Supporting Information

Nitroimidazopyrazinones with oral activity against tuberculosis and Chagas disease in mouse models of infection

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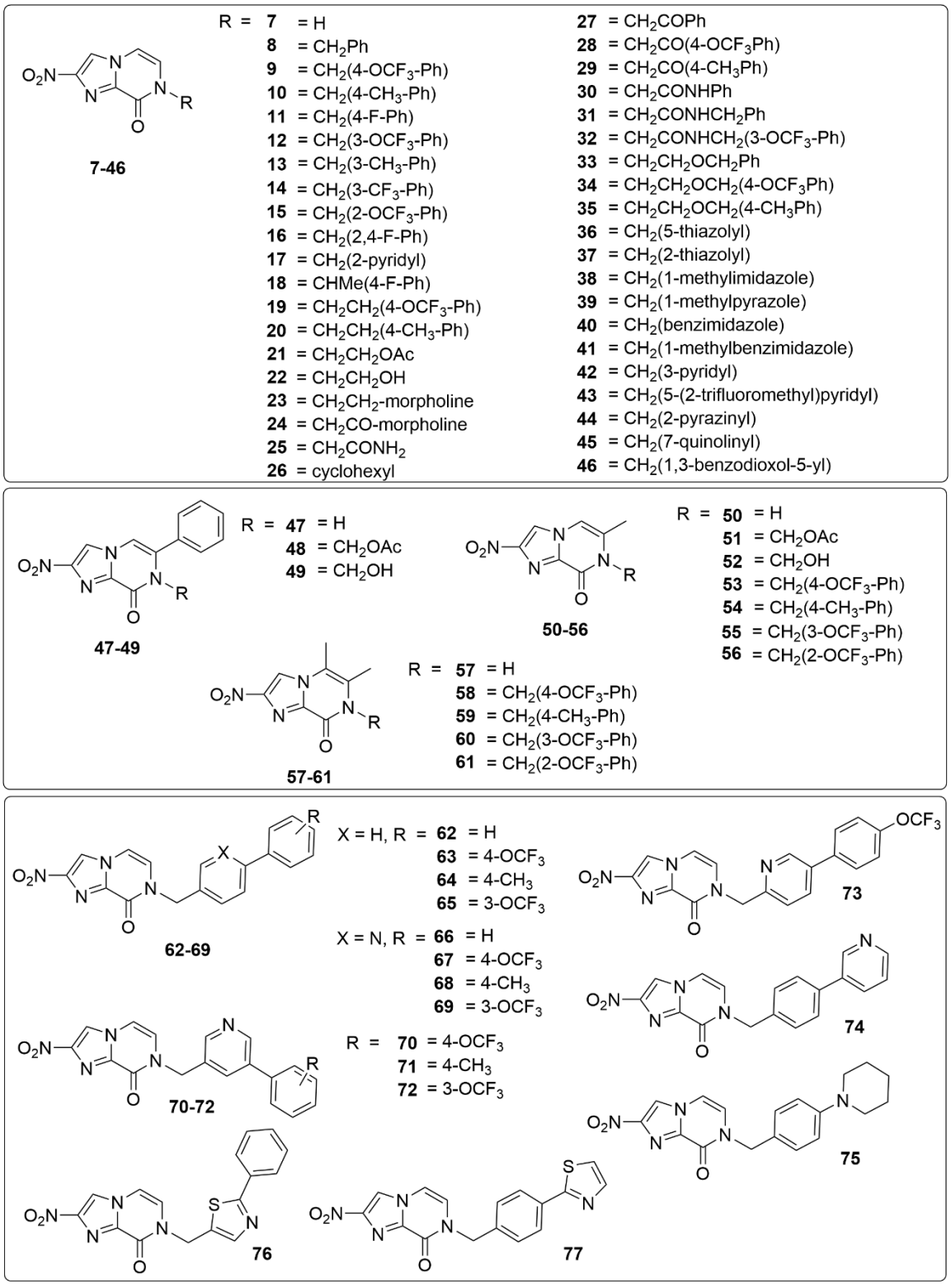


Figure S1. Chemical structures of nitroimidazopyrazinones **7–77**.

