Solvent Induced Cooperativity of Zn(II) Complexes Cleaving a Phosphate Diester RNA Analog in Methanol.

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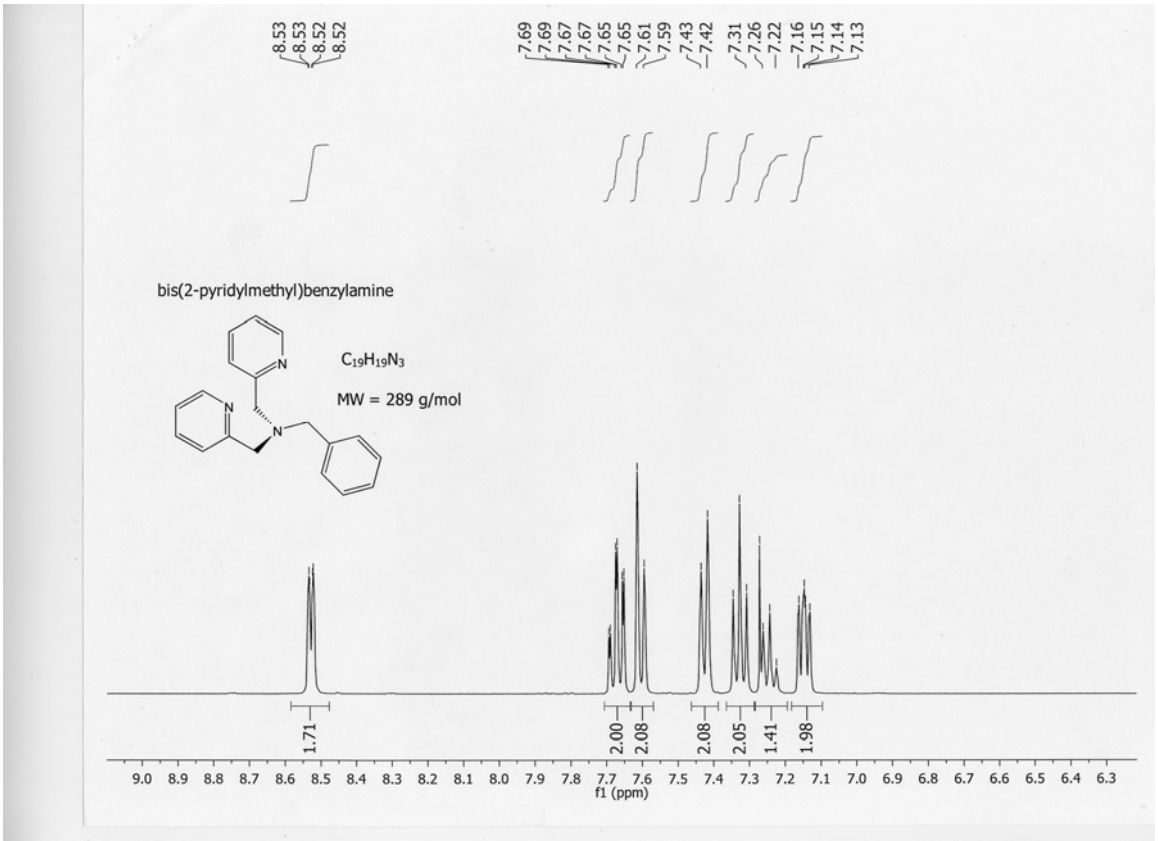
^{1}H NMR Spectrum of ligand **4** (Bis(2-pyridylmethyl)benzylamine)



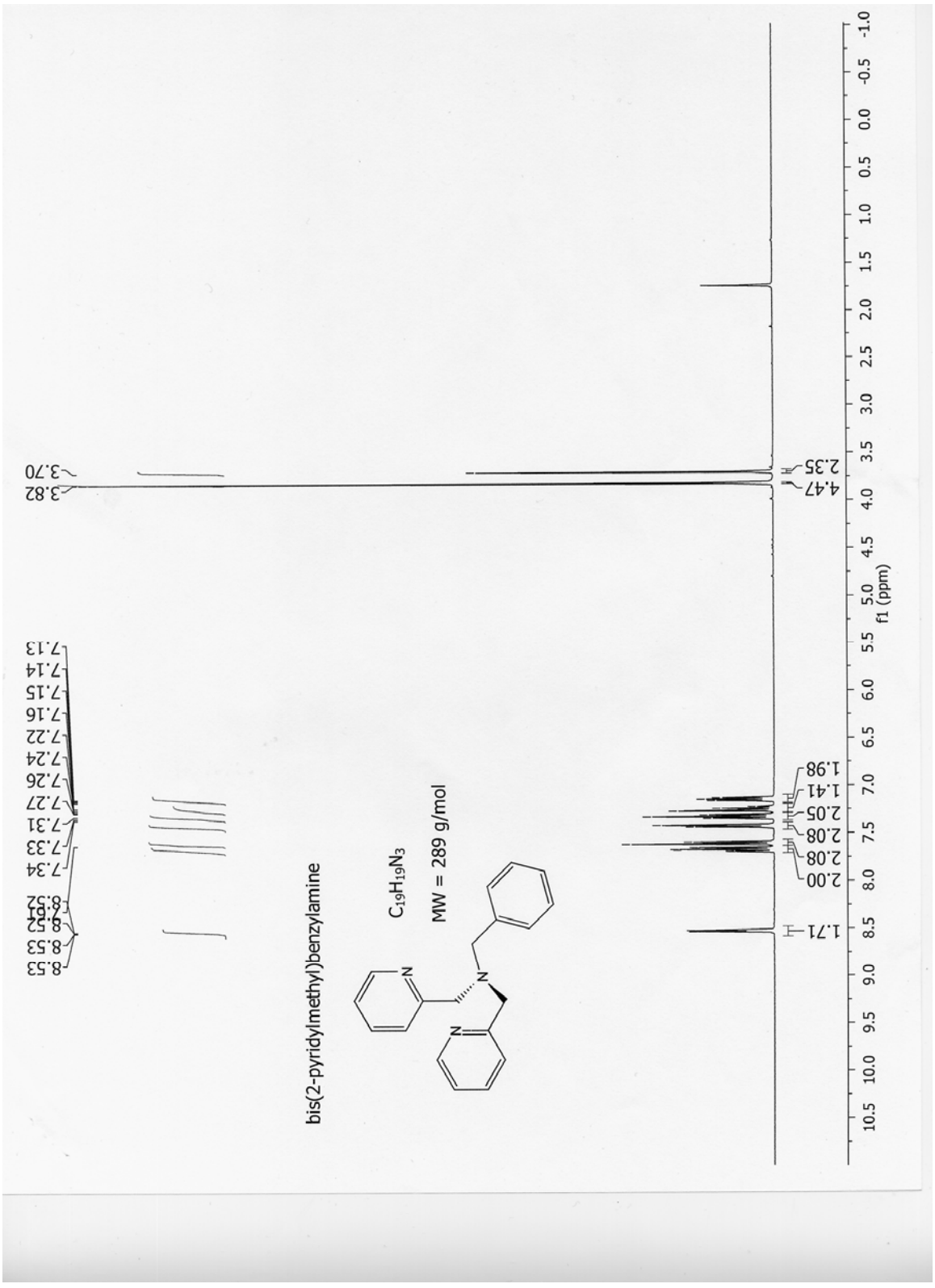


Table 1S. Average observed pseudo first order rate constants (k_{obs}) vs. [**4**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 8.0 (4-Ethylmorpholine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Values of k_{obs} are corrected for the effect of buffer on the basis of the buffer inhibition data in Table 8S.

[**4**:Zn(II)] (mmol dm^{-3})	k_{obs} (s^{-1})
0.1	0.0000073
0.2	0.000011
0.3	0.000024
0.5	0.000057
1.0	0.00014
1.5	0.00022

Table 2S. Average observed pseudo first order rate constants (k_{obs}) vs. [**4**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 8.5 (4-Ethylmorpholine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Values of k_{obs} are corrected for the effect of buffer on the basis of the buffer inhibition data in Table 9S.

[**4**:Zn(II)] (mmol dm^{-3})	k_{obs} (s^{-1})
0.1	0.000025
0.2	0.000068
0.3	0.00013
0.5	0.00029
1.0	0.00071
1.5	0.0011

Table 3S. Average observed pseudo first order rate constants (k_{obs}) vs. [**4**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 9.1 (4-Ethylmorpholine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Values of k_{obs} are corrected for the effect of buffer on the basis of the buffer inhibition data in Table 10S.

[**4**:Zn(II)] (mmol dm^{-3})	k_{obs} (s^{-1})
0.1	0.00010
0.2	0.00025
0.3	0.00045
0.5	0.0010
1.0	0.0025
1.5	0.0038

Table 4S. Average observed pseudo first order rate constants (k_{obs}) vs. [**4**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 10.1 (triethylamine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Values of k_{obs} are corrected for the effect of buffer on the basis of the buffer inhibition data in Table 11S.

[**4**:Zn(II)] (mmol dm^{-3})	k_{obs} (s^{-1})
0.1	0.00038
0.2	0.00088
0.3	0.0020
0.5	0.0040
1.0	0.010
1.5	0.016

Table 5S. Average observed pseudo first order rate constants (k_{obs}) vs. [**4**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 10.8 (triethylamine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Values of k_{obs} are corrected for the effect of buffer on the basis of the buffer inhibition data in Table 12S.

[**4**:Zn(II)] (mmol dm^{-3})	k_{obs} (s^{-1})
0.1	0.00069
0.2	0.0026
0.3	0.0035
0.5	0.0078
1.0	0.022
1.5	0.032

Table 6S. Average observed pseudo first order rate constants (k_{obs}) vs. [**4**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 11.3 (triethylamine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Values of k_{obs} are corrected for the effect of buffer on the basis of the buffer inhibition data in Table 13S.

[**4**:Zn(II)] (mmol dm^{-3})	k_{obs} (s^{-1})
0.1	0.0016
0.2	0.0042
0.3	0.0078
0.5	0.017
1.0	0.041
1.5	0.061

Table 7S. Average observed pseudo first order rate constants (k_{obs}) vs. [**4**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 12.1 (2,2,6,6-Tetramethylpiperidine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Values of k_{obs} are corrected for the effect of buffer on the basis of the buffer inhibition data in Table 14S.

