pH Stability and Antioxidant Power of CycloDOPA and Its Derivatives

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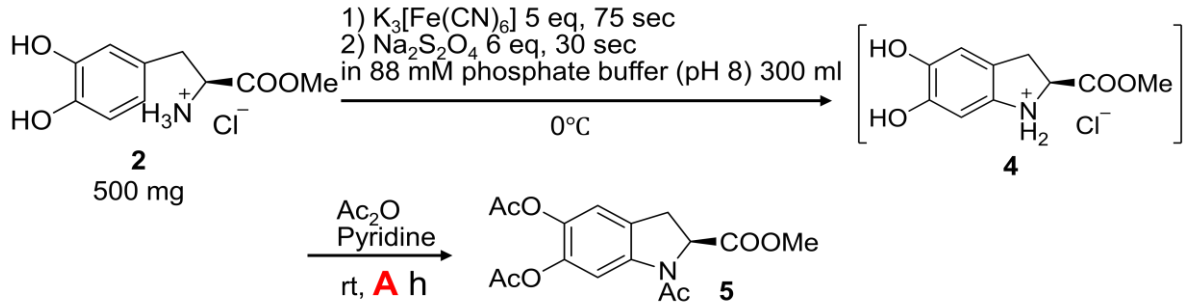
Supplementary Material

SM-1) Optimize the conditions to synthetsis of triacetyl-cycloDOPA-OMe (**5**)
SM-2) NMR data for synthetic compounds
SM-3) End-products analysis for decomposition of cycloDOPA (**8**) with ^{1}H-NMR
SM-4) Time course analysis for DPPH radical scavenge activity for cycloDOPA and its derivatives at pH 4 and 6.

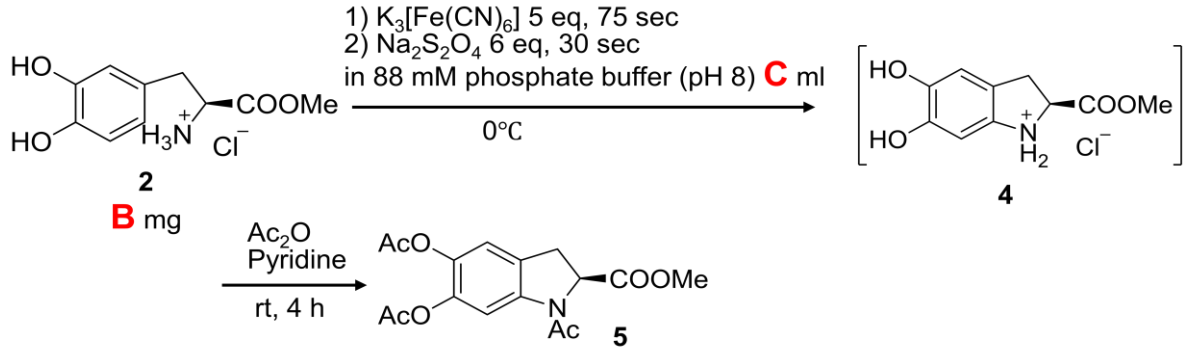
SM-1) Optimize the conditions to synthetsis of triacetyl-cycloDOPA-OMe **5**

1-1) Reaction time for acetylation



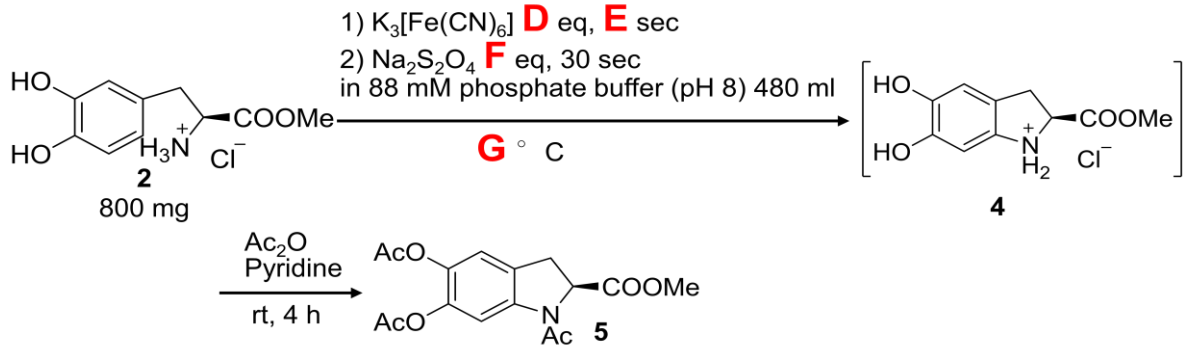
Entry	Reaction time A (h)	Yield of **5**
1	4	28
2	12	21

1-2) Reaction scale



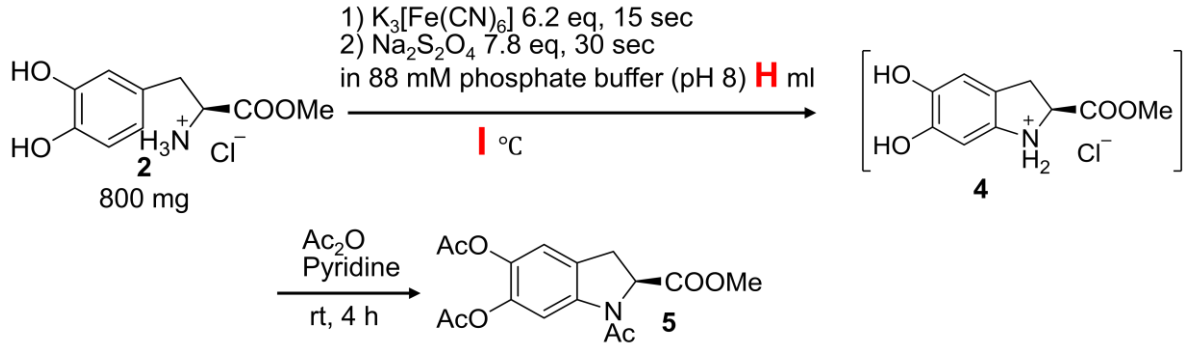
Entry	DOPA-OMe (2) B (mg)	Buffer volume C (ml)	Yield of **5**
1	500	300	28
2	800	480	34
3	1000	600	32
4	1500	900	8

1-3) Reaction time



Entry	$K_3[Fe(CN)_6]$ D (eq)	Time E (sec)	$Na_2S_2O_4$ F (eq)	Temp G (°C)	Yield of **5**
1	5	75	6	4	34
2	6.2	15	7.8	rt	41

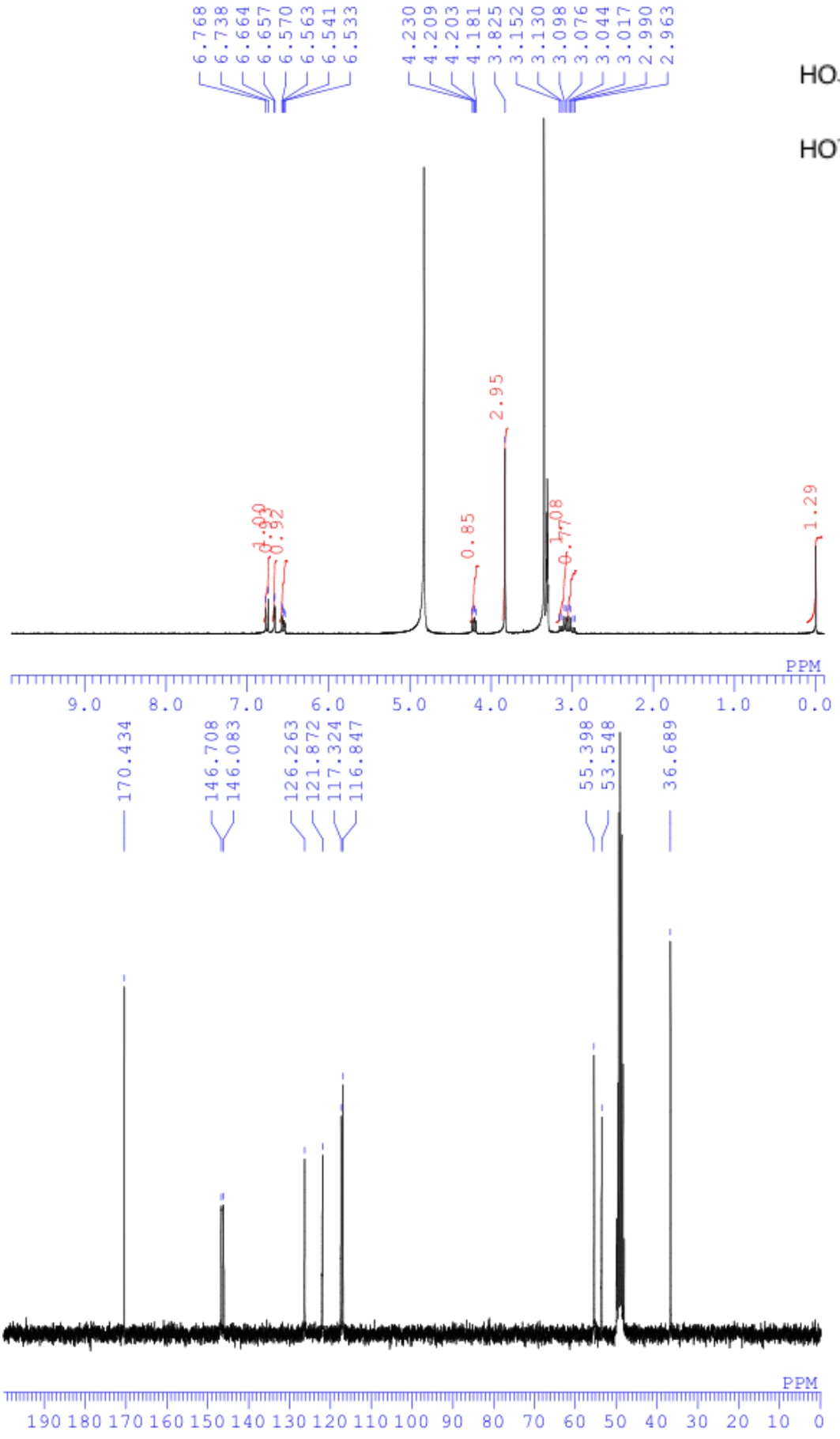
1-4) Reaction concentration of **2**

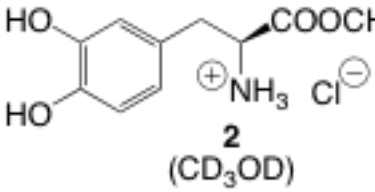


Entry	Buffer volume H (ml)	Temp I (°C)	Yield of **5**
1	480	rt	41
2	120	rt	Complex mixture
3	600	rt	49
4	480	4	52
5	600	4	60