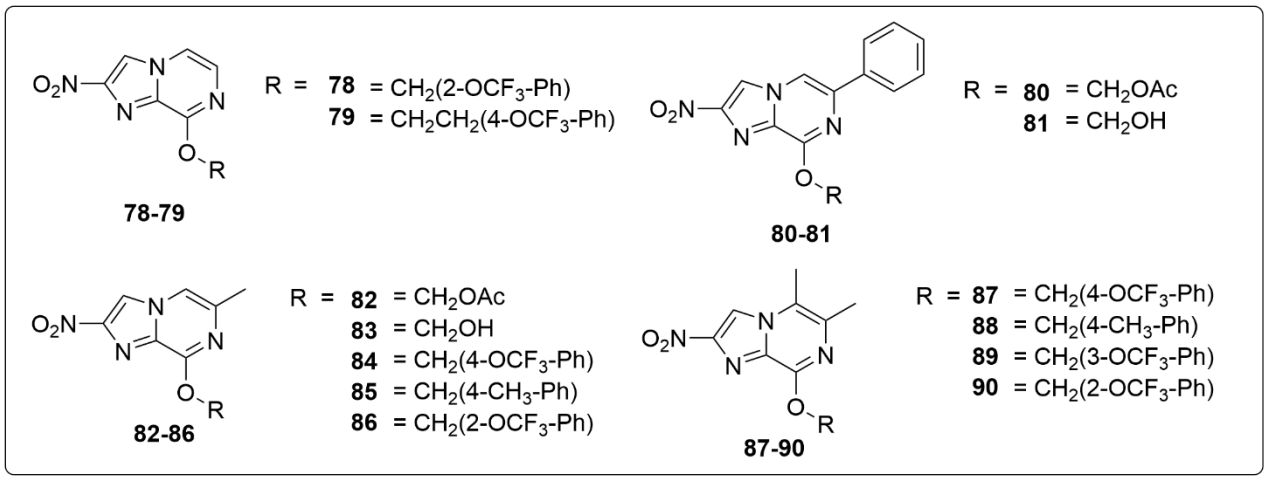


Figure S2. Chemical structures of nitroimidazopyrazines **78–90.**

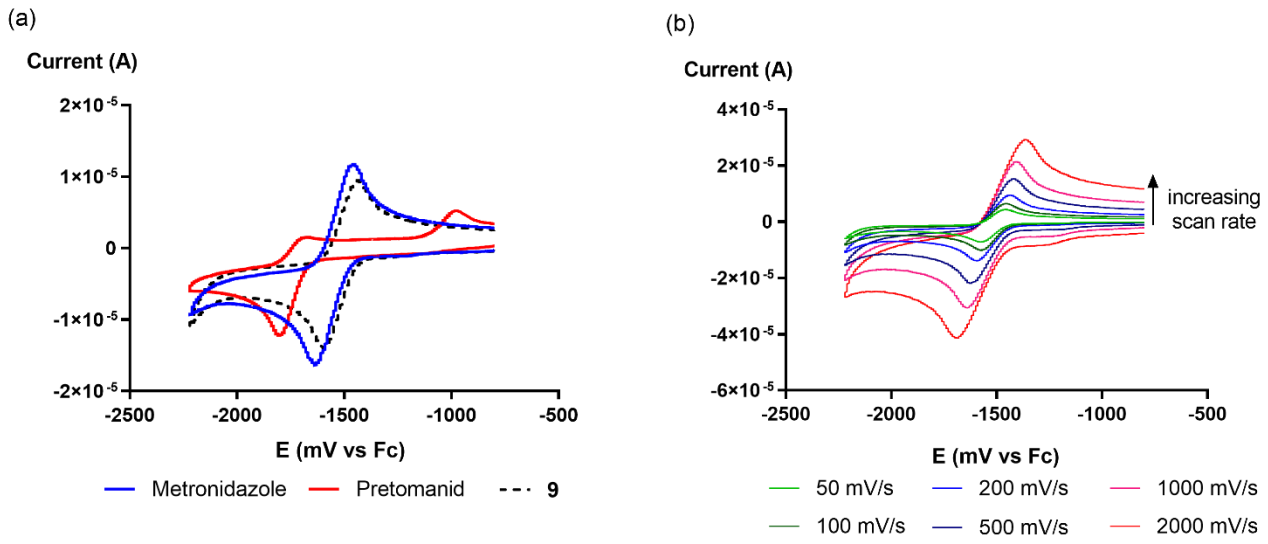


Figure S3. (a) Cyclic voltammogram of 1 mM tested compounds (metronidazole, pretomanid **4** and compound **9**) in DMSO containing 0.1M tetrabutylammonium hexafluorophosphate (TBAHFP), with sweep rate at 200 mV/s. (b) Cyclic voltammogram of **9** at different sweep rates (50, 100, 200, 500, 1000 and 2000 mV/s).

