

Supporting Information

Design, Synthesis, and Inhibitory Activity of Hydroquinone Ester Derivatives against Mushroom Tyrosinase

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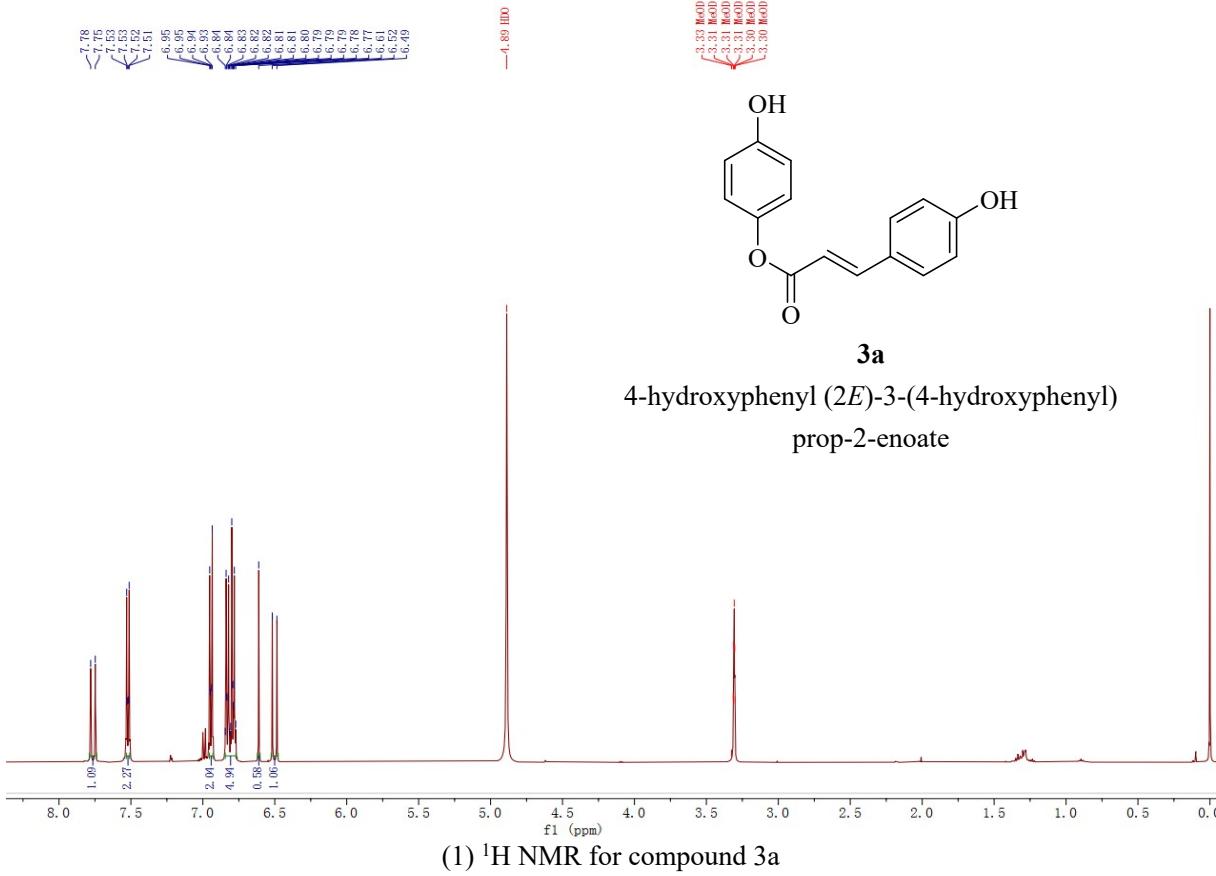
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Table S2. Docking energy and bonding condition of compounds 3a-3e with mTyr





—4.86 HDO

(3) ^1H NMR for compound 3b

XD-128.2gfid
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(4) ^{13}C NMR for compound 3b

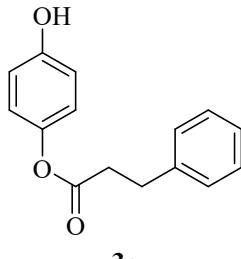
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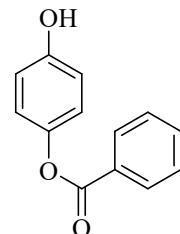
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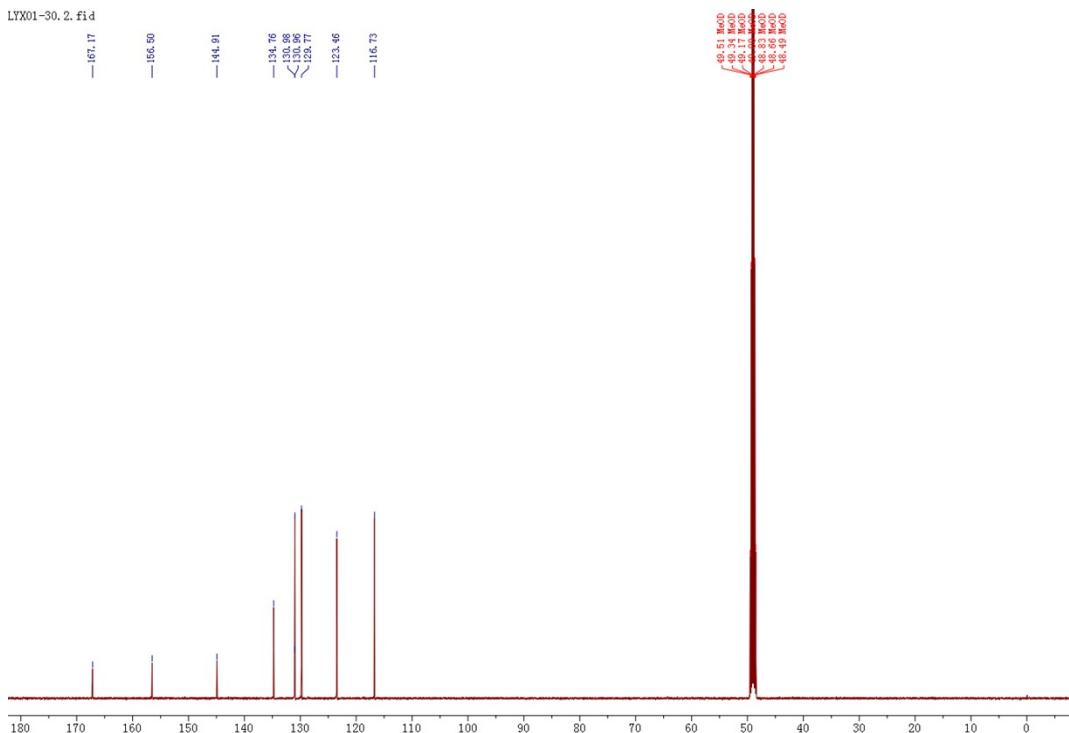
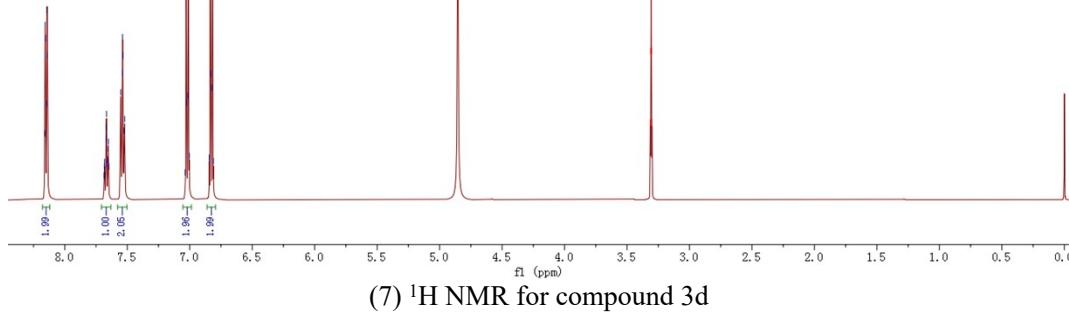
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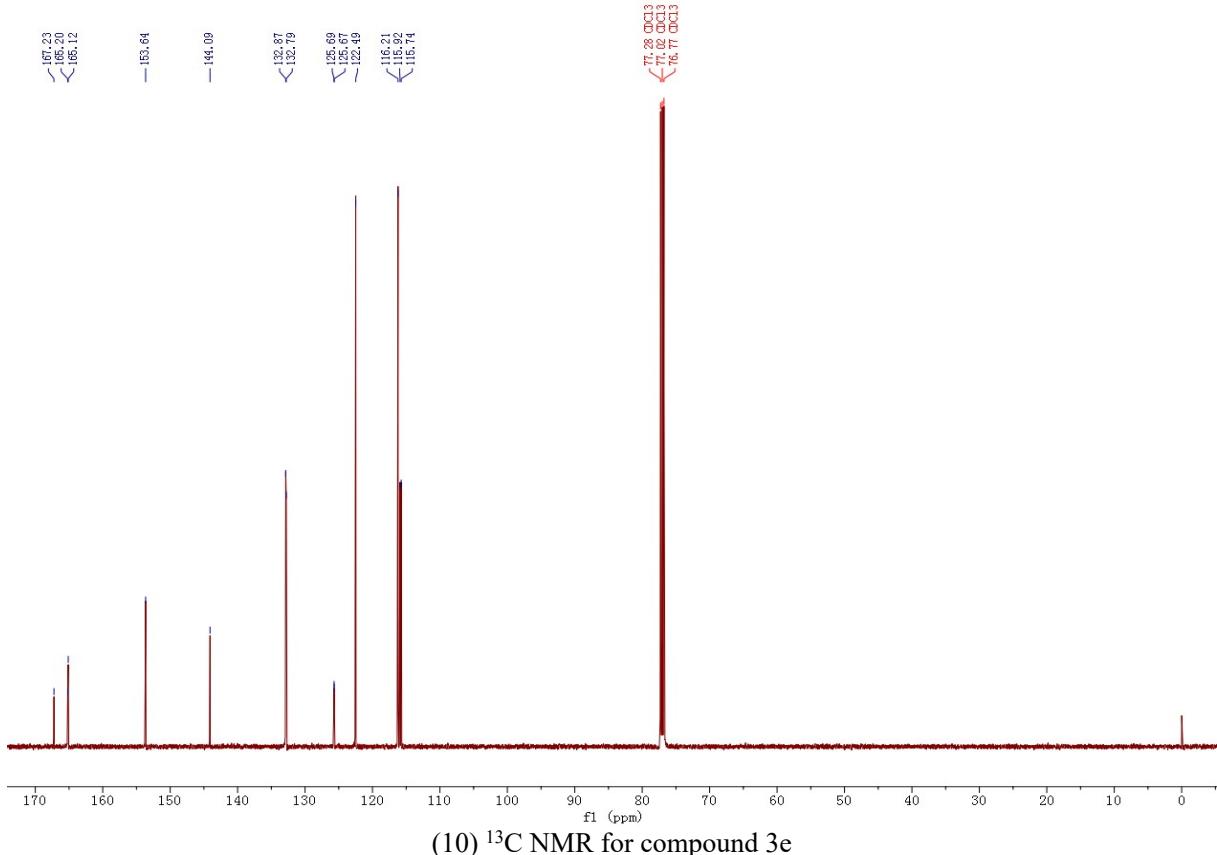
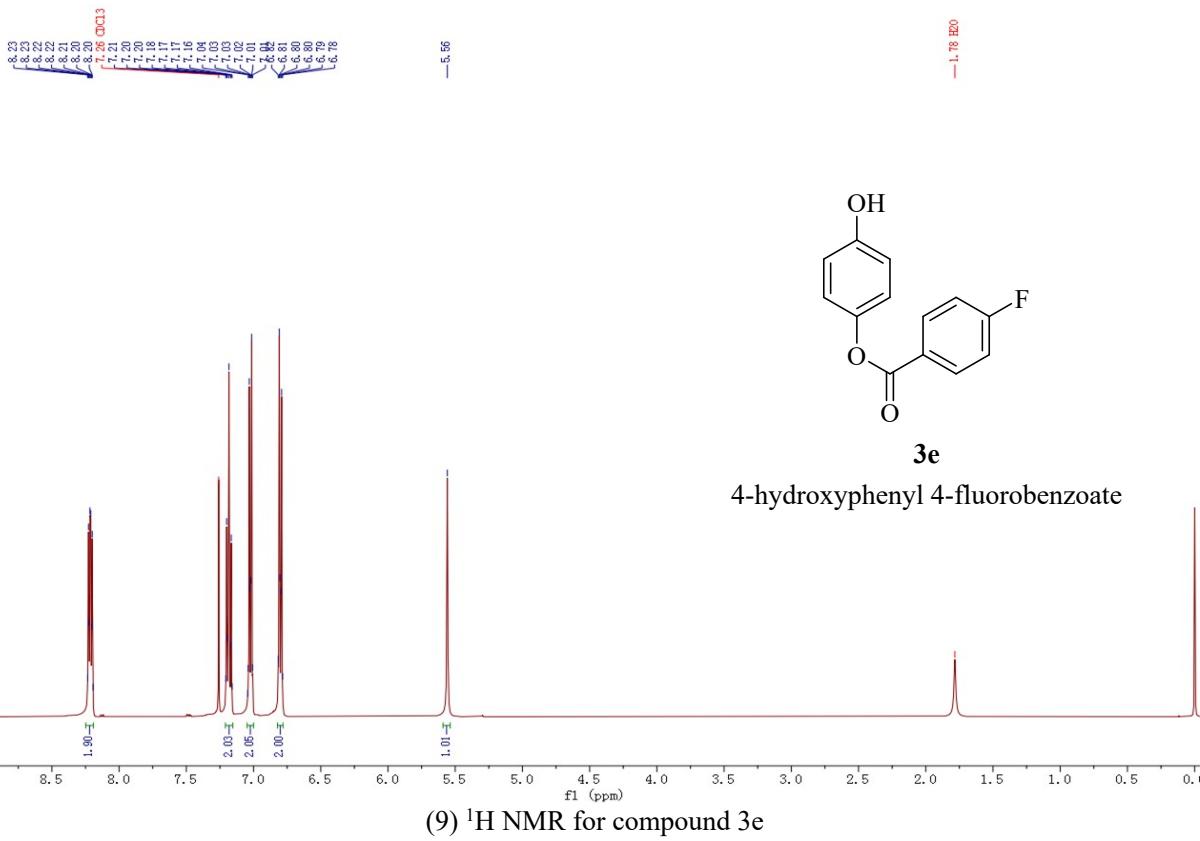