[**4**:Zn(II)] (mmol dm^{-3})	k_{obs} (s^{-1})
0.1	0.0013
0.2	0.0034

0.3	0.0043
0.5	0.012
1.0	0.031
1.5	0.047

Table 8S. Average observed pseudo first order rate constants (k_{obs}) vs. [N-ethylmorpholine] for the cleavage of HPNPP (**1**, 0.05mM) catalyzed by **4**:Zn(II) (1.0 mmol dm^{-3}) in N-ethylmorpholine buffer ($^{s}_{s}$pH = 8.0) at T=25.0 ± 0.1 °C.

[N-ethylmorpholine] (mmol dm^{-3})	k_{obs} (s^{-1})
5	0.00013
10	0.00012
20	0.00012

Table 9S. Average observed pseudo first order rate constants (k_{obs}) vs. [N-ethylmorpholine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **4**:Zn(II) (1.0 mmol dm^{-3}) in N-ethylmorpholine buffer ($^{s}_{s}$pH = 8.5) at T=25.0 ± 0.1 °C.

[N-ethylmorpholine] (mmol dm^{-3})	k_{obs} (s^{-1})
5	0.00075
10	0.00075
15	0.00071
20	0.00071

Table 10S. Average observed pseudo first order rate constants (k_{obs}) vs. [N-ethylmorpholine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **4**:Zn(II) (1.0 mmol dm^{-3}) in N-ethylmorpholine buffer ($^{s}_{s}$pH = 9.1) at T=25.0 ± 0.1 °C.

[N-ethylmorpholine] (mmol dm^{-3})	k_{obs} (s^{-1})
5	0.0023
10	0.0024
15	0.0025
20	0.0025

Table 11S. Average observed pseudo first order rate constants (k_{obs}) vs. [triethylamine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **4**:Zn(II) (1.0 mmol dm^{-3}) in Triethylamine buffer ($^{s}_{s}$pH = 10.1) at T=25.0 ± 0.1 °C.

[triethylamine] (mmol dm^{-3})	k_{obs} (s^{-1})

5	0.0096
10	0.010
15	0.010
20	0.010

Table 12S. Average observed pseudo first order rate constants (k_{obs}) vs. [triethylamine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **4**:Zn(II) (1.0 mmol dm^{-3}) in Triethylamine buffer ($^{s}_{s}$pH = 10.8) at T=25.0 ± 0.1 °C.

[triethylamine] (mmol dm^{-3})	k_{obs} (s^{-1})
5	0.0150
10	0.0130
15	0.0126

Table 13S. Average observed pseudo first order rate constants (k_{obs}) vs. [triethylamine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **4**:Zn(II) (1.0 mmol dm^{-3}) in triethylamine buffer ($^{s}_{s}$pH = 11.3) at T=25.0 ± 0.1 °C.

[triethylamine] (mmol dm^{-3})	k_{obs} (s^{-1})
5	0.029
10	0.026
15	0.023

Table 14S. Average observed pseudo first order rate constants (k_{obs}) vs. [2,2,6,6,-tetramethylpiperidine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **4**:Zn(II) (1.0 mmol dm^{-3}) in 2,2,6,6,-Tetramethylpiperidine buffer ($^{s}_{s}$pH = 12.1) at T=25.0 ± 0.1 °C.

[2,2,6,6,-tetramethylpiperidine] (mmol dm^{-3})	k_{obs} (s^{-1})
5	0.029
10	0.024
15	0.021
20	0.020

Table 15S. Average observed pseudo first order rate constants (k_{obs}) vs. [DBP] for the inhibition of the cleavage of **6** (0.05 mmol dm^{-3}) catalyzed by **4**:Zn(II) (1.0 mmol dm^{-3}) by DBP, sodium salt. Determined in anhydrous methanol at $^{s}_{s}$pH = 11.0 and T=25.0 ± 0.1 °C. The data were fit according to eqn. (S1) to give K_i = 0.18 ± 0.6 x10^{-3} mol dm^{-3}.

[DBP] (mmol dm^{-3})	k_{obs} (s^{-1})

0.0	0.019
0.4	0.011
0.8	0.0082
1.2	0.0062
1.5	0.0050
2.0	0.0038
3.0	0.0026
4.0	0.0018

Table 16S. Average observed pseudo first order rate constants (k_{obs}) for the cleavage of 5.0 x 10^{-4} mol dm^{-3} HPNPP (**1**) catalyzed by 5.0 x 10^{-5} mol dm^{-3} **4**:Zn(II) as a function of $^{s}_{s}$pH.

$^{s}_{s}$**pH**	k_{obs} (s^{-1})
8.36	0.000020
8.74	0.000052
9.15	0.00010
9.89	0.0011
10.60	0.0033
10.85	0.0034
11.26	0.0025
11.94	0.0022

Table 17S. Average observed pseudo first order rate constants (k_{obs}) vs. [**5**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 7.6 (2,6-lutidine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Values of k_{obs} are corrected for the effect of buffer on the basis of the buffer inhibition data in Table 25S.

[**5**:Zn(II)] (mmol dm^{-3})	k_{obs} (s^{-1})
0.1	0.000028
0.2	0.000083
0.3	0.00028
0.5	0.0012
0.75	0.0022
1.0	0.0036
1.5	0.0069
2.0	0.011

Table 18S. Average observed pseudo first order rate constants (k_{obs}) vs. [**5**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 8.3 (N-ethylmorpholine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Values of

k_{obs} are corrected for the effect of buffer on the basis of the buffer inhibition data in Table 26S.

[**5**:Zn(II)] (mmol dm^{-3})	k_{obs} (s^{-1})
0.1	0.000086
0.2	0.00041
0.3	0.0012
0.5	0.0040
0.75	0.0085
1.0	0.013
1.5	0.026
2.0	0.038

Table 19S. Average observed pseudo first order rate constants (k_{obs}) vs. [**5**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 8.6 (N-ethylmorpholine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Values of k_{obs} are corrected for the effect of buffer on the basis of the buffer inhibition data in Table 27S.

[**5**:Zn(II)] (mmol dm^{-3})	k_{obs} (s^{-1})
0.1	0.00023
0.2	0.00094
0.3	0.0026
0.5	0.0089
0.75	0.017
1.0	0.026
1.5	0.045
2.0	0.064

Table 20S. Average observed pseudo first order rate constants (k_{obs}) vs. [**5**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 8.9 (N-ethylmorpholine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Values of k_{obs} are corrected for the effect of buffer on the basis of the buffer inhibition data in Table 28S.

[**5**:Zn(II)] (mmol dm^{-3})	k_{obs} (s^{-1})
0.1	0.00052
0.2	0.0021
0.3	0.0045
0.5	0.013
0.75	0.025
1.0	0.038
1.5	0.077
2.0	0.10

Table 21S. Average observed pseudo first order rate constants (k_{obs}) vs. [**5**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 9.9 (N-methylpiperidine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Values of k_{obs} are corrected for the effect of buffer on the basis of the buffer inhibition data in Table 29S.

[**5**:Zn(II)] (mmol dm^{-3})	k_{obs} (s^{-1})
0.1	0.00092
0.2	0.0029
0.3	0.0063
0.5	0.016
0.75	0.034
1.0	0.053
1.5	0.10
2.0	0.15

Table 22S. Average observed pseudo first order rate constants (k_{obs}) vs. [**5**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 10.4 (triethylamine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Values of k_{obs} are corrected for the effect of buffer on the basis of the buffer inhibition data in Table 30S.

[**5**:Zn(II)] (mmol dm^{-3})	k_{obs} (s^{-1})
0.1	0.00071
0.2	0.0020
0.3	0.0035
0.5	0.0072
0.75	0.016
1.0	0.024
1.5	0.051
2.0	0.081

Table 23S. Average observed pseudo first order rate constants (k_{obs}) vs. [**5**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 10.9 (triethylamine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Values of k_{obs} are corrected for the effect of buffer on the basis of the buffer inhibition data in Table 31S.

[**5**:Zn(II)] (mmol dm^{-3})	k_{obs} (s^{-1})
0.1	0.00077
0.2	0.0020
0.3	0.0033
0.5	0.0061
0.75	0.011

1.0	0.016
1.5	0.030
2.0	0.050

Table 24S. Average observed pseudo first order rate constants (k_{obs}) vs. [**5**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 11.2 (triethylamine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Values of k_{obs} are corrected for the effect of buffer on the basis of the buffer inhibition data in Table 32S.

[**5**:Zn(II)] (mmol dm^{-3})	k_{obs} (s^{-1})
0.1	0.00089
0.2	0.0019
0.3	0.0030
0.5	0.0060
0.75	0.011
1.0	0.016
1.5	0.024
2.0	0.043

Table 25S. Average observed pseudo first order rate constants (k_{obs}) vs. [**5**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 12.0 (2,2,6,6-tetramethylpiperidine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Values of k_{obs} are corrected for the effect of buffer on the basis of the buffer inhibition data in Table 33S.

[**5**:Zn(II)] (mmol dm^{-3})	k_{obs} (s^{-1})
0.1	0.00016
0.2	0.00037
0.3	0.00055
0.5	0.0011
0.75	0.0018
1.0	0.0026
1.5	0.0044
2.0	0.0075

Table 26S. Average observed pseudo first order rate constants (k_{obs}) vs. [2,6-lutidine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **5**:Zn(II) (1.0 mmol dm^{-3}) in 2,6-Lutidine buffer ($^{s}_{s}$pH = 7.6) at T=25.0 ± 0.1 °C.

[2,6-Lutidine] (mmol dm^{-3})	k_{obs} (s^{-1})
5	0.0039
10	0.0036
20	0.0036

Table 27S. Average observed pseudo first order rate constants (k_{obs}) vs. [N-ethylmorpholine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **5**:Zn(II) (1.0 mmol dm^{-3}) in N-ethylmorpholine buffer ($^{s}_{s}$pH = 8.3) at T=25.0 ± 0.1 °C.

[N-ethylmorpholine] (mmol dm^{-3})	k_{obs} (s^{-1})
5	0.0073
10	0.0071
20	0.0068

Table 28S. Average observed pseudo first order rate constants (k_{obs}) vs. [N-ethylmorpholine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **5**:Zn(II) (1.0 mmol dm^{-3}) in N-ethylmorpholine buffer ($^{s}_{s}$pH = 8.6) at T=25.0 ± 0.1 °C.

[N-ethylmorpholine] (mmol dm^{-3})	k_{obs} (s^{-1})
5	0.018
10	0.019
20	0.019

Table 29S. Average observed pseudo first order rate constants (k_{obs}) vs. [N-ethylmorpholine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **5**:Zn(II) (1.0 mmol dm^{-3}) in N-ethylmorpholine buffer ($^{s}_{s}$pH = 8.9) at T=25.0 ± 0.1 °C.

