Electronic Supplementary Information

Conformational control over an aldehyde fragment by selective vibrational excitation of interchangeable remote antennas

António Jorge Lopes Jesus,[a,b] Cláudio M. Nunes,[a] Rui Fausto[a] and Igor Reva[a,*]

[a] *CQC, Department of Chemistry, University of Coimbra, 3004-535, Coimbra, Portugal.*

[b] *CQC, Faculty of Pharmacy, University of Coimbra, 3004-295, Coimbra, Portugal.*

* Corresponding author E-mail address: reva@qui.uc.pt

Contents

Experimental Section

Matrix-isolation of 3-substituted isoxazoles

Commercial samples of 3-amino-isoxazole (**1**, Aldrich, purity > 95%) and 3-hydroxy-isoxazole (**2**, Paragos e.K., purity > 95%) were used in the matrix-isolation experiments. A small quantity of the chosen compound was introduced into a glass tube which was connected through a needle valve to the vacuum system of a closed-cycle helium cryostat (APD Cryogenics, with a DE-202A expander), which is described elsewhere.[1] Before the experiment, air and volatile impurities were pumped out through the cryostat. In order to reduce the vapor pressure of the compounds and improve the metering function of the needle valve, the glass tube was immersed into an ice-water bath ($T \sim 0$ °C). Vapours of the chosen compound (**1** or **2**) were co-deposited with a large excess of argon (N60, supplied by Air Liquide) onto a CsI window cooled to 15 K. The temperature of the CsI window was measured directly at the sample holder by means of a silicon diode sensor connected to a digital controller (Scientific Instruments, Model 9650-1, accuracy of ± 0.1 K).[1]

Irradiations in the Near-Infrared and UV-regions

The two compounds of interest for the present study: 3-amino-2-formyl-2*H*-azyrine (**3**) and 3-hydroxy-2-formyl-2*H*-azyrine (**4**) were photogenerated *in situ* by irradiating the corresponding matrix-isolated 3-substituted isoxazoles: **1** and **2**, with UV-laser light tuned at 228 and 224 nm, respectively. These wavelengths were selected taking into account the results previously obtained for the photochemistry of matrix-isolated isoxazole[2] and 3,5-dimethyl-isoxazole.[3] The irradiations were performed through the outer quartz window of the cryostat by using monochromatic UV-radiation provided by the frequency-doubled signal beam of a Quanta-Ray MOPO-SL optical parametric oscillator (OPO): 0.2 cm^{-1} spectral width, pulse energy 2-10 mJ. The OPO was pumped with a pulsed Nd:YAG laser. The pulse duration time and repetition rate were, respectively, 10 ns and 10 Hz. The time of exposition of the sample to UV-light varied from 3 to 12 minutes. Irradiations in the near-infrared region were also performed after the photogeneration of **3** and **4** by using the idler beam of the same OPO. In this case, the time of exposition of the sample to NIR laser-light tuned at a given selected wavenumber varied between 30 minutes and 7 hours.

IR-spectroscopy

IR-spectroscopy was used to identify the matrix-isolated compounds and to monitor the changes occurring in these compounds during the UV- or NIR-irradiations. Spectra of the matrix isolated compounds in the near-infrared and mid-infrared regions were recorded using a Thermo Nicolet 6700 Fourier-transform infrared (FTIR) spectrometer. The mid-IR spectra were recorded with a resolution of 0.5 cm^{-1}, using an FTIR spectrometer equipped with a deuterated triglycine sulfate (DTGS) detector and a Ge/KBr beam splitter, while the NIR spectra were recorded with a resolution of 1 cm^{-1}, using the same spectrometer with a mercury cadmium telluride (MCT-B) detector cooled with liquid nitrogen, and a CaF_2 beam splitter.

Computational Section

The geometries of **1** and **2**, as well as of the two conformers of **3** and of **4** (here denoted as **A** and **B**), were fully optimized, followed by harmonic vibrational calculation, by using the DFT (B3LYP)[4-6] approximation method and the standard 6-311++G(d,p) basis set. To correct for the vibrational anharmonicity, basis set truncation, neglected part of electron correlation and matrix shifts, the harmonic vibrational frequencies below 3100 cm^{-1} were multiplied by 0.980, while those above 3100 cm^{-1} were multiplied by 0.950. The scaled calculated harmonic frequencies and infrared intensities were then used to simulate the IR-spectra (shown in Figures 3a and 4a of the main text) by using the Chemcraft software.[7] Spectral convolution was performed with Lorentzian functions having a full width at half-maximum (FWHM) of 2 cm^{-1}, and by setting the intensity at the band maximum equal to the calculated absolute infrared intensity.