Table S1. Average body weight of mice at day 10 (starting of treatment) and day 31 (end of treatment) for *M. tuberculosis* infection model. Each treated group composed of 7 female BALB/c mice.

Compounds	Dosages (mg/kg)	Mouse number	Average mice weights (g) each group	
			T10, before	T31, after
5% DMSO + 10% hydroxypropyl-β-cyclodextrin	-	7	22.71	22.71
Rifampicin	15	5	21.80	22.40
Pretomanid **4**	20	7	21.86	22.71
9	12.5	7	22.71	22.86
	25	7	22.43	22.57
	50	7	21.71	22.14
14	12.5	7	22.71	22.29
	25	7	22.29	22.57
	50	7	22.14	22.71

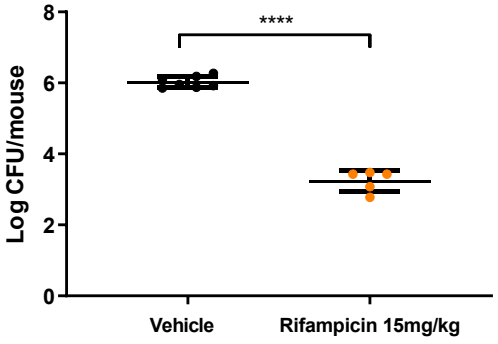
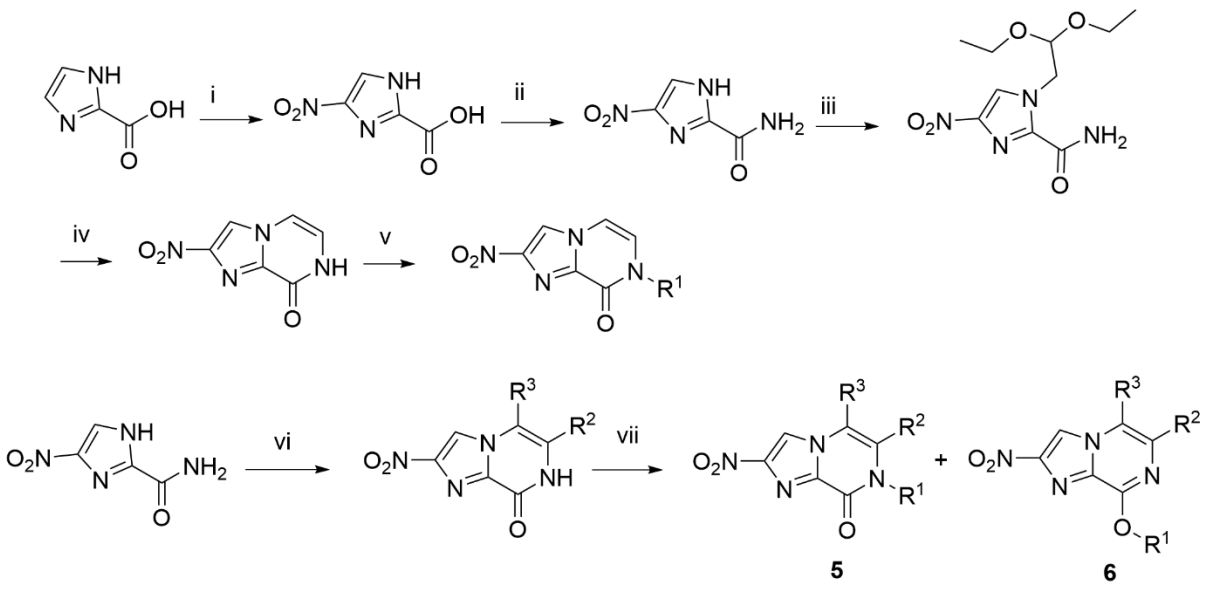


Figure S4. CFU count data in the lungs of infected mice treated with rifampicin (15 mg/kg) in comparison with the vechcle control (5% DMSO + 10% hydroxypropyl-β-cyclodextrin). Statistical significance was determined by ordinary one-way ANOVA followed by Dunnett's multiple comparison test. ****P < 0.0001.



