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Received 24th April 2013, Accepted 7th June 2013 Alexander J. Hough,^a Ivan Prokes,^a James H. R. Tucker,^{*b} Michael Shipman^{*a} and Tiffany R. Walsh^{*ac}

with pyramidal inversion[†]

Photochemical control of molecular motion associated

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Rates of pyramidal motion in an aziridine are controlled by reversible *trans* to *cis* photoisomerisation of an azobenzene unit attached to the ring nitrogen atom. The dynamics of the inversion process and activation parameters are derived by variable temperature NMR, and are supported by *ab initio* calculations.

As part of the continuing interest in the development of molecular machines and switching devices in chemistry and biology, light is considered to be an important means through which external control can be brought to bear on such systems.¹ It is well known that reversible photocontrol can be readily realised through the use of photochromic groups such as azobenzene.² There are now many examples of photoswitchable devices using this approach,²⁻⁵ for example in studies on photocontrollable reactivity and binding processes.³ Another active area within this field is photocontrollable molecular motion but despite extensive work on interlocked structures and unidirectional systems,⁴ there are just a few examples where effective photocontrol over simple dynamic processes such as bond rotation rates have been achieved.⁵ Here we demonstrate for the first time, through studies on azobenzene-linked aziridines 1 and 2 (Scheme 1), how another form of dynamic molecular motion, that of pyramidal atomic inversion, can be reversibly controlled by light.

A number of factors led to the design and construction of photoresponsive aziridines **1** and **2**. The use of aziridine based systems (in this case, **1a** \Leftrightarrow **1b** and **2a** \Leftrightarrow **2b**) allows accurate measurement of the inversion dynamics using VT-NMR spectroscopy.^{6,7} We have previously demonstrated how functionalisation



Scheme 1 Photochemical control of pyramidal inversion rates.

of aziridines and related heterocycles with various coordinating groups,⁸ as well as redox-responsive units,⁹ can dramatically affect pyramidal inversion rates. Of relevance to this work, it is well known that the rate of pyramidal inversion in simple N-aryl aziridines is very sensitive to the nature of substituents on the aromatic ring, with electron withdrawing groups lowering the barrier through greater conjugation of the nitrogen lone pair into the benzene ring.¹⁰ As far as photoresponsive units are concerned, the choice of azobenzenes was motivated by knowledge that they have been well studied as elements in light-controlled molecular devices,² and that methods for the isomerisation between the *cis* and *trans* forms are well established.¹¹ Typically, trans \rightarrow cis isomerisation occurs following UV-visible light irradiation, with the reverse reaction often being conveniently induced with heat. In this study, we aimed to use photochemically induced isomerisation to modulate the extent of conjugation of the nitrogen lone pair into the π -system by disrupting the planarity of the azobenzene unit. In 1, the trans azobenzene unit was expected to be planar with significant conjugation of the trigonal aziridine nitrogen atom in the transition state (TS) across the entire π -framework, leading to

^a Department of Chemistry, University of Warwick, Gibbet Hill Road, Coventry, CV4 7AL, UK. E-mail: m.shipman@warwick.ac.uk; Fax: +44 (0)2476 524112; Tel: +44 (0)2476 523186

^b School of Chemistry, University of Birmingham, Edgbaston, Birmingham, B15 21T, UK. E-mail: j.tucker@bham.ac.uk; Fax: +44 (0)121 414 4403

^c Institute for Frontier Materials, Deakin University, Waurn Ponds, 3216 VIC, Australia. E-mail: tiffany.walsh@deakin.edu.au; Tel: +61 352 273 116

[†] Electronic supplementary information (ESI) available: Synthesis and spectroscopic data for **1** and **2**, procedures for their interconversion, and their activation barriers (measured and computed). See DOI: 10.1039/c3cc43036g

a stable, low-lying TS and hence relatively fast rate of pyramidal motion. Conversely, in *cis*-2, the extent of this overlap in the TS would be reduced as a result of a twist¹² in the azobenzene subunit reducing interaction with the distal aromatic ring and the attached nitro group. This would be expected to lead to a slower rate of motion. In this way, light-induced conversion of 1 into 2 should lead to measurable changes in the rate of pyramidal motion at the aziridine nitrogen atom (Scheme 1).

