Electronic Supplementary Information

Title: Rapid Probing the Reactivity of P450 monooxygenases from CYP116B subfamily using Substrate-based method

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General procedure of substrates preparation from alcohols[1,2]

To a suspension of NaH (60% in mineral oil, 0.427g, 10.7 mmol) in anhydrous THF (40 mL), corresponding alcohol (9.7 mmol) was added at 0 °C under an argon atmosphere and the reaction mixture was stirred for another 30 min. After the addition of methyl iodide (2.0 g, 14.6 mmol), the reaction mixture was warmed to room temperature and stirred for 12 h. The reaction was quenched with water (20 mL). THF was removed under vacuum and the residue was extracted with ethyl acetate (20 mL × 2). The organic phase was combined, washed with brine (20 mL) and dried with anhydrous Na_2SO_4. The solvent was removed by evaporation under reduced pressure to give crude product. Flash column chromatography on silica gel with petroleum-ethyl acetate allowed purification of the methyl ether.

D-menthol methyl ether (***1***), colorless liquid (1.22 g, yield 80%, purity 98% (GC));

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.78 (d, *J* = 7.2 Hz, 3H), 0.81-1.03 (m, 9H), 1.15-1.22 (m, 1H), 1.29-1.41 (m, 1H), 2.10- 2.24 (m, 2H), 2.93 (td, *J* = 10.4, 6.4 Hz, 1H), 3.34 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 16.5, 21.1, 23.6, 25.8, 31.7, 34.8, 39.8, 48.4, 56.1, 80.6.

L-menthol methyl ether (***2***), colorless liquid (1.23 g, yield 80%, purity 98% (GC));

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.78 (d, *J* = 6.8 Hz, 3H), 0.81-1.06 (m, 9H), 1.16-1.20 (m, 1H), 1.1-1.41 (m, 1H), 1.59-1.67 (m, 2H), 2.11-2.22 (m, 2H), 2.93 (td, *J* = 10.8, 6.4 Hz, 1H), 3.33 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 16.3, 20.9, 22.3, 23.4, 25.7, 31.5, 34.6, 39.7, 48.3, 55.9, 80.4.

α-terpineol methyl ether (***3***), yellow liquid (0.3 g, yield 19.9%, purity 95% (GC));

^{1}H NMR (400MHz, $CDCl_3$): δ (ppm) 1.10 (d, *J* = 2.8 Hz, 6H), 1.18-1.29 (m, 1H), 1.65 (s, 3H), 1.67-1.72 (m, 1H), 1.74-1.84 (m, 2H), 1.92-2.06 (m, 3H), 3.18 (s, 3H), 5.38-5.40 (m, 1H).

^{13}C NMR (100MHz, $CDCl_3$): δ (ppm) 21.9, 22.4, 23.5, 24.0, 26.9, 31.2, 41.6, 48.8, 76.7, 120.9, 134.0.

4-terpineol methyl ether (***4***), colorless liquid (0.62 g, yield 40%, purity 98.2% (GC));

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.88 (t, *J* = 6.8 Hz, 6H), 1.56-1.65 (m, 1H), 1.67 (s, 3H), 1.72-1.83 (m, 2H), 1.89-2.09 (m, 4H), 3.16 (s, 3H), 5.27 (br, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 16.4, 17.5, 23.3, 26.7, 27.1, 30.0, 31.4, 48.0, 76.3, 118.0, 133.7.

Isopulegol methyl ether (***5***), colorless liquid (0.33 g, yield 20%, purity 86.8% (GC));

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.80-0.86 (m, 1H), 0.94-0.97 (m, 3H), 1.36-1.74 (m, 3H), 1.63 (s, 3H), 1.73 (d, *J* = 9.6 Hz, 3H), 1.97-2.02 (m, 1H), 2.13-2.17 (m, 1H), 3.10 (dt, *J* = 10.4, 4.0 Hz, 1H), 3.32 (d, *J* = 6.4 Hz, 3H), 4.77-4.82 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 19.6, 22.3, 31.2, 31.5, 34.5, 39.2, 51.8, 56.0, 80.7, 110.8, 148.1.

Borneol methyl ether (***9***), colorless liquid (0.75 g, yield 53.5%, purity 99.2% (GC));

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.84 (s, 3H), 0.85 (s, 3H), 0.88 (s, 3H) 1.01 (dd, *J* = 13.2, 2.4 Hz, 1H), 1.18-1.25 (m, 2H), 1.63 (t, *J* = 4.4 Hz, 1H), 1.66-1.75 (m, 1H), 1.88-1.96 (m, 1H), 2.08-2.16 (m, 1H), 3.32 (s, 3H), 3.48 (dq, *J* = 9.6, 2.4 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.1, 18.9, 19.9, 26.7, 28.3, 35.9, 45.0, 48.0, 49.1, 57.8, 88.8.

1,2,3,4-tetrahydro-6-methoxy-naphthalene (***10***) colorless liquid (0.54 g, yield 45.7%, purity 92% (GC));

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.75-1.84 (m, 4H), 2.69-2.74 (m, 4H), 3.76 (s, 3H), 6.60 (s, 1H), 6.66 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 23.2, 23.5, 28.6, 29.8, 55.3, 111.8 113.7, 129.3, 130.0, 138.2, 157.4.

1,2,3,4-tetrahydro-1-methoxy-naphthalene (***11***), colorless liquid (0.61 g, yield 54.8%, purity 98.7% (GC));

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.68-1.78 (m, 1H), 1.84-1.19 (m, 1H), 1.93-2.05 (m, 2H), 2.66-2.86 (m, 2H), 3.42 (s, 3H), 4.30 (t, *J* = 4.8 Hz, 1H), 7.07-7.09 (m, 1H), 7.14-7.19 (m, 2H), 7.33-7.35 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 18.7, 27.5, 29.1, 56.1, 76.8, 77.1, 77.4, 125.7, 127.5, 129.0, 129.3, 136.6, 137.5.