[N-ethylmorpholine] (mmol dm^{-3})	k_{obs} (s^{-1})
5	0.030
10	0.031
20	0.033

Table 30S. Average observed pseudo first order rate constants (k_{obs}) vs. [N-methylpiperidine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **5**:Zn(II) (1.0 mmol dm^{-3}) in N-methylpiperidine buffer ($^{s}_{s}$pH = 9.9) at T=25.0 ± 0.1 °C.

[N-methylpiperidine] (mmol dm^{-3})	k_{obs} (s^{-1})
5	0.051
10	0.046
20	0.041

Table 31S. Average observed pseudo first order rate constants (k_{obs}) vs. [triethylamine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **5**:Zn(II) (1.0 mmol dm^{-3}) in Triethylamine buffer ($^{s}_{s}$pH = 10.4) at T=25.0 ± 0.1 °C.

[triethylamine] (mmol dm^{-3})	k_{obs} (s^{-1})
5	0.038
10	0.040
20	0.039

Table 32S. Average observed pseudo first order rate constants (k_{obs}) vs. [triethylamine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **5**:Zn(II) (1.0 mmol dm^{-3}) in Triethylamine buffer ($^{s}_{s}$pH = 10.9) at T=25.0 ± 0.1 °C.

[triethylamine] (mmol dm^{-3})	k_{obs} (s^{-1})
20	0.015
30	0.013
50	0.011

Table 33S. Average observed pseudo first order rate constants (k_{obs}) vs. [triethylamine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **5**:Zn(II) (1.0 mmol dm^{-3}) in Triethylamine buffer ($^{s}_{s}$pH = 11.2) at T=25.0 ± 0.1 °C.

[triethylamine] (mmol dm^{-3})	k_{obs} (s^{-1})
5	0.016
10	0.012
20	0.0093

Table 34S. Average observed pseudo first order rate constants (k_{obs}) vs. [2,2,6,6-Tetramethylpiperidine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **5**:Zn(II) (1.0 mmol dm^{-3}) in 2,2,6,6-Tetramethylpiperidine buffer ($^{s}_{s}$pH = 12.0) at T=25.0 ± 0.1 °C.

[2,2,6,6-Tetramethylpiperidine] (mmol dm^{-3})	k_{obs} (s^{-1})
20	0.0028
30	0.0024
50	0.0018

Table 35S. Average observed pseudo first order rate constants (k_{obs}) vs. [DBP] for the inhibition of the cleavage of **6** (0.05 mmol dm^{-3}) catalyzed by **4**:Zn(II) (1.0 mmol dm^{-3}) by DBP, sodium salt. Determined in anhydrous methanol at $^{s}_{s}$pH = 11.0 and T=25.0 ± 0.1 °C. The data were fit according to eqn. (S1) to give K_i = 0.18 ± 0.6 x10^{-3} mol dm^{-3}.

[DBP] (mM)	k_{obs} (s^{-1})
0.0	0.049
0.4	0.033

0.8	0.021
1.2	0.012
1.5	0.0070
2.0	0.0028
3.0	0.00062

Table 36S. Average observed pseudo first order rate constants (k_{obs}) for the cleavage of 5.0 x 10^{-4} mol dm^{-3} HPNPP (**1**) Catalyzed by 5.0 x 10^{-5} mol dm^{-3} **5**:Zn(II) as a function of $^{s}_{s}$pH .

$^{s}_{s}$**pH**	k_{obs} (s^{-1})
7.60	0.000022
8.30	0.000083
8.64	0.00020
8.94	0.00033
9.90	0.00091
10.39	0.0013
10.80	0.0023
10.85	0.0016
12.00	0.00046

Figure 1S. Plot of k_{obs} vs. [**4**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 8.0 (4-Ethylmorpholine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Data corrected for buffer inhibition as described in the article text. Dashed line through the data represents fit to eqn. (1) in the main text.

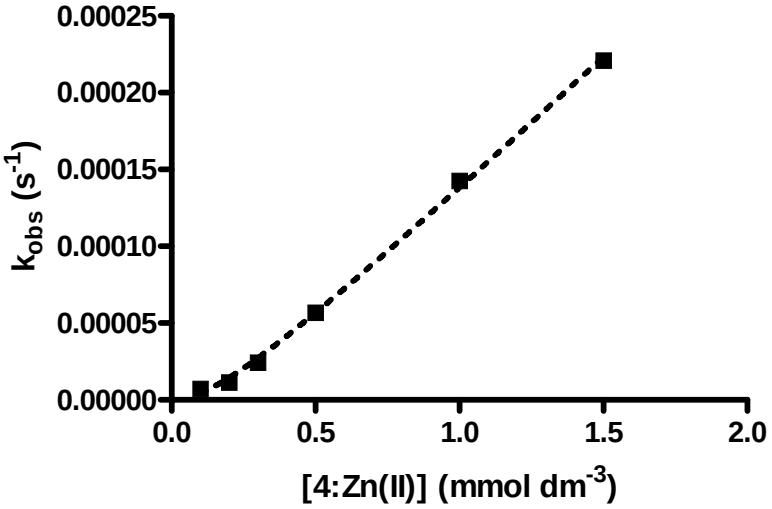


Figure 2S. Plot of k_{obs} vs. [**4**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 8.5 (4-Ethylmorpholine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Data corrected for buffer inhibition as described in the article text. Dashed line through the data represents fit to eqn. (1) in the main text.

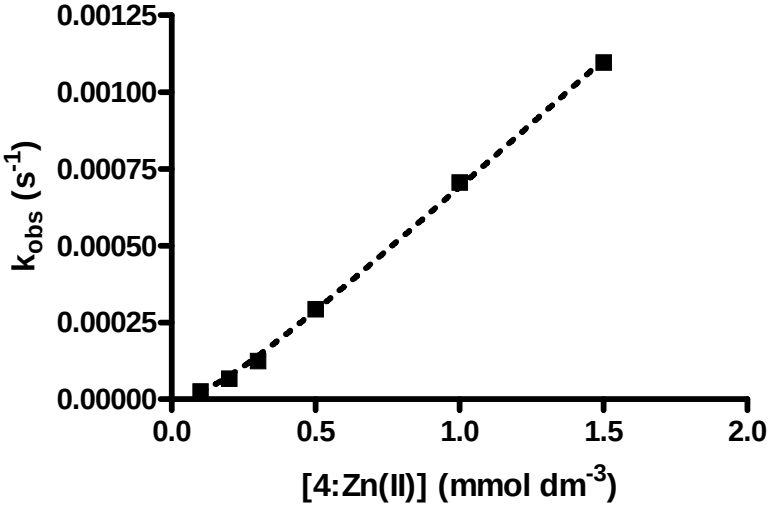


Figure 3S. Plot of k_{obs} vs. [**4**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 9.1 (4-Ethylmorpholine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Data corrected for buffer inhibition as described in the article text. Dashed line through the data represents fit to eqn. (1) in the main text.

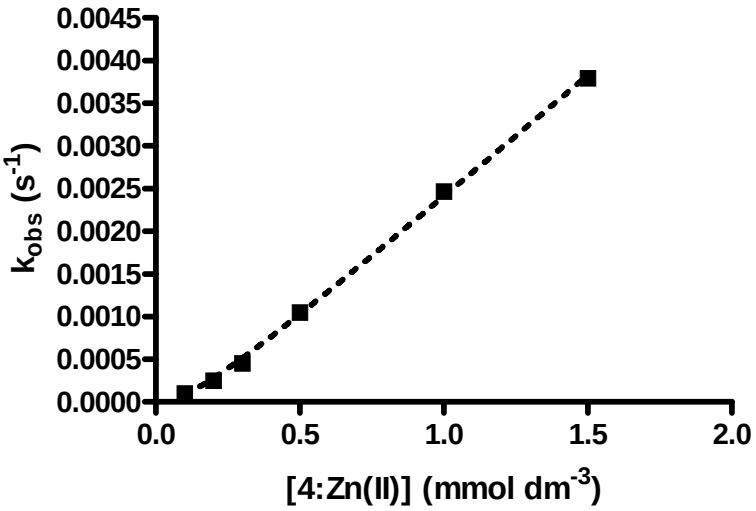


Figure 4S. Plot of k_{obs} vs. [**4**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 10.1 (triethylamine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Data corrected for buffer inhibition as described in the article text. Dashed line through the data represents fit to eqn. (1) in the main text.

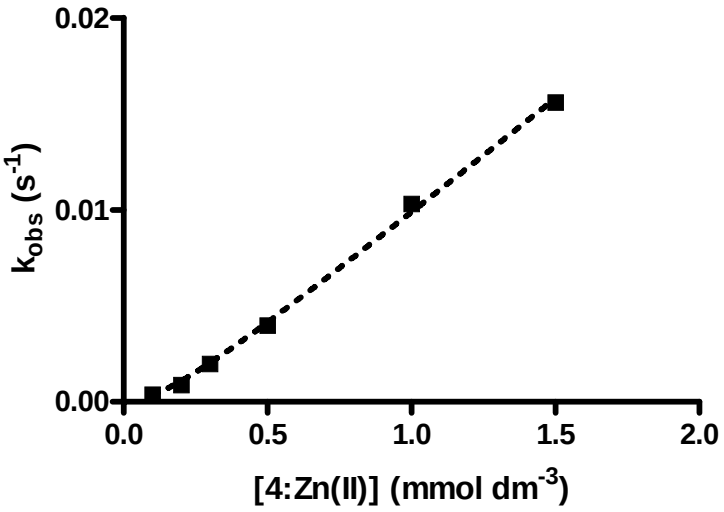


Figure 5S. Plot of k_{obs} vs. [**4**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 10.8 (triethylamine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Data corrected for buffer inhibition as described in the article text. Dashed line through the data represents fit to eqn. (1) in the main text.

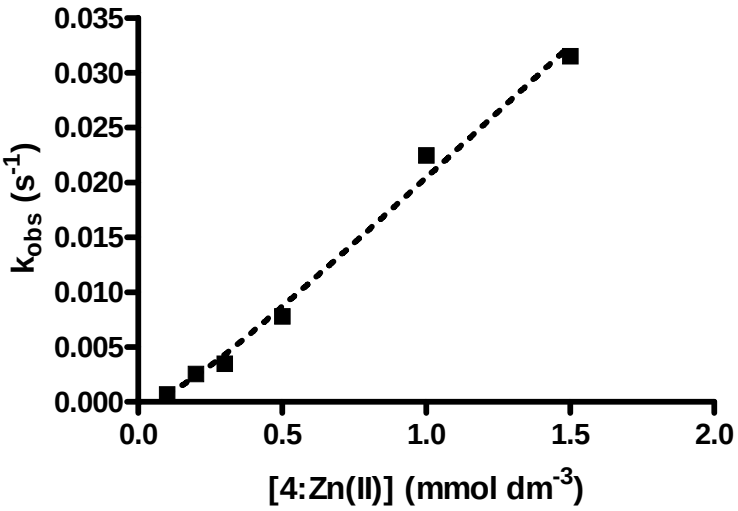


Figure 6S. Plot of k_{obs} vs. [**4**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 11.3 (triethylamine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Data corrected for buffer inhibition as described in the article text. Dashed line through the data represents fit to eqn. (1) in the main text.

