Single-Site Hydrogen-Bond Modulation Enhances Catalytic Ester Hydrolysis in a Zn(II)–TPA Scaffold

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Table S1.
Crystal data and structure refinement for Zn(II)-TPA(CH_2OH).

Parameter	Value
Identification code	SLEE1
Empirical formula	$C_{19}H_{20}Cl_2N_4O_5Zn$
Formula weight	520.695
Temperature/K	296.15
Crystal system	monoclinic
Space group	$P2_1/c$
Unit cell dimensions	$a = 13.373(3)$ Å
	$b = 13.859(4)$ Å
	$c = 13.464(5)$ Å
	$\alpha = 90^\circ$
	$\beta = 119.197(9)^\circ$
	$\gamma = 90^\circ$
Volume/Å^3	2178.2(11)
Z	4
ρ_{calc}g/cm^3	1.588
μ/mm^{-1}	1.412
F(000)	1067.2
Crystal size/mm^3	0.112 × 0.059 × 0.055
Radiation	Mo Kα ($\lambda = 0.71073$)
2Θ range for data collection/°	4.54 to 49.98
Index ranges	$-17 \le h \le 16,\ -18 \le k \le 18,\ -17 \le l \le 17$
Reflections collected	28076
Independent reflections	3818 [$R_{int} = 0.0654$, $R_{sigma} = 0.0584$]
Data/restraints/parameters	3818/204/327
Goodness-of-fit on F^2	1.075
Final R indexes [I>=2σ (I)]	$R_1 = 0.0588$, $wR_2 = 0.1541$
Final R indexes [all data]	$R_1 = 0.0885$, $wR_2 = 0.1789$
Largest diff. peak/hole / e Å^{-3}	0.70/-0.64

Table S2.
Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for Zn(II)-TPA(CH_2OH).

Atom	**U_{11}**	**U_{22}**	**U_{33}**	**U_{12}**	**U_{13}**	**U_{23}**
Zn1	54.3(4)	52.5(4)	50.5(4)	-1.5(3)	24.7(3)	2.7(3)
Cl1	94.9(12)	76.4(11)	67.5(10)	0.9(9)	27.3(9)	21.1(8)
N1	57(3)	63(3)	68(3)	-8(2)	34(2)	-14(2)
N2	69(3)	62(3)	47(3)	9(2)	21(2)	1(2)
N3	57(3)	64(3)	72(3)	-5(2)	31(3)	-16(3)
N4	56(3)	76(3)	55(3)	-11(2)	25(2)	-16(2)
C1	62(4)	86(5)	108(6)	-9(3)	41(4)	-38(4)
C2	79(5)	140(8)	128(8)	-14(5)	62(5)	-64(7)
C3	89(6)	189(11)	101(7)	-46(7)	66(6)	-74(7)
C4	119(6)	127(7)	63(4)	-58(6)	56(5)	-32(4)
C5	81(4)	84(4)	49(3)	-26(4)	39(3)	-17(3)
C6	118(6)	67(4)	63(4)	-21(4)	42(4)	8(3)
C7	77(4)	95(5)	41(3)	16(4)	15(3)	-2(3)
C8	48(3)	82(4)	79(5)	5(3)	22(3)	-32(4)
C9	76(5)	133(7)	90(6)	10(5)	9(4)	-58(6)
C10	72(5)	122(8)	154(10)	-28(5)	16(6)	-75(7)
C11	111(7)	119(8)	147(9)	-35(6)	48(7)	-49(7)
C12	77(5)	84(5)	135(7)	-26(4)	50(5)	-45(5)
C13	86(5)	78(4)	65(4)	26(4)	12(3)	-6(3)
C14	56(3)	72(4)	76(4)	1(3)	24(3)	-21(3)
C15	76(5)	94(5)	109(6)	15(4)	26(4)	-38(5)
C16	95(6)	142(8)	135(8)	6(6)	54(6)	-68(7)
C17	95(6)	135(7)	97(6)	-29(5)	63(5)	-60(6)
C18	68(4)	106(5)	62(4)	-19(4)	31(3)	-8(4)
C19	131(7)	142(8)	97(6)	-47(7)	69(6)	-28(6)
O1	128(5)	127(5)	107(5)	-14(4)	33(4)	9(4)
Cl2	67(2)	108(4)	106(3)	16(2)	47.5(17)	46(2)
O2	208(12)	134(7)	139(7)	37(4)	80(5)	51(4)
O3	97(5)	225(9)	113(5)	23(3)	59(3)	40(4)
O4	190(9)	135(6)	210(9)	17(4)	125(5)	23(4)
O5	128(6)	246(11)	157(7)	37(5)	95(4)	47(5)
O4a	115(10)	138(13)	153(11)	56(6)	88(6)	66(7)
O3a	159(11)	144(8)	216(13)	52(5)	125(7)	64(5)
Cl2a	131(7)	131(8)	170(9)	65(5)	111(5)	70(5)
O5a	137(8)	167(11)	209(11)	59(5)	116(5)	69(6)
O2a	213(16)	207(16)	186(10)	25(8)	121(6)	54(6)

Table S3

Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for Zn(II)-TPA(CH_2OH).

U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.

