– Electronic Supplementary Material (ESI)–

Kinetics and mechanism of organocatalytic aza–Michael additions: direct observation of enamine intermediates

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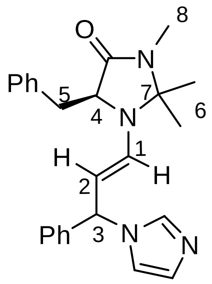
1. General

The ^{1}H and ^{13}C NMR spectra were recorded at 600, 400 or 300 MHz and at 150, 100 or 75.5 MHz, respectively. The chemical shifts (δ) for ^{1}H and ^{13}C are given in ppm relative to residual signals of the solvents (CD$_3$CN @ 1.94 ppm ^{1}H NMR, 117.4 ppm ^{13}C NMR). Coupling constants are given in Hz. Carbon multiplicities were determined from HSQC experiments. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; bs, broad singlet. NMR signal assignments are based on additional 2D-NMR experiments (COSY, NOESY, HSQC, and HMBC).

Commercially available acetonitrile (VWR, Prolabo, HPLC-gradient grade) was used without further purification for all kinetic experiments and determinations of equilibrium constants. The azoles **1a–g** were purified prior to use. The iminium ion **2** was prepared according to literature procedures.[S1]

2. Product Characterization by NMR Spectroscopy

Under an atmosphere of nitrogen, 4 equivalents (or little excess) of imidazole **1c**, were added directly to a CD$_3$CN solution of the iminium ion **2** in an NMR tube. After few minutes of shaking, the NMR study was performed, which shows the formation of the enamine **4c** as a mixture of two diastereoisomers (1:1).



4c

^{1}H NMR (400 MHz, CD$_3$CN): $\delta = 7.90$ (s, 1H), 7.24-7.50 (m, 6H), 7.10-7.20 (m, 4H), 7.00-7.07 (m, 1H), 6.94-6.99 (m, 1H), 6.56 (d, $J = 13.7$ Hz, 1H, 1-H), 5.97 (dd, $J = 9.0$ Hz, 13, 6 Hz, 1H, 3-H), 4.91-5.08 (m, 1H, 2-H), 4.25 (bs, 4-H), 4.20 (bs, 4-H), 2.98-3.44 (m, 2H, 5-H), 2.65* (s, 3H, 8-H), $2.64^{\#}$ (s, 3H, 6H), 0,66* (s, 3H, 6H), $0.65^{\#}$ (s, 3H, 6-H); ^{13}C NMR (101 MHz, CD$_3$CN) 168.8* (s, C=O), $168.7^{\#}$ (s, C=O), 142.3, 141.8, 136.9, 136.9, 136.3 , 136.2, 133.3, 132.9 (d, C–1), 130.1 (d), 130.0, 129.3, 128.93, 128.8, 128.3, 127.8, 127.8, 127.5, 126.7, 126.6, 126.5, 126.5, 118.9, 118.8, 97.8* (d, C–2), $97.7^{\#}$ (d, C–2), 78.3* (s, C–7), $78.2^{\#}$ (s, C–7), 63.3* (d, C–3), $63.2^{\#}$ (d, C–3), 59.9* (d, C–4), $59.9^{\#}$ (d, C–4), 33.4^{*} (d, C–5), $33.4^{\#}$ (d, C–5), 25.0*, $25.0^{\#}$, 24.2^{*} (q, C–8), $24.2^{\#}$ (q, C–8).

*: diasteroisomer 1; #: diastereoisomer 2

[S1] a) S. Lakhdar, T. Tokuyasu and H. Mayr, *Angew. Chem.*, 2008, **120**, 8851; *Angew. Chem., Int. Ed.*, 2008, **47**, 8723; b) S. Lakhdar, J. Ammer and H. Mayr *Angew. Chem.* 2011, **123**, 10127-10130; *Angew. Chem. Int. Ed.* 2011, **50**, 9953-9956.

3. Kinetics

All reactions of azoles with iminium ion **2** were performed in acetonitrile at 20°C. The kinetics were followed photometrically using the stopped-flow technique described previously.[S1] The kinetic runs were performed by mixing equal volumes of acetonitrile solutions of the azoles with acetonitrile solutions of **2** and monitoring the decrease of absorbances at the wavelength close to the absorption maxima of **2** (370 nm).