Scheme S1. General reaction scheme of nitroimidazopyrazin-ones/-es. (i) H_2SO_4/ HNO_3, 60 ºC; (ii) oxalyl chloride, catalytic DMF, DCM, 0 ºC → rt, then concentrated NH_4OH, 0 ºC → rt; (iii) bromoacetaldehyde diethyl acetal, K_2CO_3, DMF, µW 180 °C; (iv) 2M HCl/1,4-dioxane, µW 120 ºC; (v) various alkyl bromides, Cs_2CO_3 or K_2CO_3, DMF, µW 80–120 °C; (vi) α-halo ketones, K_2CO_3, DMF, rt, then 2M HCl, rt; (vii) various alkyl bromides, Cs_2CO_3 or K_2CO_3, DMF, rt–µW 80 °C.

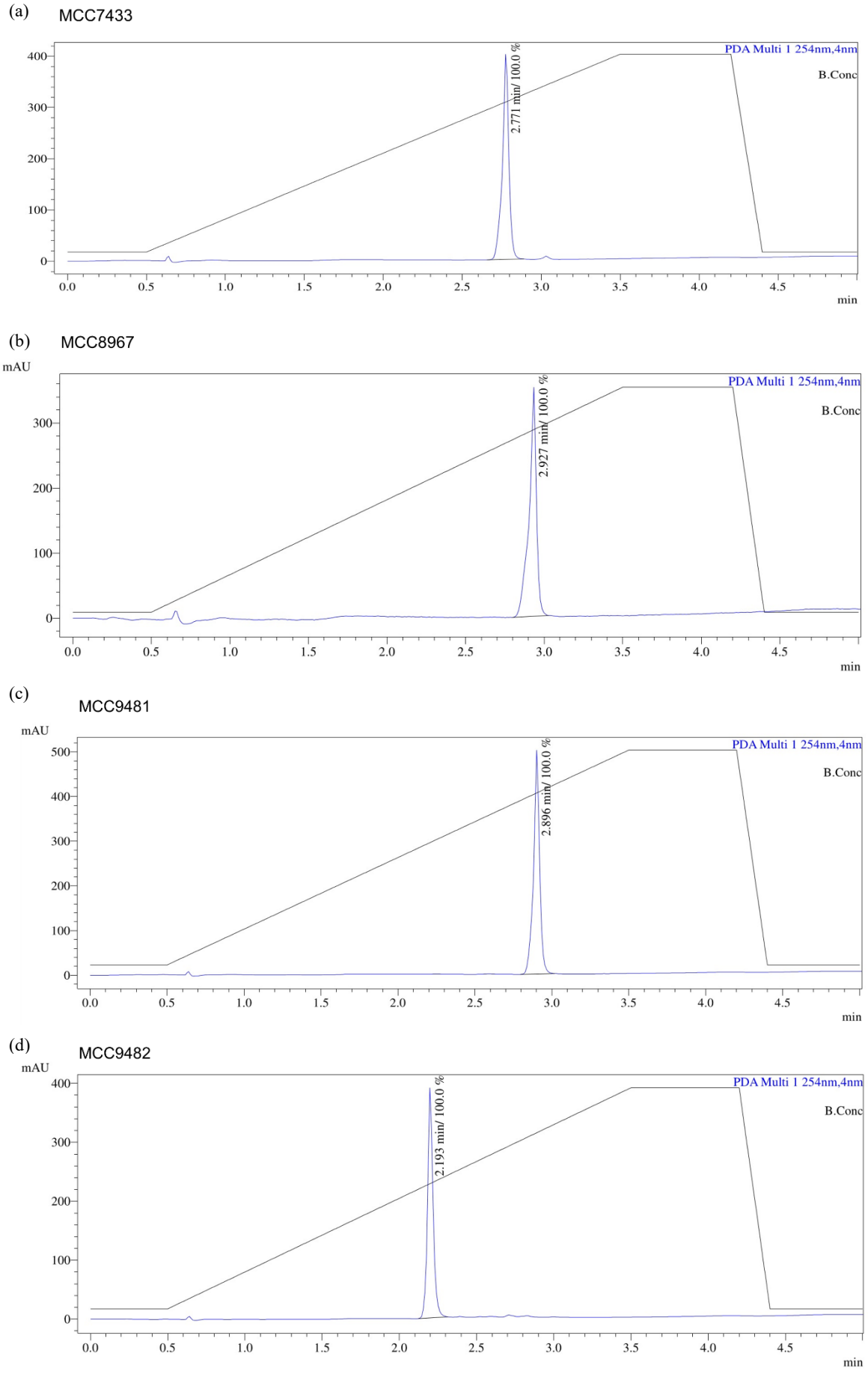
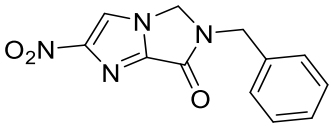


