# Pd(II)/Zn Co-catalyzed Chemo-Selective Hydrogenation of α-Methylene-γ-Keto Carboxylic Acids

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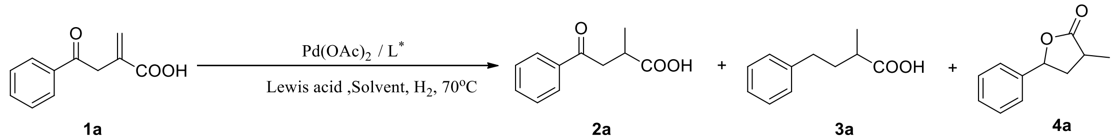
[b]Chongqing Academy of Chinese Materia Medica, Chongqing, 400065, China

***Table of Contents***

**A: Table 1. Reaction condition optimizations**

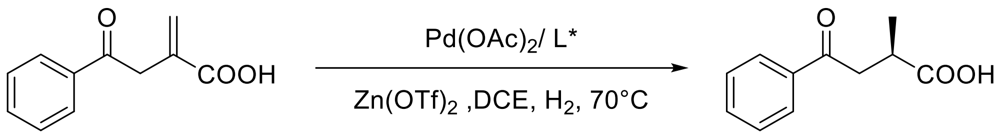



| Entry | Ligand | Additive | Solvent | Time (h) | Yield[b] (**2a**) | Yield[b] (**3a**) | Yield[b,c] (**4a**) |
|---|---|---|---|---|---|---|---|
| 1 | (±)-Binap | $Zn(OTf)_2$ | DCE | 8 | 96 | - | trace |
| 2 | $PPh_3$ | $Zn(OTf)_2$ | DCE | 24 | 70 | - | - |
| 3 | DPPF | $Zn(OTf)_2$ | DCE | 20 | 92 | - | - |
| 4 | DPPP | $Zn(OTf)_2$ | DCE | 14 | 97 | - | - |
| 5 | DPPE | $Zn(OTf)_2$ | DCE | 38 | 93 | - | - |
| 6 | DPPB | $Zn(OTf)_2$ | DCE | 15 | 99 | - | - |
| 7 | Xantphos | $Zn(OTf)_2$ | DCE | 36 | 64 | - | 31 |
| 8 | *o*-Phenanthroline | $Zn(OTf)_2$ | DCE | 24 | 72 | - | - |
| 9 | $PCy_3$ | $Zn(OTf)_2$ | DCE | 24 | 92 | - | - |
| 10 | DPPB | $Fe(OTf)_3$ | DCE | 7 | 87 | | 10 |
| 11 | DPPB | $Fe(OTf)_2$ | DCE | 10 | 97 | - | - |
| 12 | DPPB | $Cu(OTf)_2$ | DCE | 10 | 50 | 18 | 22 |
| 13 | DPPB | Cu(OTf) | DCE | 10 | 76 | - | 20 |
| 14 | DPPB | $AgBF_4$ | DCE | 7 | 75 | - | 19 |
| 15 | DPPB | AgOTf | DCE | 6 | 82 | 6 | 5 |
| 16 | DPPB | $Al(OTf)_3$ | DCE | 7 | 48 | 19 | 26 |
| 17 | DPPB | $ZnI_2$ | DCE | 48 | - | - | - |
| 18 | DPPB | - | DCE | 60 | 20 | - | - |
| 19 | DPPB | $Zn(OTf)_2$ | Toluene | 10 | 95 | - | Trace |
| 20 | DPPB | $Zn(OTf)_2$ | TFE | 6 | 53 | - | 41 |
| 21 | DPPB | $Zn(OTf)_2$ | 1,4-dioxane | 16 | 98 | - | Trace |
| 22 | DPPB | $Zn(OTf)_2$ | $CH_3CN$ | 24 | 92 | - | - |
| 23[d] | DPPB | $Zn(OTf)_2$ | DCE | 15 | 99 | - | - |
| 24[e] | DPPB | $Zn(OTf)_2$ | DCE | 18 | 98 | - | - |
| 25[f] | DPPB | $Zn(OTf)_2$ | DCE | 45 | 98 | - | - |
| 26[g)] | BPA | $Zn(OTf)_2$ | DCE | 10 | - | 98 | - |
| 27[g)] | BPA | - | DCE | 15 | - | 97 | - |
| 28 | (*R*,*S*)-PPF-$P^tBu_2$ | $Zn(OTf)_2$ | DCE | 12 | - | - | 96 |
| 29 | (*R*,*S*)-PPF-$P^tBu_2$ | - | DCE | 24 | 68 | - | - |
| 30 | HOAc | $Zn(OTf)_2$ | DCE | 48 | 48 | 34 | 15 |
| 31 | Diethyl phosphite | $Zn(OTf)_2$ | DCE | 48 | 15 | - | - |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 32 | Triphenyl phosphite | $Zn(OTf)_2$ | DCE | 48 | 19 | trace | - |
| 33[g)] | $H_3PO_4$ | $Zn(OTf)_2$ | DCE | 18 | - | 92 | trace |
| 34[g)] | $NaH_2PO_4$ | $Zn(OTf)_2$ | DCE | 24 | - | 91 | - |
| 35[g)] | $Na_2HPO_4$ | $Zn(OTf)_2$ | DCE | 22 | - | 90 | trace |
| 36[g)] | $K_3PO_4$ | $Zn(OTf)_2$ | DCE | 24 | 20 | - | - |

[a]Reaction conditions: $Pd(OAc)_2$ (0.01 mmol), Lewis acid (0.02 mmol), and ligand (0.012 mmol) in DCE (2 mL) was stirred at room temperature for 30 min under Argon. **1a** (0.2 mmol) were added, and the reaction mixture in 1 bar $H_2$ was stirred at 70 °C for indicated period of time. [b]Isolated yields. [c]*anti*/*syn* = 1.5/1.0. [d]The reaction was performed at 60 °C. [e]The reaction was performed at 50 °C. [f]The reaction was performed at 40 °C. [g)]Bronsted acid

**B: Table 2. The asymmetric hydrogenation of α-methylene-γ-keto carboxylic acids using different ligands**

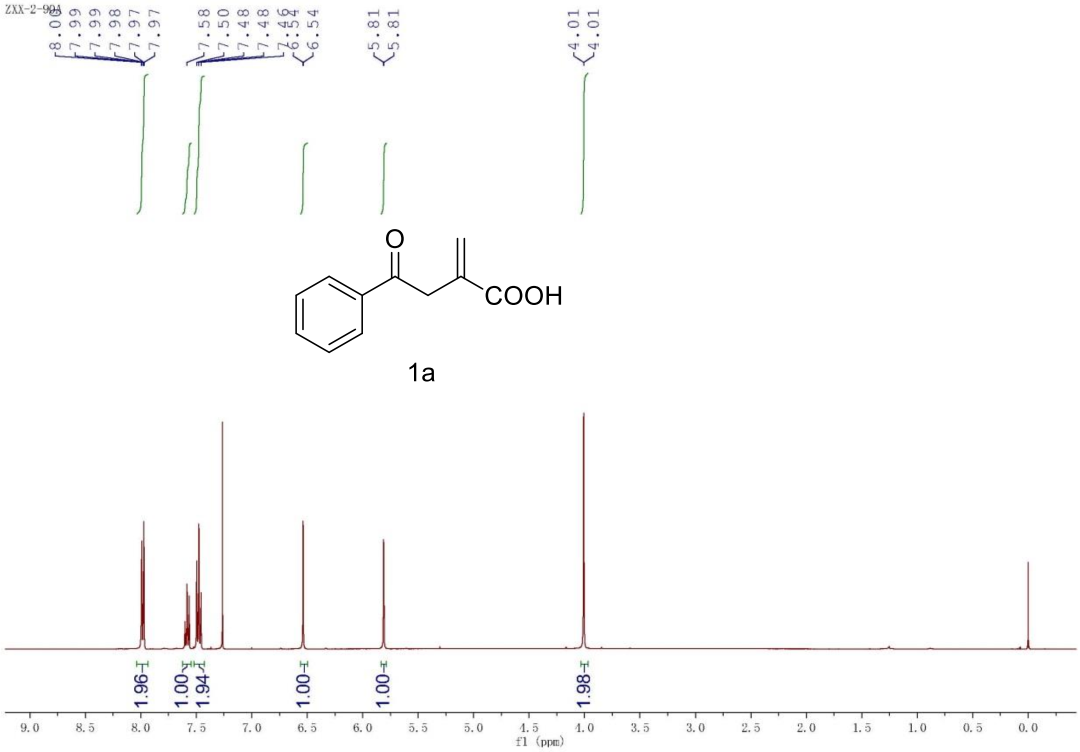


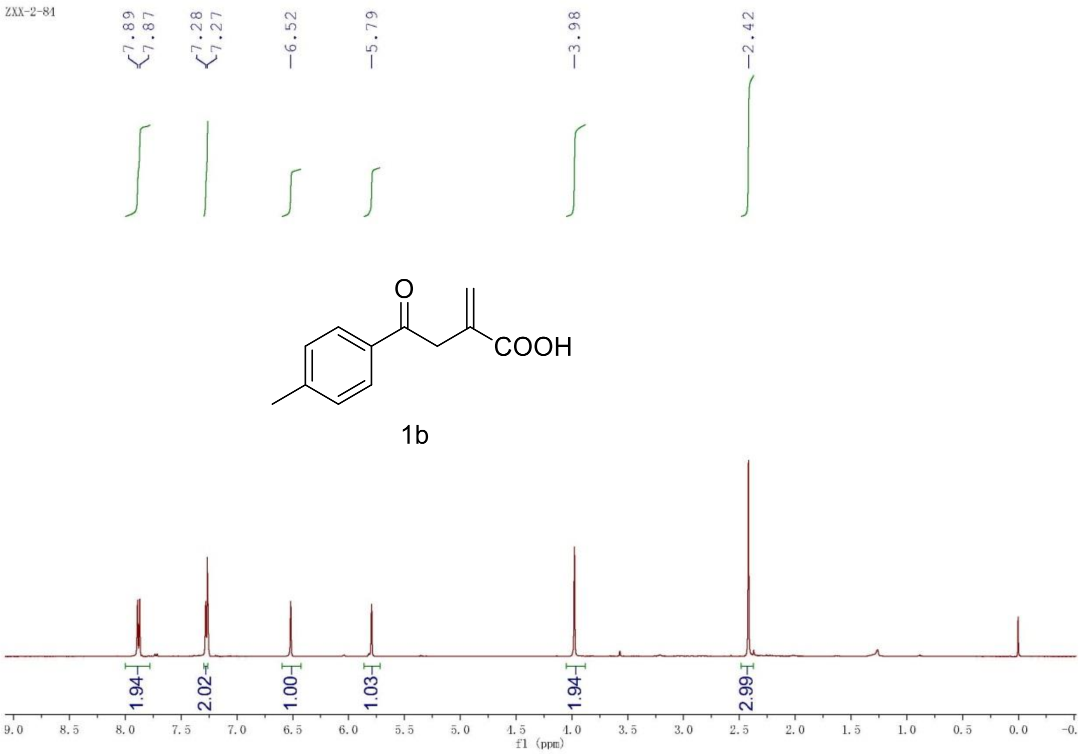

| Entry | Solvent | Ligand | Time (h) | Yield(%) | Ee(%) |
|---|---|---|---|---|---|
| 1 | DCE | (*R*)-BINAP | 12 | 98 | 21 |
| 2 | DCE | (*R*)-OMe-BIPHEP | 12 | 92 | 35 |
| 3 | DCE | (*R*)-SEGPHOS | 12 | 89 | 37 |
| 4 | DCE | (*R*)-MONOPHOS | 48 | 75 | 3 |
| 5 | DCE | (*R*)-Xyl-SDP | 11 | 98 | 43 |
| 6 | DCE | (*R*,*S*)-Ph-Bn-SIPHOX | 30 | 81 | 10 |
| 7 | DCE | (*S*,*S*)-Et-FerroTANE | 11 | 97 | 19 |
| 8 | DCE | (*R*)-DIFLUORPHOS | 15 | 94 | 5 |
| 9 | DCE | (*R*)-P-PHOS | 10 | 98 | 15 |
| 10 | DCE | (*R*)-BDPP | 10 | 98 | 9 |
| 11 | DCE | (*S*)-SYNPHOS | 10 | 81 | 41 |
| 12 | DCE | (*R*)-DIOP | 30 | 88 | 3 |
| 13 | DCE | (*R*)-An-SDP | 10 | 98 | 17 |
| 14[a] | DCE | (*R*)-Xyl-SDP | 11 | 98 | 45 |

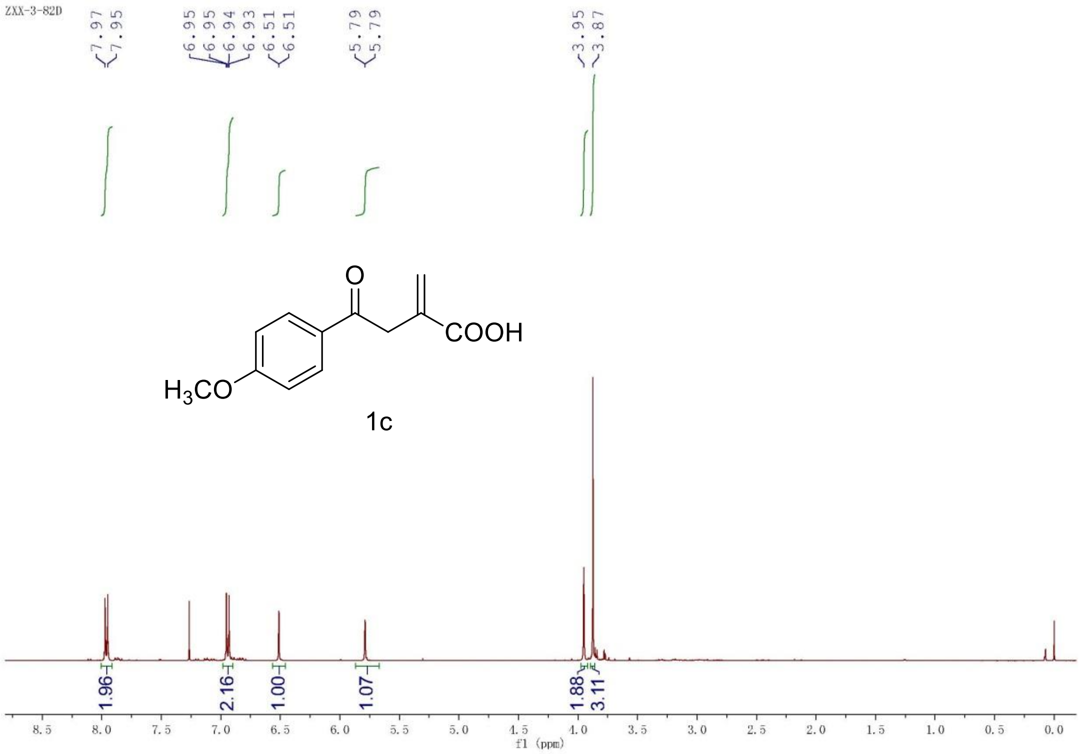
[a]Reaction conditions: $Pd(OAc)_2$ (0.01 mmol), Lewis acid (0.02 mmol), and ligand (0.012 mmol) in DCE (2 mL) was stirred at room temperature for 30 min under Argon. **1a** (0.2 mmol) were added, and the reaction mixture in 1 bar $H_2$ was stirred at 70 °C for indicated period of

time. [b]The reaction was performed at 60 °C.

**C: NMR spectra of substrates**







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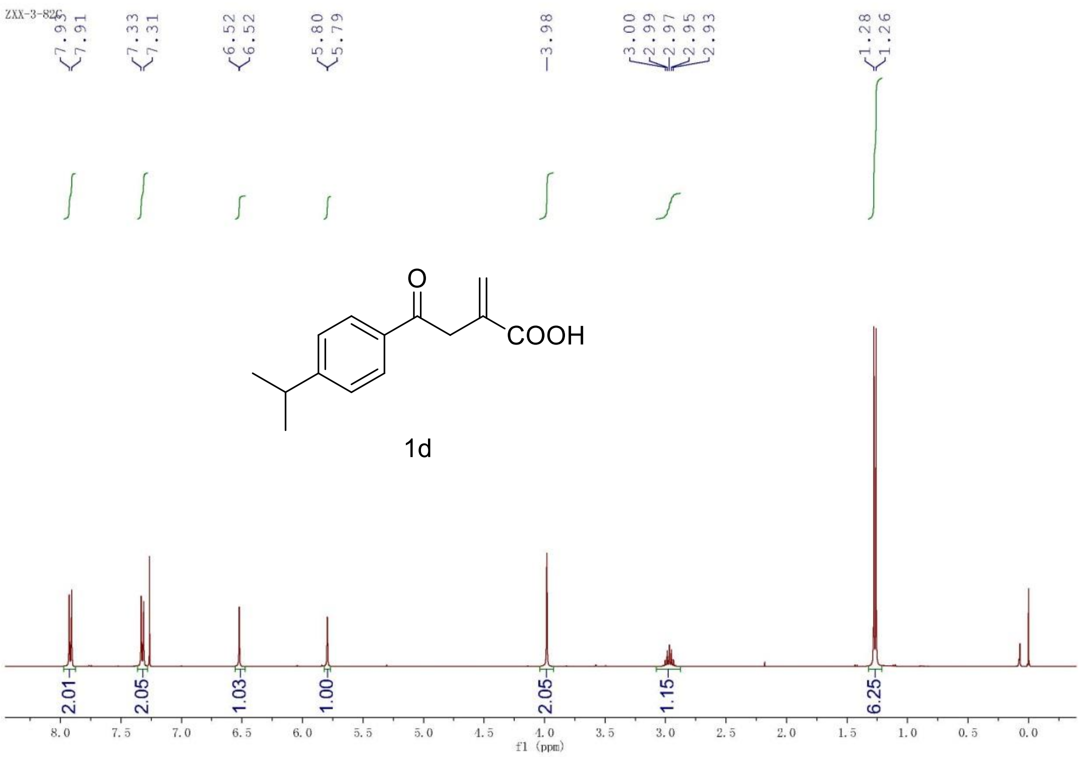

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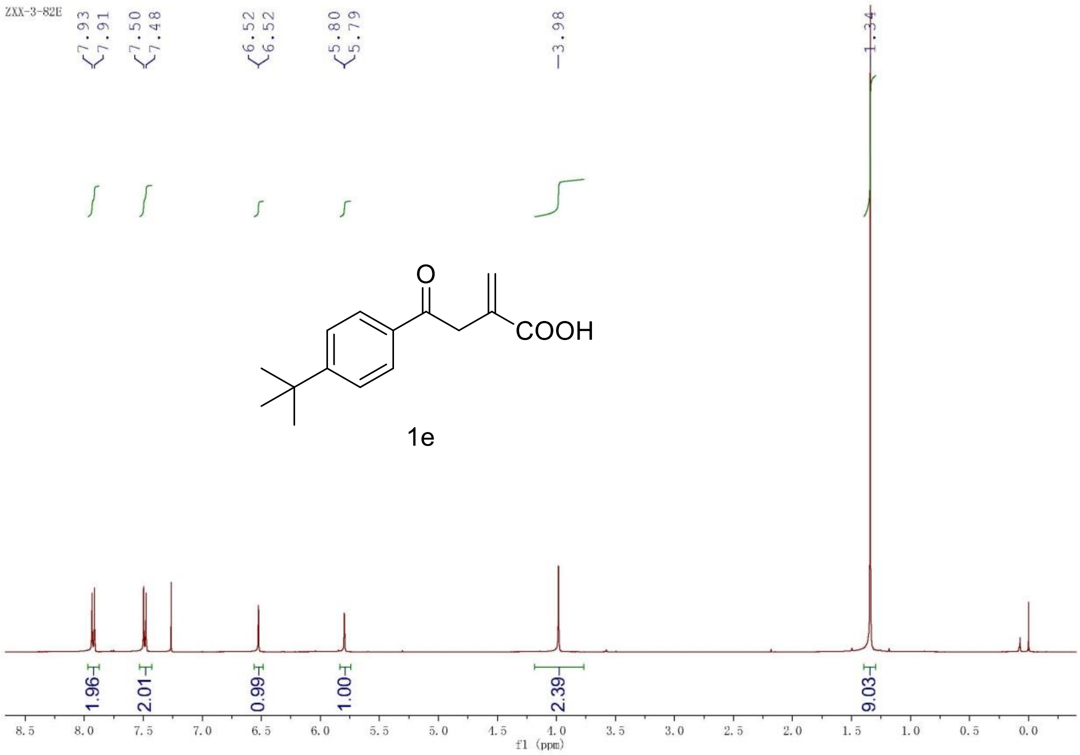
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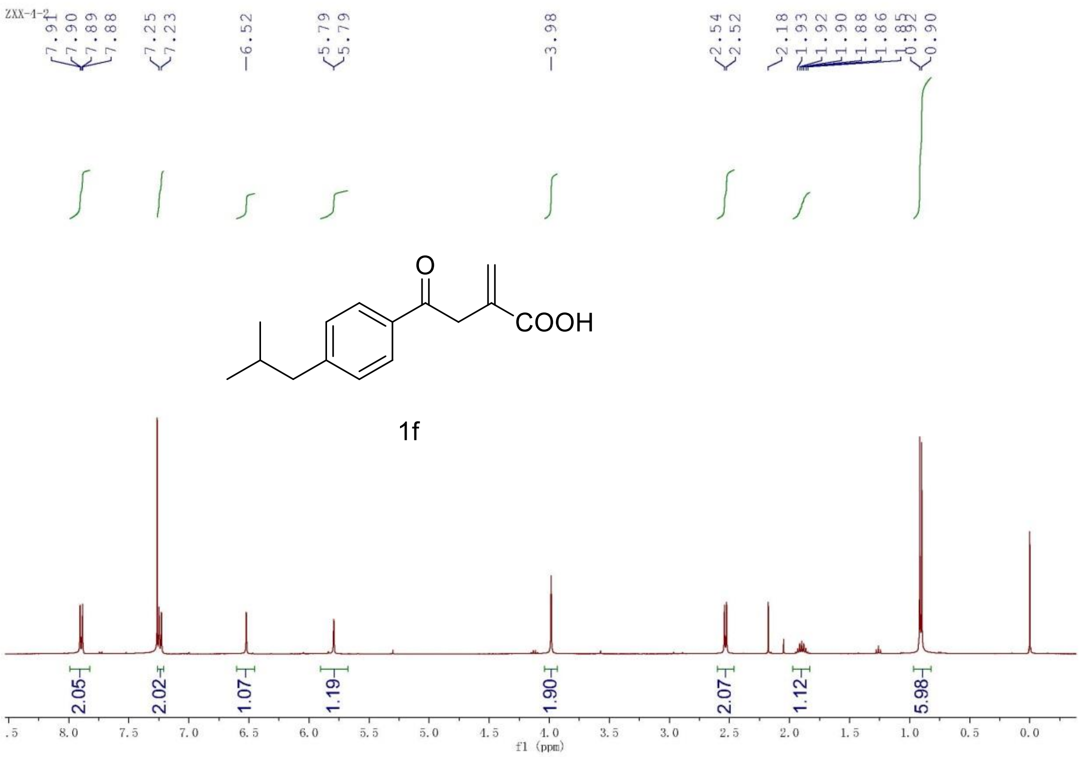
7.91
7.50
7.48
6.52
6.52
5.80
5.79
3.98
1.34
O
COOH
1.96
2.01
0.99
1.00
2.39
9.03
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
1e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7.23
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5.79
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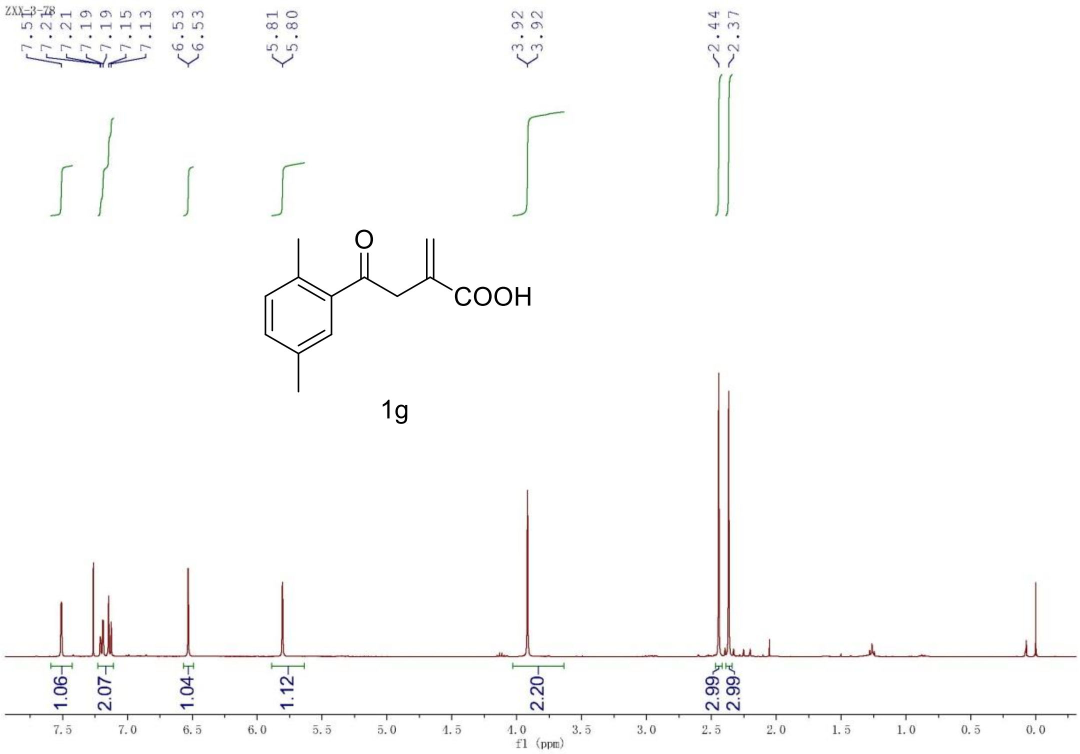
3.98
2.54
2.52
2.18
1.93
1.92
1.90
1.88
1.86
1.85
0.92
0.90
O
COOH
2.05
2.02
1.07
1.19
1.90
2.07
1.12
5.98
.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
1f



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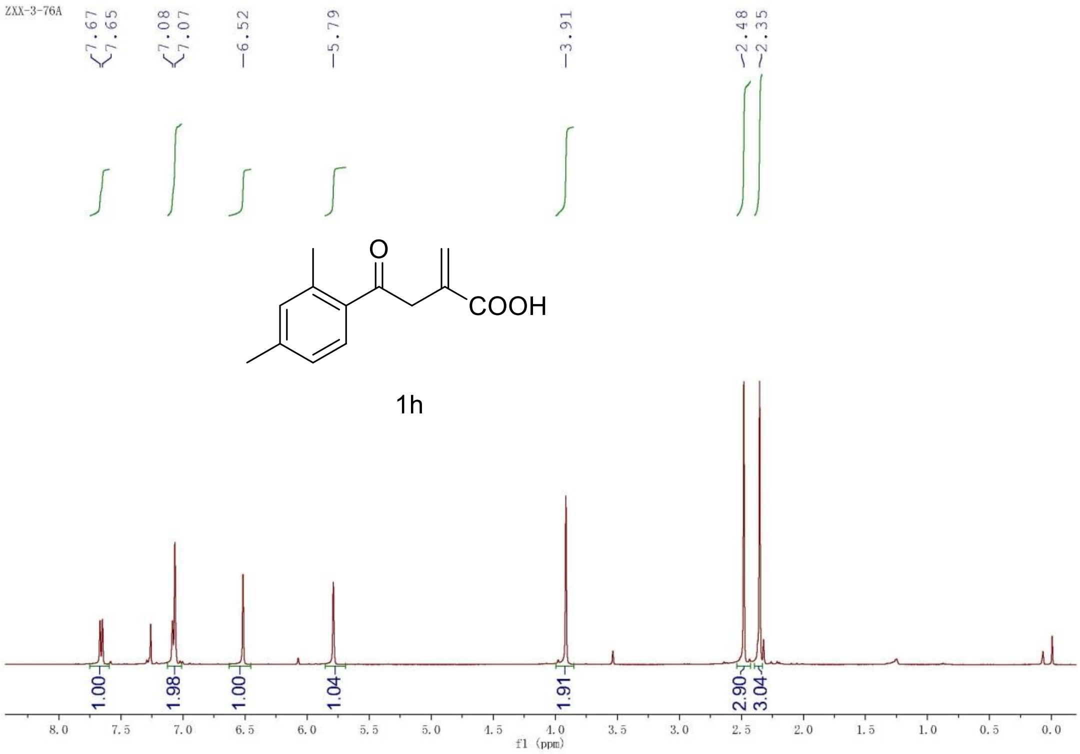

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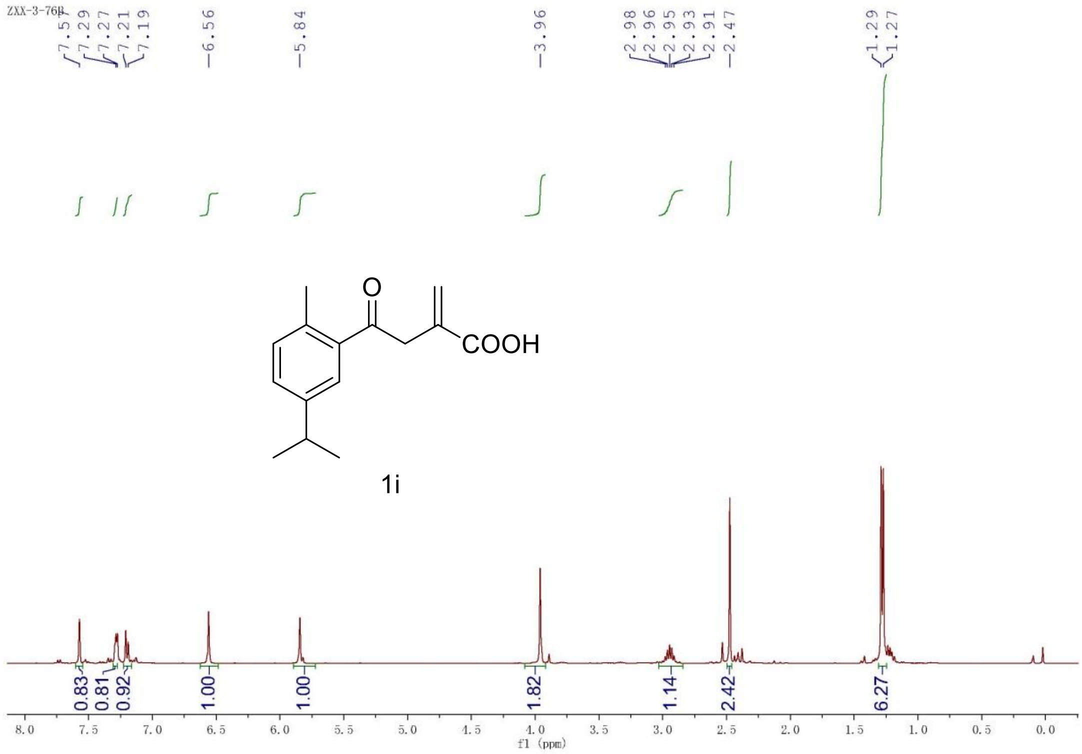
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7.19
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3.96
2.98
2.96
2.95
2.93
2.91
2.47
1.29
1.27
O
COOH
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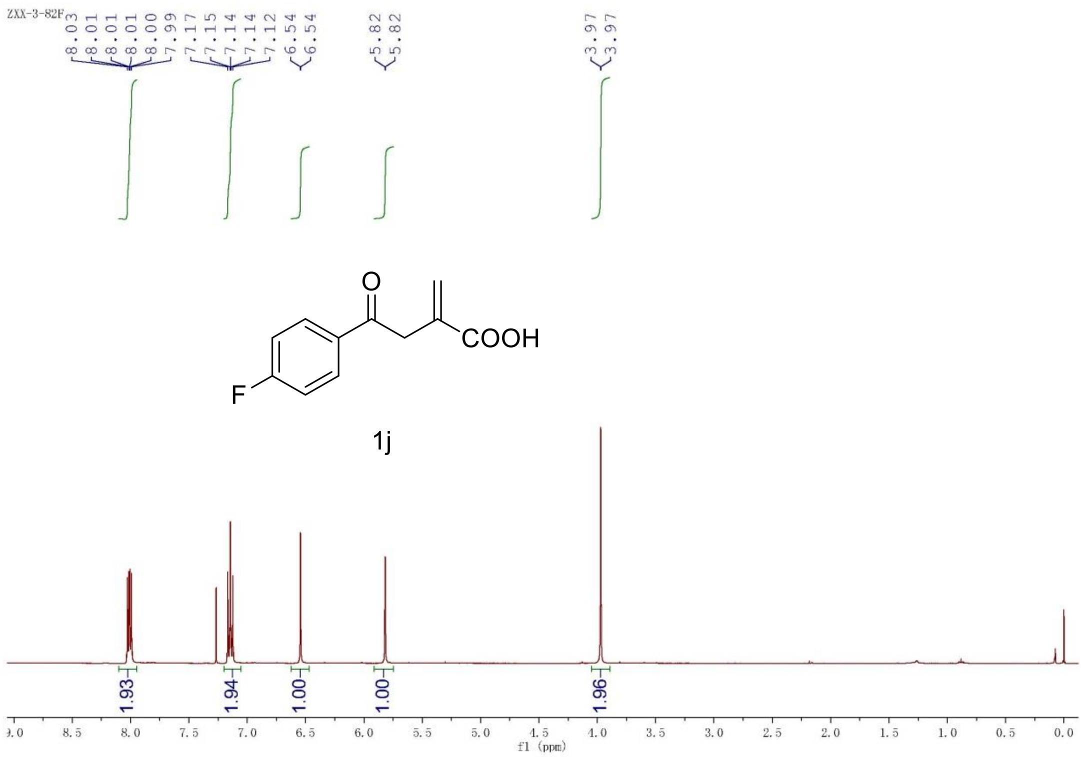
0.81
0.92
1.00
1.00
1.82
1.14
2.42
6.27
f1 (ppm)