In general, azoles were applied in high excess over iminium ion **2** for achieving pseudo-first-order conditions. The first-order rate constants k_{obs} (s^{-1}) were obtained by least-squares fitting of the absorbances (averaged from at least 6 kinetic runs) to the single exponential function $A = A_0 \exp(-k_{obs}t) + C$. Second-order rate constants k (M^{-1} s^{-1}) were then obtained from the slope of the k_{obs} vs [1a–g] curve.

Table S1. Rate constants for the reaction of **1a** with **2** in acetonitrile (0.5% DMSO) (Stopped–flow method, 20 °C, λ = 370 nm).

[**2**] (M)	[**1a**] (M)	k_{obs} (s^{-1})
1.20×10^{-4}	8.88×10^{-3}	4.56
1.20×10^{-4}	1.14×10^{-2}	5.11
1.20×10^{-4}	1.27×10^{-2}	5.45
1.20×10^{-4}	1.52×10^{-2}	6.16
1.20×10^{-4}	1.78×10^{-2}	6.99
$\mathbf{k_2 = 2.75 \times 10^{2}\ M^{-1}\ s^{-1}}$		

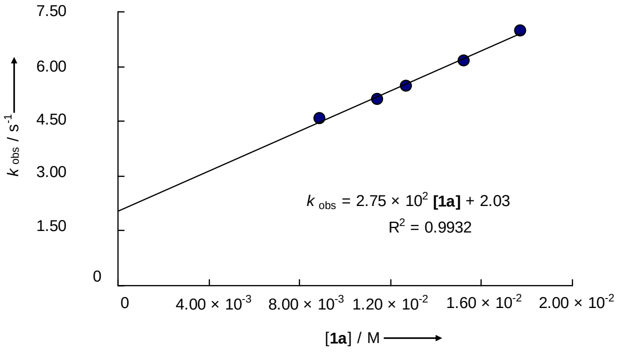


Table S2. Rate constants for the reaction of **1b** with **2** in acetonitrile (Stopped–flow method, 20 °C, λ = 370 nm).

[**2**] (M)	[**1b**] (M)	k_{obs} (s^{-1})
1.20×10^{-4}	1.51×10^{-3}	8.59
1.20×10^{-4}	3.02×10^{-3}	1.20×10^{1}
1.20×10^{-4}	4.53×10^{-3}	1.64×10^{1}
1.20×10^{-4}	6.04×10^{-3}	2.10×10^{1}
1.20×10^{-4}	7.54×10^{-3}	2.59×10^{1}
$k_2 = 2.88 \times 10^{3}$ M^{-1} s^{-1}		

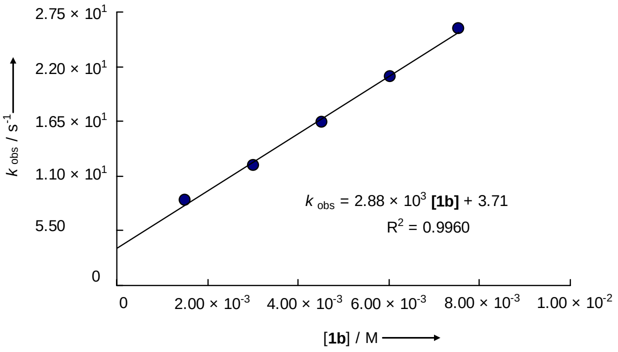


Table S3. Rate constants for the reaction of **1c** with **2** in acetonitrile (Stopped–flow method, 20 °C, λ = 370 nm).