Figure S5. HPLC traces of compounds (a) **9**, (b) **14**, (c) **73** and (d) **74.**

^{1}H and ^{13}C NMR spectra

6-Benzyl-2-nitro-5,6-dihydro-7*H*-imidazo[1,5-*a*]imidazol-7-one (92)



^{1}H NMR (600 MHz, DMSO-d_6)

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7	Pulse Sequence	zg
8	Experiment	1D
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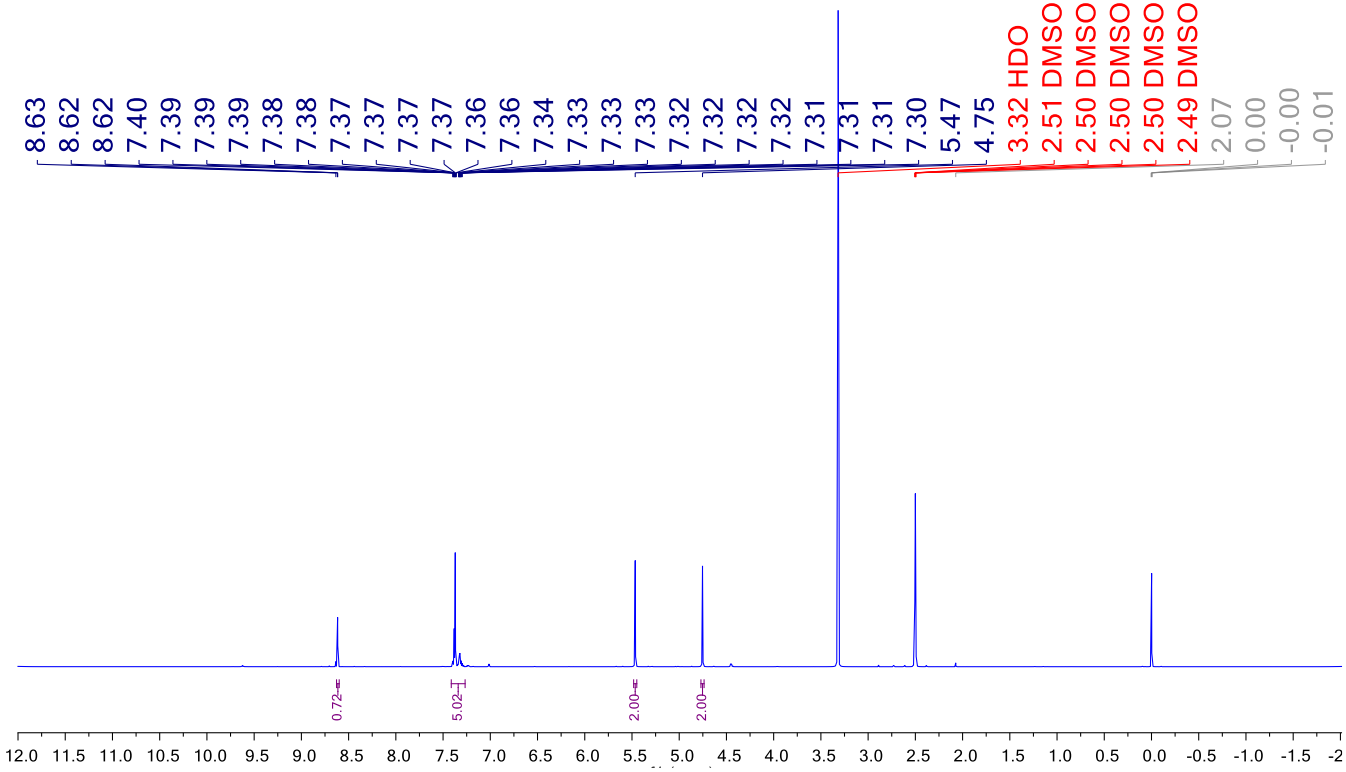
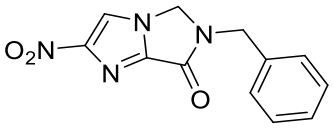
22	Acquired Size	16384
23	Spectral Size	65536