1i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8.01
8.01
8.01
8.00
7.99
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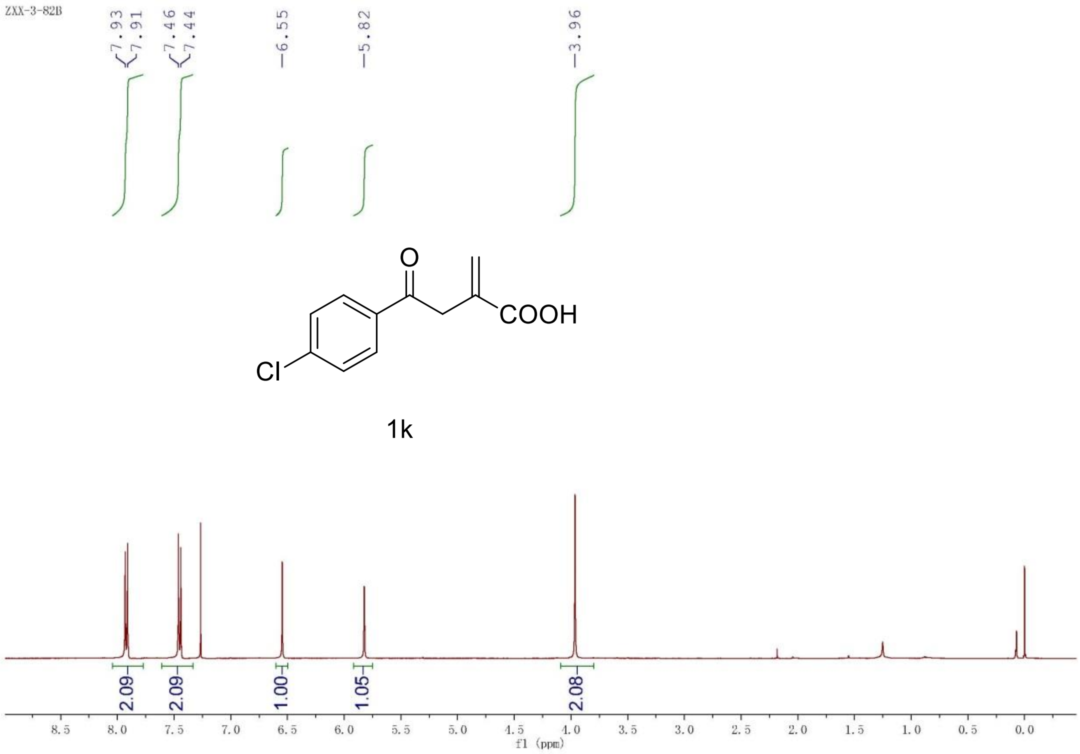
7.15
7.14
7.14
7.12
6.54
6.54
5.82
5.82
3.97
3.97
O
COOH
F
1.93
1.94
1.00
1.00
1.96
f1 (ppm)

1j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5.82
3.96
O
COOH
Cl
1k
2.09
2.09
1.00
1.05
2.08
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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2.0
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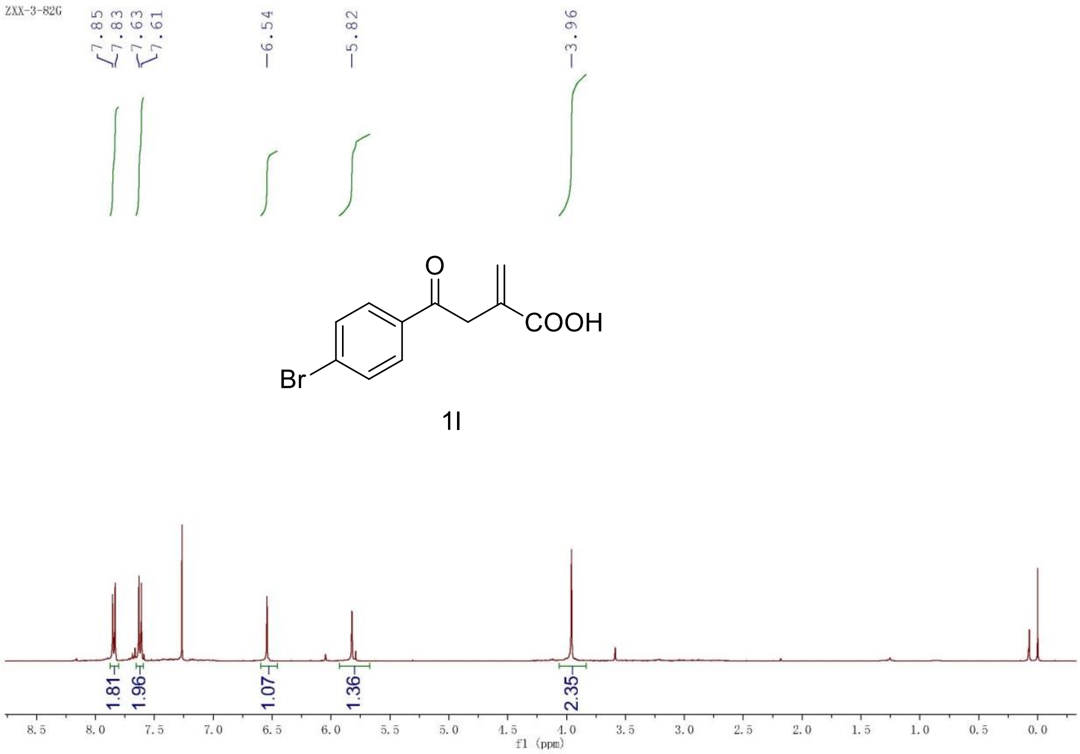
1.0
0.5
0.0
f1 (ppm)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7.61
6.54
5.82
3.96
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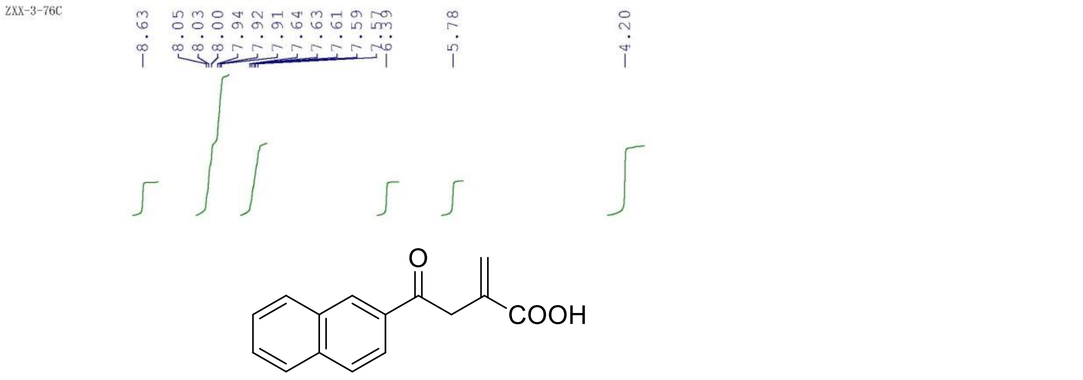
COOH
Br
1l
1.81
1.96
1.07
1.36
2.35
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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8.05
8.03
8.00
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7.91
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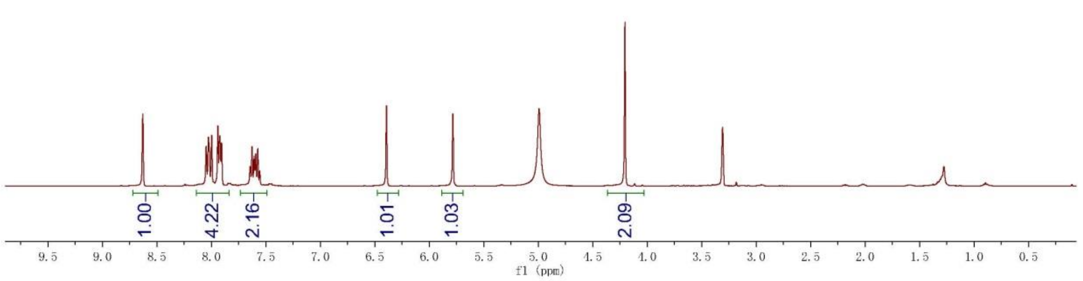
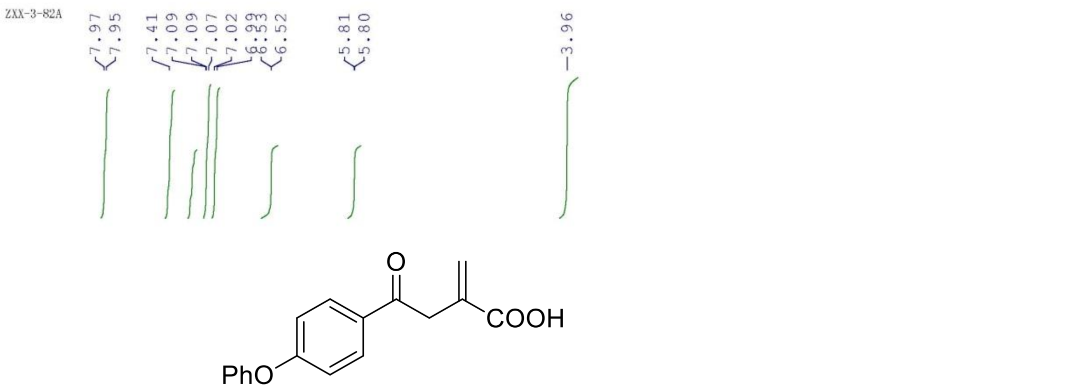
7.63
7.61
7.59
7.57
6.39
5.78
4.20
O
COOH

1m


1.00
4.22
2.16
1.01
1.03
2.09
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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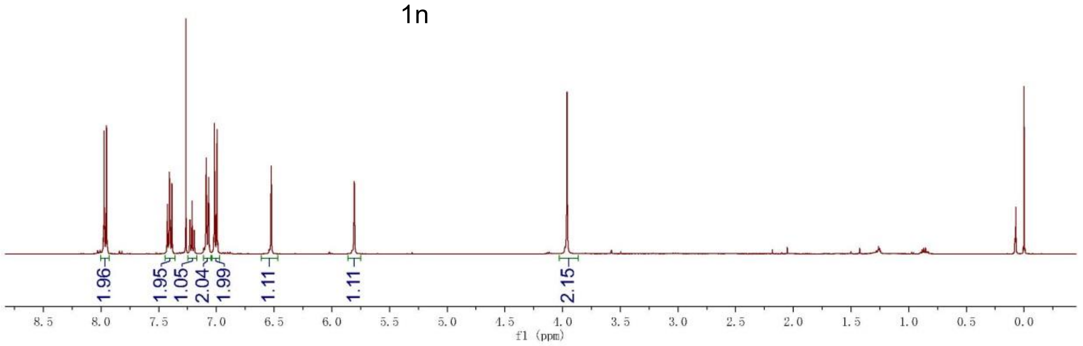
7.95
7.41
7.09
7.09
7.07
7.02
6.99
6.53
6.52
5.81
5.80
3.96
O
COOH
PhO

1n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1.95
1.05
2.04
1.99
1.11
1.11
2.15
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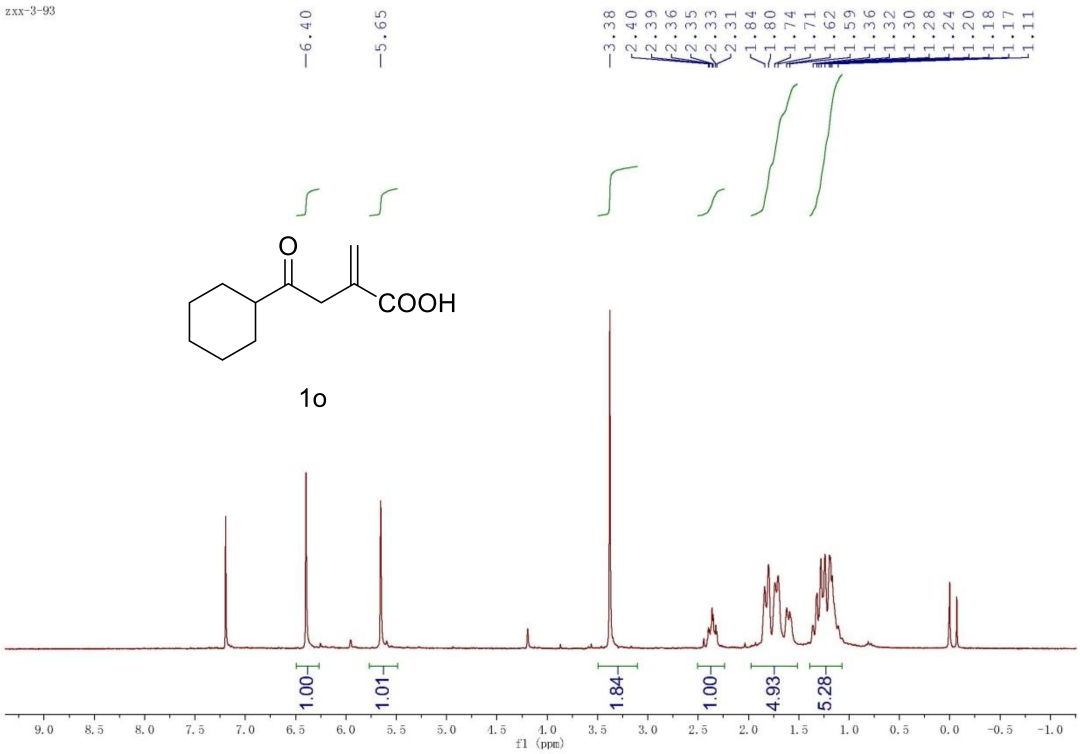
f1 (ppm)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2.35
2.33
2.31
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1.80
1.74
1.71
1.62
1.59
1.36
1.32
1.30
1.28
1.24
1.20
1.18
1.17
1.11
COOH
O
1o
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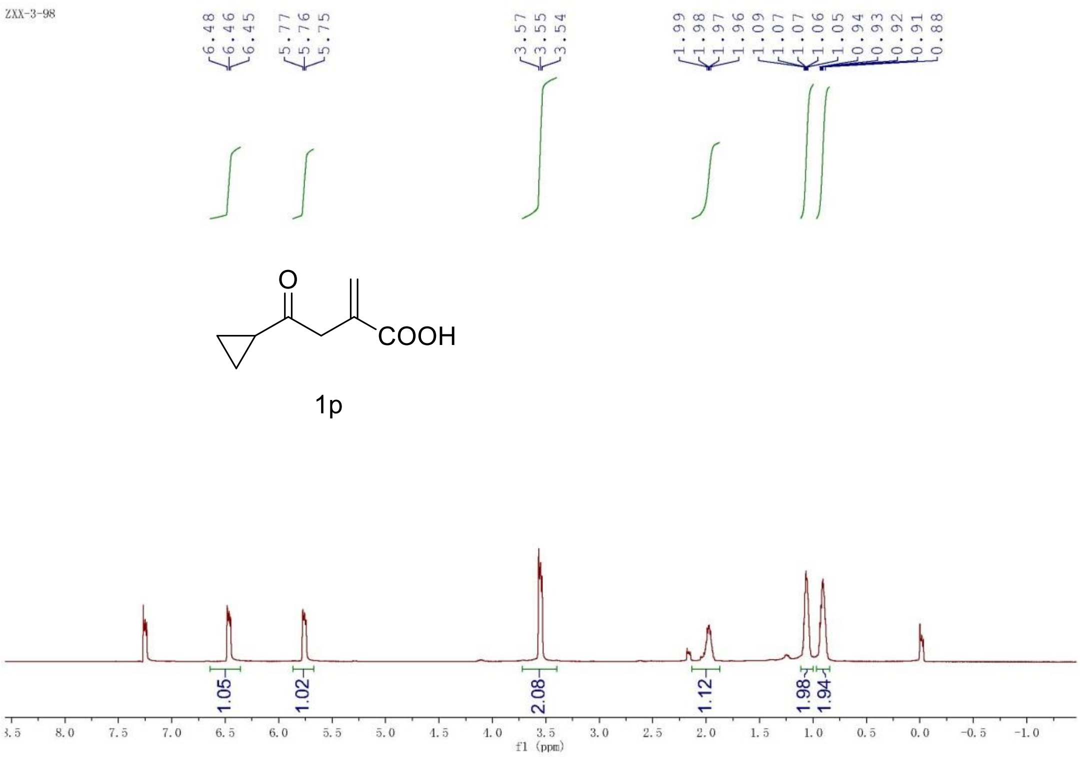
1.01
1.84
1.00
4.93
5.28
f1 (ppm)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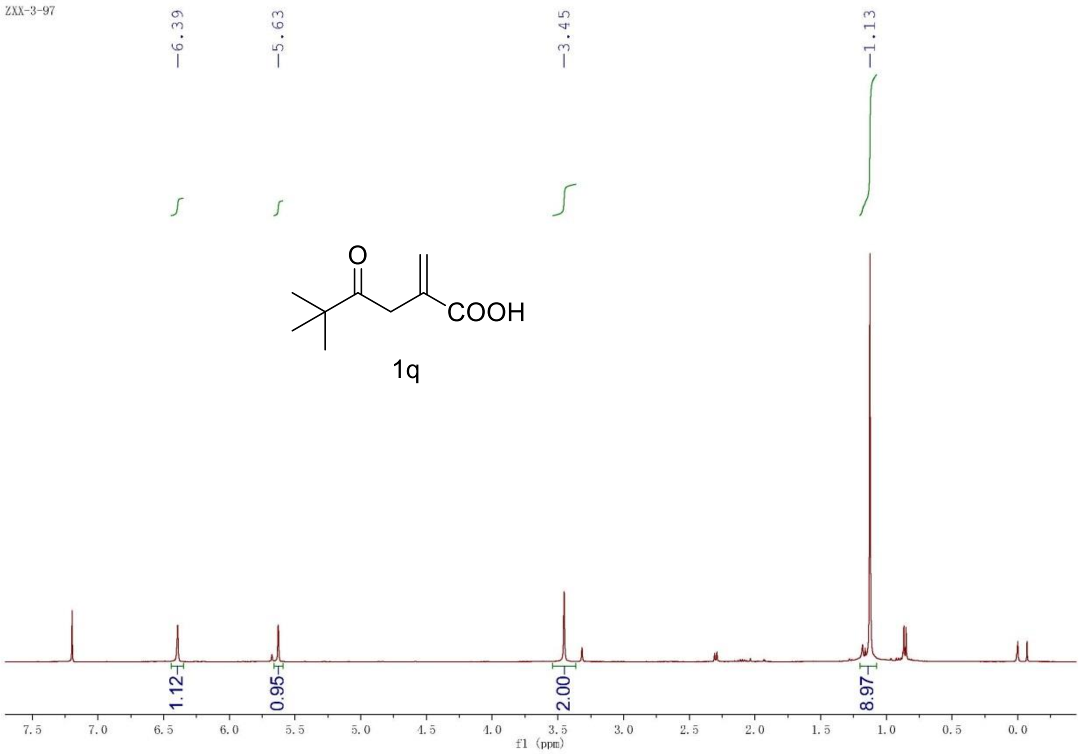
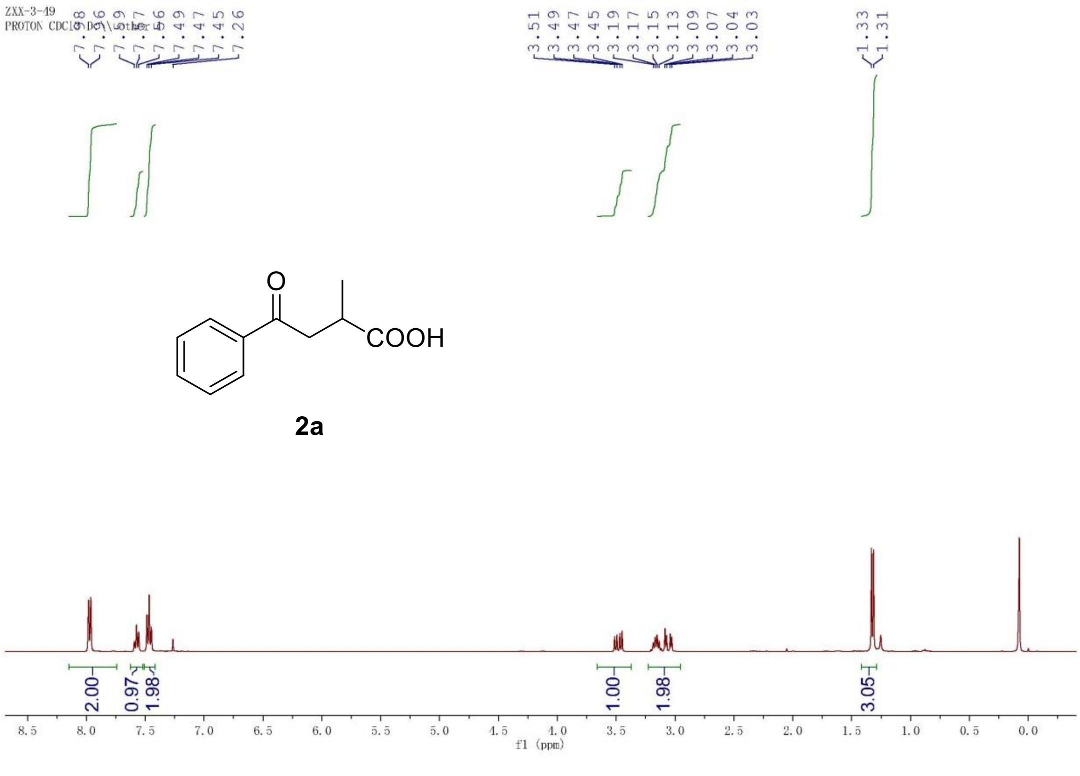
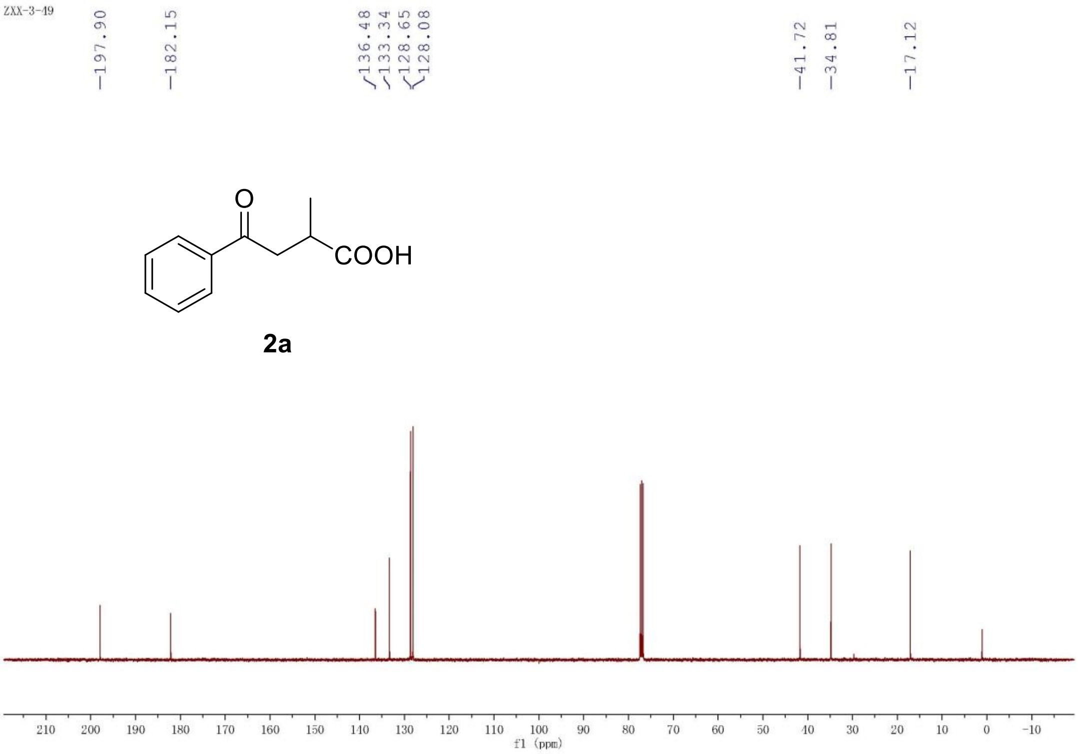
1.98
1.97
1.96
1.09
1.07
1.06
1.05
0.94
0.93
0.92
0.91
0.88
O
COOH
1p
1.05
1.02
2.08
1.12
1.98
1.94
f1 (ppm)




**D: NMR Spectra of Products**

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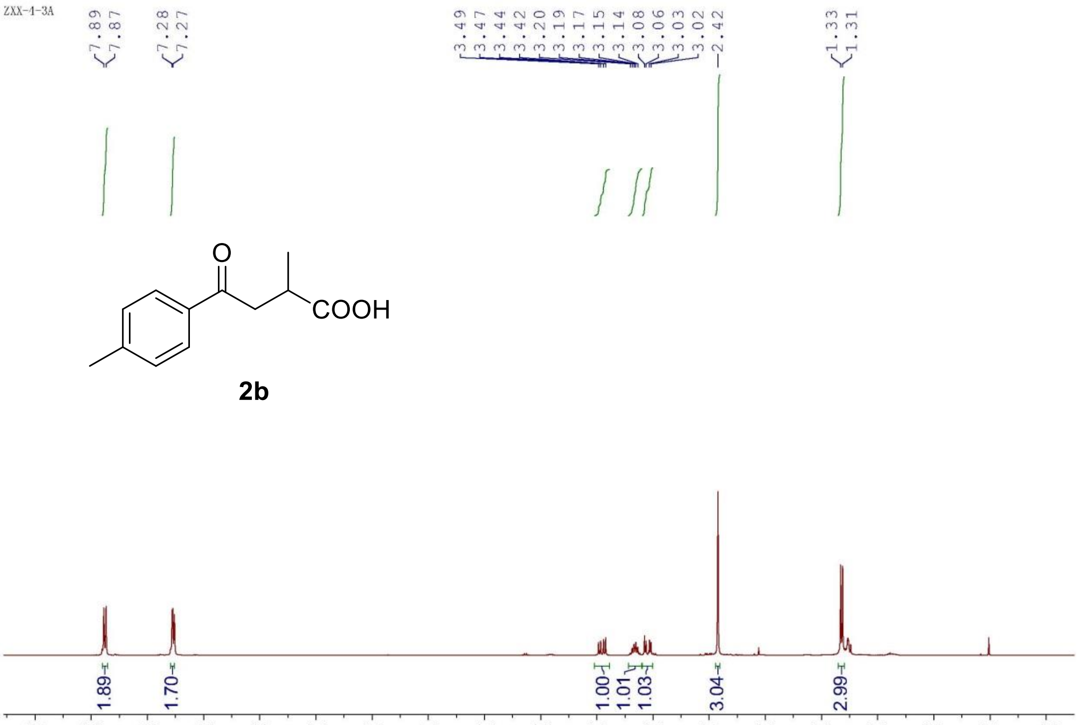
128.08
41.72
34.81
17.12
COOH
2a
f1 (ppm)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7.27
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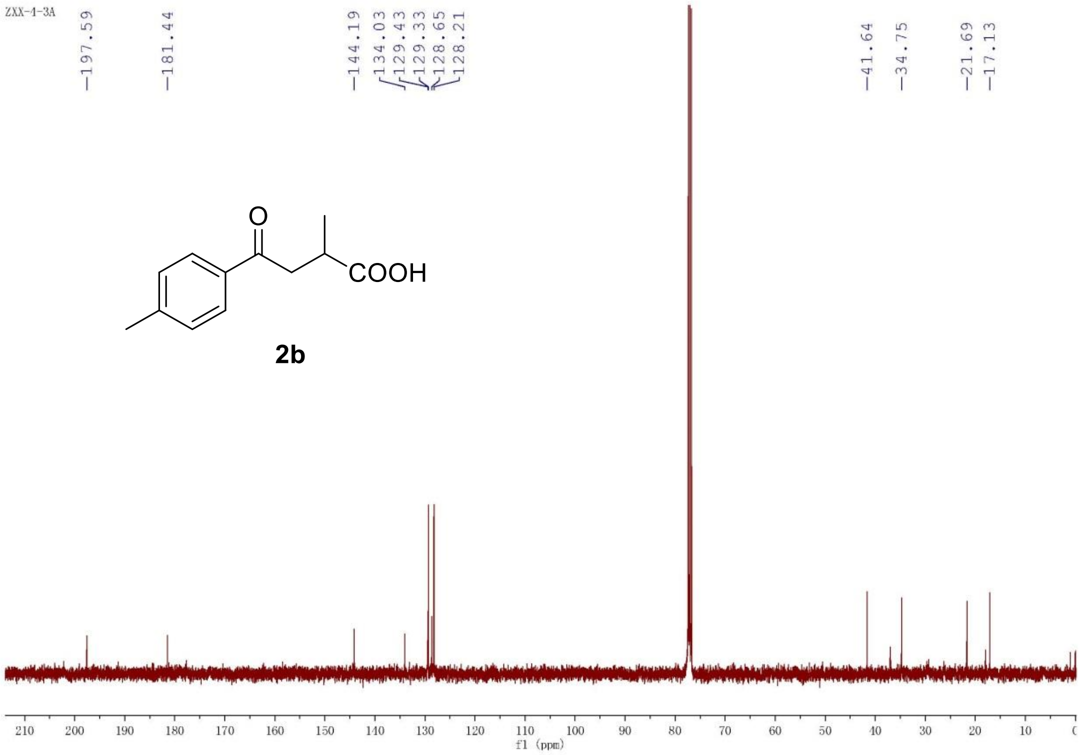
3.47
3.44
3.42
3.20
3.19
3.17
3.15
3.14
3.08
3.06
3.03
3.02
2.42
1.33
1.31
COOH
2b
1.89
1.70
1.00
1.01
1.03
3.04
2.99
f1 (ppm)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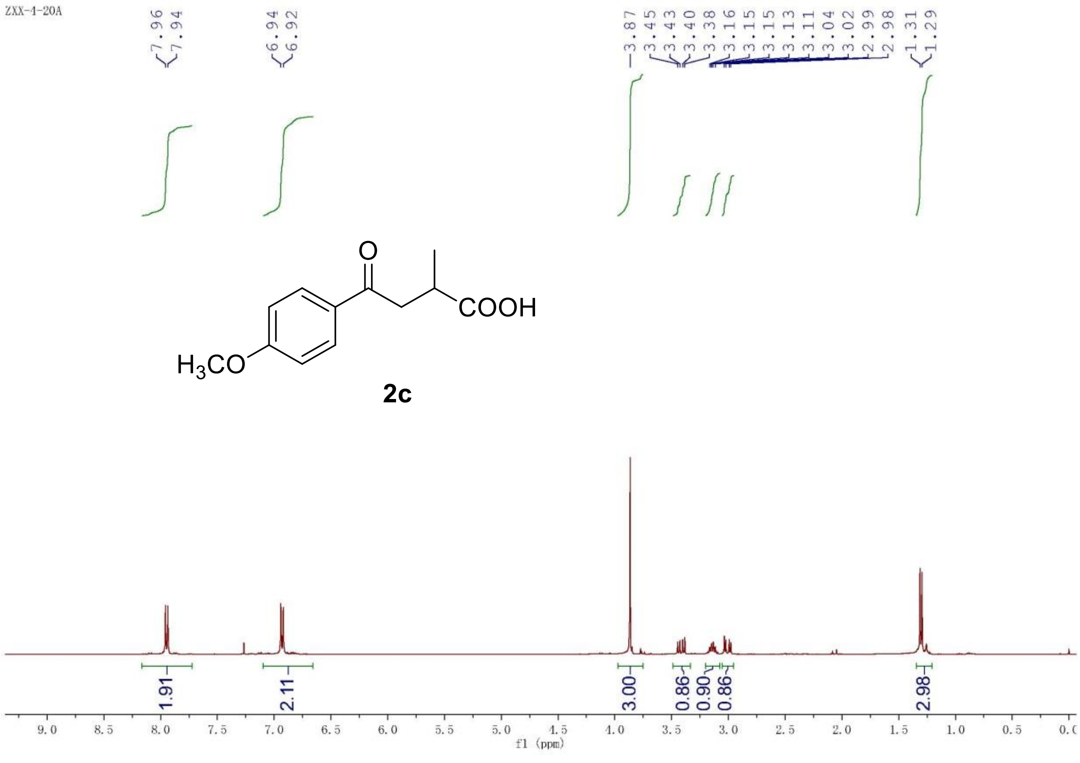
181.44
144.19
134.03
129.43
129.33
128.65
128.21
41.64
34.75
21.69
17.13
COOH
2b
f1 (ppm)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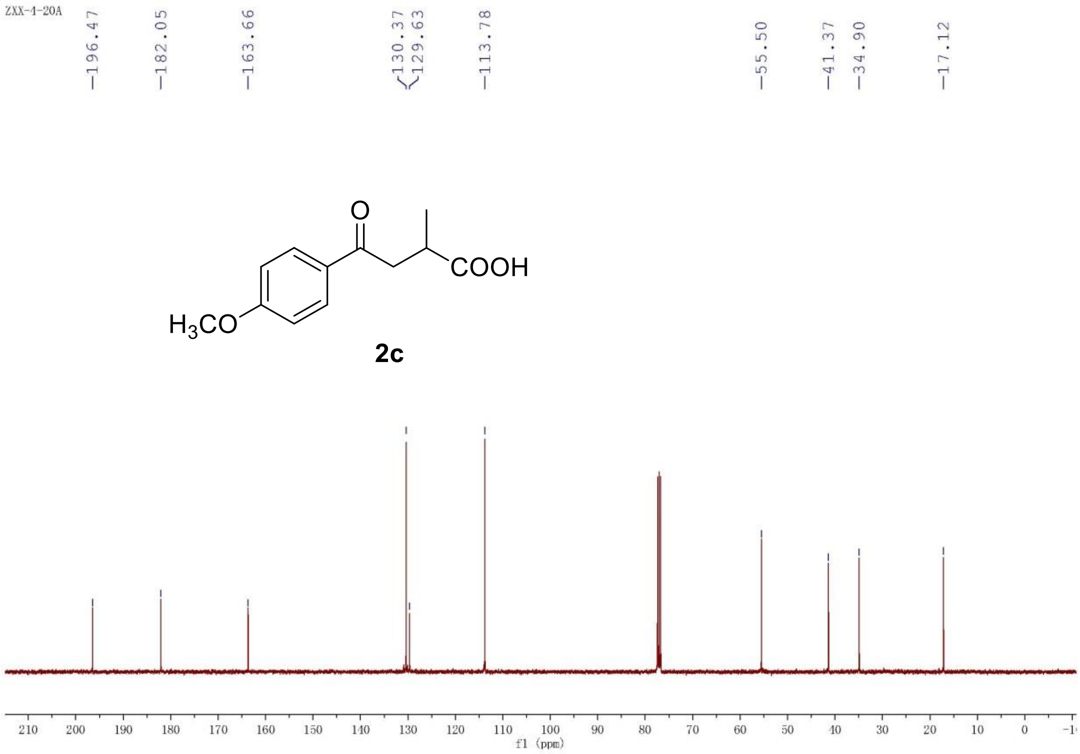
3.15
3.13
3.11
3.04
3.02
2.99
2.98
1.31
1.29
COOH
2c
1.91
2.11
3.00
0.86
0.90
0.86
2.98
f1 (ppm)