[**2**] (M)	[**1c**] (M)	k_{obs} (s^{-1})
1.20×10^{-4}	1.82×10^{-3}	9.20
1.20×10^{-4}	3.65×10^{-3}	1.39×10^{1}
1.20×10^{-4}	5.47×10^{-3}	1.96×10^{1}
1.20×10^{-4}	7.30×10^{-3}	2.51×10^{1}
1.20×10^{-4}	9.12×10^{-3}	3.10×10^{1}
$k_2 = 3.01 \times 10^{3}$ M^{-1} s^{-1}		

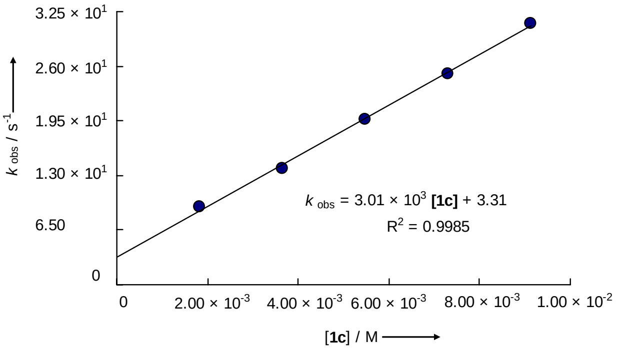


Table S4. Rate constants for the reaction of **1d** with **2** in acetonitrile (Stopped–flow method, 20 °C, $\lambda = 370$ nm).

[**2**] / M	[**1d**] / M	k_{obs} / $\mathrm{s^{-1}}$
1.20×10^{-5}	2.36×10^{-3}	7.36
1.20×10^{-5}	3.53×10^{-3}	1.11×10^{1}
1.20×10^{-5}	4.71×10^{-3}	1.47×10^{1}
1.20×10^{-5}	5.89×10^{-3}	1.81×10^{1}
1.20×10^{-5}	7.07×10^{-3}	2.15×10^{1}
$\boldsymbol{k_2 = 3.00 \times 10^{3}\ \mathrm{M^{-1}\ s^{-1}}}$		

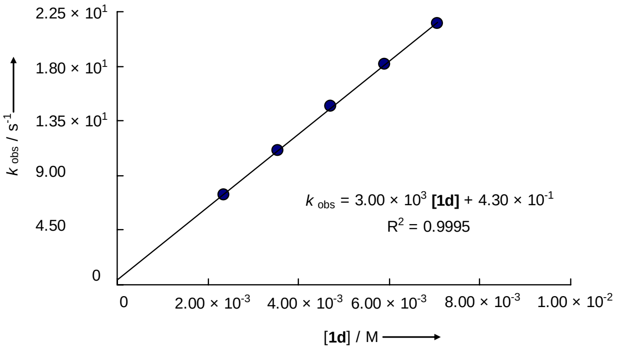


Table S5. Rate constants for the reaction of **1e** with **2** in acetonitrile (Stopped–flow method, 20 °C, $\lambda = 370$ nm).

[**2**] / M	[**1e**] / M	k_{obs} / $\mathrm{s^{-1}}$
1.20×10^{-4}	2.68×10^{-3}	7.46
1.20×10^{-4}	4.02×10^{-3}	1.10×10^{1}
1.20×10^{-4}	5.36×10^{-3}	1.48×10^{1}
1.20×10^{-4}	6.70×10^{-3}	1.88×10^{1}
1.20×10^{-4}	8.03×10^{-3}	2.26×10^{1}
$\boldsymbol{k_2 = 2.84 \times 10^{3}\ \mathrm{M^{-1}\ s^{-1}}}$		

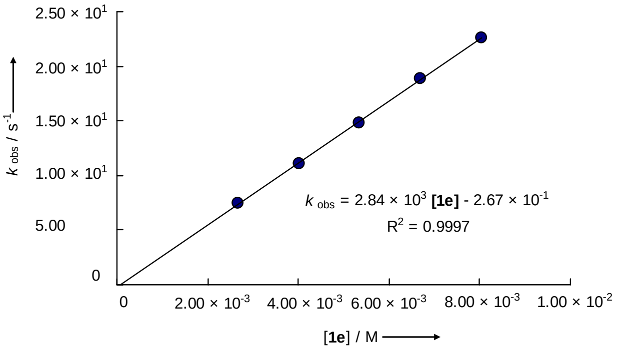


Table S6. Rate constants for the reaction of **1f** with **2** in acetonitrile (Stopped–flow method, 20 °C, λ = 370 nm).