SM-2) NMR data for synthetic compounds

2-1) L-DOPA methyl ester hydrochloride (**2**, DOPA-OMe)

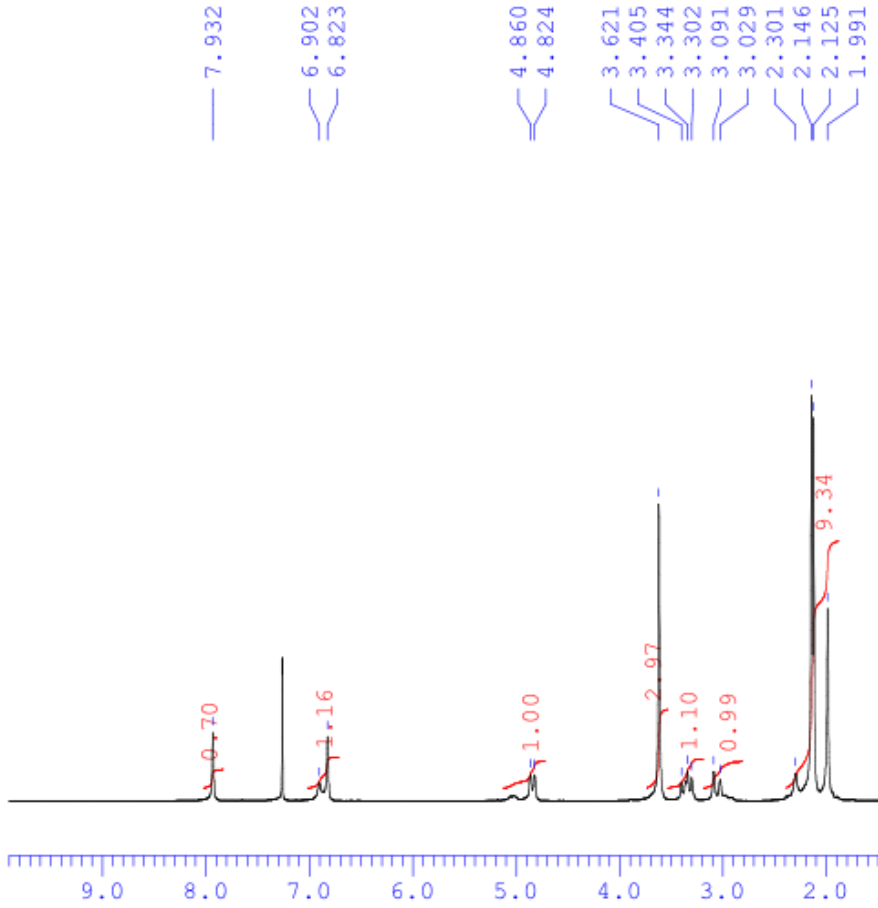


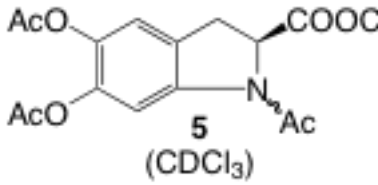


2

(CD_3OD)

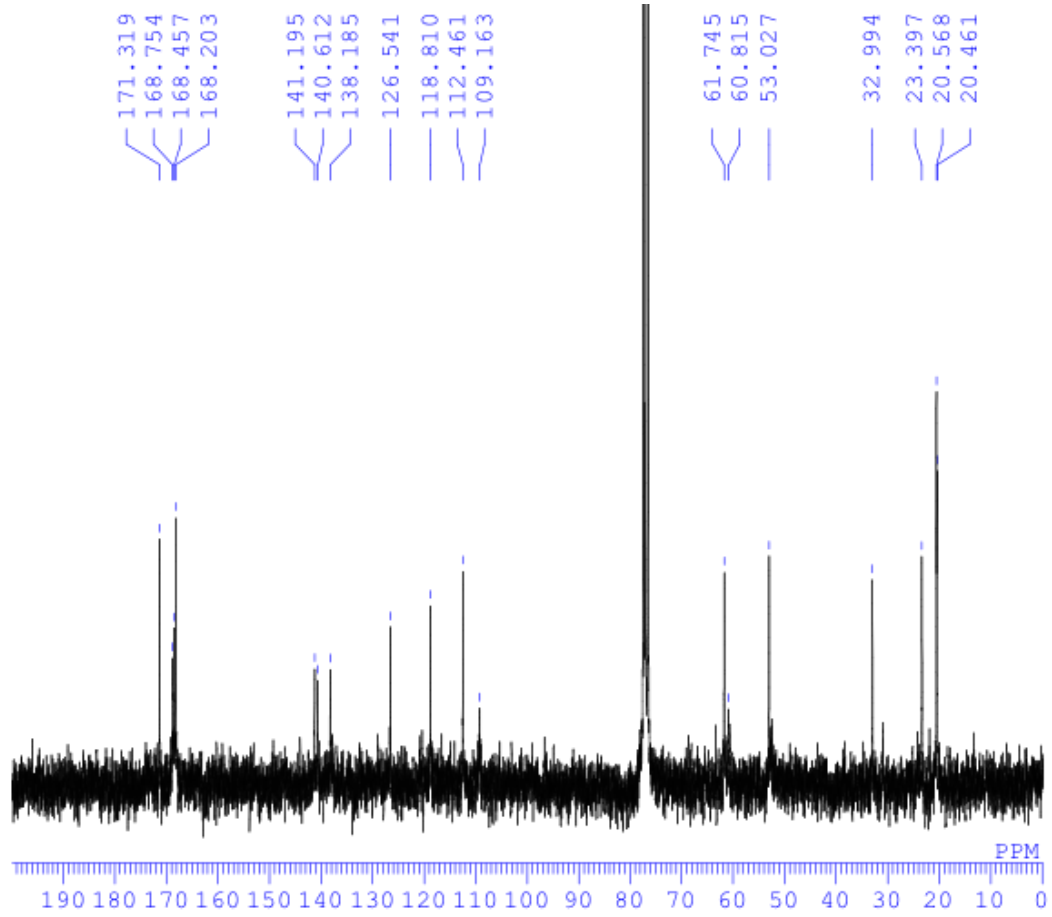
2-2) *O, O, N*- triacetyl cycloDOPA-OMe (**5**)



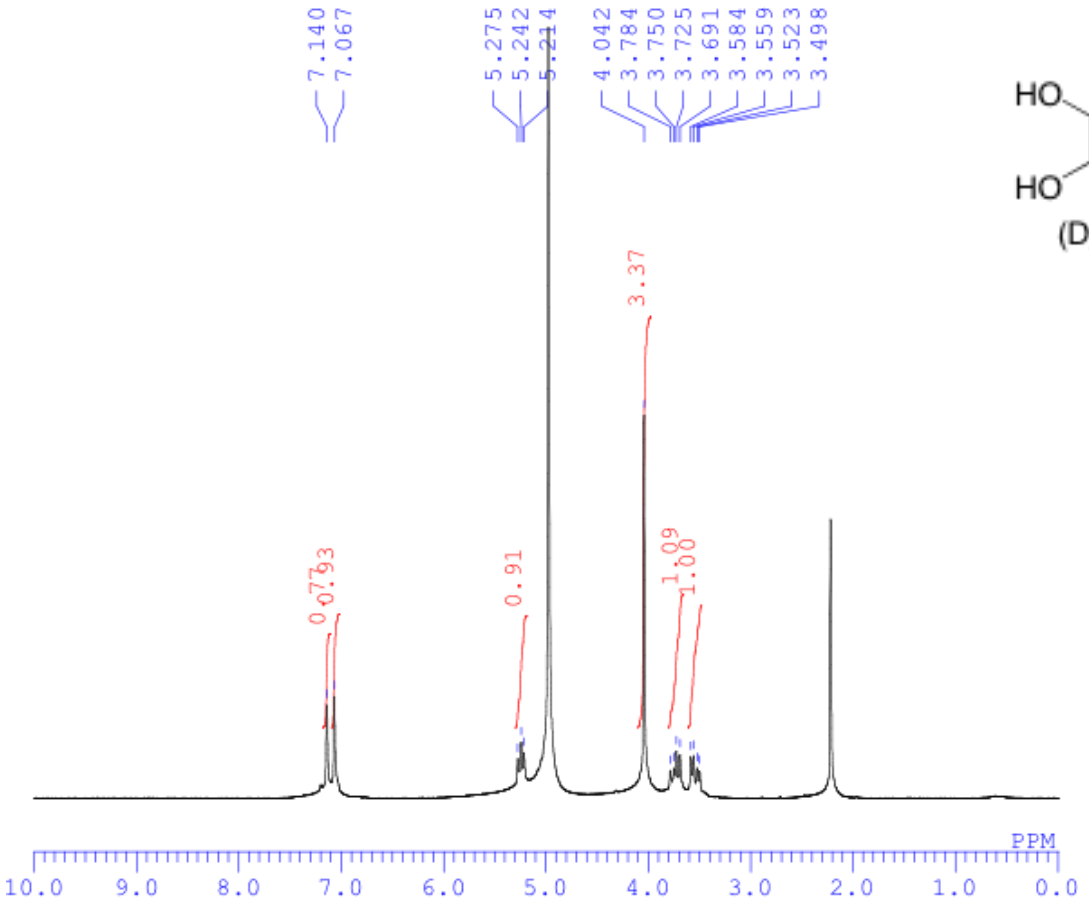


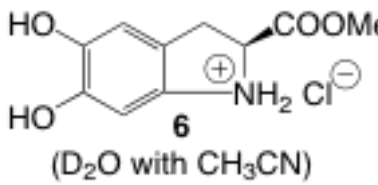
5

($CDCl_3$)