The harmonic vibrational calculations were followed by computations of anharmonic infrared spectra, at the same B3LYP/6-311++G(d,p) level, using a fully automated second-order vibrational perturbative approach of Barone and co-workers,[8, 9] allowing for the evaluation of anharmonic vibrational frequencies and anharmonic infrared intensities up to 2 quanta, including overtones and combination bands.[9-11]

The relative energies of conformers **A** and **B**, for both **3** and **4**, were additionally evaluated by using a Møller-Plesset correlation energy correction truncated at second-order (MP2) method,[12] as well as the quadratic configuration interaction with single and double excitations (QCISD) method[13] at geometries optimized at the respective (MP2 and QCISD) levels with the 6-311++G(3df,3pd) basis set. All calculations were executed with the GAUSSIAN 09 software.[14]

Electronic Supplementary Information References:

1. I. D. Reva, S. G. Stepanian, L. Adamowicz and R. Fausto, *J. Phys. Chem. A*, 2001, **105**, 4773-4780.
2. C. M. Nunes, I. Reva, T. M. V. D. Pinho e Melo and R. Fausto, *J. Org. Chem.*, 2012, **77**, 8723-8732.
3. C. M. Nunes, I. Reva and R. Fausto, *J. Org. Chem.*, 2013, **78**, 10657-10665.
4. A. D. Becke, *Phys. Rev. A*, 1988, **38**, 3098-3100.
5. C. T. Lee, W. T. Yang and R. G. Parr, *Phys. Rev. B*, 1988, **37**, 785-789.
6. S. H. Vosko, L. Wilk and M. Nusair, *Can. J. Phys.*, 1980, **58**, 1200-1211.
7. G. A. Zhurko, CHEMCRAFT, *Version 1.8*, 2016. http://www.chemcraftprog.com (last accessed on February 6, 2018).
8. V. Barone, *J. Chem. Phys.*, 2005, **122**, 014108.
9. J. Bloino and V. Barone, *J. Chem. Phys.*, 2012, **136**, 124108.
10. V. Barone, M. Biczysko and J. Bloino, *Phys. Chem. Chem. Phys.*, 2014, **16**, 1759-1787.
11. V. Barone, J. Bloino, C. A. Guido and F. Lipparini, *Chem. Phys. Lett.*, 2010, **496**, 157-161.
12. C. Møller and M. S. Plesset, *Physical Review*, 1934, **46**, 0618-0622.
13. J. A. Pople, M. Head-Gordon and K. Raghavachari, *J. Chem. Phys.*, 1987, **87**, 5968-5975.
14. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T.Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. J. A. Montgomery, J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski and D. J. Fox, GAUSSIAN 09, *Revision D.01*, Gaussian, Inc.: Wallingford CT, 2013.