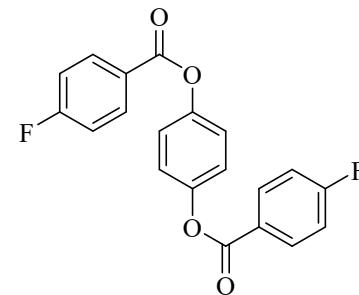


4-hydroxyphenyl benzoate

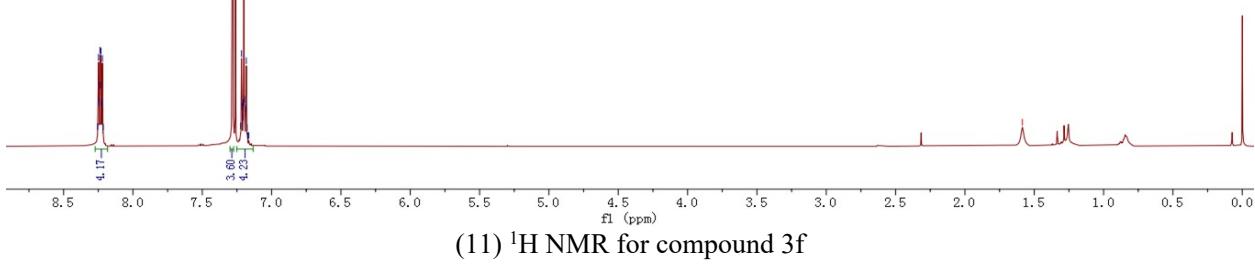


(8) ^{13}C NMR for compound 3d





1,4-phenylene bis(4-fluorobenzoate)



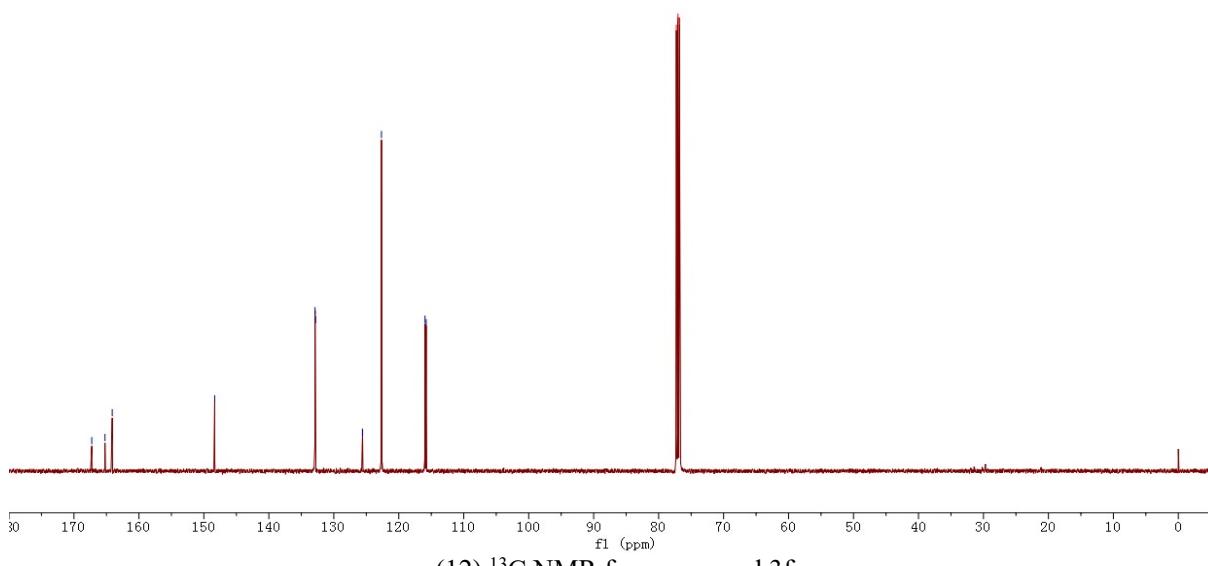
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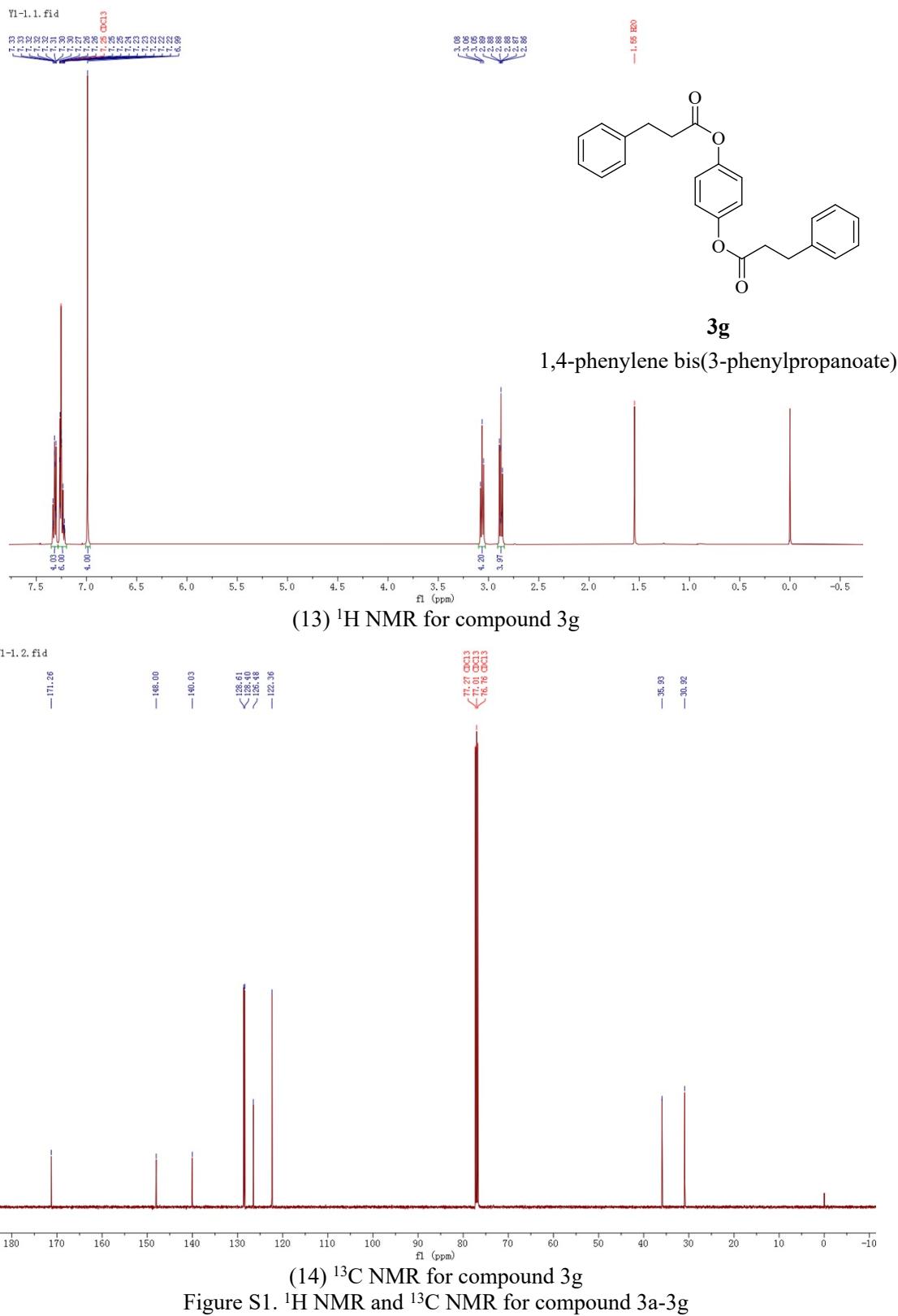
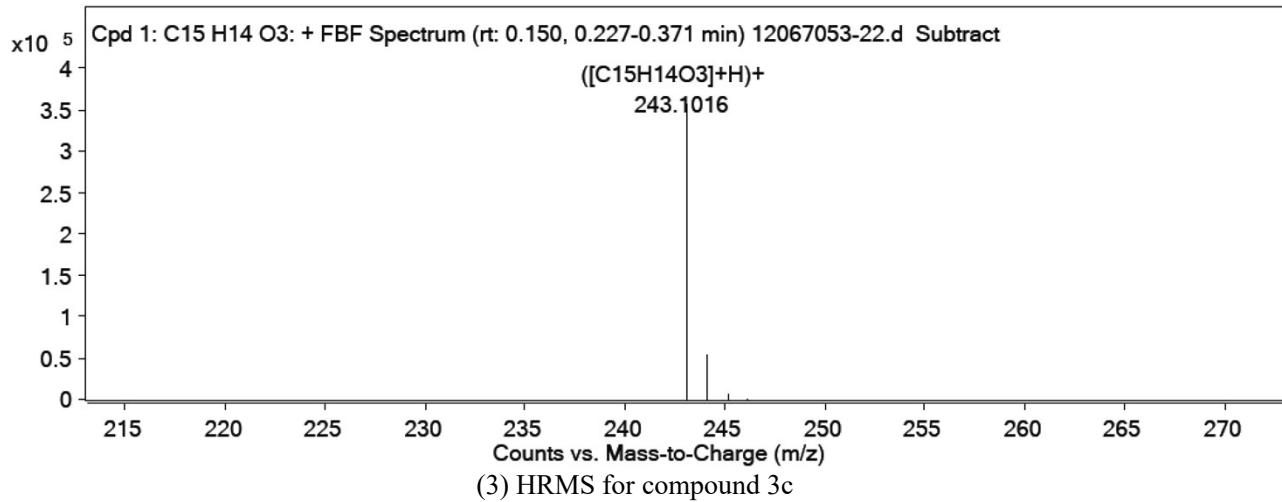
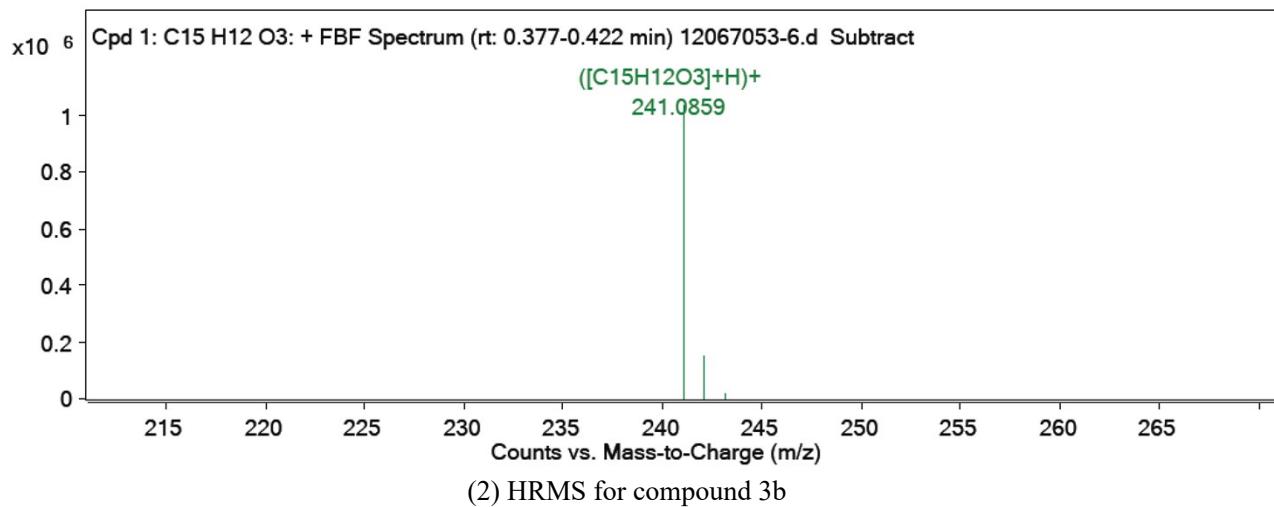
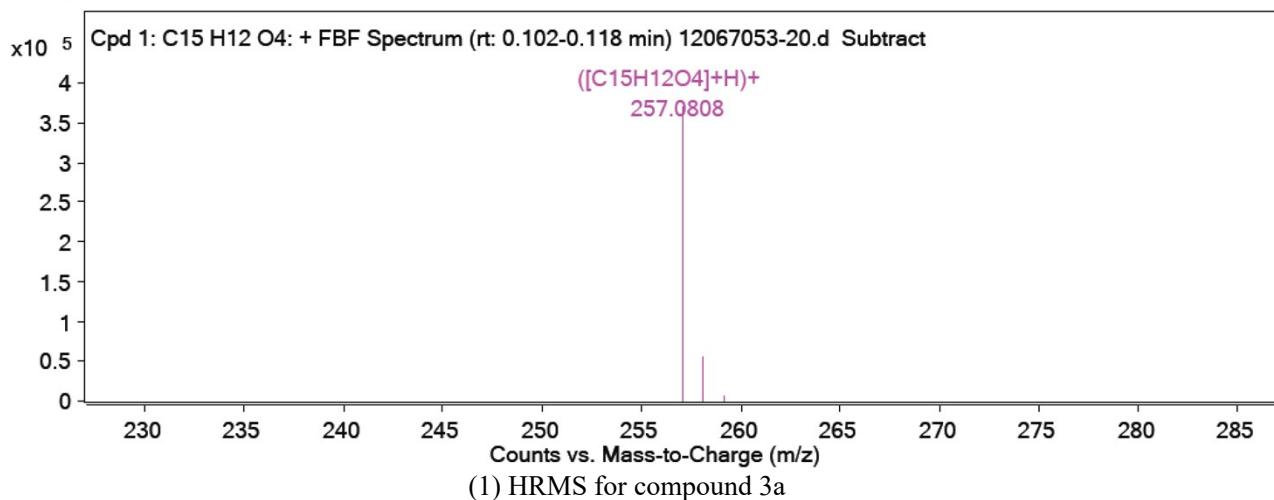
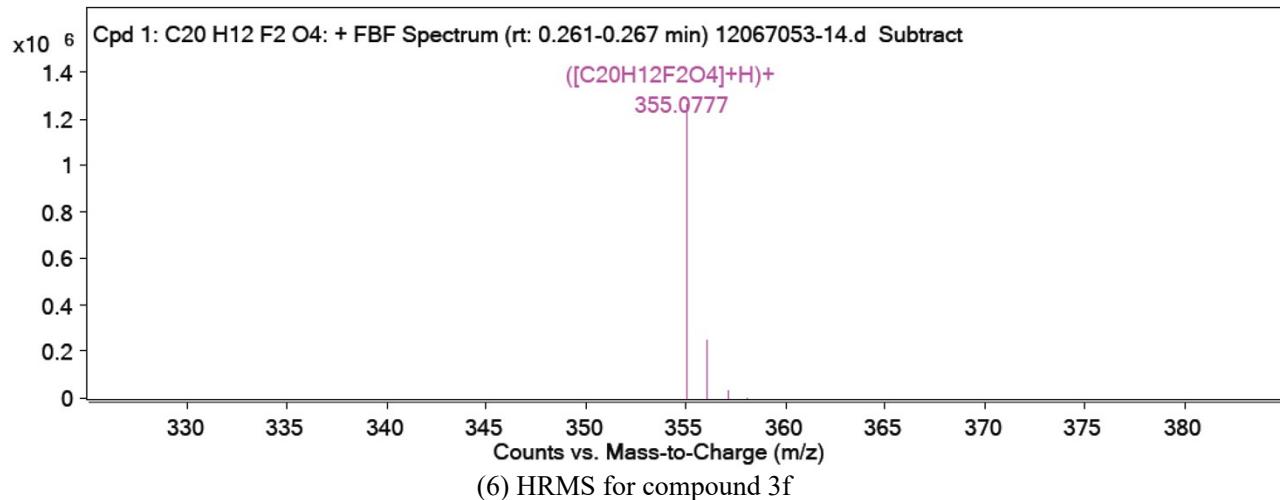
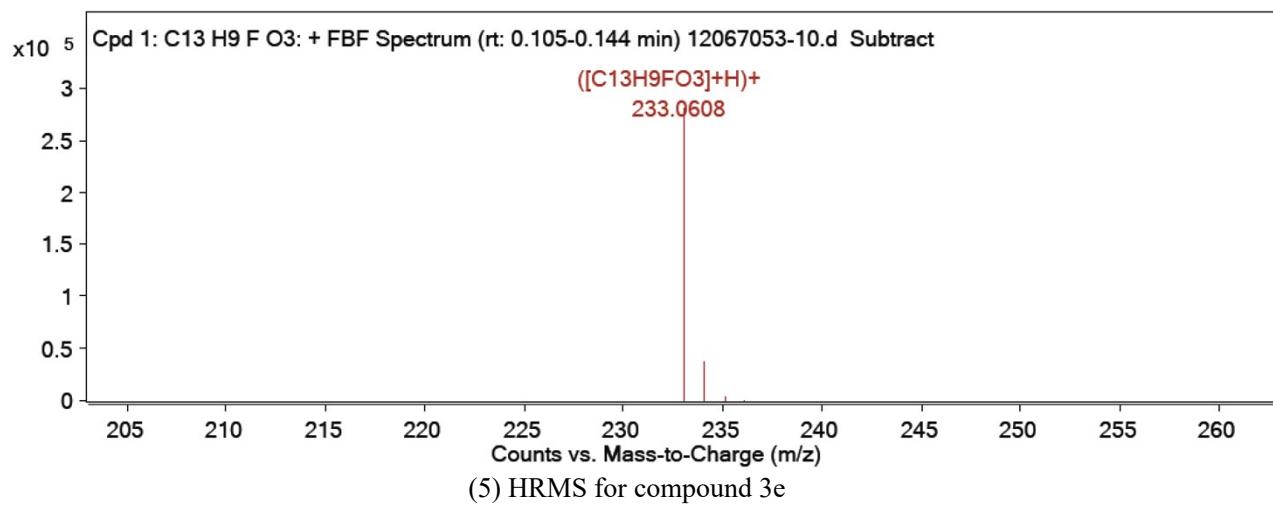
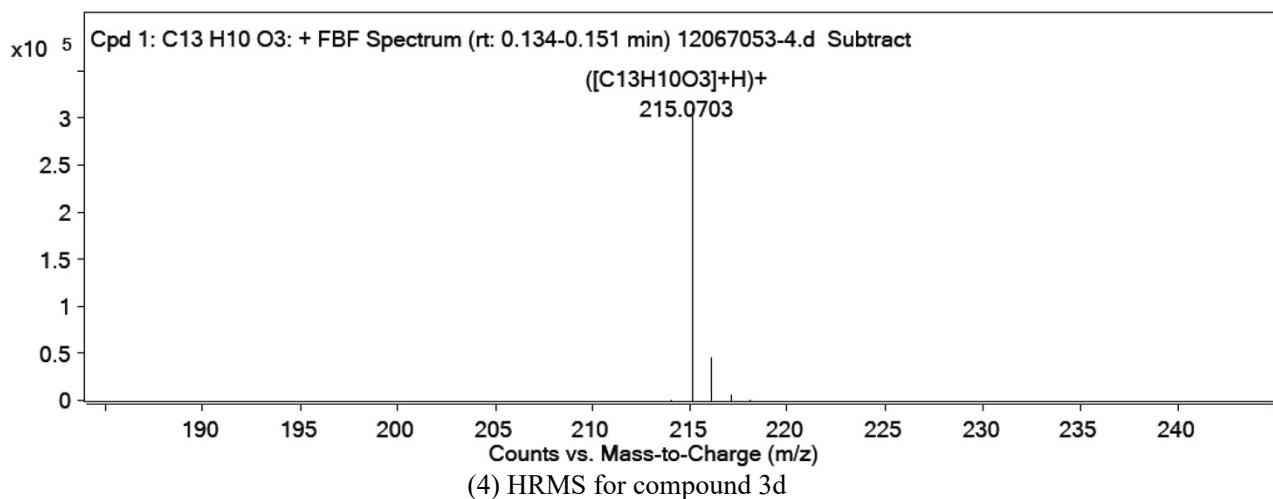