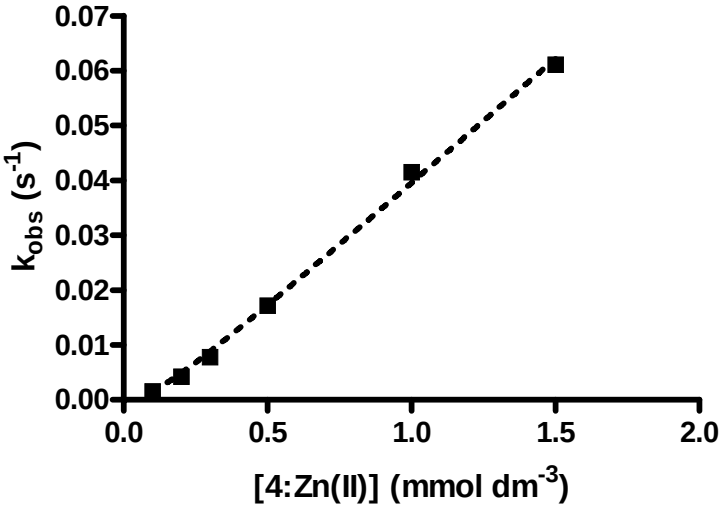


Figure 7S. Plot of k_{obs} vs. [**4**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 12.1 (2,2,6,6-Tetramethylpiperidine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Data corrected for buffer inhibition as

described in the article text. Dashed line through the data represents fit to eqn. (1) in the main text.

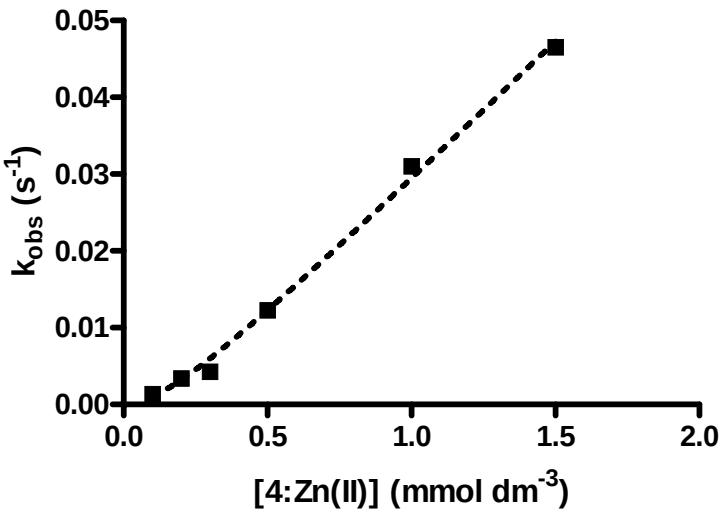


Figure 8S. Buffer inhibition plot showing observed pseudo-first order rate constants (k_{obs}) vs. [N-ethylmorpholine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **4**:Zn(II) (1.0 mmol dm^{-3}) in N-ethylmorpholine buffer at $^{s}_{s}$pH = 8.0 and T=25.0 ± 0.1 °C.

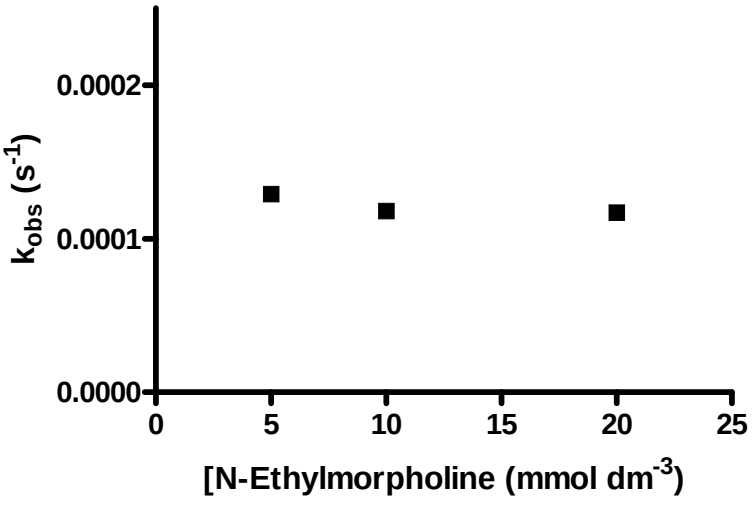


Figure 9S. Buffer inhibition plot showing observed pseudo first order rate constants (k_{obs}) vs. [N-ethylmorpholine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed

by **4**:Zn(II) (1.0 mmol dm^{-3}) in N-ethylmorpholine buffer at $^{s}_{s}$pH = 8.5 and T=25.0 ± 0.1 °C.

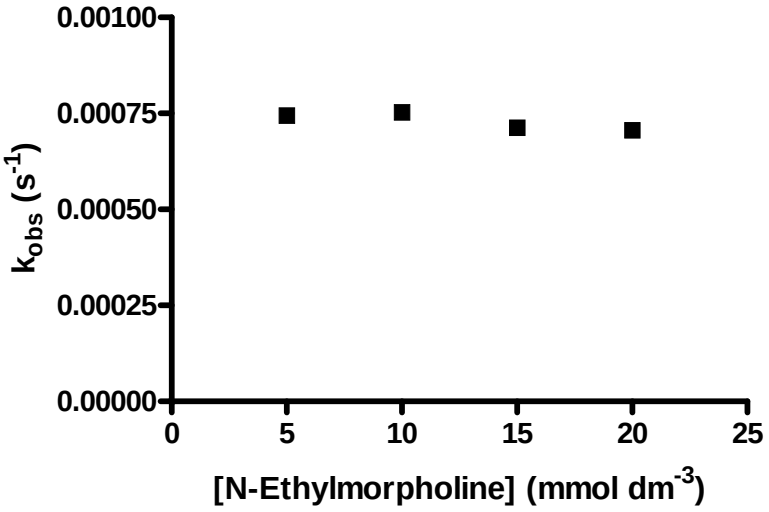


Figure 10S. Buffer inhibition plot showing observed pseudo first order rate constants (k_{obs}) vs. [N-ethylmorpholine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **4**:Zn(II) (1.0 mmol dm^{-3}) in N-ethylmorpholine buffer at $^{s}_{s}$pH = 9.1 and T=25.0 ± 0.1 °C.

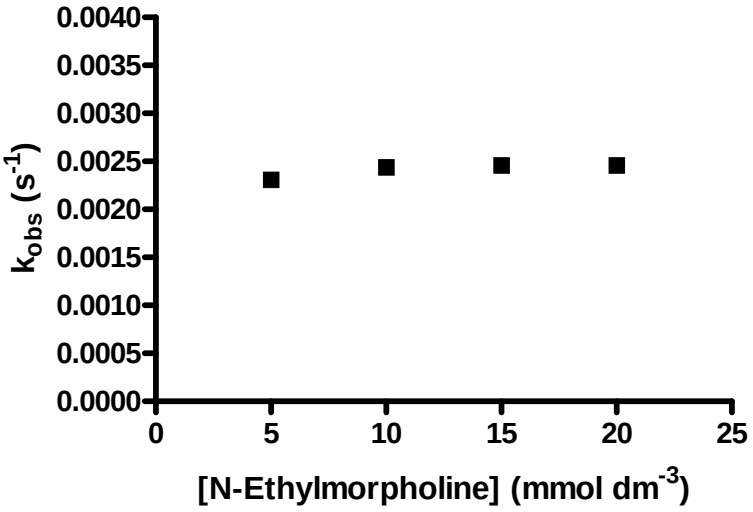


Figure 11S. Buffer inhibition plot showing observed pseudo first order rate constants (k_{obs}) vs. [triethylamine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **4**:Zn(II) (1.0 mmol dm^{-3}) in triethylamine buffer at $^{s}_{s}$pH = 10.1 and T=25.0 ± 0.1 °C.

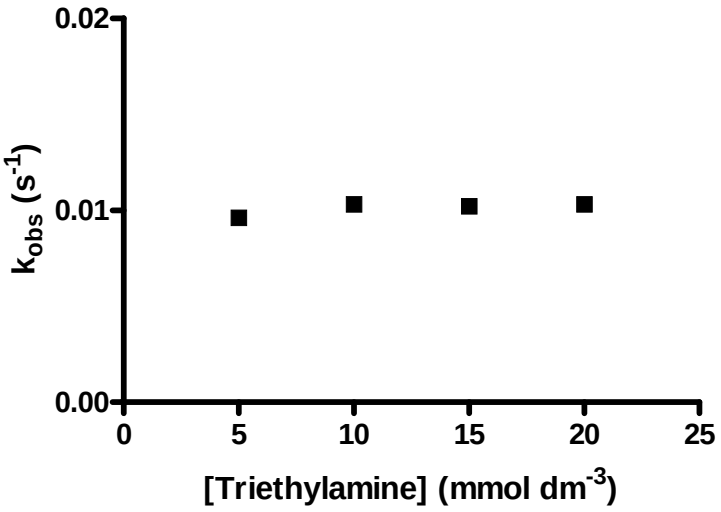


Figure 12S. Buffer inhibition plot showing observed pseudo first order rate constants (k_{obs}) vs. [triethylamine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **4**:Zn(II) (1.0 mmol dm^{-3}) in triethylamine buffer at $^{s}_{s}$pH = 10.8 and T=25.0 ± 0.1 °C.

