

# Supplementary Materials

## Discovery of novel non-oxime reactivators showing *in vivo* antidotal efficiency for sarin poisoned mice

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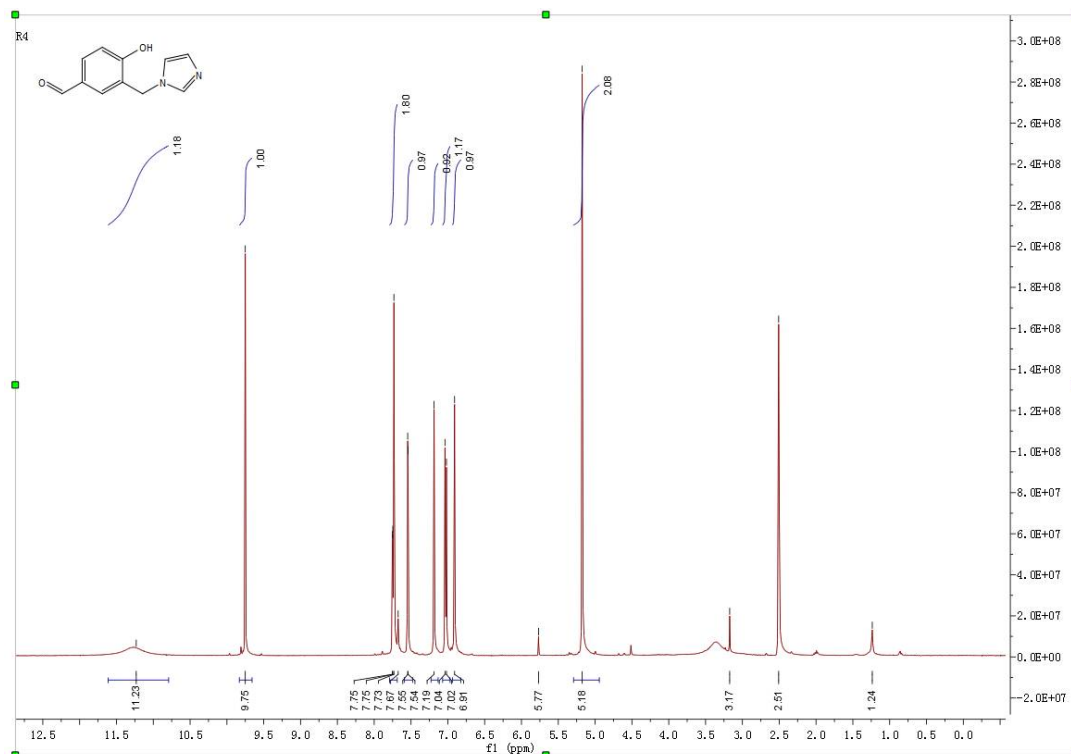
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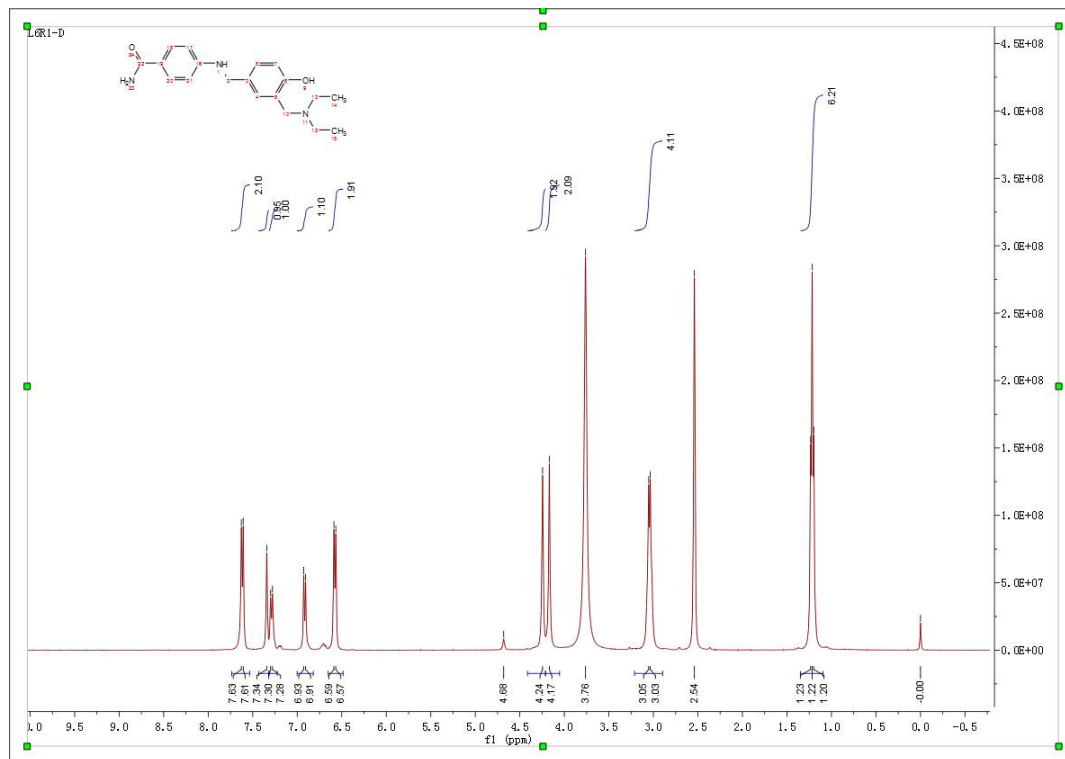
# 1. NMR and HR-MS Spectra for R4, L6R1, L10R1, L6R4 and L10R4