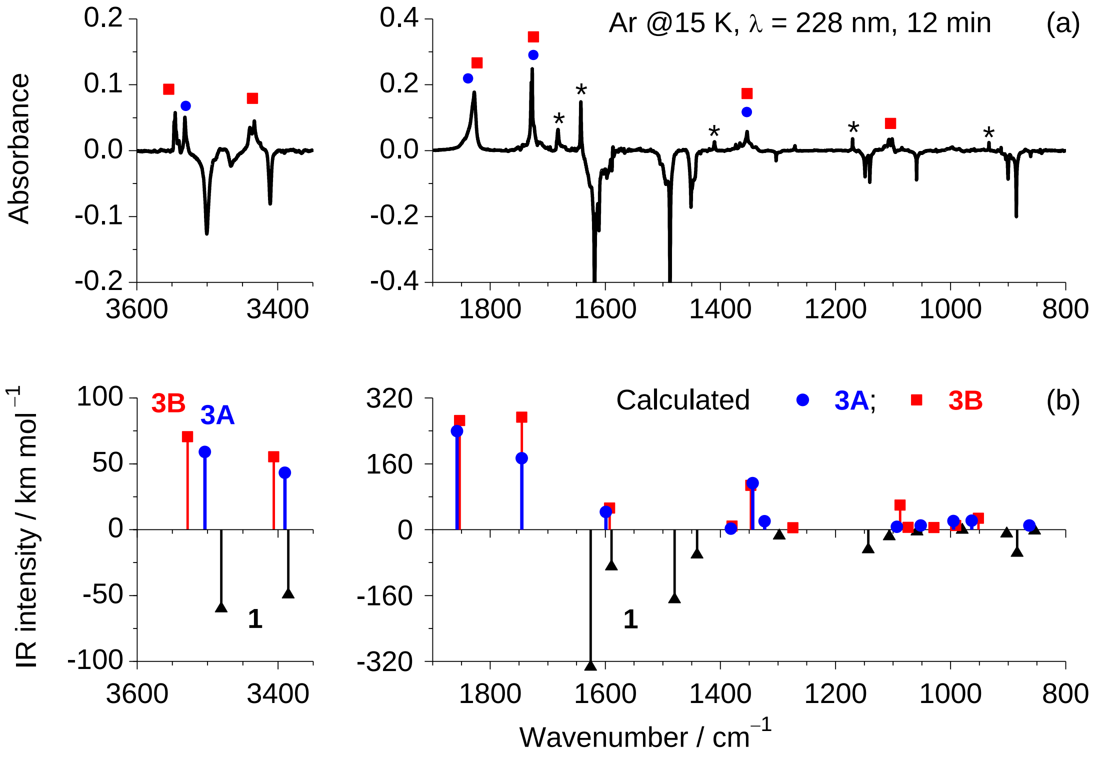


Figure S1. (a) Difference mid-IR spectrum obtained by subtracting the spectrum of 3-amino-isoxazole (**1**) isolated in an argon matrix at 15 K from that registered after UV (λ = 228 nm) irradiation of the sample for 12 minutes. Positive bands marked by blue circles and red squares are assigned to photogenerated **3A** and **3B**, while those marked with asterisks are assigned to other photoproducts of **1** whose characterization is beyond the scope of the present study. Negative bands are due to consumed **1**; (b) Mid-IR spectra calculated at the B3LYP/6-311++G(d,p) level for **3A** (blue, ●), **3B** (red, ■), and for **1** (black, ▲; intensities scaled by −2). The calculated wavenumbers were scaled by 0.95 and 0.98 above and below 3100 cm^{-1}, respectively.

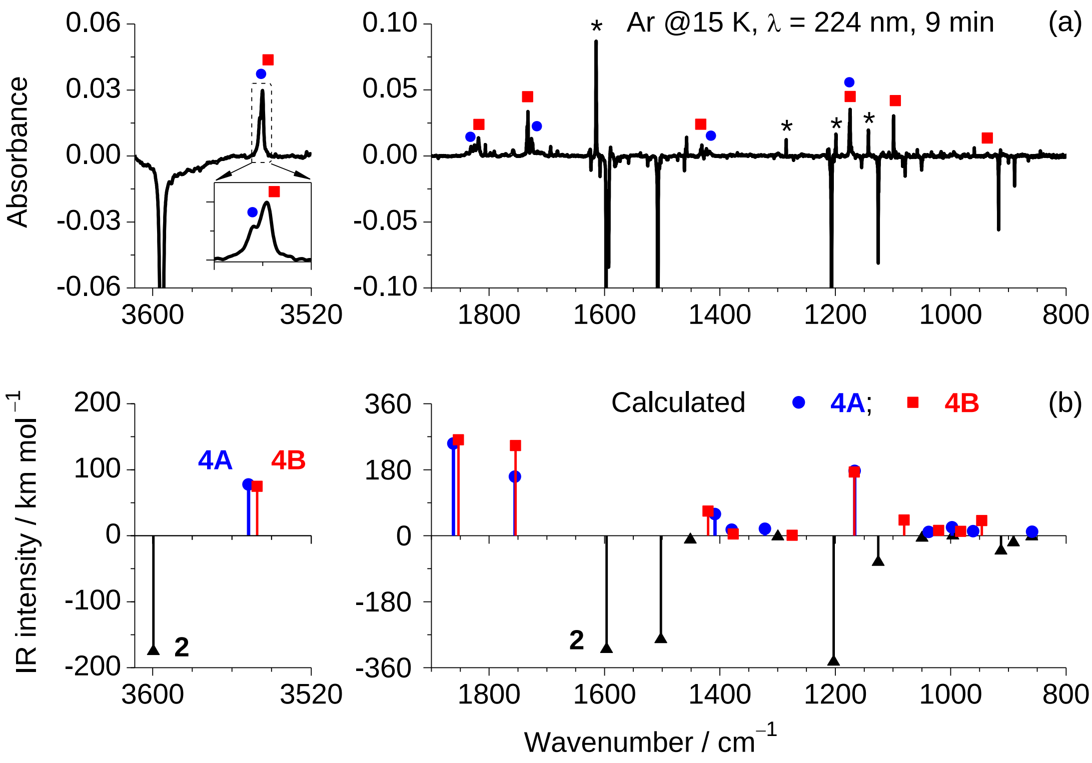


Figure S2. (a) Difference mid-IR spectrum obtained by subtracting the spectrum of 3-hydroxy-isoxazole (**2**) isolated in an argon matrix at 15 K from that registered after UV (λ = 224 nm) irradiation of the sample for 9 minutes. Positive bands marked by blue circles and red squares are assigned to photogenerated **4A** and **4B**, while those marked with asterisks are assigned to other photoproducts of **2** whose characterization is beyond the scope of the present study. Negative bands are due to consumed **2**; (b) Mid-IR spectra calculated at the B3LYP/6-311++G(d,p) level for **4A** (blue, ●), **4B** (red, ■), and for **2** (black, ▲; intensities scaled by −2). The calculated wavenumbers were scaled by 0.95 and 0.98 above and below 3100 cm^{-1}, respectively.