Atom	x	y	z	U(eq)
Zn1	6523.9(5)	6845.4(4)	7072.7(5)	52.8(2)
Cl1	5777.6(16)	8082.8(12)	5788.7(14)	84.8(5)
N1	5108(4)	6585(3)	7300(4)	61.8(12)
N2	7191(4)	5782(3)	8471(4)	62.8(12)
N3	7882(4)	7597(4)	8377(4)	64.9(12)
N4	7030(4)	5727(4)	6375(4)	63.1(12)
C1	4172(5)	7163(5)	6906(6)	85(2)
C2	3313(7)	7016(7)	7137(9)	111(3)
C3	3392(8)	6270(10)	7809(8)	118(4)
C4	4306(8)	5643(7)	8214(6)	98(3)
C5	5185(6)	5827(5)	7936(5)	68.2(16)
C6	6206(6)	5203(5)	8306(5)	84(2)
C7	7692(6)	6343(5)	9528(5)	76.9(18)
C8	8272(5)	7240(5)	9414(6)	73.3(18)
C9	9150(7)	7699(7)	10367(7)	114(3)
C10	9637(7)	8526(8)	10163(11)	132(4)
C11	9223(9)	8873(8)	9082(11)	132(4)
C12	8350(6)	8415(6)	8204(8)	99(3)
C13	8060(6)	5232(5)	8347(5)	87(2)
C14	7713(5)	5065(5)	7129(6)	71.3(16)
C15	8125(6)	4264(5)	6819(7)	101(3)
C16	7877(8)	4151(8)	5723(10)	125(3)

C17	7199(7)	4812(7)	4955(7)	102(3)
C18	6766(6)	5578(6)	5273(6)	79.0(18)
C19	6021(9)	6226(7)	4418(8)	118(3)
O1	4863(6)	6224(5)	4257(6)	131(2)
Cl2	1123(6)	6318(7)	8821(8)	91.6(18)
O2	758(14)	7102(10)	8115(11)	162(5)
O3	2290(8)	6374(9)	9552(8)	142(4)
O4	1137(13)	5482(9)	8305(13)	167(4)
O5	666(11)	6428(11)	9539(11)	166(4)
O4a	1210(20)	6938(17)	7910(20)	125(6)
O3a	630(20)	5420(20)	8520(30)	159(6)
Cl2a	1040(20)	6420(20)	8700(20)	128(5)
O5a	-170(20)	6511(18)	8050(20)	157(6)
O2a	1660(30)	6710(20)	9980(30)	191(9)

Table S4
Bond Lengths for Zn(II)-TPA(CH_2OH).

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Zn1	Cl1	2.2897(17)	C8	C9	1.400(9)
Zn1	N1	2.092(5	C9	C10	1.409(14)
Zn1	N2	2.208(4	C10	C11	1.368(14)
Zn1	N3	2.087(5)	C11	C12	1.348(11)
Zn1	N4	2.089(5)	C13	C14	1.489(9)
N1	C1	1.357(8)	C14	C15	1.391(9)
N1	C5	1.327(7)	C15	C16	1.353(12)
N2	C6	1.465(7)	C16	C17	1.348(12)
N2	C7	1.466(7)	C17	C18	1.374(10)
N2	C13	1.465(8)	C18	C19	1.417(11)
N3	C12	1.368(9)	Cl2	O2	1.367(16)
N4	C14	1.342(8)	Cl2	O3	1.383(13)
N4	C18	1.362(8)	Cl2	O4	1.356(17)
C1	C2	1.345(10)	Cl2	O5	1.381(15)
C2	C3	1.343(13)	O4a	Cl2a	1.39(3)
C3	C4	1.377(13)	O3a	Cl2a	1.48(4)
C4	C5	1.420(9)	O3a	O5a	1.79(3)
C5	C6	1.482(9)	Cl2a	O5a	1.42(3)
C7	C8	1.512(9)	Cl2a	O2a	1.56(4)

Table S5
Bond Angles for Zn(II)-TPA(CH_2OH).

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
N1	Zn1	Cl1	98.48(15)	C8	C7	N2	110.6(5)
N2	Zn1	Cl1	171.83(13)	C7	C8	N3	117.2(5)
N2	Zn1	N1	77.19(19)	C9	C8	N3	121.2(8)
N3	Zn1	Cl1	98.11(16)	C9	C8	C7	121.6(8)
N3	Zn1	N1	116.22(18)	C10	C9	C8	116.9(9)
N3	Zn1	N2	77.98(19)	C11	C10	C9	120.5(8)
N4	Zn1	Cl1	109.50(15)	C12	C11	C10	119.7(10)
N4	Zn1	N1	116.91(17)	C11	C12	N3	120.9(9)
N4	Zn1	N2	78.67(18)	C14	C13	N2	111.6(5)
N4	Zn1	N3	114.12(17)	C13	C14	N4	117.3(5)
C1	N1	Zn1	124.6(5)	C15	C14	N4	122.7(6)
C5	N1	Zn1	116.1(4)	C15	C14	C13	119.9(7)
C5	N1	C1	119.2(5)	C16	C15	C14	119.8(8)
C6	N2	Zn1	106.1(3)	C17	C16	C15	118.3(8)
C7	N2	Zn1	106.1(4)	C18	C17	C16	120.9(8)
N2	Zn1	Cl1	171.83(13)	C7	C8	N3	117.2(5)
N2	Zn1	N1	77.19(19)	C9	C8	N3	121.2(8)
N3	Zn1	Cl1	98.11(16)	C9	C8	C7	121.6(8)
N3	Zn1	N1	116.22(18)	C10	C9	C8	116.9(9)
N3	Zn1	N2	77.98(19)	C11	C10	C9	120.5(8)
N4	Zn1	Cl1	109.50(15)	C12	C11	C10	119.7(10)
N4	Zn1	N1	116.91(17)	C11	C12	N3	120.9(9)
N4	Zn1	N2	78.67(18)	C14	C13	N2	111.6(5)
N4	Zn1	N3	114.12(17)	C13	C14	N4	117.3(5)
C1	N1	Zn1	124.6(5)	C15	C14	N4	122.7(6)
C5	N1	Zn1	116.1(4)	C15	C14	C13	119.9(7)
C5	N1	C1	119.2(5)	C16	C15	C14	119.8(8)
C6	N2	Zn1	106.1(3)	C17	C16	C15	118.3(8)
C7	N2	Zn1	106.1(4)	C18	C17	C16	120.9(8)
C7	N2	C6	112.9(5)	C17	C18	N4	122.1(7)
C13	N2	Zn1	105.3(4)	C19	C18	N4	119.7(7)
C13	N2	C6	113.7(5)	C19	C18	C17	118.2(7)
C13	N2	C7	112.0(5)	O1	C19	C18	113.2(7)