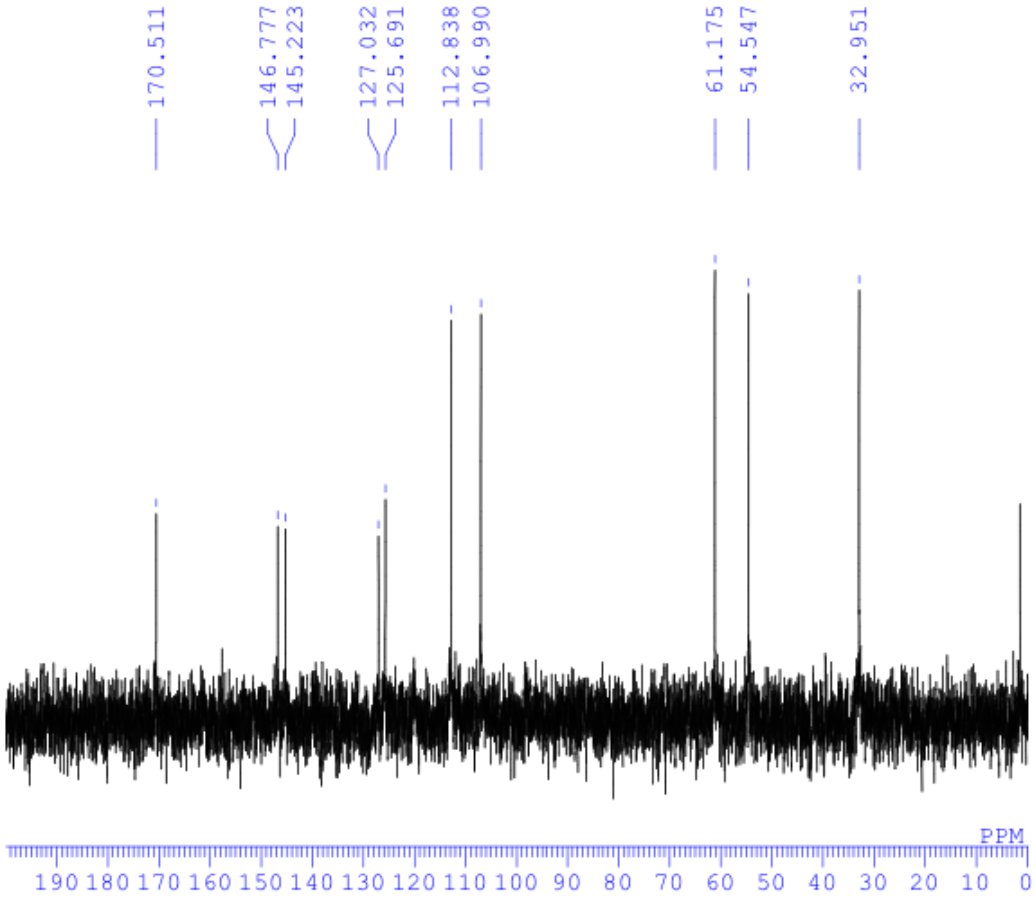
2-3) cycloDOPA-OMe (**6**, cycloDOPA-OMe)



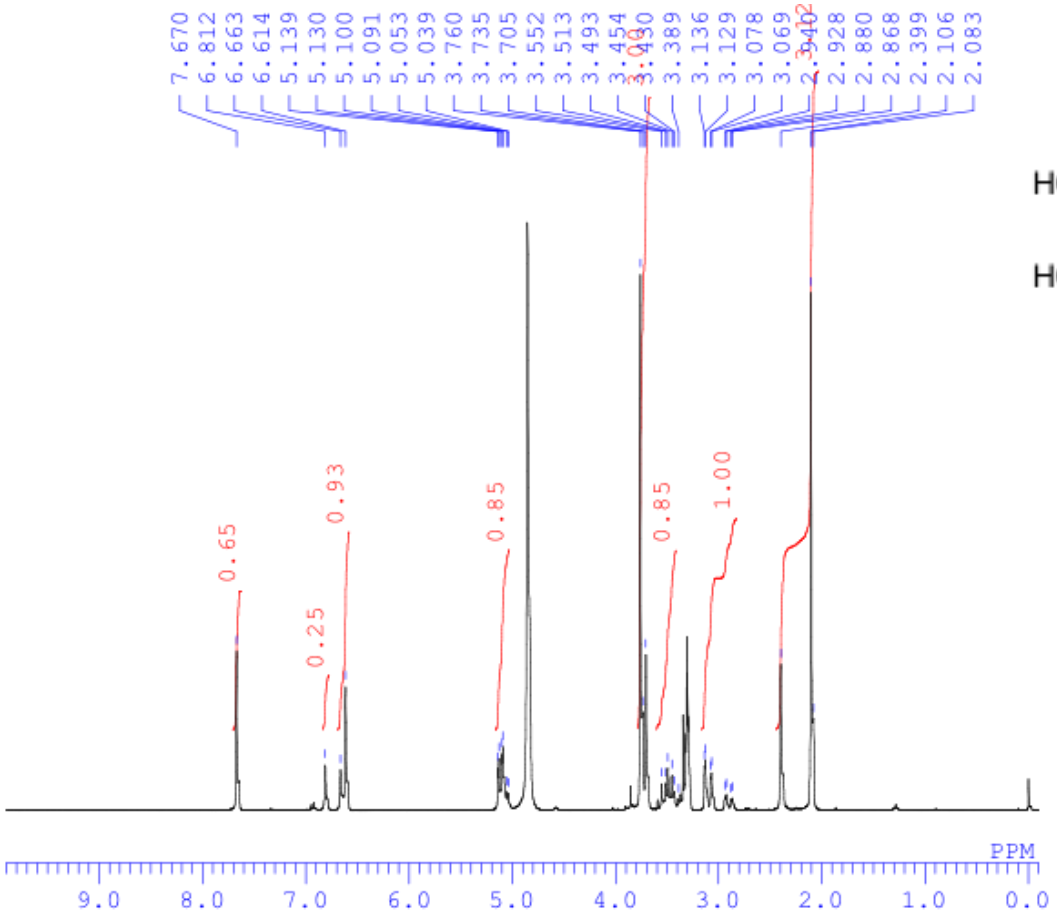


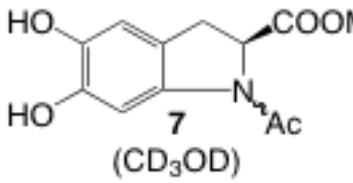
6

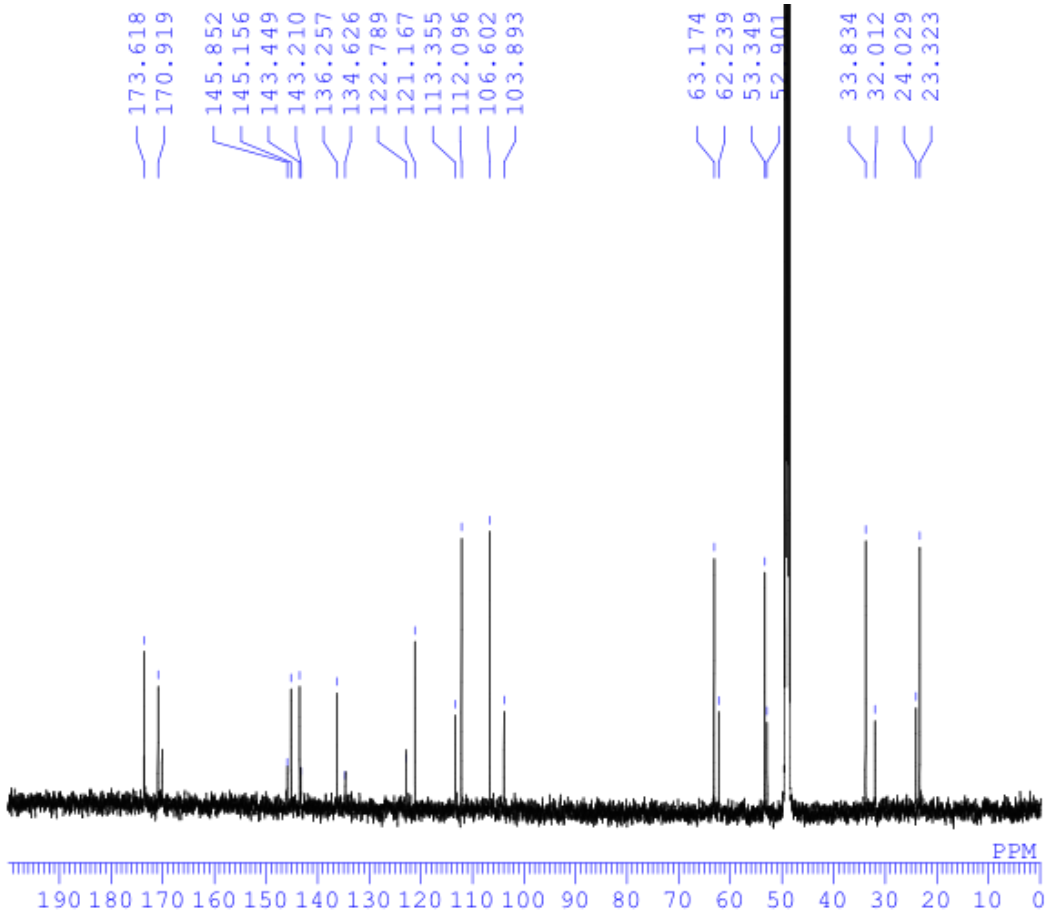
(D_2O with CH_3CN)