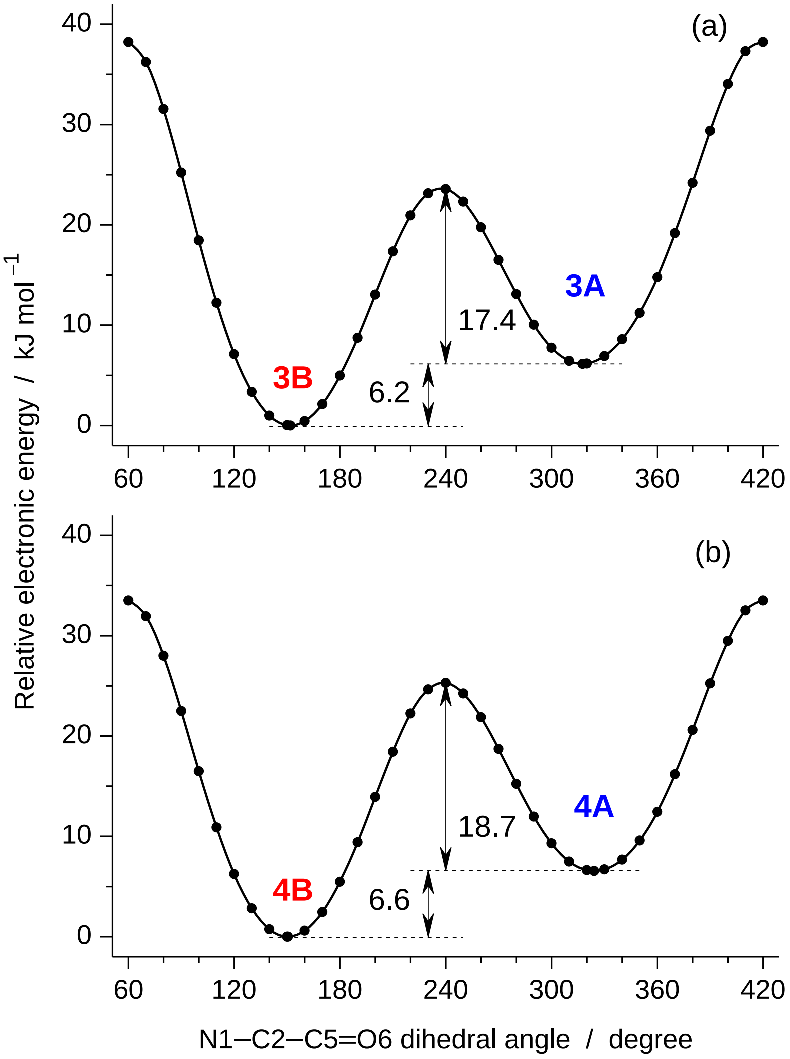


Figure S3. Relaxed potential energy scans for the internal torsion of the formyl group in (a) 3-amino-2-formyl-2*H*-azirine **3** and (b) 3-hydroxy-2-formyl-2*H*-azirine **4**, calculated at the MP2/6-311++G(3df,3pd) level. The N1−C2−C5=O6 dihedral angle was incrementally fixed, while all other internal coordinates were fully optimized. The energies of forms **3B** (frame a) and **4B** (frame b) were selected as relative zeroes. The absolute energies of the global minima are (**3B**): $E_{MP2} = -300.84134302\ E_h$; and (**4B**): $E_{MP2} = -320.69354598\ E_h$. For conformers **3A** and **4A** the C5=O6 bond of the formyl group is synperiplanar, whereas for **3B** and **4B** it is antiperiplanar with respect to the bisector of the N1−C2−C3 angle (i.e., with respect to the 3-membered azirine ring). See Table S3 for the atom numbering scheme.

