

Conformational Switching by Vibrational Excitation of a Remote NH Bond

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S Supporting Information

ABSTRACT: Here we describe an unprecedented reversible interconversion between two conformational states, accomplished by selective vibrational excitation of a bond remotely located in relation to the isomerizing fragment. In contrast to previous studies reporting conformational changes via vibrational excitation of a nearby OH group, in this study the transformations were successfully achieved by excitation of a distant NH stretching coordinate. The *syn* and *anti* forms of monomeric 6-methoxyindole, which differ in the orientation of the methoxy group, were trapped in low-temperature inert matrixes and characterized spectroscopically. These forms could be selectively shifted in both directions by using near-IR excitations tuned at the frequency of the first NH stretching overtone. The observed isomerization proves the possibility of efficient vibrational relaxation to carry the energy deposited at the NH stretching coordinate into the reactive C–O torsional mode localized on the methoxy group four bonds away from the excited NH moiety.

The first report on an IR-induced conformational isomerization in a cryomatrix was presented by Hall and Pimentel in 1963.¹ That work considered the isomerization of HONO upon broadband infrared excitation. However, the generalization of the technique was severely conditioned by the usual similarity between the vibrational spectra of different conformers. It was only much later that the technique evolved to an extremely effective and elegant strategy for optically controlling the populations of different conformers of a molecule. In a seminal work published in 1997,² Pettersson et al. were able to generate the high-energy rotamer of formic acid from the most stable form, by combining the low-temperature noble-gas matrix isolation technique with selective vibrational excitation using narrowband near-infrared (NIR) radiation. Before that, the experimental identification of the less stable conformer of this molecule was largely limited due to its vanishingly small gas-phase population (~0.1% at 298 K).²

Since this pioneering research, monochromatic NIR light excitation has been successfully applied to control in a selective way the conformational composition of various molecules trapped in low-temperature matrixes, such as carboxylic acids,^{3–9} ethanol,¹⁰ amino acids,^{11–14} parent cytosine^{15,16} and 5-substituted cytosines,¹⁷ hydroxyacetone,¹⁸ and squaric acid.¹⁹

In all of the above-mentioned studies, the photorotamerizations are triggered by tuning the NIR laser-light at a frequency characteristic of the first overtone of an OH stretching vibration (or a suitable combination tone involving the ν OH mode). Also, in most of the studied cases, the rotating group is undergoing photoexcitation or is in a neighbor position to the excited moiety.^{2,3,6–17,19} Less frequently, a somewhat more complex pattern of conformational changes was observed, where groups located more apart from the excited OH group were affected.^{4,18} However, in those cases the molecules exhibit intramolecular H-bonds, and the conformational change of the more distant groups could be explained as resulting from a reorganization of the intramolecular H-bond system subsequent to the NIR-induced initial conformational change of the photoexcited group.

To the best of our knowledge, a reversible interconversion between two conformational states resulting purely from selective excitation of the stretching vibration of a bond remotely located relatively to the isomerization coordinate has never been observed so far. Also, an efficient conformational interconversion induced by pumping a stretching overtone vibration of other than the OH group has never been reported hitherto.²⁰ If successful, this would open the opportunity for manipulating the conformational distribution of a larger variety of molecular systems.

In the present communication we report the first experimental observation of a bidirectional and large-scale conformational switching involving the intramolecular torsion of a methoxy group, induced by excitation of a stretching overtone of an NH group, located in a remote position relatively to the fragment undergoing isomerization.

The molecular system used as model is 6-methoxyindole (**6MOI**). The conformational space of this indole derivative is constituted by two conformers, whose structures have been determined by rotationally resolved electronic spectroscopy and theoretical calculations.^{21,22} Using the nomenclature adopted elsewhere,²¹ they are designated as *syn* and *anti*, depending if the OCH₃ and NH groups are pointing in the same or opposite directions, respectively (see Figure 1). By applying different levels of theory, up to CC2/cc-pVTZ,²¹ both the electronic and the ZPE corrected energy difference between the two conformers was calculated to fall between 1.8 and 3.2

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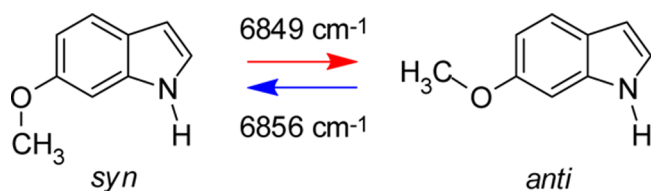


Figure 1. Conformers of 6-methoxyindole and effects of the narrowband NIR irradiations. The numbers next to the arrows correspond to the experiments with xenon matrixes.

kJ mol^{-1} , in favor of the *syn* conformer, see Table S1 of the Supporting Information (SI).^{21,22} This means that at the temperature of the evaporating compound before the matrix deposition ($T \approx 323$ K, see below), the equilibrium conformational mixture is constituted by 66–77% of *syn* and 34–23% of *anti*. Since the two forms are present in gas-phase in significant concentrations and are separated by an energy barrier of at least ~ 9 kJ mol^{-1} (see SI, Figure S1), both of them can be expected to be efficiently trapped in a low-temperature matrix.

