Umbrella motion in aziridines: use of simple chemical inputs to reversibly control the rate of pyramidal inversion

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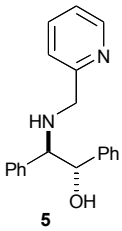
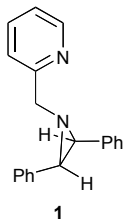
ELECTRONIC SUPPLEMENTARY INFORMATION



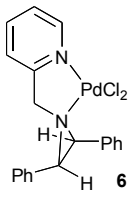
5

Synthesis of Aminoalcohol 5. A mixture of *trans*-stilbene oxide (2.0 g, 10.2 mmol) and 2-(2-aminomethyl)pyridine (1.10 g, 10.2 mmol) in a 10 mL sealed tube was heated at 200°C for 10 minutes, in a CEM Discover microwave synthesiser. The solid product was triturated with EtOAc (100 mL), filtered then washed with cold EtOAc (10 mL) to give **5** (1.71 g, 55%) as a white solid; mp 153.0-153.5°C; IR (thin film) 3305, 3061, 3026, 2893, 1593, 1420, 761 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 8.44 (d, *J* = 4.5 Hz, 1H), 7.66 (t, *J* = 7.8 Hz, 1H), 7.29-7.12 (m, 12H), 5.36 (dd, *J* = 4.3, 1.3 Hz, 1H), 4.77 (t, *J* = 5.0 Hz, 1H), 3.79 (d, *J* = 5.8 Hz, 1H), 3.60 (d, *J* = 14.6 Hz, 1H), 3.50 (d, *J* = 14.6 Hz, 1H), 2.63 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.9 (C), 148.7 (CH), 143.2 (C), 140.9 (C), 136.3 (CH), 128.5 (CH), 127.4 (CH), 127.39 (CH), 127.0 (CH), 126.8 (CH), 126.6 (CH), 121.8 (CH), 121.7 (CH), 76.2 (CH), 67.9 (CH), 52.1 (CH_2); HRMS (EI^+): calcd for $C_{20}H_{20}N_2O$, 305.1648; found, 305.1648. Anal. calcd for $C_{20}H_{20}N_2O$: C, 78.92; H, 6.62; N, 9.20%. Found C, 78.95; H, 6.61; N, 9.31%.



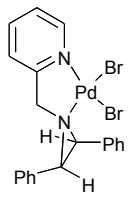
1

Synthesis of Aziridine 1. To a stirred solution of **5** (1.71 g, 5.62 mmol) and PPh_3 (1.92 g, 7.32 mmol) in THF (40 mL) at 0°C was slowly added DIAD (1.44 mL, 7.31 mmol). The reaction was allowed to warm to room temperature, stirred for a further 16 h, then the solvent removed *in vacuo*. Purification by column chromatography (Al_2O_3, Activity II, 10:1 petroleum ether/ethyl acetate) gave **1** (1.60 g, 99%) as a clear oil that solidified on standing; mp 75-76°C; IR (thin film) 3032, 2975, 2834, 1588, 1433, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.42 (m, 1H), 7.55 (dt, *J* = 7.8, 1.8 Hz, 1H), 7.50-7.21 (m, 11H), 7.06 (m, 1H), 3.81 (d, *J* = 15.6 Hz, 1H), 3.45 (br s, 1H), 3.43 (d, *J* = 15.6 Hz, 1H), 3.25 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8 (C), 148.8 (CH), 139.9 (C), 136.6 (CH), 133.7 (C), 130.1 (CH), 128.4 (CH), 128.1 (CH), 127.1 (CH), 126.3 (CH), 121.9 (CH), 121.7 (CH), 58.3 (CH_2), 50.9 (CH), 45.8 (CH); HRMS (EI^+): calcd for $C_{20}H_{18}N_2$, 286.1469; found, 286.1472. Anal. calcd for $C_{20}H_{18}N_2$: C, 83.88; H, 6.34; N, 9.78%. Found C, 83.84; H, 6.37; N, 9.80%.