C8	N3	Zn1	115.7(4)	O3	Cl2	O2	110.2(10)
C12	N3	Zn1	123.6(5)	O4	Cl2	O2	114.3(11)
C12	N3	C8	120.7(6)	O4	Cl2	O3	96.8(11)
C14	N4	Zn1	114.7(4)	O5	Cl2	O2	105.7(11)
C18	N4	Zn1	129.3(5)	O5	Cl2	O3	103.1(9)
C18	N4	C14	116.1(6)	O5	Cl2	O4	125.1(10)
C2	C1	N1	123.3(8)	O5a	O3a	Cl2a	50.5(14)
C3	C2	C1	118.5(9)	O3a	Cl2a	O4a	123(3)
C4	C3	C2	121.0(8)	O5a	Cl2a	O4a	93(2)
C5	C4	C3	118.2(8)	O5a	Cl2a	O3a	76(2)
C4	C5	N1	119.8(7)	O2a	Cl2a	O4a	121(3)
C6	C5	N1	116.6(5)	O2a	Cl2a	O3a	113(2)
C6	C5	C4	123.5(7)	O2a	Cl2a	O5a	120(2)
C5	C6	N2	110.1(5)	Cl2a	O5a	O3a	53.3(16)

Table S6
Torsion Angles for Zn(II)-TPA(CH_2OH).

A	B	C	D	Angle/°	A	B	C	D	Angle/°
Zn1	N1	C1	C2	-174.8(6)	C2	C1	N1	C5	0.8(8)
Zn1	N1	C5	C4	174.7(4)	C2	C3	C4	C5	2.2(9)
Zn1	N1	C5	C6	-6.2(4)	C3	C4	C5	C6	-179.2(6)
Zn1	N2	C6	C5	-39.7(3)	C5	C6	N2	C7	76.1(5)
Zn1	N2	C7	C8	-37.0(4)	C5	C6	N2	C13	-154.9(5)
Zn1	N2	C13	C14	-37.5(4)	C6	N2	C7	C8	-152.8(5)
Zn1	N3	C8	C7	-0.2(4)	C6	N2	C13	C14	78.2(5)
Zn1	N3	C8	C9	-177.4(4)	C7	N2	C13	C14	-152.3(6)
Zn1	N3	C12	C11	179.5(7)	C7	C8	N3	C12	179.0(5
Zn1	N4	C14	C13	-2.7(5)	C7	C8	C9	C10	179.6(7)
Zn1	N4	C14	C15	179.3(5)	C8	N3	C12	C11	0.4(7)
Zn1	N4	C18	C17	178.1(5)	C8	C7	N2	C13	77.3(6)
Zn1	N4	C18	C19	-1.9(6)	C8	C9	C10	C11	2.7(9)
N1	C1	C2	C3	1.2(8)	C9	C8	N3	C12	1.8(7)
N1	C5	C4	C3	-0.2(7)	C9	C10	C11	C12	-0.7(11)
N1	C5	C6	N2	32.4(5)	C13	C14	N4	C18	177.3(6)
N2	C6	C5	C4	-148.5(5)	C13	C14	C15	C16	-175.2(8)
N2	C7	C8	N3	26.8(6)	C14	N4	C18	C17	-1.9(6)
N2	C7	C8	C9	-156.0(5)	C14	N4	C18	C19	178.0(6)
N2	C13	C14	N4	29.0(7)	C14	C15	C16	C17	-2.1(9)
N2	C13	C14	C15	-153.0(6)	C15	C14	N4	C18	-0.7(8)
N3	C8	C9	C10	-3.3(7)	C15	C16	C17	C18	-0.4(11)
N3	C12	C11	C10	-0.9(9)	C16	C17	C18	C19	-177.5(8)
N4	C14	C15	C16	2.8(8)	C17	C18	C19	O1	115.3(7)
N4	C18	C17	C16	2.5(8)	O4a	Cl2a	O3a	O5a	-84(3)
N4	C18	C19	O1	-64.7(7)	O4a	Cl2a	O5a	O3a	123(3)
C1	N1	C5	C4	-1.2(6)	O3a	O5a	Cl2a	O2a	-108(2)
C1	N1	C5	C6	177.9(6)	O5a	O3a	Cl2a	O2a	117(2)
C1	C2	C3	C4	-2.7(9)					