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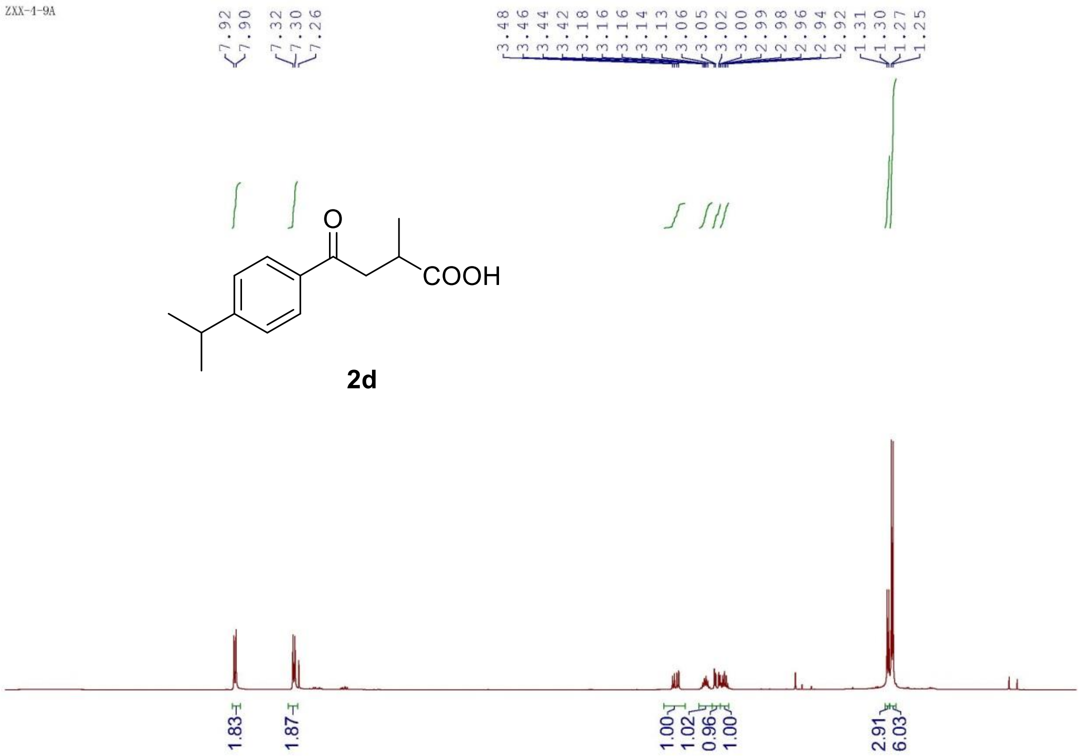
182.05
163.66
130.37
129.63
113.78
55.50
41.37
34.90
17.12
O
COOH
$H_3CO$
2c
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

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7.90
7.32
7.30
7.26
3.48
3.46
3.44
3.42
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3.16
3.14
3.13
3.06
3.05
3.02
3.00
2.99
2.98
2.96
2.94
2.92
1.31
1.30
1.27
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2d
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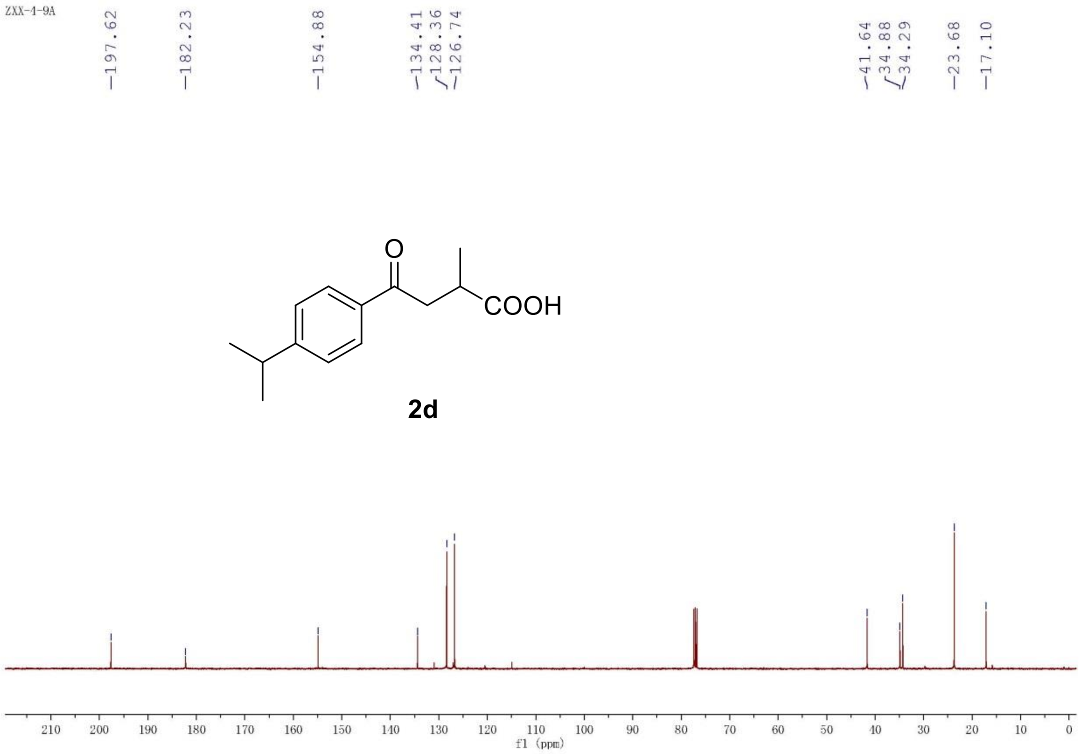
1.00
2.91
6.03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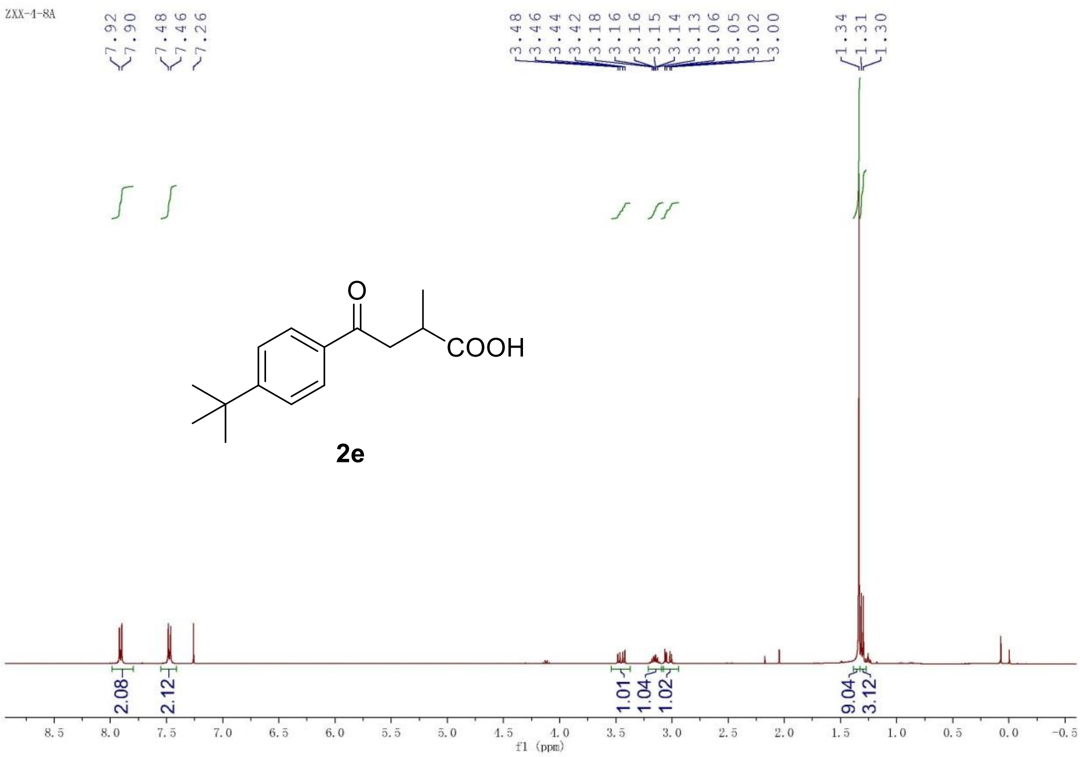
f1 (ppm)

**2d**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7.90
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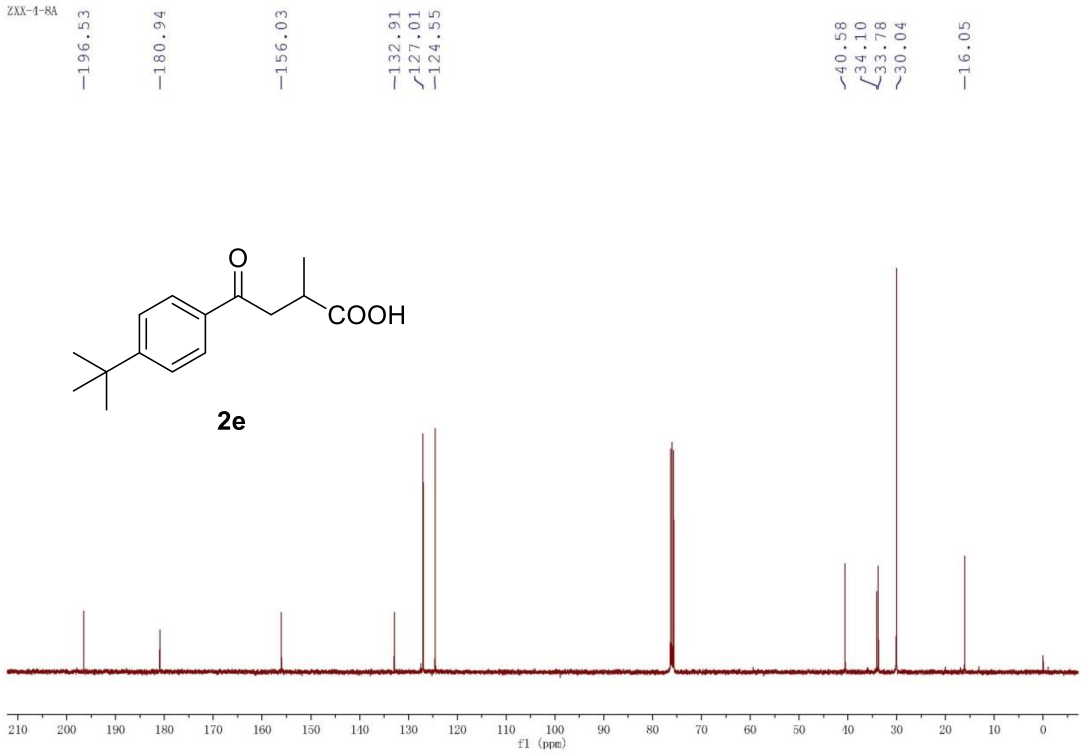
7.46
7.26
3.48
3.46
3.44
3.42
3.18
3.16
3.15
3.14
3.13
3.06
3.05
3.02
3.00
1.34
1.31
1.30
O
COOH
2.08
2.12
1.01
1.04
1.02
9.04
3.12
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

**2e**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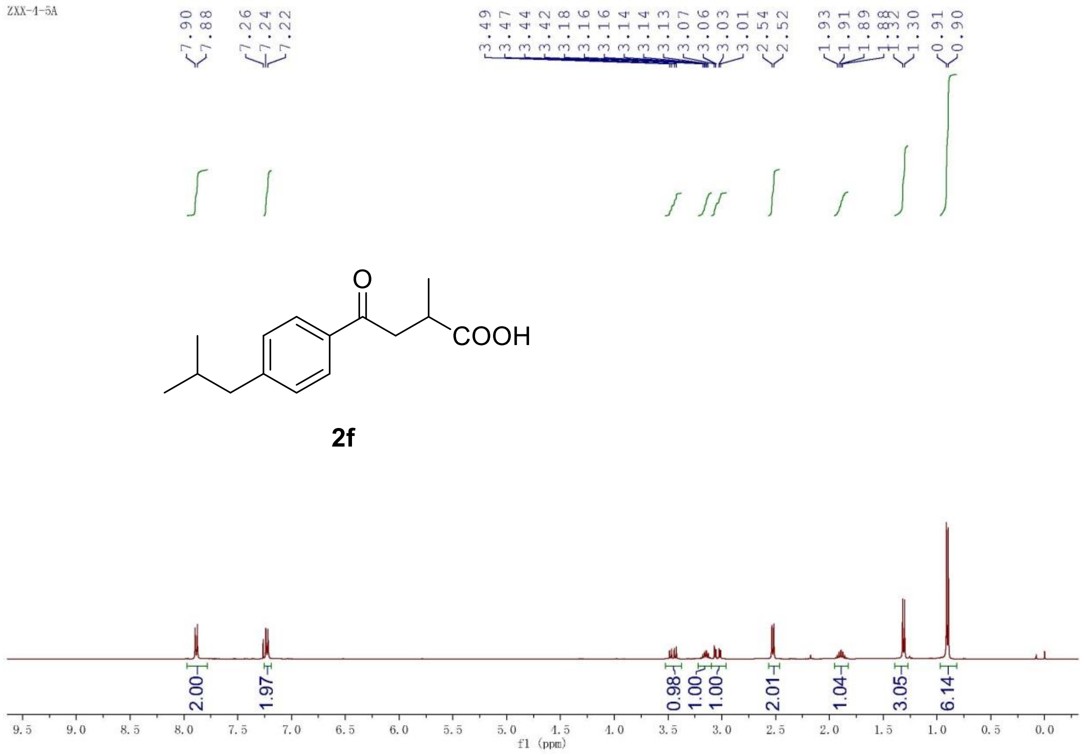
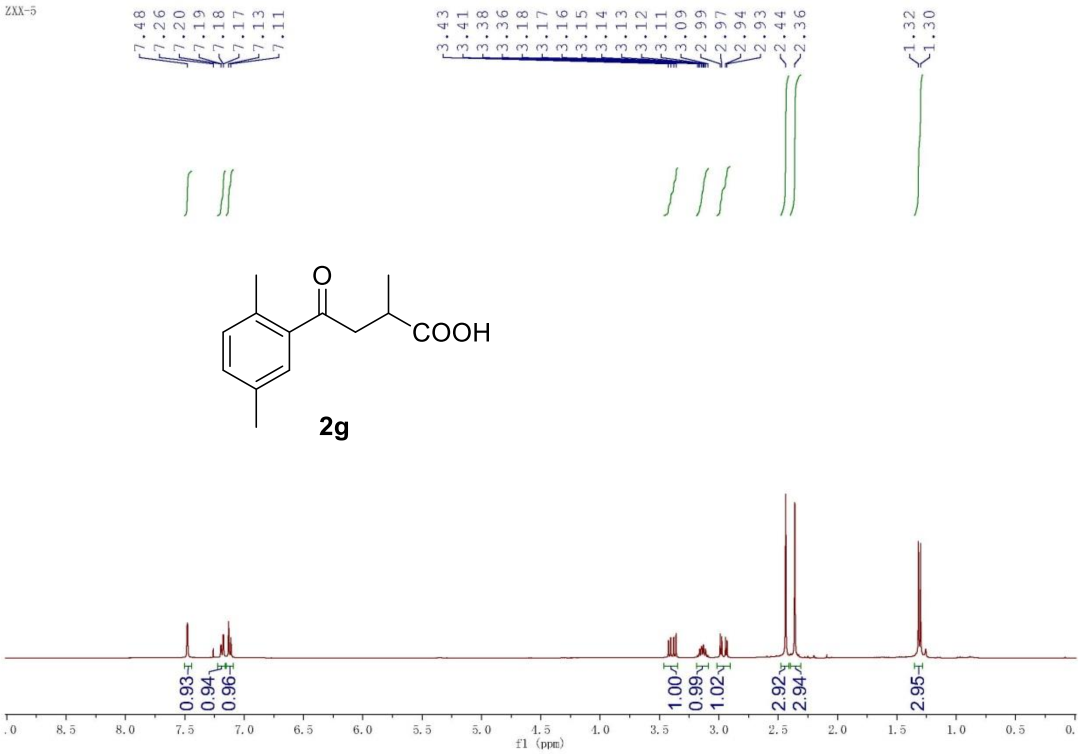
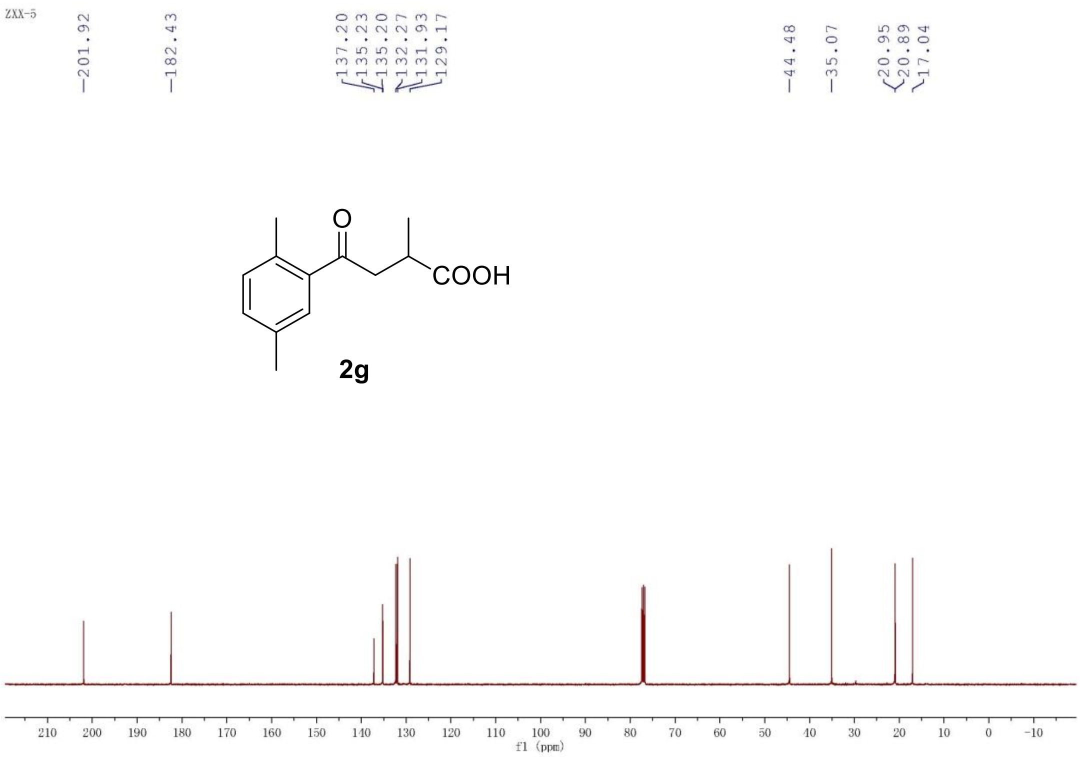
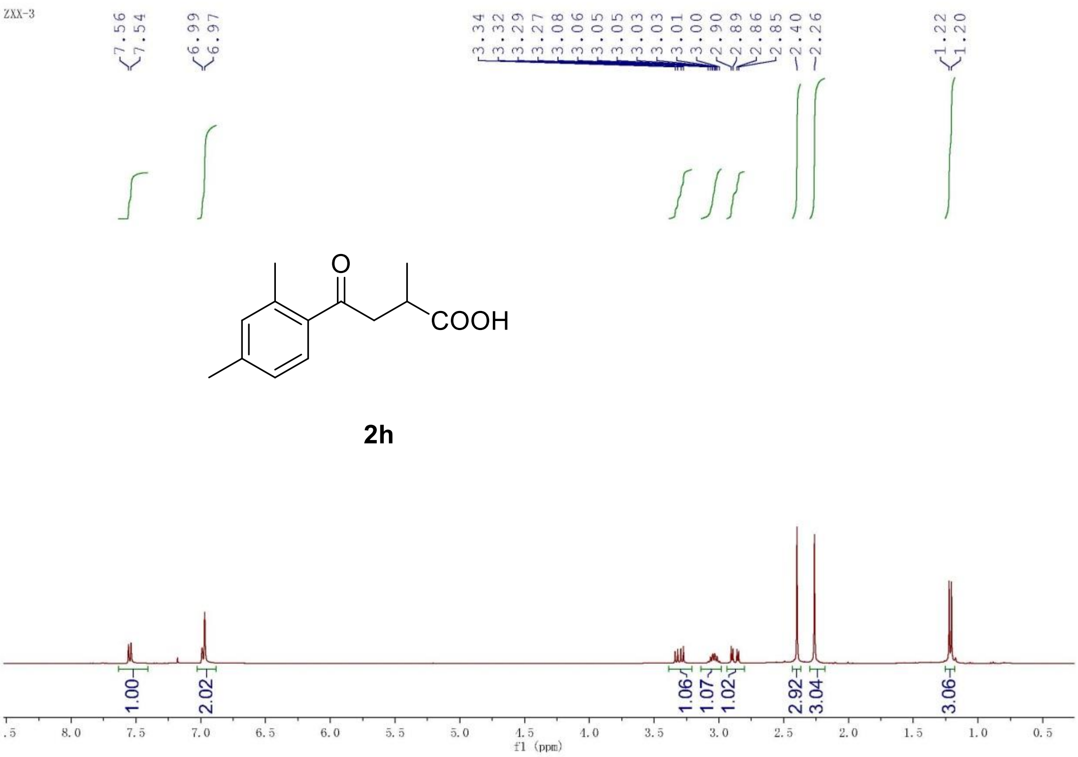
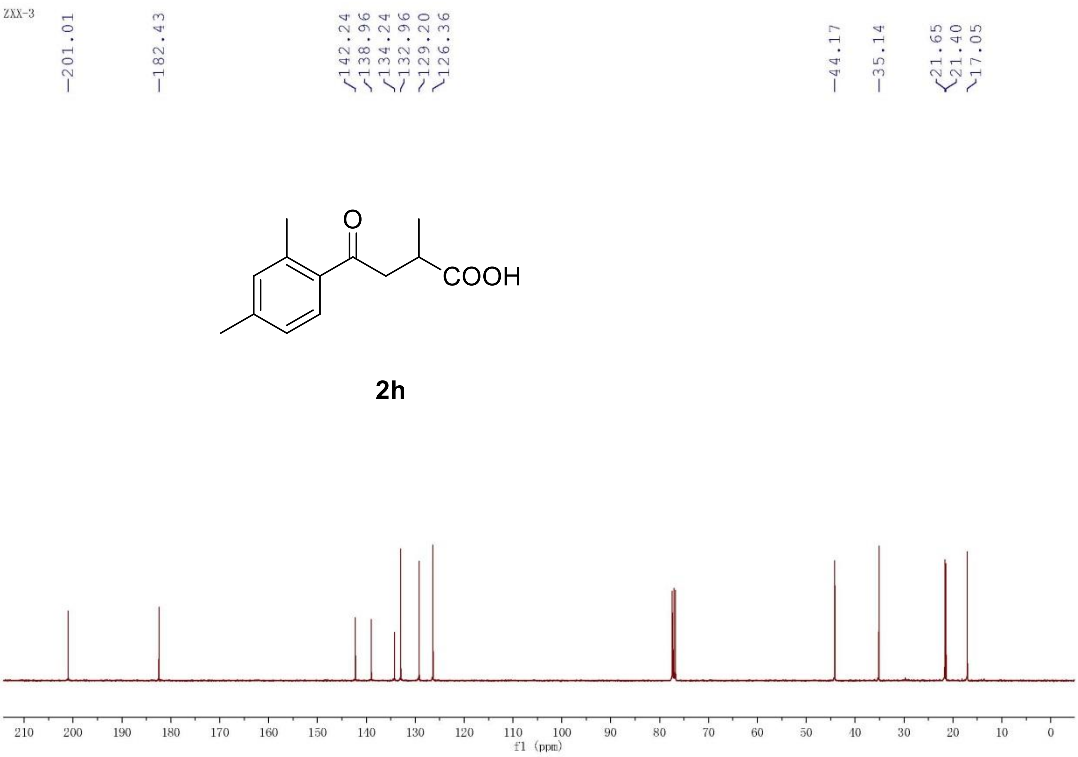
196.53
180.94
156.03
132.91
127.01
124.55
40.58
34.10
33.78
30.04
16.05
COOH
2e
f1 (ppm)

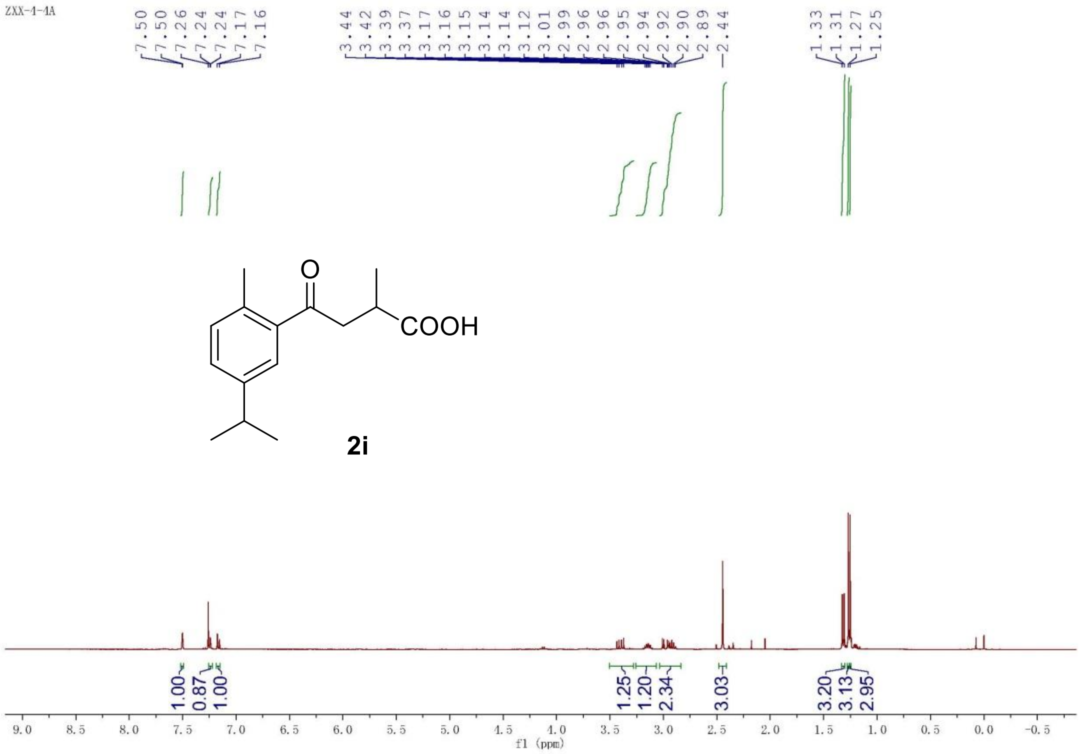

ZXX-4-5A
7.90
7.88
7.26
7.24
7.22
3.49
3.47
3.44
3.42
3.18
3.16
3.16
3.14
3.14
3.13
3.07
3.06
3.03
3.01
2.54
2.52
1.93
1.91
1.89
1.88
1.32
1.30
0.91
0.90
COOH
2f
2.00
1.97
0.98
1.00
1.00
2.01
1.04
3.05
6.14
f1 (ppm)


ZXX-5
7.48
7.26
7.20
7.19
7.18
7.17
7.13
7.11
3.43
3.41
3.38
3.36
3.18
3.17
3.16
3.15
3.14
3.13
3.12
3.11
3.09
2.99
2.97
2.94
2.93
2.44
2.36
1.32
1.30
O
COOH
2g
0.93
0.94
0.96
1.00
0.99
1.02
2.92
2.94
2.95
f1 (ppm)

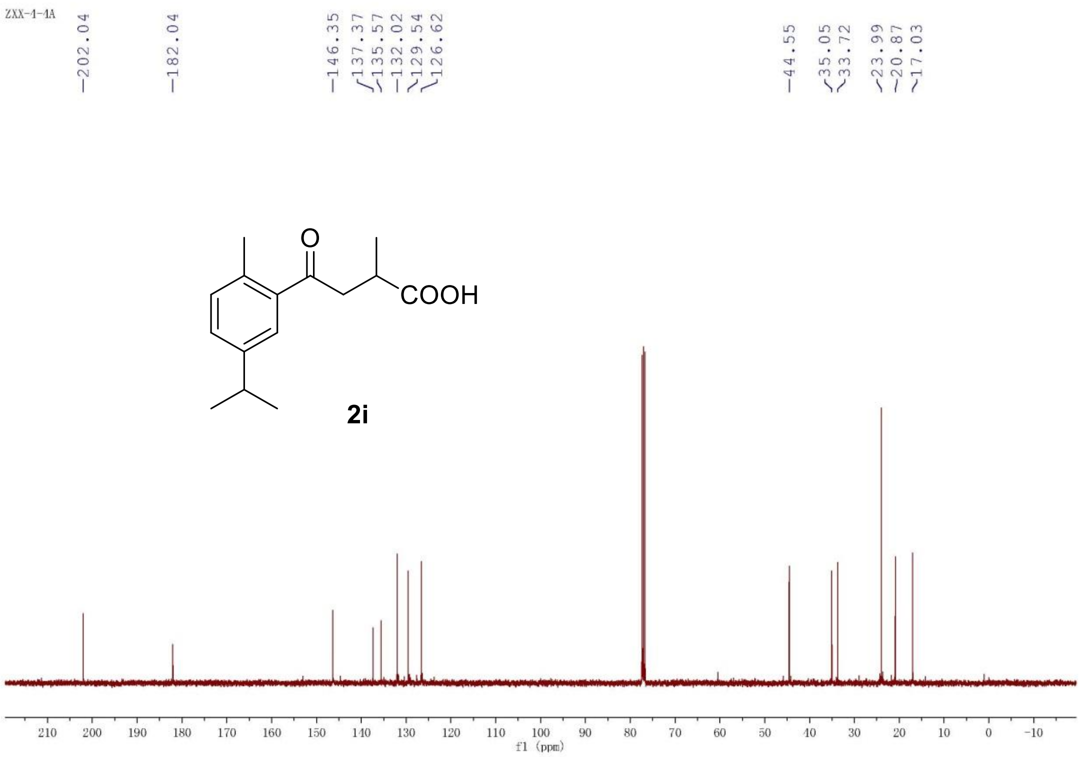

ZXX-5
201.92
182.43
137.20
135.23
135.20
132.27
131.93
129.17
44.48
35.07
20.95
20.89
17.04
O
COOH
2g
f1 (ppm)


ZXX-3
7.56
7.54
6.99
6.97
3.34
3.32
3.29
3.27
3.08
3.06
3.05
3.05
3.03
3.03
3.01
3.00
2.90
2.89
2.86
2.85
2.40
2.26
1.22
1.20
O
COOH
2h
1.00
2.02
1.06
1.07
1.02
2.92
3.04
3.06
f1 (ppm)

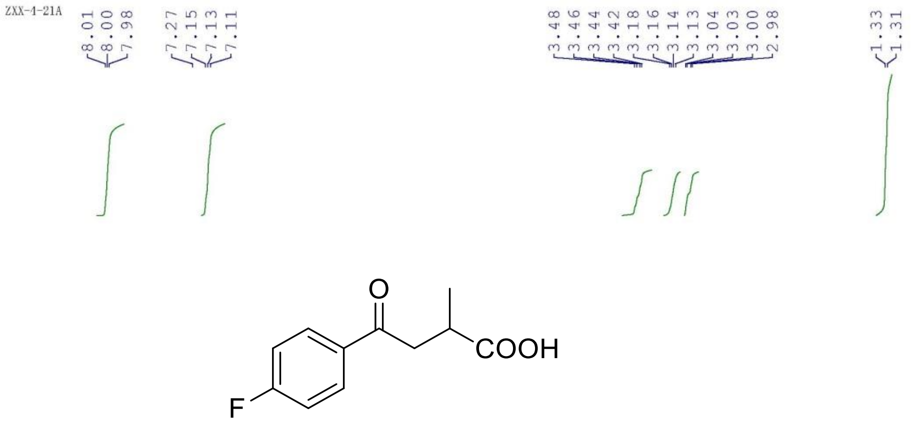

ZXX-3
201.01
182.43
142.24
138.96
134.24
132.96
129.20
126.36
44.17
35.14
21.65
21.40
17.05
O
COOH
2h
f1 (ppm)



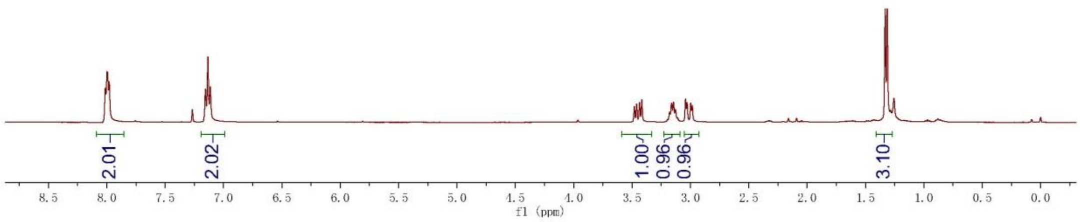

2i

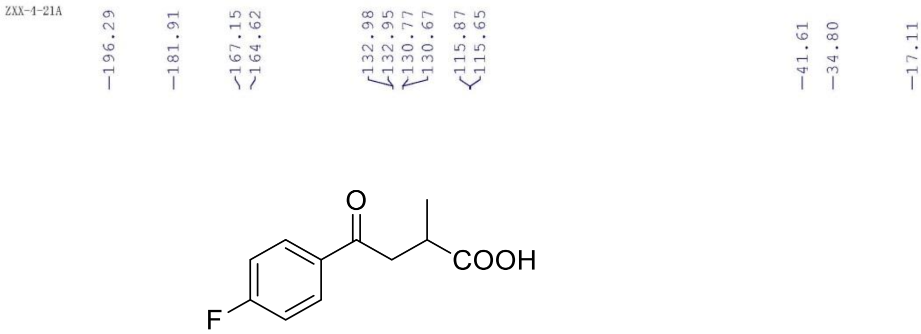



2i

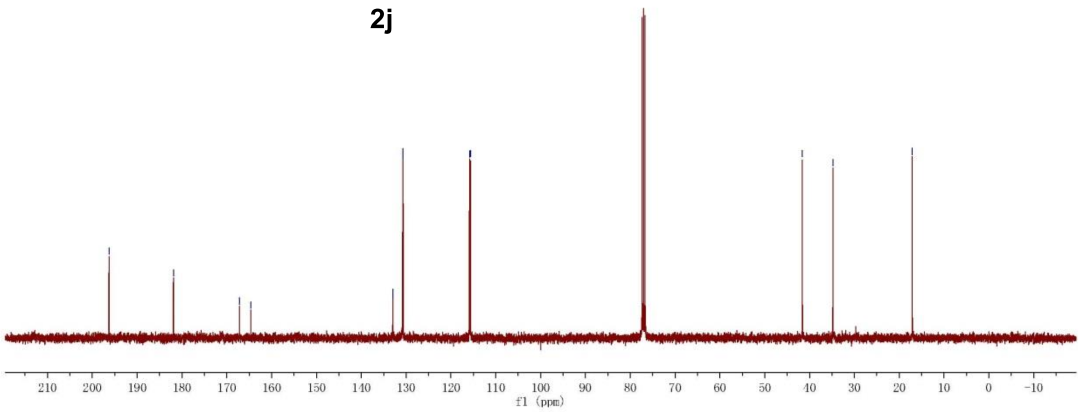

ZXX-4-21A
8.01
8.00
7.98
7.27
7.15
7.13
7.11
3.48
3.46
3.44
3.42
3.18
3.16
3.14
3.13
3.04
3.03
3.00
2.98
1.33
1.31
O
COOH
F