Figure S1. ^1H NMR and ^{13}C NMR for compound 3a-3g





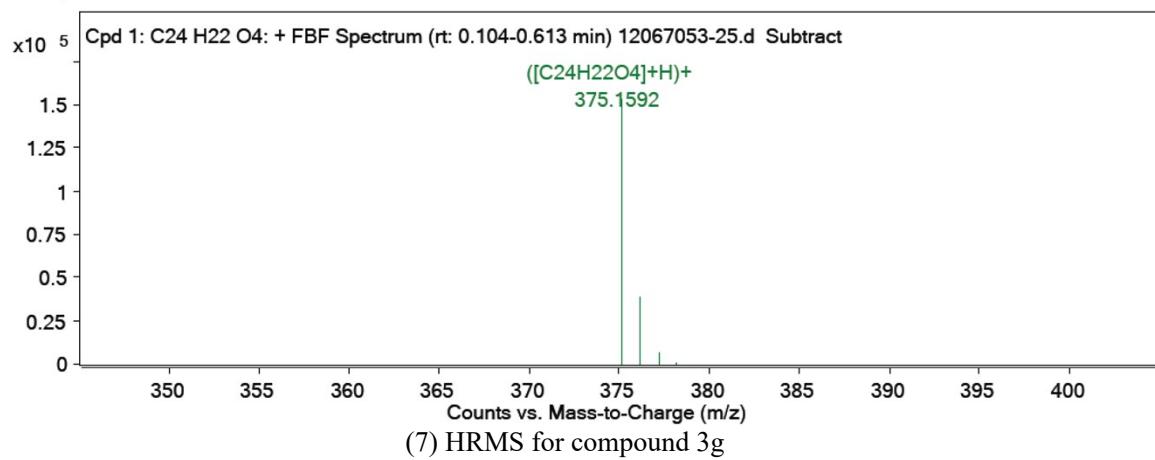
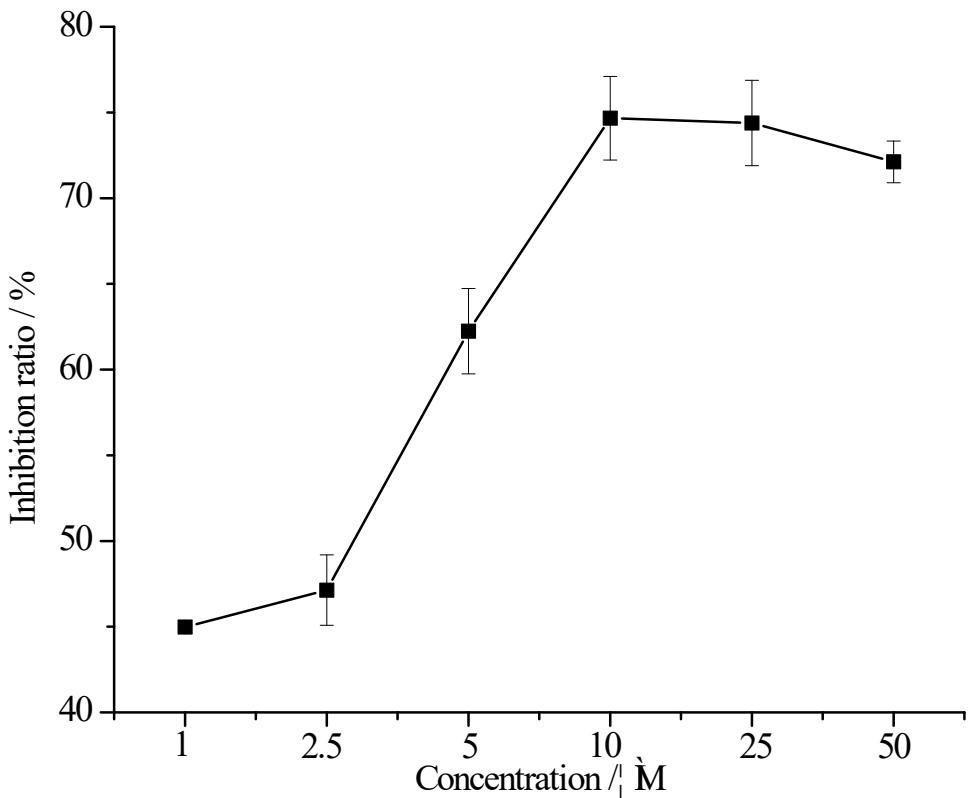
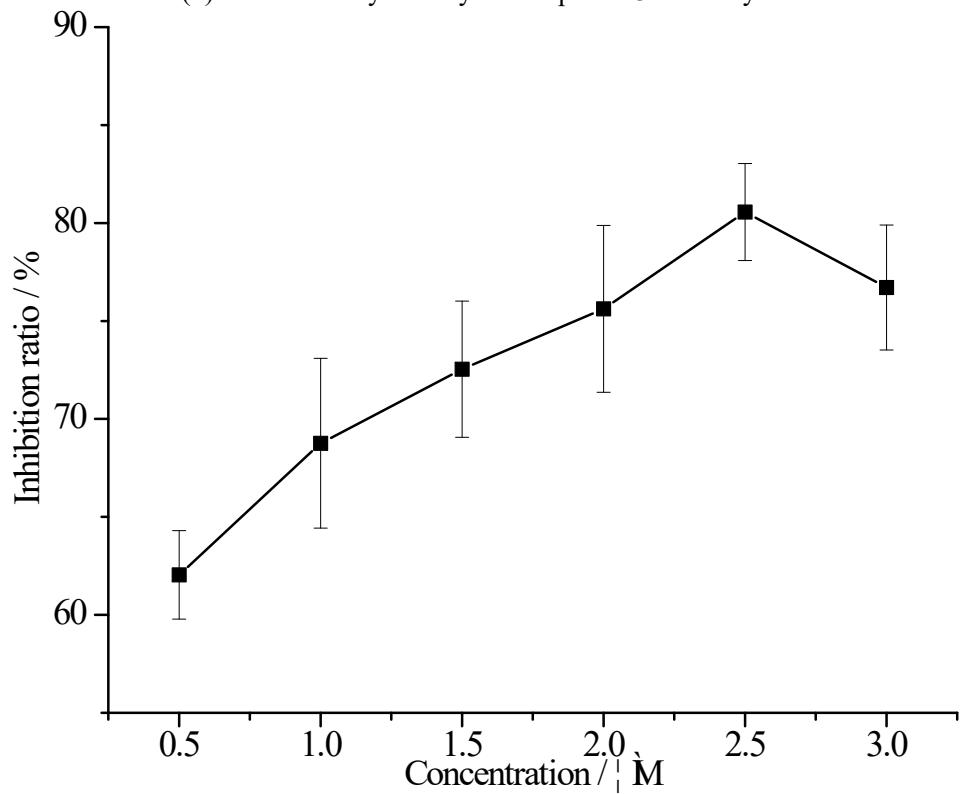


