Bond-Breaking/Bond-Forming Reactions by Vibrational Excitation: Infrared-Induced Bidirectional Tautomerization of Matrix-Isolated Thiotropolone

Cláudio M. Nunes,* Nelson A. M. Pereira, Igor Reva, Patrícia S. M. Amado, Maria L. S. Cristiano, and Rui Fausto

ABSTRACT: Infrared vibrational excitation is a promising approach for gaining exceptional control of chemical reactions, in ways that cannot be attained via thermal or electronic excitation. Here, we report an unprecedented example of a bond-breaking/bond-forming reaction by vibrational excitation under matrix isolation conditions. Thiotropolone monomers were isolated in cryogenic argon matrices and characterized by infrared spectroscopy and vibrational computations (harmonic and anharmonic). Narrowband near-infrared irradiances tuned at frequencies of first CH stretching overtone (5940 cm$^{-1}$) or combination modes (5980 cm$^{-1}$) of the OH tautomer, the sole form of the compound that exists in the as-deposited matrices, led to its conversion into the SH tautomer. The tautomerization in the reverse direction was achieved by vibrational excitation of the SH tautomer with irradiation at 5947 or 5994 cm$^{-1}$, corresponding to the frequencies of its CH stretching combination and overtone modes. This pioneer demonstration of bidirectional hydroxyl ↔ thiol tautomerization controlled by vibrational excitation creates prospects for new advances in vibrationally induced chemistry.

Selective energy deposition in a chosen vibrational mode of a given molecular species is a promising way to achieve exquisite control of chemical reactions.1−5 This approach contrasts with conventional heating, in which energy is nonselectively deposited in all molecules of the considered system. The dream of tuning light at a vibrational frequency of a particular bond and inducing a chemical reaction only at that site is extremely challenging, even using femtosecond pulses under low-pressure gas-phase conditions.8 This is partially because intramolecular vibrational energy redistribution (IVR) dissipates the deposited energy fast to other modes before the reaction arises.5,6 Alternatively, if a dominant (nonstatistical) IVR pathway exists due to the coupling between an excited vibrational mode and a reaction coordinate, this might be exploited to induce a desired chemical transformation in an elegant and selective way.3,10 One remarkable example illustrating this possibility is the vibrationally induced unimolecular reaction of the jet-cooled Criegee intermediate syn-CH$_3$CHOO, reported by Lester and co-workers11−14 The authors demonstrated that excitation of CH stretching overtones or combination modes induces a 1,4-H shift from the methyl group to the terminal oxygen and activates decomposition of the molecule (Scheme 1).11 Nevertheless, the application of this strategy to induce and control organic reactions remains scarcely explored.15−24

One noticeable exception has been the use of vibrational excitation to manipulate molecular conformations of different

Scheme 1. Reaction of a Criegee Intermediate (syn-CH$_3$CHOO) Induced by Pumping $2\nu$(CH) Overtones with Narrowband Light Tuned at ∼6000 cm$^{-1}$ (note the red vertical arrow)4

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classes of organic compounds. Typically, energy is deposited in XH (X = O or N) first stretching overtones, because these modes have substantial energy alongside with a sufficiently significant absorption cross section. This way, it has been shown that vibrational excitation can induce rotamerization of a light H atom (e.g., of an OH or SH group) or heavy fragments (e.g., aldehyde, hydroxymethyl, and methoxy), even when they are located remotely in relation to the excited vibrational mode. To the best of our knowledge, apart from conformational isomerizations, only one other type of reaction induced by vibrational excitation under matrix isolation conditions has been reported hitherto, namely the reaction of small ethylene derivatives aggregated with F2.

Looking for a less direct approach, we investigated chemical processes with low energy barriers, especially signiﬁcant noncovalent interactions. Since this condition is fulﬁlled in the B2PLYP/6-311+G(2d,p), and B3LYP/6-311+G(2d,p) Levels of Theory for the Four Most Relevant Isomers of Thiotropolone, and due to the low energy barriers, some Fermi resonance and overtone bands appearing in the range of 1500–1250 cm$^{-1}$ (Figure S5). A detailed assignment of this spectrum is provided in Table S1. Although TT was described to exist in solution and the solid state as two rapidly equilibrated hydroxy (OH-TT) and thiol (SH-TT) tautomeric structures, the presence of thiol forms under matrix isolation conditions is excluded due to the lack of strong ν(C=O) and other characteristic spectral features (Figure S6). This picture is consistent with the relative energies computed for the most relevant isomers of TT (Table 1).