5-methoxy-1,3-benzodioxole (***16***), colorless liquid (0.53 g, yield 45%, purity 96% (GC));

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.73 (s, 3H), 5.89 (s, 2H), 6.30 (dd, *J* = 8.8, 2.0 Hz, 1H), 6.48 (d, *J* = 2.0 Hz, 1H), 6.70 (d, *J* = 8.8 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 56.0, 97.5, 101.1, 104.7, 107.9, 141.6, 148.3, 155.2.

5-(1-methoxyethyl)-1,3-benzodioxole (***17***), colorless liquid (0.61 g, 54%, purity 98%(GC));

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.39 (d, *J* = 6.4 Hz, 3H), 3.19 (s, 3H), 4.20 (q, *J* = 6.4 Hz, 1H), 5.93 (s, 2H), 6.72-6.77 (m, 2H), 6.82 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 23.9, 56.2, 79.4, 100.9, 106.4, 108.0, 119.7, 137.6, 146.9, 147.9.

General procedure of substrates preparation from ketones

Under an argon atmosphere, to the solution of corresponding ketone (6.41 mmol) in isopropanol (10 mL), $NaBH_4$ (0.51 g, 12.82 mmol) was added at 0 °C and stirred for 3 h. The mixture was extracted with ethyl acetate (30 mL x 3). The organic phase was dried with anhydrous Na_2SO_4 and concentrated under reduced pressure to get light yellow liquid. To the solution of NaH (60% in mineral oil, 0.3 g, 6.69 mmol) in anhydrous THF (30 mL), corresponding alcohol was added at 0 °C and stirred for 30 min before adding the methyl iodide (0.6 mL, 9.12 mmol). The reaction mixture was warmed to room temperature and stirred for 12 h. The reaction was quenched with water (20 mL). THF was removed under reduced pressure and the residue was extracted with ethyl acetate (20 mL × 2). The collected organic portion was dried with anhydrous Na_2SO_4. The crude product was purified by flash chromatography to provide corresponding methyl ether.

β-ionone methyl ether (***6***), colorless liquid (0.31 g, yield 20%, purity 89.9% (GC));

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.00 (s, 3H), 1.01 (s, 3H), 1.28 (d, *J* = 6.4 Hz, 1H), 1.44-1.47 (m, 2H), 1.58-1.61 (m, 2H), 1.68 (s, 3H), 1.98 (t, *J* = 6.4 Hz, 2H), 3.31 (s, 3H), 3.73-3.79 (m, 1H), 5.29 (dd, *J* = 16.0, 8.0 Hz, 1H), 6.02 (d, *J* = 16.0 Hz, 1H)

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 19.2, 21.4, 21.8, 28.7, 32.6, 33.8, 39.3, 55.8, 78.8, 128.7, 130.0, 135.4, 136.8.

4-propylhexanol methyl ether (*7*), colorless liquid (0.79 g, yield 80%, purity 90% (GC));

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.88 (t, *J* = 7.2 Hz, 3H), 1.11-1.24 (m, 6H), 1.31-1.39 (m, 7H), 3.07-3.11 (m, 1H), 3.36 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.4, 20.2, 30.2, 31.2, 31.4, 31.9, 36.8, 39.1, 55.6, 79.9.

2-adamantanone methyl ether (***8***), light yellow liquid (0.55 g, yield 50%, purity 84.8% (GC));

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.45-1.48 (m, 2H), 1.63-1.66 (m, 2H), 1.71 (br, 2H), 1.77-1.86 (m, 4H), 2.00-2.03 (m, 4H), 3.32-3.34 (m, 4H)

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 27.4, 27.5, 31.3, 31.4, 36.5, 37.6, 55.2, 83.2.

(3*S*,10*S*,13*S*,17*S*)-3,17-dimethoxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*α*] phenanthrene (***25***)[S3], white solid (1.05 g, yield 60%, purity 99% (HPLC));

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.74 (s, 3H), 0.79 (s, 3H), 3.21 (t, *J* = 8.4 Hz, 1H), 3.28 (s, 3H), 3.33 (s, 3H), 3.41-3.42 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 11.4, 11.6, 20.5, 23.3, 25.1, 27.7, 28.5, 31.5, 32.6, 32.8, 35.3, 35.9, 38.1, 39.5, 43.0, 51.4, 54.4, 55.6, 57.8, 75.5, 90.9.

(3*S*,10*S*,13*S*,17*S*)-17-methoxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*α*] phenanthren-3-ol (***26***), white solid (0.63 g, yield 31.7%, purity 92% (HPLC));

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.75 (s, 3H), 0.78 (s, 3H), 3.22 (t, *J* = 8.0 Hz, 1H), 3.28 (s, 3H), 3.33 (s, 3H), 4.04-4.05 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 11.2, 11.7, 20.5, 23.3, 27.7, 28.5, 29.0, 29.7, 31.6, 32.2, 35.3, 35.9, 36.2, 38.1, 39.2, 51.4, 54.5, 57.9, 66.6, 90.9.

Synthesis of compound 14

Under an argon atmosphere, $AlCl_3$ (13.32 g, 0.1 mol) was added to the suspension of 1,4-dimethoxybenzene **1'** (6.97 g, 0.05 mol) and succinic anhydride **2'** (5.32 g, 0.05 mol) in 40.0 mL of $ClCH_2CH_2Cl$. The reaction mixture was stirred at room temperature for 12 h and quenched with water (10.0 mL x 2). Subsequently, the reaction mixture was basified with aqueous NaOH-solution (1 M, 50.0 mL) and separated using Buchner funner. Then, the aqueous layer was neutralized by HCl-solution (6.0 M, 20.0 mL). The participated residue was collected, washed with water and dried in vacuum to afford white solid **3'** (9.1g, yield 76%).