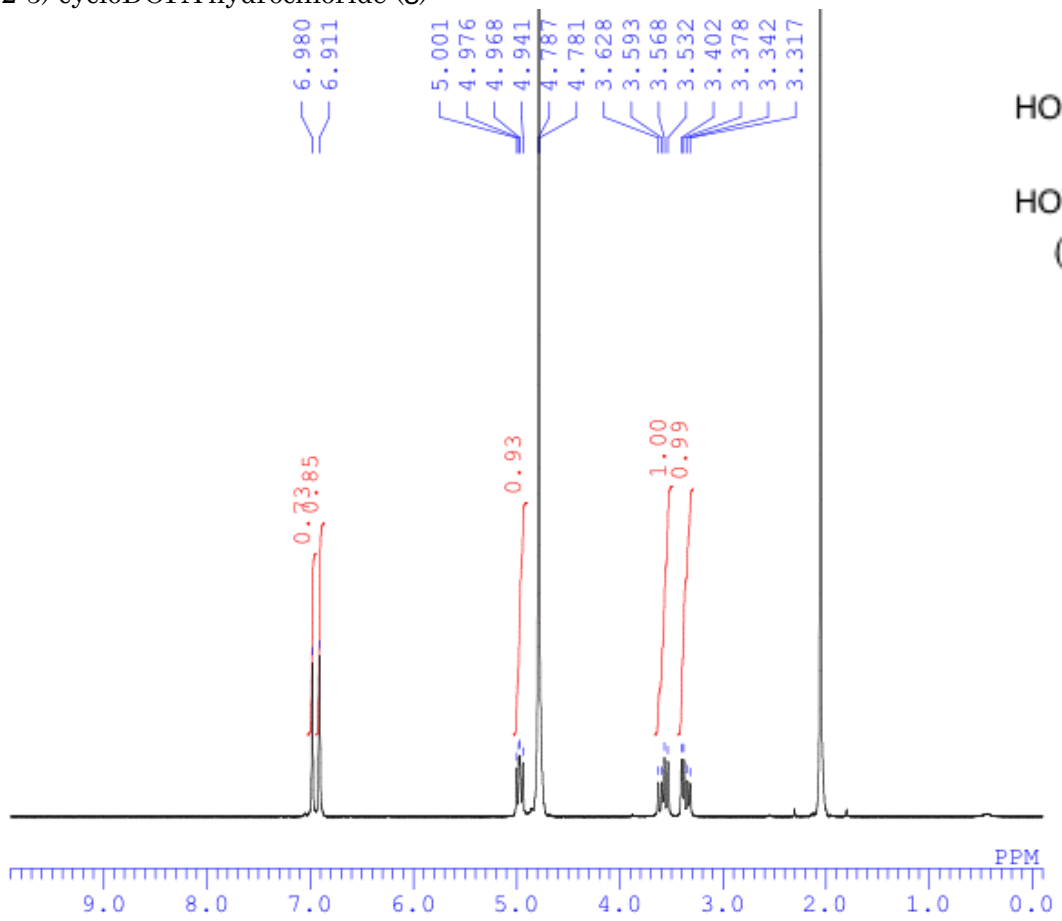
2-4) *N*-acetyl cycloDOPA-OMe (**7**)

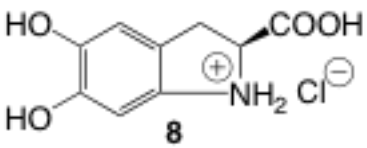

7.670
6.812
6.663
6.614
5.139
5.130
5.100
5.091
5.053
5.039
3.760
3.735
3.705
3.552
3.513
3.493
3.454
3.430
3.389
3.136
3.129
3.078
3.069
2.928
2.880
2.868
2.399
2.106
2.083
0.65
0.25
0.93
0.85
0.85
1.00
PPM
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


HO
HO
COOH
N
Ac
7
(CD3OD)


173.618
170.919
145.852
145.156
143.449
143.210
136.257
134.626
122.789
121.167
113.355
112.096
106.602
103.893
63.174
62.239
53.349
33.834
32.012
24.029
23.323
PPM
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

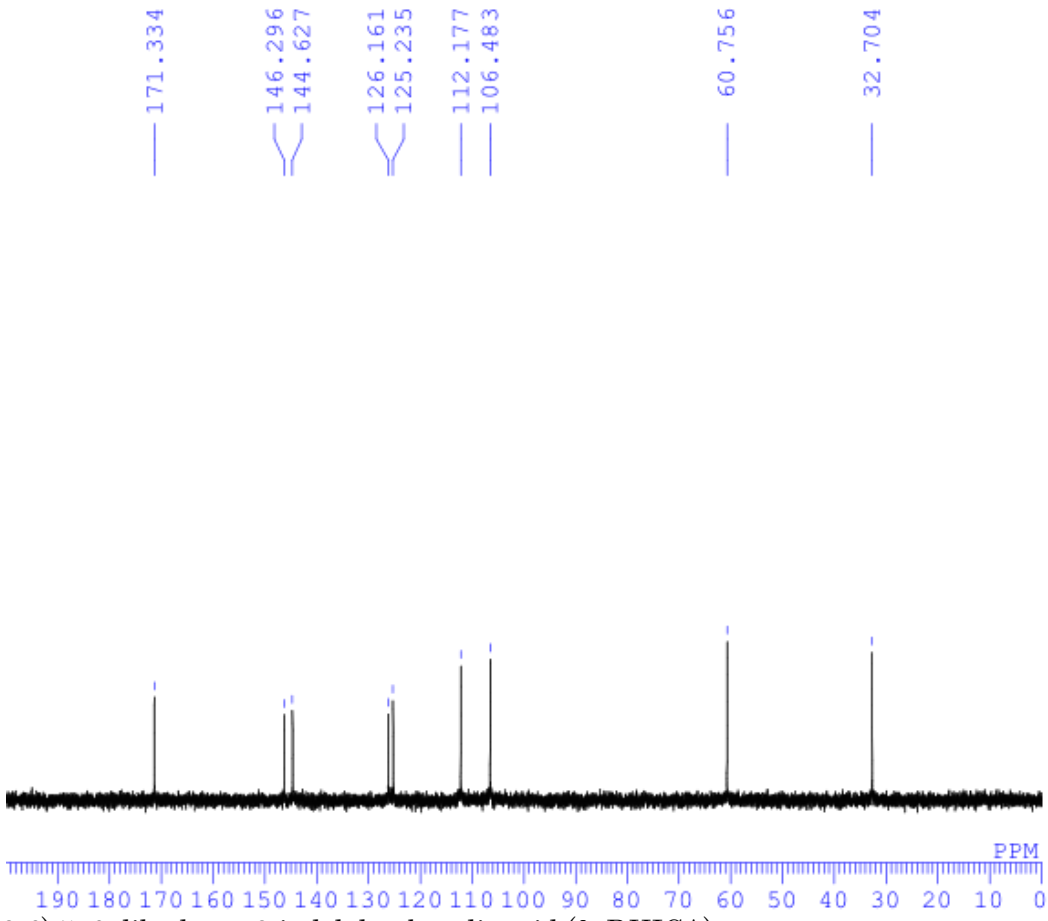
2-5) cycloDOPA hydrochloride (**8**)



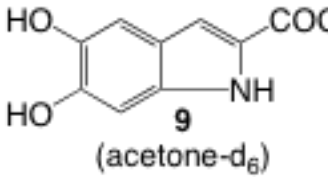


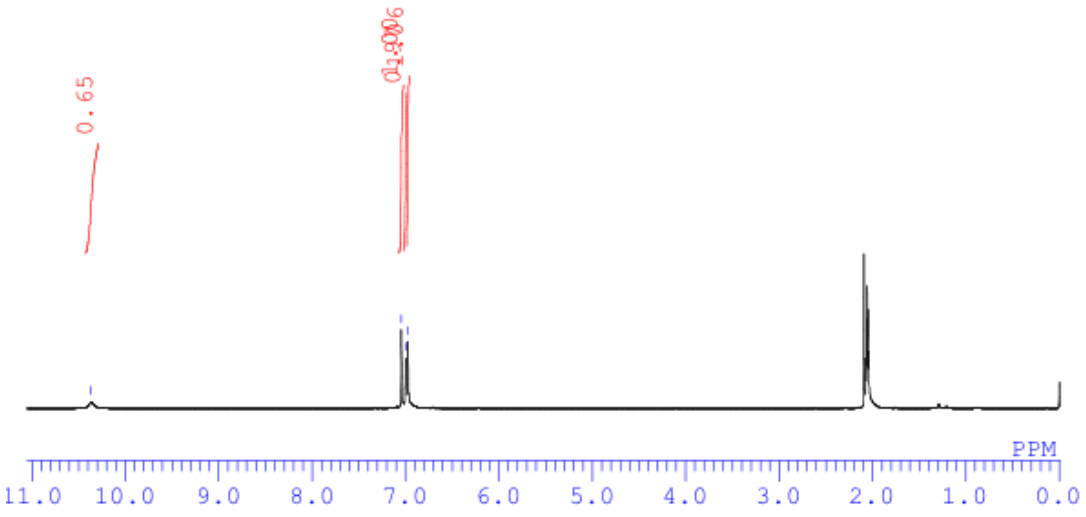
8

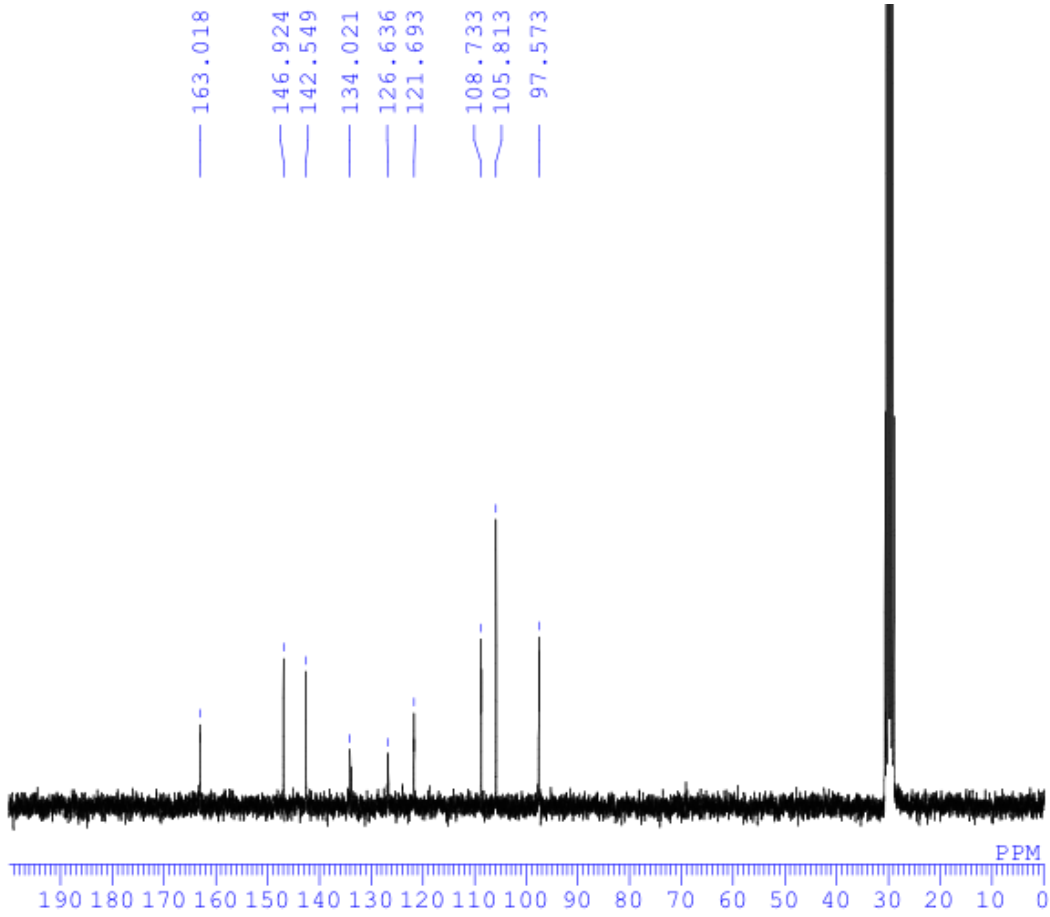
(D_2O with CH_3CN)