Table 1. Relative Gibbs Energies at 298.15 K (ΔG$_{298}$ K in kJ mol$^{-1}$) Computed at the CBS-QB3, MP2/6-311++G(3df,3pd), B2PLYP/6-311+G(2d,p), and B3LYP/6-311+G(2d,p) Levels of Theory for the Four Most Relevant Isomers of Thiotropolone and Their Equilibrium Populations at 298.15 K (Pop$_{298}$ % in %)

<table>
<thead>
<tr>
<th>Structure</th>
<th>Name</th>
<th>s-OH-TT</th>
<th>a-OH-TT</th>
<th>s-SH-TT</th>
<th>a-SH-TT</th>
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<td>8.1</td>
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<tr>
<td>Pop$_{298}$</td>
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<td>0.0</td>
<td>3.7</td>
<td>0.0</td>
<td></td>
</tr>
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</table>

Here, we demonstrate an unprecedented example of a bond-breaking/bond-forming reaction activated by vibrational excitation under matrix isolation conditions, namely the hydroxyl ↔ thiol tautomerization of thiotropolone (TT), which can be induced in both directions by excitation of CH stretching overtones or combination modes of the corresponding reactant species (Scheme 2).

Scheme 2. Bidirectional Tautomerizations in Thiotropolone (TT) Induced by Vibrational Excitation

\[ \text{s-OH-TT} \leftrightarrow \text{a-SH-TT} \]

“In the names of structures, s stands for syn and a stands for anti, corresponding to the orientation of the O−H/S==C or S−H/O==C moieties.

Thiotropolone was prepared by standard procedures, as described in the Supporting Information. The compound was sublimated at room temperature and deposited with a large excess of argon onto a CsI window (15 K). The IR spectrum of monomeric TT isolated in an argon matrix is well reproduced by the B3LYP/6-311+G(2d,p)-computed harmonic IR spectrum of the s-OH-TT hydroxy tautomeric form, except for some Fermi resonance and overtone bands appearing in the range of 1500–1250 cm$^{-1}$ (Figure S5). A detailed assignment of this spectrum is provided in Table S1. Although TT was described to exist in solution and the solid state as two rapidly equilibrated hydroxy (OH-TT) and thiol (SH-TT) tautomeric structures, the presence of thiol forms under matrix isolation conditions is excluded due to the lack of strong ν(C=O) and other characteristic spectral features (Figure S6). This picture is consistent with the relative energies computed for the most relevant isomers of TT (Table 1).

Because of the strong OH···S==C H-bond, the ν(OH) stretching mode of s-OH-TT (computed at 2688 cm$^{-1}$) causes a very broad absorption (barely noticeable) in the range of 2900–2400 cm$^{-1}$ (Figure S7). The corresponding νs(OH) overtone (computed at 4916 cm$^{-1}$) was not detected in the near-IR spectrum. However, two bands were observed at 5980 and 5940 cm$^{-1}$ (Figure 1a). On the basis of B3LYP/6-311+G(2d,p) anharmonic computations, these bands were ascribed to overtones and combinations of ν(CH) modes (Figure 1b), whose fundamentals appear near 3000 cm$^{-1}$ (Figure S7). More details about the assigned overtones and combinations of ν(CH) modes are shown in Figure S8.

