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**Photofragment Translational Spectroscopy Studies of H Atom Loss Following
Ultraviolet Photoexcitation of Methimazole in the Gas Phase**

Graham A. Cooper,¹ Christopher S. Hansen,² Tolga N.V. Karsili ³ and Michael N.R. Ashfold^{1*}

¹ School of Chemistry, University of Bristol, Bristol, BS8 1TS, U.K.

² School of Chemistry, University of New South Wales, Sydney, NSW 2052, Australia

³ Department of Chemistry, University of Louisiana at Lafayette, LA 70504, U.S.

*Author to whom correspondence should be addressed

Abstract

The ultraviolet (UV) photodissociation of gas phase methimazole has been investigated by H Rydberg atom photofragment translational spectroscopy methods at many wavelengths in the range 222.5 – 275 nm and by complementary electronic structure calculations. Methimazole is shown to exist predominantly as the thione tautomer, 1-methyl-2(3H)-imidazolinethione, rather than the commonly given thiol form, 2-mercapto-1-methylimidazole. The UV absorption spectrum of methimazole is dominated by the $S_4 \leftarrow S_0$ transition of the thione tautomer, which involves electron promotion from an a' (p_y) orbital localized on the sulfur atom to a σ^* orbital localized around the N–H bond. Two H atom formation pathways are identified following UV photoexcitation. One, involving prompt, excited state N–H bond fission, yields vibrationally cold but rotationally excited methimazolyl (Myl) radicals in their first excited ($\tilde{A}$) electronic state. The second yields H atoms with an isotropic recoil velocity distribution peaking at low kinetic energies but extending to the energetic limit allowed by energy conservation given a ground state dissociation energy $D_0(\text{Myl-H}) \sim 24\,000\text{ cm}^{-1}$. These latter H atoms are attributed to the unimolecular decay of highly vibrationally excited S_0 parent molecules. The companion electronic structure calculations provide rationales for both fragmentation pathways and the accompanying product energy disposals, and highlight similarities and differences between the UV photochemistry of methimazole and that of other azoles (*e.g.* imidazole) and with molecules like thiourea and thiouracil that contain similar N–C=S motifs.

1. Introduction

Prototypical nitrogen-containing heterocycles have featured prominently in recent studies of non-adiabatic effects in the decay of electronically excited molecules.¹⁻⁶ Pyrrole (fig. 1(a)), for example, has been investigated experimentally by gas phase photofragment translational spectroscopy (PTS),⁷⁻¹¹ and by time-resolved pump-probe photofragment ion imaging^{12,13} and photoelectron spectroscopy methods.¹⁴⁻¹⁶ The H Rydberg atom (HRA)-PTS studies confirmed N–H bond fission as the dominant primary process following photoexcitation of pyrrole (fig. 1(a)) within its weak, long wavelength absorption band ($260 \geq \lambda \geq 210$ nm) and showed that the partner pyrrolyl fragments are formed in just a few vibrational (ν) levels of the ground ($\tilde{X}^2A_2$) electronic state, and with minimal rotational excitation. The recoil velocity distributions of the H + pyrrolyl(ν) products are anisotropic; N–H bond fission in the photoexcited pyrrole molecule occurs promptly, on a timescale that is short compared with the parent rotational period – a conclusion confirmed by the time-resolved photofragment imaging and photoelectron spectroscopy studies. More strikingly, the product recoil anisotropies are found to depend on the particular ν level into which pyrrole is excited. This unusual finding can be understood by recognizing that the $\sigma^* \leftarrow \pi$ ($^1A_2 \leftarrow \tilde{X}^1A_1$) parent absorption is electric dipole forbidden, but gains transition strength by vibronic coupling with other dipole-allowed, off-resonant excited electronic states.^{17,18} Theory has played equally important roles in advancing our understanding of the excited state photochemistry of pyrrole, in the form of high level electronic structure calculations,¹⁹⁻²¹ and a variety of approaches to treating the coupled electron-nuclear dynamics.²²⁻³⁷

The corresponding ultraviolet (UV) photochemistry of imidazole (fig. 1(b)) has received less attention. The additional N atom lowers the parent symmetry and ensures that the corresponding long wavelength $\sigma^* \leftarrow \pi$ ($^1A'' \leftarrow \tilde{X}^1A'$) excitation is electric dipole allowed (albeit with low oscillator strength).³⁸ HRA-PTS experiments³⁹ and time-resolved photofragment imaging studies,⁴⁰ as well as *ab initio* electronic structure calculations and fewest-switches surface-hopping simulations^{41,42} all show that N–H bond fission following $\sigma^* \leftarrow \pi$ excitation is prompt. As with pyrrole, the radical fragments are formed in a limited number of vibrational states. These all involve a' (*i.e.* in-plane) motions, as expected on symmetry grounds. The radical fragments are also formed with little rotational excitation. Such product energy disposal is unsurprising, given the similarities between the parent and radical ring vibrations, and the fact that any impulse

associated with N–H bond fission is directed at (in pyrrole) or very close to (in imidazole) the center of mass of the radical fragment.

Replacing one or more of the H atoms bonded to a C atom in pyrrole with an alkyl group offers another way of lowering the symmetry and boosting the long wavelength $\sigma^* \leftarrow \pi$ excitation cross-section, and HRA-PTS^{43,44} along with time-resolved photofragment ion^{45,46} or photoelectron imaging⁴⁷ studies have been reported for 2,4- and 2,5-dimethylpyrrole and 2-ethylpyrrole. Again, UV excitation is found to induce prompt N–H bond cleavage, and the resulting radical fragments are formed in just a few vibrational levels, all of which involve in-plane (a') ring-breathing motions.