[**2**] / M	[**1f**] / M	k_{obs} / s^{-1}
1.20×10^{-4}	3.70×10^{-3}	1.70×10^{1}
1.20×10^{-4}	4.94×10^{-3}	2.27×10^{1}
1.20×10^{-4}	7.41×10^{-3}	3.46×10^{1}
1.20×10^{-4}	9.88×10^{-3}	4.60×10^{1}
1.20×10^{-4}	1.23×10^{-2}	5.68×10^{1}
$k_2 = 4.62 \times 10^{3}$ M^{-1} s^{-1}		

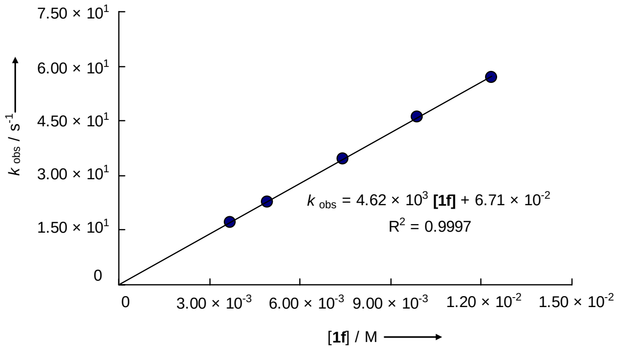
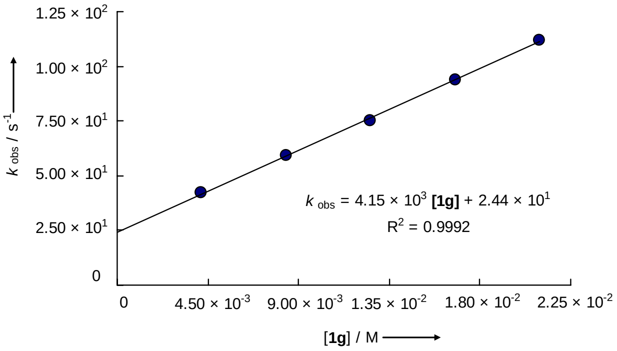


Table S7. Rate constants for the reaction of **1g** with **2** in acetonitrile (Stopped–flow method, 20 °C, λ = 370 nm).

[**2**] / M	[**1g**] / M	k_{obs} / s^{-1}
1.20×10^{-4}	4.19×10^{-3}	4.22×10^{1}
1.20×10^{-4}	8.38×10^{-3}	5.93×10^{1}
1.20×10^{-4}	1.26×10^{-2}	7.52×10^{1}
1.20×10^{-4}	1.68×10^{-2}	9.39×10^{1}
1.20×10^{-4}	2.10×10^{-2}	1.12×10^{2}
$k_2 = 4.15 \times 10^{3}$ M^{-1} s^{-1}		



4. Determination of the Equilibrium Constants

Table S8. Equilibrium constant for the reaction of **1b** with **2** in acetonitrile (20 °C, 370 nm).

Entry	A_t	$(A_0–A)$	[**2**]$_t$	[**1b**]$_t$	K (L mol^{-1})
0			7.19×10^{-5}	0	
1	0.750	0.510	4.26×10^{-5}	7.26×10^{-4}	9.95×10^{2}
2	0.437	0.818	2.48×10^{-5}	1.45×10^{-3}	1.32×10^{3}
3	0.272	0.978	1.55×10^{-5}	2.16×10^{-3}	1.68×10^{3}
4	0.200	1.045	1.14×10^{-5}	2.87×10^{-3}	1.83×10^{3}