Table S7

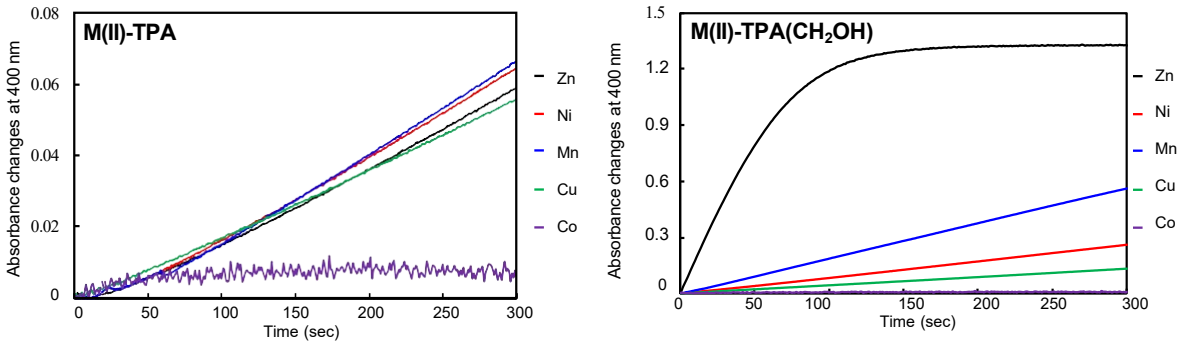
Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3 Zn(II)-TPA(CH_2OH).

Atom	x	y	z	U(eq)
H1	4123(5)	7688(5)	6453(6)	103(3)
H2	2678(7)	7422(7)	6839(9)	133(4)
H3	2820(8)	6176(10)	8003(8)	142(4)
H4	4347(8)	5114(7)	8657(6)	118(3)
H6a	6049(6)	4711(5)	7735(5)	100(2)
H6b	6378(6)	4882(5)	9012(5)	100(2)
H7a	7095(6)	6526(5)	9704(5)	92(2)
H7b	8247(6)	5950(5)	10150(5)	92(2)
H9	9401(7)	7470(7)	11100(7)	136(4)
H10	10245(7)	8837(8)	10769(11)	159(5)
H11	9541(9)	9424(8)	8953(11)	159(4)
H12	8063(6)	8657(6)	7471(8)	119(3)
H13a	8780(6)	5581(5)	8710(5)	104(2)
H13b	8178(6)	4616(5)	8730(5)	104(2)
H15	8569(6)	3807(5)	7362(7)	121(3)
H16	8166(8)	3631(8)	5507(10)	150(4)
H17	7023(7)	4749(7)	4199(7)	123(3)
H19a	6332(9)	6874(7)	4618(8)	141(4)
H19b	5990(9)	6056(7)	3704(8)	141(4)
H1a	4750(40)	6730(40)	4500(110)	197(3)

Table S8

Atomic Occupancy for Zn(II)-TPA(CH_2OH).

Atom	Occupancy	Atom	Occupancy	Atom	Occupancy
Cl2	0.677(11)	O2	0.677(11)	O3	0.677(11)
O4	0.677(11)	O5	0.677(11)	O4a	0.323(11)
O3a	0.323(11)	Cl2a	0.323(11)	O5a	0.323(11)
O2a	0.323(11)				



(II)-TPA] and [M(II)-TPA(CH_2OH)] = 1.0mM, [*p*NPA] = 10 Mm, pH 7.0 , 0.05M Tris buffer (*I* = 0.1M with NaCl)

Fig. S1. Effects of metal ions on the hydrolysis of pNPA catalyzed by M(II)–TPA and M(II) TPA(CH_2OH) complexes.

Table S9

Observed rate constants (k_{obs}) for the hydrolysis of *p*NPA (10 mM) catalyzed by various metal complexes.

Metal ion	k_{obs} (s^{-1})	
	TPA	**TPA(CH_2OH)**
Zn^{2+}	(1.50 ± 0.13) x 10^{-4}	(1.19 ± 0.10) x 10^{-2}
Ni^{2+}	(1.66 ± 0.18) x 10^{-4}	(8.19 ± 1.97) x 10^{-4}
Mn^{2+}	(1.52 ± 0.16) x 10^{-4}	(1.86 ± 0.24) x 10^{-3}
Cu^{2+}	(1.70 ± 0.16) x 10^{-4}	(4.28 ± 1.18) x 10^{-4}
Co^{2+}	(5.50 ± 2.24) x 10^{-5}	(4.60 ± 1.21) x 10^{-5}

Figure S2. Dependence of the observed rate constant (k_{obs}) for the hydrolysis of *p*-nitrophenyl acetate (10 mM) on the concentration of M(II) complexes

