S–H Rotamerization via Tunneling in a Thiol Form of Thioacetamide

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Abstract

Rotamerization of a hydroxyl (O−H) group by tunneling is well-known and has been extensively studied. On the other hand, similar tunneling processes for the thiol (S−H) group have not been reported yet. In this work, the imino-thiol forms of thioacetamide were studied in cryogenic matrices (Ar, Xe) after UV-irradiation of the common amino-thione form of the compound. Four different imino-thiol forms were generated, corresponding to the cis or trans thiol (C/T) conformers of the two imino isomers (syn and anti; s/a). Noteworthy, the syn-cis (sC) imino-thiol form was found to convert spontaneously to the syn-trans (sT) form (with a half-life of 80 min), in a process whose reaction rate is independent of the temperature (i.e., at 11 or 20 K). Such conformational transformation represents the first experimental observation of an S−H rotamerization occurring by tunneling. Computations based on the Wentzel–Kramers–Brillouin formalism predict an S−H tunneling for the syn-imino sC→sT rotamerization on the time scale of minutes, in agreement with the experimental observations.
1. Introduction

Thione–thiol tautomerization has been an intriguing and widely investigated topic. In most of the compounds only the thione tautomer is populated and can be detected under standard experimental conditions in the gas phase or isolated in rare-gas matrices. However, upon UV irradiation, the thione compounds can be converted to their thiol tautomers, which can be captured and stabilized in inert matrices at low temperatures. Such molecules include 2(1H)-pyridinethione, 4(3H)-pyrimidinethione and 3(2H)-pyridazinethione, 2(1H)-quinolinethione, methimazole, 2-thiobenzimidazole, thiourea, 6,7 and thioacetamide.8 One notable exception is thiophenol, existing as thiol tautomer only.9 Compounds with two thio groups usually have either dithione or thione–thiol as the most abundant tautomeric form, and can be successfully converted to dithiols;10–14 furthermore, the photoreversibility of the tautomerization has also been demonstrated.11

The role of tunneling in molecular conformational isomerizations has been investigated in cryogenic matrices on numerous occasions.15 Most of the reported cases involve the rotamerization of the O–H moiety of carboxylic acids isolated in different cryogenic matrices,16–18 and include investigations on formic acid monomer and dimers,19–22 acetic acid,23,24 trifluoroacetic acid,25 tribromoacetic acid,26 propionic acid,27 2-chloropropionic acid,28 propionic acid,29 several α-ketocarboxylic acids including pyruvic acid,30,31 2-furoic acid,32 and 2-chlorobenzoic acid.33 Examples of tunneling in the rotamerization of the O–H group in derivatives of carbonic acid,34,35 amino acids,36,37 and the nucleobase cytosine in cryogenic matrices have also been discussed in the literature.38,39

There are far fewer known systems that exhibit intramolecular hydrogen tunneling involving bond-breaking and making. Besides α-hydroxy carbonyls (such as tropolone) and the cyclic dimers of carboxylic acids being the most widely known examples,40–42 only a handful of such processes have been reported for (hydroxy)carbenes,43–52 ketenes,53 nitrenes,54 selones (selenourea),55 as well as thiones such as thiourea and dithiooxamide6,7,14 isolated in cryogenic matrices. Tunneling observed in the tautomerization of seleno and thio compounds follows similar trends, which are the prototrophic isomerizations opposite to those induced by UV-irradiation: the photogenerated selenols and thiols convert back to selone and thione forms, respectively.
Due to the well-known occurrence of tunneling in the rotamerization of O–H groups and also in the tautomerization of hydroxyl compounds as well as seleno- and thio-derivatives, the existence of tunneling in the rotamerization of an S–H (or Se–H) group could be envisaged. However, to the best of our knowledge, evidence of such tunneling processes has never been reported so far. Here, we demonstrate that S–H rotamerization in a thiol form of thioacetamide captured in cryogenic matrices takes place spontaneously by tunneling. This observation proves, for the first time, that tunneling plays a role not only in conformational isomerization of oxygen-containing compounds but is also possible for their sulfur counterparts and could occur more generally than it has been considered.

2. Experimental and Computational Methods

2.1 Matrix-isolation infrared spectroscopy

The experiments reported in this work were carried out in two laboratories, in Coimbra (Portugal) and in Budapest (Hungary).

In Coimbra, a commercial sample of thioacetamide obtained from Merck (99%) was used. The sample was stored in a glass tube with a Young valve, connected to the vacuum chamber of a cryostat through a stainless steel needle valve. Before the experiments, the sample was pumped through the vacuum chamber at room temperature in order to eliminate air and other volatile impurities. Then, a CsI window used as optical substrate was cooled down to 16 K using a closed-cycle helium refrigerator with a DE-202 expander (Advanced Research Systems) with a base pressure of approximately $10^{-7}$ mbar. The sample vapor was co-deposited with an excess of Ar (Air Liquide, purity 99.9999%) or Xe (Linde, 99.999%) onto the optical substrate. After the deposition, the temperature of the sample was lowered to 11 K. The temperature of the cold window was measured directly by a silicon diode sensor connected to a LakeShore 331 digital temperature controller, which also allows for the stabilization of the sample temperature with an accuracy of 0.1 K. The sample sublimation temperature was kept at 320 K to achieve the desired vapor pressure and therefore deposition rate. During and after the deposition, mid-IR spectra of the growing or deposited sample were collected (128 scans) using a Nicolet 6700 FT-IR spectrometer equipped with a deuterated triglycine sulfate (DTGS) detector and a Ge/KBr beamsplitter (experiment 1). The FT-IR spectra were also taken using a
mercury cadmium telluride (MCT) detector cooled with liquid nitrogen (experiments 2 and 3). The same spectral collection parameters (4000–400 cm\(^{-1}\) region, 128 scans, and 0.5 cm\(^{-1}\) resolution) were used for experiments 1, 2, and 3.