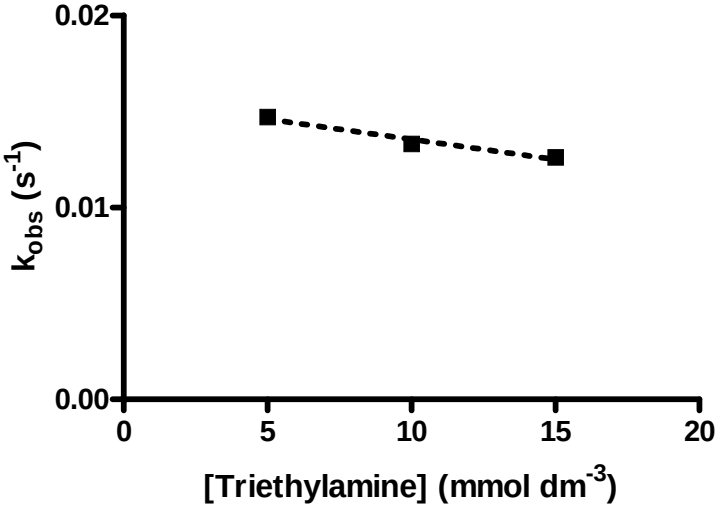


Figure 13S. Buffer inhibition plot showing observed pseudo first order rate constants (k_{obs}) vs. [triethylamine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **4**:Zn(II) (1.0 mmol dm^{-3}) in triethylamine buffer at $^{s}_{s}$pH = 11.3 and T=25.0 ± 0.1 °C.

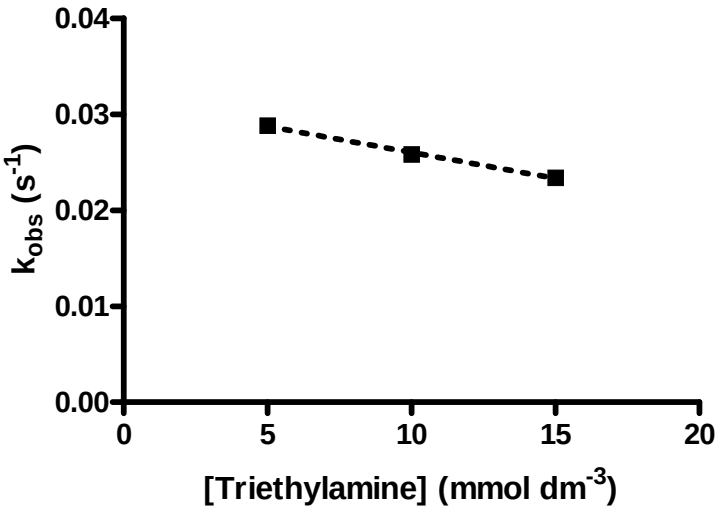


Figure 14S. Buffer inhibition plot showing observed pseudo first order rate constants (k_{obs}) vs. [2,2,6,6-tetramethylpiperidine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **4**:Zn(II) (1.0 mmol dm^{-3}) in 2,2,6,6-tetramethylpiperidine buffer at $^{s}_{s}$pH = 12.1 and T=25.0 ± 0.1 °C.

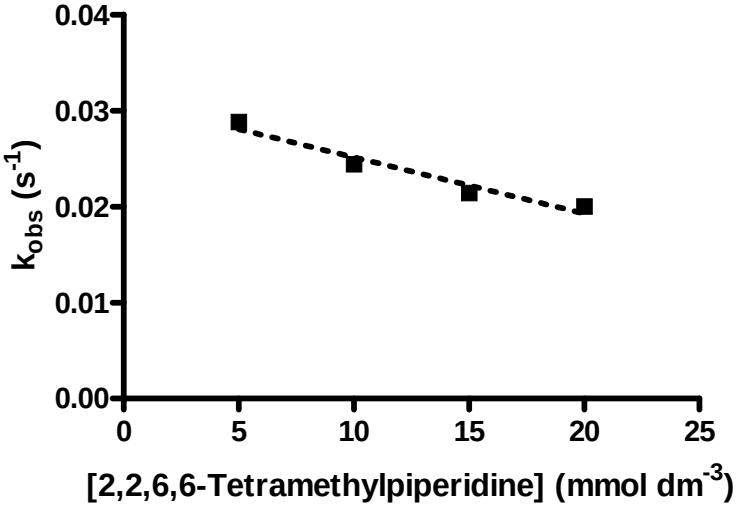
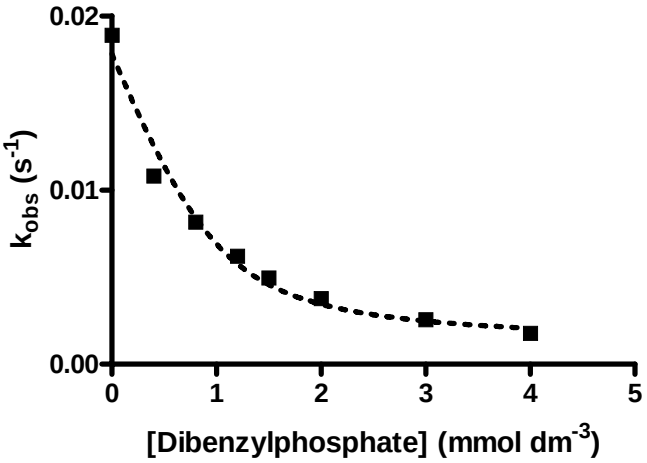


Figure 15S. Plot of (k_{obs}) vs. [DBP] for the inhibition of the cleavage of **6** (0.05 mmol dm^{-3}) catalyzed by **4**:Zn(II) (1.0 mmol dm^{-3}) by DBP, sodium salt. Determined in anhydrous methanol at $^{s}_{s}$pH = 11.0 and T=25.0 ± 0.1 °C. Dashed line through the data points represents the fit to eqn. (S1).



Eqn. S1.

$$k_{obs} = k_{cat}(1 + K_B \times [S] + [In] \times K_B - X)/(2K_B)/[S]) \times (1 + K_B \times [S] + [In] \times K_B - X)/(2K_B)/[S])$$

where:

$$X = (1 + 2K_B \times [S] + 2 \times [In] \times K_B + K_B^2 \times [S]^2 - 2 \times K_B^2 \times [In][S] + [In]^2 \times K_B^2)^{0.5}$$

Figure 16S. Plot of log k_1^{cat} vs $^{s}_{s}$pH for the cyclization of **1** (5.0×10^{-4} mol dm^{-3}) catalyzed by **4**:Zn(II) (5.0×10^{-5} mol dm^{-3}) in buffered methanol at T = 25.0 ± 0.1 °C. Dashed line through the data represents fit to eqn. (2) in the main text which gave $^{s}_{s}pK_a$ = 10.5 ± 0.2 and k_1^{max} = 0.004 ± 0.001 s^{-1}.

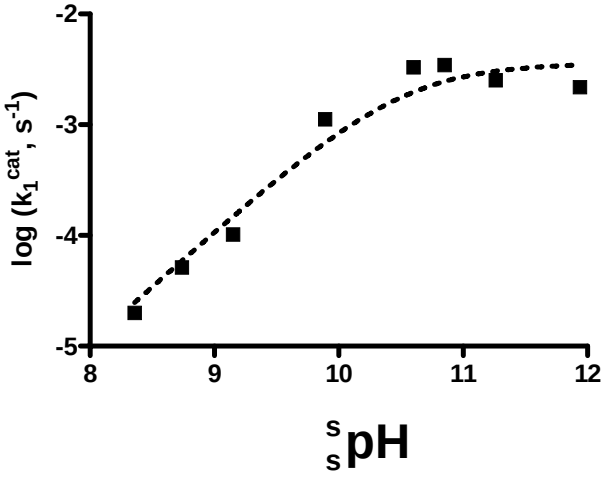


Figure 17S. Plot of k_{obs} vs. [**5**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 7.6 (2,6-Lutidine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Data corrected for buffer inhibition as described in the article text. Dashed line through the data represents fit to eqn. (1) in the main text.

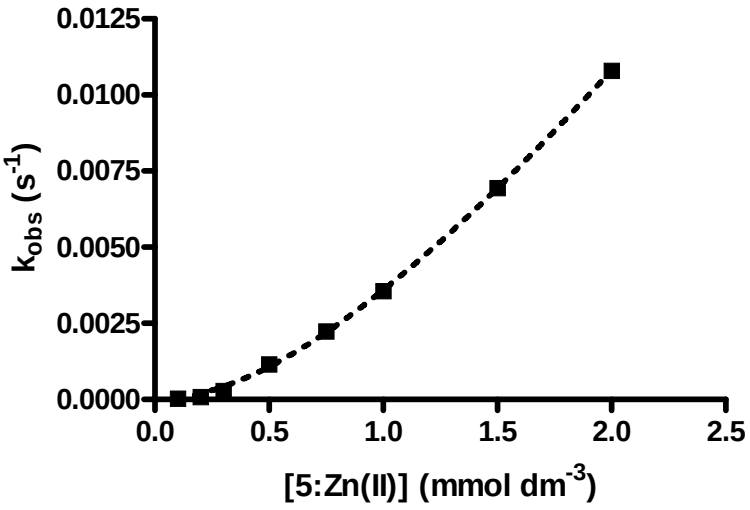


Figure 18S. Plot of k_{obs} vs. [**5**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 8.3 (N-ethylmorpholine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Data corrected for buffer inhibition as described in the article text. Dashed line through the data represents fit to eqn. (1) in the main text.

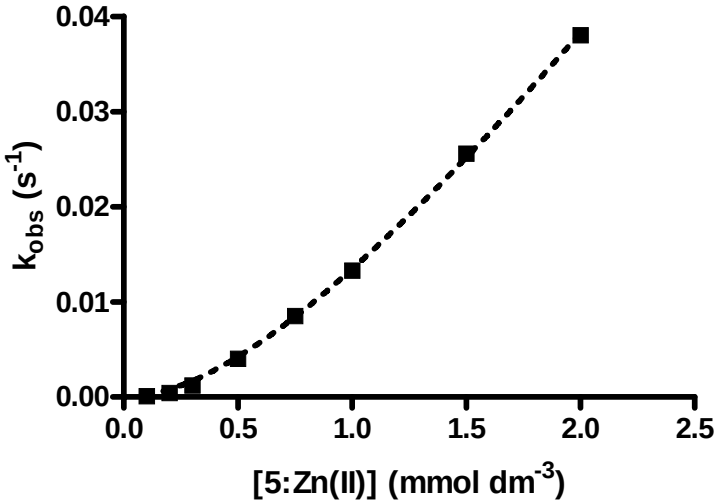


Figure 19S. Plot of k_{obs} vs. [**5**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 8.6 (N-ethylmorpholine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Data corrected for buffer inhibition as described in the article text. Dashed line through the data represents fit to eqn. (1) in the main text.