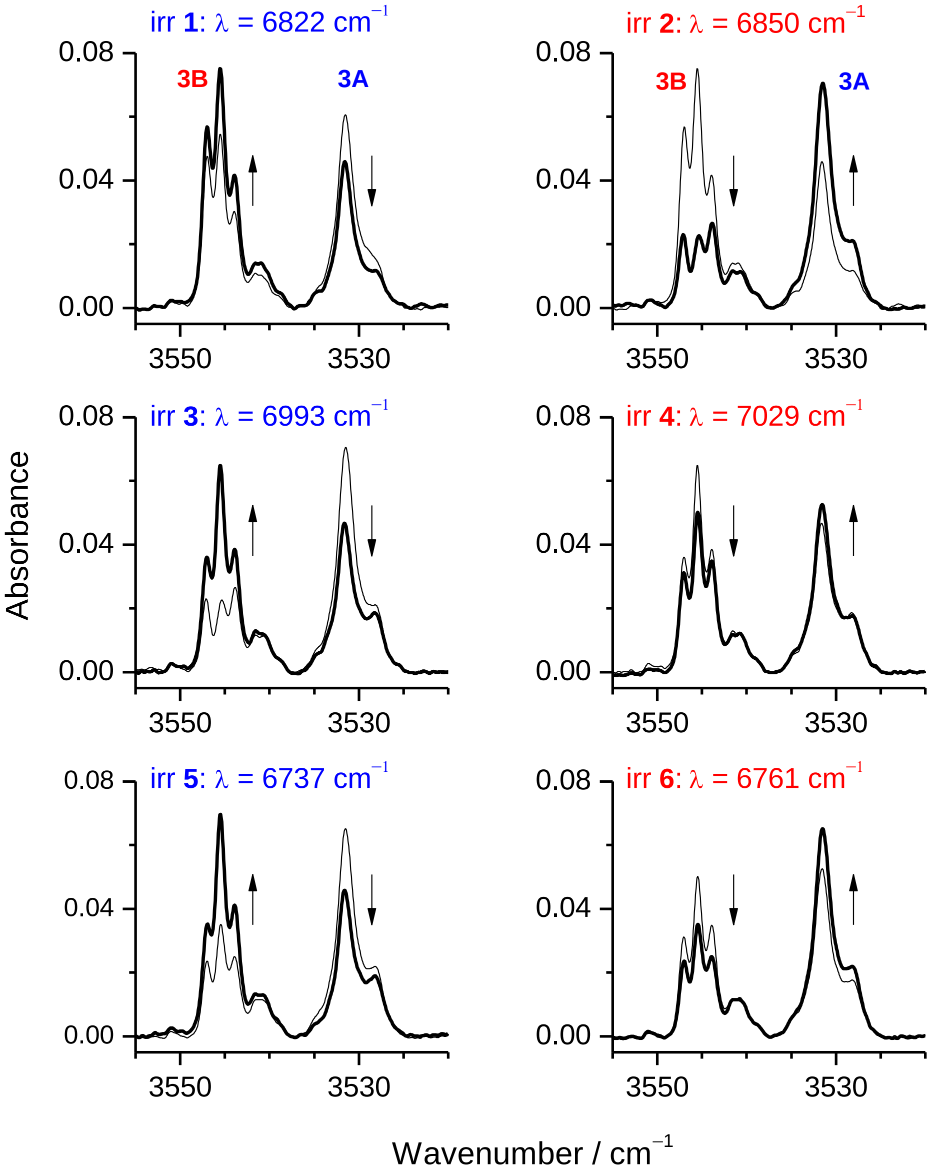


Figure S4. Changes in the intensity of the IR bands ascribed to the antisymmetric NH_2 stretching vibrations (ν_aNH_2) of conformers **3B** (~ 3545 cm^{-1}) and **3A** (~ 3532 cm^{-1}), resulting from different NIR excitations of **3** (isolated in an Ar matrix at 15 K). In each frame, the spectra represented by thin and bold traces were recorded, respectively, before and after the irradiation at the wavenumber indicated on top of the frame (arrows represent the direction of the intensity changes upon the irradiation). Irradiations **1**, **3** and **5** resulted in the **3A** → **3B** conversion, while irradiations **2**, **4** and **6** resulted in the **3B** → **3A** conversion.