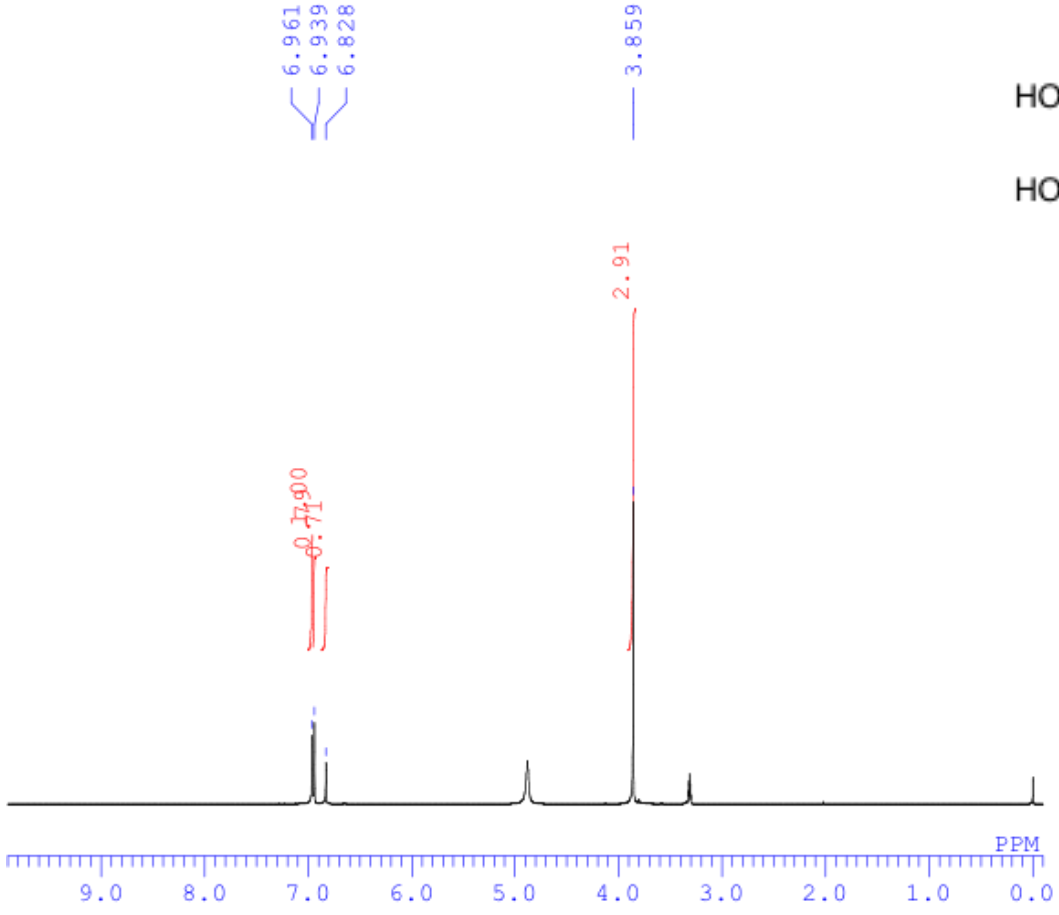
2-6) 5, 6-dihydroxy-2-indolylcarboxylic acid (**9**, DHICA).

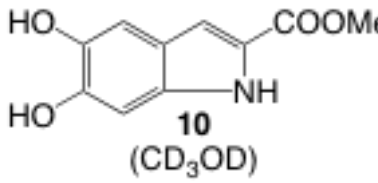


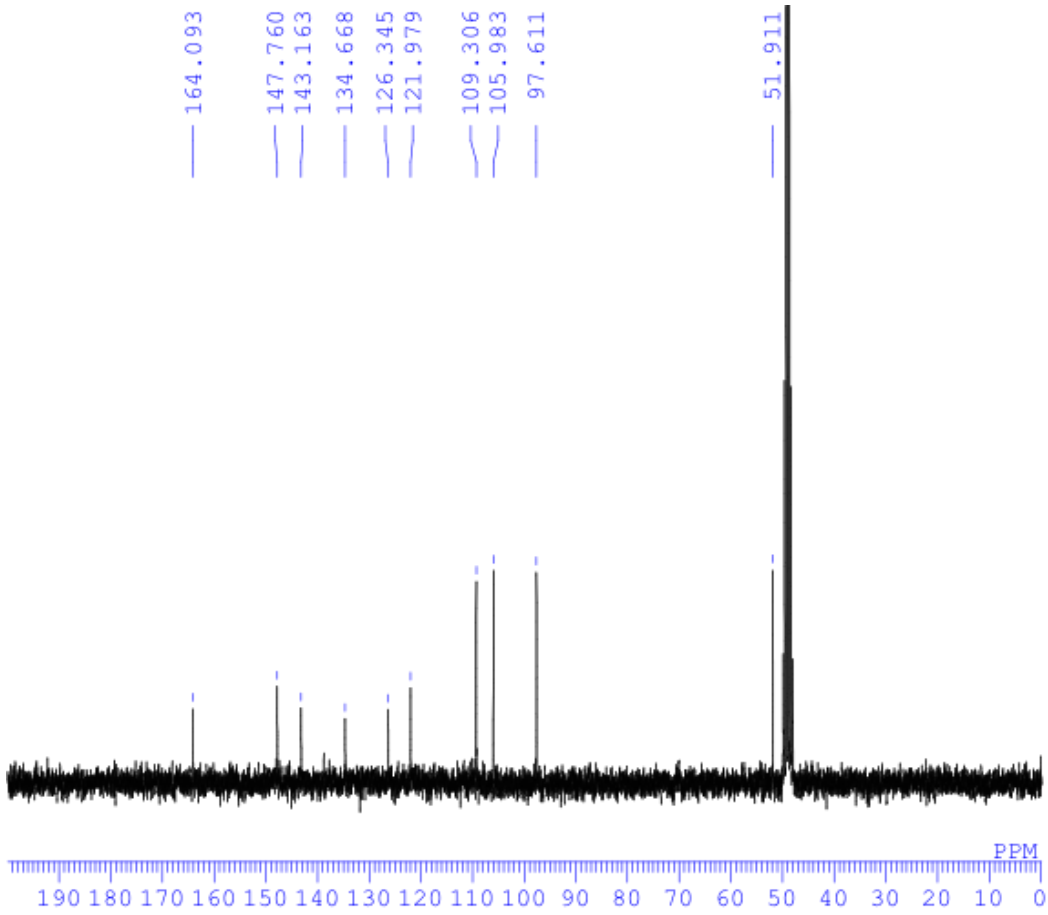




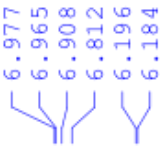
2-7) 5, 6-Dihydroxyindole-2-carboxylic acid methyl ester (**10**, DHICA-OMe)

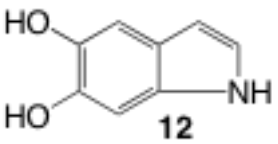






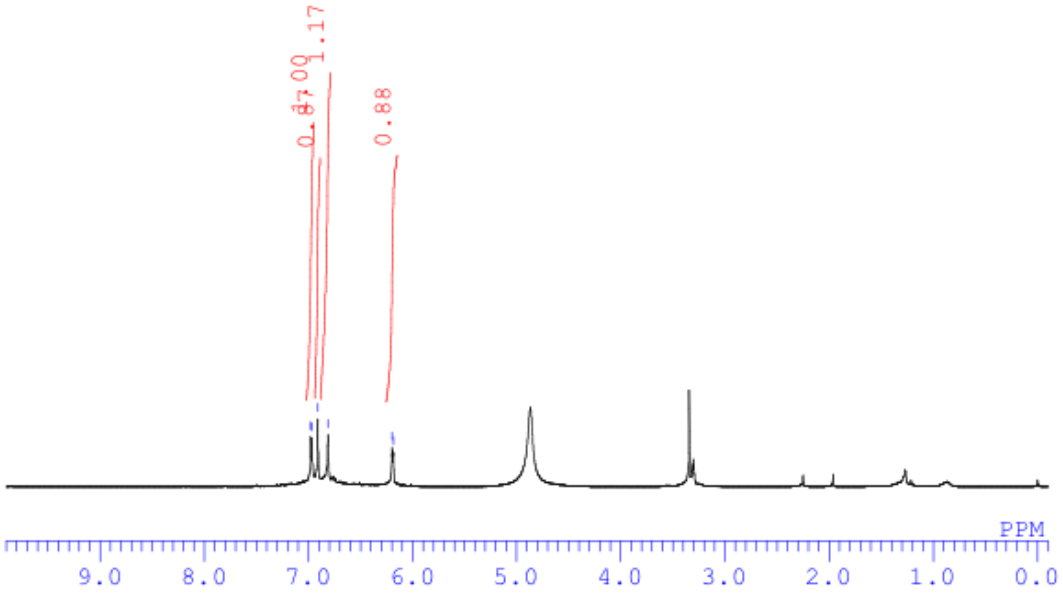
2-8) 5, 6-dihydroxyindole (**12**, DHI)