Here we explore the UV photodissociation dynamics of methimazole (CAS number 60-56-0), also known as thiamazole and marketed as tapazole for use as an antithyroid drug for treating Graves' disease (hyperthyroidism).^{48,49} Despite being commonly described as 2-mercapto-1-methylimidazole (MMI) in the literature⁵⁰⁻⁵³ and sold as such by chemical suppliers such as Sigma-Aldrich (product code 301507), methimazole exists in a tautomeric equilibrium (see figs. 1(c) and 1(d)). In the solid phase, methimazole is comprised of dimeric units of the thione form, 1-methyl-2(3H)-imidazolinethione.^{52,54,55} The N–H proton is labile in solution,^{56,57} but the thione form again dominates the equilibrium,^{56,58} with one NMR study reporting (solvent dependent) mole fractions in the range 0.98-1.00.⁵⁷

Prior computational studies (second order Møller-Plesset perturbation theory (MP2) and Density Functional Theory (DFT)) have also shown the thione form to be favored energetically^{59,60} – a finding that is confirmed by the higher-level calculations reported here. The present work also compares and contrasts the UV photophysics displayed by methimazole with those of imidazole³⁹ and thiol-containing molecules. Like imidazole, N–H bond fission following electron promotion to a σ^* orbital is a major channel, and the resulting methimazolyl (1-methyl-2-imidazolinethionyl, henceforth Myl) fragments carry little vibrational excitation. In contrast to imidazole, however, these radical fragments are formed in their first excited ($\tilde{A}$) electronic state, and with substantial rotational excitation. None of the observed signal is definitively attributable to thiol S–H bond fission, though a broad signal that underlies the peaks attributed to H + Myl($\tilde{A}$) product formation and extends to higher fragment kinetic energies (henceforth termed the 'background' signal) is tentatively ascribed to one or more rival H atom loss processes following non-radiative transfer to

the parent ground state. All these dynamical outcomes are rationalized by complementary electronic structure calculations.

2 Methods

2.1 Experimental methods

Previous publications have detailed the HRA-PTS apparatus,^{8,61} so only information pertinent to the present experiments is summarized here. Methimazole is an involatile solid at room temperature and, for the present experiments, it was necessary to heat the sample ($\geq 99\%$ purity, Sigma-Aldrich [as 2-mercapto-1-methylimidazole]) in an inline filter to $\sim 250^\circ\text{C}$, well above its melting point. The resulting vapor was seeded in argon (CP grade, 3 bar backing pressure), expanded via a pulsed valve (General Valve, Series 9, using a Vespel poppet due to the high temperatures) and skimmed prior to entering the interaction region where the molecular beam was intersected by three laser beams. The first, from a frequency doubled tunable dye laser yielding wavelengths in the range 222.5 – 275 nm, induced photodissociation and H atom loss from the parent species. These $\text{H}(n=1)$ photofragments were then excited to the $n=2$ state by a suitably delayed ($\delta t \sim 10$ ns) photon at the Lyman- α wavelength (121.6 nm) and on to high- n Rydberg states by the third laser pulse at ~ 364.6 nm.

A weak electric field (~ 50 V cm^{-1}) across the interaction region serves to remove unwanted protons formed by the laser excitations. Rydberg-tagged atoms that recoil towards the detector travel through a drift tube, then pass through a grounded mesh in front of a microchannel plate detector, where they are field ionized and detected. The times of flight (TOFs) from the interaction region to the detector (the length of which was determined to be 0.610 m by measuring H atoms from the well-characterized UV photodissociation of H_2S^{62}) were recorded and used to calculate the velocity of the hydrogen atoms, and thus the total kinetic energy release (TKER) associated with the bond fission process. TOF spectra were recorded with the electric (ϵ) vector of the photolysis laser perpendicular to the TOF axis unless stated otherwise.

2.2 Computational methods

The ground state minimum energy geometry of the thione and thiol tautomers of methimazole were optimized using the Becke-3-parameter-Lee-Yang-Parr (B3LYP) functional of Density

Functional Theory,⁶³⁻⁶⁷ coupled to a 6-311G(d) Pople basis set (henceforth B3LYP/6-311G(d)).^{68,69} Potential energy profiles were computed in the C_s symmetry group along the N–H and S–H stretch coordinates for, respectively, the thione and thiol tautomers. These potential energy cuts (PECs) were calculated using complete active space with second-order perturbation theory (CASPT2),⁷⁰⁻⁷³ coupled to Dunning's augmented correlation-consistent basis set of double- ζ quality: aug-cc-pVDZ.^{74,75} An additional tight d -polarization function was added to the sulfur atom (henceforth aug(S)-AVDZ).⁷⁶ The CASPT2 computations were based on a state-averaged complete active space self-consistent field (SA-CASSCF) reference wavefunction comprising three A' and three A'' states.^{77,78} The active space consisted of 12 electrons distributed in 9 orbitals, comprising 4 ring-centered π -orbitals, 2 ring-centered π^* -orbitals, the highest occupied $p\sigma$ lone pair and the σ and σ^* orbitals. The relevant $p\sigma$ and σ/σ^* orbitals for the thione and thiol were, respectively, the in-plane S(3p) orbital and the σ/σ^* orbitals along the N–H bond, and the in-plane N(2p) orbital and the σ/σ^* orbitals along the S–H bond. All nine orbitals included in the calculations for the dominant thione tautomer are shown in Figure S1 of the Supplementary Information (SI). An imaginary level shift of $0.5E_H$ was used to mitigate the involvement of intruder states. Oscillator strengths for excitations from the ground state to the first four singlet excited states were computed using eq. (1):