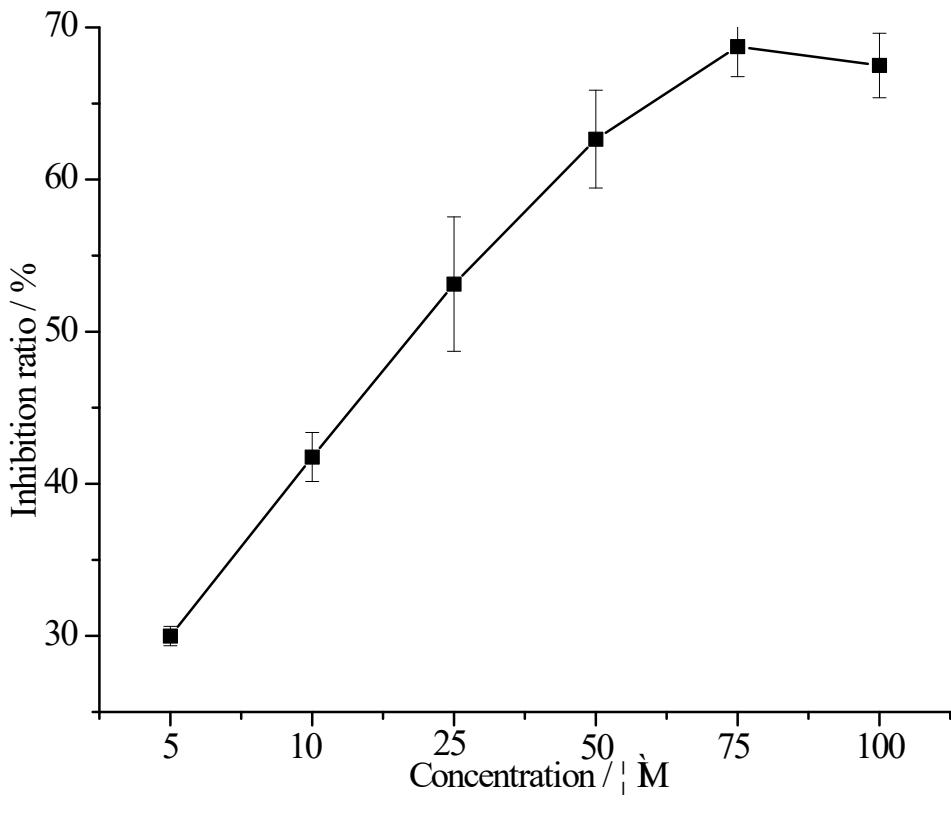
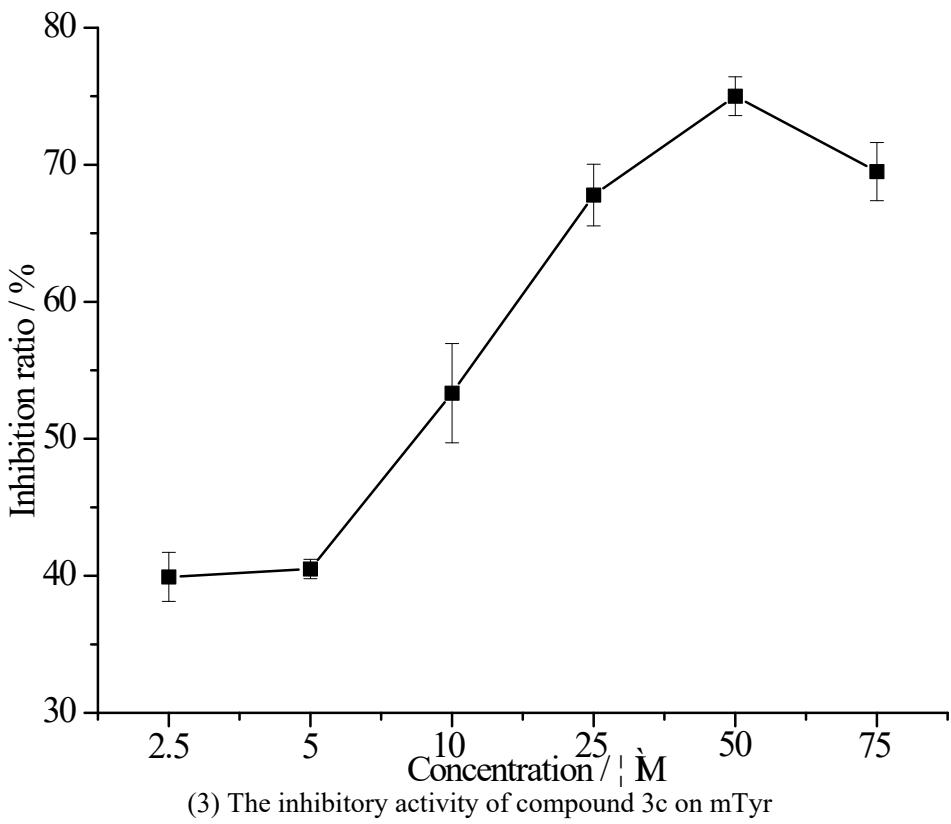
Figure S2. HRMS for compounds 3a-3g

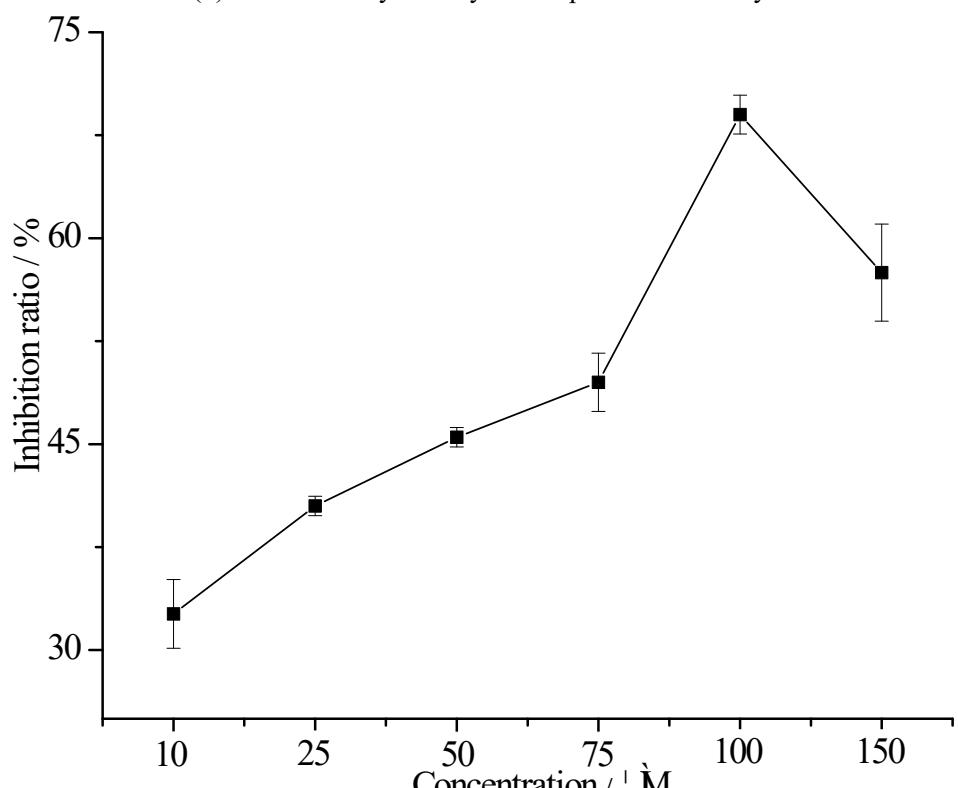
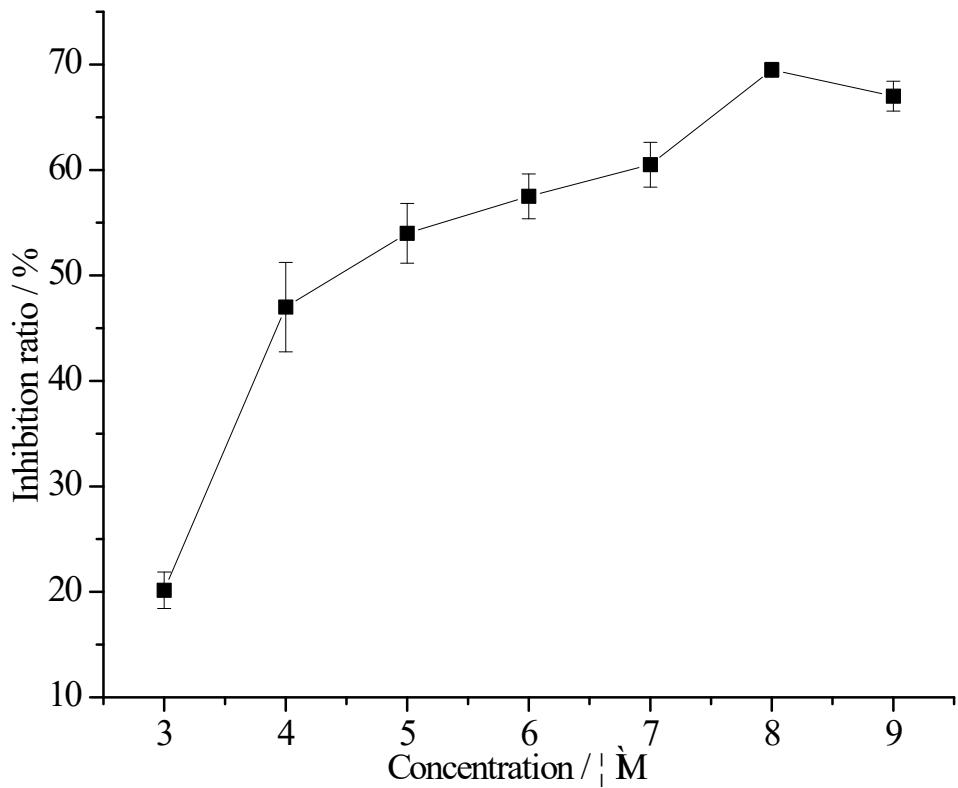


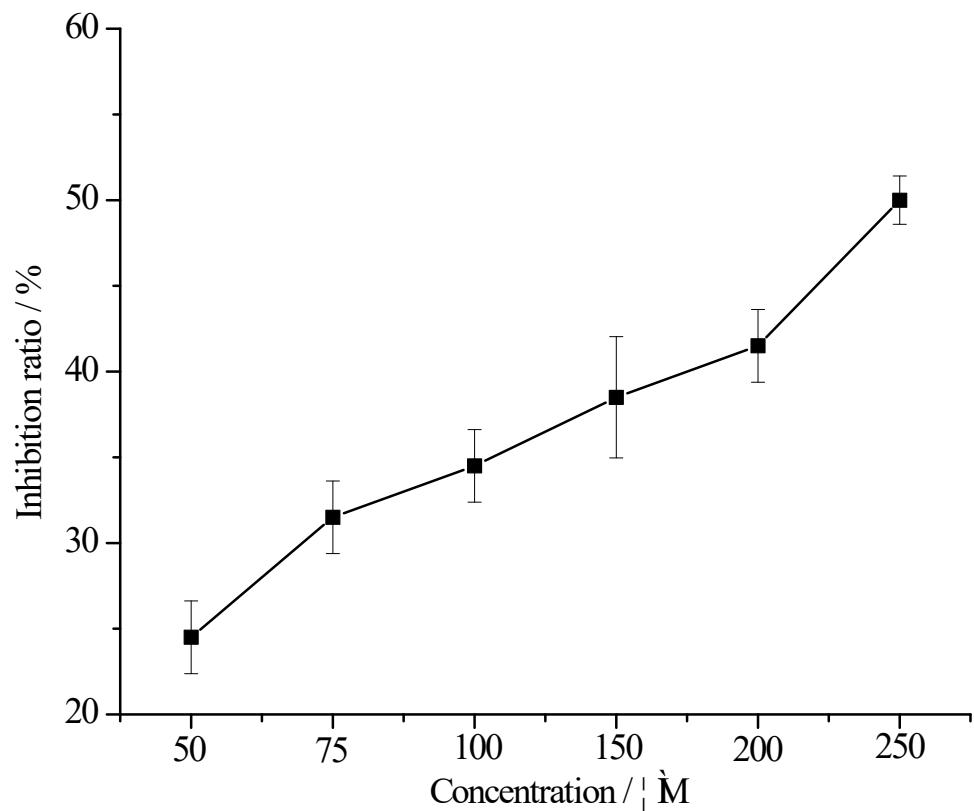
(1) The inhibitory activity of compound 3a on mTyr