## 3-((1H-imidazol-1-yl)methyl)-4-hydroxybenzaldehyde (R4) $^1\text{H}$ NMR (DMSO, 400 MHz)

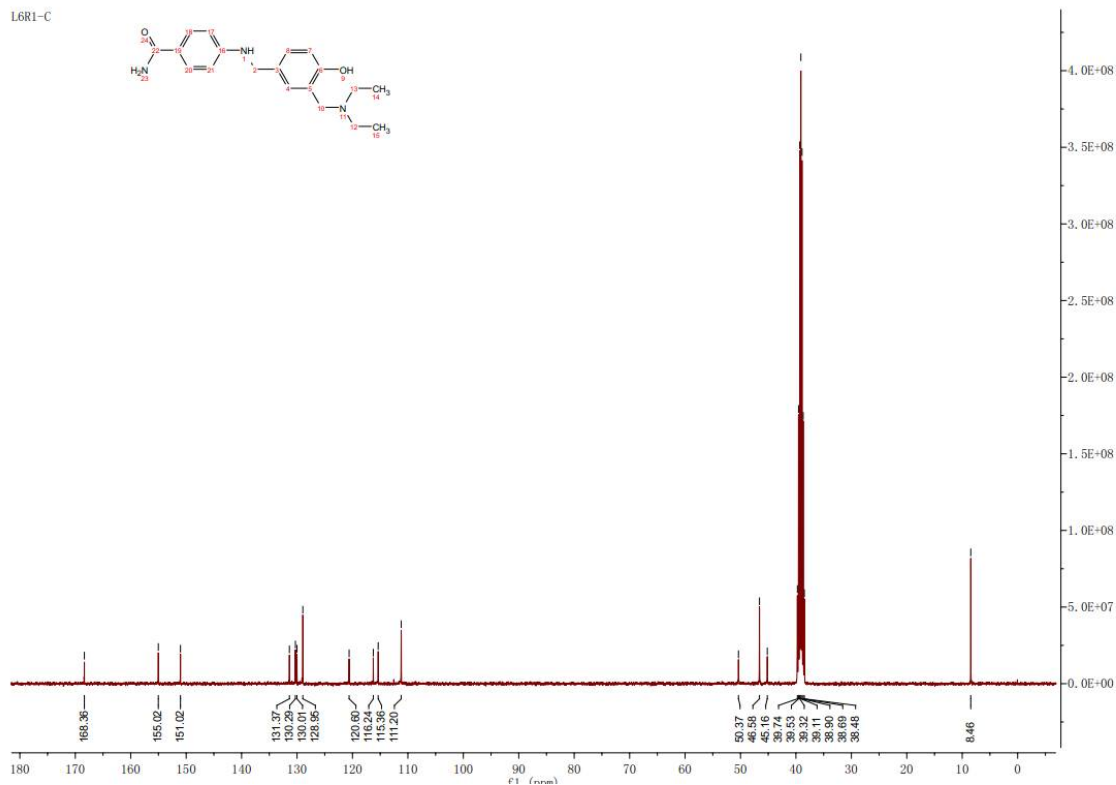


## 4-((3-((diethylamino)methyl)-4-hydroxybenzyl)amino)benzamide (L6R1)

$^1\text{H}$  NMR (DMSO, 400 MHz) and HRMS (ESI $^+$ )