$$f = \frac{2}{3}(E_j - E_i) \sum_{\alpha=x,y,z} |\hat{\mu}_{ij}|_{\alpha}^2 \quad (1)$$

where E_j (S_1 , S_2 , S_3 or S_4) and E_i (S_0) are the energies of the respective upper states and of the ground state, $\hat{\mu}_{ij}$ is the transition dipole moment associated with the given $j \leftarrow i$ electronic transition, and all quantities in eq. (1) are in atomic units. The radicals formed by N–H or S–H bond fission were optimized using the B3LYP functional and the aug-cc-pVTZ triple- ζ basis set.^{74,75,79} Normal mode wavenumbers (with anharmonic corrections) for the parent thione and thiol tautomers and for the common ground state radical formed by N(S)–H bond fission were computed at the same level of theory. For future reference, these are listed in Tables S1 – S3 of the SI. The calculated wavenumbers for the thione tautomer agree well with those published by Jian *et al.*, and the experimentally determined values are also included in Table S1 where available.⁵⁰

Additional calculations were undertaken to investigate potential rival non-radiative excited state

decay channels. Guided by recent studies of thiourea^{80,81} and thiouracil,⁸² a low energy conical intersection between the $\pi\pi^*$ (or $n\pi^*$) excited states and the ground state was identified at non-planar geometries, optimized, and energies then calculated along the coordinate Q obtained by a linear interpolation in internal coordinates (LIIC) between the ground state minimum and the minimum energy conical intersection (MECI). The MECI was optimized using Gaussian 09, at the CASSCF(6,5)/6-31G(d) level of theory. The PE profiles along Q was computed at the CASPT2/cc-pVDZ level using the same (12,9) active space as above.

All DFT calculations were undertaken in Gaussian 09,⁸³ and all CASPT2/CASSCF calculations employed Molpro 2015.^{84,85}

3 Results and Discussion

3.1 Parent Electronic Absorption Spectrum

Figure 2 shows the UV absorption spectrum of methimazole recorded in *n*-hexane solution, with an absorption maximum at $\lambda = 261$ nm. The profile of the spectrum matches well with previously reported spectra of this molecule in acetonitrile and in water.⁵⁰

Calculated PECs for the first few singlet states that may be populated by UV excitation are shown in Figure 3. The left half of this figure shows PECs along the N–H stretch coordinate for the ground and first four excited singlet states of the dominant thione tautomer. Four excited states are predicted to lie at energies < 5 eV in the Franck-Condon (FC) region and thus could contribute to the observed UV absorption. Table 1 details these states, including their vertical excitation energies (VEEs), the magnitudes and directions of the transition dipole moments (TDMs), and the nature of the molecular orbitals (MOs) involved in the excitation. The calculated oscillator strength of the $S_4 \leftarrow S_0$ transition is an order of magnitude larger than that for any other transition in this region. Thus this transition is likely to be the major contributor to the UV absorption shown in Figure 2 – contrary to the conclusions reached in the earlier DFT study.⁵⁰ The CASPT2 calculations predict that this transition involves electron excitation from the $S(3p_y)$ orbital ($2a'$) to the σ^* antibonding orbital of the N–H bond ($3a'$), both of which are shown in Figure S1. The calculated PEC for the S_4 state is repulsive at large R_{N-H} (as expected for a $\sigma^* \leftarrow n$ excitation) but, as in NH_3 , pyrrole, *etc.*,³

the excited state has significant 3s Rydberg character in the FC region which manifests as a shallow potential well with a calculated barrier of $\sim 2500\text{ cm}^{-1}$ to N–H bond cleavage.

The present calculations place the minimum of the thiol tautomer $\sim 3000\text{ cm}^{-1}$ above that of the thione. The calculated PECs along the S–H stretch coordinate ($R_{\text{S-H}}$, right side of Figure 3) are reminiscent of those for thiophenol,⁸⁶ with a dissociative $S_1(n\sigma^*)$ state correlating to ground state radical products and a conical intersection between the S_1 and S_0 potential energy surfaces (PESs) at extended S–H bond lengths. Relative to thiophenol, however, the corresponding $(n/\pi)\pi^*$ excited states are substantially raised in energy. This is a manifestation of a lower density of π and π^* orbitals, which, to first-order, increases the π – π^* energy gap.

Given the calculated minimum energies of the thiol and thione tautomers and the available experimental evidence on the tautomeric ratio in solution, we conclude that the thiol tautomer makes negligible contribution to the measured absorption or to any of the photodissociation processes discussed below.

The center panel in Figure 3 shows the energies of the ground and first four excited electronic states of the radical formed by N–H bond fission (in the thione tautomer) and S–H bond fission (in the thiol) relative to the minimum energies of the respective parents. These are calculated at the optimized geometries of the ground ($\tilde{X}$) state (solid line) and first excited ($\tilde{A}$) states. Note that the first two dissociation limits are common to both tautomers. This is self-evident for the lowest asymptote – reflecting the delocalized nature of the π singly occupied molecular orbital (SOMO) of the $\text{Myl}(\tilde{X})$ radical. Somewhat similar arguments apply in the case of the a' SOMO in the $\text{Myl}(\tilde{A})$ radical, which is predominantly S-centered but extends onto the N atom(s). Such is not the case at higher energies, however; as shown in Fig. S1, the odd electron in the third ($\tilde{C}$) excited state of the Myl radical, which correlates diabatically with the ground state thione tautomer, is very clearly an N-centered in-plane orbital.