6

Preparation of palladium(II) dichloride complex 6. To a stirred solution of **1** (150 mg, 0.52 mmol) in CH_2Cl_2 (6 mL) was added [$PdCl_2(MeCN)_2$] (136 mg, 0.52 mmol). The reaction was stirred for 15 minutes, then the solvent removed *in vacuo* to give **6** (242 mg, 100%) as an orange solid; mp 230°C (dec); IR (thin film) 3062, 2999, 1611, 1448, 753, 695 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.92 (d, *J* = 5.6 Hz, 1H), 7.89 (dt, *J* = 7.8, 1.6 Hz, 1H), 7.62-7.56 (m, 2H), 7.53-7.32 (m, 10H), 5.19 (d, *J* = 6.6 Hz, 1H), 4.44 (d, *J* = 15.6 Hz, 1H), 3.61 (d, *J* = 6.6 Hz, 1H), 3.10 (d, *J* = 15.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.3 (C), 151.1 (CH), 139.5 (CH), 132.2 (C), 130.0 (CH), 129.9 (CH), 129.7 (CH), 129.65 (C), 129.3 (CH), 129.1 (CH), 124.6 (CH), 121.4 (CH), 65.4 (CH_2), 54.0 (CH), 47.5 (CH); HRMS (EI^+): calcd for $C_{20}H_{17}ClN_2{}^{105}Pd$, 425.0126; found, 425.0126 (M^+–HCl). Anal. calcd for $C_{20}H_{18}Cl_2N_2Pd$: C, 51.80; H, 3.91; N, 6.04; Cl, 15.29%. Found C, 51.41; H, 3.91; N, 5.87; Cl, 15.29%.



7

Preparation of palladium(II) dibromide complex 7. To a stirred solution of **7** (100 mg, 0.35 mmol) in CH_2Cl_2 (10 mL) was added $PdBr_2$ (93 mg, 0.35 mmol). The reaction was stirred for 16 hours, and the solvent removed *in vacuo* to give **7** (193 mg, 100 %) as an orange solid; mp 197-198°C; IR (thin film) 3031, 2950, 2912, 1609, 1448, 1292, 693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.18 (d, *J* = 4.7 Hz, 1H), 7.92 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.64-7.58 (m, 2H), 7.55-7.48 (m, 3H), 7.46-7.32 (m, 7H), 5.44 (d, *J* = 6.5 Hz, 1H), 4.51 (d, *J* = 15.6 Hz, 1H), 3.53 (d, *J* = 6.5 Hz, 1H), 3.09 (d, *J* = 15.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1 (C), 152.3 (CH), 139.3 (CH), 132.1 (C), 130.1 (C), 130.0 (CH), 129.9 (CH), 129.7 (CH), 129.3 (CH), 129.0 (CH), 124.9 (CH), 121.4 (CH), 65.2 (CH_2), 53.4 (CH), 48.3 (CH); HRMS (EI^+): calcd for $C_{20}H_{17}BrN_2{}^{105}Pd$, 468.9620; found, 468.9621 (M^+–HBr). Anal. calcd for $C_{20}H_{18}Br_2N_2Pd$: C, 43.47; H, 3.28; N, 5.07; Br, 28.92%. Found C, 43.32; H, 3.27; N, 4.96; Br, 28.75%.

Method for the determination of activation parameters for aziridine 1. Variable temperature NMR spectra were recorded at 500 MHz on a Bruker DRX spectrometer in $CDCl_3$ at temperatures ranging from 283-334 K. Temperature calibration of the spectrometer was performed using CH_3OH/CD_3OD (<279K) and $HOCH_2CH_2OH/d_6$-DMSO (>298K). Natural line width was determined using a spectator signal (3.44 ppm). The chemical shifts of the aziridine resonances at close to coalescence were determined from a plot of $\nu_A - \nu_B$ (in Hz) vs T at temperatures well below coalescence. Simulated spectra for the AX spin system of the aziridine methine hydrogens were generated using the WINDNMR package (version 7.1.10) and compared with the acquired spectra using difference spectra. From these simulations, the rate constant k for inversion could be determined as a function of temperature (see overleaf). Hence, from the Eyring equation, the activation parameters could be determined by plotting $\ln(k/T)$ versus $1/T$ wherein:

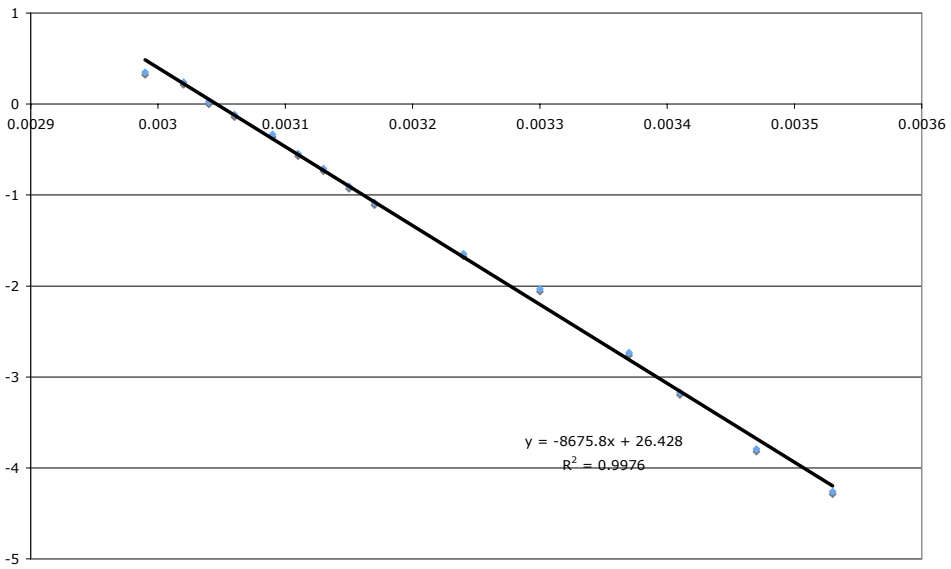
$$\Delta H^{\ddagger} = -(\text{slope})R$$

$$\Delta S^{\ddagger} = [\text{intercept} + \ln(h/K_b)]R$$

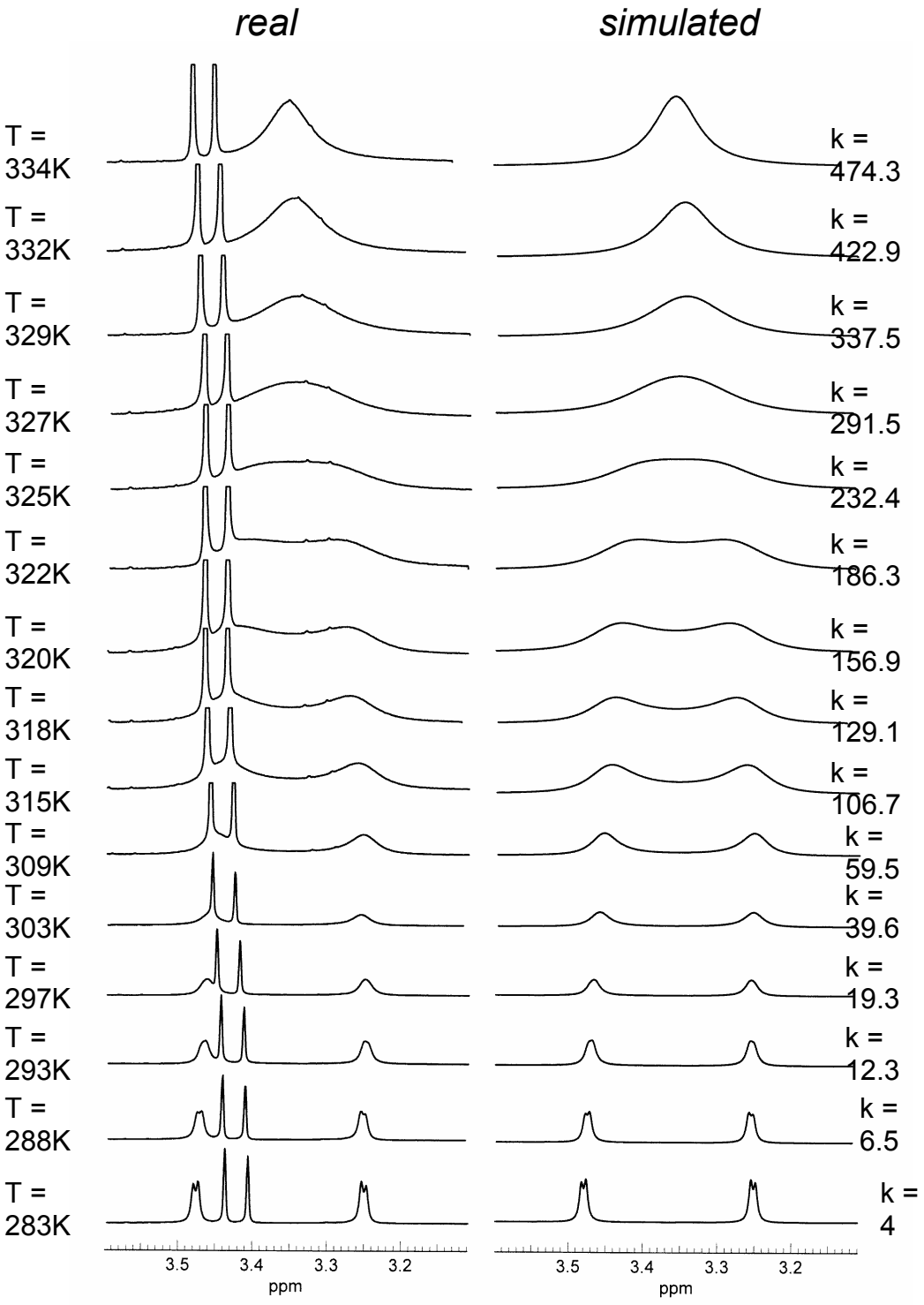
Where R = gas constant; h = Planck's constant; and k_b = Boltzmann's constant.