In Budapest, a commercial sample of thioacetamide obtained from Sigma-Aldrich (>99.0%) was used. Similarly to the experiments undertaken in Coimbra, the compound was kept in a glass tube with a Young valve, connected to the vacuum chamber of a cryostat, and, before the experiments, the sample was pumped through the vacuum chamber in order to eliminate air and other volatile impurities. The CsI optical substrate of the cryostat was cooled down to 11 K using a closed-cycle helium refrigeration system (Janis CCS-350R cold head cooled by a CTI Cryogenics 22 refrigerator) with a base pressure of approximately 10\(^{-6}\) mbar. The sample vapor was co-deposited with an excess of Ar (Messer, 99.9999%) onto the optical substrate. The temperature of the cold window was measured by a silicon diode sensor connected to a LakeShore 321 digital temperature controller. The sample sublimation temperature was 318 ± 5 K. The mid-IR spectra obtained during and after the deposition of the samples were collected (64 scans) in the 4000–400 cm\(^{-1}\) region with 1 cm\(^{-1}\) resolution using a Bruker IFS 55 FT-IR spectrometer equipped with an MCT detector cooled with liquid nitrogen and a KBr beamsplitter (experiment 4).

2.2 Irradiation experiments

In Coimbra, the deposited matrices were irradiated through a quartz window of the cryostat. In experiments 1 and 2, the UV irradiation of the thione precursor was done using a frequency-tunable monochromatic light provided as signal beam of an Optical Parametric Oscillator (Spectra-Physics MOPO-SL, fwhm ≈ 0.2 cm\(^{-1}\), duration = 10 ns) pumped with a pulsed Nd:YAG laser (Spectra-Physics PRO-230, output power \(P\) ≈ 4.5 W, wavelength \(\lambda\) = 355 nm, repetition rate \(f\) = 10 Hz). A frequency-doubling unit (Spectra-Physics MOPO FDO-970) was utilized, with the wavelength of the irradiating beam set to 269.5 nm or 285 nm in experiments 1 and 2, respectively. The overall irradiation time was 3 min \(P\approx 13\) mW in experiment 1, and 31 min \(P\approx 10\) mW in experiment 2. In experiment 3, a Hg(Xe) lamp (Newport model 6697; output power: 250 W), coupled to a water filter, was used as UV source, with the irradiation time being 60 min. All the above irradiation wavelengths fall within the first UV-absorption band of thioacetamide, with an onset near 300 nm and a maximum near 266 nm.
In the Budapest experiment (4), the deposited matrices were irradiated *in situ* through the outer KBr window of the cryostat applying a frequency-tunable monochromatic light provided as signal beam of an Optical Parametric Oscillator (OPO; GWU/Spectra-Physics VersaScan MB 240, fwhm $\approx 5$ cm$^{-1}$) pumped by a pulsed Nd:YAG laser (Spectra-Physics Quanta Ray Lab 150, $P \approx 2.1–2.2$ W, $\lambda = 355$ nm, $f = 10$ Hz, duration = 2–3 ns). The OPO beam was perpendicular to the FT-IR spectrometer beam. The CsI cold window was rotated 45° relatively to both the FT-IR and the OPO beams. The wavelength of the irradiating beam was set to 275 nm, with the overall irradiation time being 60 min ($P \approx 25$ mW).

### 2.3 Kinetic studies

In experiment 1, the thione→thiol conversion was achieved by means of UV-irradiation, in a similar way as reported in Ref. 8. After that, the kinetics of the spontaneous decay of the thiol isomers was monitored. These decays were monitored in independent experiments at 11 K (experiment 1a) and 20 K (experiment 1b). In order to protect the sample against infrared irradiation with photons exceeding the energy of 10.4 kJ mol$^{-1}$, a Spectrogon LP11500 nm longwave-pass cut-off filter (transmitting only below 870 cm$^{-1}$) was placed between the spectrometer light source and the cryostat. The effect of complete blocking of the spectrometer beam source was investigated after the irradiation of the deposited sample in experiment 2. In experiment 3, a different matrix gas (xenon, instead of argon) was examined, to study the effect of matrix host on the spontaneous decay (at 11 K). In order to further investigate the spontaneous decay in the presence or absence of filters, the kinetic studies were repeated again, for the compound in argon matrix, without using any filter (experiment 4a) or using a longwave-pass filter having a cut-off wavenumber of 1960 cm$^{-1}$ (experiment 4b).