3.2 Photodissociation of methimazole

H atom TOF spectra were recorded following excitation of methimazole at 13 different wavelengths in the range 222.5 – 275 nm (or, in wavenumbers, $44\,900 \geq E_{\text{phot}} \geq 36\,400\text{ cm}^{-1}$) shown in Figure 2, and converted to TKER spectra (and displayed in units of cm^{-1}) assuming that the partner fragment has chemical formula $\text{C}_4\text{N}_2\text{H}_5\text{S}$ and mass $m = 113.16\text{ u}$. Five TKER spectra

are shown in Figure 4; the remainder are available in the SI (Figure S2). All show one or more peaks at higher TKER, on top of the broad background signal that maximizes at lower TKER. At this point it is worth re-emphasizing the challenge of studying this molecule by the HRA-PTS technique. Even with the sample heating, the signals are small and details of the background signal (its profile and its magnitude relative to that of the sharper features) are sensitively dependent upon how well the experiment is working, the chosen discriminator settings, *etc.* Nonetheless, some characteristics of this background signal are clear; it peaks at low TKER, has an isotropic angular distribution (*vide infra*), extends to TKERs greater than that of the sharp features, and declines in relative importance at the higher photolysis photon energies (E_{phot}). Such background signals are often seen in HRA-PTS studies and typically attributed to H atom loss channels from highly internally excited ground (S_0) state parent molecules formed by non-radiative transfer (internal conversion, IC) from the photoexcited state. We return to consider the origin of this underlying signal in the present TKER spectra in section 3.5. For now, we simply fit it with a split Gaussian function as shown in Figure 4 and subtract it, in order to focus attention on the region of each TKER spectrum that displays the sharper structure.

The spectrum recorded at 275 nm shows a pair of peaks at TKER $\sim 6000 \text{ cm}^{-1}$, which shift to higher TKER, broaden and merge together upon increasing E_{phot} . 275 nm was the longest excitation wavelength at which such a feature was discerned yet, as Figure 2 shows, the parent still shows an appreciable absorption cross-section at longer excitation wavelengths. A second, less intense, pair of peaks at lower TKER are recognizable in the spectra recorded at shorter wavelengths (but are too weak to be seen at $\lambda = 275 \text{ nm}$). These peaks also broaden and merge together as E_{phot} is increased, and become increasingly obscured by an additional cluster of sharp features (identified on the TKER spectra shown in Figure 4). These sharp features are attributable to photolysis of residual H_2S (left over from the periodic TOF calibration experiments and fortuitously persisting as a reliable internal standard for TOF calibration) that has desorbed from the heated sample delivery line. The increased showing of these additional features at higher E_{phot} reflects the H_2S absorption cross-section, which is negligible at $\lambda > 260 \text{ nm}$ but increases strongly upon tuning towards 225 nm. The observation of these H_2S -related features is further testimony to the challenge of studying methimazole by HRA-PTS methods. One further peak, not related to H_2S photolysis, is evident at TKER $\sim 10\,000 \text{ cm}^{-1}$ in the spectrum obtained at 230 nm. The H atom recoil anisotropy was investigated at just two wavelengths (265 and 230 nm), by comparing spectra measured with

ϵ aligned at 0° and 90° to the TOF axis. Analyses of these data (shown in Figure S3 of the SI) return recoil anisotropy parameters $\beta \sim -0.5$ for the pair of peaks at high TKER and $\beta \sim 0$ for the background signal at lower TKER.

These observations are all broadly consistent with the predicted dominance of the $S_4 \leftarrow S_0$ transition. As Table 1 and Figure 1 show, the calculated $S_4 \leftarrow S_0$ TDM is at an angle $\chi \sim 70^\circ$ to the N–H bond axis. Given $\beta = 2P_2(\cos\chi)$ in the limit of axial recoil (where $P_2(\cos\chi) = \frac{1}{2}(3\cos^2\chi - 1)$, the second Legendre polynomial),⁸⁷ $\chi = 70^\circ$ would imply $\beta = -0.65$. This value matches well with the measured anisotropy of the structured features in the TKER spectra (particularly given that the structured features sit on some background signal with $\beta \sim 0$), and supports the view that these features arise via direct N–H bond fission following $S_4 \leftarrow S_0$ excitation.

Table 1 and the PECs shown in Figure 3 also provide a rationale for the decline, and eventual disappearance of these features on tuning to the long wavelength end of the parent absorption spectrum (Figure 2). First, absorption to the S_3 state (which is predicted to be diabatically bound with respect to N–H bond fission) becomes relatively more important. Second, the S_4 state levels populated when exciting at long wavelengths are likely to be at least quasi-bound (by virtue of the barrier in the R_{N-H} coordinate). Even if the magnitude of this barrier is insufficient to preclude transmission by tunneling, the presence of the barrier will slow the rate – thereby enhancing the relative probabilities of any rival non-radiative decay pathways.

The magnitudes of the energy separations between the various peaks in the TKER spectra imply population of different vibrational levels of the Myl radicals formed by N–H bond fission. The peak at highest TKER is the dominant (methimazole related) feature in each spectrum, and the number of peaks in each spectrum is small. The latter, viewed in a Franck-Condon context, implies minimal geometry change in the remainder of the molecule either during photoexcitation or during the subsequent evolution to the asymptotic radical. We assign the peak at highest TKER in each spectrum to formation of H atoms together with Myl($v=0$) radicals; the other peaks are thus associated with formation of vibrationally excited radicals.