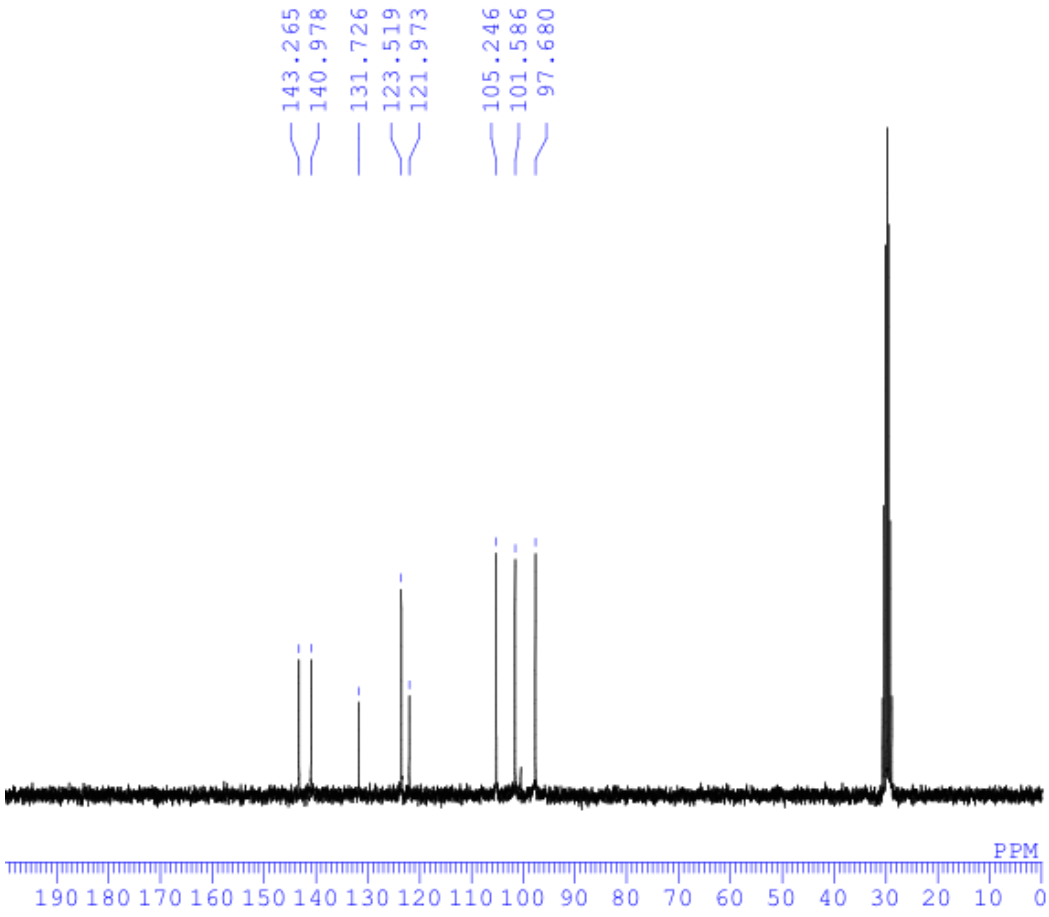




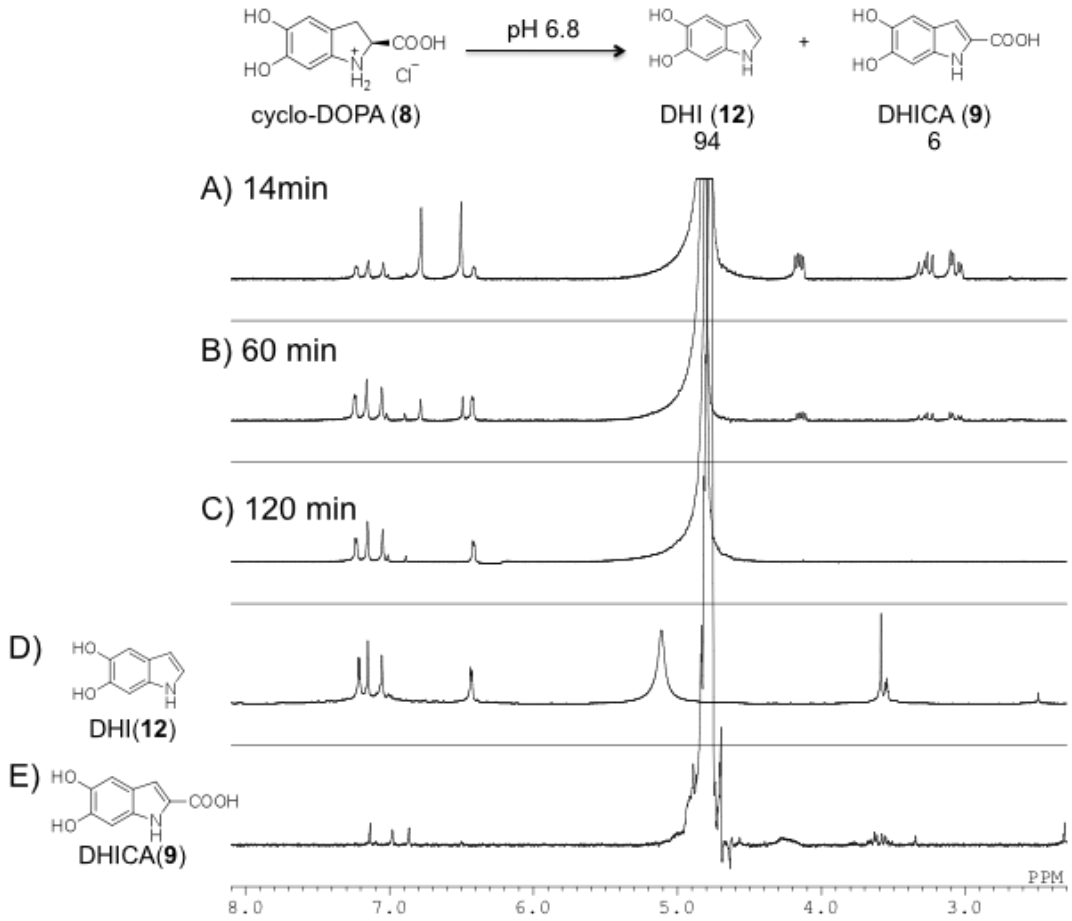
12

(CD_3OD for H
acetone-d_6 for C



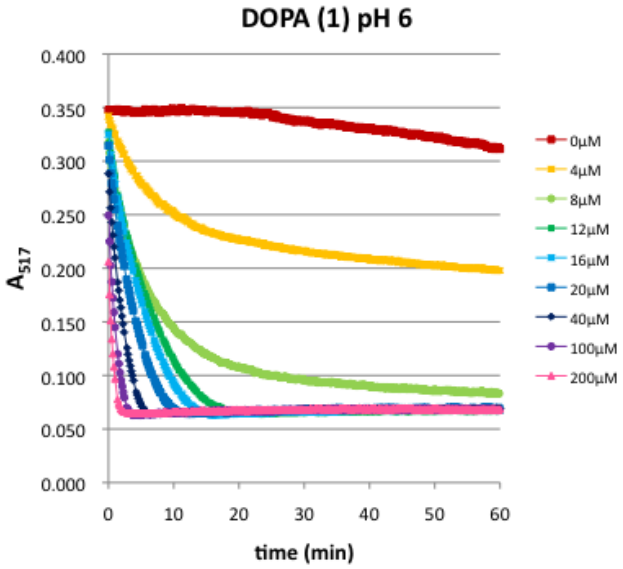


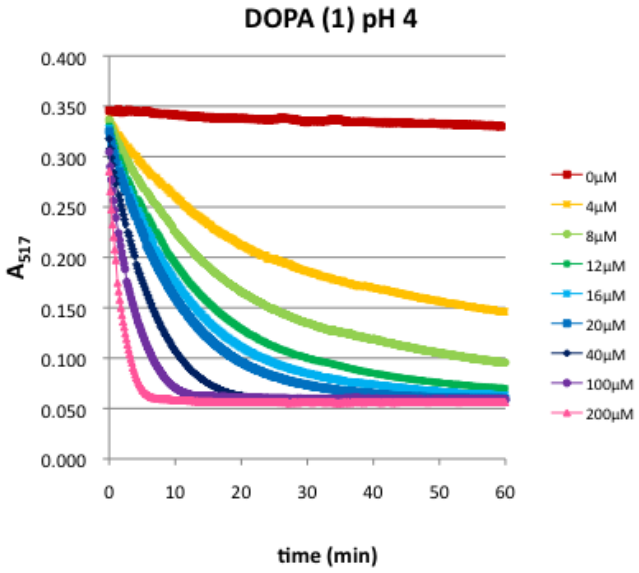
SM-3) End-products analysis for decomposition of cycloDOPA (**8**) with ^{1}H-NMR

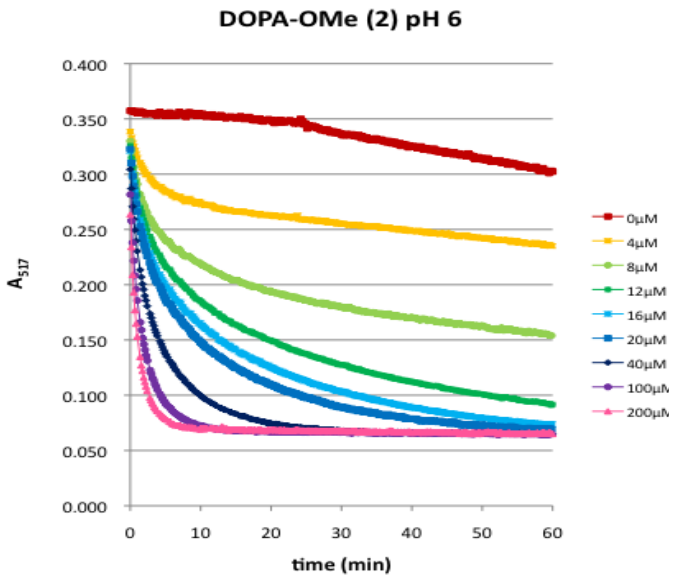


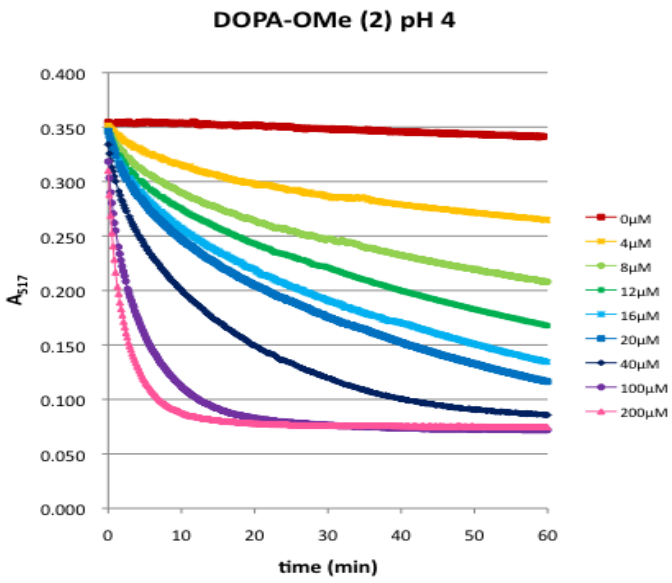
CycloDOPA (**8**) in D_2O (pH 1), pH of D_2O solution was adjusted to pH 6.8 with NaOD/D_2O and NMR spectrum was measured after 14, 60 and 120 min for A), B) and C), respectively. D) and E) are NMR spectrum for DHI (**12**) and DHICA (9), respectively