Experimentally, the crystals of the studied compound (98%, supplied by Apollo Scientific) were sublimated by heating up to $T \approx 323$ K using a miniature glass oven placed inside a helium-cooled cryostat. Vapors of the compound were codeposited with a large excess of inert gas onto a cold CsI window. Argon and xenon matrixes were deposited at 16 and 30 K, respectively. Narrowband tunable NIR-light of the idler beam of a Quanta-Ray MOPO-SL optical parametric oscillator (pulse energy 10 mJ, duration 10 ns, repetition rate 10 Hz) pumped with a pulsed Nd:YAG laser was used to irradiate the deposited matrixes. Spectra in the mid- and near-infrared regions, with a resolution of 0.5 and 1 cm^{-1} , respectively, were collected with a Thermo Nicolet 6700 FTIR spectrometer. Further details of the experimental setup are given elsewhere.^{8,23} To assist the interpretation of the experimental spectra, the geometries of the *syn* and *anti* forms were fully optimized (see Tables S2 and S3 of the SI), and harmonic and anharmonic vibrational frequencies and infrared intensities of the two **6MOI** conformers were calculated at the B3LYP/6-311++G(d,p) level of theory, using the Gaussian 09 program package.²⁴ The results of these vibrational calculations are summarized in the SI, Tables S4 and S5.

The same type of experiments have been conducted both in xenon and argon matrixes. In general, no major differences were detected between the mid- and near-IR spectra registered in both matrixes, except for the much more pronounced site-splitting effects observed in argon than in xenon spectra, in particular in the NH-stretching region (see SI, Figure S2).

The NH stretching region of **6MOI** isolated in a freshly deposited xenon matrix at 30 K is shown in Figure 2a (solid red trace). The doublet band with maxima separated by 3.5 cm^{-1} corresponds to the NH-stretching vibration (νNH) of the two conformers. By comparison with the calculated vibrational frequencies (Figure 2c), the lower frequency component (3494.5 cm^{-1}) can be assigned to the *syn* form and that at higher frequency (3498.0 cm^{-1}) to the *anti* conformer. Using the integrated areas of the two band components and the absolute intensities calculated for the respective vibrations, the relative abundance of both conformers in the freshly deposited matrix is estimated to be $\sim 65\%$ *syn*/ $\sim 35\%$ *anti*, a ratio that is in a very good agreement with the theoretical predictions.

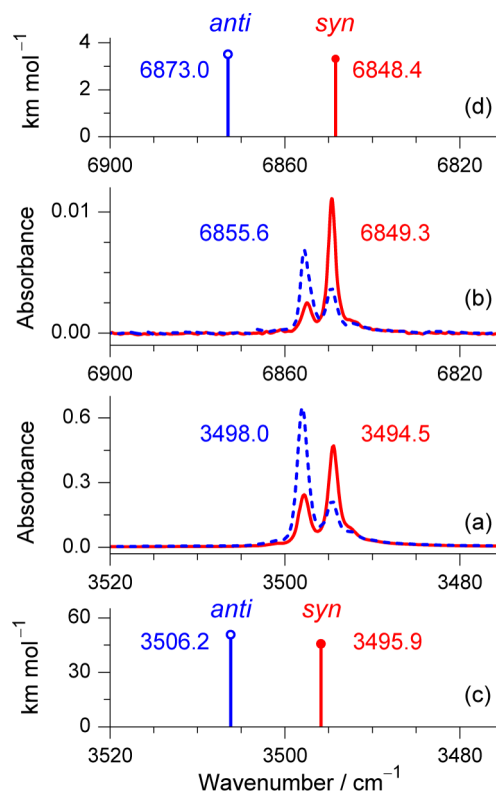


Figure 2. Fragment of the mid-infrared (a) and near-infrared (b) spectrum of **6MOI** isolated in a xenon matrix at 30 K before any irradiation (red, solid trace) and after 30 min of irradiation at 6849 cm^{-1} (blue, dashed trace). The experimental bands are compared with the anharmonic wavenumbers (unscaled) and IR intensities calculated for the νNH (c) and $2\nu\text{NH}$ (d) vibrations of the *syn* (red, closed circle) and *anti* (blue, open circle) conformers at the B3LYP/6-311++G(d,p) level of theory.