A mixture of the white solid **3'** (9.1 g, 0.04 mol), potassium hydroxide (6.73 g, 0.12 mol) and 80% of hydrazine monohydrate (6.0 ml, 0.10 mol) in 30.0 mL of triethylene glycol was stirred at 110 °C for 4 h. Then, the reaction mixture was slowly heated to 190 °C to remove the excess of hydrazine monohydrate and heated for another 4 h. Upon cooling, it was poured into ice water (20 mL) and washed with ethyl acetate (20 mL). The aqueous layer was neutralized by HCl-solution (6.0 M, 20 mL) and extracted with ethyl acetate (30 mL x 3). The combined organic layer was washed with water (10 mL x 2), dried with anhydrous Na_2SO_4 and concentrated under reduced pressure. The final product was purified by flash chromatography with petroleum ether-EtOAc (5:1) given **4'** (4.9 g, yield 69.1%) as white solid.

The white solid **4'** (4.9 g, 27.5 mmol) was added to a stirred solution of PPA (polyphosphoric acid) (10 mL) at 80 °C for 40 min. Subsequently, the reaction mixture was quenched with ice water (20 mL) and extracted with ethyl acetate (30 mL x 2). The combined organic layers were washed with saturated aqueous Na_2CO_3 solution (20 mL x 2) and water (10 mL x 2). The extract was dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Flash column chromatography on silica gel using petroleum ether-EtOAc (3:1) allowed purification of 5,8-dimethoxy- 3,4-dihydronaphthalen-1(2*H*)-one 14 as yellow solid.

5,8-dimethoxy-3,4-dihydronaphthalen-1(2*H*)-one (***14***), yellow solid (3.04 g, yield 53%, purity 98% (GC));

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.04-2.07 (m, 2H), 2.61 (t, *J* = 6.0 Hz, 2H), 2.88 (t, *J* = 6.0 Hz, 2H), 3.82 (s, 3H), 3.86 (s, 3H), 6.78 (d, *J* = 8.8 Hz, 1H), 6.98 (d, *J* = 8.8 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 22.2, 23.6, 40.7, 56.0, 56.3, 109.8, 115.4, 123.0, 135.3, 150.1, 153.9, 198.1.

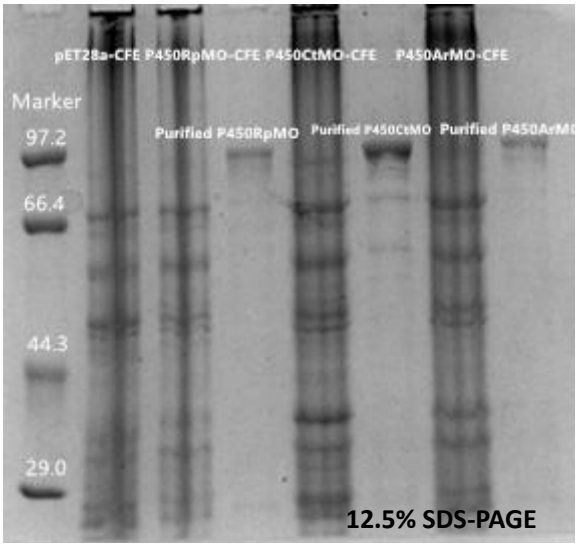

Fig. S1 The purity analysis of three P450s by SDS-PAGE

The original data of fingerprint and gas chromatography in Fig. 2

Table S1 The original data of colorimetric method in Fig. 2 (Unit: nmol product/ nmol P450/h)

				$P450_{RpMO}$			$P450_{CtMO}$			$P450_{ArMO}$		
I	**1**	**2**	**3**	0.00	0.31	1.27	0.00	0.00	0.00	0.00	0.28	0.38
	4	**5**	**6**	2.03	1.74	1.30	0.78	0.00	0.00	0.35	0.19	0.21
II	**7**	**8**	**9**	0.00	1.73	1.95	0.00	0.00	0.00	0.00	0.34	0.00
III	**10**	**11**	**12**	5.03	4.37	4.94	0.00	0.00	0.93	0.00	0.76	1.46
	13	**14**	**15**	6.57	15.9	4.47	0.58	2.03	0.43	1.28	2.40	0.55
	16	**17**	**18**	0.35	0.30	8.62	2.11	0.00	0.99	1.12	0.00	2.42
	19	**20**	**21**	4.06	0.50	24.7	1.65	0.00	0.00	1.65	0.00	0.00
	22	**23**	**24**	3.24	7.57	2.63	0.00	0.96	0.00	0.00	1.95	0.68
IV	**25**	**26**	-	0.00	0.00	-	0.00	0.00	-	0.00	0.00	-

Table S2 The original data of gas chromatography in Fig. 2 (Unit: nmol product/ nmol P450/h)

				$P450_{RpMO}$			$P450_{CtMO}$			$P450_{ArMO}$		
I	**1**	**2**	**3**	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	4	**5**	**6**	0.1	0.1	0.0	0.1	0.0	0.0	0.00	0.00	0.0
II	**7**	**8**	**9**	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
III	**10**	**11**	**12**	15.6	10.4	15.3	8.9	5.5	2.6	0.2	5.6	0.7
	13	**14**	**15**	10.2	94	0.2	4.0	5.3	10.7	0.2	10.7	0.0
	16	**17**	**18**	0.0	0.0	26.3	0.0	0.0	5.3	0.0	0.0	0.3
	19	**20**	**21**	0.0	0.0	48	0.0	0.0	0.0	0.0	0.0	0.0
	22	**23**	**24**	0.0	0.0	12	0.0	0.0	0.0	0.0	0.0	0.0
IV	**25**	**26**		0.0	0.0	-	0.0	0.0	-	0.0	0.0	-

Table S3 GC or GC/MS analysis for the reaction of substrates **1-23**

Substrate	GC or GC/MS	Column, Conditions	Retention time for substrate (min)
1	GC	Rxi-5sil Ms column, thickness 0.25 μm; length 30.0 m; 0.25 mm ID 100°C hold for 1 min 10°C /min to 200, hold for 1min; 20°C /mim to 260°C, hold for 1 min; inlet 280°C, detector 280°C	11.0
2			10.4
3			11.9
4			11.8
5			10.3
6			14.3
7			10.4
8			12.6
9			10.1
10	GC/MS	InterCap DB-5 ms column, splitless, SCAN, thickness 0.25 μm; length 30.0m; 0.25 mm ID 50°C hold for 2 min; 10°C /min to 280°C hold for 2 min, inlet 280°C, detector 280°C.	14.3
11			13.1
12			17.6
13			16.9
14			19.4
15			16.9
16			12.3
17			13.3
18			12.6
19			13.9
21			17.1
22			12.3
23			15.2