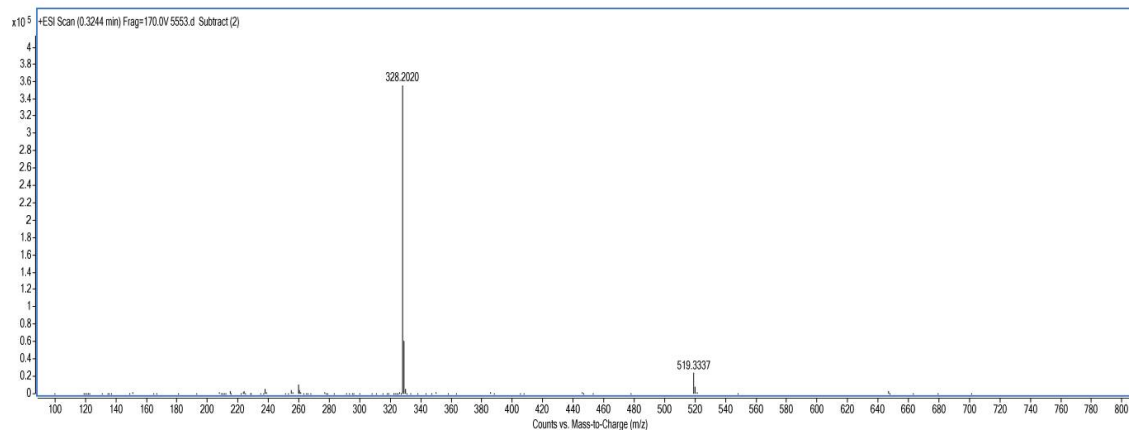


L6R1-C



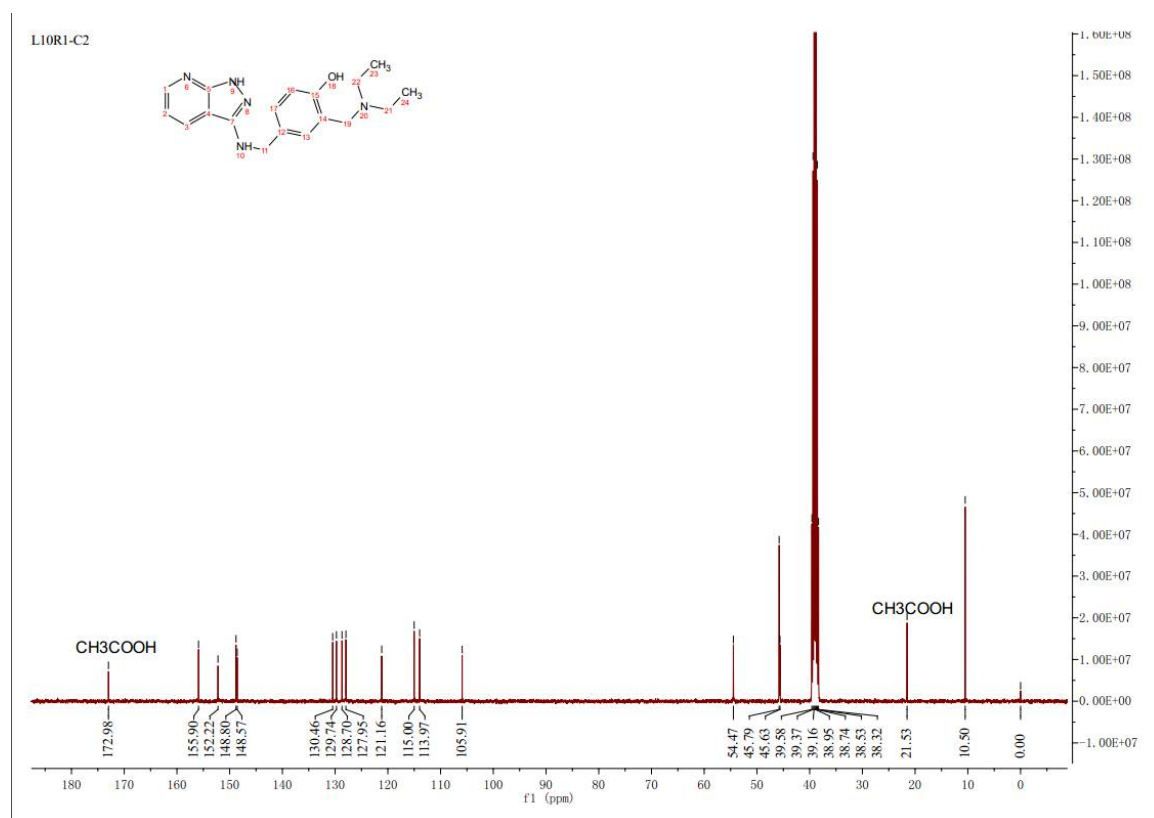
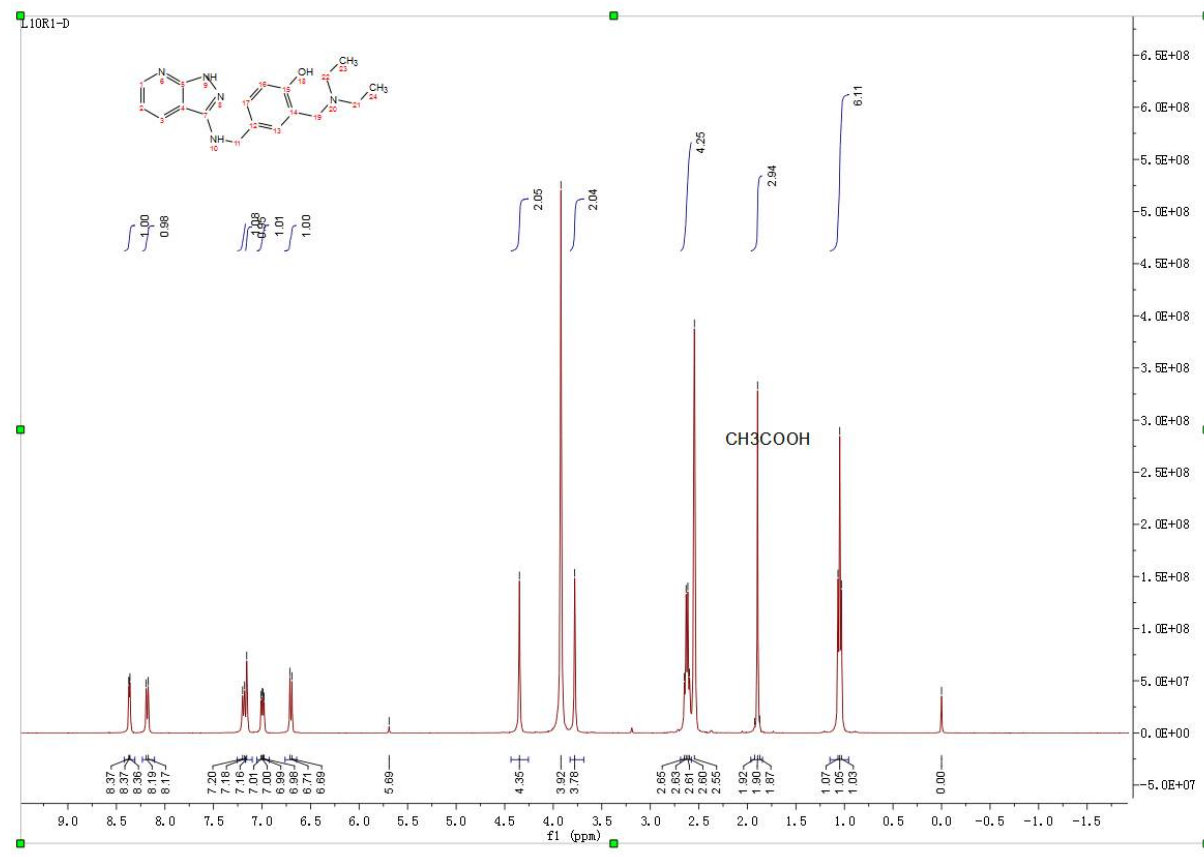
## Qualitative Analysis Report

Data Filename	5553.d	Sample Name	L6R1
Instrument Name	TOF G6230A	Acquired Time	2021-09-28
Acq Method	YCLM	Acquired SW	6200 series TOF/6500 series
IRM Calibration Status	Success		
User Chormatograms			