### 2.4 Theoretical computations

The quantum chemical computations were performed using the Becke’s three parameter hybrid functional B3LYP, with the non-local and local correlation described by the Lee–Yang–Parr and the Vosko–Wilk–Nusair III functionals, respectively,$^{59–61}$ together with the Pople-type 6-311+G(3df,3pd) basis set,$^{62}$ as implemented in Gaussian 09.$^{63}$ The isomerization barriers were investigated starting by the optimization of the transition states (TSs) using the Berny algorithm,$^{64}$ followed by the computation of the
intrinsic reaction paths (IRPs) in Cartesian coordinates. The tunneling rates were computed using the Wentzel–Kramers–Brillouin (WKB) model, described in detail elsewhere. The energies of the thioacetamide conformers and those of the TSs were also obtained from the structures optimized with the complete basis set (CBS-QB3) and Gaussian-4 (G4) methods, which are well-known to allow for very accurate determination of energies.

3. Results and Discussion

3.1 Computations on the Thioacetamide Isomeric Forms

Figure 1 presents the structures of thione and thiol isomeric forms of thioacetamide as optimized at the B3LYP/6-311++G(3df,3pd) level of theory. The structures of the TSs between these forms were also optimized and are shown in Figure 2. Table 1 summarizes the energetics of all the structures (the geometries, energies, and harmonic vibrational frequencies are shown in Tables S1–S31; Supporting Information). Overall, the results support the previous theoretical findings.

According to the computed energies of the different thioacetamide isomeric forms, it is expected that it adopts exclusively the amino-thione form (hereafter denoted as Tn) in the sample after deposition, since this form is stabilized by more than 38 kJ mol\(^{-1}\) comparing to the imino-thiol forms. The imino-thiol forms can have two orientations of the N–H group (denoted as anti (a) and syn (s), differing in their dihedral angle H–N–C–S, \(\varphi_1\)), as well as two orientations of the S–H group (denoted as trans (T) and cis (C), differing in their torsional angle H–S–C=N, \(\varphi_2\)). For the definition of \(\varphi_1\) and \(\varphi_2\) and their values please refer to Figure 1 and Table 1. All possible combinations of a/s and T/C orientations result in four different thiol isomers. Based on the computational results syn (s) imino forms are relatively more stable than the anti (a) forms (stability order: sT > sC > aC > aT). Furthermore, five different TS structures were considered, one accounting for the Tn to thiol conversion (Tn–aC, Table 1), whereas the others interconnect the anti and syn imino isomers in keeping the conformation of the thiol group (aC–sC and aT–sT), or the trans and cis thiol conformers of each imino isomer (aC–aT, sC–sT). It should be noted that both the aC–aT and sC–sT TSs exist in pairs, as mirror-images of each other (1 and 2) and therefore have identical energies. An interesting structural feature is the fact that the orientation of the methyl group is different in thione
compared to the thiol tautomer and the TSs, with one methyl hydrogen atom eclipsing the sulphur atom in the former, whereas eclipsing the nitrogen atom in the latter.

In order to obtain the relative energies, especially for the cis (C) and trans (T) thiol forms, the use of the B3LYP/6-311++G(3df,3pd) level of theory was necessary. Compounds containing sulfur atoms notoriously require the extensive use of polarization and diffuse functions in order to accurately predict their energies; it has been shown that this applies not only to hypervalent but to divalent sulfur atoms as well.\textsuperscript{71,72} Computations applying the CBS-QB3 and G4 methods, known for the reliable prediction of the relative energies and barrier heights,\textsuperscript{73,74,75} were then also performed in the present study (Tables S32–S57). The obtained results were found to agree with the energies of the thioacetamide isomeric forms computed at the B3LYP/6-311++G(3df,3pd) level of theory. Therefore, computations at the B3LYP/6-311++G(3df,3pd) level of theory were also used to characterize the intrinsic reaction paths (IRC computations) that were used in this work to estimate the tunneling probabilities (Section 3.4).

3.2 Thioacetamide Thiol Forms Generated and Captured in Cryogenic Matrices

The IR spectra obtained after matrix deposition indicate the sole presence of the thione (Tn) monomeric form in the as-deposited matrices (Figure S1a). Upon the performed UV irradiations, Tn gradually converts into the four thiol isomers (Figure S1b). This observation generally agrees with the results described before by Lapinski et al.\textsuperscript{8} Interestingly, in the case of the oxo-counterpart of the studied compound, i.e., acetamide, only two syn-imino-enol isomers exist in the matrix after irradiation.\textsuperscript{76} After generating the thiol forms by UV irradiation of their thione precursor, we found that the bands due to sC form spontaneously decreased in intensity, while those ascribed to sT simultaneously increased. This observation, testifying the occurrence of a conformational change through S–H rotamerization, is shown in Figure 3b, depicting the overnight spectral changes in the 855–600 cm\textsuperscript{-1} region that occurred in the dark, for an argon matrix kept at 11 K. The experimentally observed UV-induced and subsequent spontaneous (with or without filter, as will be discussed further) IR spectral changes (Table 2), supported by the comparison between the experimental and the simulated IR spectra allowed for the unambiguous assignment of all four photogenerated thiol forms in the above-mentioned region of the IR spectrum (Figure 3).
3.3. Kinetics of the Observed S-H Rotamerization