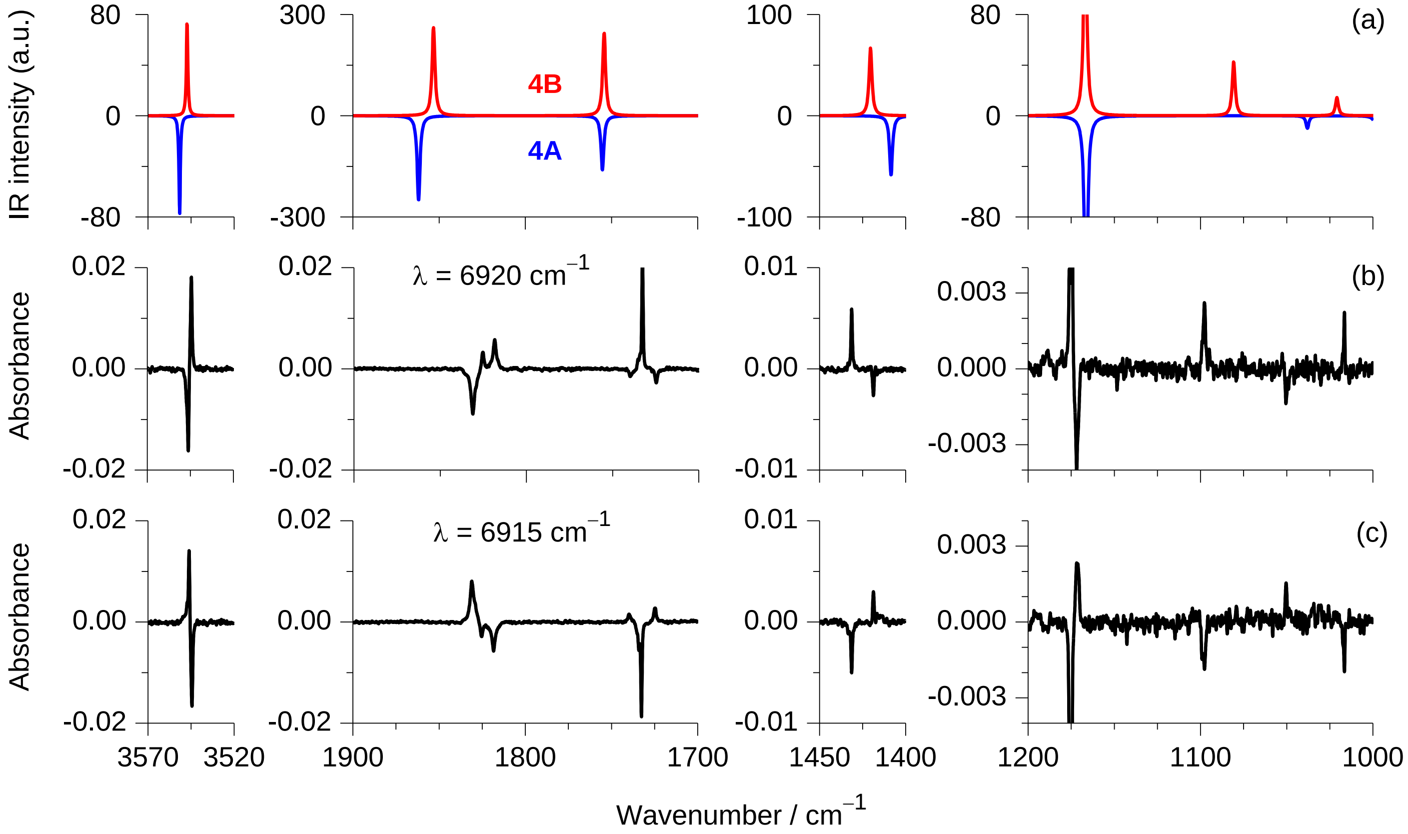


Figure S5. (a) Simulated IR spectra for conformers **4A** (blue, intensities multiplied by −1) and **4B** (red) using the results of the harmonic vibrational calculations performed at the B3LYP/6-311++G(d,p) level of theory. Details of the simulations are given in the computational section; (b) Spectral changes resulting from irradiation at 6920 cm^{-1} of **4** isolated in an Ar matrix at 15 K. (c) Spectral changes resulting from irradiation at 6915 cm^{-1} of **4** isolated in an Ar matrix at 15 K. The positive bands correspond to those growing upon the NIR irradiation. The strong bands near 1170 cm^{-1} are truncated.

Table S1. Experimental IR spectral signature of 3-amino-2-formyl-2*H*-azirine (**3**) isolated in an argon matrix at 15 K and B3LYP/6-311++G(d,p) calculated harmonic vibrational wavenumbers ($\tilde{\nu}$ / cm^{-1}) and infrared intensities (I / km mol^{-1}) for the two conformers of this molecule.

Experimental, Ar (15 K) [a]	Calc. (conf. **3A**) [b]		Calc. (conf. **3B**) [b]		Approximate description [c]
	$\tilde{\nu}$	I	$\tilde{\nu}$	I	
3532 / 3545	3503.8	59.0	3528.3	70.5	ν_aNH$_2$
3410 / 3440	3390.2	43.2	3405.9	55.3	ν_sNH$_2$
	3049.8	30.0	3061.6	13.7	νC2H
2826 / 2817	2832.0	141.7	2832.1	79.5	νC5H
1831 / 1827	1857.6	239.2	1853.0	265.0	νC=N
1724 / 1727	1745.1	173.3	1745.2	273.0	νC=O
1591 / 1587	1599.0	43.0	1592.4	52.3	δNH$_2$
			1379.8	8.8	δC5H
1338 / 1353	1343.9	112.8	1347.2	107.3	νC2C3
	1323.1	20.5			δC2H
– / 1106			1087.7	59.4	νC2C5
	1093.3	6.9	1073.9	5.6	ρNH$_2$
	1051.9	9.8	1028.9	5.0	νC3−N4
997 / 959	994.9	20.6	951.6	27.4	γC2H + γC5H iop
964 / 985	963.4	21.5	991.0	10.0	γC2H + γC5H isp
871 / –	863.1	10.0			δCCC
752 / –	743.8	28.2			δCC=O + δN=CN
	634.8	13.7	644.3	7.5	νC2−N1