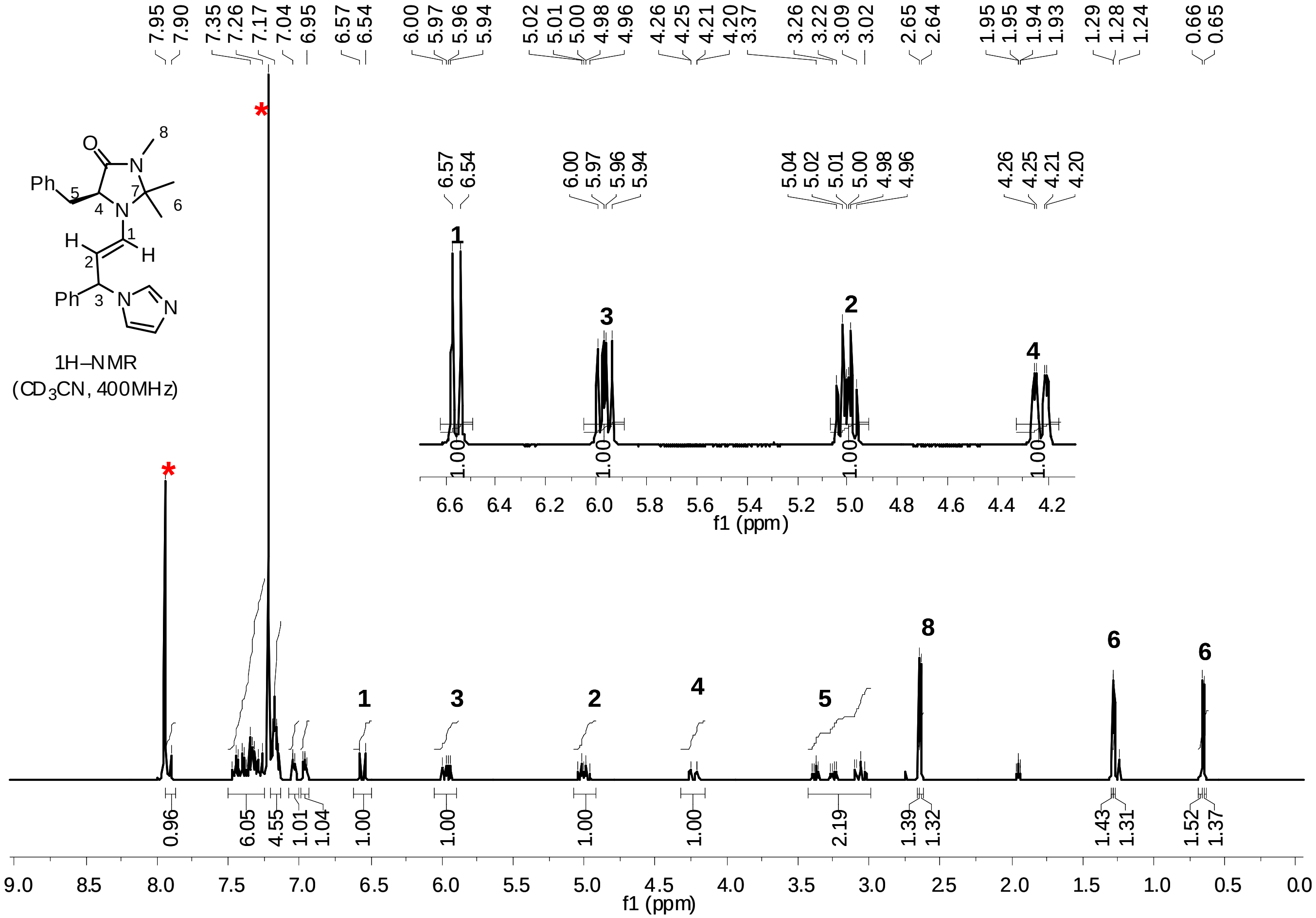
$K = (1.61 \pm 0.26) \times 10^3$ L mol^{-1}

Table S9. Equilibirium constant for the reaction of **1e** with **2** in acetonitrile (20 °C, 370 nm).