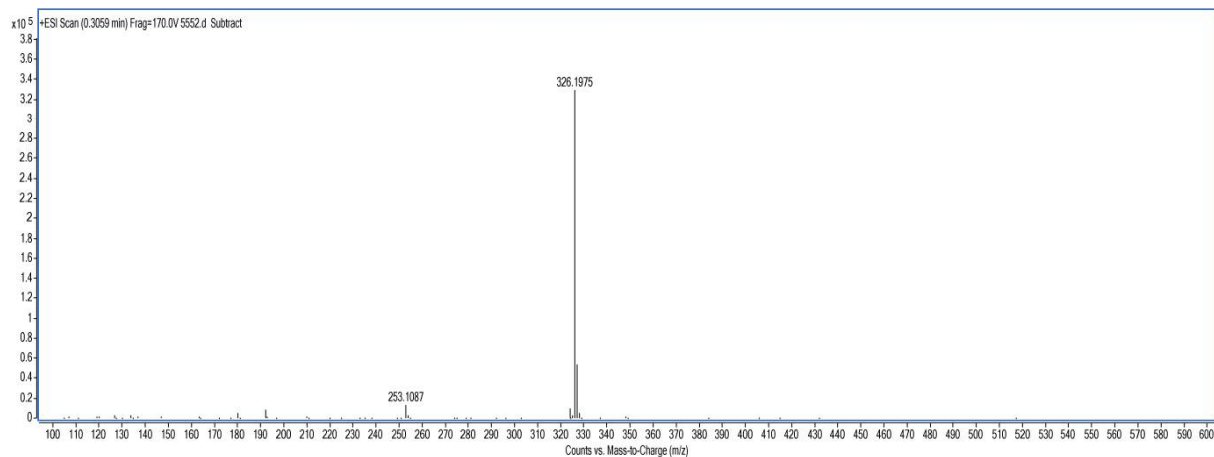
**4-(((1H-pyrazolo[3,4-b]pyridin-3-yl)amino)methyl)-2-((diethylamino)methyl)phenol (L10R1):**

$^1\text{H}$  NMR (DMSO, 400 MHz) and HRMS (ESI $^+$ )