[a] The identification of the bands assigned to the photogenerated species **3** was based on the comparison of the spectral changes induced by the UV-irradiations at λ = 228 nm carried out on matrix isolated **1** (see Figure S1) and of the spectral changes induced by the NIR-irradiations after the photoproduction of **3** (see Figure 3 in the main text) with the spectra calculated for the two conformers of **3**. The spectral modifications resulting from the NIR irradiations were particularly useful in the identification of bands of **3** overlapped with bands of **1** and in the identification of features assigned to conformers **3A** and **3B**. Wavenumbers before and after the slash are assigned to conformers **3A** and **3B**, respectively. [b] Calculated wavenumbers scaled by 0.95 and 0.98, above and below 3100 cm^{-1}, respectively. Only the vibrations having calculated frequencies above 600 cm^{-1} and infrared intensities above 5 km mol^{-1} are included.[c] Based on ChemCraft animations of the vibrations of conformers **3A** and **3B**. Abbreviations: ν, stretching; δ, in-plane deformation; γ, out-of-plane deformation; ρ, rocking; tw, twisting; ω, wagging; τ, torsion; s, symmetric; a, antisymmetric; isp, in the same phase; iop, in the opposite phase. Assignments for conformers **3A** and **3B** are common.

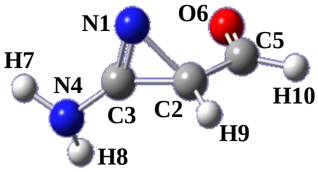
Table S2. Experimental IR spectral signature of 3-hydroxy-2-formyl-2*H*-azirine (**4**) isolated in an argon matrix at 15 K and B3LYP/6-311++G(d,p) calculated harmonic vibrational wavenumbers ($\tilde{\nu}$ / cm^{-1}) and infrared intensities (I / km mol^{-1}) for the two conformers of this molecule.

Experimental, Ar (15 K) [a]	Calc. (conf. **4A**) [b]		Calc. (conf. **4B**) [b]		Approximate description [c]
	$\tilde{\nu}$	I	$\tilde{\nu}$	I	
3546 / 3544	3551.6	77.7	3547.3	74.8	νOH
	3064.8	19.9	3079.4	6.6	νC2H
2833 / 2833	2843.0	127.0	2840.0	73.5	νC5H
1831 / 1818	1861.9	251.3	1853.2	261.3	νC=N
1740,1725 / 1733	1755.3	161.1	1754.3	245.7	νC=O
1419 / 1431	1408.5	58.9	1420.4	66.9	νC2C3 + δOH
1382 / –	1379.5	16.2	1376.9	4.7	δC5H
1329 / –	1322.0	18.6	1274.6	0.9	δC2H
1172 / 1174	1166.4	176.8	1166.9	173.6	δOH
1051 / 1098	1038.0	9.9	1080.8	42.7	νC3−O / νC2C5
– / 1016	997.5	22.7	1020.9	14.4	νC2C5 / γC2H+ γC5H iop
– / 970	961.0	12.2	982.5	11.7	γC2H + γC5H isp
– / 936	858.7	10.5	946.1	41.1	δCCC / νC3−O
763, 756	750.7	20.6			δCC=O + δN=CO
597 / 633	608.1	57.8	634.8	44.3	νC2−N + δNCO
540 / 558	556.4	71.6	574.7	42.1	γC−O

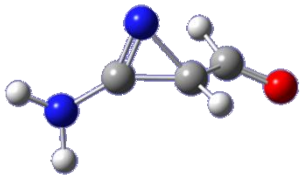
[a] The identification of the bands assigned to the photogenerated species **4** was based on the comparison of the spectral changes induced by the UV-irradiations at λ = 224 nm carried out on matrix isolated **2** (see Figure S2) and of the spectral changes induced by the NIR-irradiations after the photoproduction of **4** (see Figure 4 in the main text) with the spectra calculated for the two conformers of **4**. The spectral modifications resulting from the NIR irradiations were particularly useful in the identification of bands of **4** overlapped with bands of **2** and in the identification of features assigned to conformers **4A** and **4B**. Wavenumbers before and after the slash are assigned to conformers **4A** and **4B**, respectively. [b] Calculated wavenumbers scaled by 0.95 and 0.98, above and below 3100 cm^{-1}, respectively. Only the vibrations having calculated frequencies above 500 cm^{-1} are included. [c] Based on ChemCraft animations of the vibrations of conformers **4A** and **4B**. Abbreviations: ν, stretching; δ, in-plane deformation; γ, out-of-plane deformation; τ, torsion; s, symmetric; a, antisymmetric; isp, in the same phase; iop, in the opposite phase. Assignments before and after the slash (if it is present) correspond to conformers **4A** and **4B**, respectively, otherwise the assignments are common.