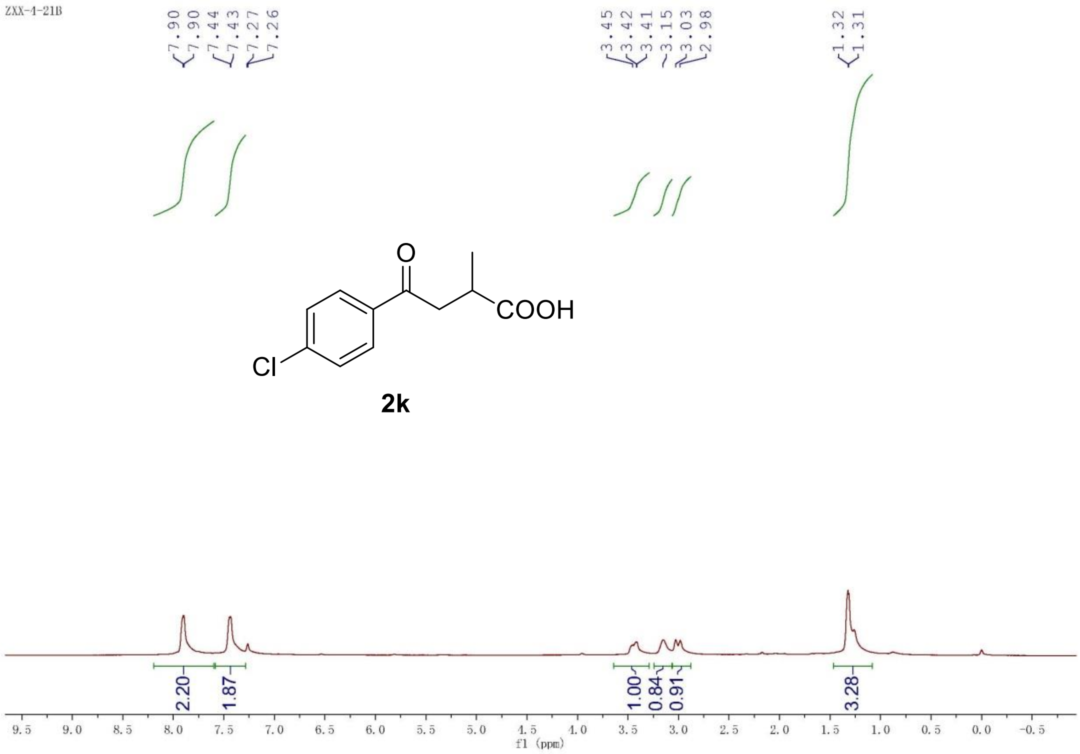
**2j**

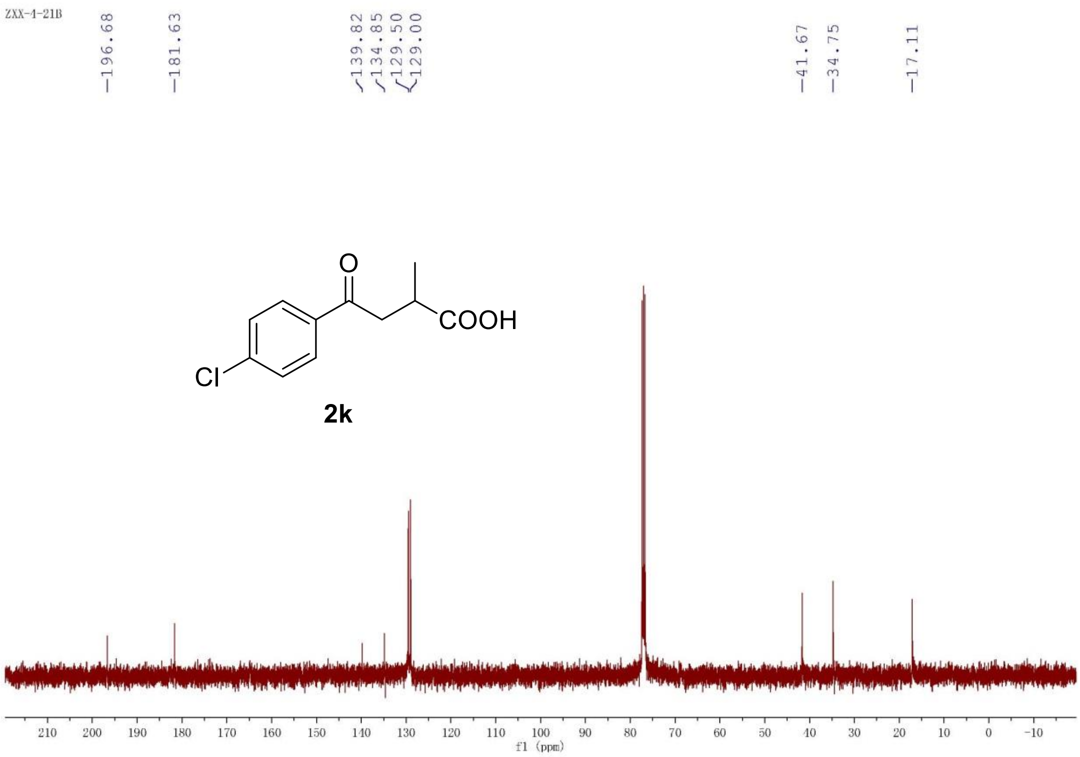

2.01
2.02
1.00
0.96
0.96
3.10
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

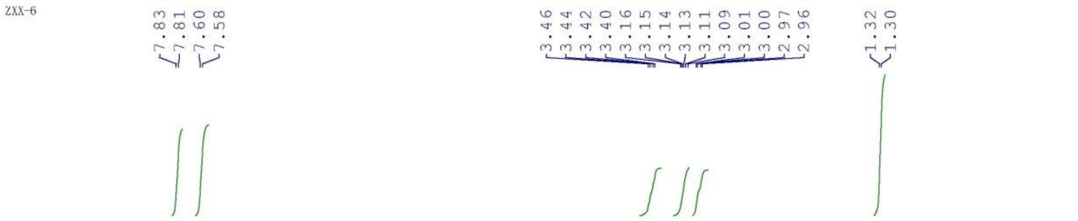

ZXX-4-21A
196.29
181.91
167.15
164.62
132.98
132.95
130.77
130.67
115.87
115.65
41.61
34.80
17.11
O
COOH
F

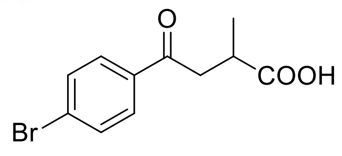
**2j**


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

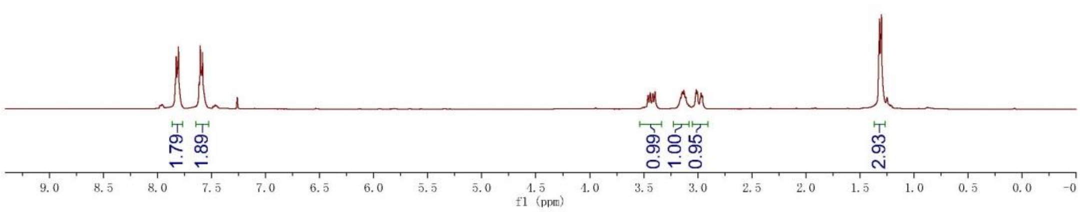

ZXX-4-21B
7.90
7.90
7.44
7.43
7.27
7.26
3.45
3.42
3.41
3.15
3.03
2.98
1.32
1.31
O
COOH
Cl
2k
2.20
1.87
1.00
0.84
0.91
3.28
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

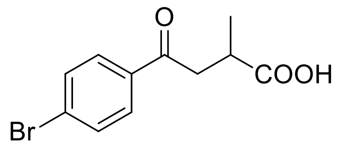

ZXX-4-21B
196.68
181.63
139.82
134.85
129.50
129.00
41.67
34.75
17.11
O
COOH
Cl
2k
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



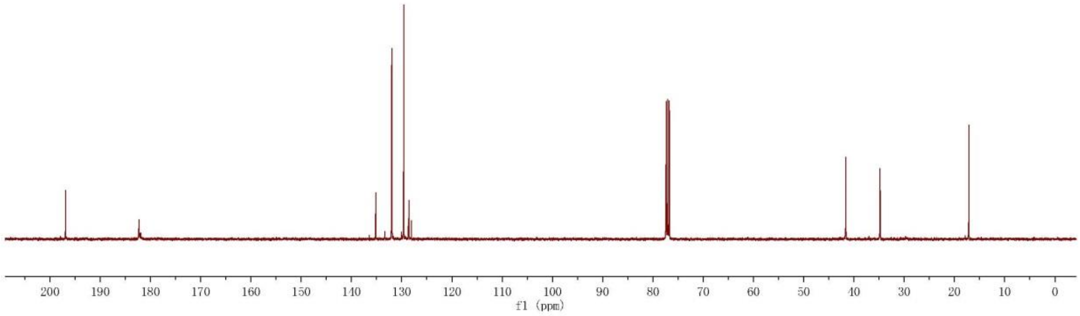


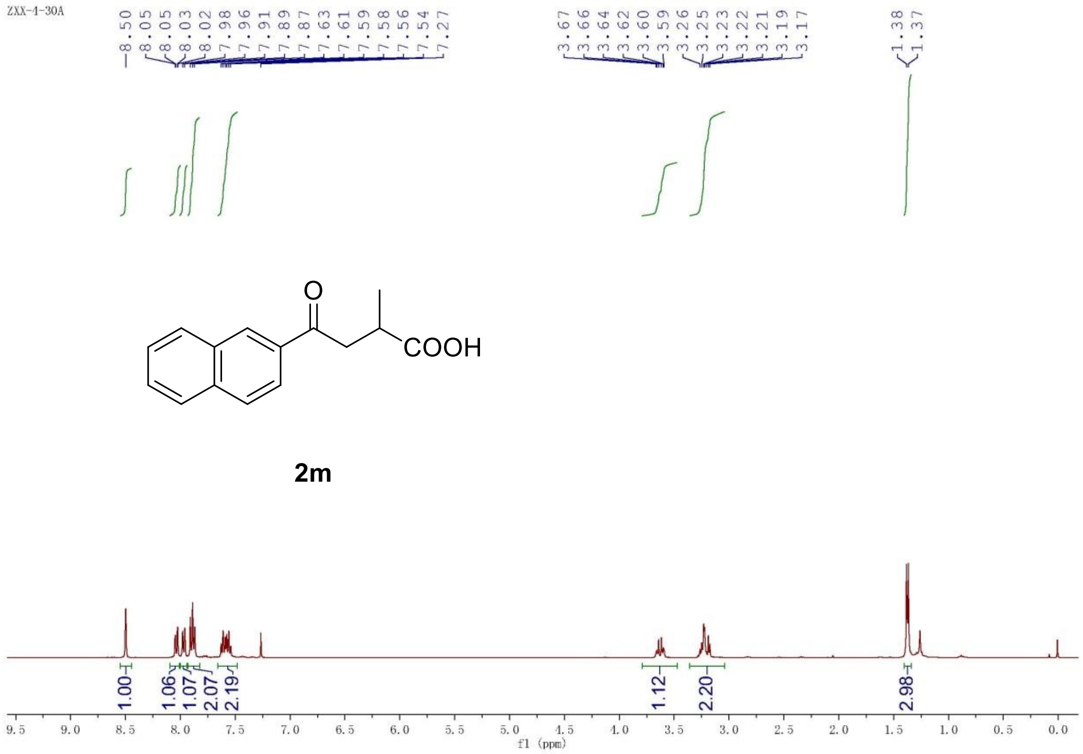
2l

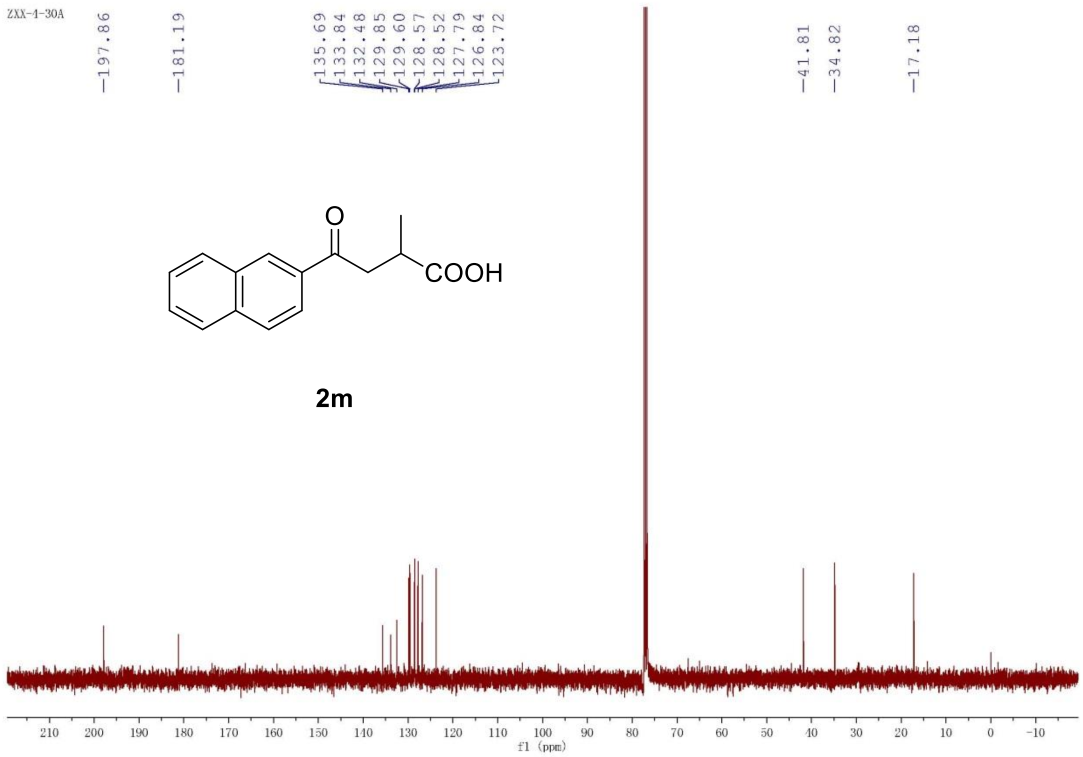


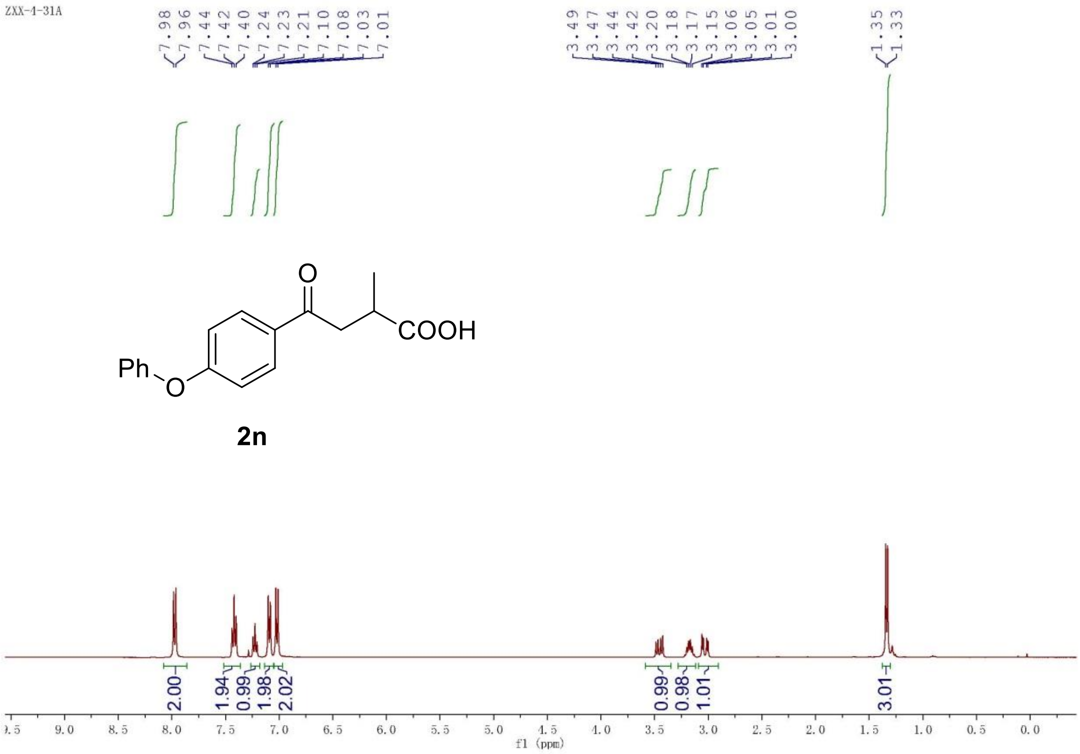


2l

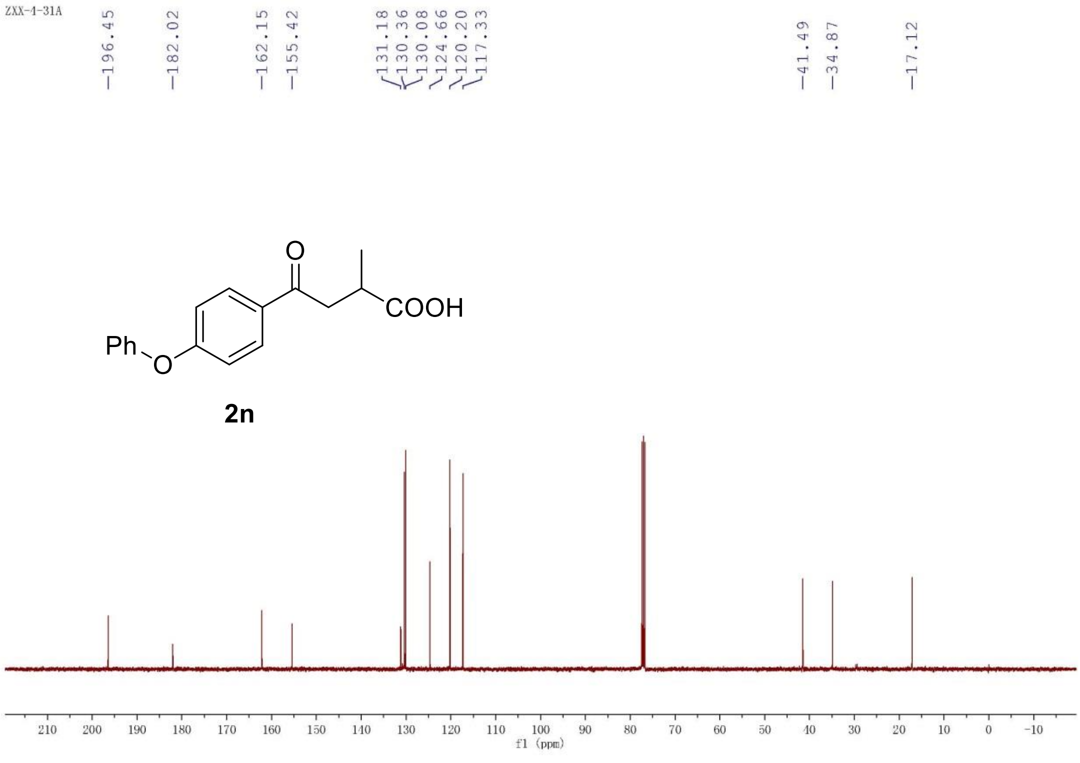



ZXX-4-30A
8.50
8.05
8.05
8.03
8.02
7.98
7.96
7.91
7.89
7.87
7.63
7.61
7.59
7.58
7.56
7.54
7.27
3.67
3.66
3.64
3.62
3.60
3.59
3.26
3.25
3.23
3.22
3.21
3.19
3.17
1.38
1.37
O
COOH
2m
1.00
1.06
1.07
2.07
2.19
1.12
2.20
2.98
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

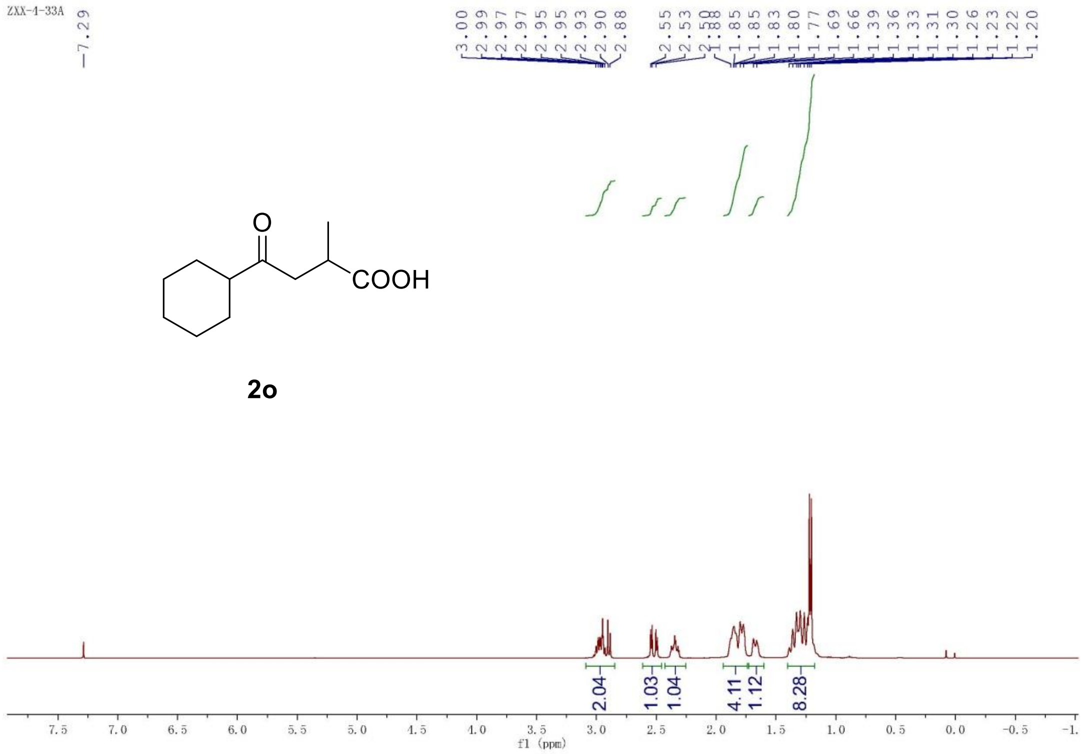

ZXX-4-30A
197.86
181.19
135.69
133.84
132.48
129.85
129.60
128.57
128.52
127.79
126.84
123.72
41.81
34.82
17.18
O
COOH
2m
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

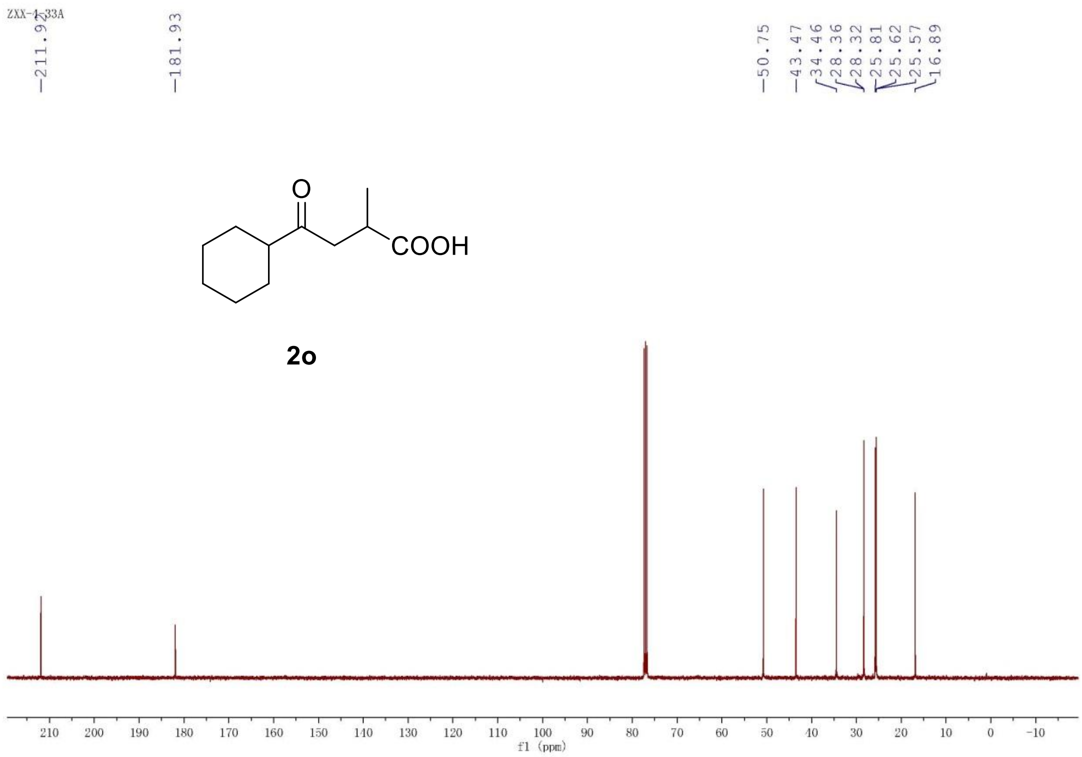


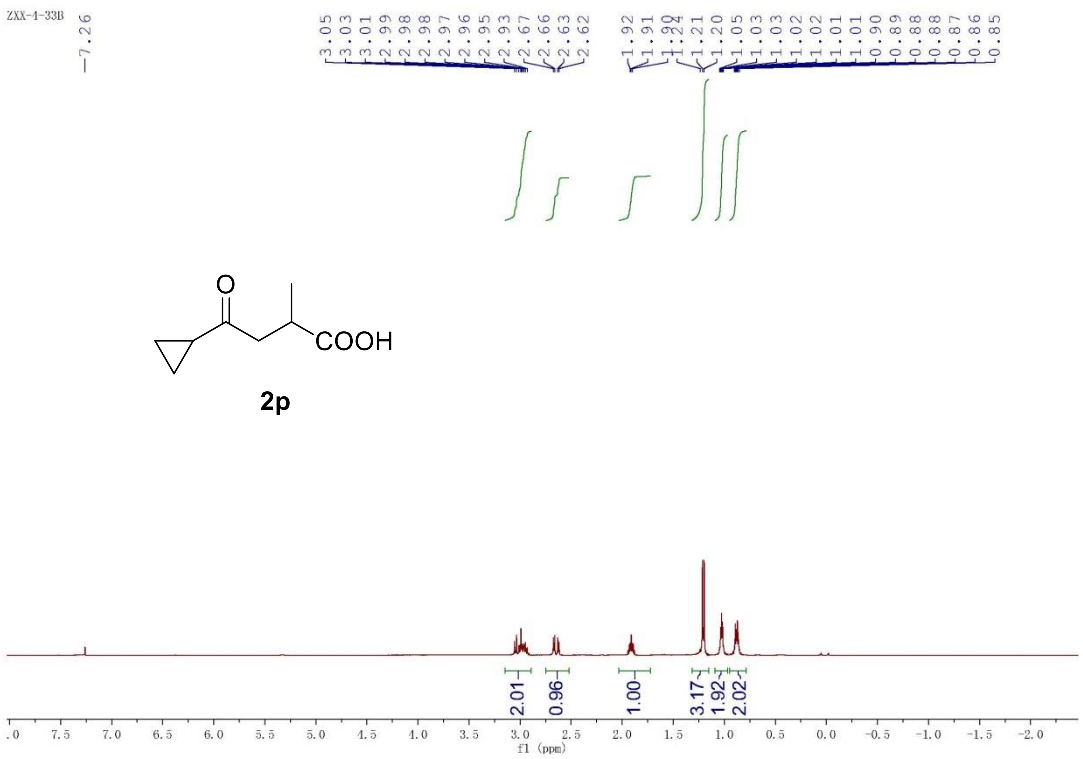
ZXX-4-31A
7.98
7.96
7.44
7.42
7.40
7.24
7.23
7.21
7.10
7.08
7.03
7.01
3.49
3.47
3.44
3.42
3.20
3.18
3.17
3.15
3.06
3.05
3.01
3.00
1.35
1.33
O
COOH
Ph
O
2n
2.00
1.94
0.99
1.98
2.02
0.99
0.98
1.01
3.01
f1 (ppm)

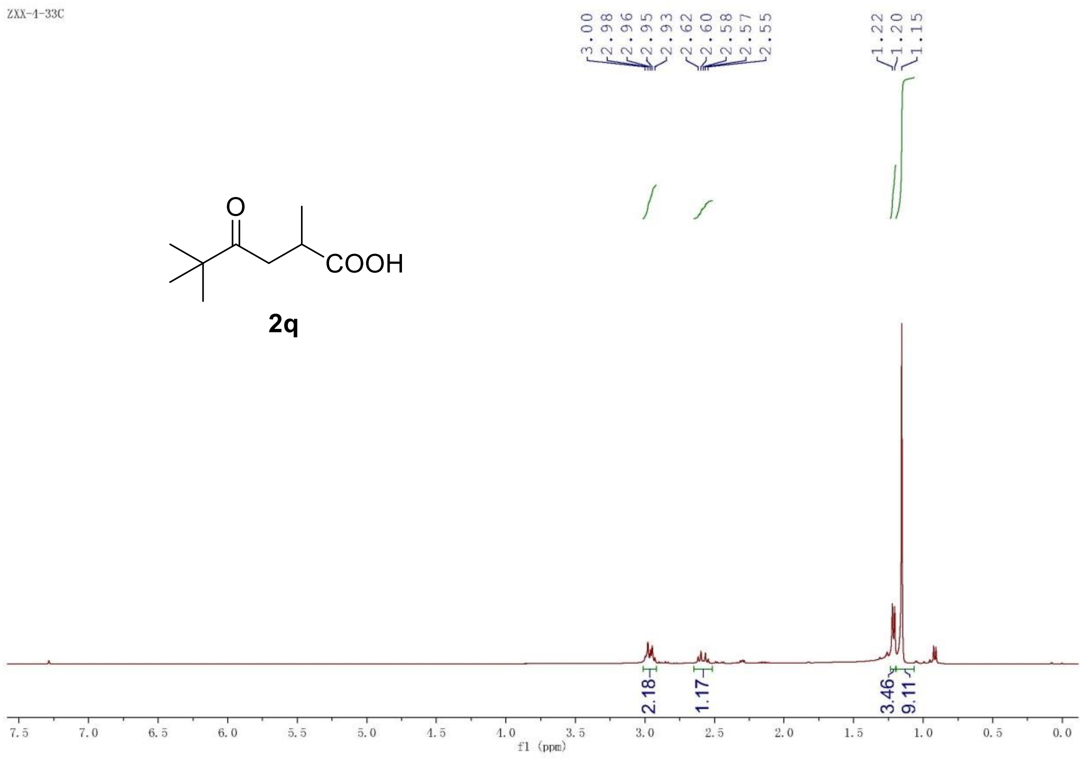
ZXX-4-31A
196.45
182.02
162.15
155.42
131.18
130.36
130.08
124.66
120.20
117.33
41.49
34.87
17.12
O
COOH
Ph
O
2n
f1 (ppm)


ZXX-4-33A
7.29
3.00 2.99 2.97 2.97 2.95 2.93 2.90 2.88 2.55 2.53 2.50 1.88 1.85 1.85 1.83 1.80 1.77 1.69 1.66 1.39 1.36 1.33 1.31 1.30 1.26 1.23 1.22 1.20
O
COOH
2o
2.04 1.03 1.04 4.11 1.12 8.28
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

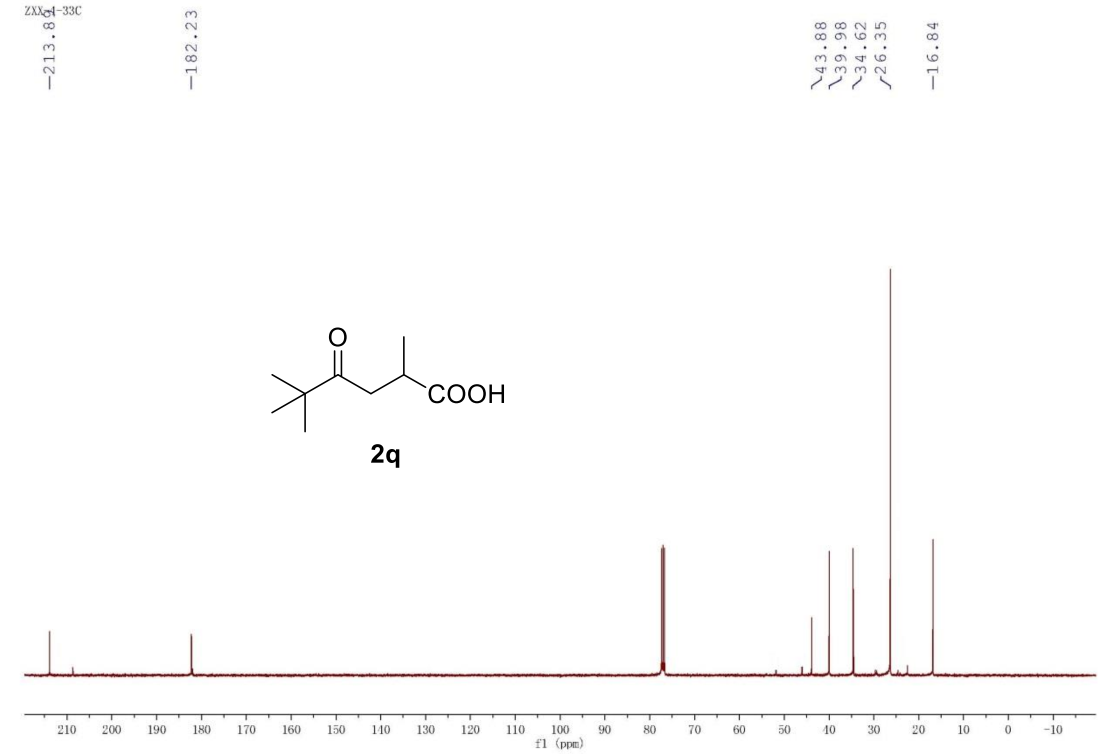

ZXX-4-33A
211.9
181.93
50.75 43.47 34.46 28.36 28.32 25.81 25.62 25.57 16.89
O
COOH
2o
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