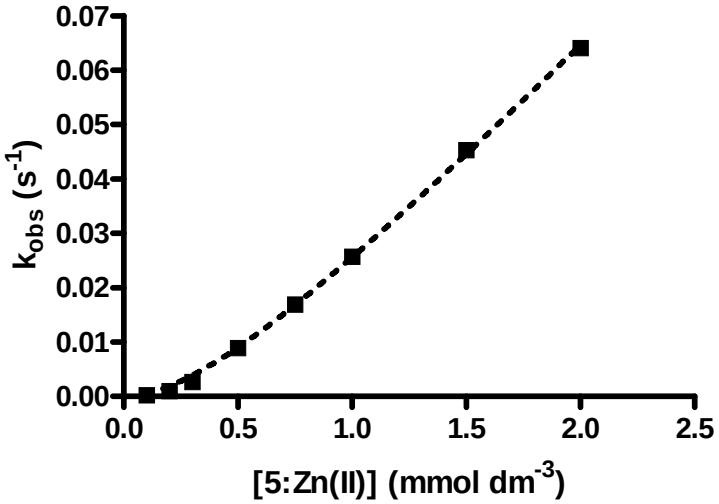


Figure 20S. Plot of k_{obs} vs. [**5**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 8.9 (N-ethylmorpholine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Data corrected for buffer inhibition as described in the article text. Dashed line through the data represents fit to eqn. (1) in the main text.

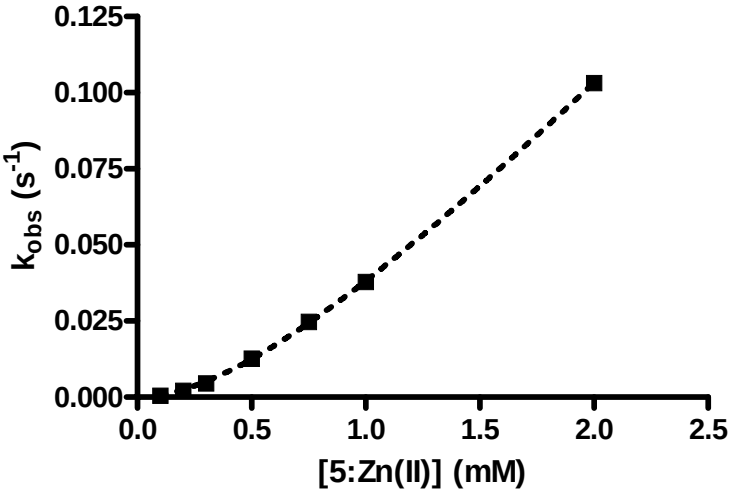


Figure 21S. Plot of k_{obs} vs. [**5**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 9.9 (N-methylpiperidine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Data corrected for buffer inhibition as described in the article text. Dashed line through the data represents fit to eqn. (1) in the main text.

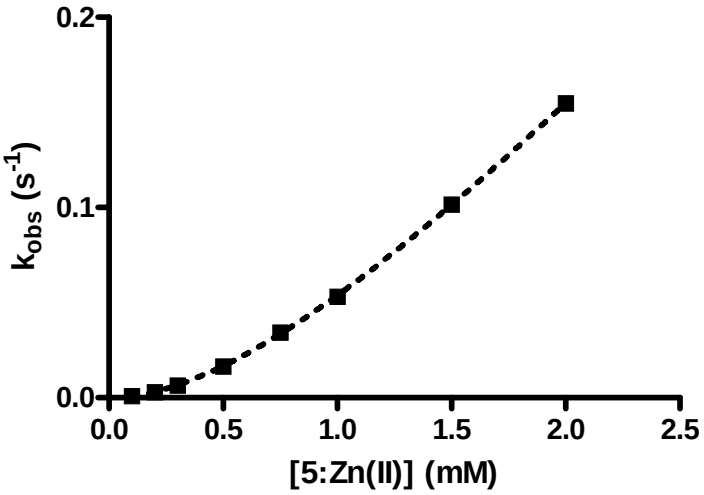


Figure 22S. Plot of k_{obs} vs. [**5**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 10.4 (triethylamine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Data corrected for buffer inhibition as described in the article text. Dashed line through the data represents fit to eqn. (1) in the main text.

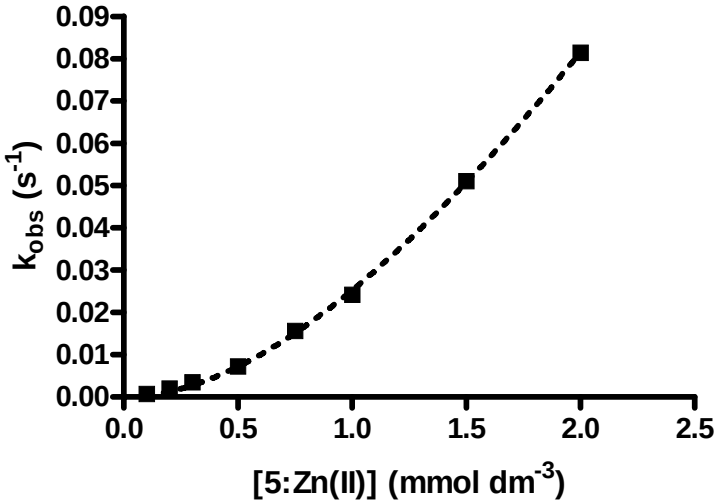


Figure 23S. Plot of k_{obs} vs. [**5**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 10.9 (triethylamine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Data corrected for buffer inhibition as described in the article text. Dashed line through the data represents fit to eqn. (1) in the main text.

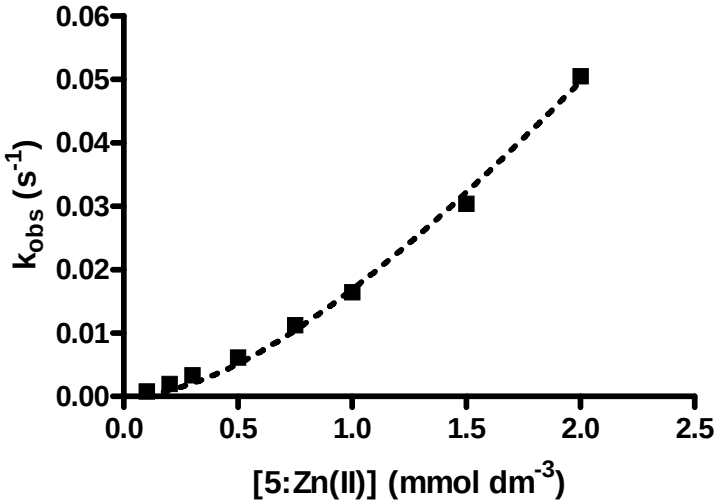


Figure 24S. Plot of k_{obs} vs. [**5**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 11.2 (triethylamine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Data corrected for buffer inhibition as described in the article text. Dashed line through the data represents fit to eqn. (1) in the main text.

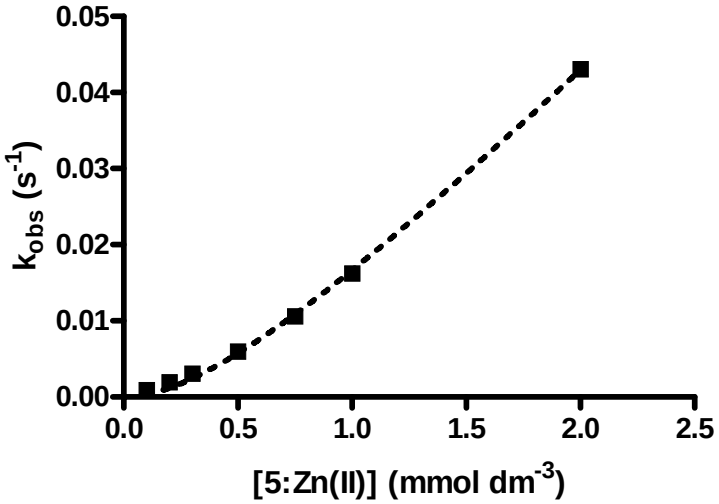


Figure 25S. Plot of k_{obs} vs. [**5**:Zn(II)] for the catalyzed cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) determined in anhydrous methanol at $^{s}_{s}$pH = 12.0 (2,2,6,6-Tetramethylpiperidine buffer, 20 mmol dm^{-3}) and T=25.0 ± 0.1 °C. Data corrected for buffer inhibition as described in the article text. Dashed line through the data represents fit to eqn. (1) in the main text.

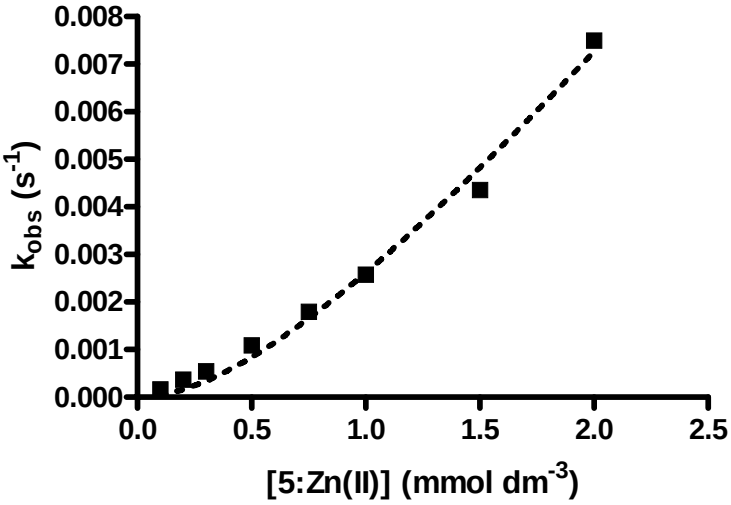


Figure 26S. Buffer inhibition plot showing observed pseudo first order rate constants (k_{obs}) vs. [2,6-Lutidine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **5**:Zn(II) (1.0 mmol dm^{-3}) in 2,6-Lutidine buffer at $^{s}_{s}$pH = 7.6 and T=25.0 ± 0.1 °C.

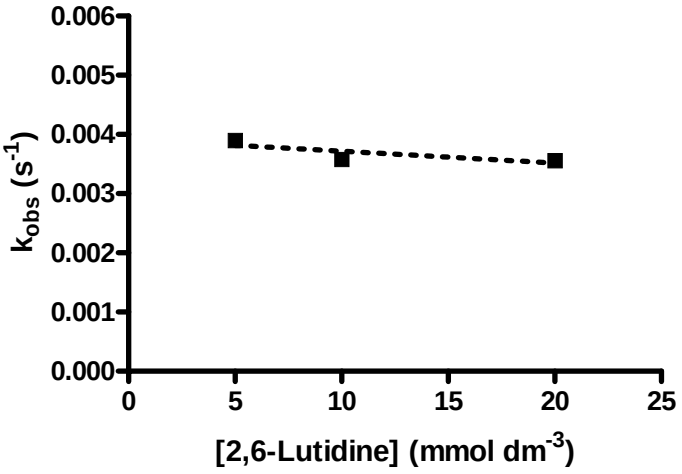


Figure 27S. Buffer inhibition plot showing observed pseudo first order rate constants (k_{obs}) vs. [N-ethylmorpholine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **5**:Zn(II) (1.0 mmol dm^{-3}) in N-ethylmorpholine buffer at $^{s}_{s}$pH = 8.3 and T=25.0 ± 0.1 °C.