The synthesis of aziridine 1 was readily achieved in 3 steps from 4-nitroaniline and β -hydroxyethylaniline (see ESI[†]).[‡] Next, photochemical conversion of 1 into 2 was investigated. At first, when 1 in CD₂Cl₂ (ca. 80 mM) was irradiated using a 125 W medium pressure Hg lamp for 1 h, using a <355 nm cutoff filter, no trace of 2 was seen. Fast thermal isomerisation of 2 \rightarrow 1 could, in part, account for the apparent lack of reactivity of 1. Indeed, push-pull azobenzenes such as 4-(diethylamino)-4'nitroazobenzene (3) are known to have unstable *cis* isomers which rapidly isomerise back to the *trans* form.¹³ Noting that solvents with a small dielectric constant slow the $cis \rightarrow trans$ thermal isomerisation of 3, leading to much longer half-lives of the *cis* isomer,¹³ we repeated the photoisomerisation of **1** in less polar solvents. Gratifyingly, when **1** in d_6 -benzene ($\varepsilon = 2.3$) was irradiated for 1 h at room temperature with a <355 nm cutoff filter, quantities of 2 were observed by ¹H NMR spectroscopy (1:2; 83:17). High levels of conversion of push-pull azobenzenes to the cis-isomer are further hampered by the fact that their UV-vis spectra are broad and poorly resolved, with overlap of the $\pi \to \pi^*$ and $n \to \pi^*$ transitions.^{11,13} The UV-vis spectrum of 1 displayed such characteristics with a broad absorption centred at 416 nm (see ESI⁺). Several filters were investigated to increase the production of 2 (see ESI⁺). For example, the use of a bandpass filter based on 0.75% w/v iodine in carbon tetrachloride,¹⁴ which has a modest transmission of $\sim 40\%$, but is highly selective for λ_{max} = 390 nm, did result in some improvement (1:2; 74:26). In combination with lower photoirradiation temperatures to slow the thermal back reaction, sufficient quantities of 2 could be produced to determine its pyramidal inversion rate (vide infra). Thus, photoirradiation below 10 °C (ice-water bath) for 3 h, allowed 2 to be formed as the major product (1:2; 44:56).§ Similar results were achieved in d_8 -toluene ($\varepsilon = 2.4$), with the added advantage that NMR spectra could be recorded down to -95 °C (see ESI⁺).

At room temperature, *cis*-2 isomerised to *trans*-1 in d_s -toluene, according to first order kinetics, with $k = 2 \times 10^{-4} \text{ s}^{-1}$ (see ESI[†]). This is significantly slower than values reported for classical push–pull azobenzenes (*e.g.* 3 (in C₆H₆): $k = 3 \times 10^{-2} \text{ s}^{-1}$),¹³ highlighting the effect of ring strain on the ability of the nitrogen to delocalise into the π -system. From a practical standpoint, heating 2 in toluene at 60 °C for 10 min resulted in clean conversion back to 1, providing a simple method to complete the switching cycle. Several iterations of this cycle (1 \rightarrow 2 \rightarrow 1) were completed without any sign of degradation.¶

To study the molecular motion within **1** and **2**, their activation parameters were determined by two different VT-NMR methods (Table 1). Firstly, the ¹H NMR spectra were recorded over a wide range of temperatures above and below coalescence

Aziridine	Measured ^a					MP2 calculations ^c	
	T _c	$\Delta G_{ m coal}^{\ddagger}$	$\Delta G^{\ddagger b}$	ΔH^{\ddagger}	ΔS^{\ddagger}	Gas-phase	Solvent ^d
trans-1	207	38.9	39.2	34.4	-16.3	52.0	49.3
cis-2	223	42.2	41.7	35.3	-21.4	56.3	52.9
$^{a}\Delta G^{\ddagger}$ and with estim	ΔH^{\ddagger} is	n kJ mol rrors for	$^{-1}, \Delta S^{\ddagger}$	in J K⁻ kI mol	$^{-1}$ mol ⁻¹ .	$^{b}\Delta G^{\dagger}$ values +1.1 kI mol ⁻	s at 298 K

with estimated errors for 1: ± 0.8 kJ mol⁻¹ and 2: ± 1.1 kJ mol⁻¹ (see ESI for full details). ^{*c*} Using MP2/aug-cc-pVDZ level. ^{*d*} Using the implicit solvent model (toluene).

