

Supporting Information

Pyridine-2,6-dithiocarboxylic Acid and Its Metal Complexes: New Inhibitors of New Delhi Metallo β -lactamase-1

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* Organisms tested: *E. coli* 2692, *E. coli* BAA-2452, and *K. pneumoniae* BAA-2146

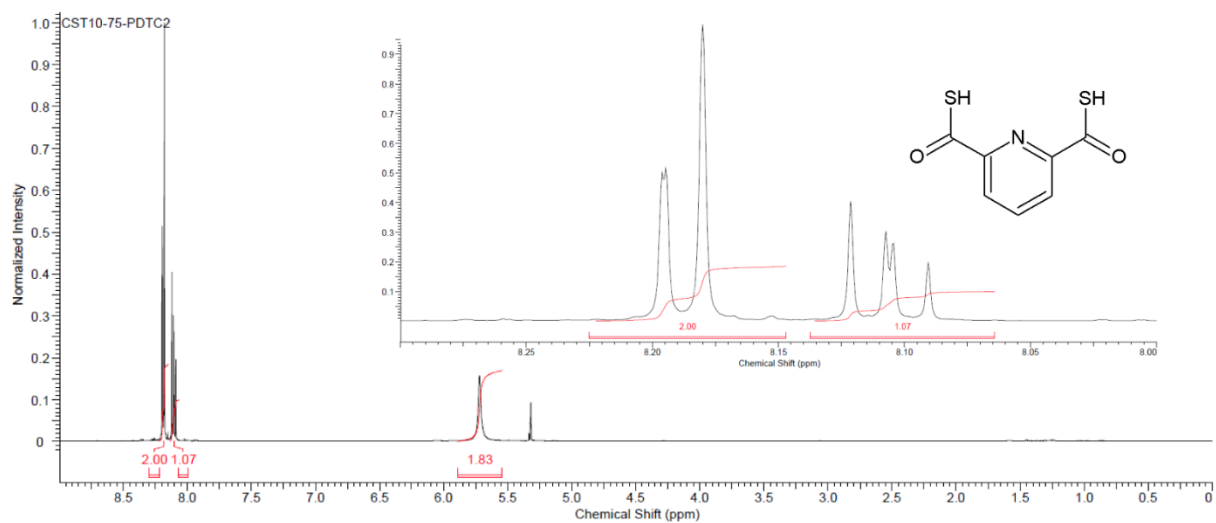


Figure S1. ¹H NMR spectrum and integration of synthesized PDTC. Inset expands the region between 8 and 8.3 ppm to highlight the second order coupling pattern – pattern identified as AB₂.

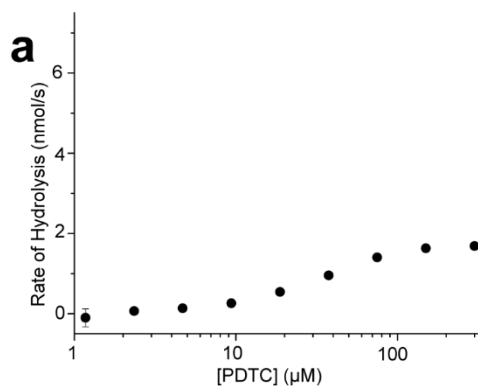


Figure S2. Rate of CENTA hydrolysis in the presence of PDTC with no NDM-1.