The effect of selective vibrational excitation of s-OH-TT was explored. Using narrowband light provided by an optical parametric oscillator, the matrix-isolated s-OH-TT was irradiated at 5980 and 5940 cm$^{-1}$, and the process followed by mid-IR spectroscopy (using a cutoff filter blocking IR light above 2200 cm$^{-1}$). Excitation at both frequencies was found to induce tautomerization of s-OH-TT into a-SH-TT. As shown in panels a and b of Figure 2, the experimental difference IR spectrum is reproduced well by the B3LYP/6-311+G(2d,p)-computed difference spectrum simulating this transformation. Some distinctive bands of a-SH-TT were observed at 1628, 1587, 1007, 770, and 563 cm$^{-1}$, corresponding to the vibrational modes computed at 1625 [ν$_1$(C=O)], 1586 [ν$_2$(C═C) − δ(SH)], 765 [ν$_2$(C=C) − γ(CH)], and 556 cm$^{-1}$ [ν$_1$(C=S)], respectively. A more detailed account of these bands and their assignments is given in the Supporting Information.
Figure 1. (a) Near-IR spectrum of the s-OH-TT form of thiotropolone in an argon matrix at 15 K. (b) Anharmonic wavenumbers and IR intensities of s-OH-TT computed at the B3LYP/6-311+G(2d,p) level of theory. Filled (■) and empty (□) circles depict $\nu_5$(CH) and $\nu_2$(CH) overtone modes, respectively. Filled (●) and empty (○) circles depict $\nu_5$(CH) + $\nu_2$(CH) and $\nu_5$(CH) + $\nu_4$(CH) combination modes, respectively. Only overtone or combination modes with a computed IR intensity of $>$0.4 km mol$^{-1}$ are shown.

Figure 2. Experimental difference IR spectrum (spectrum after matrix irradiation “minus” spectrum of the same matrix before irradiation): (a) irradiation at 5940 cm$^{-1}$ (60 mW, 1 h) and (c) irradiation at 5994 cm$^{-1}$ (30 mW, 1 h). Bands marked with circles (●) are due to a-SH-TT, which is produced by irradiation at 5940 cm$^{-1}$ (a) and consumed by irradiation at 5994 cm$^{-1}$ (c). (b) Simulated difference IR spectrum based on B3LYP/6-311+G(2d,p) vibrational data considering quantitative (1:1) transformation of s-OH-TT into a-SH-TT. The tilde symbols designate truncated bands.

detailed assignment is provided in Table S2. Although the computed IR spectra of a-SH-TT and s-SH-TT are very similar, a detailed analysis of some spectral regions suggests the exclusive formation of a-SH-TT upon irradiation (Figure S9). As demonstrated below, s-SH-TT is expected to be a fleeting species that cannot be isolated or observed even under the cryogenic conditions of the performed experiments.

After an argon matrix containing exclusively the a-SH-TT form had been produced [using irradiation at 440 nm (see the Supporting Information for details)], a near-IR spectrum was recorded allowing the identification of two bands at 5994 and 5947 cm$^{-1}$ (Figure S10a), which can be ascribed to $\nu$(CH) overtone and combination modes (Figures S10b and S11). The sample was then irradiated at these wavenumbers, and tautomerization of a-SH-TT back to s-OH-TT was observed (Figure 2c). The experimental difference IR spectrum perfectly mirrors the inverse process of the transformation of s-OH-TT to a-SH-TT described above (Figure 2a,c). The only distinctive feature is that the transformation of a-SH-TT into s-OH-TT occurs on a much larger scale.69 These results demonstrate that the hydroxy/thiol tautomerization in TT is achieved in both directions by vibrational excitation at the $\nu$(CH) overtone or combination modes of the corresponding reactant tautomeric species (Scheme 2).