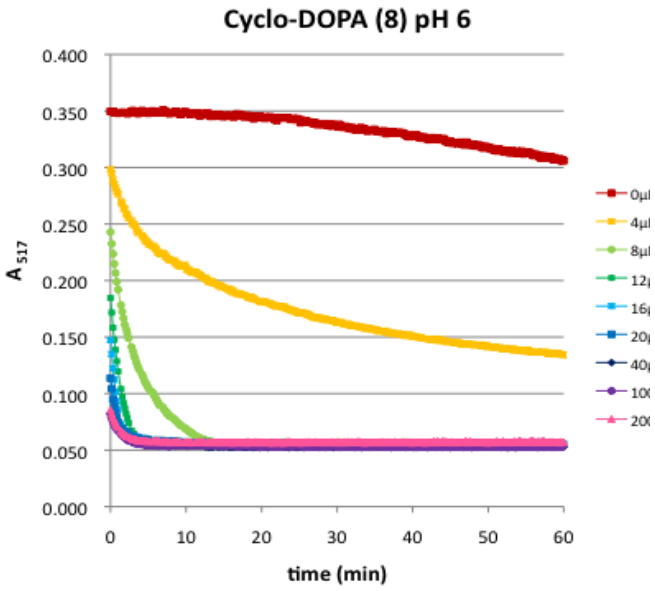
SM-4) Time course analysis for DPPH radical scavenge activity for cycloDOPA and its derivatives at pH 4 and 6.

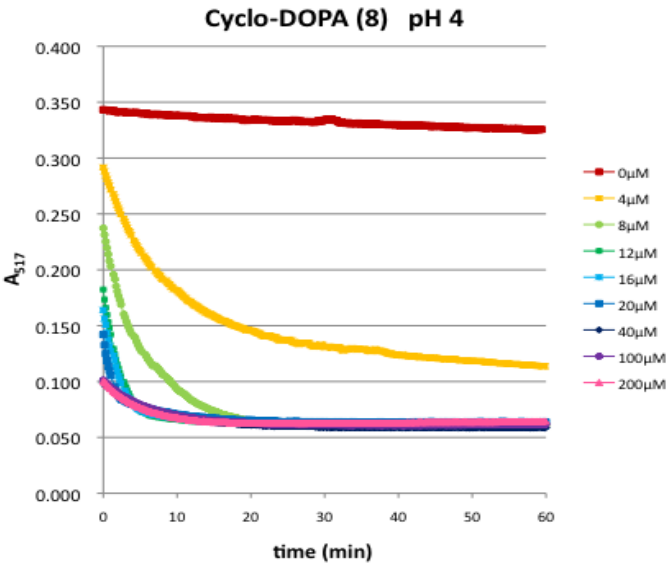


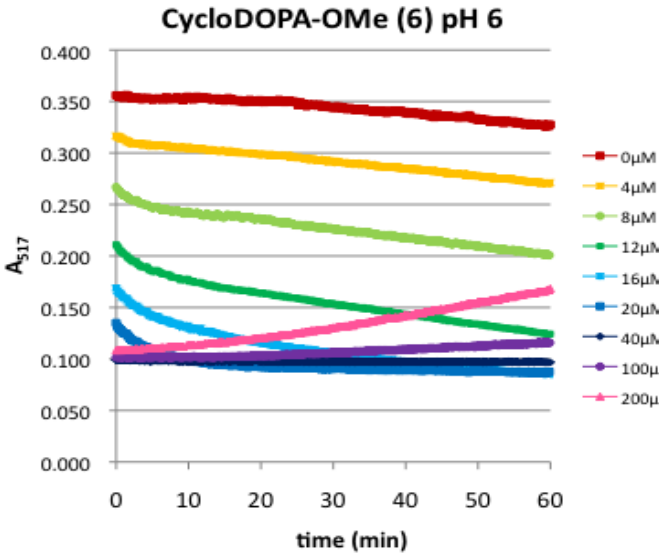


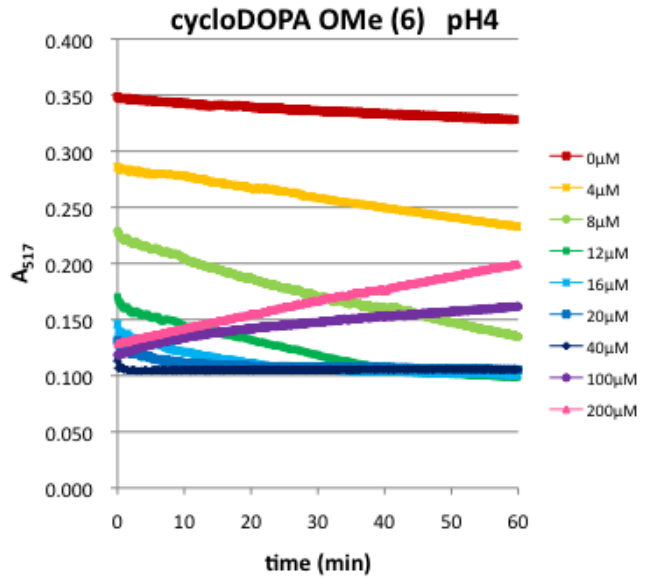


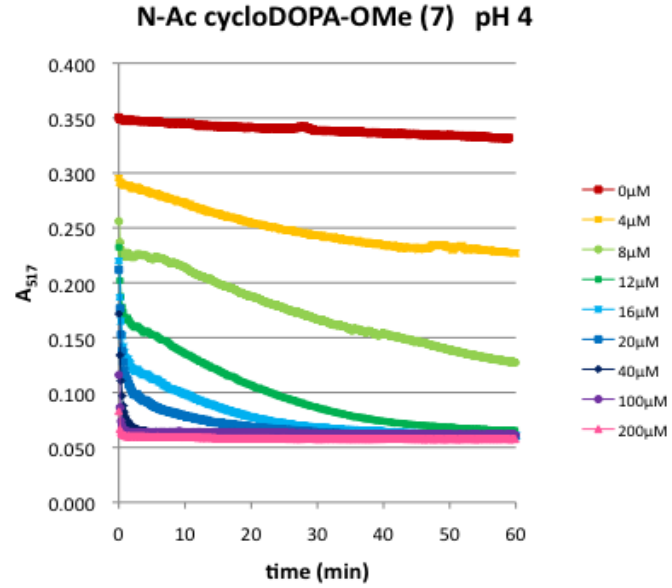


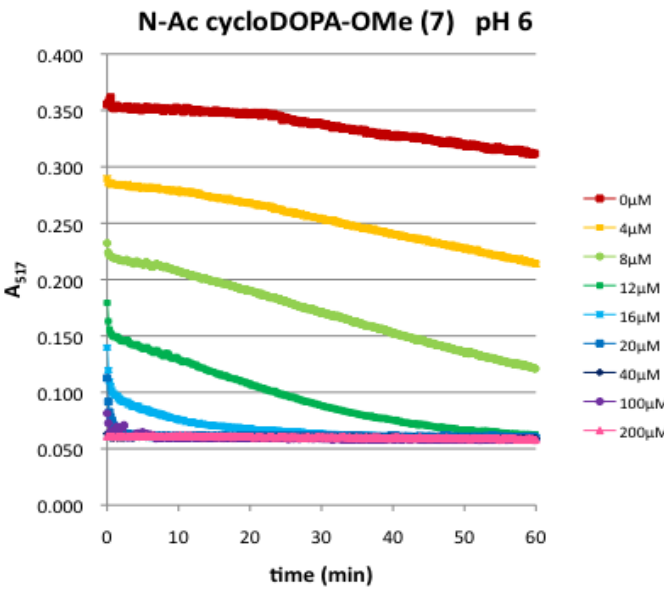

Cyclo-DOPA (8) pH 6
A 517
time (min)

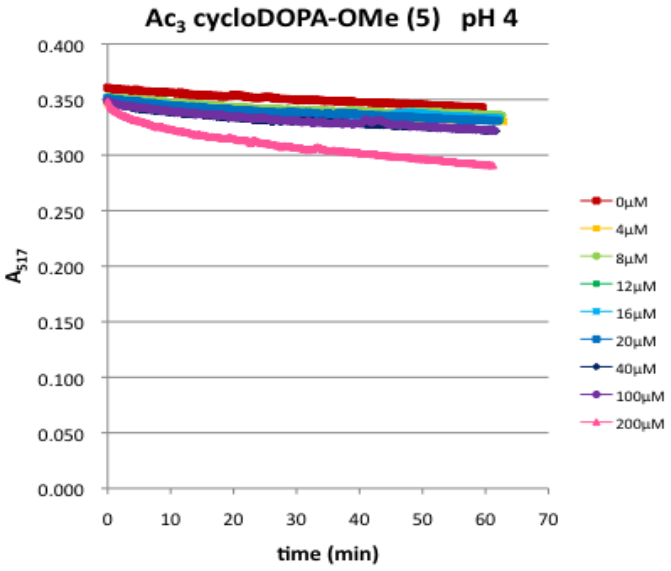

Cyclo-DOPA (8) pH 4
A517
time (min)
0μM
4μM
8μM
12μM
16μM
20μM
40μM
100μM
200μM

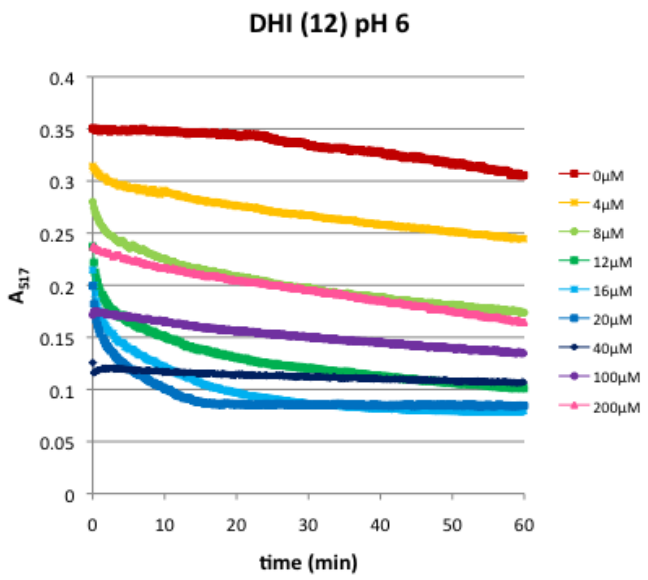

CycloDOPA-OMe (6) pH 6
A517
time (min)