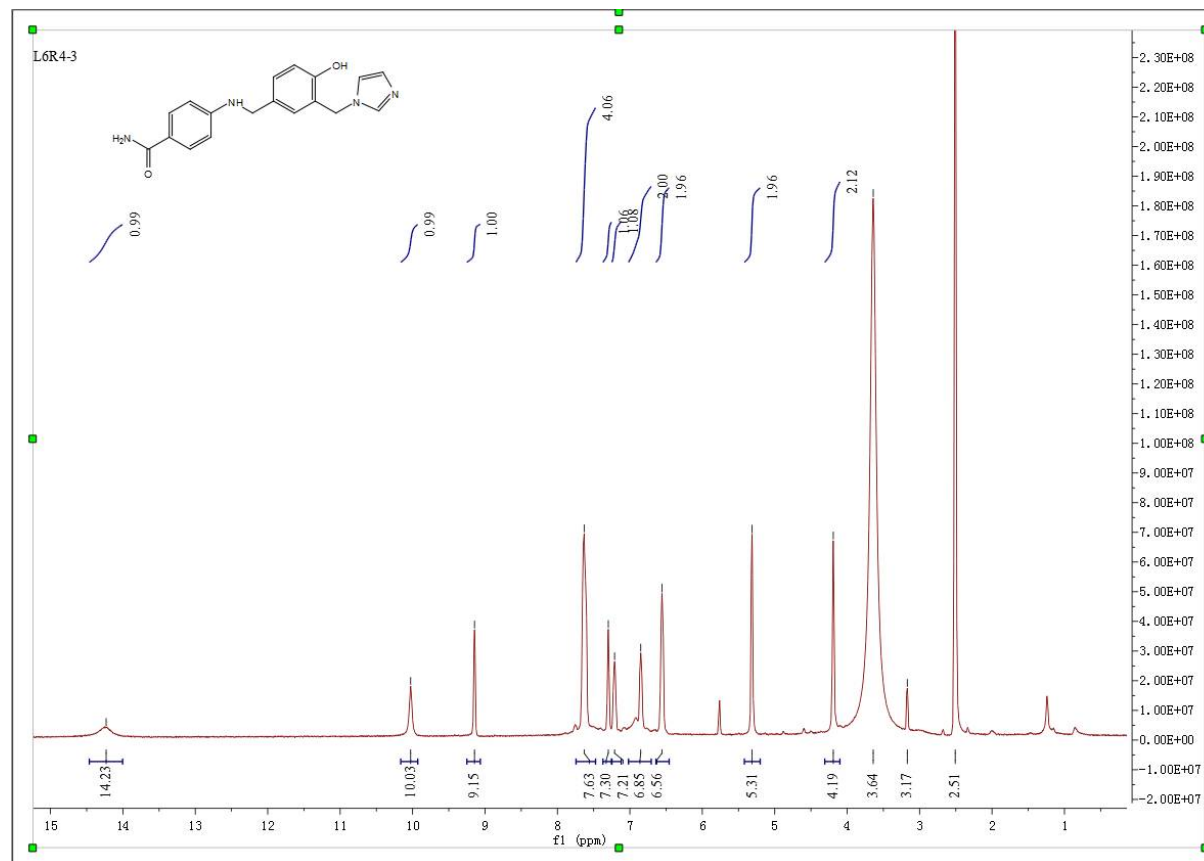
## Qualitative Analysis Report

Data Filename	5552.d	Sample Name	L10R1-2
Instrument Name	TOF G6230A	Acquired Time	2021-09-28
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IRM Calibration Status	Success		
User Chromatograms			



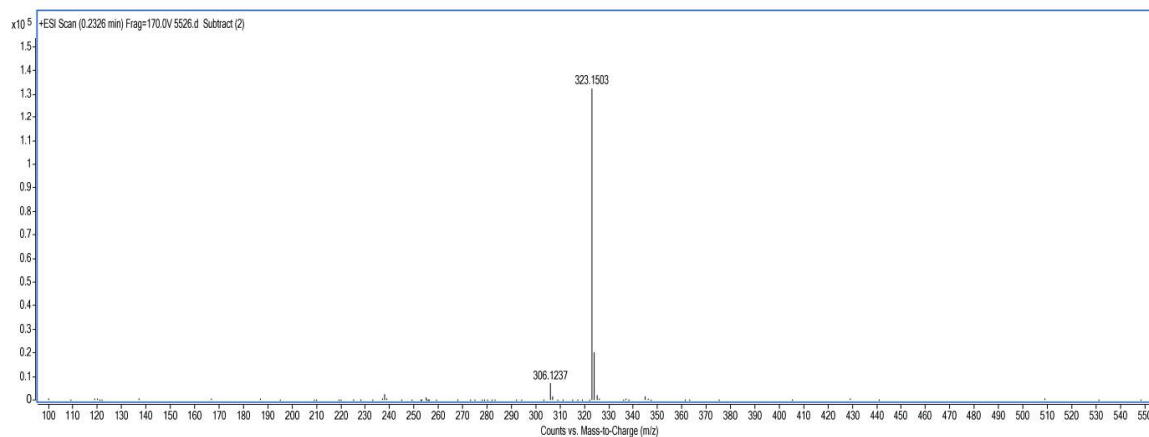
### 4-((3-((1H-imidazol-1-yl)methyl)-4-hydroxybenzyl)amino)benzamide (L6R4):

<sup>1</sup>H NMR (DMSO-D<sub>2</sub>O, 400 MHz) and HRMS (ESI<sup>+</sup>)