To rationalize the experimental observations, the potential energy surface (PES) profiles for tautomerization and rota merizations of the most relevant isomers of TT (Figure 3) were computed. Upon excitation of s-OH-TT at 5980 or 5940 cm$^{-1}$, $\sim$71 kJ mol$^{-1}$ is introduced in the molecule. Such an energy is below the transition state (TS) for OH tautomerization ($\sim$76 kJ mol$^{-1}$) but well above the TS for tautomerization to a-SH-TT ($\sim$17 kJ mol$^{-1}$), as computed at the B3LYP/6-311+G(2d,p) level (for energies computed with other methods, see Table S4). However, s-SH-TT should not persist and will promptly tautomerize back to s-OH-TT because of a low ($\sim$9 kJ mol$^{-1}$) and thin ($\sim$0.63 Å) barrier (Figure S12). With such a barrier, the occurrence of extremely fast quantum tunneling is expected, making s-SH-TT a fleeting species even under cryogenic conditions [estimated $\tau_{1/2}$ of $\sim$1 $\times$ 10$^{-11}$ s applying the Wentzel–Kramers–Brillouin (WKB) model (see the Supporting Information)].60–64 Note, for instance, that the thiol $\rightarrow$ thione tautomerization in thiourea has a much higher ($\sim$93 kJ mol$^{-1}$) and wider ($\sim$1.18 Å) barrier (Figure S13), and even for that system, tunneling under cryogenic conditions was found to occur on a time scale of hours$^{65}$ [estimated $\tau_{1/2}$ of $\sim$5 $\times$ 10$^{-3}$ s, in fair agreement with experiment (see the Supporting Information)]. These data unequivocally endorse the experimental capture and identification of thiol a-SH-TT (and not s-SH-TT) upon vibrational excitation of s-OH-TT. The formation of a-SH-TT has a barrier of $\sim$53 kJ mol$^{-1}$, clearly below the energy introduced in s-OH-TT upon vibrational excitation. The observed process shows that the excited $\nu$(CH) overtone/combination modes are coupled to some extent to the reaction coordinates for tautomerization and subsequent SH rotation, leading to a-SH-TT through an IVR process crossing two reaction coordinates. The alternative occurrence of a two-step process, involving the formation of a thermalized s-SH-TT at an intermediate stage, is unlikely, because s-SH-TT is expected to have both a very short lifetime and no significant bright transitions near 5980 or 5940 cm$^{-1}$ (Table S6). Under these circumstances, the occurrence of vibrational excitation of s-SH-TT with subsequent activation of SH rotation is impossible in practice.68

The observed tautomerization of a-SH-TT back to s-OH-TT on a much larger scale is easier to conceptualize.
Upon irradiation of a-SH-TT at 5994 or 5947 cm$^{-1}$, the vibrational energy deposited in the molecule ($\sim$71 kJ mol$^{-1}$) is high enough to activate SH rotamerization to s-SH-TT ($\sim$33 kJ mol$^{-1}$ is required), which will rapidly tautomerize by tunneling to s-OH-TT. None of these phenomena (SH rotamerization induced by vibrational excitation and thiol tautomerization by tunneling) is entirely unprecedented.$^{26,67}$

The existence of coupling between the excited $\nu$(CH) overtone/combination modes with the reaction coordinates for SH rotamerization and subsequent tautomerization is also conceivable, allowing the direct formation of s-OH-TT from a-SH-TT, similar to the process proposed for the opposite tautomerization.

In conclusion, we demonstrated that bidirectional tautomerization of thiotropolone is achieved by vibrational excitation. The s-OH-TT $\leftrightarrow$ a-SH-TT transformations involve bond-breaking/bond-forming processes as a result of vibrational excitation, which is a fascinating unprecedented observation. The observed processes also show that intramolecular vibrational redistribution in TT can transport energy deposited in the CH stretching overtone or combination modes toward the distant reaction coordinates leading to the hydroxy $\leftrightarrow$ thiol tautomerizations. These pioneering results of a bond-breaking/bond-forming reaction activated by vibrational excitation under matrix isolation conditions can be expected to lead to new exciting advances in vibrationally induced chemistry.

**ASSOCIATED CONTENT**

Supporting Information
The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.jpcl.0c02272.

Experimental and computational procedures, additional experimental results, vibrational assignments, and computational data (PDF)

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**Author Contributions**
C.M.N. conceived the original working hypothesis and wrote the first draft of the manuscript. C.M.N. and N.A.M.P. performed the experiments. C.M.N., N.A.M.P., I.R., and R.F. performed the computations and analyzed the data. P.S.M.A. and M.L.S.C. performed the synthesis. All authors discussed and co-wrote the final version of the manuscript.