More quantitative analysis is complicated by the observation that the H + Myl($v=0$) feature broadens and merges with the adjacent feature upon tuning to higher E_{phot} . Thus, the following fitting approach was adopted. Guided by the observed peak profiles in TKER spectra obtained at lower E_{phot} , both peaks were modelled using a common split Gaussian function, with a sharper

drop-off on the high TKER side. Fitting the separation between the peak centers in spectra taken at longer wavelengths yielded a value of $w_{\text{sep}} = 264 \text{ cm}^{-1}$ – which was held fixed in the subsequent analysis. The widths (in cm^{-1}) of both halves of the split Gaussian function were modelled by equations of the form

$$w = \sqrt{w_0^2 + w_1(E_{\text{phot}})^2}, \quad (2)$$

where the w_0 are intrinsic experimental widths and the w_1 values are E_{phot} dependent. The w_1 values for the high and low energy sides of both peaks in the spectra recorded at low E_{phot} were found to scale linearly with E_{phot} , and these trends were assumed to extrapolate for the merged profiles recorded at higher E_{phot} . At each photolysis wavelength, the peak pair (or the feature produced by their merger) was then fitted as the sum of two split Gaussians, with $w_{\text{sep}} = 264 \text{ cm}^{-1}$ and w_0 and w_1 values predicted by the above model (with $w_0 = 42 \text{ cm}^{-1}$ and $w_1 = 0.007E_{\text{phot}}$ for the high TKER side of the peak, and $w_0 = 38 \text{ cm}^{-1}$ and $w_1 = 0.014E_{\text{phot}}$ for the low TKER side), varying just the relative peak amplitudes and the TKER of the $v=0$ peak center (TKER_0). Figure 5 shows the TKER_0 values returned in this way plotted as a function of E_{phot} , along with example fits to the peaks at two wavelengths (as insets).

The energy balance in the one-photon induced N–H bond fission is given by

$$E_{\text{phot}} + E_{\text{int}}(\text{MylH}) = BDE(\text{Myl–H}) + E_{\text{int}}(\text{Myl}) + \text{TKER}, \quad (3)$$

where $BDE(\text{Myl–H})$ is the dissociation energy of the bond of interest, and $E_{\text{int}}(\text{MylH})$ and $E_{\text{int}}(\text{Myl})$ are the respective internal energies of methimazole (assumed to be negligible under the conditions prevailing in a molecular beam) and of the Myl radical. (The internal energy of the H atom partner is zero). Eq. (3) implies that a plot of TKER associated with any given product quantum state (*e.g.* TKER_0) vs E_{phot} should be linear with unit gradient – as has indeed been observed in PTS studies of other N-containing heterocycles like pyrrole and imidazole.^{8,39} Such is not the case in the present methimazole studies, however. This can be seen most easily by transforming the TKER spectra into E_{int} space using eq. (3) assuming a value for $BDE(\text{Myl–H}) = 30\,000 \text{ cm}^{-1}$ (justified below). Several such spectra are shown in fig. 6, which clearly demonstrates that the peaks broaden and shift to higher E_{int} with increasing E_{phot} ; this shift is $\sim 350 \text{ cm}^{-1}$ over the 8600 cm^{-1} range of E_{phot} values studied. The extra internal energy is too small and its E_{phot} dependence too smooth to be

attributable to vibrational excitation of the Myl fragment. Rather, it indicates that the energy partitioning into fragment rotation increases with increasing E_{phot} .

The much greater implied product rotational excitation in the photodissociation of methimazole (*cf.* pyrrole or imidazole) can be rationalized by considering the respective molecular geometries. As Figure 1 showed, the centers of mass of the unsubstituted heterocycles lie on (or very close to) the axis defined by the N–H bond. Any impulse arising as a result of N–H bond fission will be directed at the center of mass and thus will not generate a torque on (and thus induce rotational excitation of) the resulting radical. The center of mass of methimazole, in contrast, is ~ 1 Å off the axis defined by the N–H bond (Figure 1(d)) and any impulse from the departing H atom could plausibly map into Myl product rotation. We note that such an effect was not recognized in earlier PTS studies of UV photoinduced N–H bond fission of 2-ethylpyrrole (for which the center of mass of the resulting radical is similarly off axis),⁴⁴ but the ethyl side chain in that case is much more flexible than the C=S group in methimazole, enabling energy partitioning into substituent torsional and/or wagging vibrations. Qualitatively, an impact parameter model would predict that the product rotational excitation should scale with the available energy, E_{avl} (*i.e.* with $E_{\text{phot}} - BDE(\text{Myl-H})$), but any quantitative treatment will require a value for this bond strength and an estimate of the ‘stiffness’ of the radical, *i.e.* the extent to which the impulse induces in plane ring breathing vibrational excitation *vs.* rotational excitation of the radical.