It is always tempting to assume that at cryogenic temperatures (of a few K, as in the present experiments) spontaneous changes in the IR spectra are due to tunneling. Nonetheless, to unequivocally establish the occurrence of such a process, the possibility of other contributions has to be considered. In particular, the effect of the IR globar source of the spectrometer and the thermal energy may induce conformational isomerization processes in matrix-isolated samples.\textsuperscript{38,39,77} Accordingly, the broadband IR beam of the spectrometer either needs to be completely blocked between the measurements or the photons energetic enough to induce changes in the sample have to be filtered. Moreover, thermal effects need to be completely ruled out. Therefore, in order to separate different factors that may affect the spontaneous decay rate of thioacetamide thiol forms (temperature, effect of the spectrometer source, and also the effect of the matrix host), we conducted a series of dedicated experiments under different conditions: (i) spectra were recorded using a longpass filter with a cut-off wavenumber of 870 cm\(^{-1}\) (experiment 1 as described in Section 2) at two different temperatures (experiments 1a and 1b); (ii) the spectrometer beam was blocked overnight, therefore keeping the sample in dark (experiment 2); (iii) the compound was isolated in a different host matrix (Xe, experiment 3); (iv) no filter (experiment 4a), or a longpass filter with the cut-off wavenumber of 1960 cm\(^{-1}\) (experiment 4b) were used during recording of spectra. Note that the filter cut-off at 870 cm\(^{-1}\) (10.4 kJ mol\(^{-1}\)) is significantly lower than the computed barrier for the sC to sT rotamerization (16.4 kJ mol\(^{-1}\)) and other isomerizations (Table 1). Thus, with this filter, the impending photons of the filtered beam should not have enough energy to induce any over-the-barrier isomerization. With the cut-off value set at the higher value of 1960 cm\(^{-1}\) (23.4 kJ mol\(^{-1}\)), the impending photons have enough energy to induce over-the-barrier \(sC \rightarrow sT\), \(sT \rightarrow sC\), and \(aT \rightarrow aC\) rotamerizations. Without filter, all the \(C \rightarrow T\) or \(T \rightarrow C\) over-the-barrier rotamerizations of the S–H group may be stimulated by the infrared light.

In experiment 4a (sample exposed to the IR light from the globar without filter), intensity changes could be observed for bands ascribed to all four thiol conformers. Some of these changes must be caused by the photons originating from the spectrometer source (Figure S2). Furthermore, the final \(sC : sT\) population ratio is significantly higher in experiment 4a (\(sC_f : sT_f \approx 0.2\), Table 3) than in experiments 1a, 1b, and 4b (\(sC_f : sT_f \approx 0.1\), Table 3). This implies that the unfiltered radiation from the spectrometer source leads
to a different stationary state compared to the measurements conducted with filters. This also applies to the experiment during which the IR globar source was completely blocked (experiment 2) and the sample was kept in dark, thus excluding the effect of broadband IR irradiation and thermal effects.

Figure 4 shows the kinetic decay/growth curves of conformers $sC$ and $sT$ during experiment 1a, whereas Figures S3–S7 allow to visualize the same for experiments 1a (extended version), 1b, 3, 4a, and 4b, respectively. For fitting the decay curves, a single exponential decay function was used:

$$A_t(sX,\nu_y) = A_{t=\infty}(sX,\nu_y) + A_{t=0}(sX,\nu_y) e^{-kt}$$

(1)

where $A_t(vX)$ is the integrated area (in cm$^{-1}$) of the band $\nu_y$ of conformer $sX$ ($X = C$ or T; $y = 623$ or 836 cm$^{-1}$ if $X = C$ and $y = 626$ or 849 cm$^{-1}$ if $X = T$), $t$ is time (in min), $k$ is the first-order rate constant (in min$^{-1}$), $t_{1/2}$ is the half-life (in min). The following equation was used to fit the growth curves:

$$A_t(sX,\nu_y) = A_{t=\infty}(sX,\nu_y) \left(1 - e^{-kt}\right)$$

(3)

Table 3 summarizes the decay/growth rates determined by using the functions described in equations (1) and (3). The $sC$ and $sT$ decay/growth rates do not significantly differ from each other at 11 and 20 K suggesting a non-Arrhenius behavior and, therefore, the occurrence of tunneling. Indeed, using the Eyring–Polányi equation (classical rate model assuming exclusively the thermal over-the-barrier reaction),

$$k = \kappa \frac{k_B T}{h} e^{-\frac{\Delta^\ddagger G^\ominus}{RT}}$$

(4)