6-Benzyl-2-nitro-5,6-dihydro-7*H*-imidazo[1,5-*a*]imidazol-7-one (92)



^{13}C NMR (150 MHz, DMSO-d_6)

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4	Spectrometer	spect
5	Solvent	DMSO
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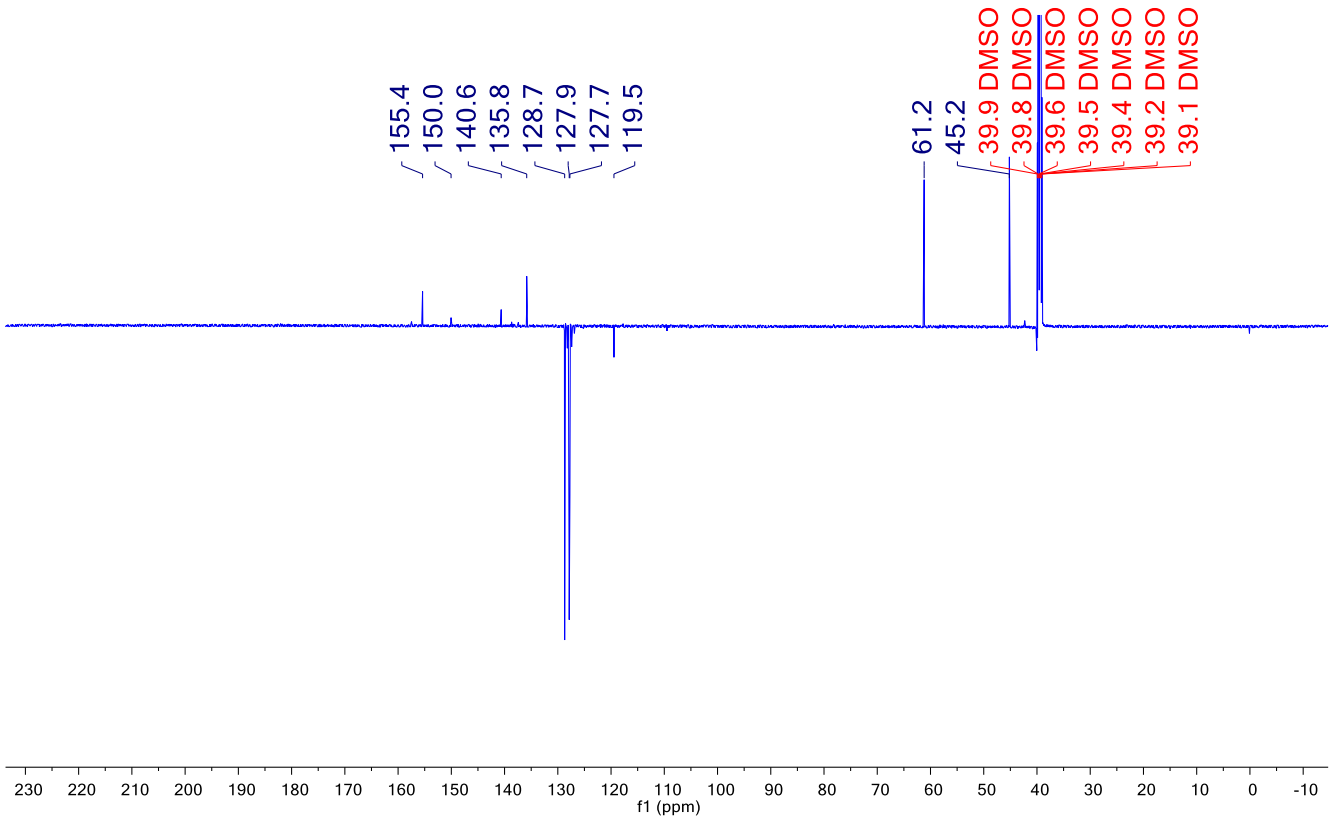
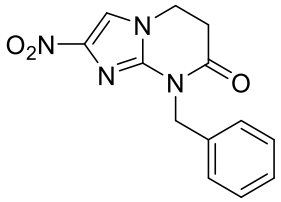
22	Acquired Size	32768
23	Spectral Size	65536