Table S3. Optimized geometries of the conformers of 3-amino-2-formyl-2*H*-azirine (**3**) and 3-hydroxy-2-formyl-2*H*-azirine (**4**), relative electronic energies (ΔE_{el}), and values of selected dihedral angles optimized at the QCISD/6-311++G(3df,3pd) level of theory.[a]

3-amino-2-formyl-2*H*-azirine (**3**)



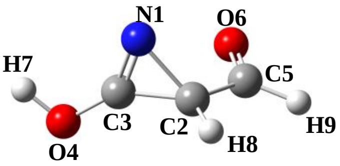
3A



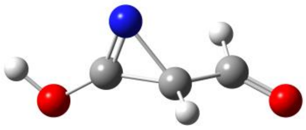
3B [b]

	3A	**3B** [b]
ΔE_{el} / kJ mol^{-1}	6.2	0.0
Dihedral angle / °		
N4–C3=N1–C2	175.766	-177.075
N1–C2–C5=O6	-45.396	154.103
C3–C2–C5=O6	10.725	-149.869
N4–C3–C2–C5	83.676	77.839
H7–N4–C3=N1	20.520	-17.532
H8–N4–C3=N1	158.824	-164.817
H9–C2–C5=O6	171.952	10.748
H9–C2–C5–H10	-7.905	-168.123

3-hydroxy-2-formyl-2*H*-azirine (**4**)



4A



4B [c]

	4A	**4B** [c]
ΔE_{el} / kJ mol^{-1}	6.8	0.0
Dihedral angle / °		
O4–C3=N1–C2	-179.363	178.882
N1–C2–C5=O6	-37.086	152.311
C3–C2–C5=O6	18.204	-152.688
O4–C3–C2–C5	80.186	83.536
H7–O4–C3=N1	2.673	-0.184
H8–C2–C5=O6	-178.756	10.657
H8–C2–C5–H9	1.136	-168.592

[a] Atom numbering schemes are shown for conformers **3A** and **4A**. The Cartesian coordinates corresponding to the optimized geometries are shown in Table S4;

[b] Absolute energy (**3B**): $E_{QCISD} = -300.8551998\ E_h$;

[c] Absolute energy (**4B**): $E_{QCISD} = -320.7025510\ E_h$.

Table S4. QCISD/6-311++G(3df,3pd) optimized Cartesian coordinates for the conformers of 3-amino-2-formyl-2*H*-azirine (**3**) and 3-hydroxy-2-formyl-2*H*-azirine (**4**)

3A

```
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          7           0        0.544656    1.049494    0.785944
      2          6           0       -0.281226    0.752100   -0.494500
      3          6           0        0.940247    0.159788   -0.004096
      4          7           0        1.942304   -0.711089   -0.243222
      5          6           0       -1.570789    0.027037   -0.294260
      6          8           0       -1.682894   -0.940494    0.418405
      7          1           0        2.518613   -0.940367    0.550804
      8          1           0        1.712019   -1.490057   -0.834935
      9          1           0       -0.267269    1.522864   -1.258248
     10          1           0       -2.438319    0.429131   -0.846773
```

3B

```
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          7           0       -0.758390    1.278380   -0.187499
      2          6           0        0.264308    0.321916    0.491105
      3          6           0       -1.092570    0.092669    0.054149
      4          7           0       -2.087609   -0.800770   -0.087286
      5          6           0        1.404999   -0.104384   -0.362862
      6          8           0        2.478044   -0.442241    0.070953
      7          1           0       -3.005033   -0.444937   -0.296750
      8          1           0       -2.044960   -1.634871    0.468848
      9          1           0        0.491788    0.491097    1.538174
     10          1           0        1.195419   -0.077833   -1.448752
```

4A

```
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          8           0       -1.731357   -0.889419    0.395041
      2          6           0       -1.561393    0.058034   -0.329083
      3          6           0       -0.248148    0.766657   -0.455374
      4          7           0        0.582503    0.901093    0.875167
      5          6           0        0.954694    0.119579   -0.021304
      6          1           0       -2.381738    0.461586   -0.947567
      7          1           0       -0.213614    1.621327   -1.121952
      8          8           0        1.877177   -0.760181   -0.347516
      9          1           0        2.480361   -0.859383    0.397717
```

4B

```
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          8           0        2.492296   -0.381039    0.079005
      2          6           0        1.403823   -0.114816   -0.361351
      3          6           0        0.251260    0.296520    0.489351
      4          7           0       -0.810334    1.223886   -0.228743
      5          6           0       -1.094239    0.045231    0.062647
      6          1           0        1.185229   -0.145375   -1.444946
      7          1           0        0.478789    0.521537    1.524915
      8          8           0       -2.057880   -0.851232    0.017057
      9          1           0       -2.832071   -0.446797   -0.391151
 ---------------------------------------------------------------------
```