(2) The inhibitory activity of compound 3b on mTyr

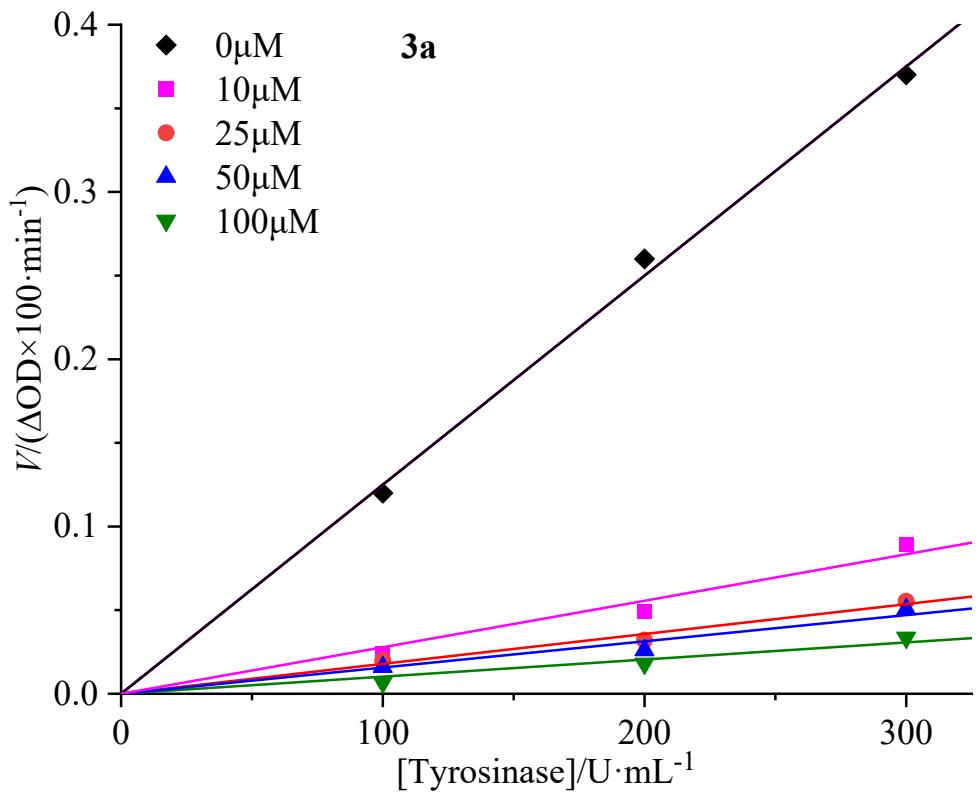




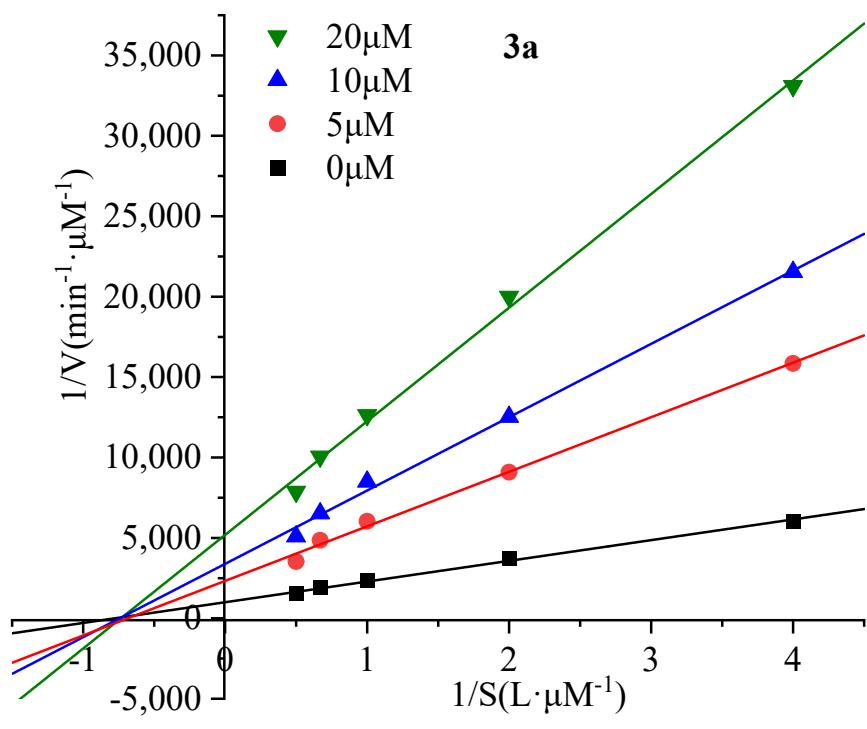


(7) The inhibitory activity of compound 3g on mTyr

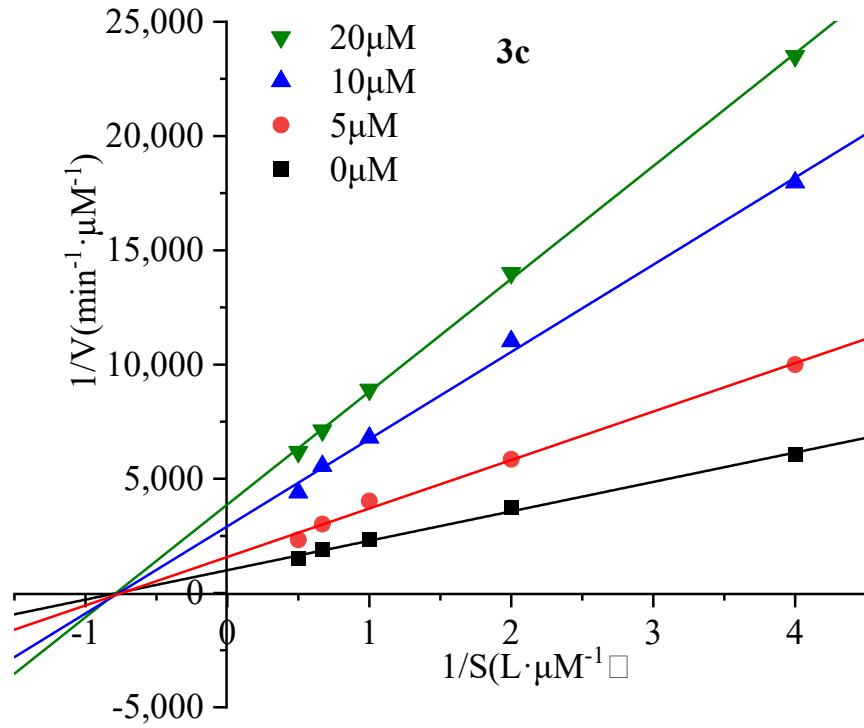
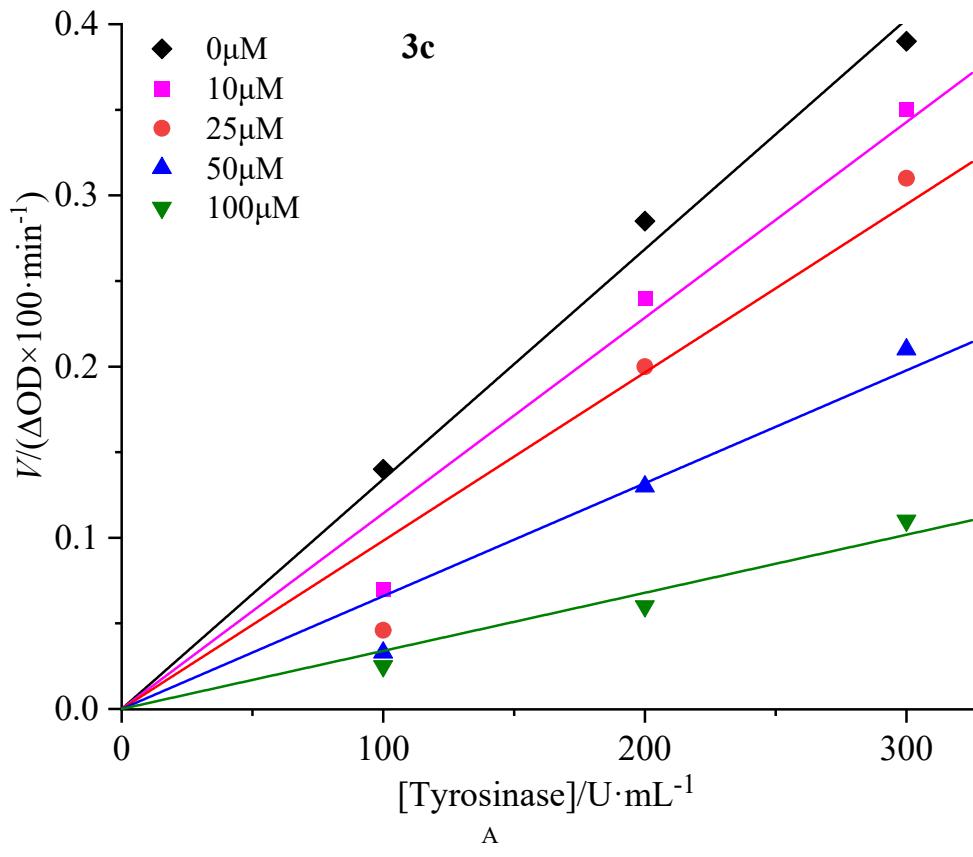
Figure S3. The inhibitory activity of compounds 3a-3g on mTyr