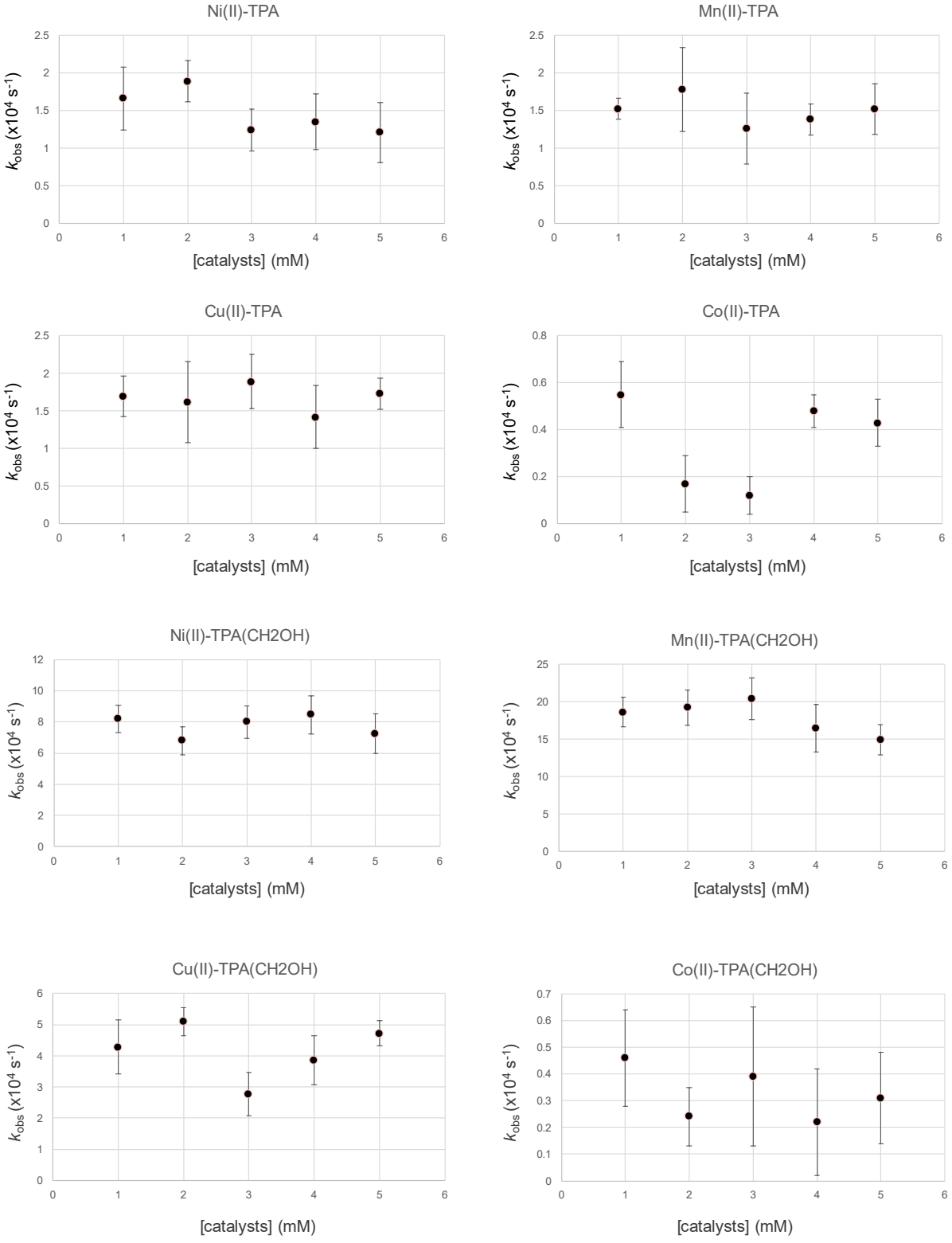


Table S10

Observed rate constants for the hydrolysis of *p*NPA (10 mM) in the presence of varying concentrations of Zn(II) complexes

Concen-tration (mM)	k_{obs} (s^{-1})		Concen-tration (mM)	k_{obs} (s^{-1})
	Zn(II)-TPA	Zn(II)-Cyclen		Zn(II)-TPA(CH_2OH)
1.0	(1.02 ± 0.10) x 10^{-4}	(2.18 ± 0.22) x 10^{-4}	0.1	(7.78 ± 1.22) x 10^{-4}
2.0	(1.47 ± 0.12) x 10^{-4}	(3.11 ± 0.28) x 10^{-4}	0.2	(1.37 ± 0.18) x 10^{-3}
3.0	(2.02 ± 0.19) x 10^{-4}	(3.64 ± 0.21) x 10^{-4}	0.3	(1.98 ± 0.16) x 10^{-3}
4.0	(2.62 ± 0.20) x 10^{-4}	(4.31 ± 0.18) x 10^{-4}	0.4	(2.37 ± 0.19) x 10^{-3}
5.0	(3.34 ± 0.21) x 10^{-4}	(4.92 ± 0.22) x 10^{-4}	0.5	(2.85 ± 0.20) x 10^{-3}
6.0	(3.94 ± 0.23) x 10^{-4}	(5.68 ± 0.20) x 10^{-4}	0.6	(3.60 ± 0.27) x 10^{-3}
7.0	(4.86 ± 0.31) x 10^{-4}	(6.28 ± 0.28) x 10^{-4}	0.7	(3.89 ± 0.30) x 10^{-3}

Experimental

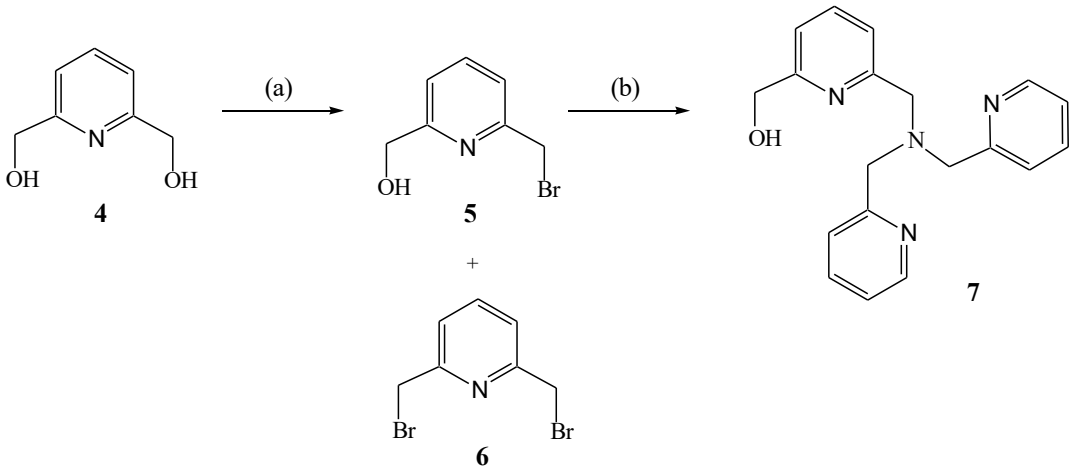
General information.