where $k$ is the reaction rate (in s$^{-1}$), $\kappa$ is the transmission coefficient usually assumed to be 1 (no tunneling), $k_B$ the Boltzmann constant ($1.38 \times 10^{-23}$ J K$^{-1}$), $T$ is the temperature (in K), $h$ is Planck’s constant ($6.626 \times 10^{-34}$ J s), $R$ is the gas constant ($8.314$ J mol$^{-1}$ K$^{-1}$), and $\Delta^\ddagger G^\ominus$ is the standard Gibbs free energy of activation of the studied compound. The half-life of the $sC \rightarrow sT$ reaction is calculated to be some $10^{27}$ years at 11 K (c.f. the measured value of 80 minutes, Table 3, $\Delta^\ddagger G^\ominus = 18$ kJ mol$^{-1}$ was extracted from the theoretical harmonic vibrational computations).
It should be emphasized that $s\text{C}$ has a nonzero abundance after 18 hours of the monitoring of its decay, which cannot be caused by the excitation of the source beam, since this can be observed in each case even if filters are used. The residual integrated band area for the band at 836 cm$^{-1}$ is roughly 0.005 ± 0.001 cm$^{-1}$ in the cases when filters were used and approximately twice as large (0.010 ± 0.001 cm$^{-1}$) in the absence of a filter (experiment 4a). The non-zero final concentration of the higher-energy form in tunneling processes is not unusual. It may indicate the existence of a matrix site where tunneling does not occur, or occurs extremely slowly, which could explain the nonzero integrated areas after tens of hours of kinetic monitoring (18 hours in this work). Indeed, Schreiner and co-authors studied tunneling in oxalic acid and “developed a general kinetic model to explain the temporal evolution of numerous experimental infrared bands as a tool to deconvolute the experimental spectra acquired over long time periods (up to 19 days).” Their phenomenological model was based on only two classes of matrix sites, “fast” and “slow”. The “fast” tunneling half-lives (30–43 hours) were in an excellent agreement with those determined from high-level quantum chemical computations in the gas phase. However, the “slow” half-lives, differing from “fast” kinetics by an order of magnitude (260–355 hours), were also detected implying that tunneling sensitively depends on the environment. Earlier, some of the present authors studied tunneling in matrix-isolated squaric acid, and also observed “fast” and “slow” tunneling decays, with respective half-lives differing by more than an order of magnitude. An important observation in the study of squaric acid was that the two trapping sites characterized by “fast” and “slow” decays could be spectroscopically distinguished in some spectral ranges (band doublets with spectrally different maxima), while some other vibrations exhibited only one maximum with the “fast” and “slow” sites spectrally non-distinguishable (appearing at the same peak frequency). The experimental findings of the present study also point out that the $s\text{C}$ imino-thiol form of thioacetamide exhibits “fast” and “slow” tunneling decay, however, the respective trapping sites cannot be spectroscopically distinguished for the $s\text{C}$ bands appearing in the range below 840 cm$^{-1}$ accessible for the decay monitoring.

### 3.4 Tunneling Computations

In order to better understand the role of tunneling in the isomerization reactions of thioacetamide, tunneling rates were theoretically estimated for multiple possible pathways. First, the TSs were identified and then the intrinsic reaction paths were obtained by running IRCs computations, thus allowing for the estimation of the width and
height of the barriers. Figure 5 and Figure S8 show the IRC profiles between the thioacetamide isomers as computed at the B3LYP/6-311++G(3df,3pd) level of theory. Then, based on the WKB approximation mentioned in Section 2.4, the equation for a parabolic barrier was used to predict the tunneling rates via the computed reaction paths:

$$P(E) = e^{-\frac{\pi w^2 m}{h} \sqrt{V_0 - E}}$$

(5)

where $m$ is the particle mass ($1.68 \times 10^{-27}$ kg for H), $(V_0 - E)$ is the difference in energy of the particle $(E)$ with respect to the barrier height $(V_0$, both in $J$), $h$ is Planck’s constant and $w$ is the width of the barrier (in m) at the particle energy $E$. By multiplying $P(E)$ with the frequency of attempts $(v$, in $s^{-1}$) estimated by the frequency of the vibrational mode participating in the process $(\tilde{v}$, in $m^{-1}$) one obtains the tunneling rate $(k$, in $s^{-1}$), which can be converted to the half-life $(t_{1/2} = \ln 2 / k$, in $s^{-1}$). Note that $\tilde{v} = v/c$, where $c$ is the speed of light and equals 299 792 458 m s$^{-1}$. Table 4 summarizes the calculated tunneling rates of the selected processes. The hydrogen tunneling for the tautomerization resulting in the formation of $Tn$ from $aC$ was estimated to have a $t_{1/2}$ of 100 days (Table 4). This agrees with the lack of detection of any spontaneous process yielding the $Tn$ precursor. The computed tunneling for the $anti\rightarrow syn$ imine isomerization from $aC$ to $sC$ has a similar $t_{1/2}$ value (100 days), whereas for the $anti\rightarrow syn$ imine isomerization from $aT$ to $sT$ the $t_{1/2}$ value was computed to be an order of magnitude faster (roughly 5 days). Taking into account the uncertainty of the computational results, the only two processes that have computed tunneling half-lives compatible with the time scale of our experiments are the $trans\rightarrow cis$ S–H rotamerization of the $anti$-imine ($aT \rightarrow aC$, $t_{1/2} \approx 2.3$ h) and $cis\rightarrow trans$ S–H rotamerization of the $syn$-imine ($sC \rightarrow sT$, $t_{1/2} \approx 3$ min). Moreover, both processes can take place through two symmetry-equivalent barriers (characterized by mirror-image TSs, Figure 2), and, therefore, the chance of tunneling becomes twice as high, meaning theoretical half-lives of 1.1 h and 1.5 min. However, the computed tunneling half-life values are extremely sensitive to the shape of IRC profiles, and therefore, not expected to be completely accurate. For instance, Nunes et al. showed that a slight increase of 5% in the width of a barrier ($w$) can cause a six-fold decrease in the calculated tunneling rates. The tunneling transformation with the shortest computed half-life ($S–H$ rotamerization of $sC \rightarrow sT$), i.e. with the higher tunneling probability, was the only one observed experimentally. The measured tunneling half-life time $t_{1/2}$ for the $sC \rightarrow sT$ process was approximately 80 minutes in argon matrices (Table 3). No other spontaneous decay was detected during the measurements.
According to the tunneling computations, the $sC \rightarrow sT$ process is estimated to be approximately 46 times faster than the $aC \rightarrow aT$ process (Table 4). Using the $t_{1/2}$ value for the $sC \rightarrow sT$ process obtained experimentally (80 minutes) and based on the ratio of the computed values, the $aT \rightarrow aC$ tunneling should take place in roughly 2.6 days. The half-life values for the other pathways are 270 days ($aT \rightarrow sT$), and 15 years ($aC \rightarrow sC$ as well as $aC \rightarrow Tn$) when applying the same calculation. Therefore, an additional but slower $S$–$H$ rotamerization corresponding to the $aT \rightarrow aC$ conversion is still predicted to occur by tunneling within the timescale of the experiments. However, there was no discernible evidence for such a process during the performed overnight experiments (after 18 hours, approximately 18% conversion could be expected). This finding seems to contradict both what one would think intuitively (before the tunneling calculations) and the theoretical results, i.e. the occurrence of tunneling in the $S$–$H$ rotamerization should be expected for both the anti- and syn-imine forms, considering the similarity of their structures, as well as the relatively close predicted values for barrier heights and widths. However, the experimental results point to a selective tunneling $S$–$H$ rotamerization in the syn-imine form of thioacetamide. This may be either caused by different interaction of the matrices with the anti- and syn-imines, which may change the shape of the barriers or by the different energy gaps between the donor (in the reactant) and acceptor (in the product) levels, which may favor or disfavor the two processes in a considerably different way as well as by the assumptions made by the applied tunneling computational method. This also indicates that imino-thiol systems need further, more advanced, theoretical investigations to be completely understood.