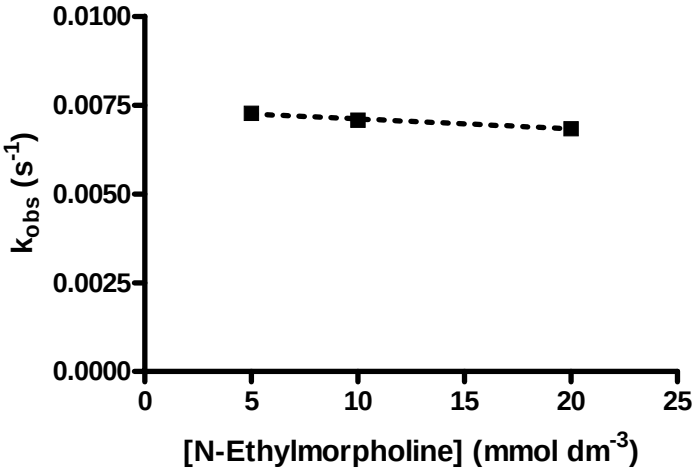


Figure 28S. Buffer inhibition plot showing observed pseudo first order rate constants (k_{obs}) vs. [N-ethylmorpholine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **5**:Zn(II) (1.0 mmol dm^{-3}) in N-ethylmorpholine buffer at $^{s}_{s}$pH = 8.6 and T=25.0 ± 0.1 °C.

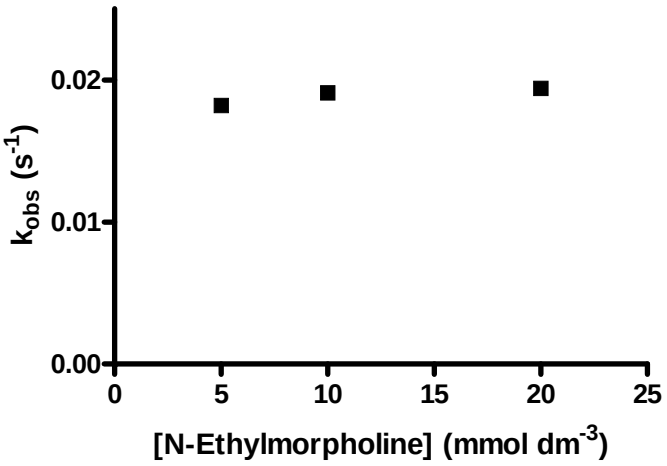


Figure 29S. Buffer inhibition plot showing observed pseudo first order rate constants (k_{obs}) vs. [N-ethylmorpholine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **5**:Zn(II) (1.0 mmol dm^{-3}) in N-ethylmorpholine buffer at $^{s}_{s}$pH = 8.9 and T=25.0 ± 0.1 °C.

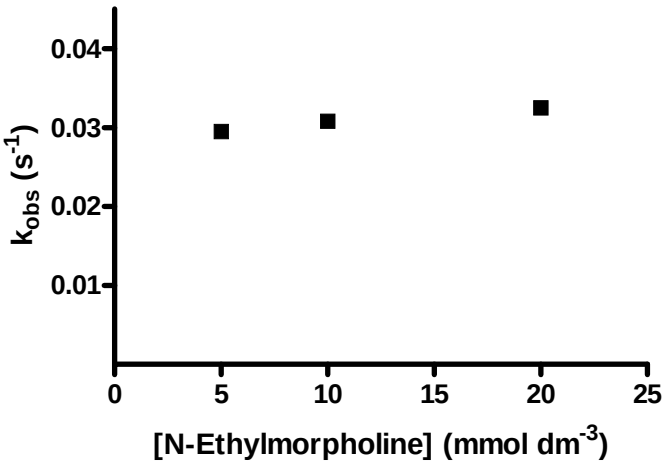


Figure 30S. Buffer inhibition plot showing observed pseudo first order rate constants (k_{obs}) vs. [N-methylpiperidine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **5**:Zn(II) (1.0 mmol dm^{-3}) in N-methylpiperidine buffer at $^{s}_{s}$pH = 9.9 and T=25.0 ± 0.1 °C.

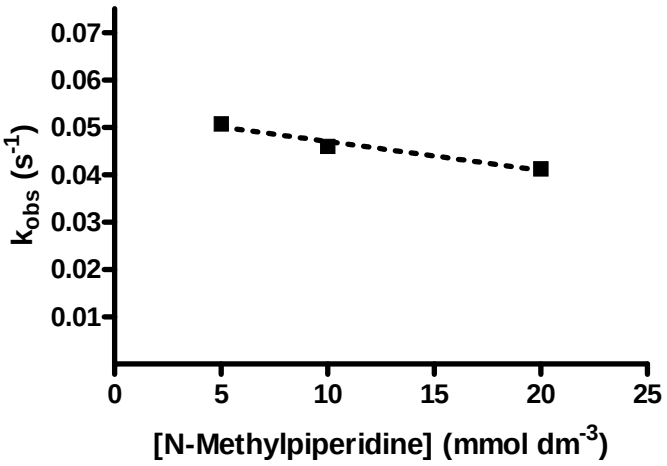


Figure 31S. Buffer inhibition plot showing observed pseudo first order rate constants (k_{obs}) vs. [triethylamine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **5**:Zn(II) (1.0 mmol dm^{-3}) in Triethylamine buffer at $^{s}_{s}$pH = 10.4 and T=25.0 ± 0.1 °C.

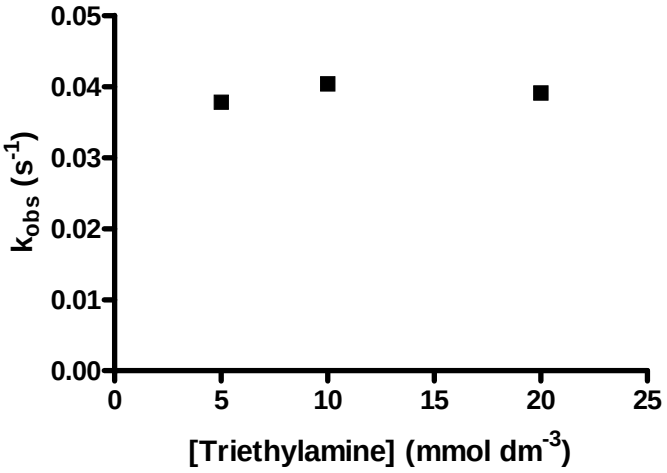


Figure 32S. Buffer inhibition plot showing observed pseudo first order rate constants (k_{obs}) vs. [triethylamine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **5**:Zn(II) (1.0 mmol dm^{-3}) in triethylamine buffer at $^{s}_{s}$pH = 10.9 and T=25.0 ± 0.1 °C.

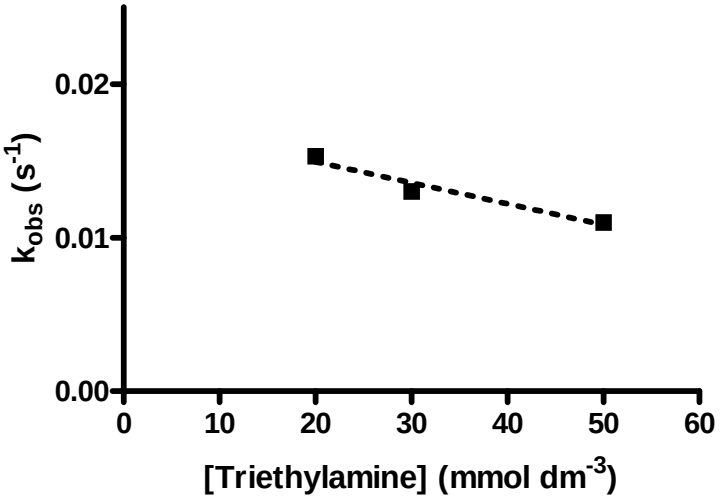


Figure 33S. Buffer inhibition plot showing observed pseudo first order rate constants (k_{obs}) vs. [triethylamine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **5**:Zn(II) (1.0 mmol dm^{-3}) in triethylamine buffer at $^{s}_{s}$pH = 11.2 and T=25.0 ± 0.1 °C.

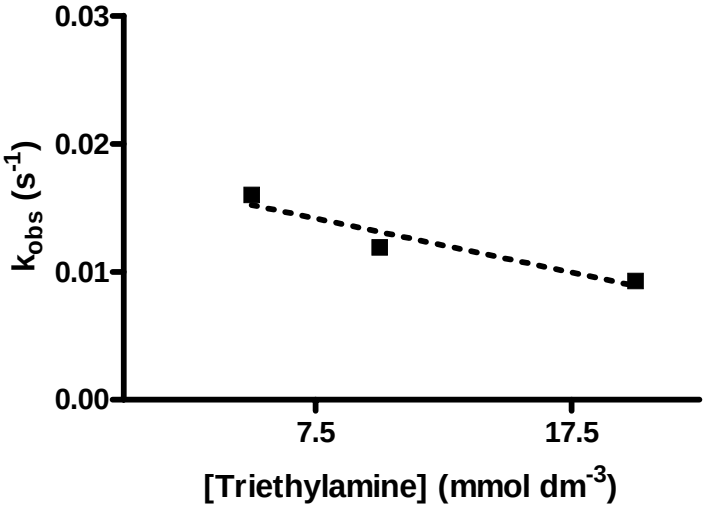


Figure 34S. Buffer inhibition plot showing observed pseudo first order rate constants (k_{obs}) vs. [2,2,6,6-tetramethylpiperidine] for the cleavage of HPNPP (**1**, 0.05 mmol dm^{-3}) catalyzed by **5**:Zn(II) (1.0 mmol dm^{-3}) in 2,2,6,6-tetramethylpiperidine buffer at $^{s}_{s}$pH = 12.0 and T=25.0 ± 0.1 °C.