Using the above method, the following rates were obtained (see Table). The resulting Eyring plot was used to obtain the following data: $\Delta H^{\ddagger} = 72.1$ kJ mol^{-1}; $\Delta S^{\ddagger} = 22.2$ J K^{-1}mol^{-1} and $\Delta G^{\ddagger}$ (at 298 K) = 65.5 kJ mol^{-1}.

T (in K)	*k (s^{-1})*
283	4
288	6.5
293	12.3
297	19.3
303	39.6
309	59.5
315	106.7
318	129.1
320	156.9
322	186.3
325	232.4
327	291.5
329	337.5
332	422.9
334	474.3



Plot of ^{1}H NMR spectra (500 MHz, $CHCl_3$) as a function of temperature for aziridine **1**:



***In situ* Switching of Inversion "off" and "on" within aziridine 1**. The ^{1}H NMR spectrum of aziridine **1** (2.8 mg, 9.8 μmol) in d_2-tetrachloroethane (0.75 mL) was recorded (400 MHz, 338 K). $[PdCl_2(MeCN)_2]$ (2.6 mg, 10 μmol) was added, and the spectrum rerecorded at 338 K. Finally, dppe (4.0 mg, 9.7 μmol) was added and the spectrum rerun. Expansions pertaining to these ^{1}H NMR spectra are given in Fig 1.

Multiple switching cycles. The ^{1}H NMR spectrum of aziridine **6** (4.0 mg, 8.6 μmol) in d_2-tetrachloroethane (0.75 mL) was recorded (400 MHz, 338 K). Dppp (3.6 mg, 8.7 μmol) was added and the spectrum re-recorded at 338 K. Then, $[PdCl_2(MeCN)_2]$ (2.2 mg, 8.5 μmol) was added and the ^{1}H spectrum rerun at 338 K. Three additional cycles of this switching experiment were performed by adding further amounts of dppp (3.6 mg, 8.7 μmol) and $[PdCl_2(MeCN)_2]$ (2.2 mg, 8.5 μmol) in turn. Through integration of the aziridine signals for the inversion "on" and "off" states, it was possible to assess the efficiency of the switching process.

	^{1}H NMR integrals		
Added chemical input	**complexed ("off" state)**	**uncomplexed ("on" state)**	**% inversion "on"**
none	2.0148	0.0126	0.01
dppp	0.0492	1.9174	0.97
$PdCl_2(MeCN)_2$	2.0111	0	0
dppp	0.0647	1.906	0.97
$PdCl_2(MeCN)_2$	2.0056	0.0129	0.01
dppp	0.0895	1.9035	0.95
$PdCl_2(MeCN)_2$	2.0026	0	0
dppp	0.1335	1.9305	0.93
$PdCl_2(MeCN)_2$	2.2115	0.3217	0.14