**Notes**
The authors declare no competing financial interest.

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REFERENCES


(11) Another landmark is the recently reported acceleration of urethane and polyurethane formation in solution by vibrational excitation at the OH and NCO stretching of their alcohol and isocyanate reactants, respectively (see ref 13). For the first case of a vibrationally driven bimolecular reaction in solution, see ref 14.


(37) Wassermann, T. N.; Suhm, M. A.; Roubin, P.; Cousseau, S. Isomerization around C–C and C–O bonds in 1-propanol:
Collisional relaxation in supersonic jets and selective IR photo-
(40) Bazsi, G.; Magyarfalvi, G.; Tarczay, G. Tunneling lifetime of the
(41) Lapinski, L.; Nowak, M. J.; Reva, I.; Rostkowska, H.; Fausto, R.
NIR-laser-induced selective rotamerization of hydroxy formylnitrene
(42) Sharma, A.; Reva, I.; Fausto, R. Conformational switching
induced by near-infrared laser irradiation. J. Am. Chem. Soc. 2009, 131,
8752−8753.
(43) Khrachtchev, L. Rotational isomers of small molecules in
noble-gas solids: From monomers to hydrogen-bonded complexes. J.
(44) Dian, B. C.; Longarte, A.; Zwier, T. S. Conformational
dynamics in a dipeptide after single-mode vibrational excitation.
Science 2002, 296, 2369−2373.
(45) Pettersson, M.; Lundell, J.; Khrachtchev, L.; Rasane, M. IR
spectrum of the other rotamer of formic acid, cis-HCOOH. J. Am.
(46) It was recently demonstrated that selective conformational
isomerizations can also be achieved using excitation to second
stretching overtones. See: Nunes, C. M.; Reva, I.; Fausto, R.
Conformational isomerizations triggered by vibrational excitation of
second stretching overtones. Phys. Chem. Chem. Phys. 2019, 21,
24993−25001.
(47) We have recently reported a heavy-atom tunneling event
involving the ring expansion of a fused-ring benzanilide into a seven-
membered ring ketenimine. Interestingly, broadband IR radiation,
from the spectrometer globar, was found to increase the rate of this
transformation, which may indicate that the reaction is also promoted
by vibrational excitation. See: Nunes, C. M.; Reva, I.; Kozuch, S.;
McMahon, R. J.; Fausto, R. Photochemistry of 2-formylphenylnitrene:
A doorway to heavy-atom tunneling of a benzazirine to a cyclic
(48) Catalano and Barletta also tentatively reported a bimolecular
reaction between SF6 and nitrogen oxides induced by vibrational
excitation under matrix isolation conditions. However, no product
assignments could be made to show conclusively that IR laser-induced
photochemistry is really occurring. See: Catalano, E.; Barletta, R. E.
Infrared laser single photon absorption reaction chemistry in the solid
Chem. 1980, 84, 1686−1694.
(49) Frei, H.; Fredin, L.; Pimentel, G. C. Vibrational excitation of
(50) Cesaro, S. N.; Frei, H.; Pimentel, G. C. Vibrational excitation of
the reaction between vinyl bromide and fluoride in solid argon. J.
(51) Knudsen, A. K.; Pimentel, G. C. Vibrational excitation of the
allene-fluorine reaction in cryogenic matrices: Possible mode
(52) The IR spectrum of matrix-isolated tropolone, a structurally
similar species, also shows significant complexity in the range of
1650−1400 cm−1 due to the existence of Fermi resonances and
overtones bands. See: Redington, R. L.; Redington, T. E.; Montgomery,
(53) Machiguchi, T.; Hasegawa, T.; Saitoh, H.; Yamabe, S.; Yamazaki, S. Solid-state thiotropolone: An extremely rapid intra-
(54) The possibility of H-atom tunneling from OH-TT to SH-TT
was clearly ruled out at low temperatures. See: Fernández-Ramos, A.
Correct interpretation of how tunneling proceeds at low temperatures
in the proton transfer reactions involving thiotropolone: A comment.
Angew. Chem., Int. Ed. 2013, 52, 8204−8205.
(55) A similar effect was observed for other molecules with a strong
OH···X (X = S, O, or N) intramolecular H-bond. See for instance refs
56−58.