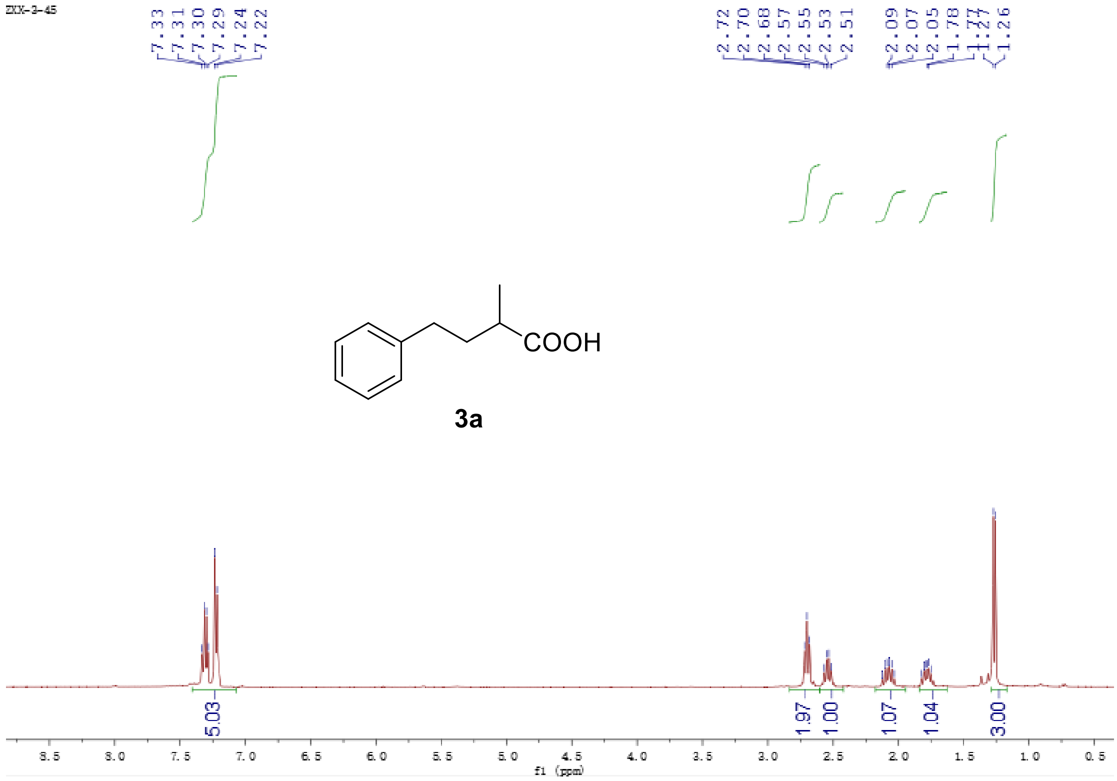

**2p**



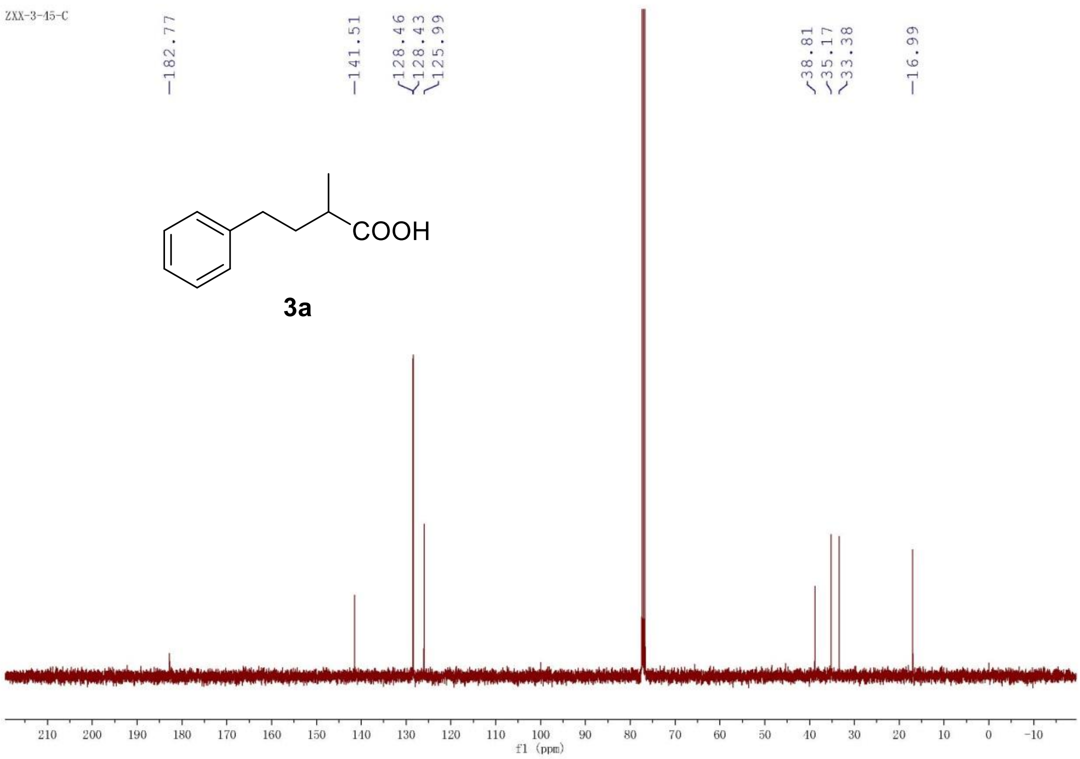

**2q**

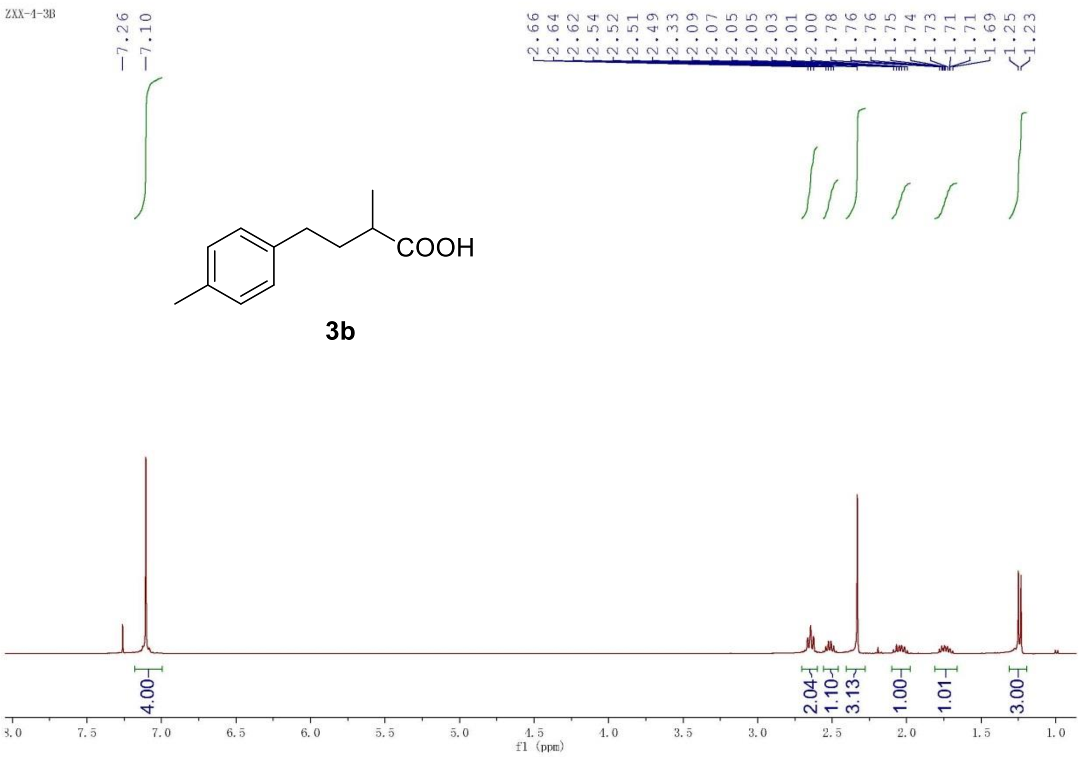

ZXX-4-33C
213.80
182.23
43.88
39.98
34.62
26.35
16.84
COOH
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

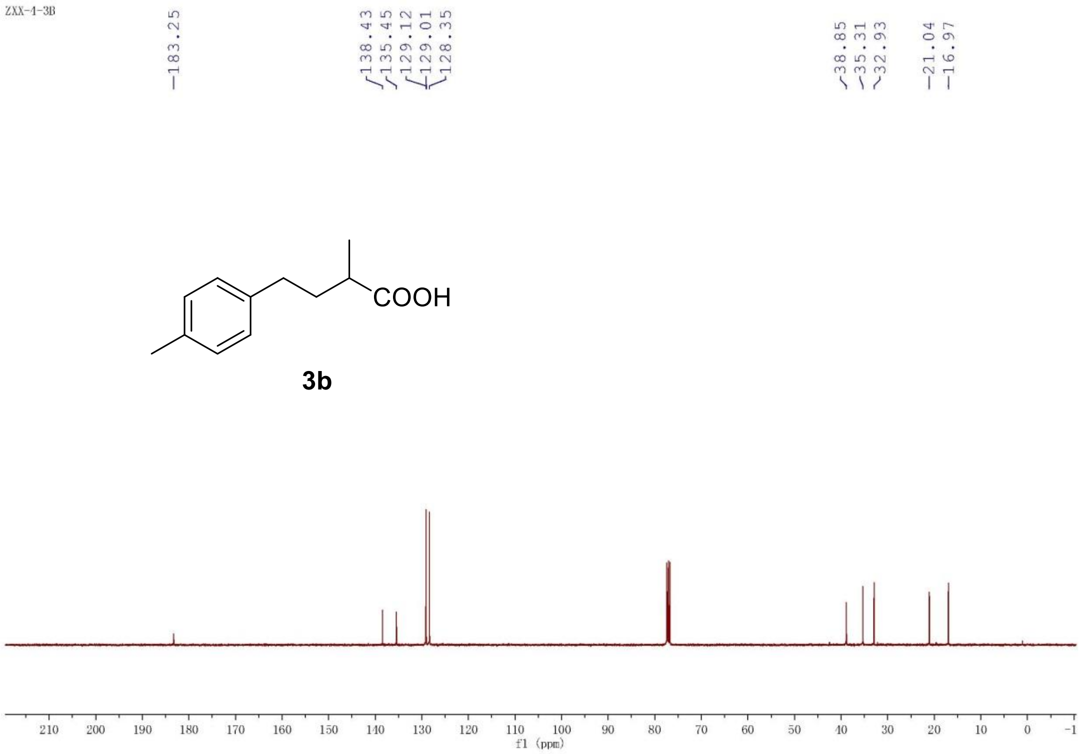
**2q**

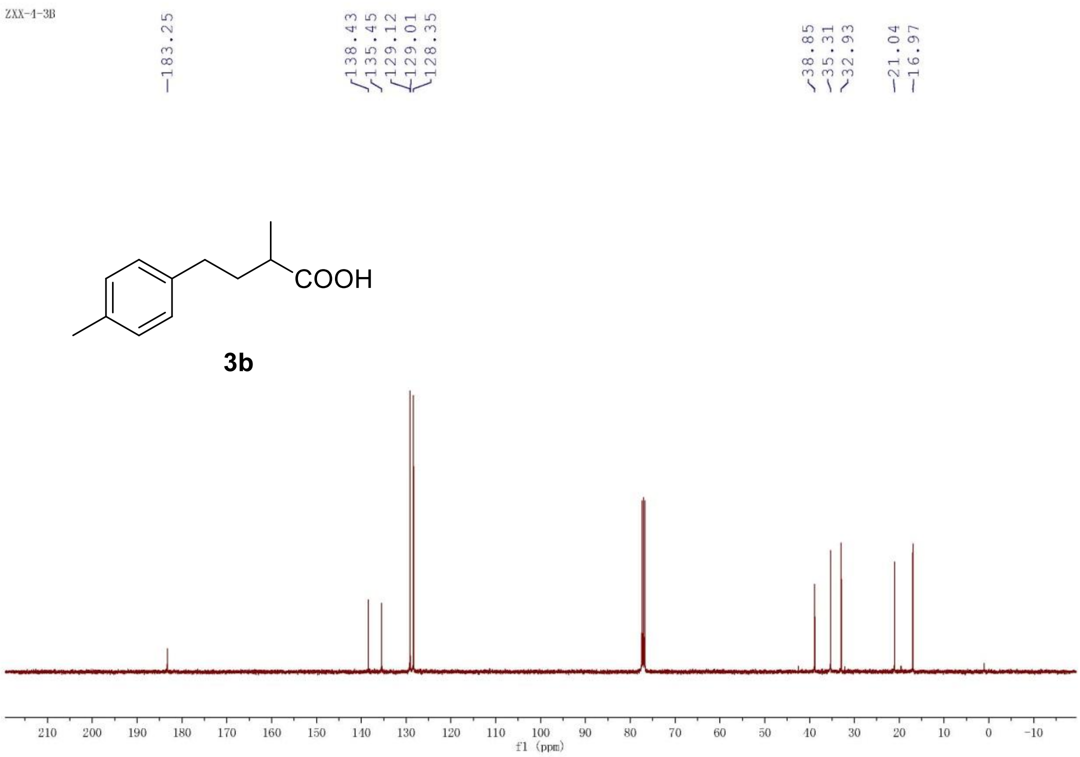

ZXX-3-45
7.33 7.31 7.30 7.29 7.24 7.22
2.72 2.70 2.68 2.57 2.55 2.53 2.51
2.09 2.07 2.05 1.78 1.77 1.26
COOH
5.03
1.97 1.00 1.07 1.04 3.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

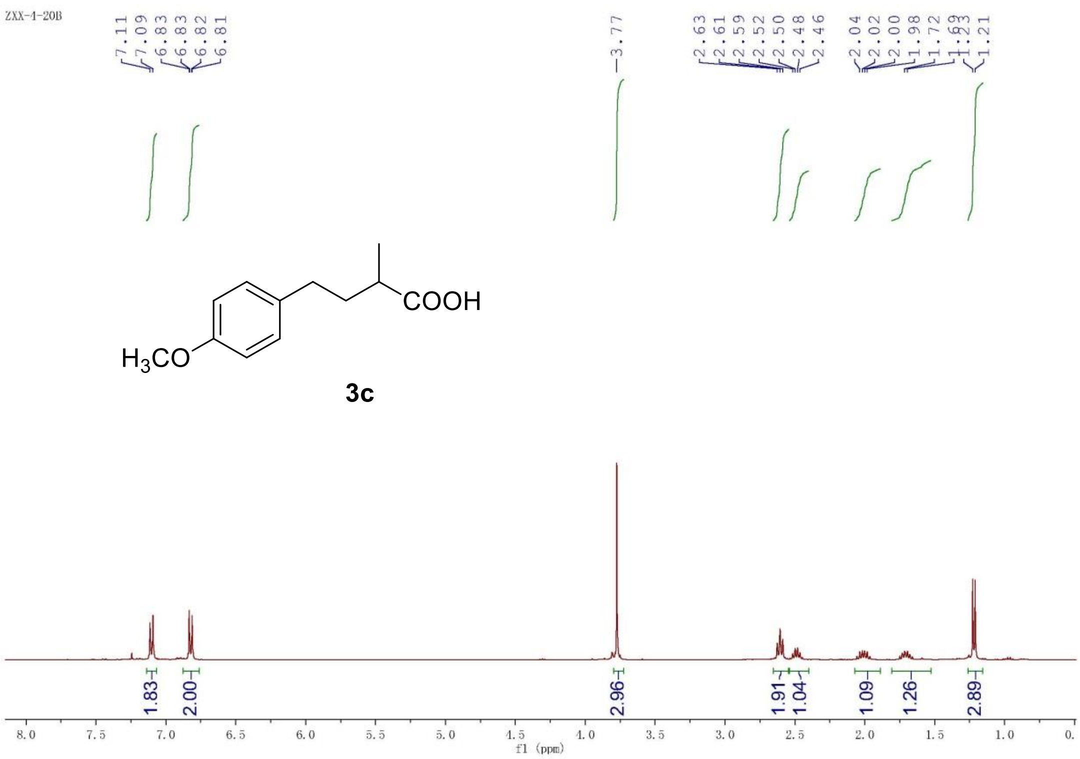
**3a**

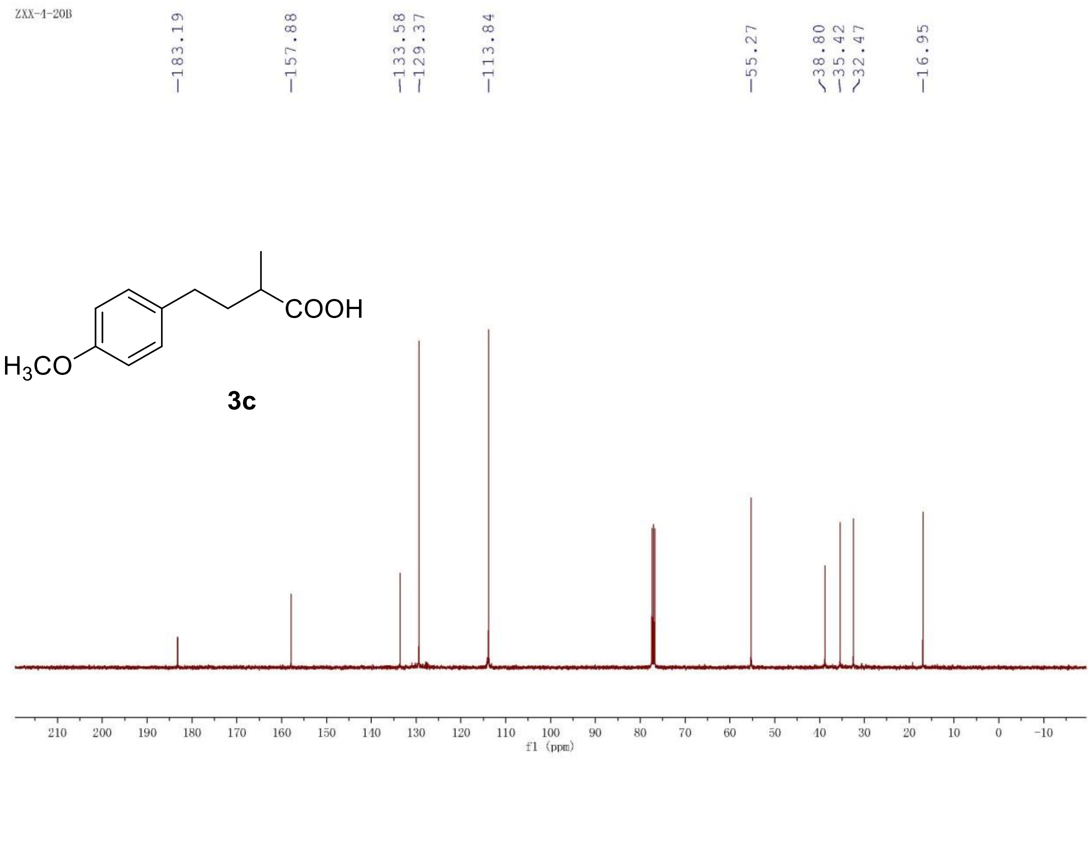

ZXX-3-45-C
182.77
141.51
128.46
128.43
125.99
38.81
35.17
33.38
16.99
COOH
3a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

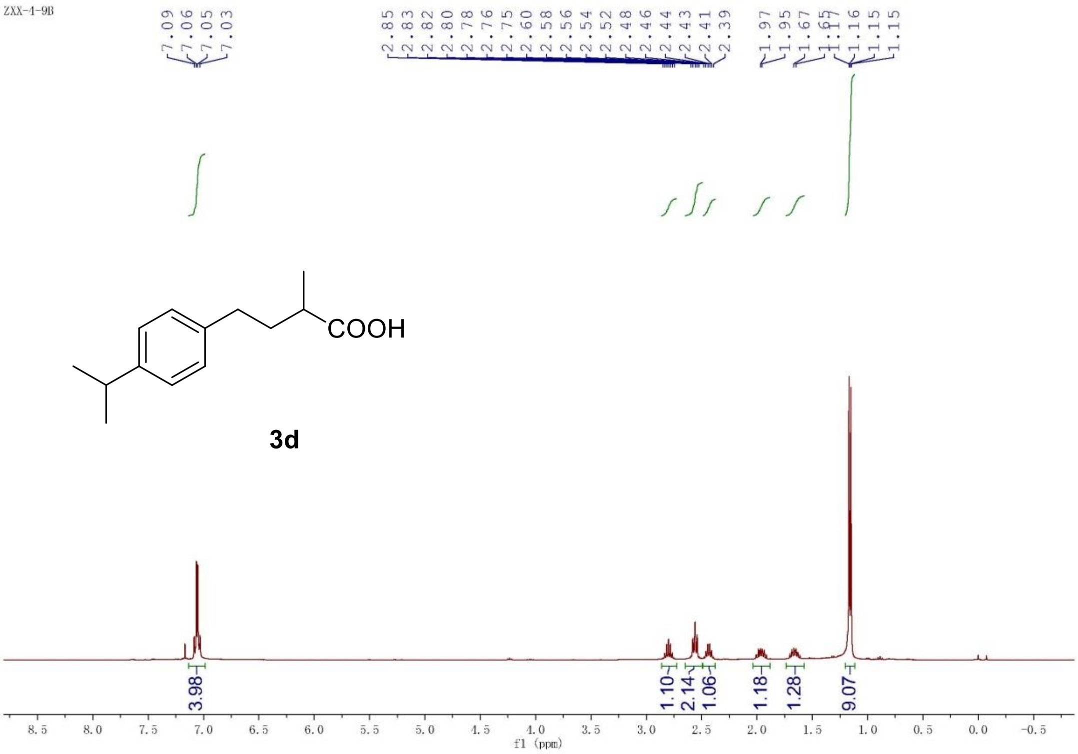

ZXX-4-3B
7.26
7.10
2.66 2.64 2.62 2.54 2.52 2.51 2.49 2.33 2.09 2.07 2.05 2.05 2.03 2.01 2.00 1.78 1.76 1.76 1.75 1.74 1.73 1.71 1.69 1.25 1.23
COOH
3b
4.00
2.04
1.10
3.13
1.00
1.01
3.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
f1 (ppm)


ZXX-4-3B
183.25
138.43
135.45
129.12
129.01
128.35
38.85
35.31
32.93
21.04
16.97
COOH
3b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)


ZXX-4-3B
183.25
138.43
135.45
129.12
129.01
128.35
38.85
35.31
32.93
21.04
16.97
COOH
3b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


ZXX-4-20B
7.11
7.09
6.83
6.83
6.82
6.81
3.77
2.63
2.61
2.59
2.52
2.50
2.48
2.46
2.04
2.02
2.00
1.98
1.72
1.69
1.23
1.21
COOH
$H_3CO$
3c
1.83
2.00
2.96
1.91
1.04
1.09
1.26
2.89
f1 (ppm)


ZXX-4-20B
183.19
157.88
133.58
129.37
113.84
55.27
38.80
35.42
32.47
16.95
COOH
$H_3CO$
3c
f1 (ppm)


ZXX-4-9B
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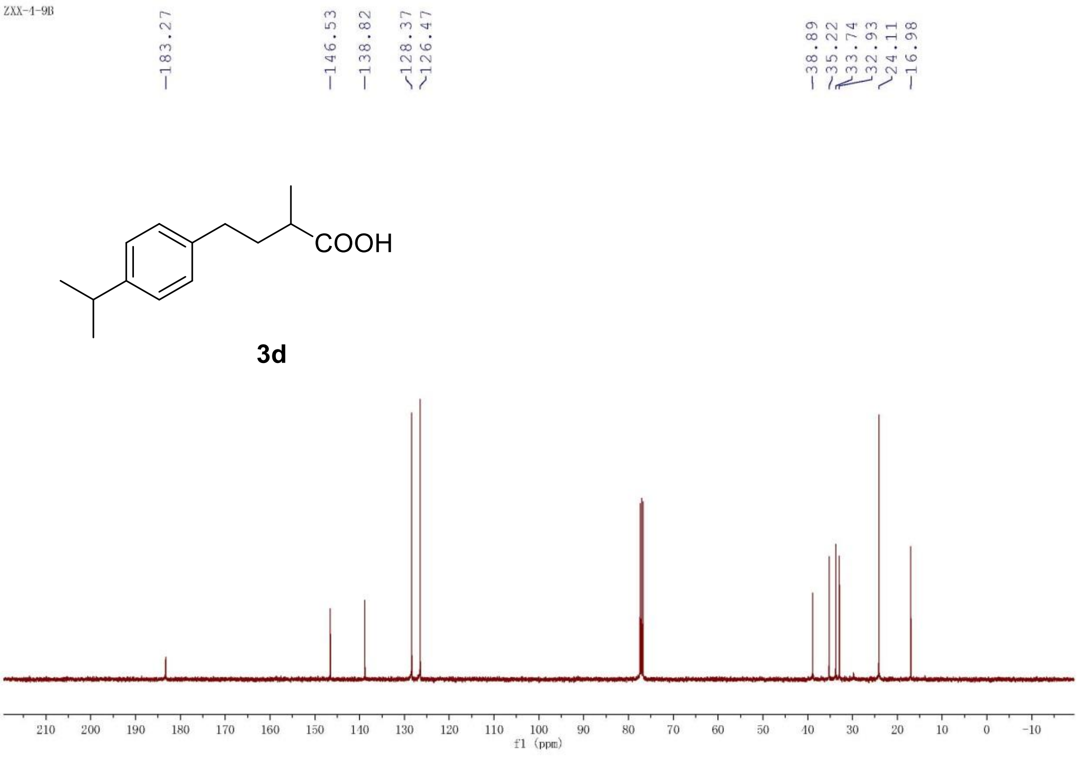
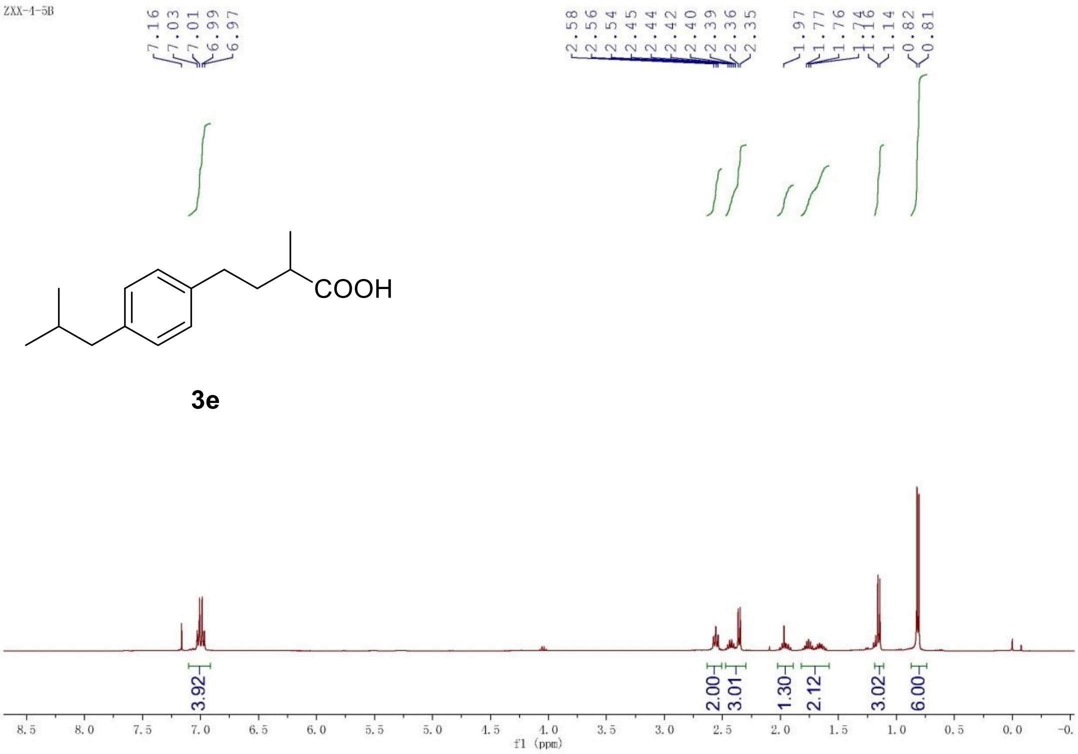
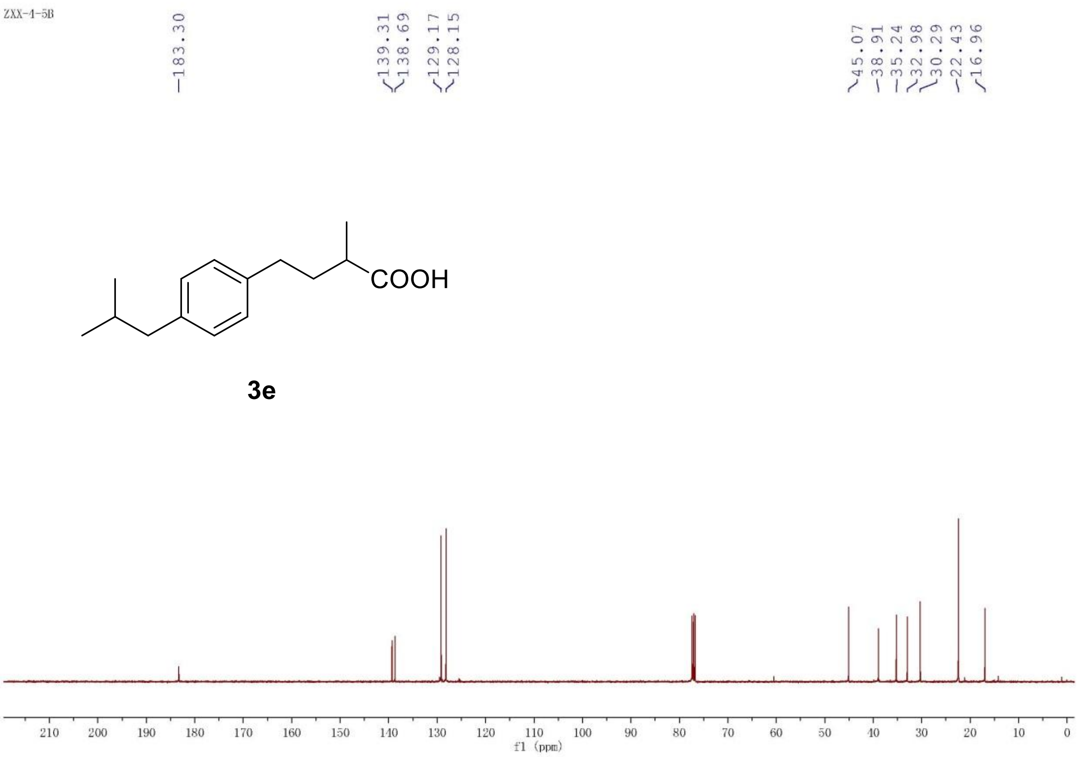
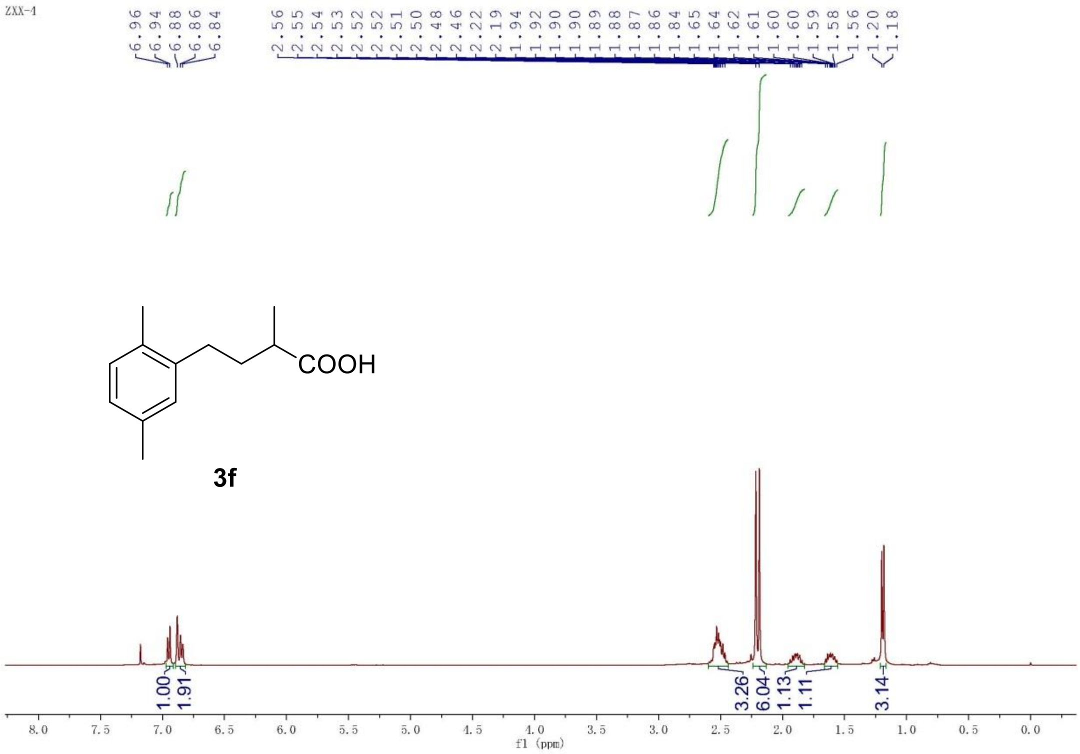
7.06
7.05
7.03
2.85
2.83
2.82
2.80
2.78
2.76
2.75
2.60
2.58
2.56
2.54
2.52
2.48
2.46
2.44
2.43
2.41
2.39
1.97
1.95
1.67
1.65
1.17
1.16
1.15
1.15
COOH
3d
3.98
1.10
2.14
1.06
1.18
1.28
9.07
f1 (ppm)