(188–219 K). For each aziridine, the temperature of coalescence $(T_{\rm c})$ was determined and the free energy of activation at coalescence $(\Delta G_{\text{coal}}^{\ddagger})$ derived. Significantly, 2 $(T_{\text{c}} = 223 \text{ K})$ coalesced at a measurably higher temperature than 1 (T_c = 207 K), consistent with our prediction of a higher barrier to N-inversion in 2. In a second approach, dynamic line-shape simulations of the aziridine A2X2 spin system performed using WINDNMR¹⁵ enabled the rates of exchange over a range of temperatures to be determined (Fig. 1). || Eyring plots $\left[\ln(k/T) vs.\right]$ 1/T were then used to extract the activation parameters for these aziridines which are presented in Table 1. The measured difference in inversion barrier between **1** and **2** $(\Delta\Delta G^{\dagger})$ is *ca.* 3 kJ mol⁻¹ [3.3 kJ mol⁻¹ (from coalescence) and 2.5 kJ mol⁻¹ (from line shape analysis)]. These data confirm our supposition that inversion occurs faster in 1, with a difference in barrier that equates to ca. 3-fold difference in the inversion rate at 223 K $(1, k = 5.9 \times 10^3; 2, 1.9 \times 10^3 \text{ s}^{-1}).$

Ab initio calculations were performed to verify the measured barriers and gain insights into the origin of the differences in the rates of motion for **1** and **2**. To determine the ground state (GS) and transition state (TS) energies for **1** and **2**, the geometries of the minima and TS were optimised at the MP2/6-31G* level of theory. For **2**, a conformational search was conducted to identify the GS minimum (see ESI† for full details). Single-point energies (SPE) for the lowest energy structures were then calculated at the higher MP2/aug-cc-pVDZ level with and



Fig. 1 Measured (left) and simulated (right) ¹H NMR spectrum (d_8 -toluene, 500 MHz) of aziridine **2** (as a *ca.* 1 : 1 mixture with **1**) over 183–248 K temperature range. NMR plots for **1** are provided in the ESI.†



Fig. 2 Ground state and transition state structures for 1 and 2 optimised at the MP2/aug-cc-pVDZ level.

without implicit solvent. The optimised structures are presented in Fig. 2, with the numerical values given in Table 1. Although the absolute values derived from these MP2/aug-ccpVDZ level calculations using toluene as implicit solvent overestimate the barriers for both 1 and 2, they successfully predict a higher barrier for 2, and compute a difference $(\Delta\Delta G^{\dagger})$ of 3.6 kJ mol⁻¹ between the *cis* and *trans* isomers that agrees closely with the experimental values (vide supra). Significant distortion away from planarity as evidenced in the minima and TS for 2 disrupts conjugation of the aziridine lone pair into the extended π -system, leading to a higher barrier. This can be quantified using a natural bond orbital analysis which revealed not only the greater extent of delocalisation from the nitrogen into the ring for 1 compared with 2, but also a greater change in this delocalisation in moving from the GS \rightarrow TS for 1 $(46.3 \text{ kJ mol}^{-1})$ compared with 2 $(44.5 \text{ kJ mol}^{-1})$ (see ESI⁺).

These studies demonstrate how it is possible to modify the atomic pyramidal inversion rates in an aziridine using only the physical inputs of light and heat. Switching $1 \rightarrow 2$ is successfully achieved photochemically, with the reverse reaction facilitated with simple heating. Careful choice of solvent and conditions are required to achieve acceptable conversion during the photoreaction. Experimental and computed differences in the activation barrier ($\Delta\Delta G^{\dagger}$) for the pyramidal motion for **1** and 2 are of the order of 3 kJ mol⁻¹, with *cis*-2 inverting more slowly due to a twist in the azo system which reduces the extent of conjugation of the aziridine lone pair into the π -system. The process proceeds without degradation and can be cycled several times. As such, it represents the first example of the use of light to control the rate of pyramidal atomic inversion and it also illustrates how dynamic molecular motion may be principally controlled by changes in bond conjugation rather than sterics.⁵ Future studies will focus on increasing the magnitude of the rates differences between the two states, and the development of molecular devices that exploit this phenomena.

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Notes and references

[‡] Aziridine **1** has been reported previously by Hallas and Choi who indicated that it is best prepared by base induced ring closure to form the aziridine as the final step.¹⁶ This approach was adopted herein although considerable refinement of the synthetic route was required to obtain **1** in a satisfactory state of purity. Full details are provided in ESI.[†] § Lowering of the photoirradiation temperature to -20 °C led to no improvement in the ratio of **1**:2. Below 10 °C, the *cis* isomer was observed to be thermally stable, so that during the VT-NMR experiments (see Fig. 1), the ratio of **1** to **2** did not change.

¶ Aziridine 1 is stable provided it was kept away from sources of acid. \parallel In aziridines 1 and 2, a complex AA'BB' spin system is predicted.¹⁷ Fortuitously, the aziridine signals were observed as pairs of singlets at low temperature, coalescing to one singlet on warming. As such they could be analysed as A₂B₂ spin systems, simplifying the line shape analysis.

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