Reagents and materials All chemicals used for the synthesis of TPA derivatives, including 2,6-pyridinedimethanol, 48% hydobromic acid, 2-(chloromethyl)pyridine hydrochloride, 2-picolylamine, and triethylamine were of analytical grade and were purchased from Sigma-Aldrich Chemical Co. (St. Louis, MO, USA). The metal ions containing chlorides as anions such as zinc(II) chloride, copper(II) chloride, cobalt(II) chloride, nickel(II) chloride, manganese(II) chloride, and iron(II) chloride were obtained from Sigma-Aldrich Chemical Co. Tris(2-pyridylmethyl)amine (TPA), 1,4,7,10-tetraazacyclododecane (Cyclen) and p-nitrophenyl acetate (*p*NPA) were purchased from Sigma-Aldrich. 50 mM Tris buffer was prepared by adding 6.06 g tris(hydroxymethyl)-aminomethane (Tris) and 5.84 g sodium chloride (NaCl) to double distilled water and diluting to 1.0 L, and then adjusting the pH from 4.5 to 11.0 with 0.1M hydrochloric acid solution or 0.1 M sodium hydroxide solution. Doubly distilled water was obtained from the Milli-Q Water Purification System (18 MΩ, Millipore, Bedford, MA, USA).

Physical Measurements UV-Vis spectra and kinetic measurements were recorded on a UV-

2450 UV-Vis spectrophotometer (Shimadzu, Kyoto, Japan) equipped with a thermostated cell holder. Nuclear magnetic resonance (NMR) spectra were recorded using a ECS 400 MHz NMR spectrometer (Jeol, Tokyo, Japan). Chemical shift values (□) are expressed in ppm relative to tetramethylsilane (TMS) as the internal standard. Mass spectra were measured on HX110/110A (Jeol, Tokyo, Japan) using the electrospray ionisation technique. Finally, elemental analysis and X-ray crystallography was performed at the Korea Basic Science Institute Seoul Center (Seoul, Korea).

Preparations



(a) 48% HBr, reflux, 12 h (b) Bis(2-pyridylmethyl)amine (1.0 eq.), Et_3N (2.0 eq.), CH_3CN, 25^{o}C, 24 h

6-(Bromomethyl)-2-(hydroxymethyl)pyridine (5) 2,6-pyridinedimethanol (**4**, 10 g, 72.0 mmol) was dissolved in 150 mL of 48% hydrobromic acid and gently refluxed under nitrogen atmosphere for 12 h. The resulting solution was cooled in an ice bath, and neutralised by adding saturated aqueous sodium carbonate to obtain a white precipitate. The neutralisation process should be performed on an ice bath. The precipitate was then filtered and washed with distilled water to obtain a white solid which was 2,6-bis(bromomethyl)pyridine (**6**). The filtrate was extracted with dichlorometane (CH_2Cl_2, 3 × 100 ml). The combined extracts were collected, washed with a saturated aqueous NaCl, and dried over anhydrous magnesium sulphate ($MgSO_4$). The solvent was removed under reduced pressure to give a light pink solid which was purified by recrystallisation from n-hexane to give the desired product (**5**) as a white solid (5.2 g, 35.8%), mp. 75-77 °C. ^{1}H NMR ($CDCl_3$, ppm) 3.70 (bs, 1H), 4.55 (s, 2H, CH_2Br), 4.77 (d, 2H), 7.17 (d, 1H), 7.35 (d, 1H), 7.70 (t, 1H). ^{13}C NMR ($CDCl_3$, ppm) 38.7, 68.6, 120.0, 120.3, 136.2, 158.2, 158.4.

[6-(Hydroxymethyl)-2-pyridylmethyl]bis(2-pyridylmethyl)-amine, TPA(CH_2OH) (7), A solution of 6-(Bromomethyl)-2-(hydroxymethyl)pyridine (**5**, 4.0 g, 20.0 mmol) in acetonitrile (50 ml) was added dropwise to a solution of bis(2-pyridylmethyl)amine (4.0 g, 20.0 mmol) and triethylamine (5.6 ml, 40.0 mmol) in acetonitrile (50 ml). The reaction mixture was stirred for 24 h under a N_2 atmosphere at room temperature. After the completion of the reaction, the solvent was removed under vacuum and the residue was treated with dichlorometane (150 ml), and then washed with saturated $NaHCO_3$ and brine. The organic layer was dried over anhydrous $MgSO_4$ and evaporated under reduced pressure to yield a product (**7**) as a yellow oil (4.1 g, 64 %). ESI-MS: m/z (321.25, $[M+H]^+$) ^{1}H NMR ($CDCl_3$, ppm) 3.49 (bs, 1H), 3.89 (s, 6H), 4.72 (s, 2H), 7.07-7.12 (m, 3H), 7.39 (d, 1H), 7.52-7.62 (m, 5H), 8.53 (d, 2 H). ^{13}C NMR ($CDCl_3$, ppm) 58.9, 59.2, 68.6, 120.0, 120.6, 123.0, 135, 135.8, 136.1, 149.4, 158.2, 158.6

General procedures of synthesis of Zn(II)-TPA, Zn(II)-TPA(CH_2OH) and Zn(II)-Cyclen
A solution of TPA, TPA(CH_2OH) or Cyclen (0.5 mmol) in methanol (15 mL) was added dropwise to a solution of zinc(II) chloride hexahydrate ($ZnCl_2 \cdot 6H_2O$, 0.5 mmol) in methanol (10 mL). After stirring for 24 h at room temperature, the resulting solution was filtered and treated with 1.0 mL of saturated solution of $NaClO_4$ and then left to crystallize at room temperature. The precipitate which separated within a few days was collected by filtration and recrystallized from H_2O.