Table S4 HPLC analysis for the reaction of substrates **24-26**

Substrate	Column and Eluent	Flow rate (mL/min)	Retention time for substrate (min)	Wavelength (nm)
24	(methanol/water, 90/10, C18)	1.0	4.2	210
25	(acetonitrile/water, 70/30, C18)	1.0	6.2	205
26	(acetonitrile/water, 70/30, C18)	1.0	7.5	205

Table S5 GC/MS analysis of aromatic compounds oxygenation reaction catalyzed by P450$_{RpMO}$ (take P450$_{RpMO}$ as the example)

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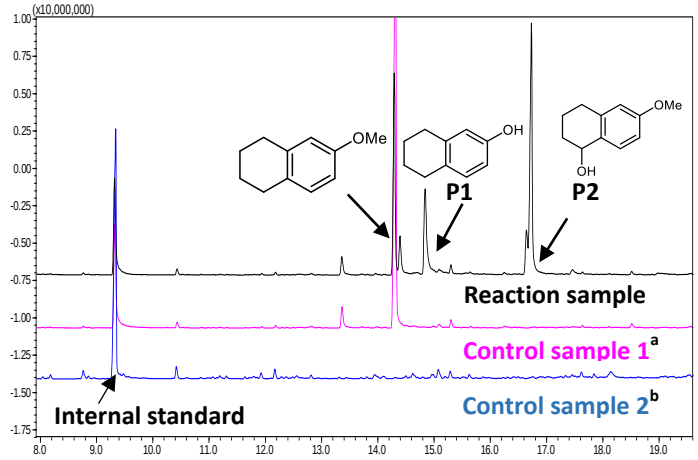
<td> 

[a] The red line is the negative control with the substrate and cell free extracts from cells containing pET28a empty plasmid. [b] The blue line is the negative control in the absence of substrate containing cell free extracts from heterologous expression of pET28a-p450rpmo plasmid in BL21 (DE3) cells.</td>
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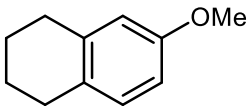
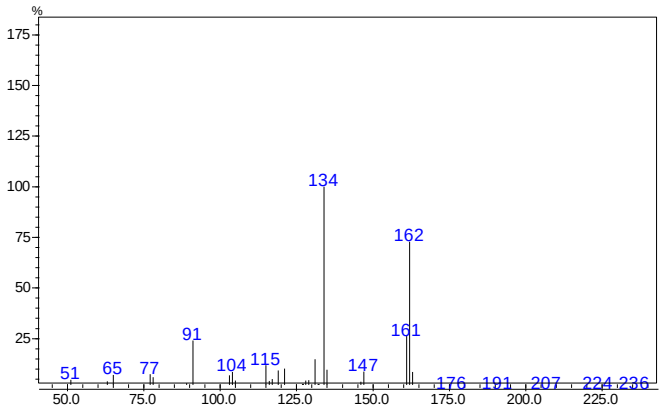
<td>10
 

1,2,3,4-tetrahydro-6-methoxy-naphthalene
Retention time: 14.3 min</td>
<td> 
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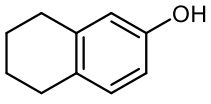
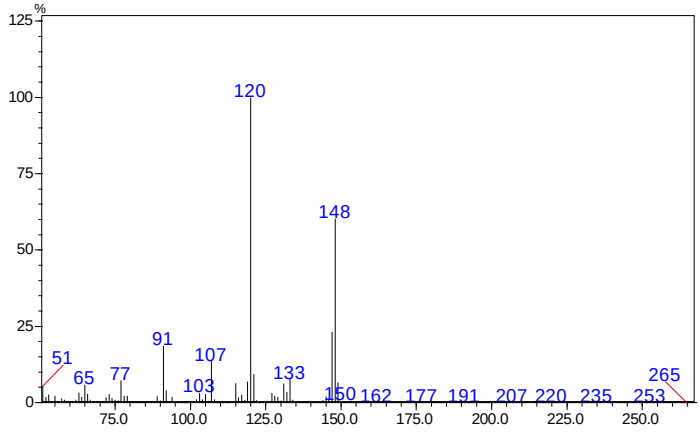
(P1)
 