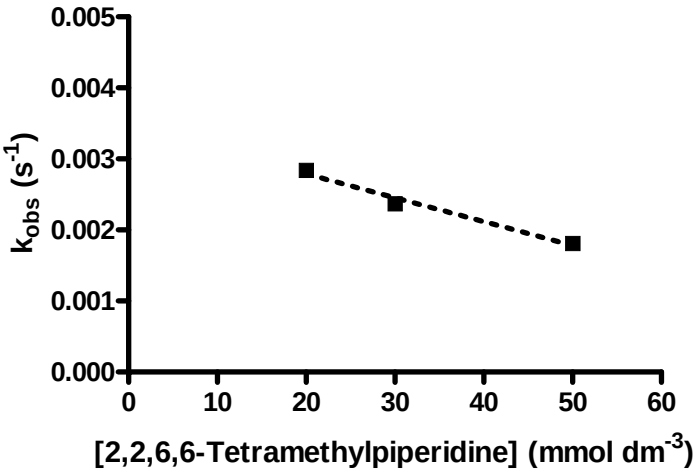


Figure 35S. Plot of (k_{obs}) vs. [DBP] for the inhibition of the cleavage of **6** (0.05 mmol dm^{-3}) catalyzed by **5**:Zn(II) (1.0 mmol dm^{-3}) by DBP, sodium salt. Determined in anhydrous methanol at $^{s}_{s}$pH = 10.2 and T=25.0 ± 0.1 °C. Dashed line through the data points represents the fit to eqn. (S1).

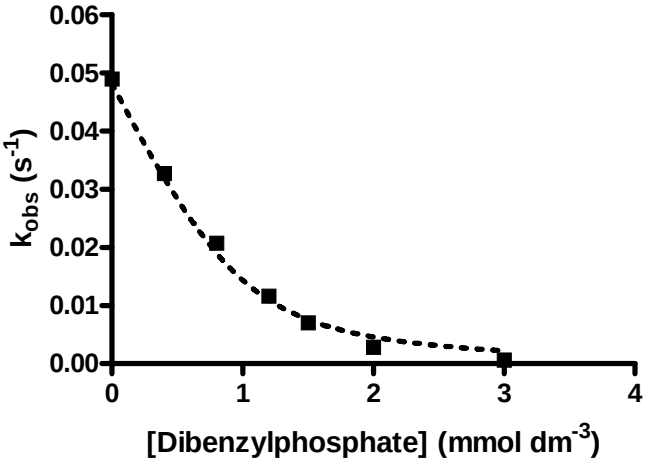


Figure 36S. Plot of log k_1^{cat} vs $^{s}_{s}pH$ for the cyclization of **1** (5.0×10^{-4} mol dm^{-3}) catalyzed by **5**:Zn(II) (5.0×10^{-5} mol dm^{-3}) in buffered methanol at T = 25.0 ± 0.1 °C. Dashed line through the data represents fit to eqn. (3) in the main text which gave values of $^{s}_{s}pK_a^1$ = 9.6 ± 0.1, $^{s}_{s}pK_a^2$ = 11.5 ± 0.2, and k_1^{max} = 0.0020 ± 0.0003 s^{-1}.

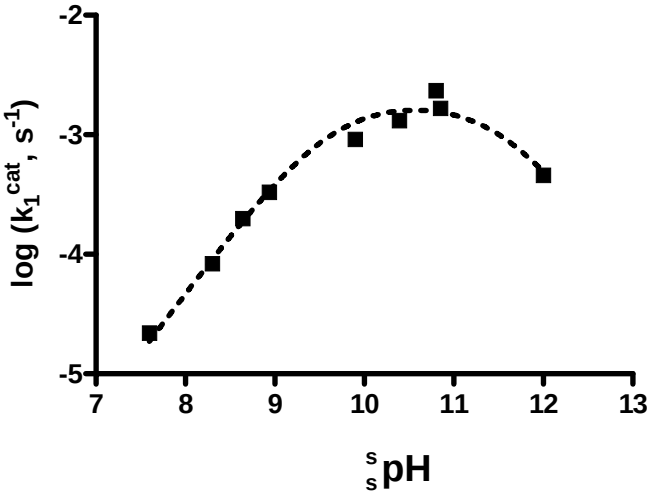


Figure 37S. Spectrophotometric titration of **4** (1.0×10^{-4} mol dm^{-3}) with $Zn(OTf)_2$ in methanol buffered at $^{s}_{s}pH$ = 9.1 and T=25.0 ± 0.1 °C.

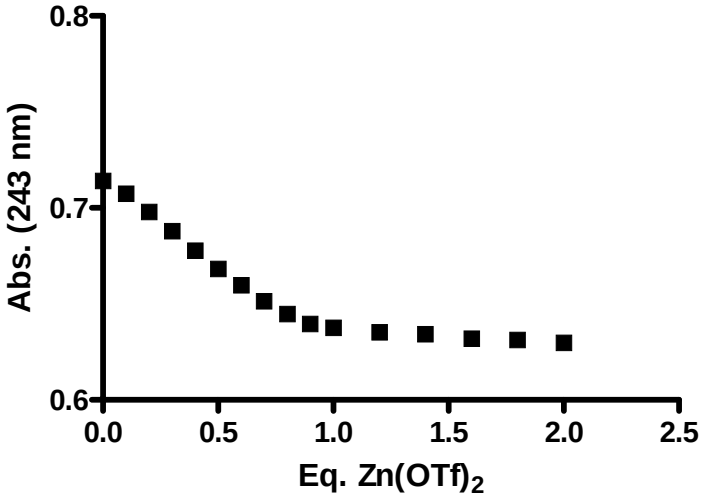
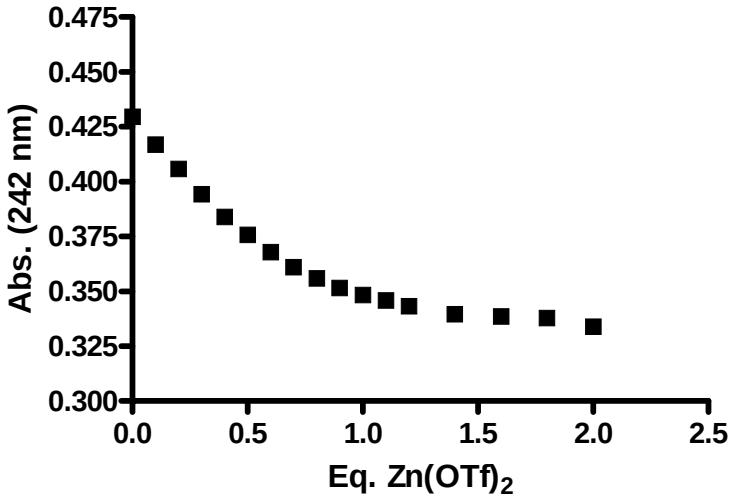


Figure 38S. Spectrophotometric titration of **5** (1.0 x 10^{-4} mol dm^{-3}) with $Zn(OTf)_2$ in methanol buffered at $^{s}_{s}$pH = 10.0 and T=25.0 ± 0.1 °C.



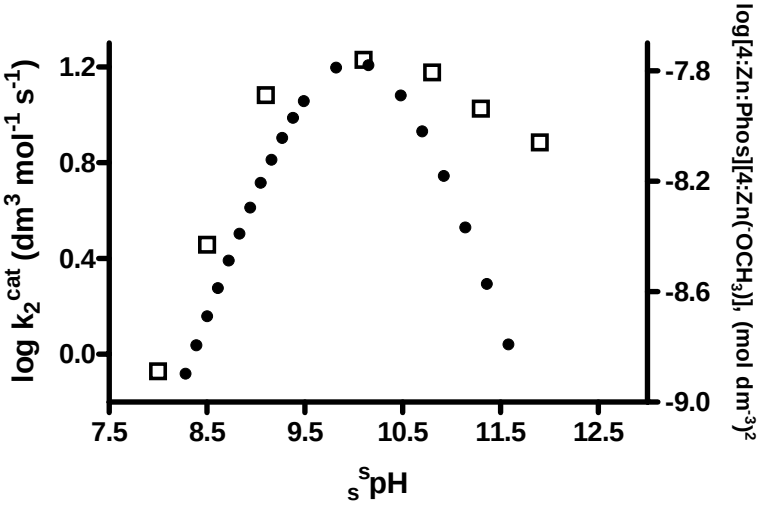


Figure 39S. Plot of log k_2^{cat} vs. $^{s}_{s}$pH for the cleavage of HPNPP (**1**) (5 x 10^{-5} mol dm^{-3}) by [**4**:Zn(II)] (□). Data superimposed on the figure as (•) are computed log [**4**:Zn:**6**$^{-}$][**4**:Zn($^{-}$$OCH_3$)] in accordance with the bimolecular reaction pathway given in Scheme 1 (main text) at 25 °C.

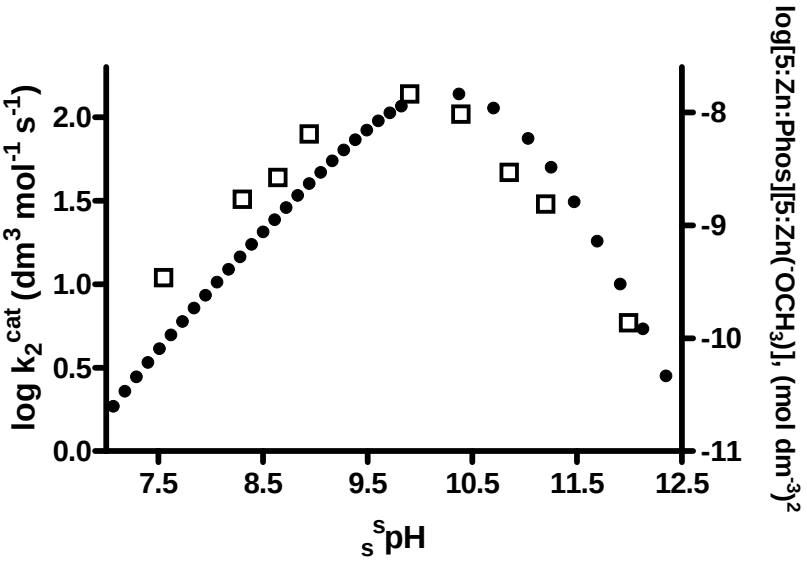


Figure 40S. Plot of log k_2^{cat} vs. $^{s}_{s}$pH for the cleavage of HPNPP (**1**) (5 x 10^{-5} mol dm^{-3}) by [**5**:Zn(II)] (□). Data superimposed on the figure as (•) are log [**5**:Zn:$\mathbf{6}^{-}$][**5**:Zn($^{-}OCH_3$)] in accordance with the bimolecular reaction pathway given in Scheme 1 (main text) at 25 °C.