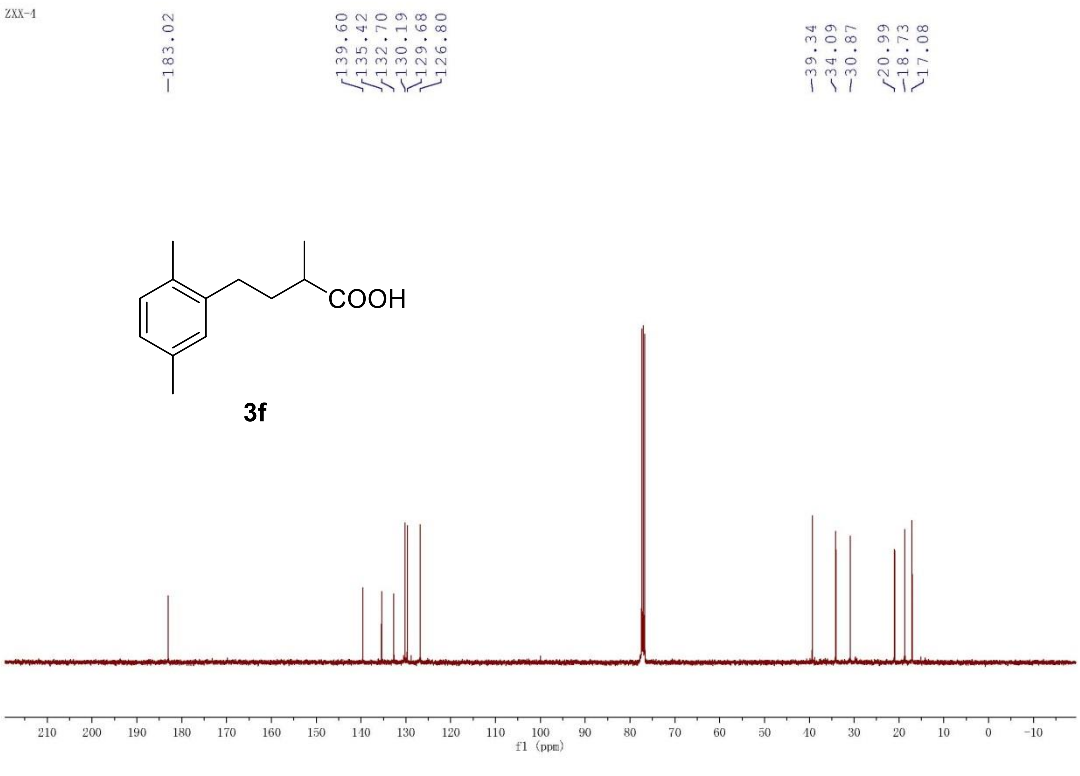

ZXX-4-9B
183.27
146.53
138.82
128.37
126.47
38.89
35.22
33.74
32.93
24.11
16.98
COOH
3d
f1 (ppm)


ZXX-4-5B
7.16
7.03
7.01
6.99
6.97
2.58
2.56
2.54
2.45
2.44
2.42
2.40
2.39
2.36
2.35
1.97
1.77
1.76
1.74
1.16
1.14
0.82
0.81
COOH
3e
3.92
2.00
3.01
1.30
2.12
3.02
6.00
f1 (ppm)

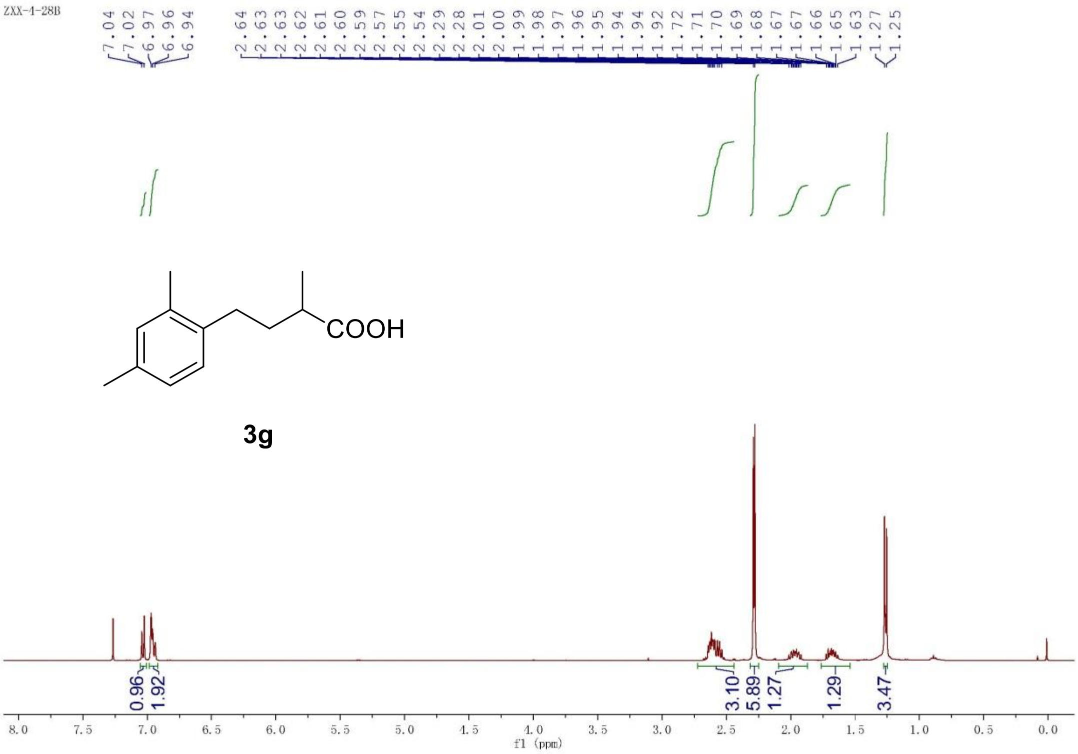

ZXX-4-5B
183.30
139.31
138.69
129.17
128.15
45.07
38.91
35.24
32.98
30.29
22.43
16.96
COOH
3e
f1 (ppm)

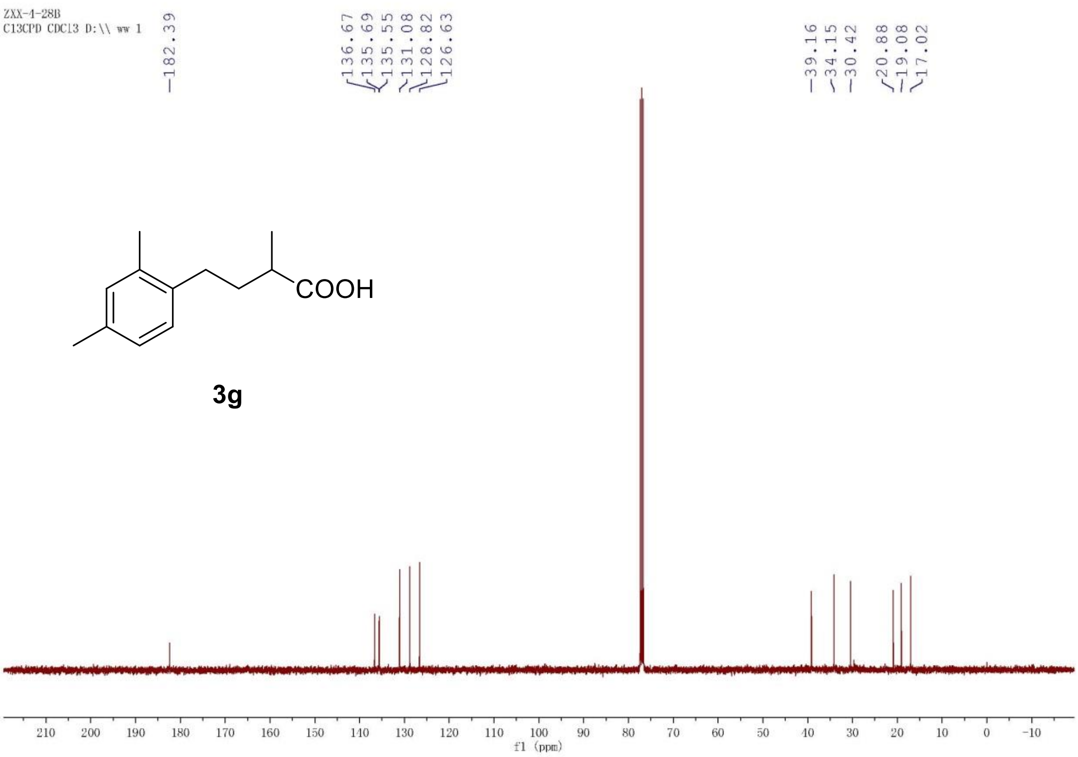


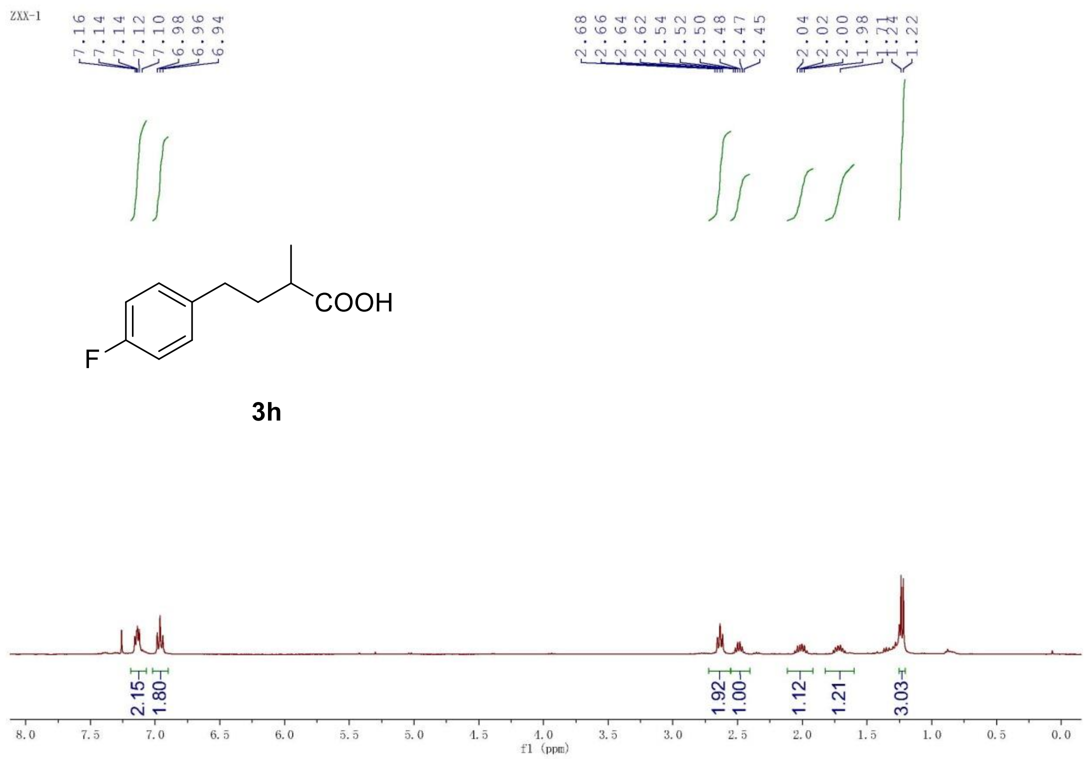
ZXX-4
6.96
6.94
6.88
6.86
6.84
2.56
2.55
2.54
2.53
2.52
2.52
2.51
2.50
2.48
2.46
2.22
2.19
1.94
1.92
1.90
1.90
1.89
1.88
1.87
1.86
1.84
1.65
1.64
1.62
1.61
1.60
1.60
1.59
1.58
1.56
1.20
1.18
COOH
3f
1.00
1.91
3.26
6.04
1.13
1.11
3.14
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

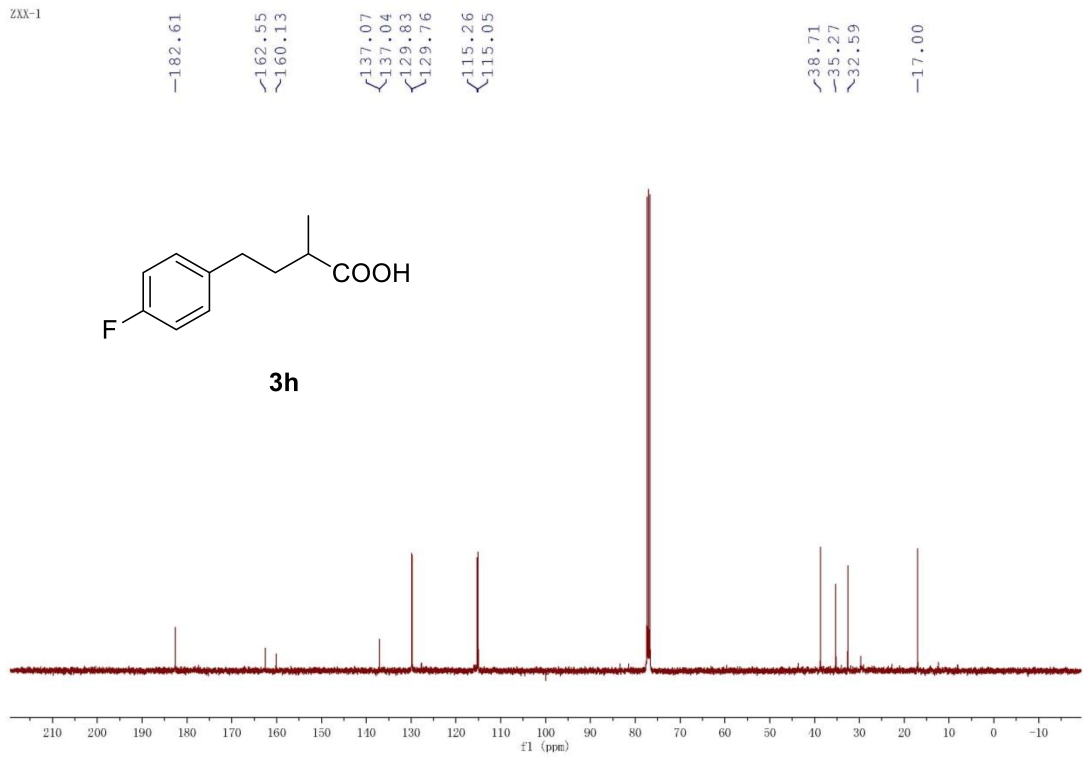



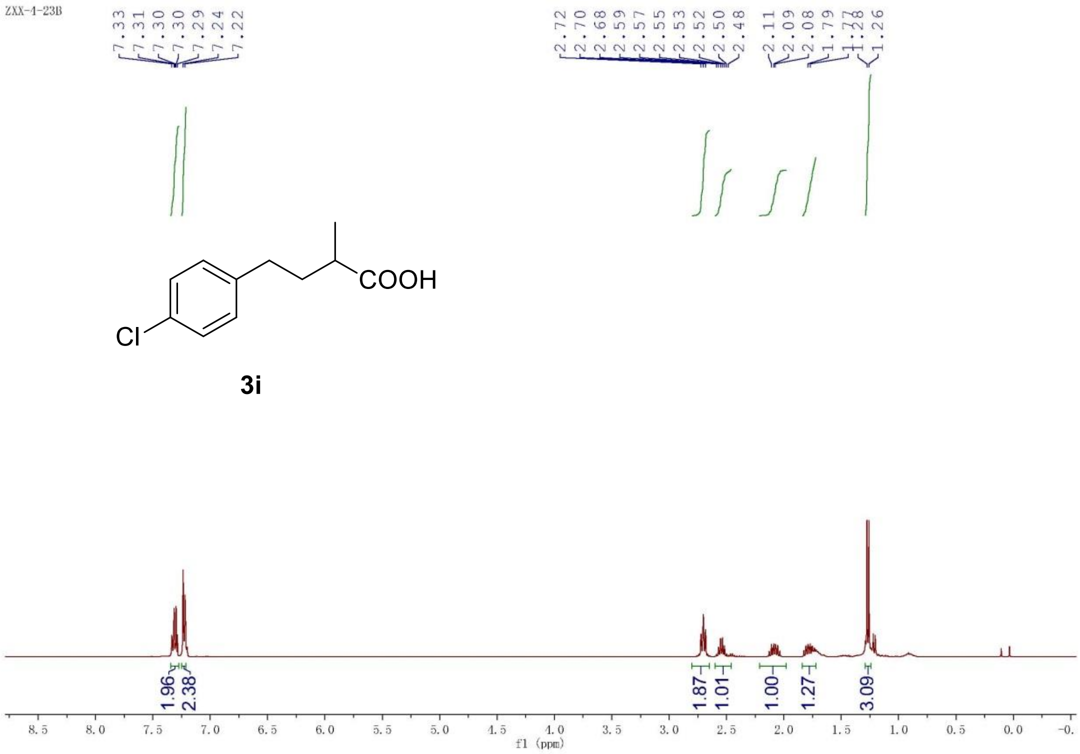
ZXX-4
183.02
139.60
135.42
132.70
130.19
129.68
126.80
39.34
34.09
30.87
20.99
18.73
17.08
COOH
3f
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


ZXX-4-28B
7.04
7.02
6.97
6.96
6.94
2.64
2.63
2.63
2.62
2.61
2.60
2.59
2.57
2.55
2.54
2.29
2.28
2.01
2.00
1.99
1.98
1.97
1.96
1.95
1.94
1.94
1.92
1.72
1.71
1.70
1.69
1.68
1.67
1.67
1.66
1.65
1.63
1.27
1.25
COOH
3g
0.96
1.92
3.10
5.89
1.27
1.29
3.47
f1 (ppm)

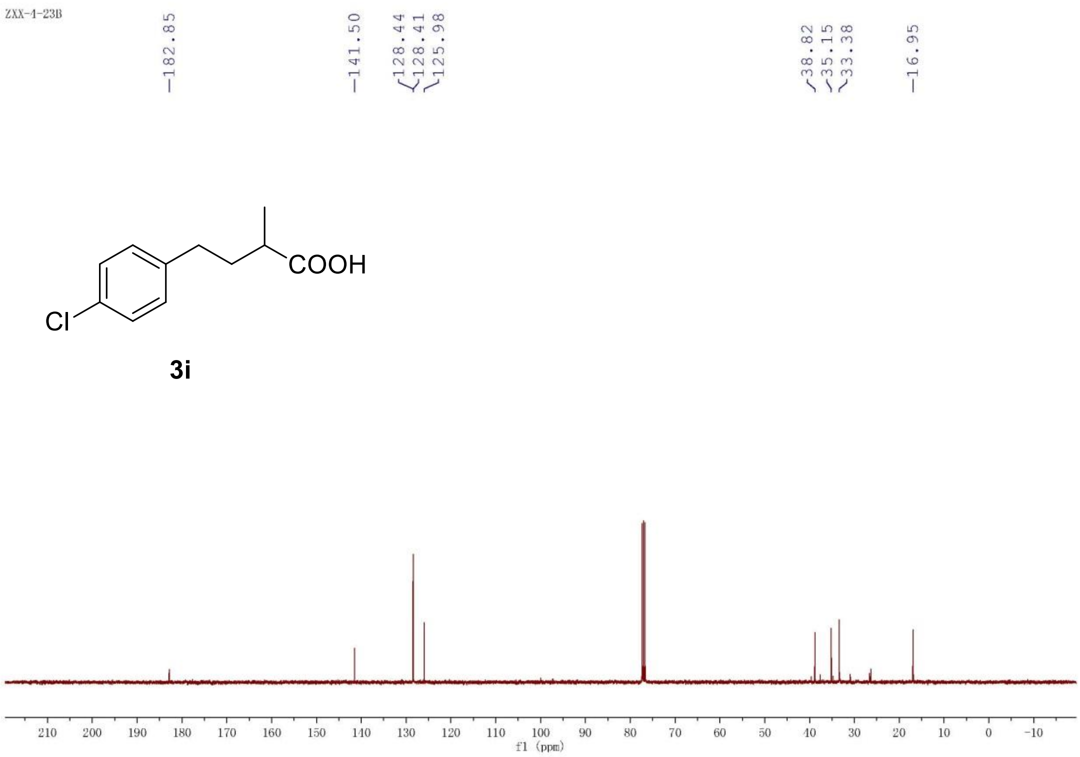

ZXX-4-28B
C13CPD CDCl3 D:\\ ww 1
182.39
136.67
135.69
135.55
131.08
128.82
126.63
39.16
34.15
30.42
20.88
19.08
17.02
COOH
3g
f1 (ppm)



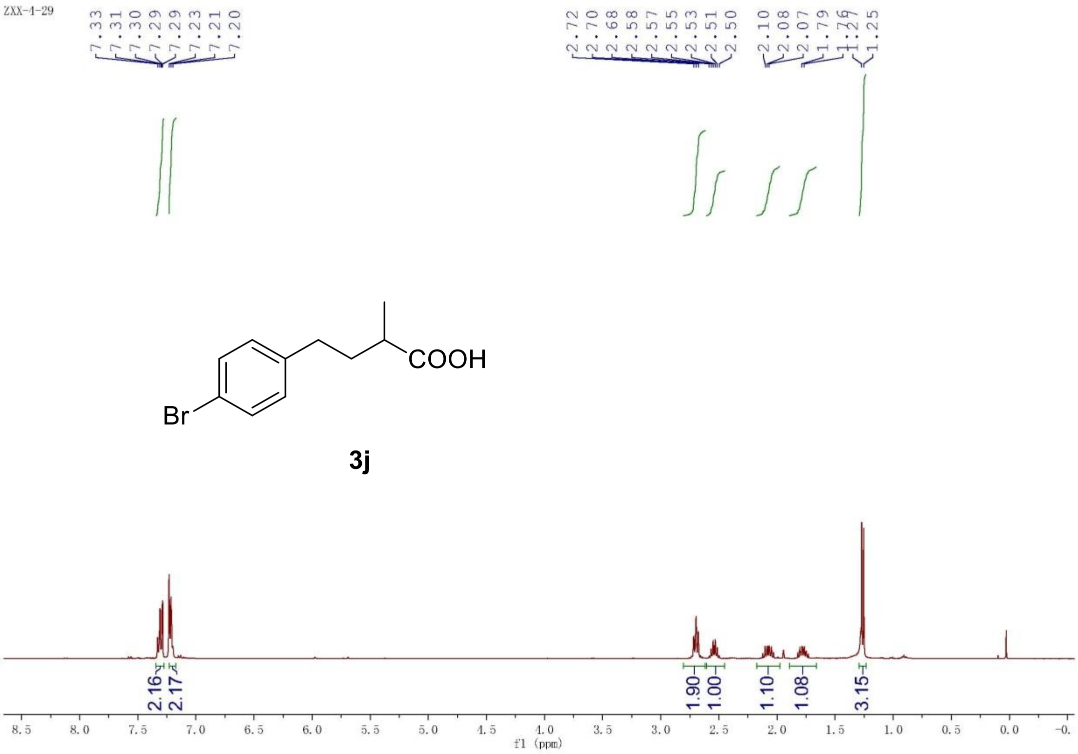


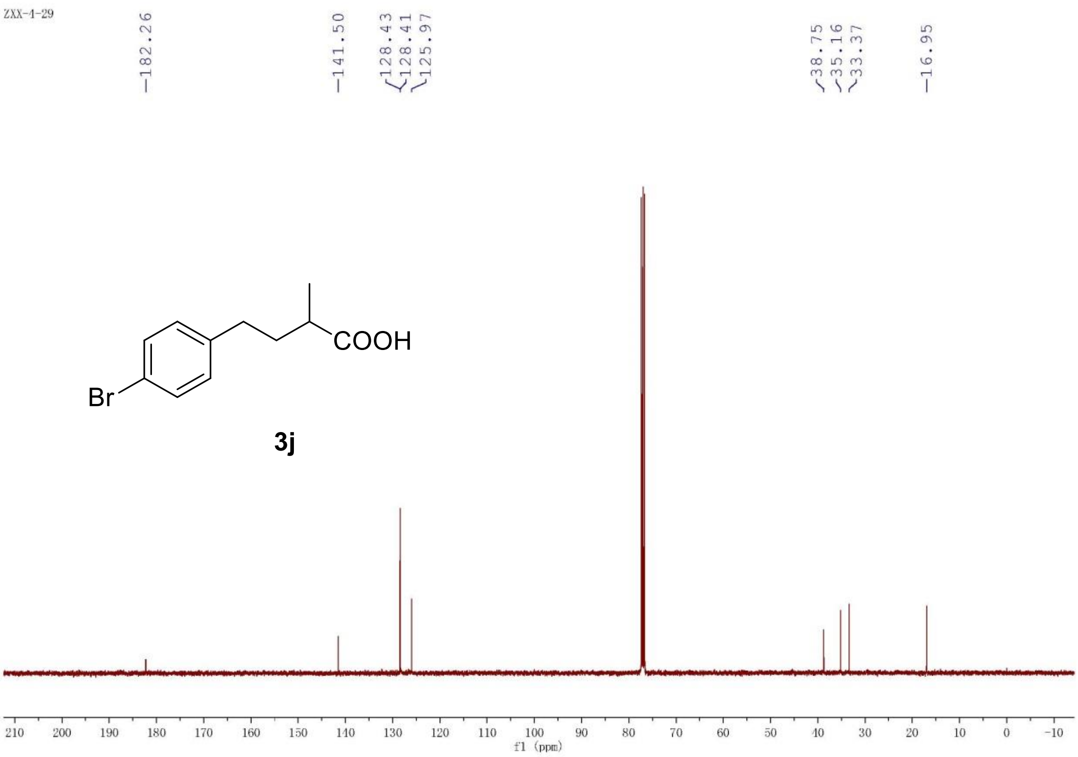

ZXX-4-23B
7.33
7.31
7.30
7.30
7.29
7.24
7.22
2.72
2.70
2.68
2.59
2.57
2.55
2.53
2.52
2.50
2.48
2.11
2.09
2.08
1.79
1.77
1.28
1.26
1.96
2.38
1.87
1.01
1.00
1.27
3.09
COOH
Cl
f1 (ppm)

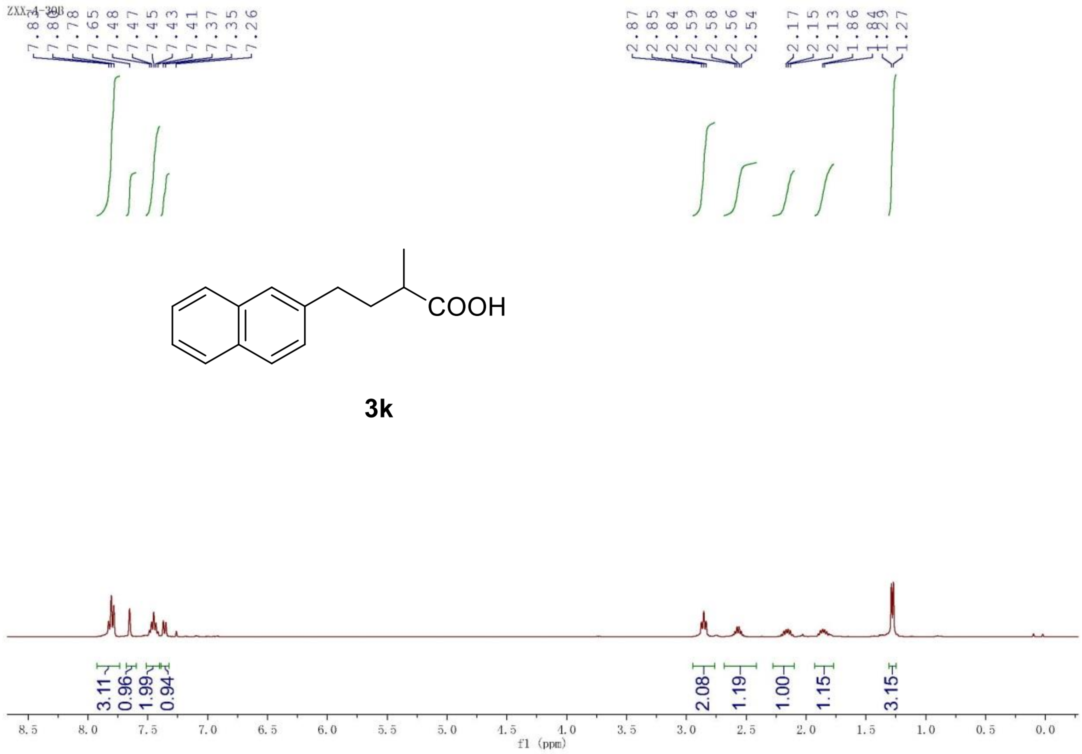
**3i**

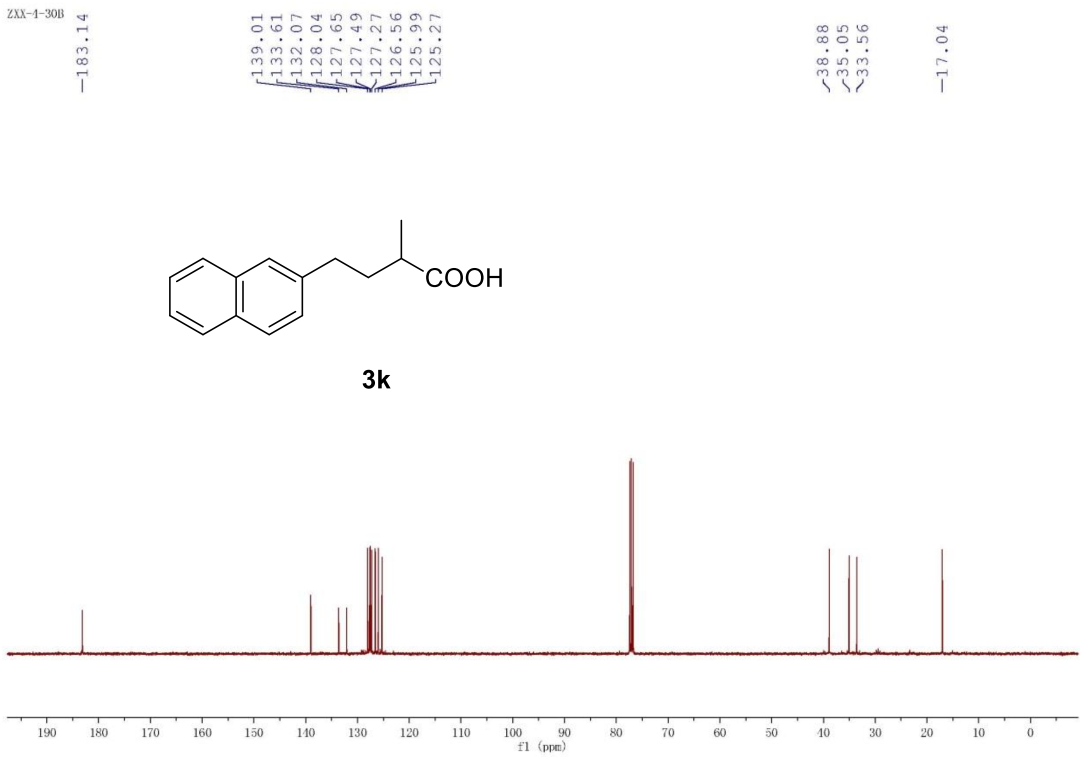

ZXX-4-23B
182.85
141.50
128.44
128.41
125.98
38.82
35.15
33.38
16.95
COOH
Cl
f1 (ppm)

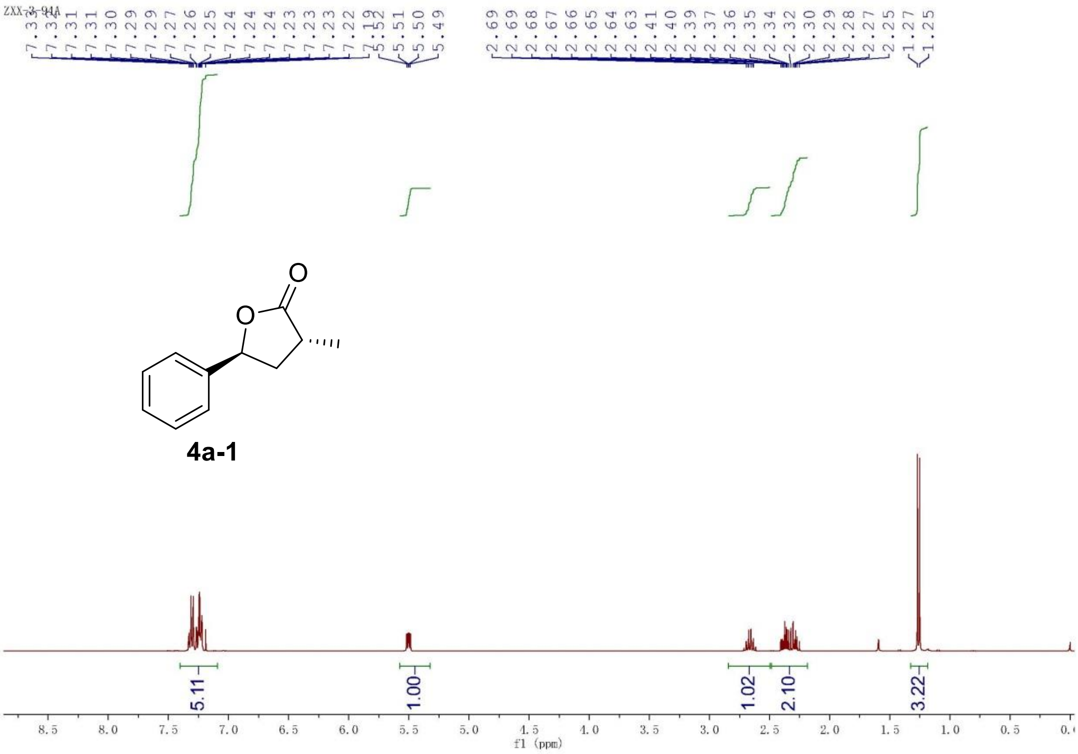
**3i**

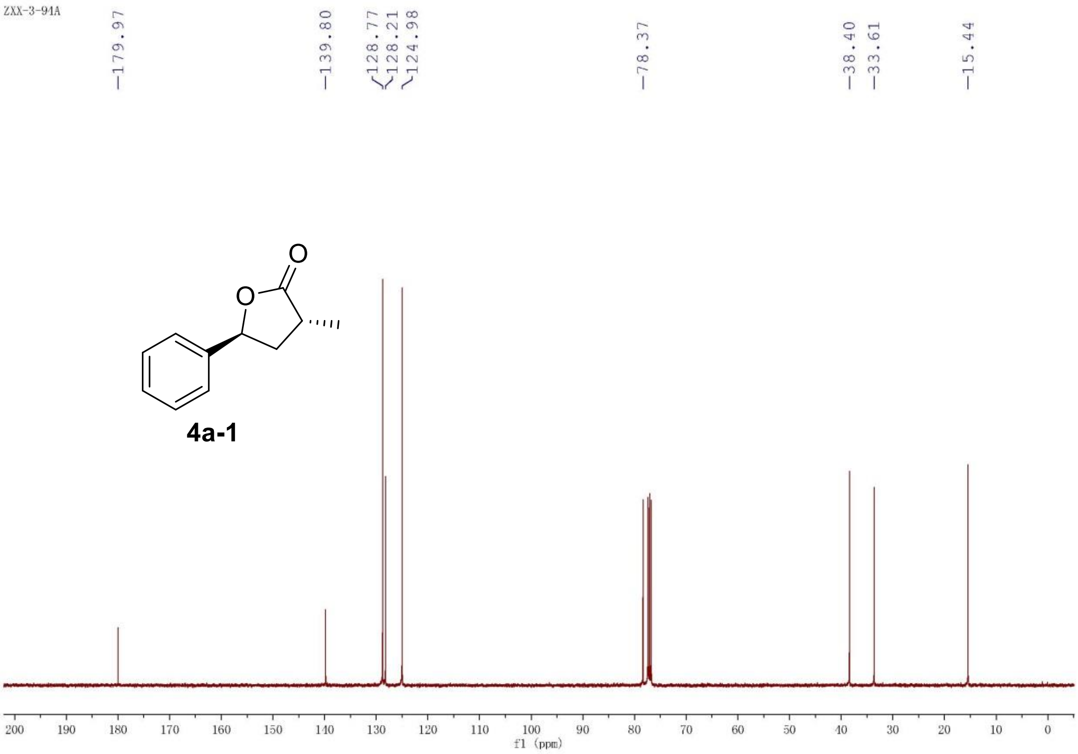

ZXX-4-29
7.33
7.31
7.30
7.29
7.29
7.23
7.21
7.20
2.72
2.70
2.68
2.58
2.57
2.55
2.53
2.51
2.50
2.10
2.08
2.07
1.79
1.26
1.27
1.25
COOH
Br
3j
2.16
2.17
1.90
1.00
1.10
1.08
3.15
f1 (ppm)