[Zn(II)-TPA·Cl]ClO_4 (**1**) Anal. Calc. for $C_{18}H_{18}N_4O_4Cl_2Zn$ (MM=490.66g/mol): C, 44.06; H, 3.70; N, 11.42. Found: C, 44.23; H, 3.63; N, 11.46 %. HRMS calc. for 489.0069 ($M+H^+$), found 489.0058 ^{1}H NMR (D_2O) □ 4.20 (6H, s), 7.48 (3H, d), 7.53 (3H, t), 7.98 (3H, t), 8.72 (3H, d)

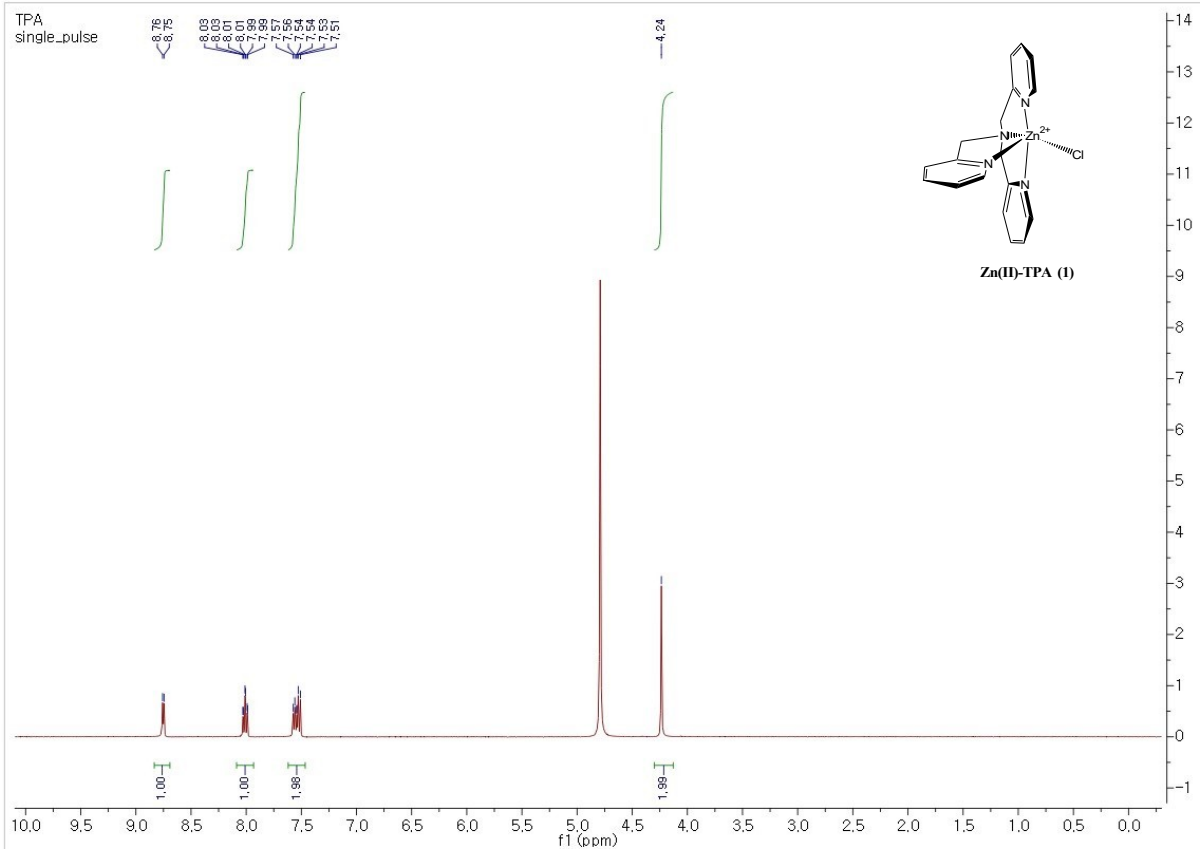
[Zn(II)-TPA(CH_2OH)·Cl]ClO_4 (**2**) Anal. Calc. for $C_{19}H_{20}Cl_2N_4O_5Zn$ (MM=520.68g/mol): C, 43.88; H, 3.87; N, 10.76. Found: C, 43.94; H, 3.83; N, 10.71 %. HRMS calc. for 519.0175, ($M+H^+$), found 519.0170 ^{1}H NMR (D_2O) □ 4.17 (2H, s), 4.39 (4H, s), 5.01 (2H, s), 7.19 (1H, d), 7.28 (1H, d), 7.43-7.48 (4H, m), 7.77 (1H, t), 7.92 (2H, t), 8.57 (2H, d)