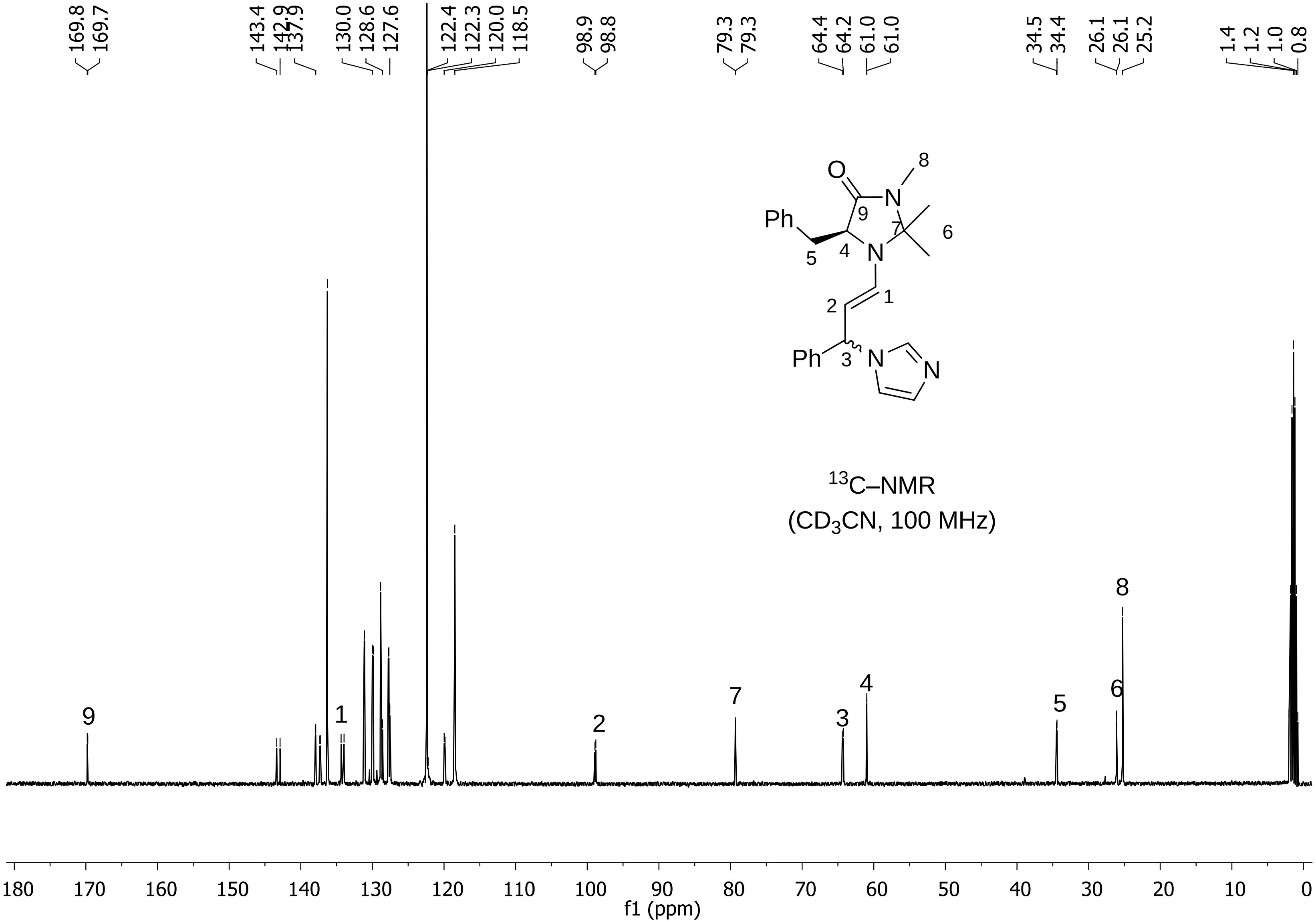
Entry	A_t	$(A_0–A)$	[**2**]$_t$	[**1b**]$_t$	K (L mol^{-1})
0			7.26×10^{-5}	0	
1	1.010	0.209	5.97×10^{-5}	1.01×10^{-3}	2.18×10^{2}
2	0.894	0.315	5.28×10^{-5}	2.01×10^{-3}	1.81×10^{2}
3	0.790	0.410	4.67×10^{-5}	2.98×10^{-3}	1.76×10^{2}
4	0.691	0.499	4.08×10^{-5}	3.95×10^{-3}	1.85×10^{2}
5	0.609	0.571	3.60×10^{-5}	4.89×10^{-3}	1.93×10^{2}