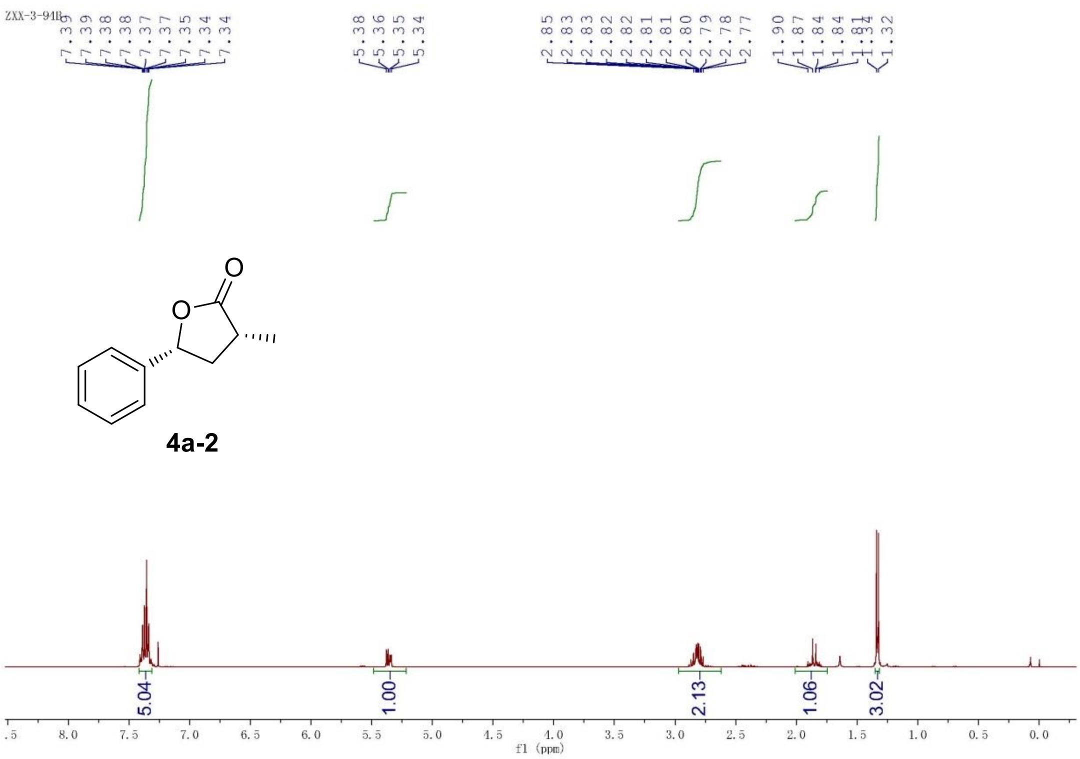

ZXX-4-29
182.26
141.50
128.43
128.41
125.97
38.75
35.16
33.37
16.95
COOH
Br
3j
f1 (ppm)

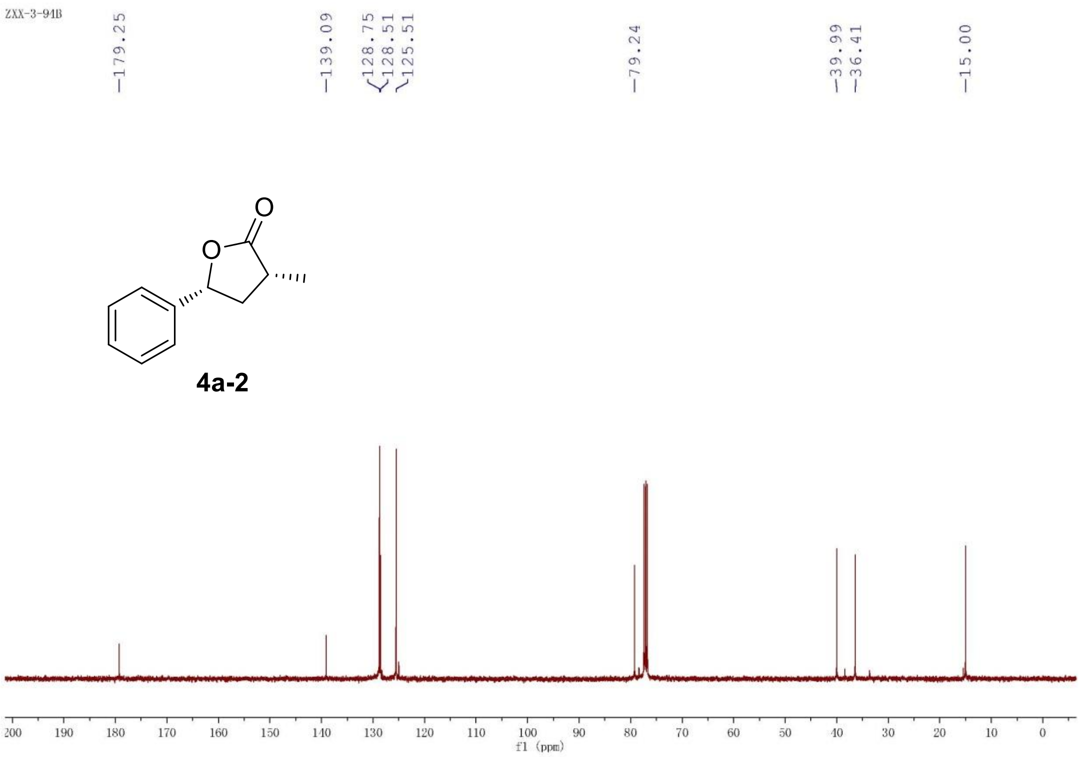

ZXX-4-30B
7.80
7.78
7.65
7.48
7.47
7.45
7.43
7.41
7.37
7.35
7.26
2.87
2.85
2.84
2.59
2.58
2.56
2.54
2.17
2.15
2.13
1.86
1.84
1.29
1.27
COOH
3k
3.11
0.96
1.99
0.94
2.08
1.19
1.00
1.15
3.15
f1 (ppm)

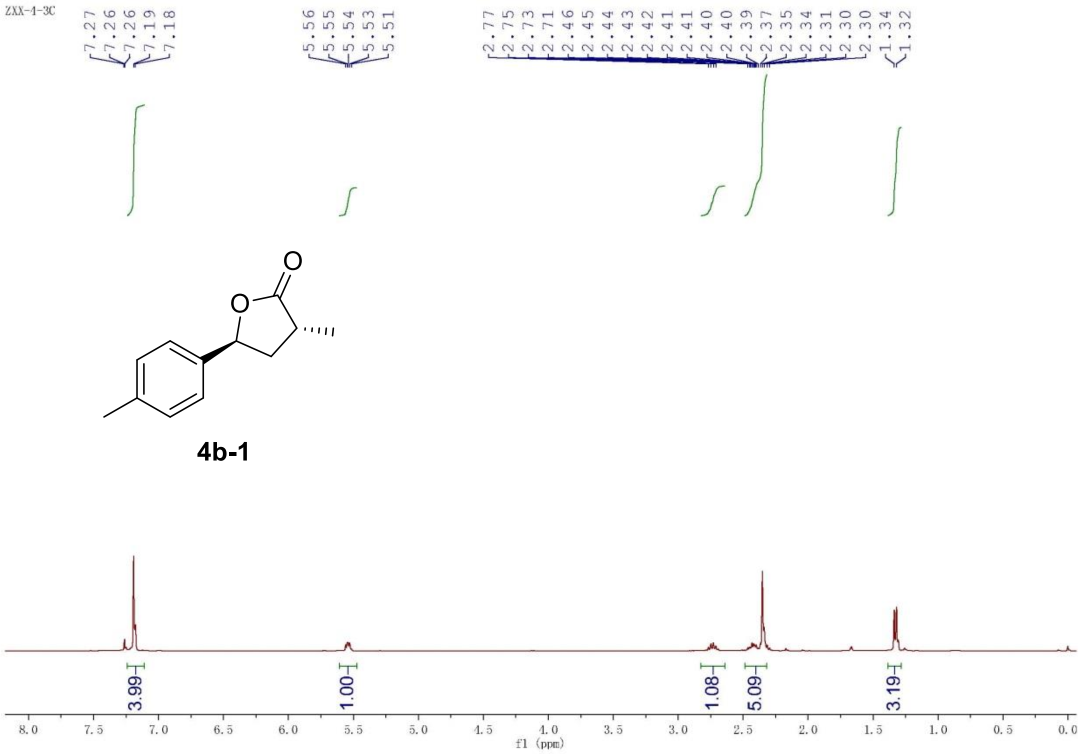

ZXX-4-30B
183.14
139.01
133.61
132.07
128.04
127.65
127.49
127.27
126.56
125.99
125.27
38.88
35.05
33.56
17.04
COOH
3k
f1 (ppm)


4a-1
5.11
1.00
1.02
2.10
3.22
f1 (ppm)

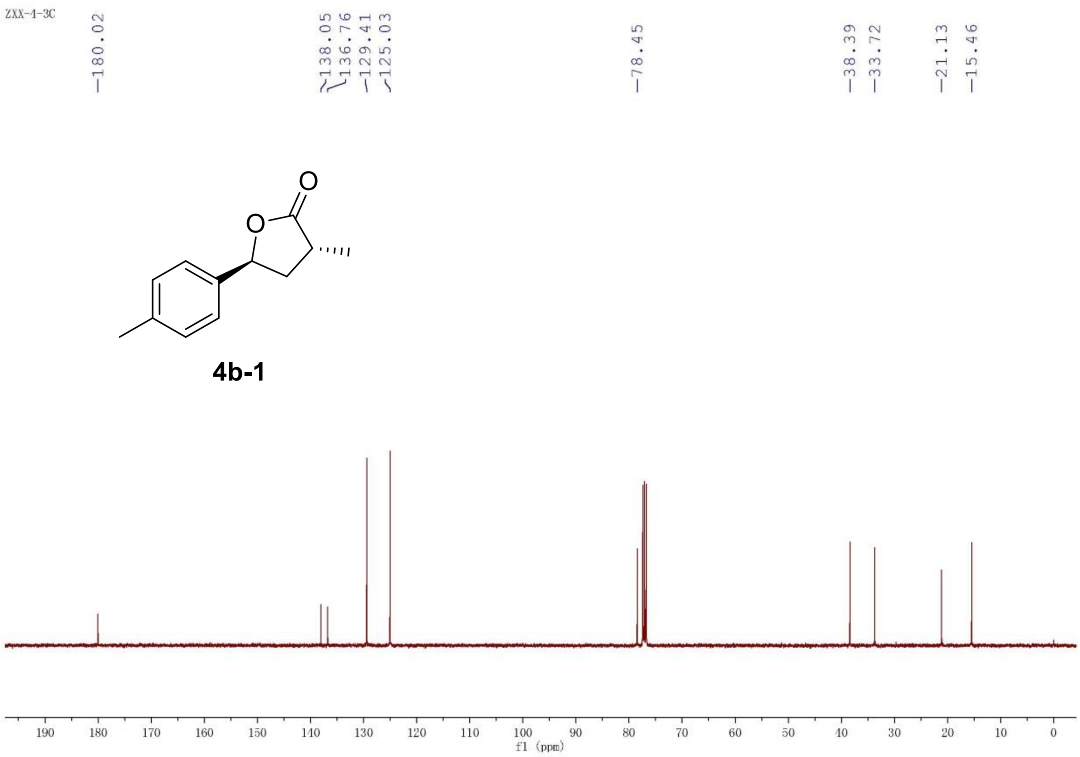

ZXX-3-94A
179.97
139.80
128.77
128.21
124.98
78.37
38.40
33.61
15.44
4a-1
f1 (ppm)


ZXX-3-94B
7.39
7.39
7.38
7.38
7.37
7.37
7.35
7.34
7.34
7.34
5.38
5.36
5.35
5.34
2.85
2.83
2.83
2.82
2.82
2.81
2.81
2.80
2.79
2.78
2.77
1.90
1.87
1.84
1.84
1.81
1.34
1.32
O
O
4a-2
5.04
1.00
2.13
1.06
3.02
f1 (ppm)

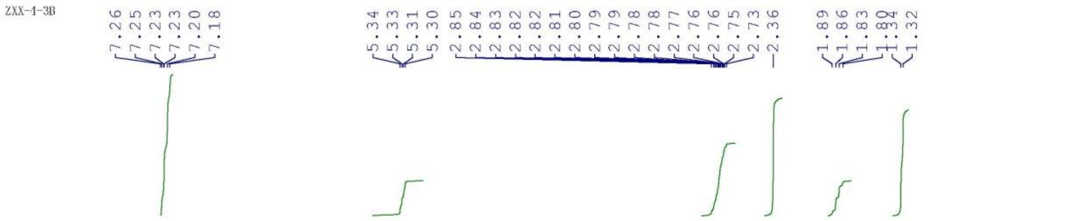

ZXX-3-94B
179.25
139.09
128.75
128.51
125.51
79.24
39.99
36.41
15.00
O
O
4a-2
f1 (ppm)

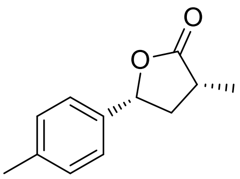

ZXX-4-3C
7.27
7.26
7.26
7.19
7.18
5.56
5.55
5.54
5.53
5.51
2.77
2.75
2.73
2.71
2.46
2.45
2.44
2.43
2.42
2.41
2.41
2.40
2.40
2.39
2.37
2.35
2.34
2.31
2.30
1.34
1.32
O
O
3.99
1.00
1.08
5.09
3.19
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

**4b-1**

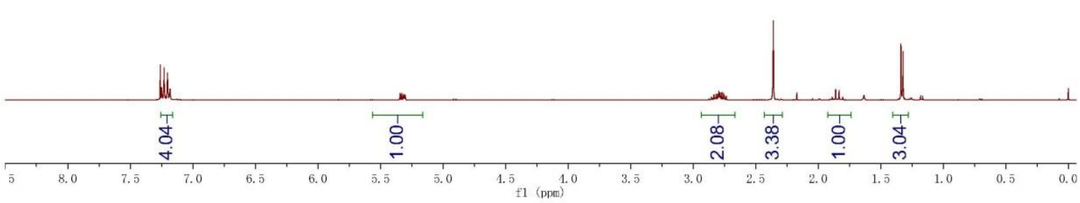

ZXX-4-3C
180.02
138.05
136.76
129.41
125.03
78.45
38.39
33.72
21.13
15.46
O
O
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

**4b-1**

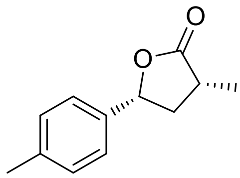

ZXX-4-3B
7.26
7.25
7.23
7.23
7.20
7.18
5.34
5.33
5.31
5.30
2.85
2.84
2.83
2.82
2.82
2.81
2.80
2.79
2.79
2.78
2.78
2.77
2.76
2.76
2.75
2.73
2.36
1.89
1.86
1.83
1.80
1.34
1.32


O
O

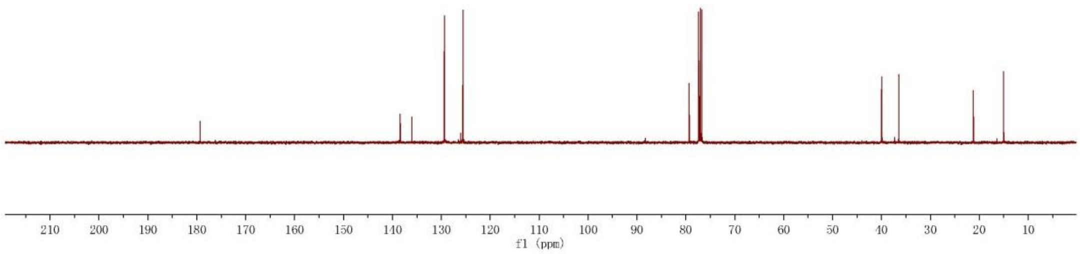
**4b-2**

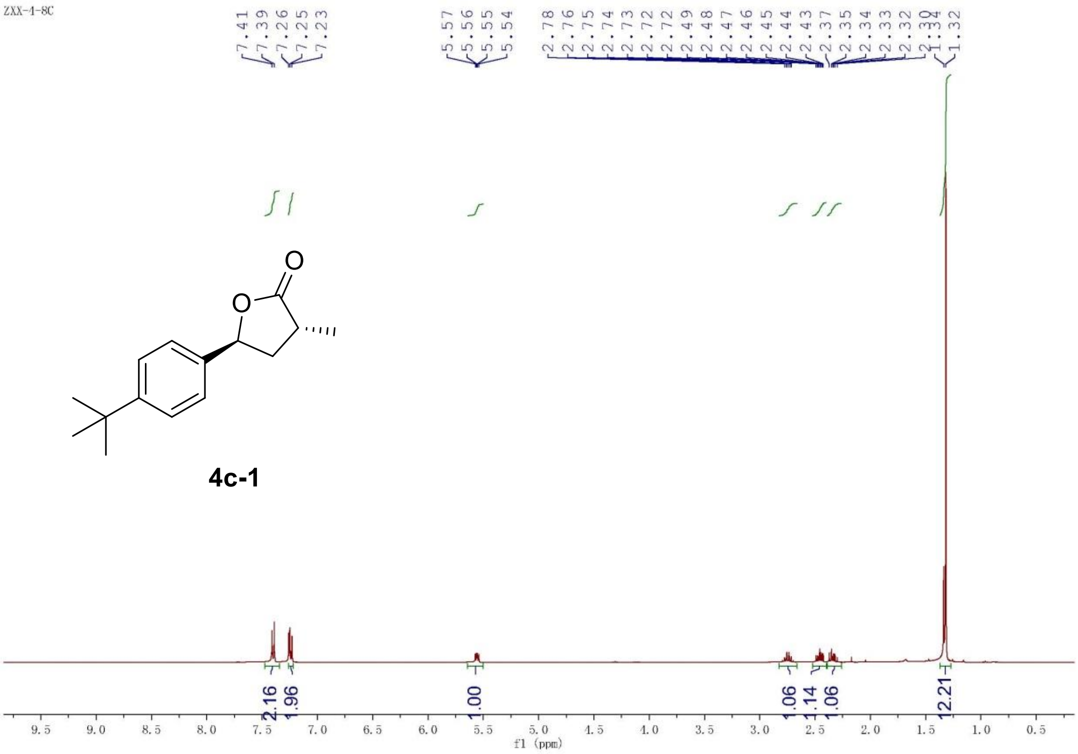

4.04
1.00
2.08
3.38
1.00
3.04
f1 (ppm)


ZXX-4-3B
179.30
138.40
136.01
129.38
125.60
79.32
39.98
36.47
21.20
15.01

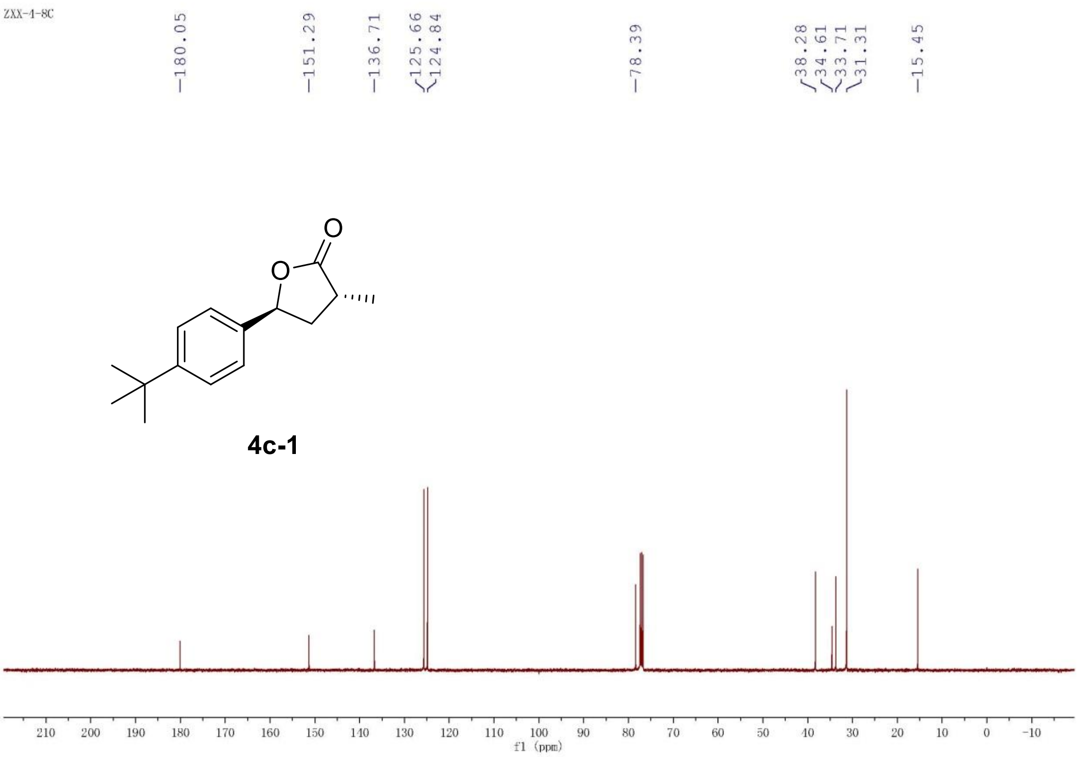

O
O

**4b-2**

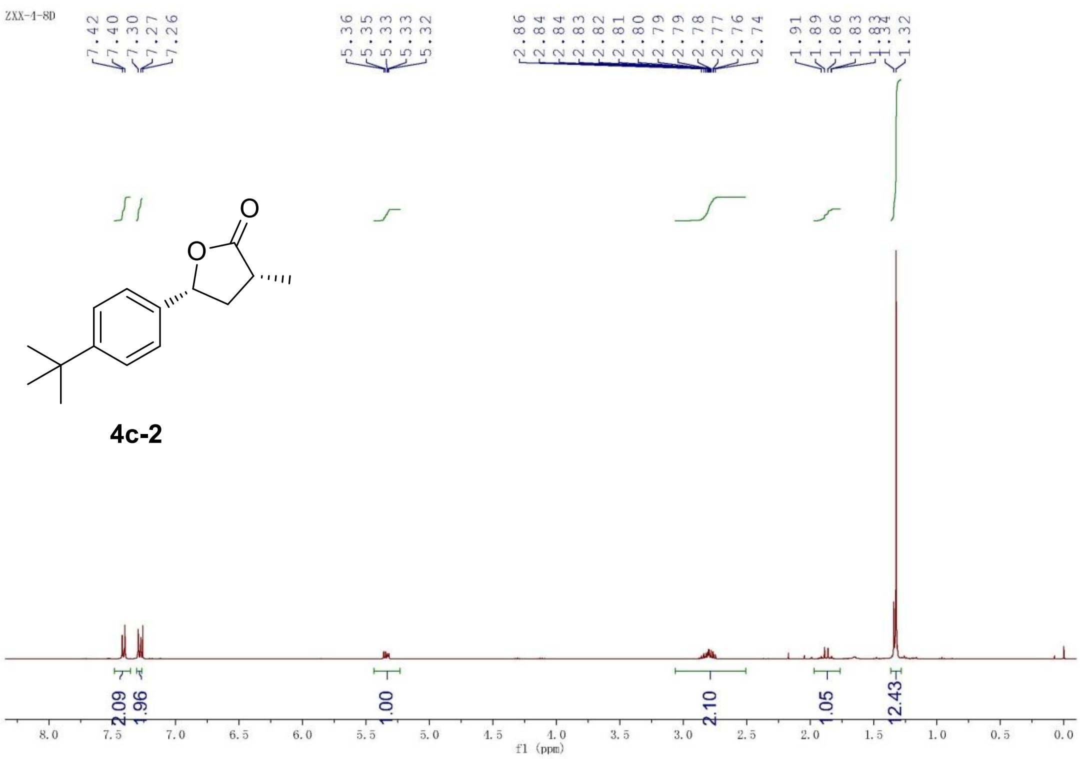

f1 (ppm)



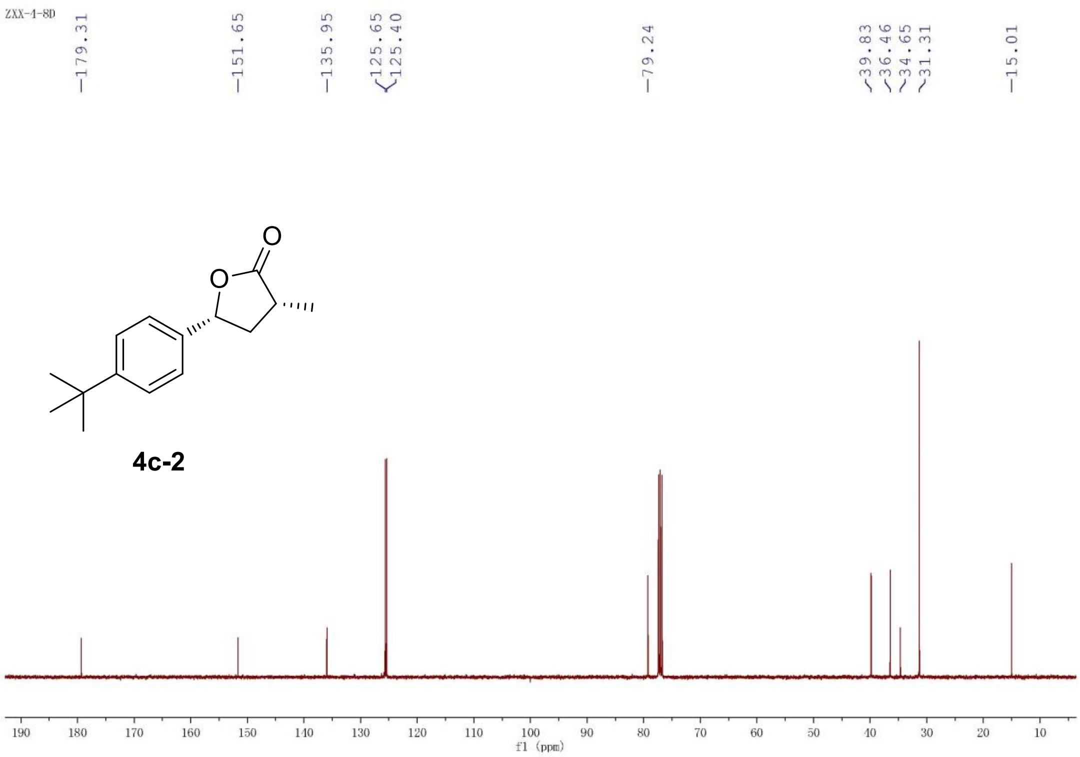
ZXX-4-8C
7.41
7.39
7.26
7.25
7.23
5.57
5.56
5.55
5.54
2.78
2.76
2.75
2.74
2.73
2.72
2.72
2.49
2.48
2.47
2.46
2.45
2.44
2.43
2.37
2.35
2.34
2.33
2.32
2.30
1.34
1.32
O
O
4c-1
2.16
1.96
1.00
1.06
1.14
1.06
12.21
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

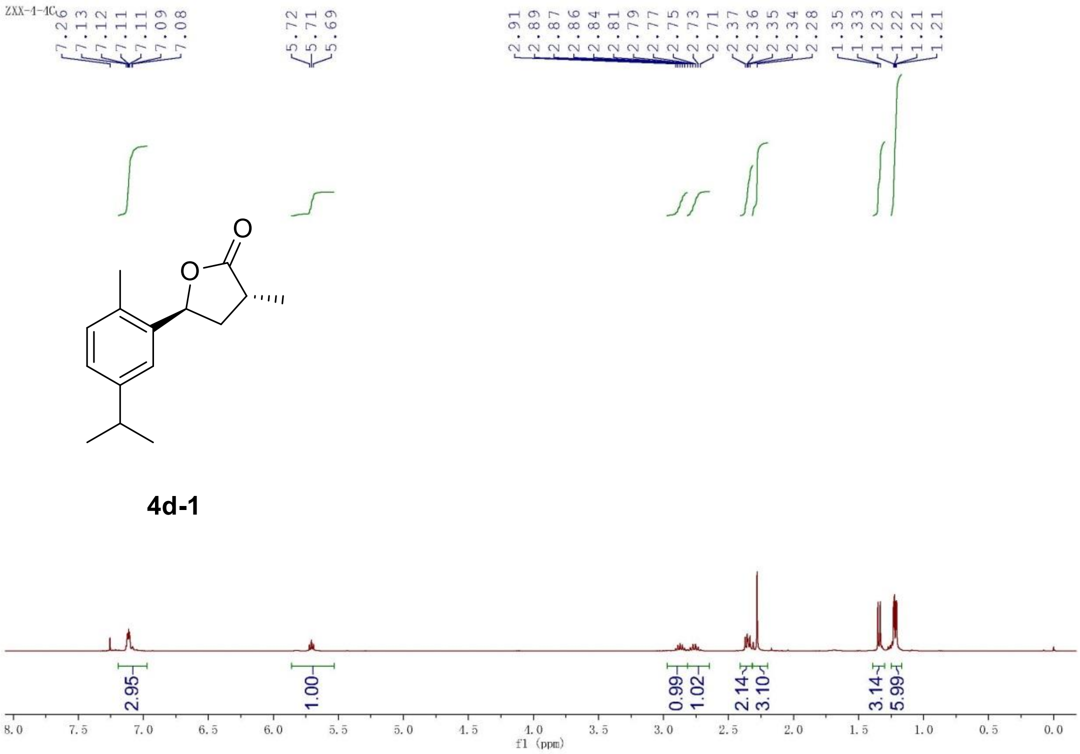
ZXX-4-8C
180.05
151.29
136.71
125.66
124.84
78.39
38.28
34.61
33.71
31.31
15.45
O
O
4c-1
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


ZXX-4-8D
7.42
7.40
7.30
7.27
7.26
5.36
5.35
5.33
5.33
5.32
2.86
2.84
2.84
2.83
2.82
2.81
2.80
2.79
2.79
2.78
2.77
2.76
2.74
1.91
1.89
1.86
1.83
1.83
1.34
1.32
2.09
1.96
1.00
2.10
1.05
12.43
f1 (ppm)

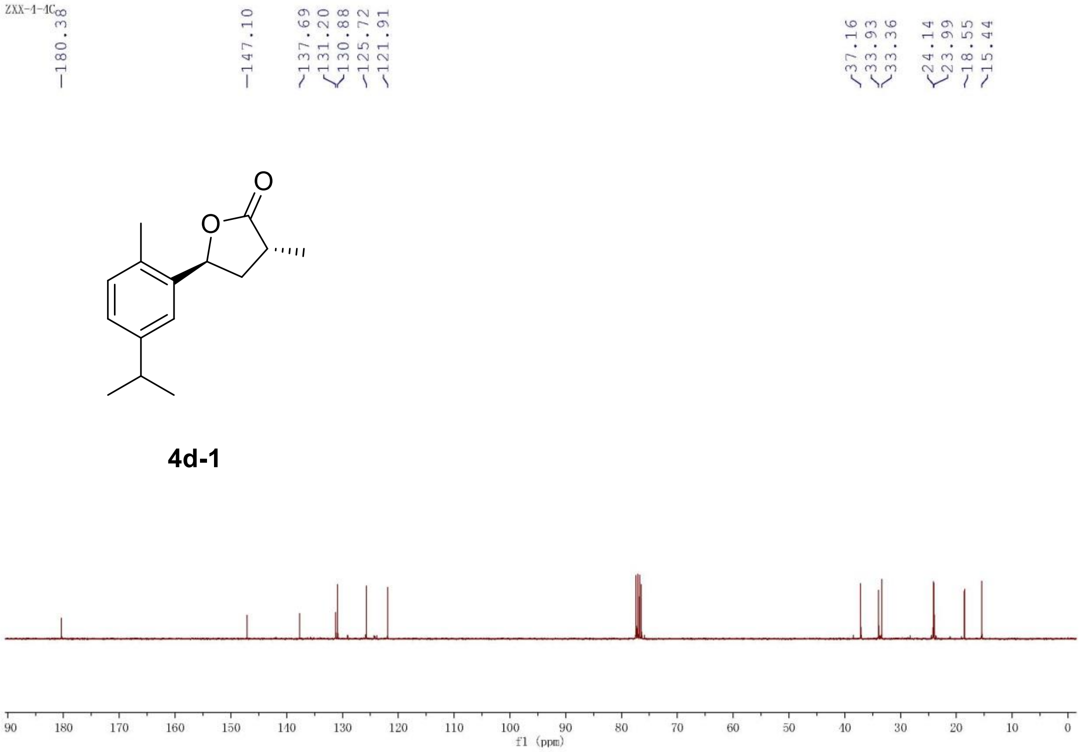
4c-2


ZXX-4-8D
179.31
151.65
135.95
125.65
125.40
79.24
39.83
36.46
34.65
31.31
15.01
f1 (ppm)