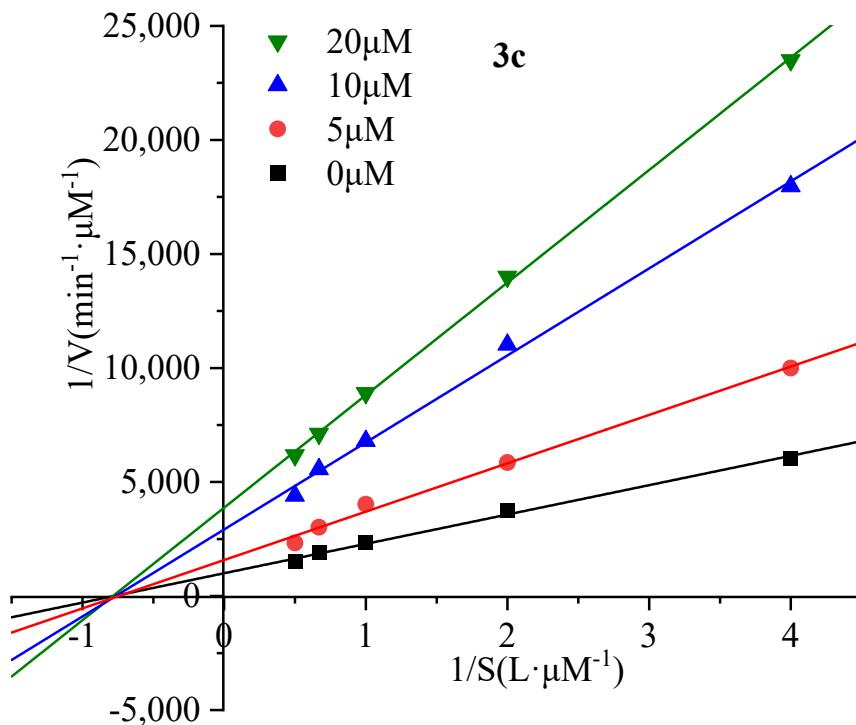


A

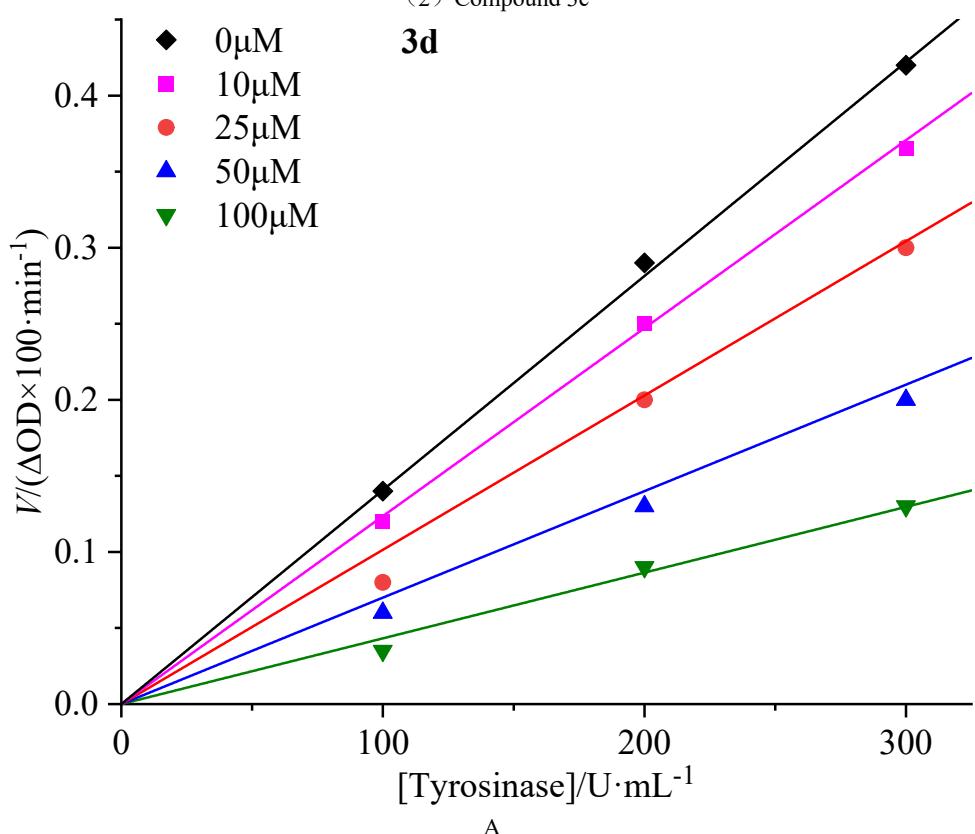


(1) Compound 3a

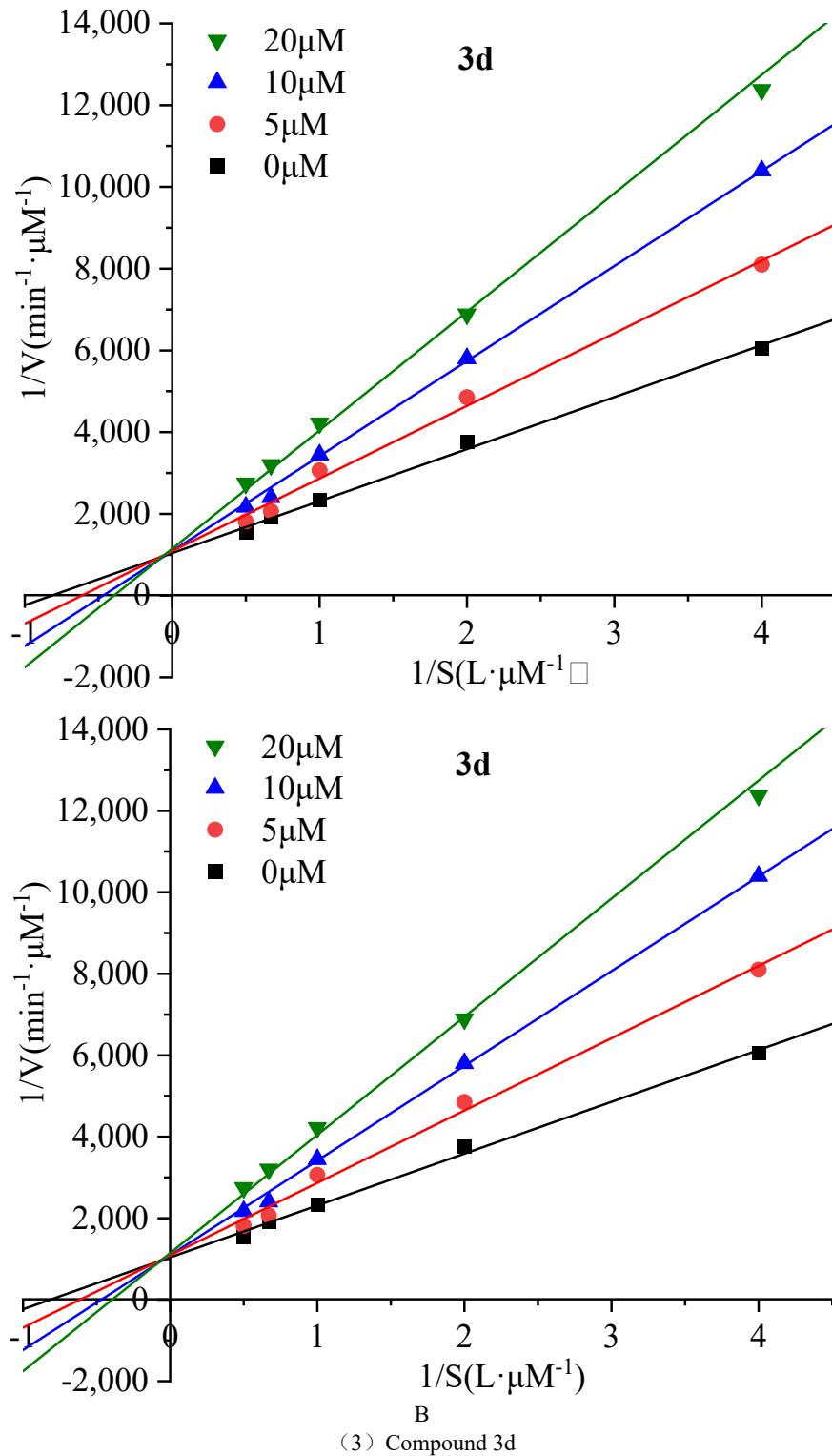


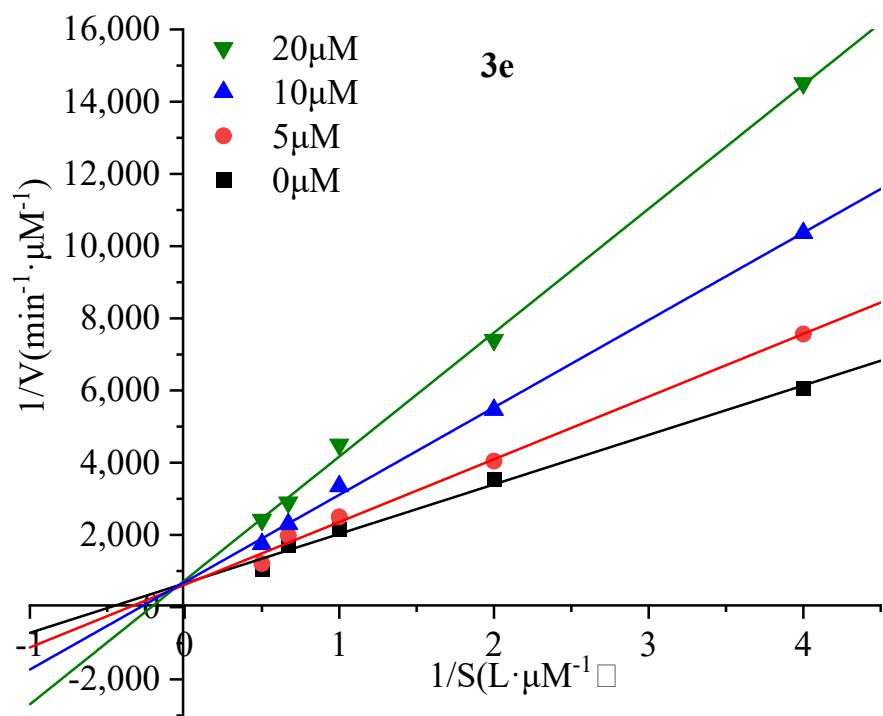
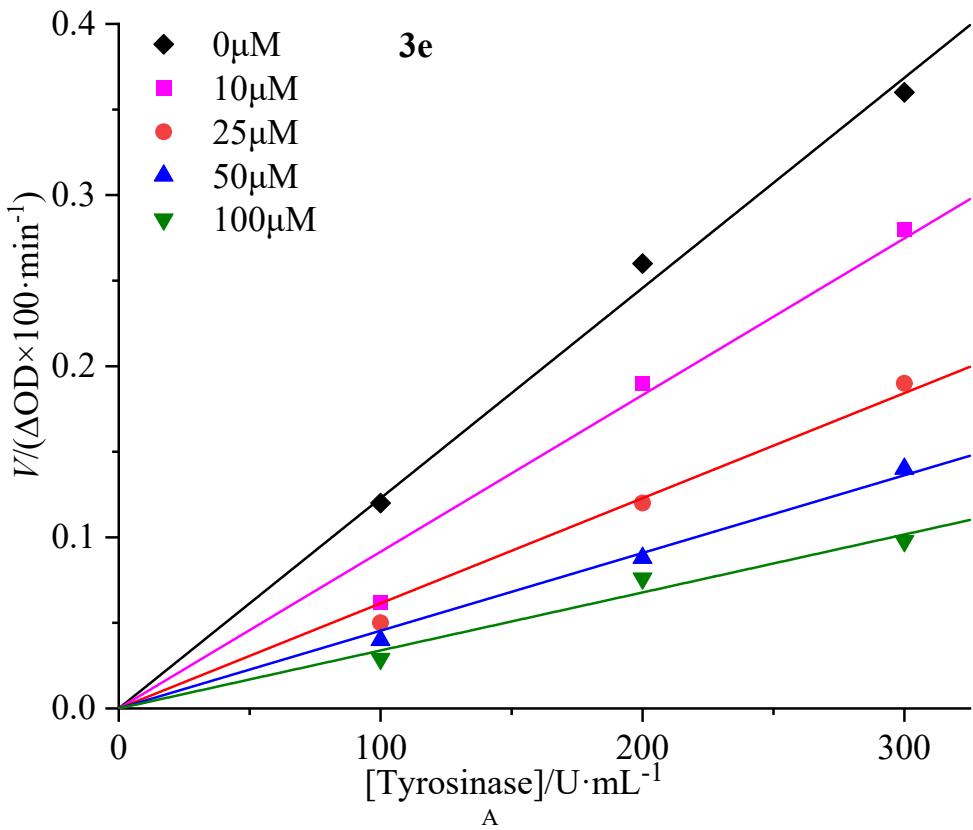


B
(2) Compound 3c



A





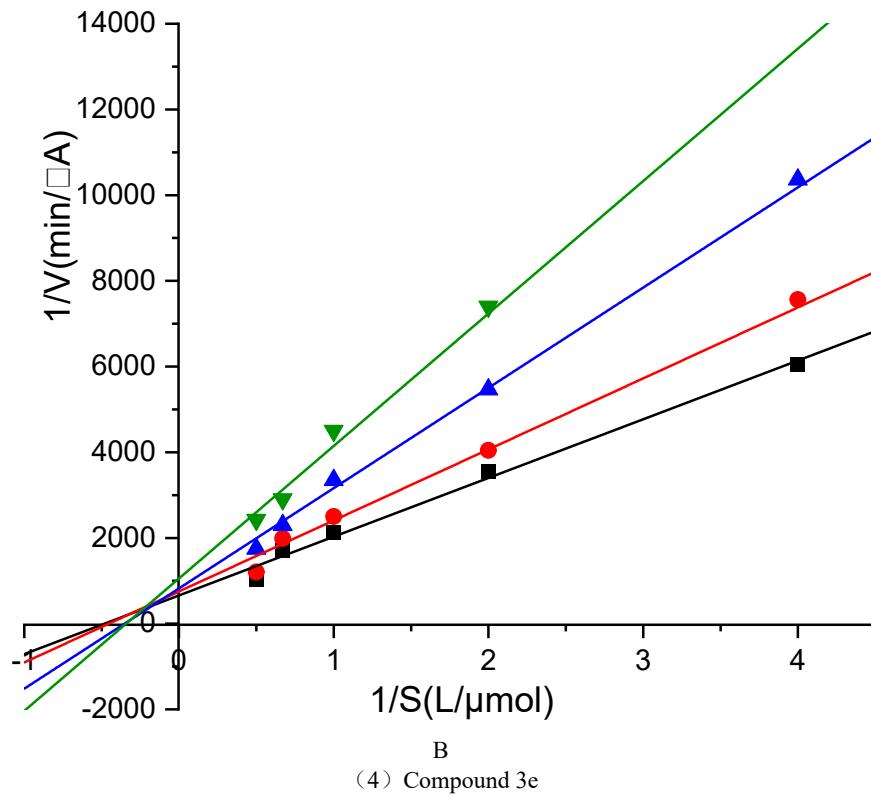
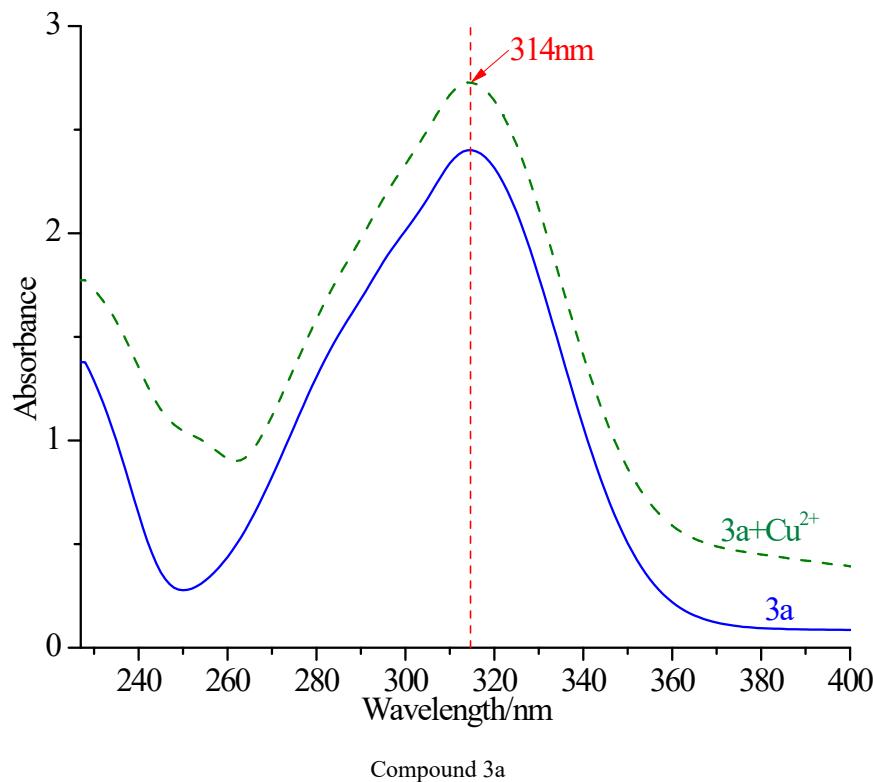
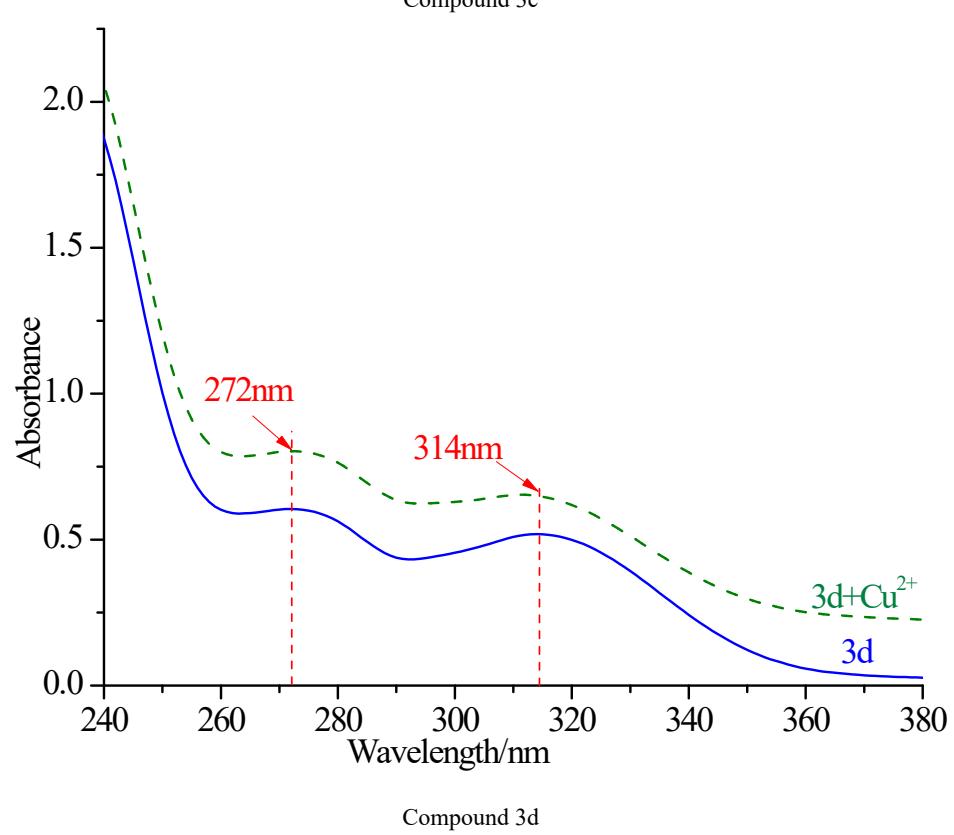
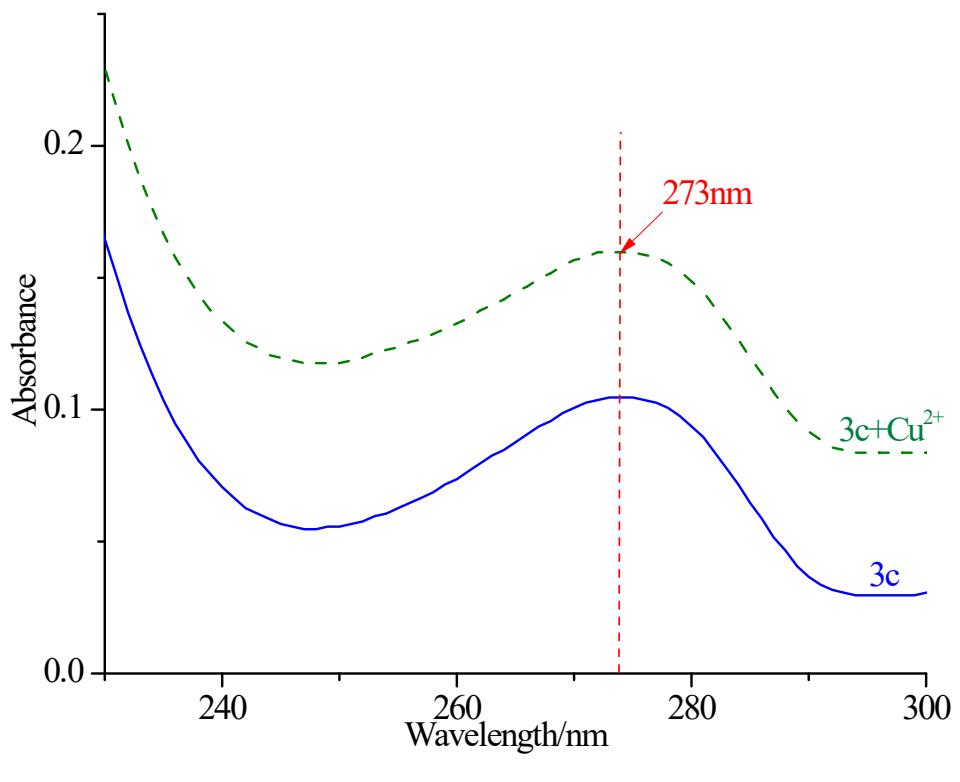
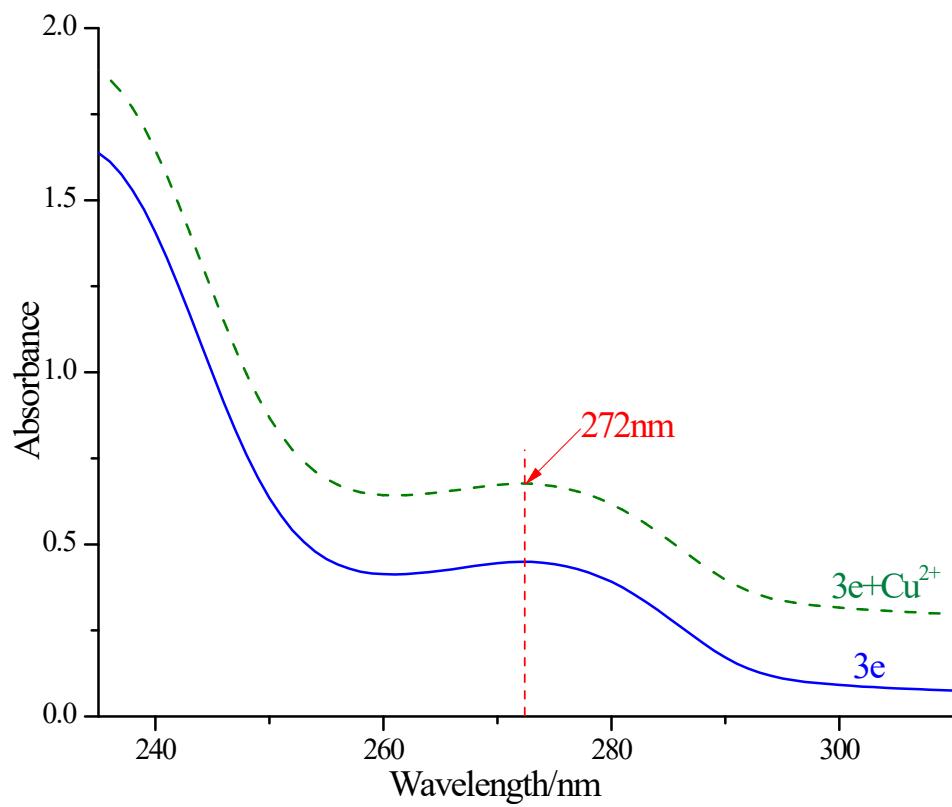