8-Benzyl-2-nitro-5,6-dihydroimidazo[1,2-*a*]pyrimidin-7(8*H*)-one (93)



^{1}H NMR (600 MHz, DMSO-d_6)

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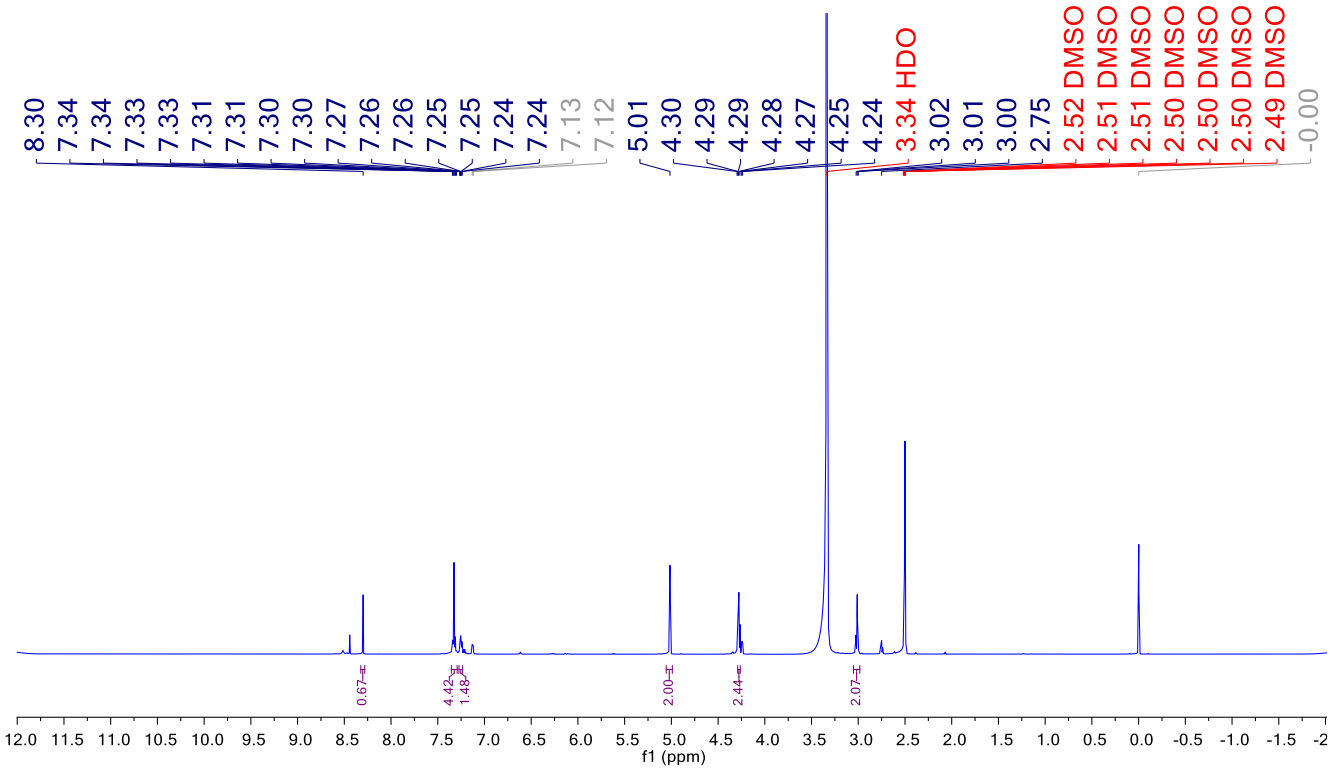
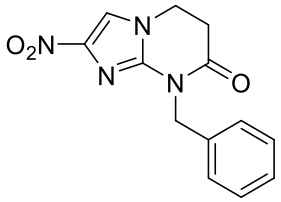
23	Spectral Size	65536



8-Benzyl-2-nitro-5,6-dihydroimidazo[1,2-*a*]pyrimidin-7(8*H*)-one (93)



^{13}C NMR (150 MHz, DMSO-d_6)

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6	Site	
7	Instrument	spect
8	Author	
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