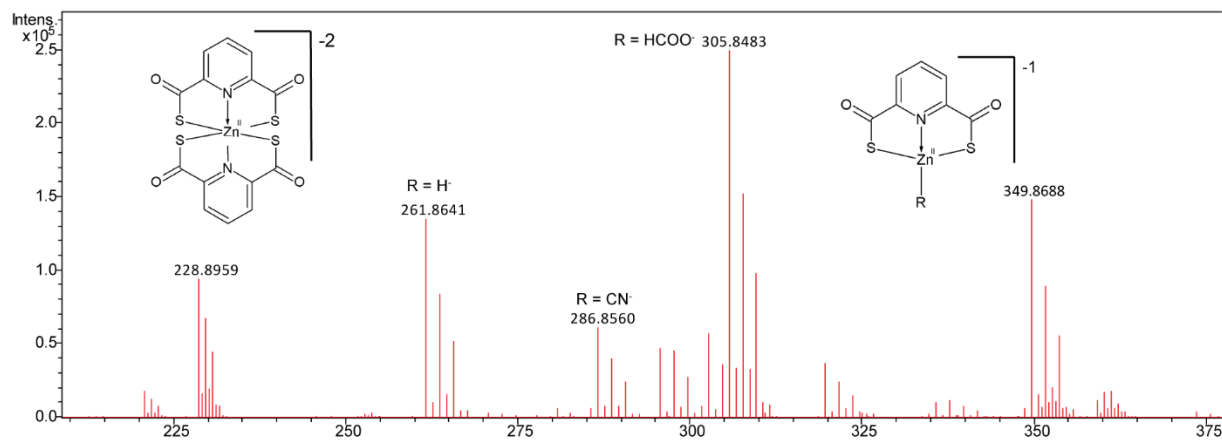


Figure S3. Mass spectra acquired for PDTC in the presence of ZnSO_4 , revealing a 2:1 PDTC₂-Zn complex for 228.8959 m/z $[\text{M}-2\text{H}]^{-2}$. Several 1:1 PDTC-Zn complexes were identified where able.

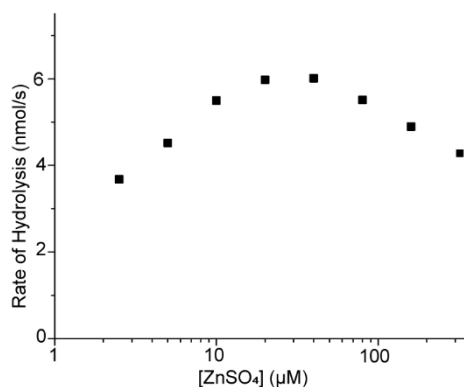


Figure S4. Rate of CENTA hydrolysis by NDM-1 at different concentrations of ZnSO_4 in the assay buffer. Optimal rate of hydrolysis takes place between 20 and 40 μM .

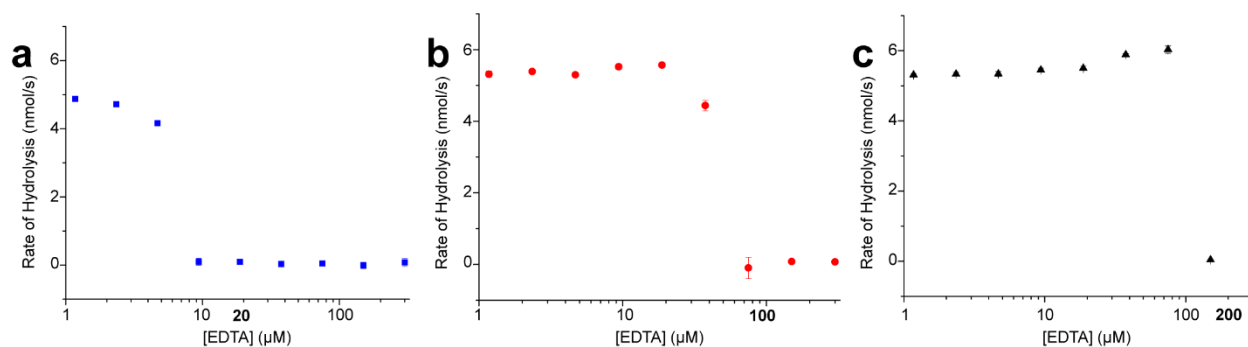


Figure S5. Initial rates of CENTA hydrolysis by NDM-1 vs. EDTA concentration with (a) 10 μM ZnSO_4 , (b) 50 μM ZnSO_4 , (c) 100 μM ZnSO_4 supplementing the reaction buffer. EDTA eliminates in a 1:1 equivalency with the amount of ZnSO_4 incorporated, as compared with PDTC, which reduced activity at 2 equiv. of ZnSO_4 (denoted by bold type on x axis).