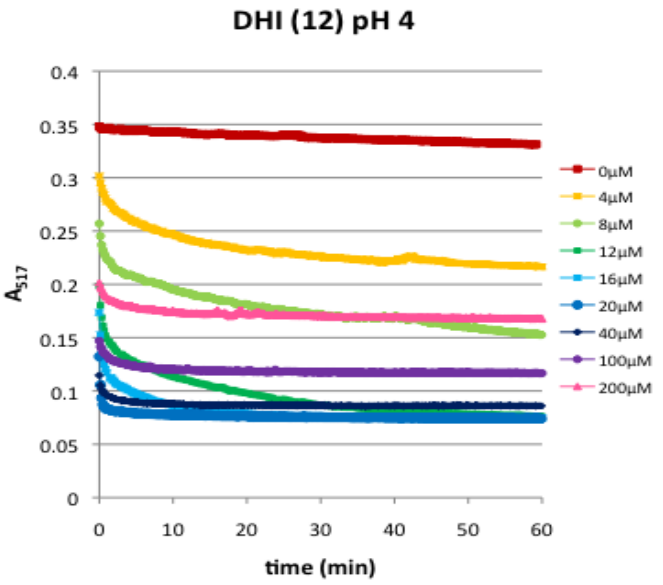

cycloDOPA OMe (6) pH4
A517
time (min)
0μM
4μM
8μM
12μM
16μM
20μM
40μM
100μM
200μM

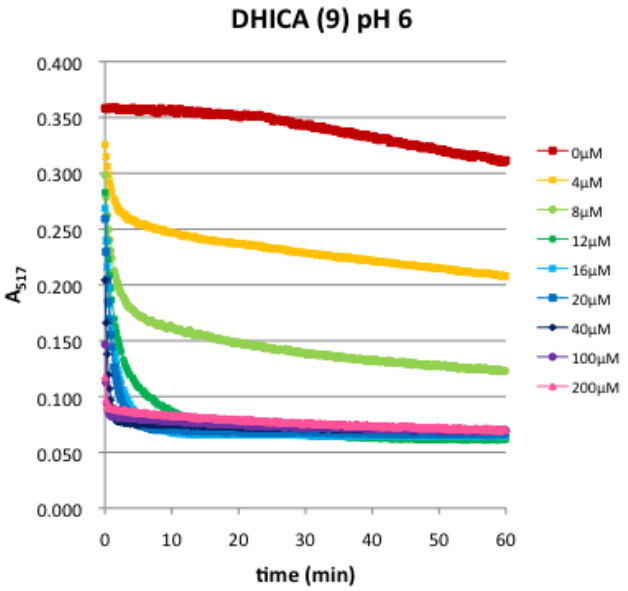

N-Ac cycloDOPA-OMe (7) pH 4
A517
time (min)
0μM
4μM
8μM
12μM
16μM
20μM
40μM
100μM
200μM

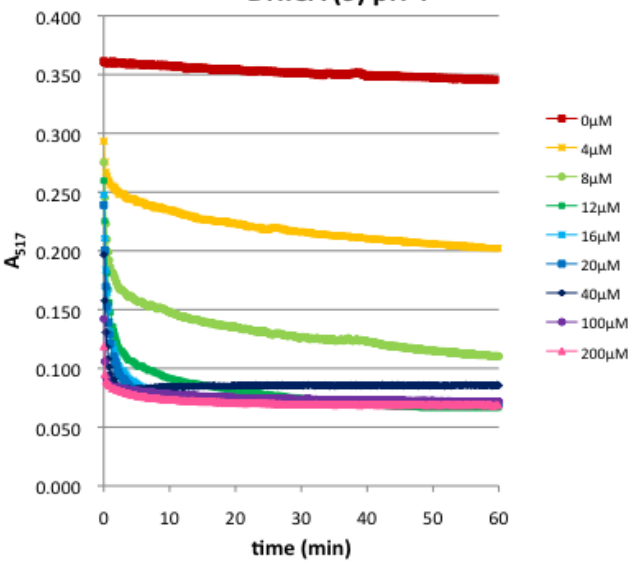

N-Ac cycloDOPA-OMe (7) pH 6
A517
time (min)
0μM
4μM
8μM
12μM
16μM
20μM
40μM
100μM
200μM

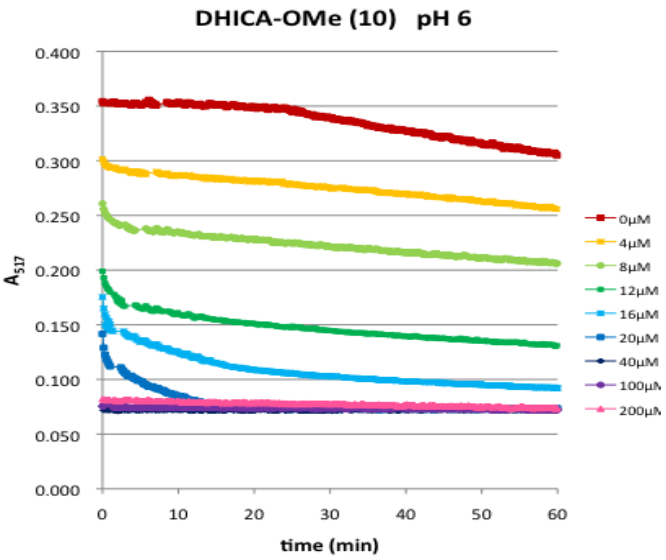

Ac3 cycloDOPA-OMe (5) pH 4
A517
time (min)
0μM
4μM
8μM
12μM
16μM
20μM
40μM
100μM
200μM

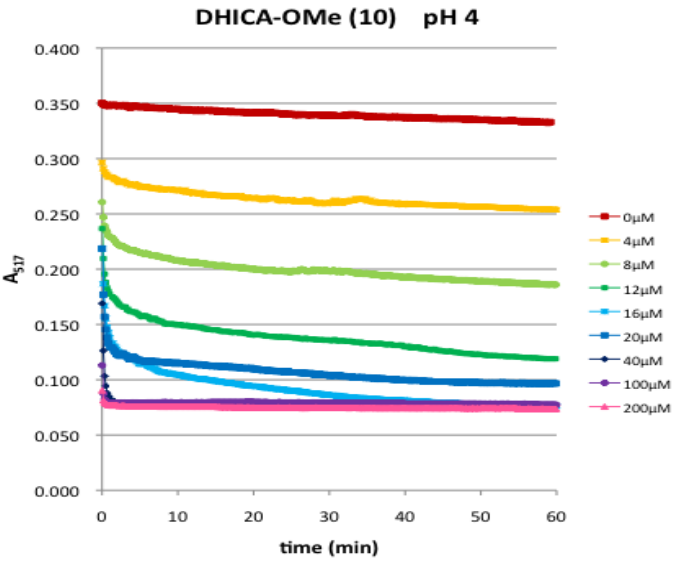

DHI (12) pH 6
A517
time (min)
0μM
4μM
8μM
12μM
16μM
20μM
40μM
100μM
200μM

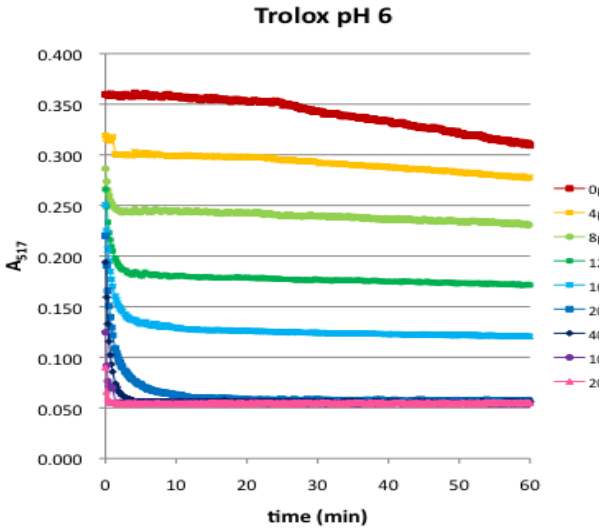

DHI (12) pH 4
A517
time (min)
0μM
4μM
8μM
12μM
16μM
20μM
40μM
100μM
200μM

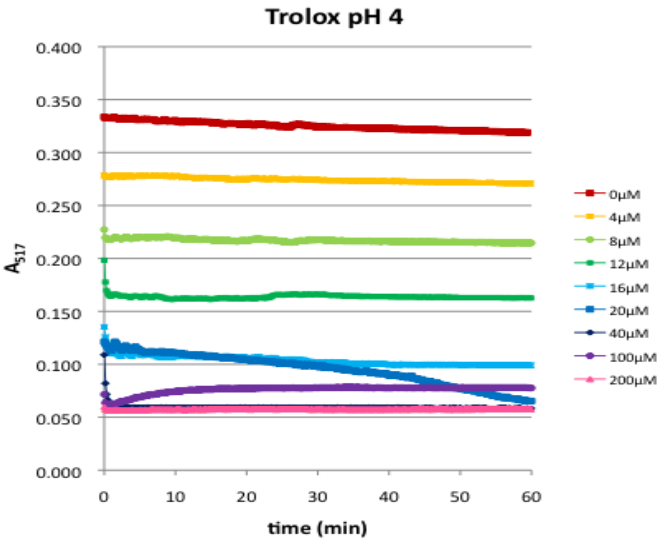

DHICA (9) pH 6
A517
time (min)
0μM
4μM
8μM
12μM
16μM
20μM
40μM
100μM
200μM


DHICA (9) pH 4
A517
time (min)
0μM
4μM
8μM
12μM
16μM
20μM
40μM
100μM
200μM


DHICA-OMe (10) pH 6
A517
time (min)
0μM
4μM
8μM
12μM
16μM
20μM
40μM
100μM
200μM


DHICA-OMe (10) pH 4
A517
time (min)
0μM
4μM
8μM
12μM
16μM
20μM
40μM
100μM
200μM


Trolox pH 6
A517
time (min)


Trolox pH 4
A517
time (min)
0μM
4μM
8μM
12μM
16μM
20μM
40μM
100μM
200μM