3.3 Determination of the N–H bond strength

The E_{phot} -dependent internal (rotational) energy deposition into the Myl radical complicates determination of $BDE(\text{Myl-H})$. One limiting approach assumes that the Myl products from photolysis at the lowest E_{phot} investigated carry negligible rotational excitation. Analyzing the $\lambda = 275$ nm data in this way, using eq. (3) with $E_{\text{int}}(\text{Myl}) = 0$, yields an upper limit of $BDE(\text{Myl-H}) \leq 30\,220 \pm 80$ cm⁻¹. An alternative approach uses eq. (4) to estimate a rotational energy of the Myl($v=0$) products at each E_{phot} investigated.

$$E_{\text{int}}(\text{Myl}(v=0)) = E_{\text{phot}} - BDE(\text{Myl-H}) - \text{TKER}_0, \quad (4)$$

(This equation derives from eq. (3) if we neglect $E_{\text{int}}(\text{MylH})$ and use the best-fit TKER_0 value at each E_{phot}). As Figure 6 shows, the $E_{\text{int}}(\text{Myl}(v=0))$ values derived from Figures 4 and 5 increase with E_{phot} . This dependence appears to be linear over the investigated E_{phot} range (SI, Figure S4)

and extrapolates to $BDE(\text{Myl-H}) = 29\,940 \pm 110 \text{ cm}^{-1}$ in the limit that $E_{\text{int}}(\text{Myl}(v=0)) = 0$. We regard this as a lower limit, and recommend the bond dissociation energy $BDE(\text{Myl-H}) = 30\,000 \pm 250 \text{ cm}^{-1}$ used in constructing figure 6.

The dissociation energy for forming $\text{H} + \text{Myl}$ radicals in their ground ($\tilde{X}$) state returned by the CASPT2 calculations (Figure 3) is $D_e(\text{Myl-H}) \sim 27\,400 \text{ cm}^{-1}$. The DFT calculated anharmonic vibrational mode wavenumbers of ground state methimazole and of the $\text{Myl}(\tilde{X})$ radical (SI) imply a zero-point energy correction upon N-H bond fission, $\Delta(\text{ZPE}) \sim 2700 \text{ cm}^{-1}$. Thus, theory predicts that the dissociation energy of the ground state molecule to form ground state products, $D_0(\text{Myl-H})$, is $\sim 24\,700 \text{ cm}^{-1}$ – significantly smaller than the value determined experimentally. But the CASPT2 calculations also place the first excited ($\tilde{A}$) state of the Myl radical $\sim 6600 \text{ cm}^{-1}$ above the $\tilde{X}$ state (after geometry relaxation). Assuming that the normal mode wavenumbers in the $\tilde{X}$ and $\tilde{A}$ states of the radical are similar, the present theory predicts a (zero-point corrected) dissociation energy for forming $\text{H} + \text{Myl}(\tilde{A})$ products, $BDE(\text{Myl-H}) \sim 31\,300 \text{ cm}^{-1}$, that is close to the experimental value. Thus, we conclude that the peaks featured in Figures 4 and 5 arise from UV photolysis of methimazole yielding $\text{H} + \text{Myl}(\tilde{A})$ products. Such an outcome is consistent with the PECs displayed in Figure 3 if molecules evolving on the S_4 potential undergo non-adiabatic coupling in the region of the conical intersection at $R_{\text{N-H}} \sim 2 \text{ \AA}$ to access the $\text{H} + \text{Myl}(\tilde{A})$ asymptote. In passing, we note that the corresponding (zero-point corrected) bond strengths predicted for forming $\text{H} + \text{Myl}(\tilde{X})$ or $\text{H} + \text{Myl}(\tilde{A})$ products from the thiol tautomer are $\sim 22\,500$ and $\sim 29\,100 \text{ cm}^{-1}$, respectively. The latter is reasonably close to the experimental value, but we reject this possible alternative assignment for two reasons. First, and most compellingly, because of the tautomeric preference deduced in Section 3.1. Second, the non-observation of any faster peaks in the TKER spectra indicating formation of $\text{H} + \text{Myl}(\tilde{X})$ products which would be expected by analogy with prior studies of thiophenol photofragmentation^{86,88} and the predicted planar equilibrium geometry of the excited state thiol tautomer.

Deduction of $D_0(\text{Myl-H})$ requires that we call on at least one computationally derived value. If we assume an energy separation between the $\tilde{A}$ and $\tilde{X}$ states of the Myl radical, $\Delta E(\tilde{A}-\tilde{X}) = 6600 \text{ cm}^{-1}$, then the experimentally derived $BDE(\text{Myl-H})$ value yields $D_0(\text{Myl-H}) = 23\,400 \text{ cm}^{-1}$. Alternatively, we could regard the computed $D_0(\text{Myl-H})$ value ($24\,700 \text{ cm}^{-1}$) as likely to be the more reliable estimate. Either way, it is clear that the N-H bond strength in methimazole ($\sim 24\,000$

cm⁻¹) is much lower than that reported for other N-containing heterocycles like pyrrole (32 850 ± 40 cm⁻¹),⁸ alkylated pyrroles (31 000 – 32 000 cm⁻¹)⁴⁴ or imidazole (33 240 ± 40 cm⁻¹).³⁹ In all of these cases, the S₀ potential along the R_{N-H} stretch coordinate correlates diabatically with the second excited state of the radical and, to first order, shows a similar well depth. The reduced N–H bond strength in methimazole reflects the greater resonance stabilization (electron delocalization) provided by the S atom in the ground state Myl radical (*cf.* the pyrrolyl or imidazolyl radicals), as well as the fact that, unlike pyrrole and imidazole (whose aromaticity is lost in the ground state product radicals), methimazole is not an aromatic ring.