1,2,3,4-tetrahydro-6-hydroxyl-naphthalene
Retention time: 14.9 min</td>
<td> 
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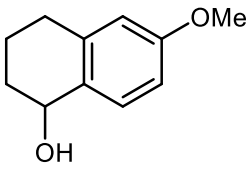
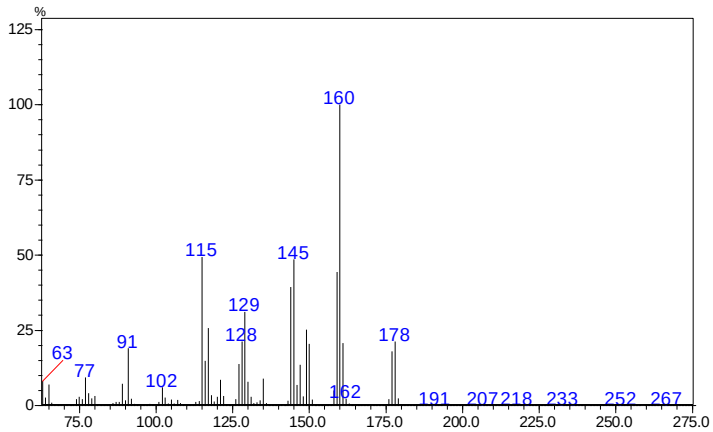
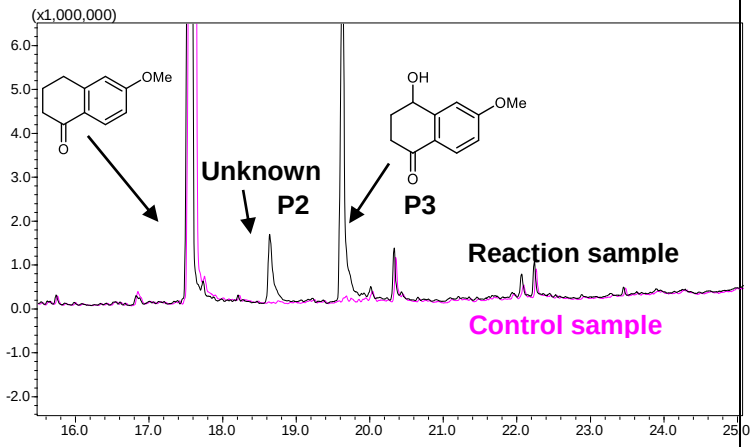
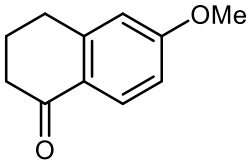
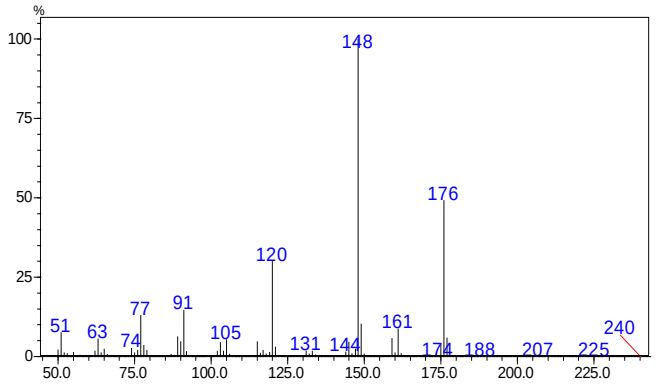
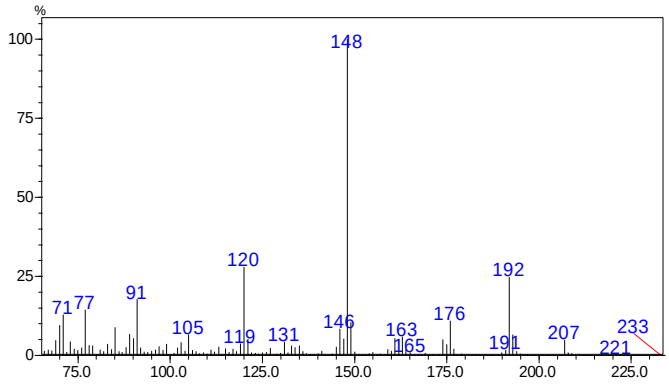
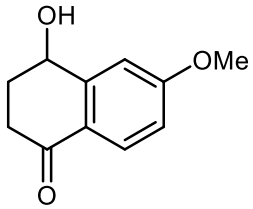
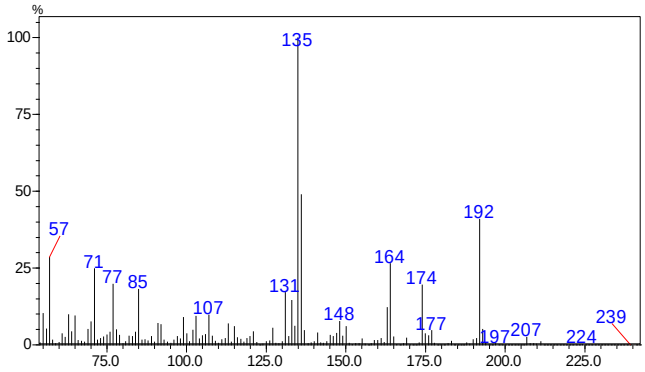
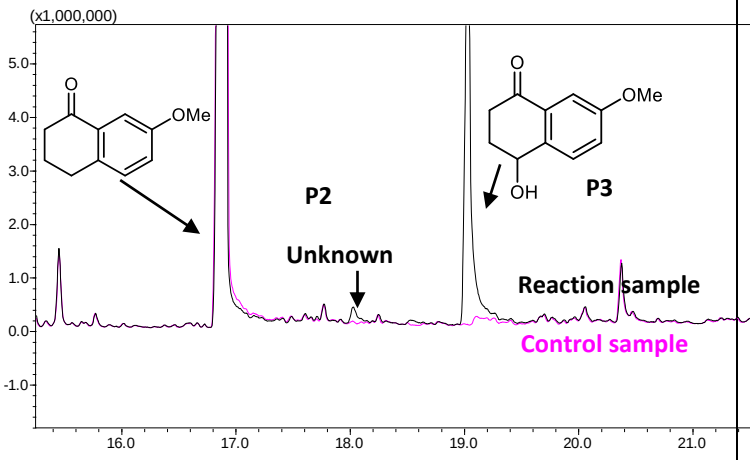
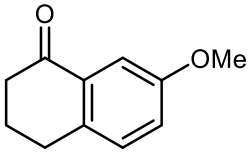
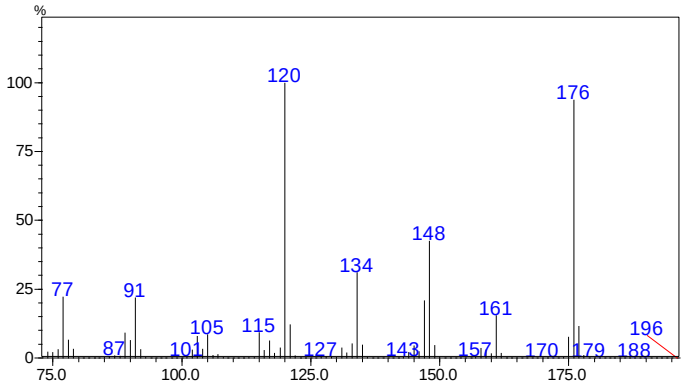
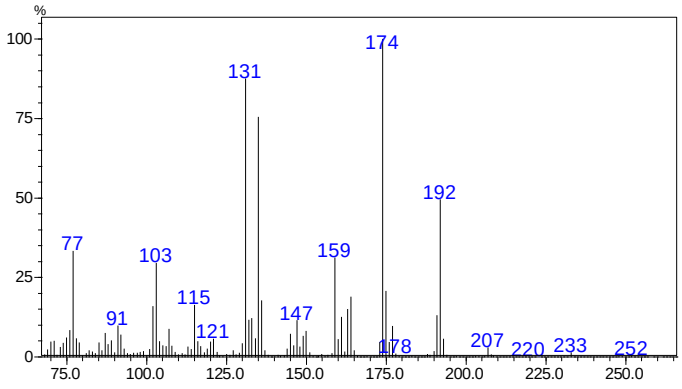
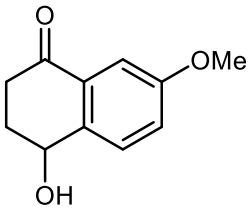
Product 2 **(P2)**  Retention time: 16.8 min	
Substrate **12**	
12  6-methoxy-1-tetralone Retention time: 17.6 min	
Product 2 **(P2)** **Unknown** Retention time: 18.9 min	