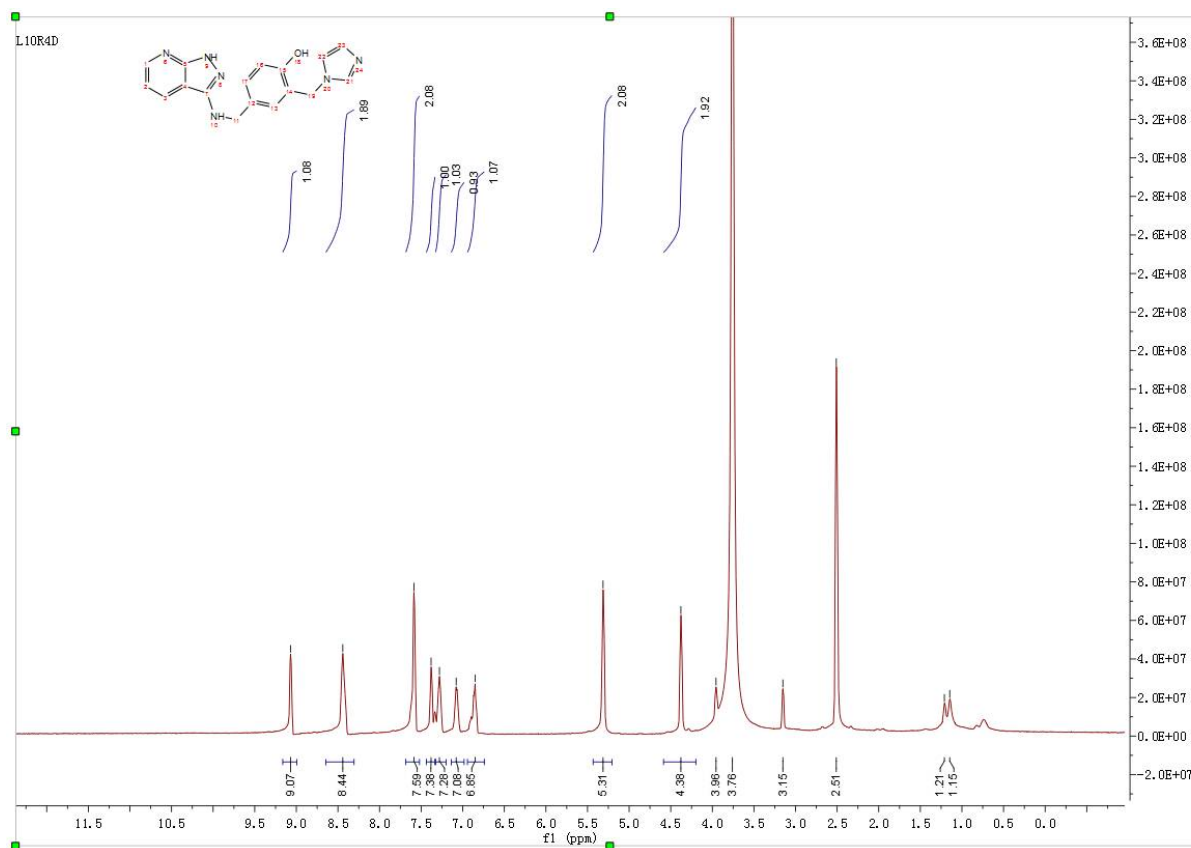
## Qualitative Analysis Report

Data Filename	5526.d	Sample Name	L6R4
Instrument Name	TOF G6230A	Acquired Time	2021-09-27
Acq Method	YCL.M	Acquired SW	6200 series TOF/6500 series
IRM Calibration Status	Success		
User Chromatograms			



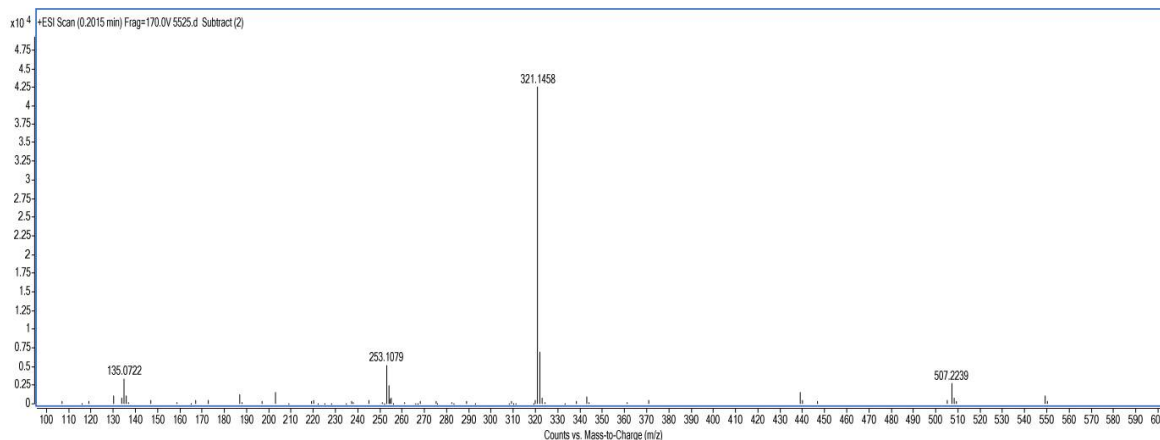
### 2-((1H-imidazol-1-yl)methyl)-4-(((1H-pyrazolo[3,4-b]pyridin-3-yl)amino)methyl)phenol (L10R4):