3.4 Assignment of Vibrational Structure

Most of the TKER spectra show four methimazole-related peaks with internal energies (defined relative to the $\nu = 0$ peak) of 0, ~260, ~740 and ~1040 cm⁻¹. As Figure 6 shows, the more closely spaced pairs merge to form two broader features upon increasing E_{phot} and an additional broad peak at ~2850 cm⁻¹ is evident at the shortest excitation wavelength. Lacking any obvious electronic or tautomeric source of a ~264 cm⁻¹ energy splitting in the radical, we attribute these peaks to population of different vibrational levels of the Myl($\tilde{A}$) radical and the evident peak broadening to increased product rotation with increasing E_{avl} . Our assignments of these product levels are guided by the DFT predicted anharmonic wavenumbers (of the $\tilde{X}$ state radical) listed in Table S3 in the SI, and the CASPT2 predicted planar equilibrium geometry of the radical. The ~260 cm⁻¹ feature is most plausibly attributed to one quantum of excitation in mode ν_{20} (an in-plane wagging motion of the N–CH₃ and C=S groups). In-plane mode ν_{17} (calculated anharmonic wavenumber: 681 cm⁻¹) is the closest match to the observed ~740 cm⁻¹ peak, but unique assignments of the higher peaks are hampered by the multiplicity of modes in each energy window. Three in-plane ring-breathing modes have predicted wavenumbers close to 1040 cm⁻¹: ν_{15} (1027 cm⁻¹), ν_{14} (1048 cm⁻¹), and ν_{13} (1082 cm⁻¹). This interval also matches reasonably with the combination ($\nu_{20} = 1 + \nu_{17} = 1$). Finally, the ~2850 cm⁻¹ peak is likely attributable to population of one or more of the C–H stretch fundamentals (with predicted wavenumbers in the range 2950 – 3125 cm⁻¹).

3.5 The background H atom signal

The TKER spectra all present some underlying background signal that peaks at low TKER, has an isotropic angular distribution, extends to TKERs greater than that of the sharp features, and declines in relative importance at higher photolysis photon energies. Such background signals are

plausibly attributable to H atom loss from highly internally excited ground state parent molecules formed by IC from the photoexcited state. As expected by analogy with previous studies of the excited state decay dynamics of molecules like thiourea and thiouracil,⁸⁰⁻⁸² we find a low energy CI between the S_0 and $S_1(n\pi^*)$ states at a non-planar geometry (characterized by pyramidalization about the C atom bounded by the N and S atoms). Figure 7 shows CASPT2 calculated PECs for the first five singlet states of the thione tautomer of methimazole along Q , the LIIC linking the S_0 minimum energy configuration to this CI geometry.

Excited state PECs returned by such interpolations are almost always over-estimates of the minimum energy path. Nonetheless, several features of these calculated PECs merit note. First, distortion to the CI geometry on the S_1 PES is energetically ‘down-hill’ from the Franck-Condon region. Second, the S_2 PEC along Q has a similar topography to that of the S_1 state and the displayed PECs hint at a CI between the S_2 and S_1 states at $Q \sim 0.5$. Third, the S_3 and S_2 PECs are tightly nested in the Franck-Condon region. Thus, very much as in the case of thiouracil,⁸² it is plausible that molecules excited to the S_3 PES of methimazole undergo a sequence of non-adiabatic transitions to high vibrational levels of the S_0 state, which then undergo unimolecular decay to yield the various low energy dissociation products – including the H atoms (along with $\text{Myl}(\tilde{X})$ radicals) implied by the measured TKER spectra.

4 Conclusions

The UV photodissociation of methimazole has been studied in the gas phase at 13 different wavelengths in the range 222.5–275 nm using the H Rydberg atom photofragment translational spectroscopy technique. Aided by complementary CASPT2 calculations, methimazole is shown to exist predominantly as the thione tautomer, 1-methyl-2(3H)-imidazolinethione. The UV absorption of this tautomer is dominated by the $S_4 \leftarrow S_0$ transition (associated with electron promotion from an a' (p_y) orbital localized on the sulfur atom to a σ^* orbital on the N–H bond). UV photoexcitation results in N–H bond fission. A substantial fraction of the H atom fragments display anisotropic recoil velocity distributions, and the partner Myl radicals are formed in their first excited ($\tilde{A}$) electronic state. The population inversion between the ground ($\tilde{X}$) and $\tilde{A}$ states of the radical follows naturally from considering the topographies of, and non-adiabatic couplings between, the PECs of methimazole upon extending $R_{\text{N-H}}$. The $\text{Myl}(\tilde{A})$ radicals are formed with

little vibrational but discernible rotational excitation. The extent of rotational excitation is found to increase near-linearly with increasing photon energy. These internal energy disposals reflect (i) the minimal geometric changes in the heavy atom framework upon photoexcitation and subsequent N–H bond fission, and (ii) the perpendicular separation of the methimazole center of mass from the axis defined by the N–H bond, which ensures that any impulse from the recoiling H atom maps into Myl product rotation.

An isotropic background signal is also evident in all measured H atom TOF spectra, particularly those recorded at lower photon energies. These H atoms are attributed to the unimolecular decay of highly vibrationally excited ground state parent molecules. The companion electronic structure calculations suggest that these internally ‘hot’ S_0 molecules arise via a sequence of non-adiabatic couplings from the initially photoexcited state, some (at least) of which involve conical intersections at non-planar geometries characterized by pyramidalization about the C atom bounded by the N and S atoms and reminiscent of those implicated in recent studies of excited state non-radiative decay pathways in thiourea and thiouracil.^{80–82} The deduced dissociation energy for forming ground state products, $D_0(\text{Myl-H})$, is $\sim 24\,000\text{ cm}^{-1}$. The comparative weakness of this bond in methimazole (which is $\sim 25\%$ less than the N–H bond dissociation energy in pyrrole⁸ or imidazole³⁹) can be understood by recognizing the greater resonance stabilization provided by the S atom in the Myl($\tilde{X}$) radical (*cf.* the pyrrolyl or imidazolyl radicals) and noting that, unlike pyrrole and imidazole, the ring in methimazole is not aromatic.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the [ACS Publications website](#) at DOI: [??????????????](#).