4. Conclusion

Tunneling in molecular conformational isomerizations is an important topic that has been reported by dozens of works in the literature in the past few decades. With a few notable exceptions, most of these papers examine the spontaneous rotamerization occurring in molecules containing $O$–$H$ group(s). In contrast, although several thioxo- (and selenoxo-) compounds have been studied and provided evidence for the tautomeric thiol $\rightarrow$ thione (selenol $\rightarrow$ selone) conversions via spontaneous intramolecular hydrogen atom transfer, the $cis$–$trans$ isomerization of $S$–$H$ ($Se$–$H$) groups via tunneling has never been described before. In this work, thiol forms of thioacetamide isolated in Ar (and Xe) matrices were investigated by the help of matrix-isolation mid-IR spectroscopy, and
kinetic studies were carried out at different temperatures and in the presence of various filters in order to exclude chemistry induced by the photons originating from the spectrometer light source. The measurements were accompanied by quantum chemical computations, which allowed for the estimation of the energies of the isomers as well as the TSs. IRC pathways were also computed in order to help interpret the experimental results.

Although UV irradiation produces the more energetic thiol forms, no evidence of spontaneous conversion could be found for the reverse thiol (aC) to thione (Tn), nor for between the anti and syn forms, or isomerizations between the two anti-imino forms (aC and aT). However, hydrogen atom tunneling takes place resulting in the selective conversion of one of the syn-imino thiol isomers (sC) to the other (sT). Therefore, this work shows, for the first time, that this type of spontaneous rotamerization exists not only in hydroxy compounds but also in their thiol analogs as well, which hopefully opens a new chapter in the study of hydrogen atom tunneling in molecules with thiol groups.

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References


Table 1. Relative zero-point corrected energies ($\Delta E_{ZPE}$) of the thioacetamide isomers (minima) and the first-order TSs computed at the B3LYP/6-311++G(3df,3pd) level of theory, as well as conformationally-relevant dihedral angles ($\varphi_1$ and $\varphi_2$).

<table>
<thead>
<tr>
<th>Structures</th>
<th>$\varphi_1$</th>
<th>$\varphi_2$</th>
<th>$\Delta E_{ZPE}$</th>
<th>$\Delta \Delta E^\prime$ (→)</th>
<th>$\Delta \Delta E^\prime$ (←)</th>
</tr>
</thead>
<tbody>
<tr>
<td>minima</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tn</td>
<td>–</td>
<td>–</td>
<td>–38.4</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>aC</td>
<td>180.0</td>
<td>0.0</td>
<td>1.7</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>aT</td>
<td>180.0</td>
<td>180.0</td>
<td>6.5</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>sC</td>
<td>0.0</td>
<td>0.0</td>
<td>0.6</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>sT</td>
<td>0.0</td>
<td>180.0</td>
<td>0.0</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>TSs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tn–aC</td>
<td>180.0</td>
<td>0.0</td>
<td>108.5</td>
<td>146.9</td>
<td>106.8</td>
</tr>
<tr>
<td>aC–sC</td>
<td>–180.0</td>
<td>0.0</td>
<td>88.9</td>
<td>87.2</td>
<td>88.3</td>
</tr>
<tr>
<td>aT–sT</td>
<td>180.0</td>
<td>180.0</td>
<td>90.9</td>
<td>84.4</td>
<td>90.9</td>
</tr>
<tr>
<td>aC–aT–1</td>
<td>178.8</td>
<td>88.6</td>
<td>29.4</td>
<td>27.7</td>
<td>22.9</td>
</tr>
<tr>
<td>aC–aT–2</td>
<td>–178.8</td>
<td>–88.6</td>
<td>29.4</td>
<td>27.7</td>
<td>22.9</td>
</tr>
<tr>
<td>sC–sT–1</td>
<td>–0.6</td>
<td>85.1</td>
<td>17.0</td>
<td>16.4</td>
<td>17.0</td>
</tr>
<tr>
<td>sC–sT–2</td>
<td>0.6</td>
<td>–85.1</td>
<td>17.0</td>
<td>16.4</td>
<td>17.0</td>
</tr>
</tbody>
</table>

a All energies in kJ mol$^{-1}$, the energy of isomer sT was chosen as the relative zero.

b In degrees, $\varphi_1 = H–N=C–S$, $\varphi_2 = H–S–C=N$, see also Figure 1.
Table 2. Assignment of the infrared spectra of thioacetamide and its isomers isolated in an Ar matrix and spectral changes of the sample in the region of 855–500 cm\(^{-1}\).