$^1\text{H}$  NMR (DMSO- $\text{D}_2\text{O}$ , 400 MHz) and HRMS (ESI $^+$ )



## Qualitative Analysis Report

Data Filename	5525.d	Sample Name	L10R4
Instrument Name	TOF G6230A	Acquired Time	2021-09-27
Acq Method	YCL.M	Acquired SW	6200 series TOF/6500 series
IRM Calibration Status	Success		
User Chromatograms			



## 2. Biological evaluation

**Table S1. %Reactivation of non-oxime reactivators for VX and sarin inhibited hAChE**

VX-hAChE				
	100 $\mu$ M	50 $\mu$ M	25 $\mu$ M	10 $\mu$ M
HI-6	74.02 $\pm$ 2.28	64.61 $\pm$ 0.72	49.38 $\pm$ 1.36	32.72 $\pm$ 1.05
L6R1	68.40 $\pm$ 0.80	48.26 $\pm$ 1.36	29.74 $\pm$ 1.82	13.21 $\pm$ 1.07
L10R1	-	-	20.29 $\pm$ 1.54	20.76 $\pm$ 0.10
L6R4	90.62 $\pm$ 2.47	68.63 $\pm$ 3.39	34.55 $\pm$ 0.25	19.12 $\pm$ 2.12
L10R4	96.42 $\pm$ 0.90	92.85 $\pm$ 4.21	75.66 $\pm$ 2.13	44.74 $\pm$ 1.10
sarin-hAChE				
	100 $\mu$ M	50 $\mu$ M	25 $\mu$ M	10 $\mu$ M
HI-6	51.20 $\pm$ 0.69	46.27 $\pm$ 0.88	28.47 $\pm$ 1.00	21.25 $\pm$ 6.86
L6R1	22.72 $\pm$ 0.88	13.90 $\pm$ 0.18	5.86 $\pm$ 3.25	5.83 $\pm$ 0.86
L10R1	-	9.12 $\pm$ 0.70	7.51 $\pm$ 0.24	7.91 $\pm$ 2.58
L6R4	30.38 $\pm$ 1.58	21.84 $\pm$ 1.39	14.99 $\pm$ 0.40	13.68 $\pm$ 0.78
L10R4	22.52 $\pm$ 0.24	17.10 $\pm$ 0.09	7.94 $\pm$ 1.94	6.33 $\pm$ 0.21

**Table S2. Selected observed first-order rate constant  $K_{obs}$  of HI-6 and novel non-oxime reactivators.**

	VX-hAChE/ $k_{obs}$ ( $10^{-3}\text{min}^{-1}$ )			Sarin-hAChE/ $k_{obs}$ ( $10^{-4}\text{min}^{-1}$ )			IC <sub>50</sub> ( $\mu$ M)
	50 $\mu$ M	25 $\mu$ M	10 $\mu$ M	100 $\mu$ M	50 $\mu$ M	20 $\mu$ M	
HI-6	20.8 $\pm$ 1.4	12.3 $\pm$ 0.7	6.7 $\pm$ 0.3	137.4 $\pm$ 8.4	121.0 $\pm$ 6.4	65.3 $\pm$ 3.0	668 $\pm$ 61
L6R1	11.8 $\pm$ 1.1	5.8 $\pm$ 0.6	2.4 $\pm$ 0.2	41.2 $\pm$ 2.3	22.8 $\pm$ 1.4	10.7 $\pm$ 0.9	439 $\pm$ 18
L10R1	-	4.0 $\pm$ 0.2	4.3 $\pm$ 0.2	-	14.2 $\pm$ 0.8	13.8 $\pm$ 1.1	30.9 $\pm$ 0.4
L6R4	191.1 $\pm$ 21.9	56.8 $\pm$ 4.0	13.6 $\pm$ 0.9	68.4 $\pm$ 4.0	41.3 $\pm$ 3.6	22.7 $\pm$ 1.3	402 $\pm$ 19
L10R4	89.7 $\pm$ 10.4	31.4 $\pm$ 2.7	10.6 $\pm$ 0.6	47.2 $\pm$ 2.0	31.1 $\pm$ 1.6	15.8 $\pm$ 1.0	483 $\pm$ 33

Experiments were performed in duplicate at 25 °C in phosphate buffer (0.10 M, pH 7.4), data shows the nonlinear fitting results and

standard deviation.

Plot of  $k_{obs}$  vs concentrations of **HI-6** and new synthesized compounds.