In the fragment of the NIR spectrum (6900–6810 cm^{-1}) displayed in Figure 2b, one can clearly identify two well-defined bands at 6849.3 and 6855.6 cm^{-1} , which correspond to the $2\nu\text{NH}$ overtones of the *syn* and *anti* conformers, respectively. This assignment is supported by the results of the anharmonic frequency calculations of the overtone modes shown in Figure 2d and also by the changes in the spectra induced by NIR-irradiations as described below.²⁵

In the performed NIR irradiation experiments, we started by exposing the deposited xenon matrix to monochromatic light tuned at 6849 cm^{-1} for 30 min. This irradiation promoted a large-scale *syn* \rightarrow *anti* transformation. More than 50% of *syn* form was converted to *anti*, as clearly reflected by the magnitude of the changes in intensity of the νNH and $2\nu\text{NH}$ absorptions: see differences between the solid (red) and dashed (blue) traces in Figure 2a,b.

This conformational conversion is also well evidenced in the fingerprint region. Figure 3a shows a difference spectrum constructed by subtracting the spectrum of the deposited matrix from that obtained after irradiation at 6849 cm^{-1} , in selected ranges, where characteristic bands of the two conformers are observed. The comparison of this spectrum with the calculated spectra of both conformers (Figure 3b) allows the doubtless assignment of the bands that decrease upon NIR excitation (negative bands in the experimental difference spectrum) to the lower-energy *syn* conformer, and of

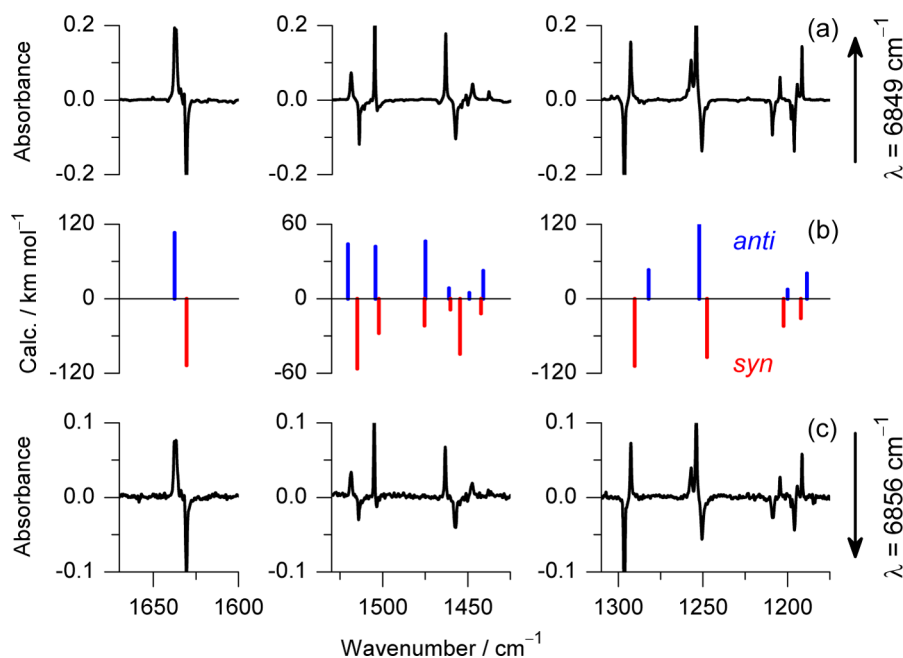


Figure 3. Fragments of experimental (Xe, 30 K) and theoretical spectra of **6MOI** in the fingerprint region showing the effect of the NIR irradiations: (a) experimental spectrum registered after irradiation at 6849 cm^{-1} minus that obtained before any irradiation; (c) experimental spectrum registered before any irradiation at 6856 cm^{-1} minus that obtained after irradiation at this frequency. Arrows indicate the direction of the bands growing upon irradiation; (b) theoretical spectra of the *anti* (upward bars, blue) and *syn* (downward bars, red) conformers calculated at the B3LYP/6-311++G(d,p) level of theory. The calculated harmonic vibrational frequencies were scaled by a factor of 0.98.

those that concomitantly are growing up to the higher-energy *anti* form.