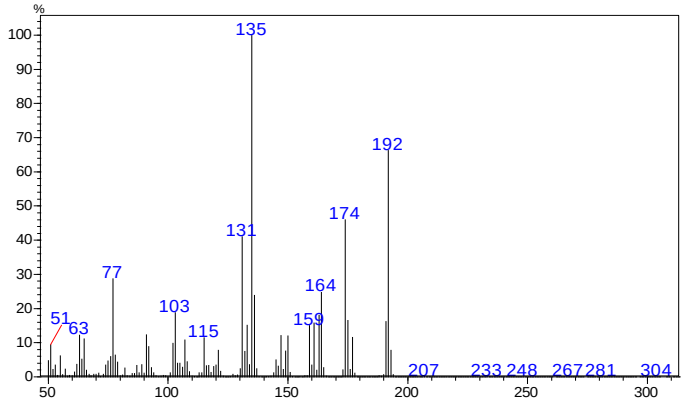
Product 3 **(P3)**  Hydroxylated 7-methoxy-1-tetralone Retention time: 18.0 min	
Substrate **13**	
13  7-methoxy-1-tetalone Retention time: 16.9 min	
Product 2 **(P2)** **Unknown** Retention time: 18.0 min	

Product 3
(P3)

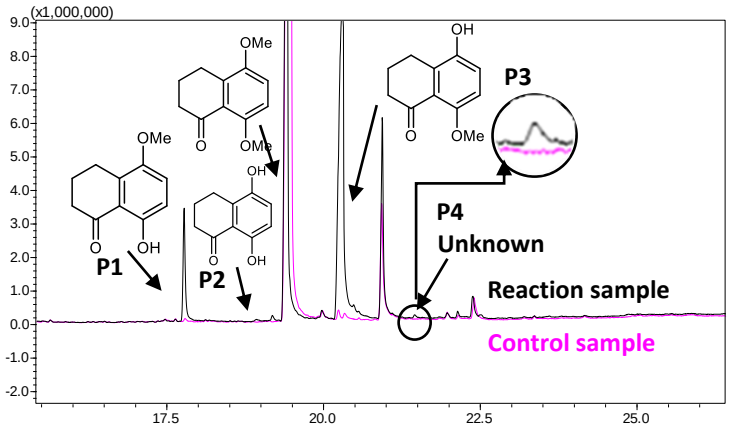


Hydroxylated
7-methoxy-1-tetralone

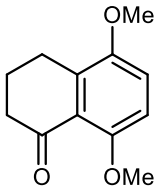
Retention time: 19.0 min



Substrate **14**

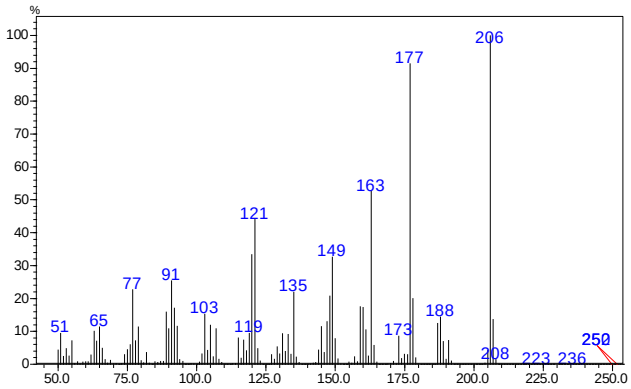


14

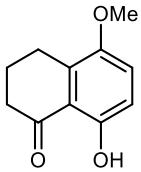


3,4-dihydro-5,8-dimethoxy-1(2*H*)-naphthalene