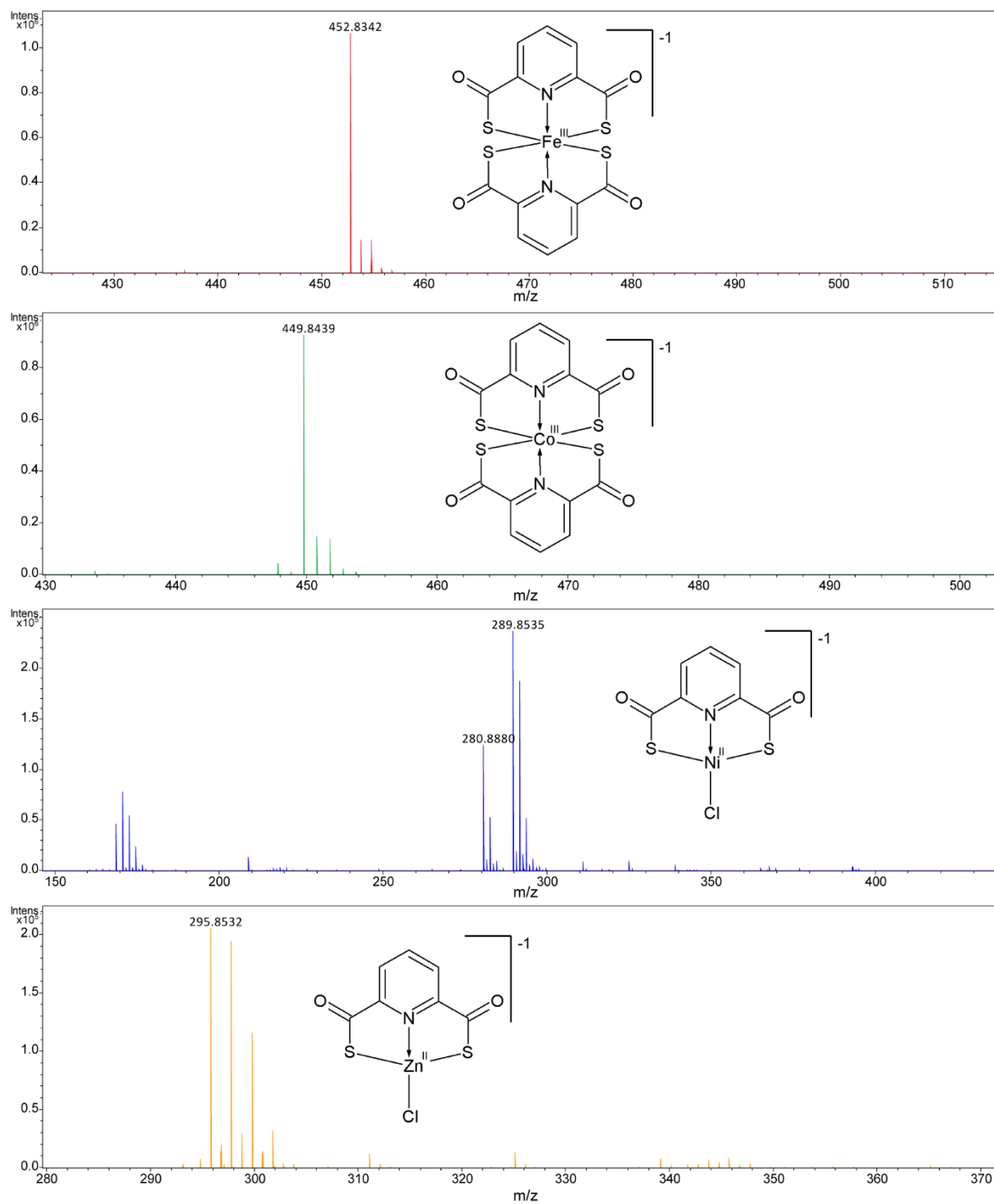


Figure S6. Mass Spectra of the PDTC complexes collected in ESI (-) mode.

Table S1. PDTC complex and PDTC MIC data. MICs shown are an average of 4 replicates.

	Observed MIC (mM)		
	<i>E. coli</i> 2692	<i>E. coli</i> BAA-2452	<i>K. pneumoniae</i> BAA-2146
PDTC ₂ -Fe	>1.6	>1.6	1.6
PDTC ₂ -Co	>1.6	>1.6	1.6
PDTC-Ni	>1.6	>1.6	1.6
PDTC-Zn	0.2	0.2	0.4
PDTC (no metal)	0.4	0.4	0.4

Table S2. Metal salt MIC data. MICs shown are an average of 4 replicates.

	Observed MIC (mM)		
	<i>E. coli</i> 2692	<i>E. coli</i> BAA-2452	<i>K. pneumoniae</i> BAA-2146
ZnCl ₂	> 1.6	> 1.6	1.6
FeCl ₃	> 1.6	> 1.6	> 1.6
NiCl ₂	> 1.6	> 1.6	> 1.6
CoCl ₂	1.6	> 1.6	1.6

Table S3. Meropenem MIC data with metal salts. MICs shown are an average of 4 replicates.

	Observed Meropenem MIC (µg/mL)		
	<i>E. coli</i> 2692	<i>E. coli</i> BAA-2452	<i>K. pneumoniae</i> BAA-2146
(no salt)	64	16	128
ZnCl ₂	64	32	128
FeCl ₃	64	8	128
NiCl ₂	64	32	128
CoCl ₂	64	10	64

Metal salts were screened at a constant concentration of 400 µM, equivalent to 0.25 x MIC or the highest concentration tested for Table S2