After the first irradiation, the source of the NIR laser-light was tuned at the $2\nu_{\text{NH}}$ overtone assigned to the *anti* conformer (6855.6 cm^{-1}) to test the photoreversibility of the isomerization. The spectral modifications observed in the course of this second irradiation (Figure 3c; note that in this figure the negative bands are those growing up, as indicated by the arrow) undoubtedly demonstrate that the higher-energy form is converted back into the most stable conformer, i.e., the NIR induced isomerization is indeed reversible. Similar bidirectional large-scale NIR-induced interconversions between the *syn* and *anti* **6MOI** conformers could also be induced for the compound isolated in an argon matrix at 16 K (see SI, Figures S4 and S5).

The conformational mixture, whether it was enriched in either *syn* or *anti* forms, was found to be thermally stable in dark under conditions of the experiment, i.e., both in argon matrix at 16 K and in xenon matrix at 30 K.²⁶ Mechanistically, the fact that selective excitation is bidirectional can be explained as follows. Whichever conformer is excited, the relaxation can then occur to any of the two conformers. However, exciting repeatedly only one chosen conformer (several minutes of excitation with relaxation times of nanoseconds) will eventually depopulate the form under excitation.²⁷

In conclusion, this communication reports the first experimental observation of a selective and reversible conformational interconversion induced by excitation of a stretching overtone of an NH group. Remarkably, this process takes place at a remote fragment (OCH_3 group) that is separated from the excited (NH) group by four covalent bonds. The observed processes are nondestructive and take place in large-scale, proving the efficiency of the intramolecular vibrational relaxation to carry the energy deposited in the

distant NH stretching coordinate into the reactive C–O torsional mode. We believe that similar effects should work in other molecules but just have not been reported yet. We hope that this investigation may contribute to expanding our knowledge on fundamental energetic, mechanistic, and dynamical aspects of unimolecular reactions of vibrationally excited species,^{28,29} which is a research area with relevance for the sunlight-driven atmospheric photochemistry.

■ ASSOCIATED CONTENT

📄 Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b08588.

Table of relative energies, optimized Cartesian coordinates, and calculated harmonic and anharmonic infrared spectra of the two conformers, as well as the calculated torsional barrier separating the two forms. Comparative experimental infrared and near-infrared spectra of **6MOI** isolated in argon and xenon matrixes for freshly deposited samples, as well as the changes in the experimental spectra of matrix-isolated **6MOI** induced by near-infrared irradiations (PDF)

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Notes

The authors declare no competing financial interest.