Retention time: 19.4 min

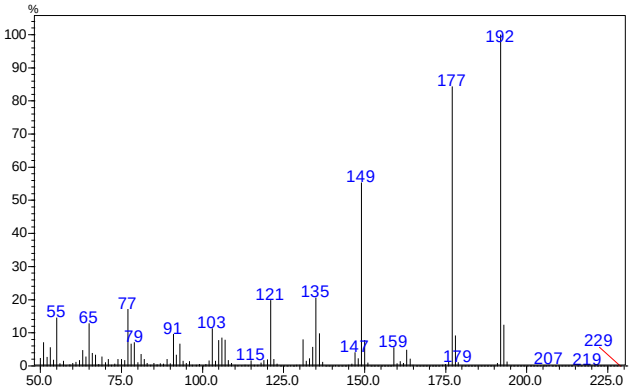


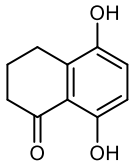
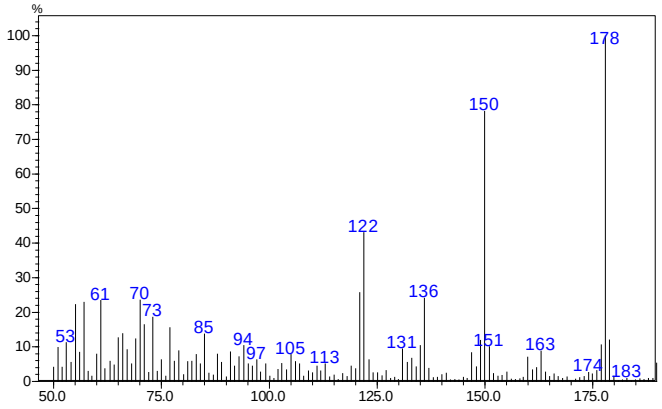
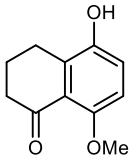
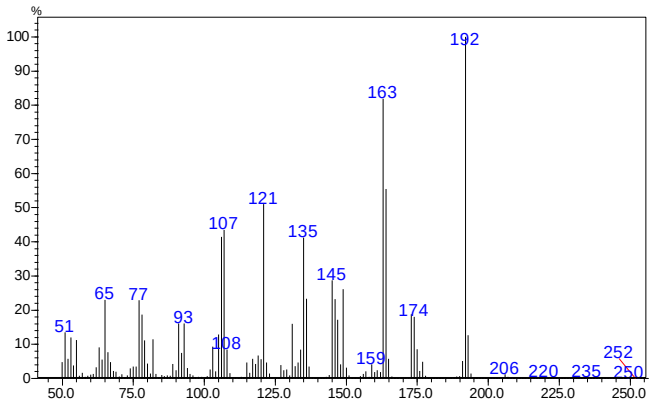
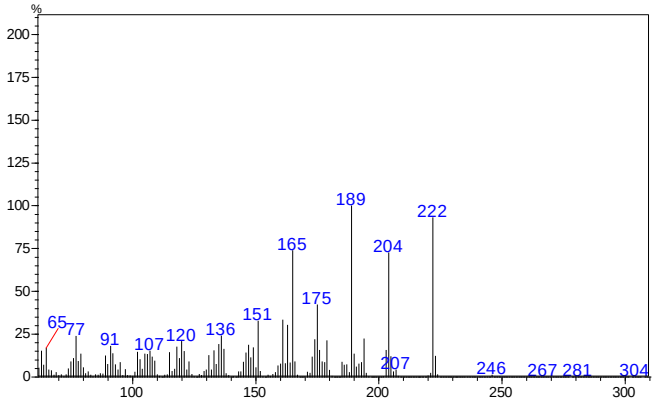
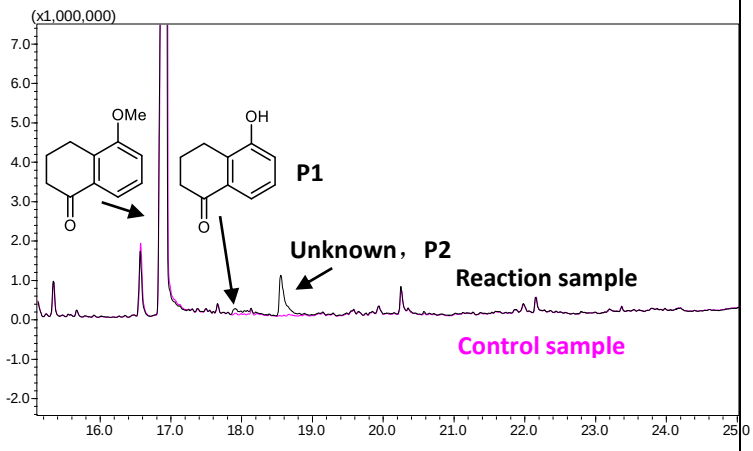
Product 1
(P1)

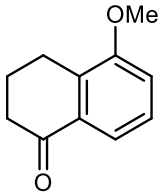
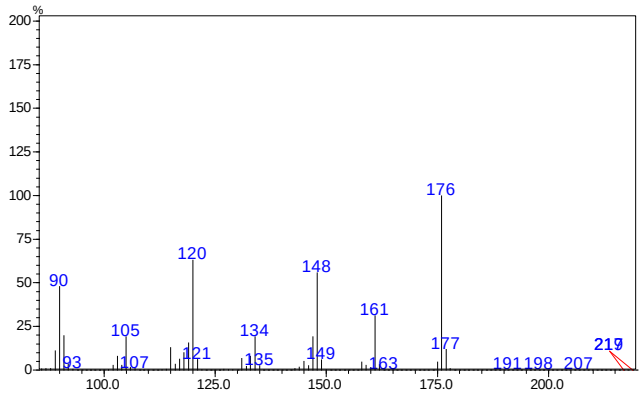
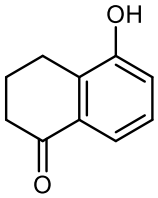
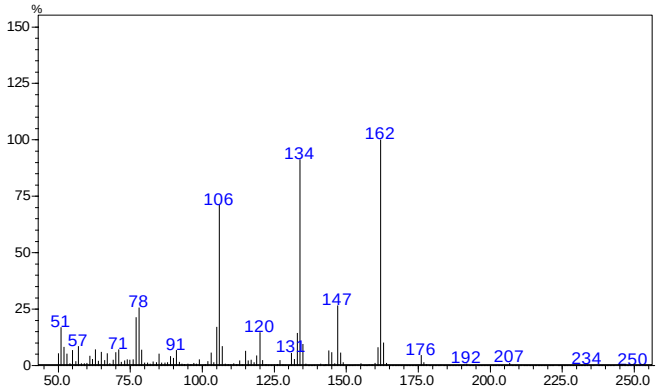
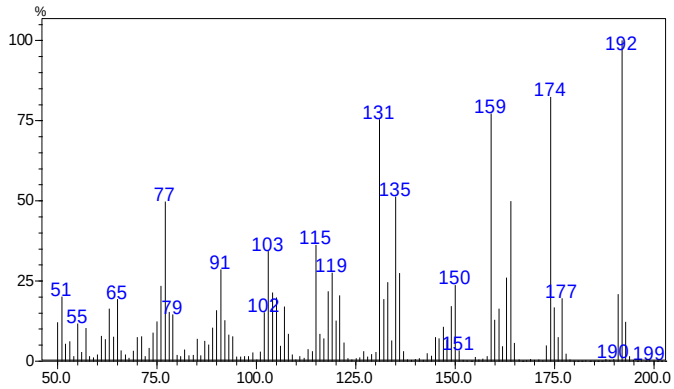
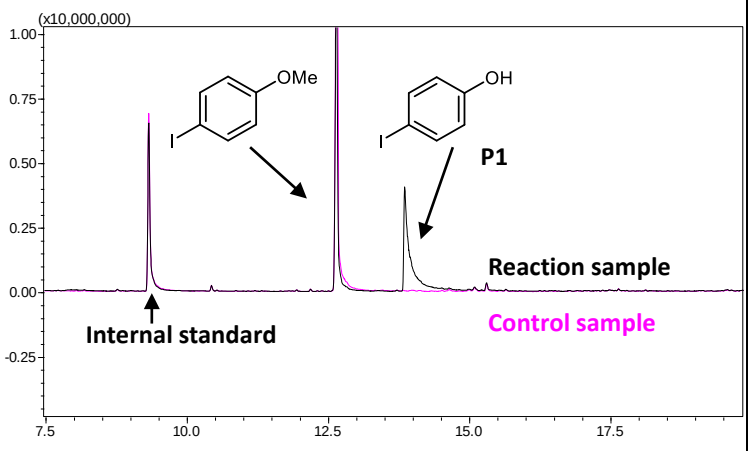