<table>
<thead>
<tr>
<th>Wavenumber (cm(^{-1}))</th>
<th>Exp.</th>
<th>Calc.(^a)</th>
<th>(I_{\text{calc.}})(^a)</th>
<th>Sym.</th>
<th>Change (^b)</th>
<th>Approx. assign.(^c)</th>
<th>Form(^d)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>upon UV irr.</td>
<td>spont. (no filter)</td>
<td>spont. (with filter)</td>
</tr>
<tr>
<td>850sh, 849</td>
<td>870.62</td>
<td>49.97</td>
<td>A''</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>τ(N–H) sT</td>
</tr>
<tr>
<td>837, 836</td>
<td>855.98</td>
<td>54.64</td>
<td>A''</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>τ(N–H) sC</td>
</tr>
<tr>
<td>820, 818</td>
<td>832.28</td>
<td>58.48</td>
<td>A''</td>
<td>+</td>
<td>−</td>
<td>0</td>
<td>τ(N–H) aT</td>
</tr>
<tr>
<td>817, 816</td>
<td>829.46</td>
<td>54.12</td>
<td>A''</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>τ(N–H) aC</td>
</tr>
<tr>
<td>774</td>
<td>−</td>
<td>−</td>
<td>A'</td>
<td>−</td>
<td>0</td>
<td>0</td>
<td>2ω(NH(_2)) Tn</td>
</tr>
<tr>
<td>729</td>
<td>732.91</td>
<td>7.50</td>
<td>A'</td>
<td>−</td>
<td>0</td>
<td>0</td>
<td>ν(CS) Tn</td>
</tr>
<tr>
<td>645</td>
<td>636.88</td>
<td>49.21</td>
<td>A'</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>ν(C–S) aC</td>
</tr>
<tr>
<td>640</td>
<td>637.94</td>
<td>48.39</td>
<td>A'</td>
<td>+</td>
<td>−</td>
<td>0</td>
<td>ν(C–S) aT</td>
</tr>
<tr>
<td>626</td>
<td>621.61</td>
<td>33.51</td>
<td>A'</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>ν(C–S) sT</td>
</tr>
<tr>
<td>623</td>
<td>616.44</td>
<td>42.31</td>
<td>A'</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>ν(C–S) sC</td>
</tr>
<tr>
<td>592</td>
<td>613.23</td>
<td>5.18</td>
<td>A''</td>
<td>−</td>
<td>0</td>
<td>0</td>
<td>τ(NH(_2)) Tn</td>
</tr>
<tr>
<td>508</td>
<td>518.39</td>
<td>3.59</td>
<td>A''</td>
<td>−</td>
<td>0</td>
<td>0</td>
<td>γ(CS) Tn</td>
</tr>
</tbody>
</table>

\(^a\) Unscaled harmonic frequencies and absolute infrared intensities (km mol\(^{-1}\)) computed at the B3LYP/6-311++G(3df,3pd) level of theory.

\(^b\) −/+: decrease/increase of signal, 0: no change upon irradiation

\(^c\) ν: stretching, γ: out-of-plane bending, ω: wagging, τ: torsion

\(^d\) Assignment based on spectral changes and computed frequencies.
Table 3. Kinetic decay/growth rates ($k_d$ and $k_g$, respectively, in min$^{-1}$) of the thiols. Kinetic half-lives ($t_{1/2}$, in min) of the sC isomer calculated from the respective $k_d$ values are also visualized.

<table>
<thead>
<tr>
<th>Exp. no.</th>
<th>Matrix gas (temperature)</th>
<th>Filter</th>
<th>$k_d$(sC)</th>
<th>$t_{1/2}$(sC)</th>
<th>$k_g$(sT)</th>
<th>$sC_f / sT_f$</th>
<th>$k_g$(aC)</th>
<th>$k_d$(aT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>Ar (11 K)</td>
<td>870 cm$^{-1}$</td>
<td>(8.6 ± 0.2) × 10$^{-3}$</td>
<td>80 ± 2</td>
<td>(7.1 ± 0.7) × 10$^{-3}$</td>
<td>0.11</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>1b</td>
<td>Ar (20 K)</td>
<td>870 cm$^{-1}$</td>
<td>(7.4 ± 0.5) × 10$^{-3}$</td>
<td>94 ± 6</td>
<td>(9.5 ± 0.2) × 10$^{-3}$</td>
<td>0.12</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>2</td>
<td>Ar (11 K)</td>
<td>870 cm$^{-1}$</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0.10</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>4b</td>
<td>Ar (11 K)</td>
<td>1960 cm$^{-1}$</td>
<td>(1.1 ± 0.1) × 10$^{-2}$</td>
<td>63 ± 6</td>
<td>(1.1 ± 0.1) × 10$^{-2}$</td>
<td>0.09</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>4a</td>
<td>Ar (11 K)</td>
<td>No filter</td>
<td>(1.4 ± 0.2) × 10$^{-2}$</td>
<td>50 ± 7</td>
<td>(1.2 ± 0.2) × 10$^{-2}$</td>
<td>0.20</td>
<td>(3.0 ± 1.0) × 10$^{-3}$</td>
<td>(4.0 ± 2.3) × 10$^{-3}$</td>
</tr>
<tr>
<td>3</td>
<td>Xe (11 K)</td>
<td>870 cm$^{-1}$</td>
<td>(1.8 ± 0.4) × 10$^{-2}$</td>
<td>39 ± 9</td>
<td>(1.3 ± 0.5) × 10$^{-2}$</td>
<td>0.22</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

$^a$ Ratio of the integrated band areas of the two syn imino forms at the end of the kinetic study.