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REFERENCES

- (1) Hall, R. T.; Pimentel, G. C. *J. Chem. Phys.* **1963**, *38*, 1889.
- (2) Pettersson, M.; Lundell, J.; Khriachtchev, L.; Räsänen, M. *J. Am. Chem. Soc.* **1997**, *119*, 11715.
- (3) Maçôas, E. M. S.; Khriachtchev, L.; Pettersson, M.; Fausto, R.; Räsänen, M. *J. Am. Chem. Soc.* **2003**, *125*, 16188.
- (4) Halasa, A.; Lapinski, L.; Reva, I.; Rostkowska, H.; Fausto, R.; Nowak, M. J. *J. Phys. Chem. A* **2014**, *118*, 5626.
- (5) Maçôas, E. M. S.; Fausto, R.; Pettersson, M.; Khriachtchev, L.; Räsänen, M. *J. Phys. Chem. A* **2000**, *104*, 6956.
- (6) Maçôas, E. M. S.; Khriachtchev, L.; Pettersson, M.; Fausto, R.; Räsänen, M. *J. Phys. Chem. A* **2005**, *109*, 3617.
- (7) Reva, I.; Nunes, C. M.; Biczysko, M.; Fausto, R. *J. Phys. Chem. A* **2015**, *119*, 2614.
- (8) Araujo-Andrade, C.; Reva, I.; Fausto, R. *J. Chem. Phys.* **2014**, *140*, 064306.
- (9) Halasa, A.; Lapinski, L.; Reva, I.; Rostkowska, H.; Fausto, R.; Nowak, M. J. *J. Phys. Chem. A* **2015**, *119*, 1037.
- (10) Coussan, S.; Bouteiller, Y.; Perchard, J. P.; Zheng, W. Q. *J. Phys. Chem. A* **1998**, *102*, 5789.
- (11) Bazsó, G.; Magyarfalvi, G.; Tarczay, G. *J. Phys. Chem. A* **2012**, *116*, 10539.
- (12) Bazsó, G.; Najbauer, E. E.; Magyarfalvi, G.; Tarczay, G. *J. Phys. Chem. A* **2013**, *117*, 1952.
- (13) Nunes, C. M.; Lapinski, L.; Fausto, R.; Reva, I. *J. Chem. Phys.* **2013**, *138*, 125101.
- (14) Kuş, N.; Sharma, A.; Peña, I.; Bermúdez, M. C.; Cabezas, C.; Alonso, J. L.; Fausto, R. *J. Chem. Phys.* **2013**, *138*, 144305.
- (15) Lapinski, L.; Nowak, M. J.; Reva, I.; Rostkowska, H.; Fausto, R. *J. Phys. Chem. Chem. Phys.* **2010**, *12*, 9615.
- (16) Reva, I.; Nowak, M. J.; Lapinski, L.; Fausto, R. *J. Chem. Phys.* **2012**, *136*, 064511.
- (17) Lapinski, L.; Reva, I.; Rostkowska, H.; Fausto, R.; Nowak, M. J. *J. Phys. Chem. B* **2014**, *118*, 2831.
- (18) Sharma, A.; Reva, I.; Fausto, R. *J. Am. Chem. Soc.* **2009**, *131*, 8752.
- (19) Lapinski, L.; Reva, I.; Rostkowska, H.; Halasa, A.; Fausto, R.; Nowak, M. J. *J. Phys. Chem. A* **2013**, *117*, 5251.
- (20) There are only a few studies of NH-containing molecules (pyrrole and dimethylamine), reporting their experimental infrared spectra in the NH stretching overtone range. See, for example, Miller, B. J.; Du, L.; Steel, T. J.; Paul, A. J.; Södergren, A. H.; Lane, J. R.; Henry, B. R.; Kjaergaard, H. G. *J. Phys. Chem. A* **2012**, *116*, 290.
- (21) Brand, C.; Oeltermann, O.; Wilke, M.; Schmitt, M. *J. Chem. Phys.* **2013**, *138*, 024321.
- (22) Lopes Jesus, A. J.; Redinha, J. S. *Struct. Chem.* **2015**, *26*, 655.
- (23) Reva, I. D.; Jarmelo, S.; Lapinski, L.; Fausto, R. *J. Phys. Chem. A* **2004**, *108*, 6982.
- (24) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09*, revision D.01; Gaussian, Inc.: Wallingford, CT, 2009.
- (25) The $2\nu_{\text{NH}}$ overtone range in the experimental spectra of **6MOI** isolated in an argon matrix (see Figure S3 of the SI), similar to the ν_{NH} fundamental range (shown in Figure S2 of the SI), appears as multiplet bands. We attribute these splittings as resulting from both conformational effects (presence of two conformers in the matrix) and site-splitting effects (different local environments for each conformer).
- (26) The *anti* \rightarrow *syn* thermal conversion could be induced by annealing the matrix-isolated **6MOI** up to temperatures of 50 K. The spectral changes were similar to those induced by NIR irradiations at 6856 cm^{-1} , as shown in Figure 3c. Such effect was only possible to be detected in the case of xenon matrixes because solid argon can only be conserved up to temperatures no higher than 40 K.
- (27) Such NIR-induced isomerizations may occur for other molecules, but should not be generalized. Recently some of us have experimentally studied two matrix-isolated isomers of phenylnitrile imine. See Nunes, C. M.; Reva, I.; Fausto, R.; Bégué, D.; Wenstrup, C. *Chem. Commun.* **2015**, *51*, 14712. Phenylnitrile imine can adopt allenic and propargylic forms, which are almost isoenergetic and are separated by a very small energy barrier. These two species have relatively intense infrared absorptions in the $2\nu_{\text{NH}}$ overtone range of spectrum, with calculated IR intensities of 14.6 and 12.6 km mol^{-1} , respectively. The attempts to convert these two species of phenylnitrile imine into one another by NIR induced excitations, tuned at the respective overtone, were not successful. Therefore, the occurrence, or lack of it, of the NIR-induced conformational interconversion cannot be directly related with the energy difference between the two conformers, or the energy barrier separating them.
- (28) Vaida, V.; Donaldson, D. J. *J. Phys. Chem. Chem. Phys.* **2014**, *16*, 827.
- (29) Donaldson, D. J.; George, C.; Vaida, V. *Environ. Sci. Technol.* **2010**, *44*, 5321.

NOTE ADDED IN PROOF

Recently a paper reporting rotamerization in thiocytosine induced by near-IR selective excitation of NH_2 stretching overtones was published by A. Halasa, L. Lapinski, H. Rostkowska, and M. J. Nowak. See *J. Phys. Chem. A* **2015**, *119*, 9262–9271. DOI: 10.1021/acs.jpca.5b06221.