[Zn(II)-Cyclen·Cl]ClO_4 (**3**) Anal. Calc. for $C_9H_{23}Cl_2N_4O_4Zn$ (MM=370.02g/mol): C, 25.95; H, 5.45; N, 15.14. Found: C, 25.99; H, 5.39; N, 15.19 %. HRMS calc. for 371.0231, ($M+H^+$), found 371.0226 ^{1}H NMR (D_2O) □ 2.68-2.71 (8H, m), 2.80-2.84 (8H, m)

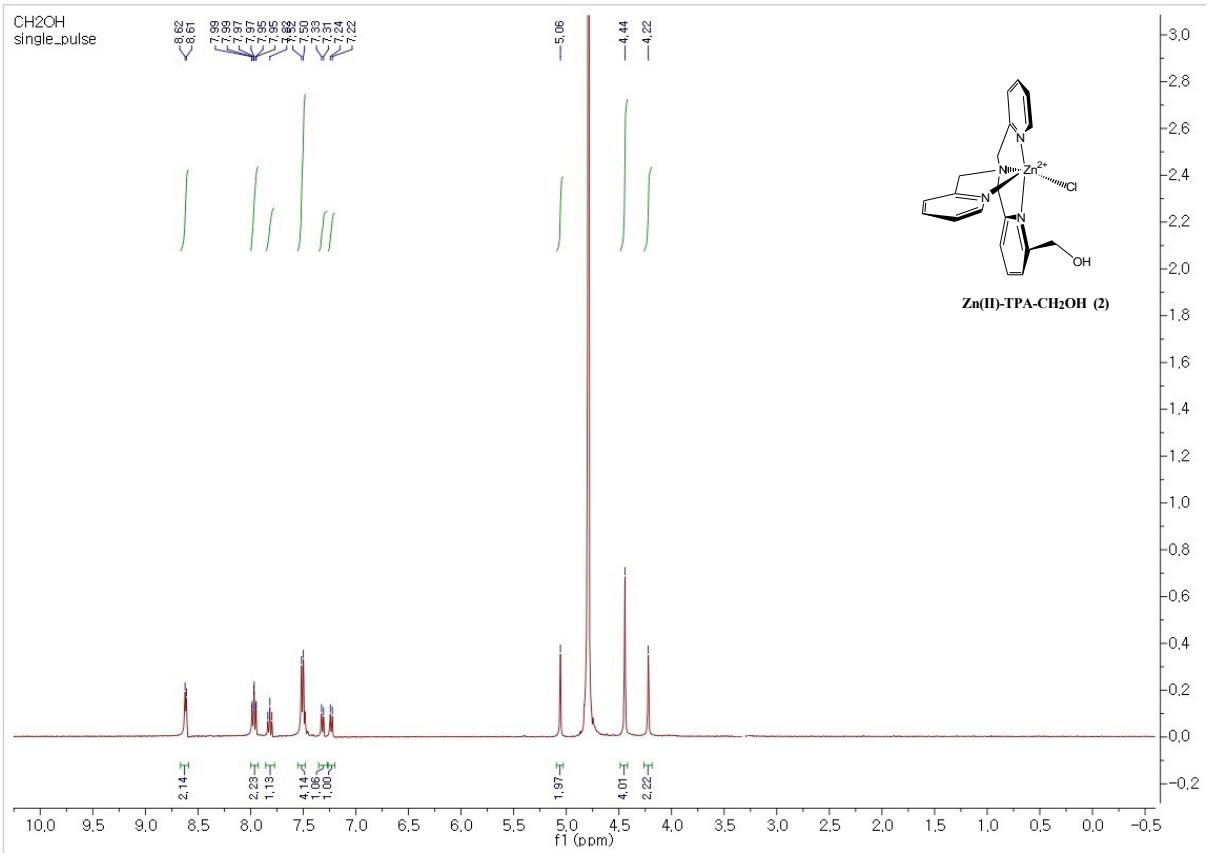
Kinetics The catalytic hydrolysis of *p*-nitrophenyl acetate (*p*NPA) in aqueous media in the presence of Zn(II) complexes was investigated by monitoring the formation of p-nitrophenolate at 400 nm using a Shimadzu UV-2450 UV-Vis spectrophotometer equipped with a temperature-controlled cell holder. All kinetic measurements were carried out at 25 °C under strictly controlled solution conditions. The reaction medium consisted of a 0.05 M Tris buffer (pH 7.0), and the ionic strength (I = 0.10) was carefully adjusted using sodium chloride to minimize activity coefficient variations during the reaction. The general experimental procedure was as follows: solutions of Zn(II)–TPA and Zn(II)–Cyclen (final concentrations: 1.0–7.0 mM), Zn(II)–TPA(CH_2OH) (final concentrations: 0.1–0.7 mM), and *p*NPA (final concentration: 10 mM) were prepared in 5% acetonitrile–water mixtures to ensure complete solubility of the substrate. Immediately after mixing the catalyst and substrate solutions, the time-dependent absorbance at 400 nm was recorded continuously or at appropriate intervals to follow the progress of the reaction. The observed pseudo-first-order rate constants (k_{obs}) were obtained from the linear portion of the absorbance–time plots by fitting the data to a first-order kinetic model. All kinetic measurements were performed in triplicate to ensure reproducibility, and the reported values represent the arithmetic mean of these independent determinations.

^{1}H NMR Spectra of Zn(II) complexes in D_2O

[Zn(II)-TPA·Cl]ClO_4 (**1**)



[Zn(II)-TPA(CH_2OH)·Cl]ClO_4 (**2**)



Zn(II)-Cyclen·Cl]ClO_4 (**3**)