$K = (1.84 \pm 0.70) \times 10^2$ L mol^{-1}

Copies of the ^{1}H, ^{13}C, NMR spectra



*: excess imidazole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98.9
98.8
79.3
79.3
64.4
64.2
61.0
61.0
34.5
34.4
26.1
26.1
25.2
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2
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3
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N
^{13}C–NMR
(CD$_3$CN, 100 MHz)
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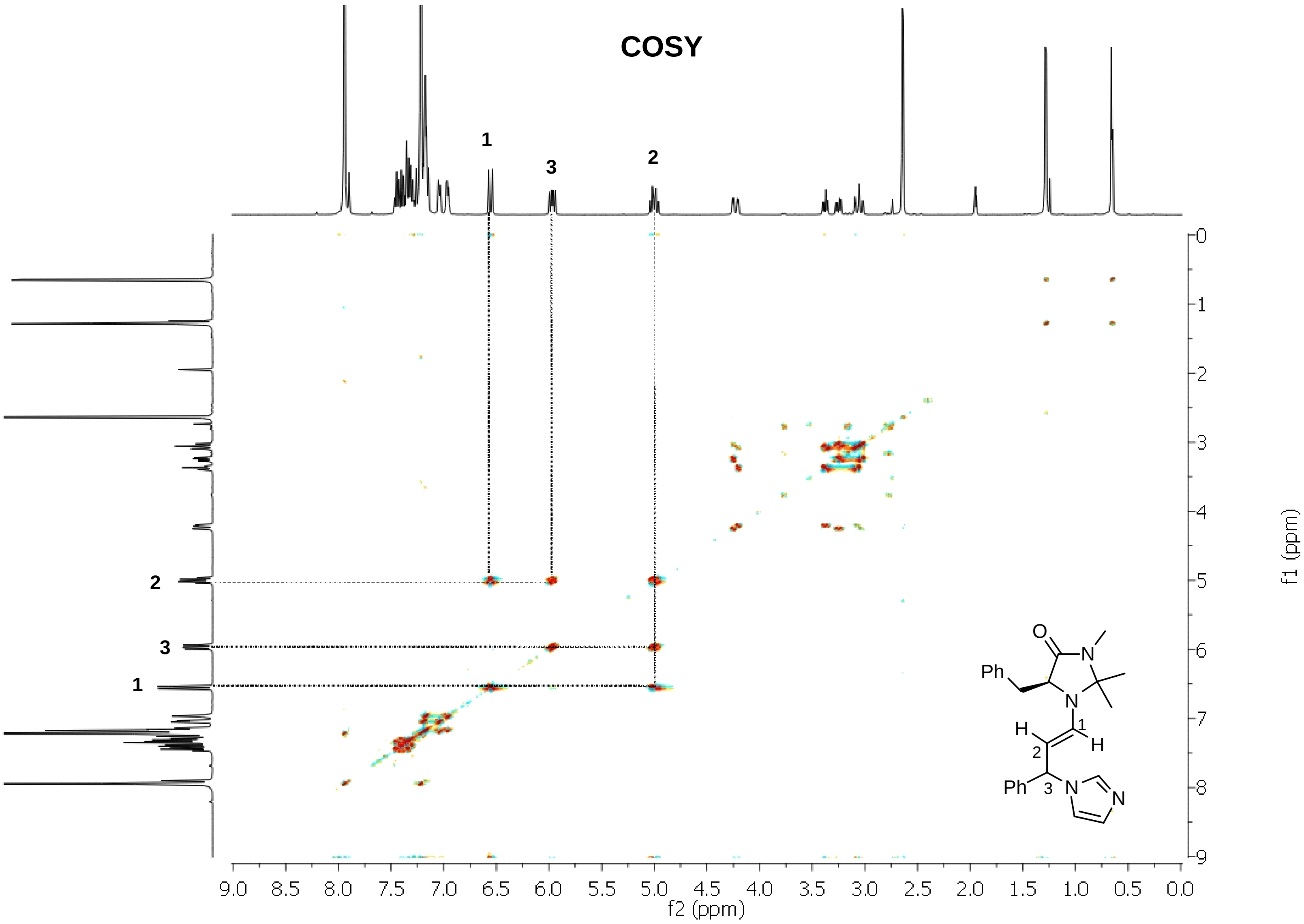
f1 (ppm)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f2 (ppm)
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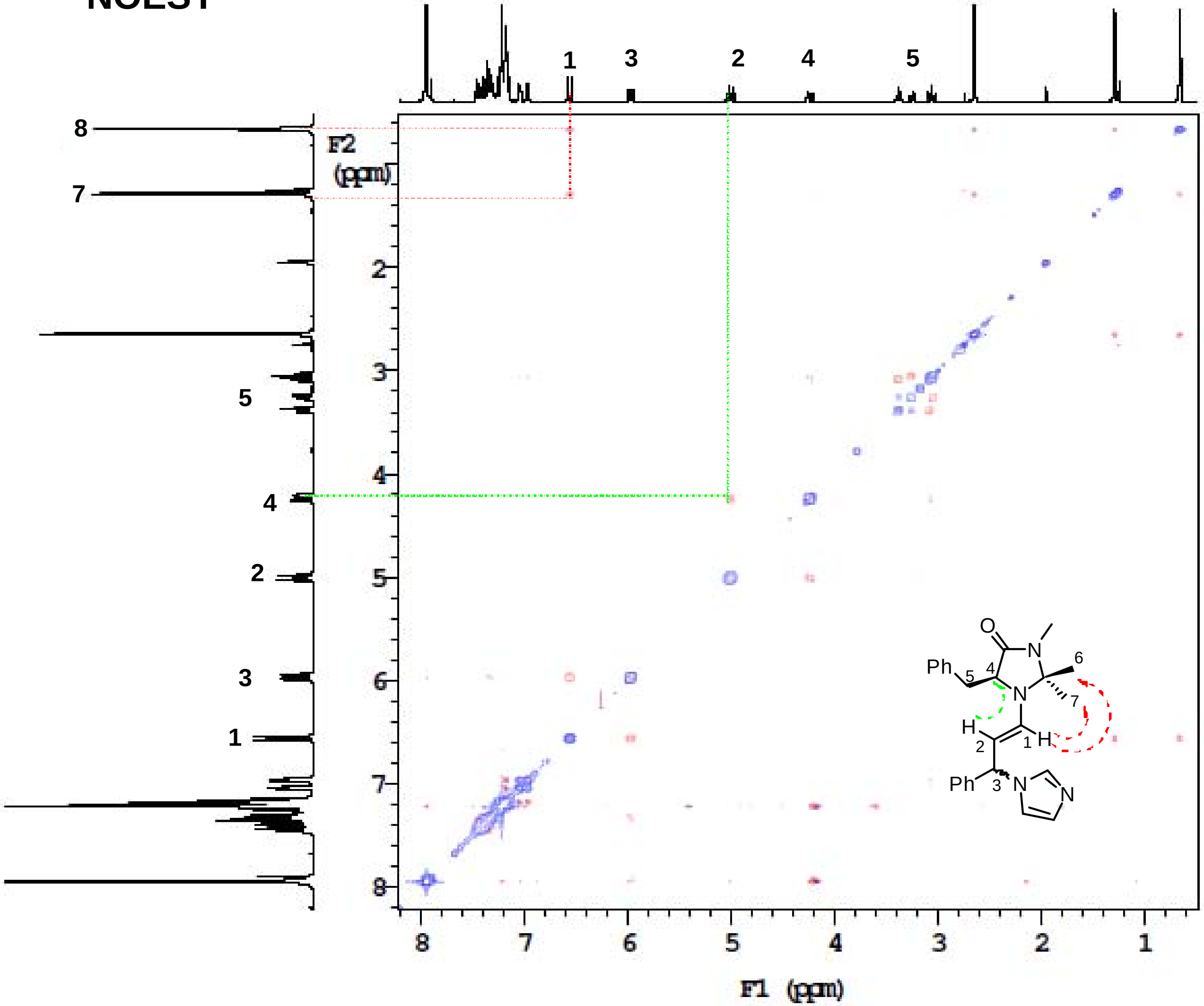
NOESY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