Figure S4 Inhibition reversibility (A) and inhibition type (B) of compound 3a, 3c-3e on mTyr.







Compound 3e
Figure S5. UV Spectra of compound 3a, 3c-3e before and after interaction with mTyr

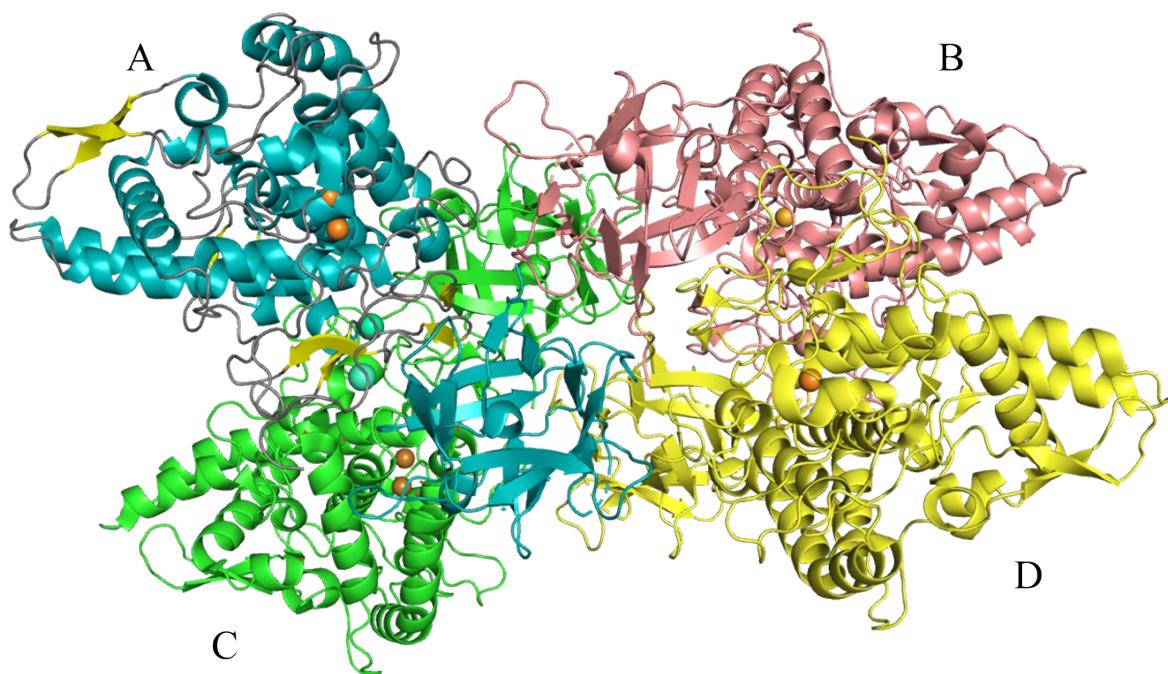
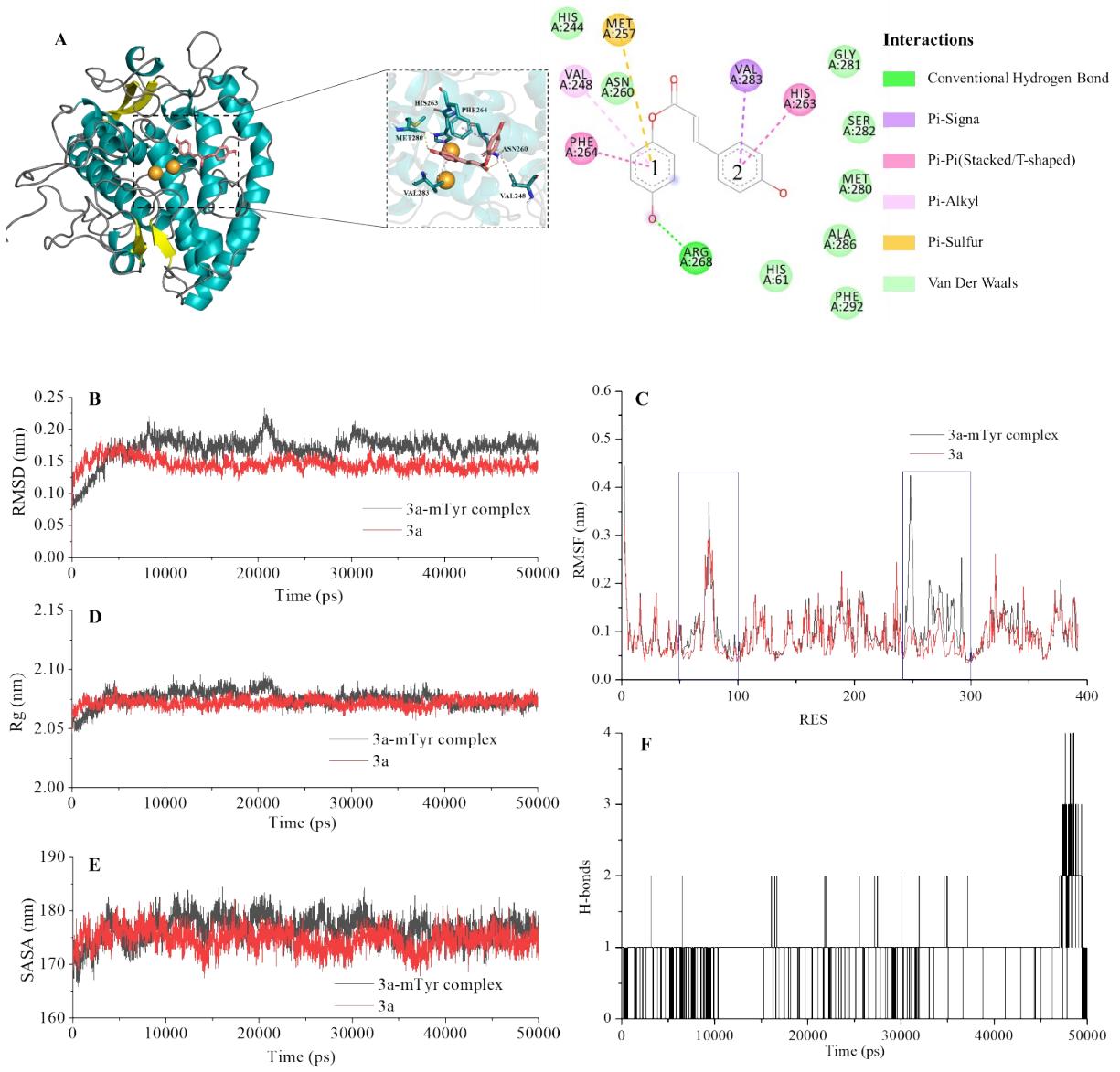
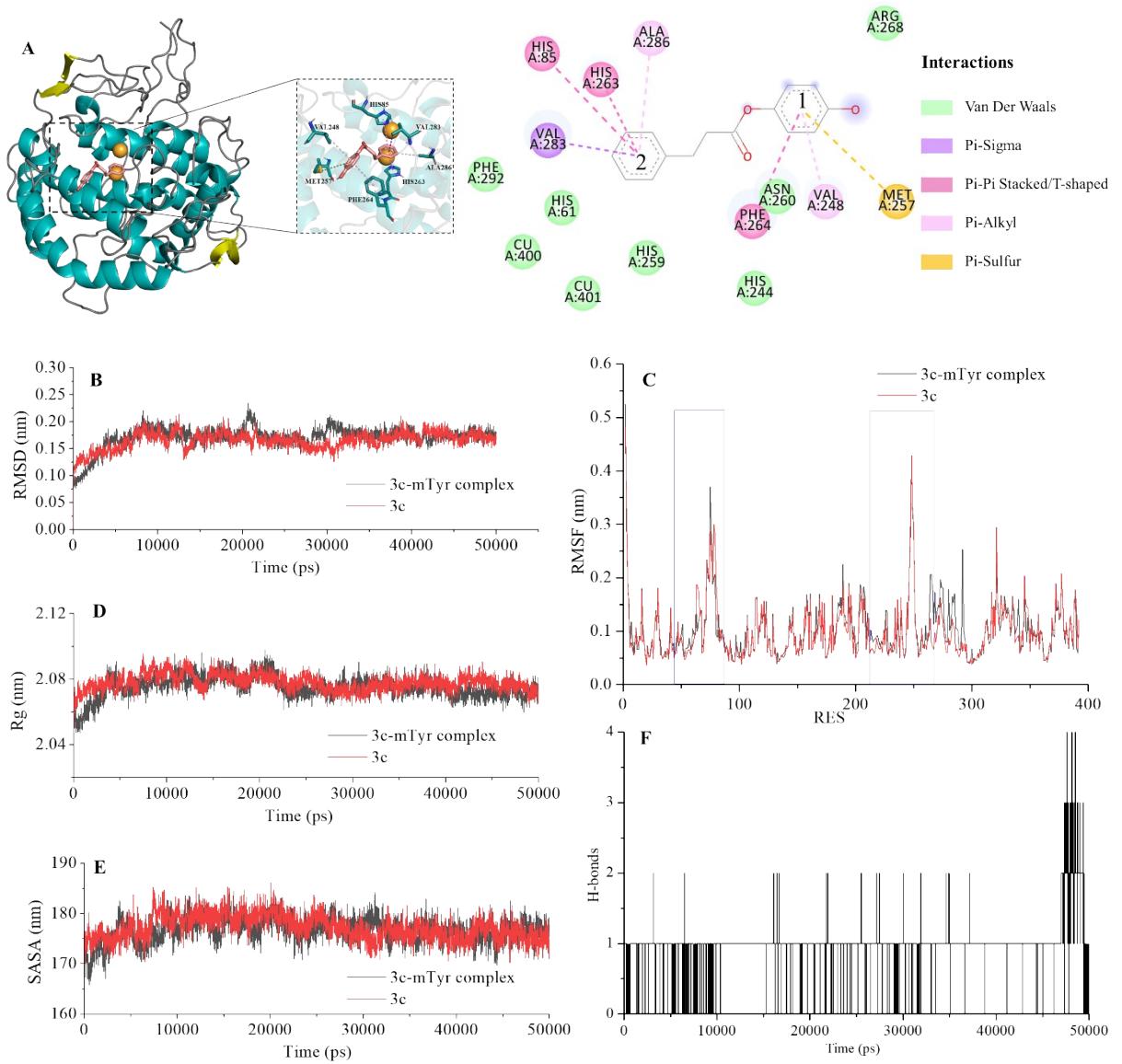