$^b$ The spectrometer beam was blocked between the measurements, the time interval was 620 min.
Table 4. Tunneling rates of the thiol forms computed using the WKB approximation and based on intrinsic reaction paths calculated at the B3LYP/6-311++G(3df,3pd) level of theory.

<table>
<thead>
<tr>
<th>Process</th>
<th>$w \times 10^{-10}$ m</th>
<th>$V_0-E$ (J)</th>
<th>$\nu$ (s$^{-1}$)</th>
<th>$t_{1/2}$ (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>aC $\rightarrow$ Tn</td>
<td>1.29</td>
<td>$1.78 \times 10^{-19}$</td>
<td>$2.55 \times 10^{13}$</td>
<td>$8.63 \times 10^{6}$</td>
</tr>
<tr>
<td>aC $\rightarrow$ sC</td>
<td>1.44</td>
<td>$1.45 \times 10^{-19}$</td>
<td>$3.90 \times 10^{13}$</td>
<td>$9.00 \times 10^{6}$</td>
</tr>
<tr>
<td>aT $\rightarrow$ sT</td>
<td>1.37</td>
<td>$1.41 \times 10^{-19}$</td>
<td>$3.90 \times 10^{13}$</td>
<td>$4.33 \times 10^{5}$</td>
</tr>
<tr>
<td>aT $\rightarrow$ aC</td>
<td>2.30</td>
<td>$3.82 \times 10^{-20}$</td>
<td>$7.35 \times 10^{12}$</td>
<td>$8.27 \times 10^{3}$</td>
</tr>
<tr>
<td>sC $\rightarrow$ sT</td>
<td>2.47</td>
<td>$2.73 \times 10^{-20}$</td>
<td>$8.35 \times 10^{12}$</td>
<td>$1.79 \times 10^{2}$</td>
</tr>
</tbody>
</table>
**Figure 1.** Structures of the thioacetamide isomers as optimized at the B3LYP/6-311++G(3df,3pd) level of theory.

170x120mm (300 x 300 DPI)
Figure 2. Structures of the thioacetamide TSs as optimized at the B3LYP/6-311++G(3df,3pd) level of theory. Only one of the mirror-image structures of both the aC–aT and sC–sT TSs, differing only in the orientation of their S–H groups, are shown.
Figure 3. (a) Selected regions of the mid-IR spectrum showing new bands of thiol isomers after UV irradiation of thioacetamide in an Ar matrix at 11 K; (b) changes in the spectrum when monitoring the spontaneous decay process overnight. Increasing bands show the formation of the respective isomer. The spectra were collected using the longpass filter with a cut-off wavenumber of 870 cm$^{-1}$. The filter was placed between the spectrometer light source and the cryostat and remained there also between the spectral collections; (c) simulated difference spectrum showing a quantitative $sC \rightarrow sT$ conversion. The absorptions were convoluted with Lorentzian functions (FWHM $= 0.5$ cm$^{-1}$) centered at the B3LYP/6-311++G(3df,3pd) computed wavenumbers. The computed infrared intensities of $sC$ were multiplied by $(-1)$. 

82x118mm (600 x 600 DPI)
Figure 4. (a) Kinetic decay of the band at 836 cm$^{-1}$ ($sC$), (b) kinetic growth of the band at 849 cm$^{-1}$ ($sT$) using the longpass filter with a cut-off wavenumber of 870 cm$^{-1}$ (experiment 1a, at 11 K).
Figure 5. Structures of the thioacetamide isomers discussed in this work. The names are shown in bold, followed by relative energies with respect to the \textit{sT} thiol isomer. The numbers near the dashed lines represent the relative energies of the first-order TSs (with respect to the \textit{sT} form), as well as the barrier widths (in bohr) along the respective intrinsic reaction paths [in brackets]. Energies of all the stationary points (in kJ mol$^{-1}$) include the zero-point vibrational energy corrections, computed at the B3LYP/6-311++G(3df,3pd) level of theory. See also Figure S8.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure5.png}
\caption{Structures of the thioacetamide isomers discussed in this work. The names are shown in bold, followed by relative energies with respect to the \textit{sT} thiol isomer. The numbers near the dashed lines represent the relative energies of the first-order TSs (with respect to the \textit{sT} form), as well as the barrier widths (in bohr) along the respective intrinsic reaction paths [in brackets]. Energies of all the stationary points (in kJ mol$^{-1}$) include the zero-point vibrational energy corrections, computed at the B3LYP/6-311++G(3df,3pd) level of theory. See also Figure S8.}
\end{figure}
Rotamerization of the S–H group via hydrogen tunneling in one of the thiol isomers of matrix-isolated thioacetamide is reported.