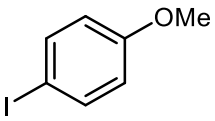
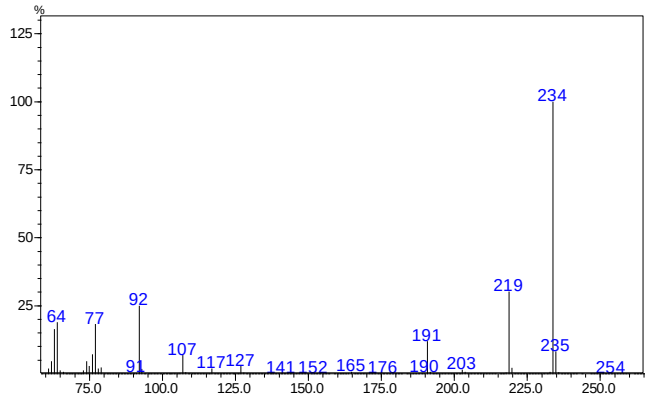
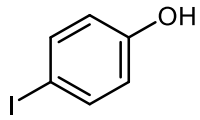
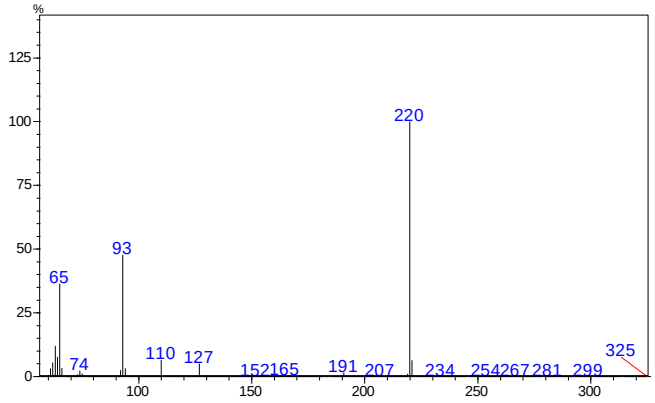
3,4-dihydro-8-hydroxy-1(2*H*)-naphthalene

Retention time: 17.7 min



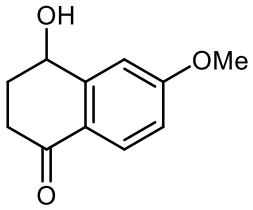
Product 2 **(P2)**  3,4-dihydro-8-hydroxy-1(2*H*)-naphthalene Retention time: 19.3 min	
Product 3 **(P3)**  3,4-dihydro-8-hydroxy-1(2*H*)-naphthalene Retention time: 20.3 min	
Product 4 **(P4)** **Unknown** Retention time: 21.3 min	
Substrate **15**	

15  5-methoxy-1-tetralone Retention time: 16.9 min	
Product 1 **(P1)**  5-hydroxy-1-tetralone Retention time: 17.9 min	
Product 2 **(P2)** **Unknown** Retention time: 18.6 min	
Substrate **18**	

18  4-methoxy-iodobenzene Retention time: 12.5 min	
Product 1 **(P1)**  *p*-iodophenol Retention time: 12.8 min	

NMR analysis of product

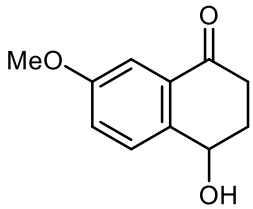
^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, $CDCl_3$) analysis of **P3** of substrate **12**



^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.16-2.20 (m, 1H), 2.36-2.45 (m, 1H), 2.54-2.62 (m, 1H), 2.84-2.93 (m, 1H), 3.90 (s, 3H), 4.93-4.96 (m, 1H), 6.93 (dd, *J* = 8.8 Hz, 2.0 Hz, 1H), 7.10 (d, *J* = 2.0 Hz, 1H), 8.02 (d, *J* = 8.8 Hz, 1H)

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 32.5, 35.2, 55.6, 68.3, 110.8, 114.7, 124.7, 129.8, 148.0, 164.3, 196.0

^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, $CDCl_3$) analysis of **P3** of substrate **13**



^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.16-2.22 (m, 1H), 2.36-2.41 (m, 1H), 2.56-2.64 (m, 1H), 2.92-3.00 (m, 1H), 3.86 (s, 3H), 4.95 (dd, *J* = 6.8, 3.6 Hz, 1H), 7.16 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.49-7.51 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 32.1, 34.8, 55.6, 67.4, 109.3, 122.0, 128.8, 132.3, 138.0, 160.0, 197.4

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3 B. T. Ngatcha, V. L. The, F. Labrie and D. Poirier, *J. Med. Chem.,* 2005, **48**, 5257-5268.

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