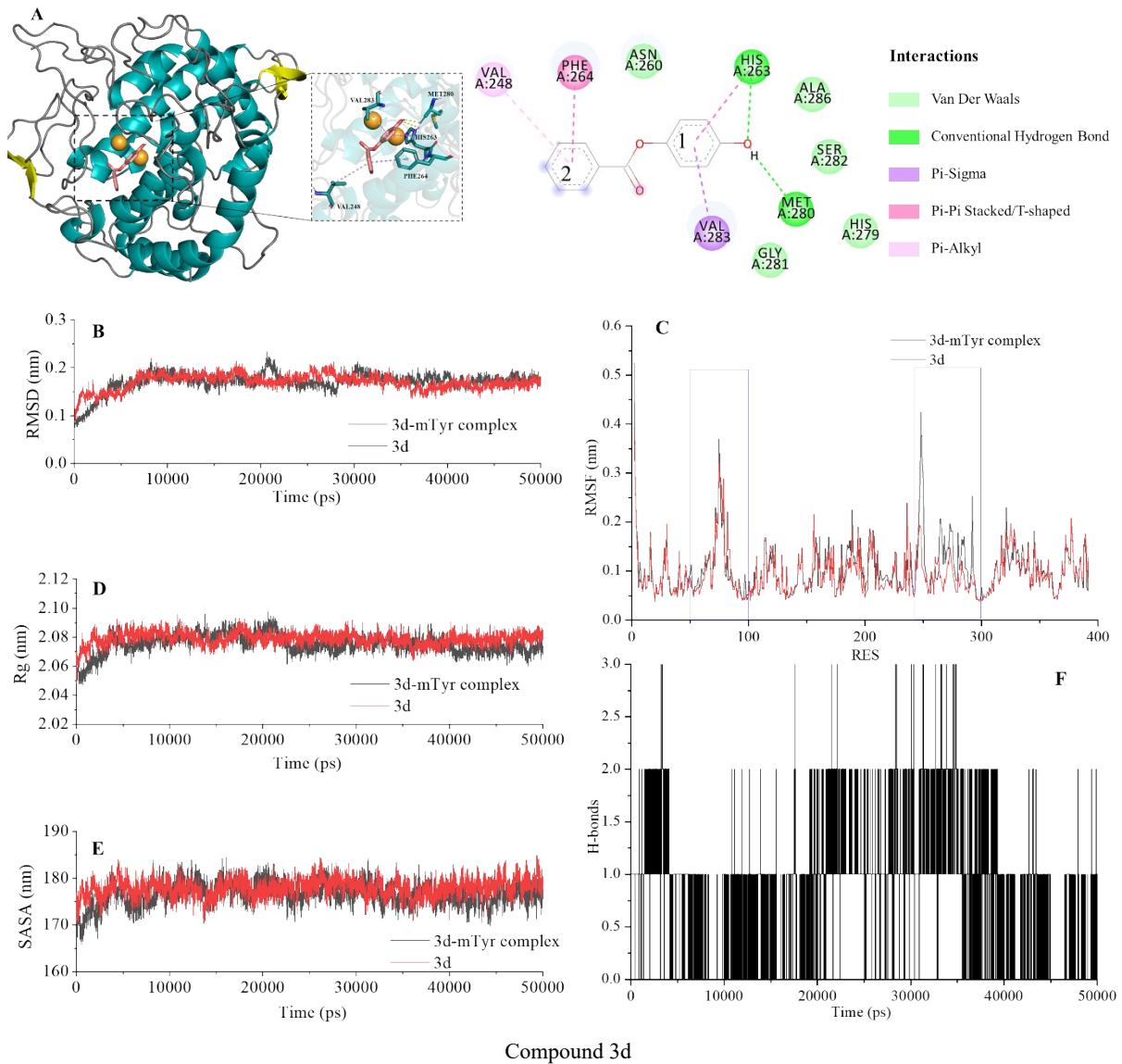
Figure S6. The crystal structure of mTyr (PDB ID: 2Y9X)

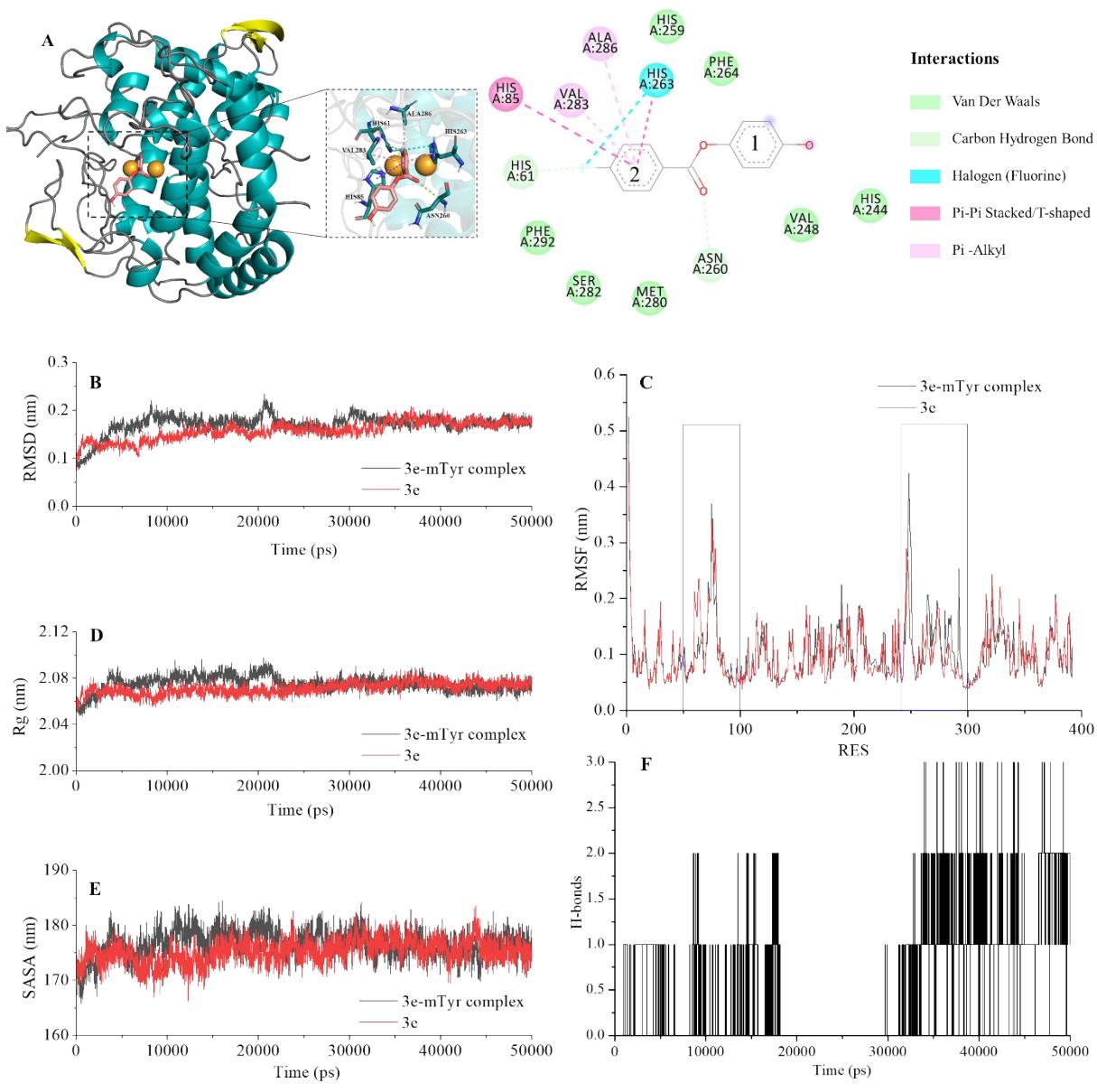


Compound 3a



Compound 3c





Compound 3e

Figure S7. Docking model for compound 3a, 3c-3e with mTyr (A) and Molecular dynamics results of compound 3a, 3c-3e and (3a, 3c-3e)-mTyr complex with: B. RMSD, C. RMSF, D. Rg, E. SASA, and F. H-bonds

Table S1. Linear fitting equation, Michaelis constant (K_m), maximum reaction rate (V_m), and inhibition type for mTyr at varying concentrations of compounds 3a-3e

Compound	Concentration (μM)	Linear fitting equation	R^2	K_m (μM)	V_m ($\times 10^3, \text{min}^{-1}$)	Inhibition type
3a	0	$Y=1000.25+1287.41X$	0.9991	1.2871	0.9998	Noncompetitive
	5	$Y=2340.91+3012.40X$	0.9958	1.2870	0.4272	
	10	$Y=3516.19+4525.44X$	0.9963	1.2867	0.2843	
	20	$Y=5446.87+7064.94X$	0.9965	1.2869	0.1836	
3b	0	$Y=333.72+1645.85X$	0.9902	4.9318	2.9965	Mix-noncompetitive
	1	$Y=1320.62+2456.41X$	0.9949	2.6173	0.7572	
	2	$Y=2889.49+3833.45X$	0.9964	1.3267	0.3461	
	4	$Y=4662.26+5183.79X$	0.9982	1.1119	0.2145	
3c	0	$Y=1000.25+1287.41X$	0.9991	1.2871	0.9998	Noncompetitive
	5	$Y=1580.45+2034.21X$	0.9990	1.2870	0.6327	
	10	$Y=2920.18+3759.70X$	0.9991	1.2873	0.3424	
	20	$Y=3875.12+4950.54X$	0.9999	1.2774	0.2581	
3d	0	$Y=1084.97+1272.89X$	0.9961	1.1732	0.9217	Competitive
	5	$Y=1085.12+1776.46X$	0.9985	1.6371	0.9216	
	10	$Y=1086.06+2324.89X$	0.9996	2.1407	0.9208	
	20	$Y=1085.95+2900.15X$	0.9967	2.6706	0.9209	
3e	0	$Y=679.35+1370.31X$	0.9904	2.0171	1.472	Competitive
	5	$Y=678.55+1736.97X$	0.9943	2.5598	1.474	
	10	$Y=680.49+2419.72X$	0.9983	3.5558	1.470	
	20	$Y=681.12+3431.14X$	0.9983	5.0375	1.468	

Table S2 Docking energy and bonding condition of compounds 3a-3e with mTyr

Compounds	Docking energy (kcal·mol ⁻¹)	Bonding condition			
		Hydrogen Bonds	Hydrophobic	Miscellaneous (Pi-Sulfur)	Halogen (Fluorine)
3a	-7.6	Ph1O←Arg 268 (6.66 Å, Conventional Hydrogen Bond) Ph1OH←Met280(5.01 Å, Conventional Hydrogen Bond)	Ph1←Phe264 (6.68 Å, Pi-Pi Stacked/T-shaped); Ph1←Val248 (5.16 Å, Pi-Alkyl); Ph2←His263 (5.57 Å, Pi-Pi Stacked/T-shaped); Ph2←Val283 (5.11 Å, Pi-Sigma).	Ph1←Met257 (6.50 Å)	
3b	-7.2		Ph1←His263 (5.32 Å, Pi-Pi Stacked); Ph1←Val283 (4.89 Å, Pi-Sigma); Ph2←Val248 (5.31 Å, Pi-Sigma).	Ph2←Met257 (6.57 Å)	
3c	-6.7		Ph1←Val248 (5.57 Å, Pi-Alkyl); Ph1←Phe264 (6.74 Å, Pi-Pi Stacked/T-shaped); Ph2←Val283 (4.26 Å, Pi-Sigma); Ph2←His85/His263 (5.47/5.48 Å, Pi-Pi Stacked/T-shaped); Ph2←Ala 286 (6.53 Å, Pi-Alkyl).	Ph1←Met257(7.58 Å)	
3d	-7.0	Ph1OH←Met280(4.88 Å, Conventional Hydroge n Bond; Ph1O←His 263 (4.06 Å, Conventional Hydrogen Bond)	Ph1←His 263 (5.52 Å, Pi-Pi Stacked/T-shaped); Ph1←Val283 (4.82 Å, Pi-Sigma); Ph2←Val248 (6.29 Å, Pi-Alkyl); Ph2←Phe264 (6.62 Å, Pi-Pi Stacked/T-shaped).		
3e	-6.7	Ph2F←His6 1 (5.50 Å, Carbon Hydrogen Bond)	Ph2←Val283 (4.42 Å, Pi-Sigma); Ph2←Val283/Ala286 (4.63/6.95 Å, Pi-Alkyl); Ph2←His85/His263 (7.42/4.57 Å, Pi-Pi Stacked/T-shaped).	Ph2F←Hi s 263 (5.41 Å Halogen (Fluorine))	