Harmonic and anharmonic normal mode wavenumbers for the ground states of the parent thione and thiol tautomers and of the Myl radical. Depictions of the SA-CASSCF active orbitals at the ground state equilibrium geometries of the thione and thiol tautomers, and the SOMO of the ground and selected excited states of the Myl radical. TKER spectra derived from H atom TOF spectra following photolysis of methimazole at (i) other wavelengths in the range 222.5 – 275 nm and (ii) 265 and 230 nm with ϵ aligned at, respectively, 0° and 90° to the TOF axis, along with the β vs

TKER plots derived from these measurements. Plot showing the variation of $E_{\text{int}}(\text{Myl}(v=0))$ with E_{phot} derived from Figures 4 and 5.

Author Information

Corresponding Authors

*(TNVK) E-mail: tolga.karsili@louisiana.edu.

*(MNRA) E-mail: mike.ashfold@bristol.ac.uk. Tel: +44 117 9288312.

Notes

The authors declare no competing financial interest.

All underlying data are available at the University of Bristol data repository, [data.bris](https://data.bris.ac.uk), at DOI: 10.5523/bris.2ml54cg0ry4jb2exegii8nk4wj.

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Table 1 Vertical Excitation Energies (E in cm^{-1}), Transition Dipole Moments (μ in a.u.) and Oscillator Strengths (f) for Transitions to the First Four Singlet Excited States of the Thione Tautomer of Methimazole.

Transition	Dominant orbital promotion	E / cm^{-1}	f	$ \mu / \text{a.u.}$	$\mu_{\alpha} / \text{a.u.}^a$		
					μ_x	μ_y	μ_z
$S_1 \leftarrow S_0$	$4a'' \rightarrow 3a' (\pi\sigma^*)$	34800	1.3×10^{-2}	0.36	-0.36	0	0
$S_2 \leftarrow S_0$	$2a' \rightarrow 5a'' (n\pi^*)$	36500	4.6×10^{-5}	0.02	-0.02	0	0
$S_3 \leftarrow S_0$	$4a'' \rightarrow 5a'' (\pi\pi^*)$	37700	2.7×10^{-2}	0.48	0	0.46	-0.15
$S_4 \leftarrow S_0$	$2a' \rightarrow 3a' (n\sigma^*)$	40000	6.5×10^{-1}	2.31	0	0.08	2.31

^a Atomic units: $1 ea_0 = 2.54$ Debye

FIGURES

Fig. 1 Structures of (a) pyrrole, (b) imidazole, (c) 2-mercapto-1-methylimidazole and (d) 1-methyl-2(3H)-imidazolinethione, including their inertial axes (with x out of the plane of the page). The red dots indicate the center of mass of the radical formed by $X-H$ bond fission ($X = N, S$).

Fig. 2 UV absorption spectrum of methimazole recorded in *n*-hexane. Black arrows indicate photolysis wavelengths at which photodissociation experiments were performed.

Fig. 3 PECs for the ground and first few singlet excited states for 1-methyl-2(3H)-imidazolinethione (along R_{N-H}) (left) and for 2-mercapto-1-methylimidazole (along R_{S-H}) (right) calculated by extending the bond of interest with the rest of the structure held fixed at the minimum energy geometry of the ground state. The energies of the thresholds corresponding to different electronic states of the Myl radical at the optimized geometries of its ground ($\tilde{X}$) and first excited ($\tilde{A}$) states are shown in the center (solid and dashed lines, respectively).

Fig. 4 Selected TKER spectra derived from measured H atom TOF spectra (black traces). The red curves indicate the fit to the underlying signal which, in each case, was subtracted as described in the text. Peaks indicated by asterisks are from H + SH(X) products from photolysis of H₂S impurities in the molecular beam.

Fig. 5 Plot of $TKER_0$ (*i.e.* the $H+Myl(v=0)$ peak center determined by fitting) vs E_{phot} , where the displayed error bars are the average of the standard deviations for each half of the split Gaussian function used. The blue line is a fit through the points with a gradient of unity. **Insets:** Two sample TKER spectra (black) with the curves fitted to the peaks (red), and the position of the $H+Myl(v=0)$ peak center determined by the fit (vertical blue line). Peaks indicated by asterisks in the lower inset originate from H_2S impurities in the molecular beam. The ticks on the inset axes are at 1000 cm^{-1} increments in both cases.

Fig. 6 $E_{\text{int}}(\text{Myl})$ spectra derived assuming a dissociation energy $BDE(\text{Myl-H}) = 30000 \text{ cm}^{-1}$. Guidelines indicate E_{int} values of 0, 250, 500, and 750 cm^{-1} and the starred peaks originate from H_2S contaminant.

Fig. 7 PECs for the ground and first few singlet excited states on the thione tautomer of methimazole along Q , the LIIC linking the ground state minimum and the MECI between the S_1 and S_0 states. Inset: the optimized structure at the MECI.

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Figure 1

82x75mm (300 x 300 DPI)

Figure 2

82x65mm (600 x 600 DPI)

Figure 3

177x99mm (300 x 300 DPI)

Figure 4

82x116mm (300 x 300 DPI)

Figure 5

82x85mm (300 x 300 DPI)

Figure 6

82x120mm (300 x 300 DPI)

Figure 7

82x100mm (300 x 300 DPI)

TOC graphic

46x44mm (300 x 300 DPI)