were classified into 12 groups, according to an intramolecular hydrogen bonding pattern. Comparison of the IR spectra calculated for nine most stable conformers of serine with experimental spectrum of monomers of the compound isolated in low-temperature Ar matrix led to the conclusion that all nine conformers are populated in inert-gas matrixes. Analysis of the experimental IR spectra in terms of coexistence of different groups of conformers frozen in a matrix was significantly facilitated by the effects of UV irradiation and annealing of the solid argon matrix. Upon UV ( $\lambda > 200\text{ nm}$ ) irradiation, serine underwent photodecarboxylation. Efficiency of this process depended on the conformational structure adopted by the conformers. Also effects of annealing of the matrix were different for different groups of conformers. This allowed grouping of the observed IR bands and their assignment to particular types of conformers or to individual conformers. The conclusions derived from the study of serine were reinforced by the results of the analogous investigation carried out for 3,3-dideutero serine.

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**Supporting Information Available:** Figure S1 and Tables S1–S22. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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