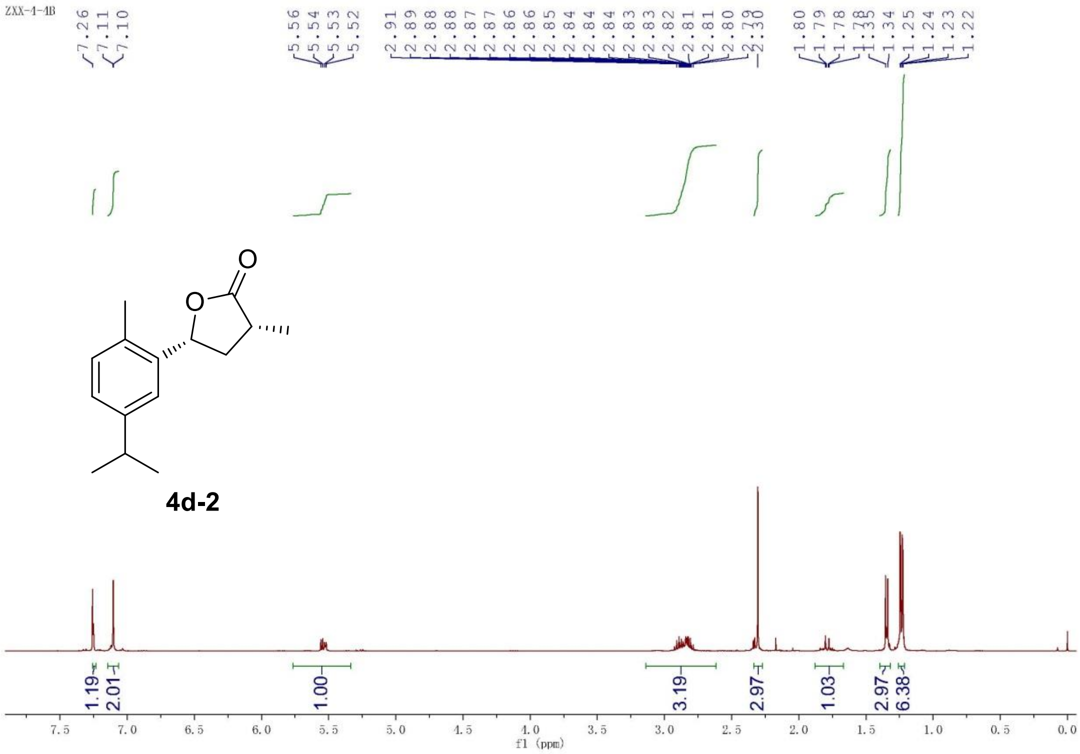
4c-2

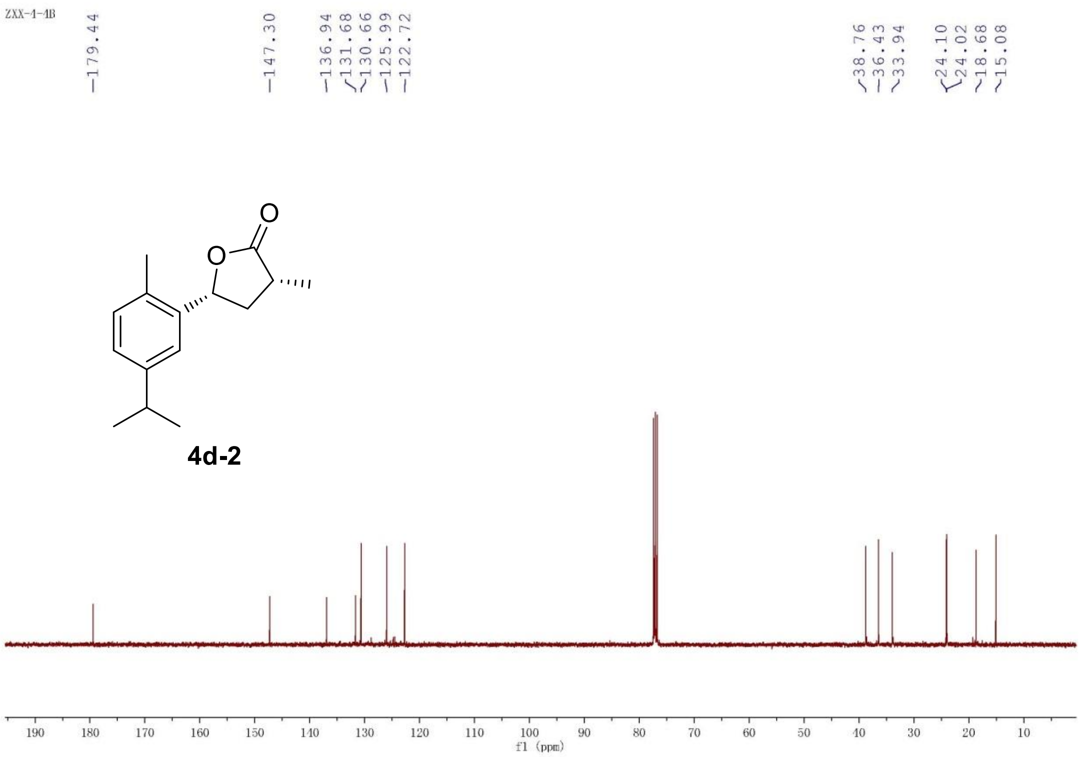

ZXX-4-1C
7.26
7.13
7.12
7.11
7.11
7.09
7.08
5.72
5.71
5.69
2.91
2.89
2.87
2.86
2.84
2.81
2.79
2.77
2.75
2.73
2.71
2.37
2.36
2.35
2.34
2.28
1.35
1.33
1.23
1.22
1.21
1.21
O
2.95
1.00
0.99
1.02
2.14
3.10
3.14
5.99
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

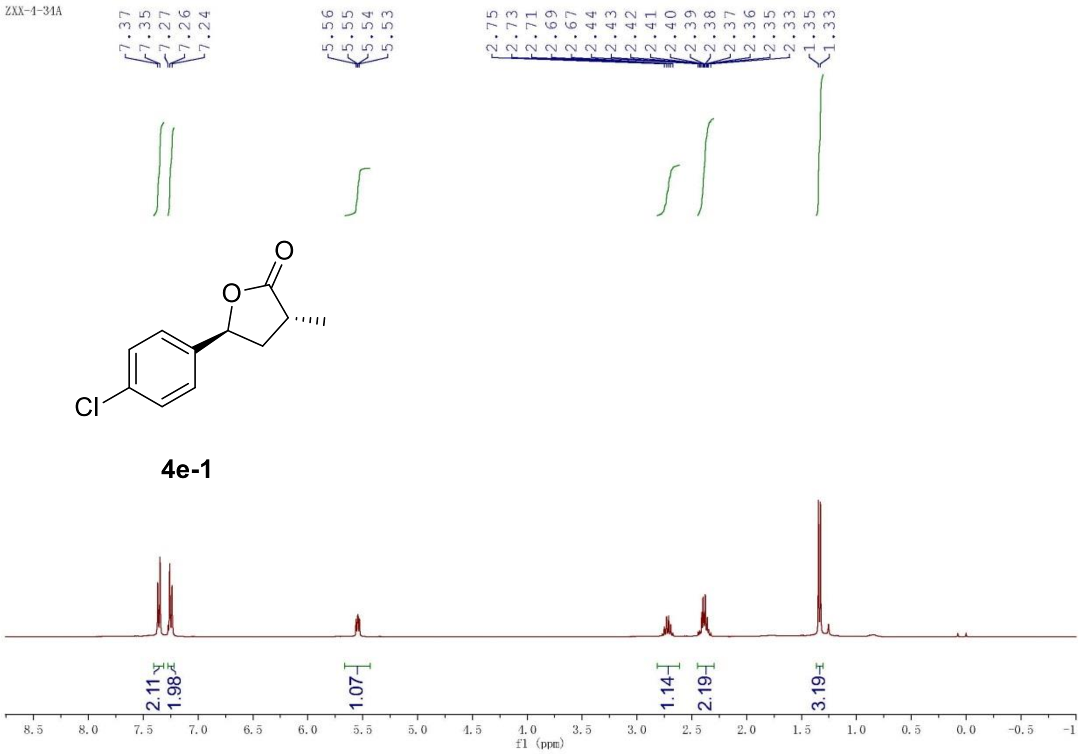
**4d-1**

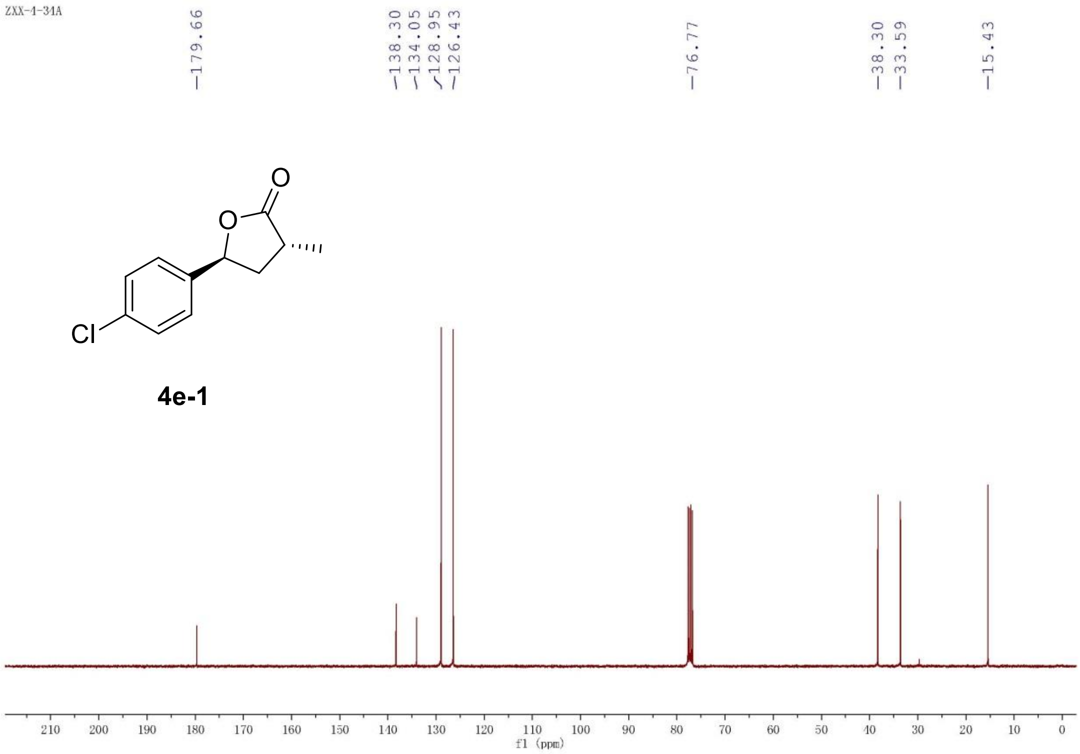

ZXX-4-1C
180.38
147.10
137.69
131.20
130.88
125.72
121.91
37.16
33.93
33.36
24.14
23.99
18.55
15.44
O
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

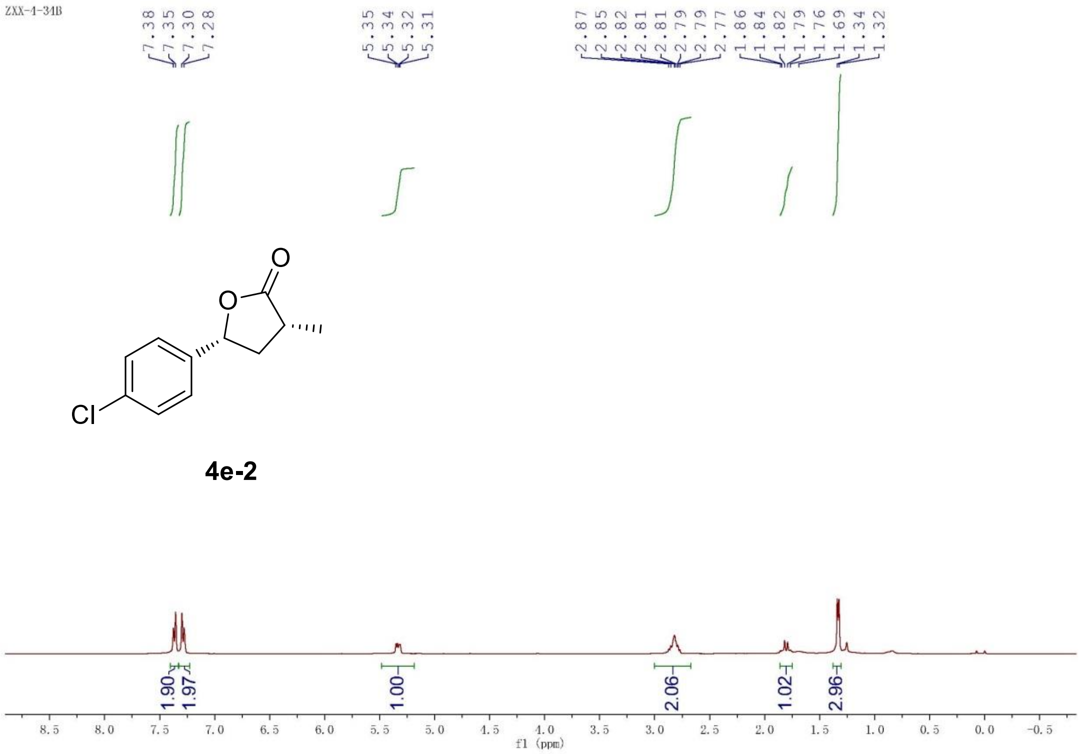
**4d-1**


ZXX-4-4B
7.26
7.11
7.10
5.56
5.54
5.53
5.52
2.91
2.89
2.88
2.88
2.87
2.87
2.86
2.86
2.85
2.84
2.84
2.84
2.83
2.83
2.82
2.82
2.81
2.81
2.80
2.79
2.30
1.80
1.79
1.78
1.78
1.35
1.34
1.25
1.24
1.23
1.22
O
O
4d-2
1.19
2.01
1.00
3.19
2.97
1.03
2.97
6.38
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

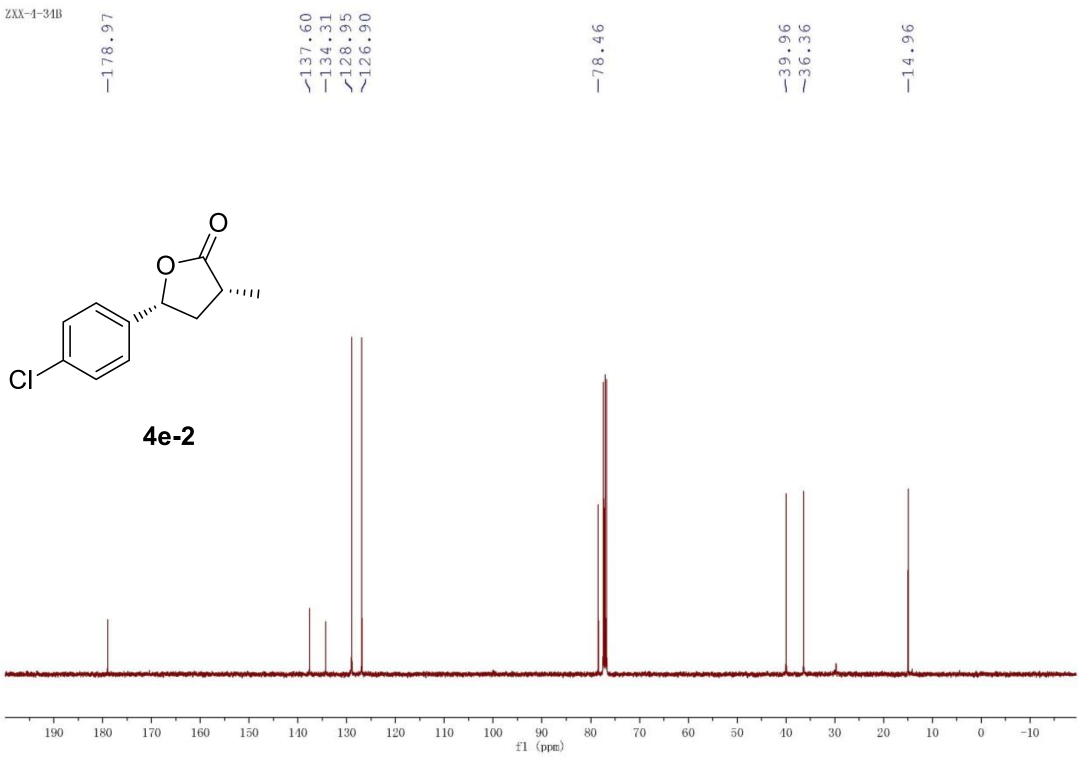

ZXX-4-4B
179.44
147.30
136.94
131.68
130.66
125.99
122.72
38.76
36.43
33.94
24.10
24.02
18.68
15.08
O
O
4d-2
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


ZXX-4-34A
7.37
7.35
7.27
7.26
7.24
5.56
5.55
5.54
5.53
2.75
2.73
2.71
2.69
2.67
2.44
2.43
2.42
2.41
2.40
2.39
2.38
2.37
2.36
2.35
2.33
1.35
1.33
4e-1
2.11
1.98
1.07
1.14
2.19
3.19
f1 (ppm)

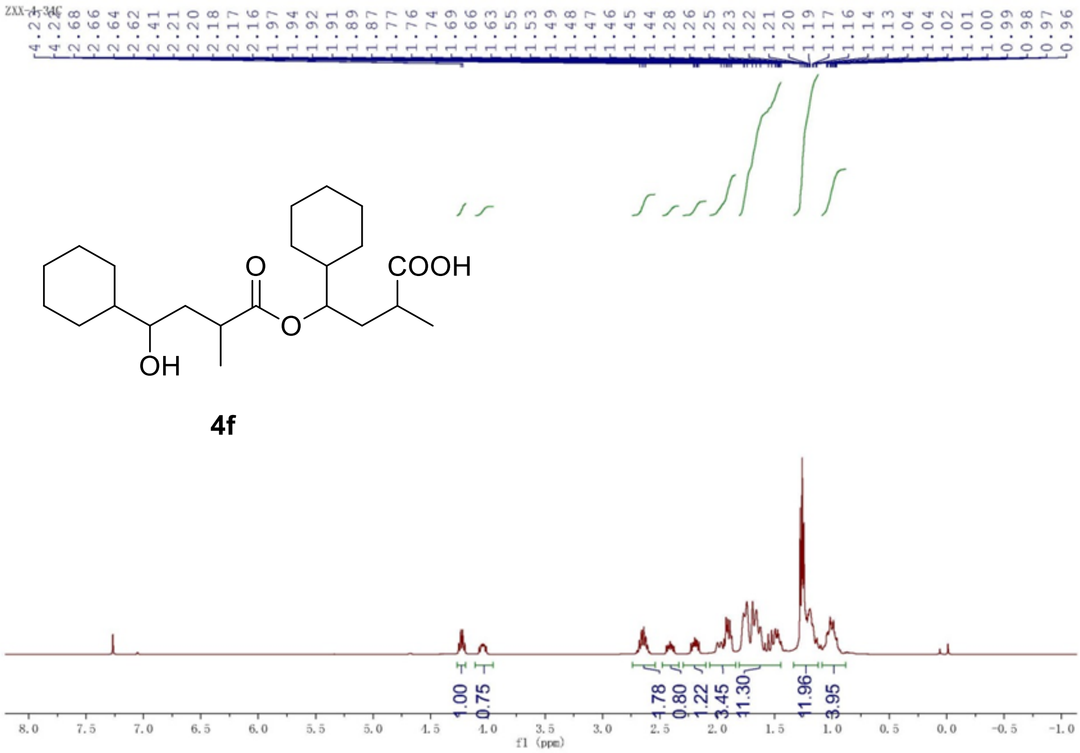

ZXX-4-34A
179.66
138.30
134.05
128.95
126.43
76.77
38.30
33.59
15.43
4e-1
f1 (ppm)

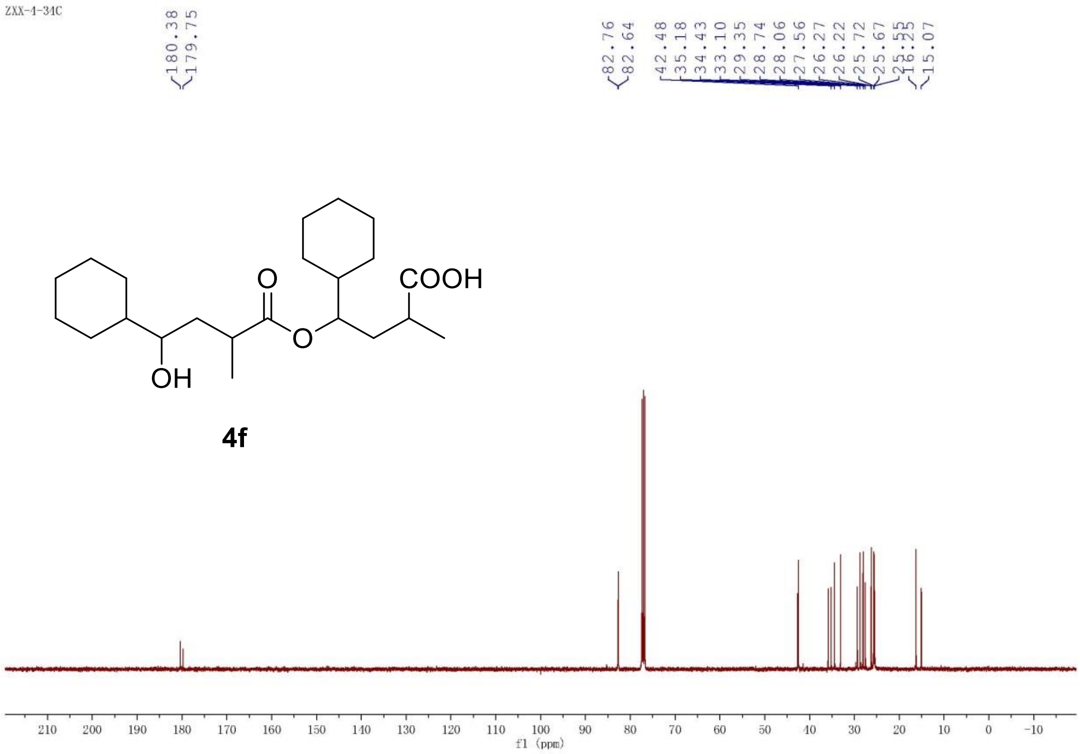

ZXX-4-34B
7.38 7.35 7.30 7.28
5.35 5.34 5.32 5.31
2.87 2.85 2.82 2.81 2.81 2.79 2.79 2.77 1.86 1.84 1.82 1.79 1.76 1.69 1.34 1.32
O
O
Cl
1.90 1.97 1.00 2.06 1.02 2.96
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

**4e-2**

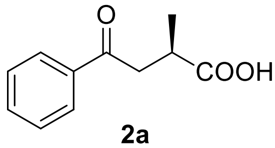

ZXX-4-34B
178.97
137.60 134.31 128.95 126.90
78.46
39.96 36.36
14.96
O
O
Cl
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

**4e-2**



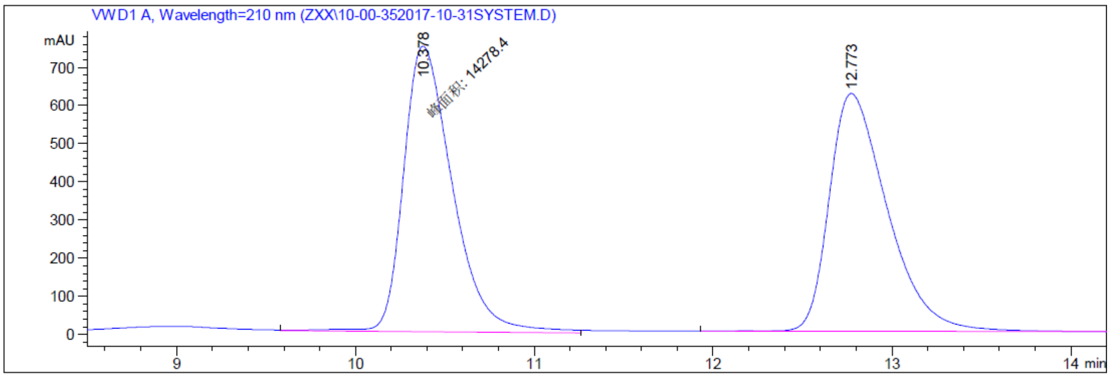


**E: HPLC Spectra of Products**

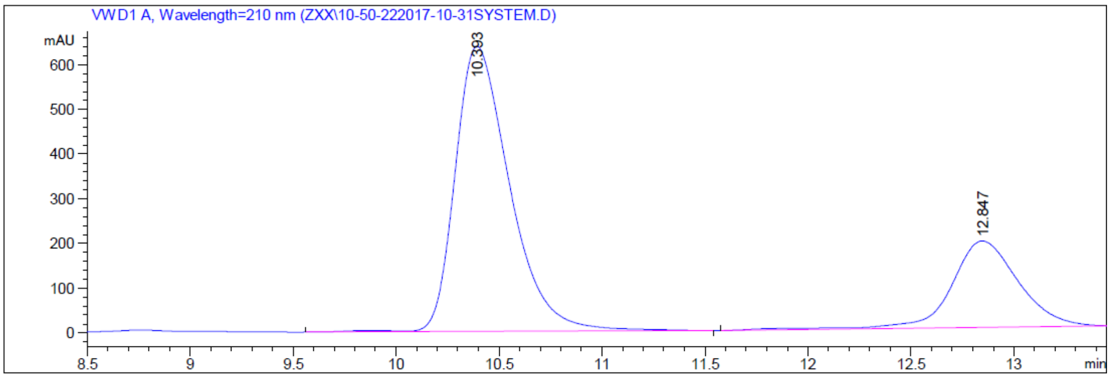


**2a**

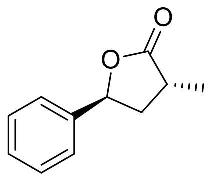
white solid, 96% yield, 45% *ee*, $[\alpha]_D^{20}$= -9.0(c=0.4, $CH_2Cl_2$). The ee of **2a** was determined by HPLC analysis using Daicel Chiralcel OJ-H column (25 cm × 0.46 cm ID), conditions: *n*-hexane/*i*-PrOH = 90/10, 1.0mL/min, 210 nm; $t_{major}$ =10.393 min, $t_{minor}$ = 12.847 min.




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 10.378 | MM | 0.3179 | 1.42784e4 | 748.68951 | 50.2502 |
| 2 | 12.773 | VBAR | 0.3454 | 1.41362e4 | 623.67511 | 49.7498 |

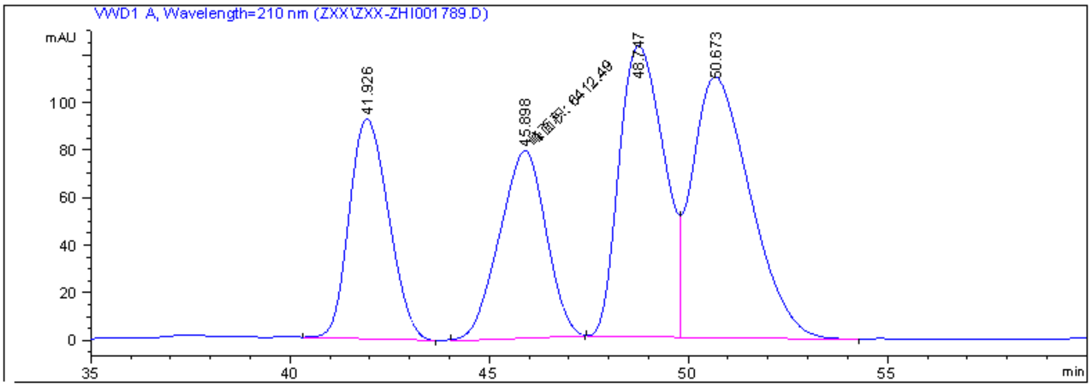



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 10.393 | VB R | 0.2803 | 1.17759e4 | 638.23584 | 72.8186 |
| 2 | 12.847 | BBA | 0.3434 | 4395.64648 | 193.26276 | 27.1814 |

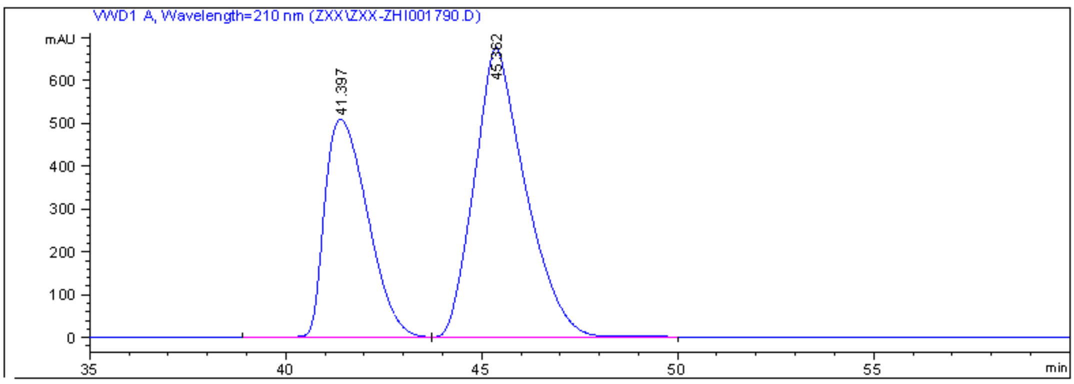


**4a-1**

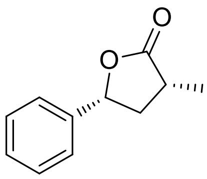
white solid, 50% yield, 22% *ee*, $[\alpha]_D^{25}$= -1.0(c=0.4, $CH_2Cl_2$).The ee of **4a-1** was determined by HPLC analysis using Daicel Chiralcel OJ-H column (25 cm × 0.46 cm ID), conditions: *n*-hexane/*i*-PrOH = 95/5, 0.5mL/min, 210 nm; $t_{major}$ =45.362 min, $t_{minor}$ = 41.397 min.




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 41.926 | BB | 1.0792 | 6348.04639 | 92.43748 | 18.9303 |
| 2 | 45.898 | MM | 1.3546 | 6412.49316 | 78.90000 | 19.1224 |
| 3 | 48.747 | BV | 1.2353 | 9629.09180 | 122.33156 | 28.7145 |
| 4 | 50.673 | VB | 1.5388 | 1.11442e4 | 109.64556 | 33.2328 |

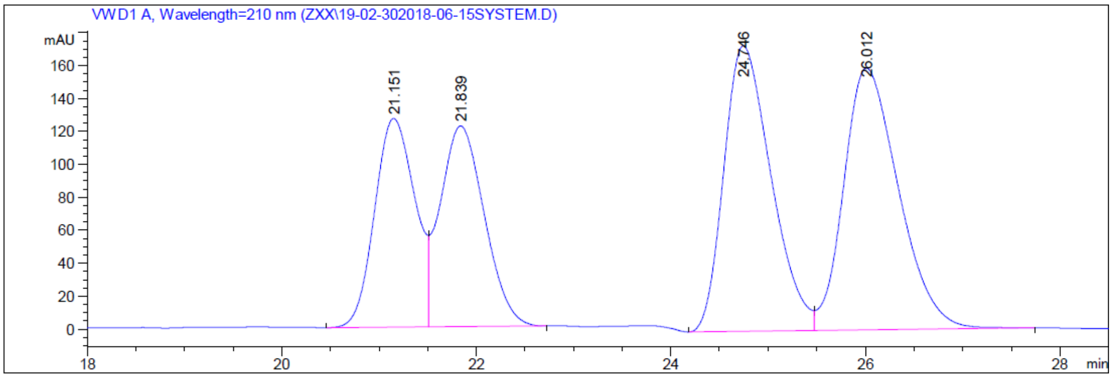


| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 41.397 | BB | 1.2178 | 3.84919e4 | 507.52402 | 38.7016 |
| 2 | 45.362 | BB | 1.2772 | 6.09663e4 | 674.71521 | 61.2984 |

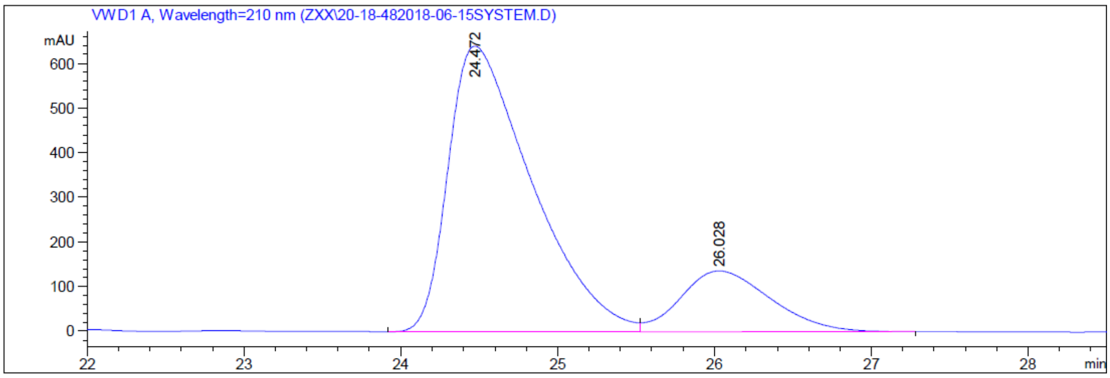


**4a-2**

White solid, 46% yield, 63% *ee*, $[\alpha]_D^{25}$= -24.0(c=0.42, $CH_2Cl_2$).The ee of **4a-2** was determined by HPLC analysis using Daicel Chiralcel OJ-H column (25 cm × 0.46 cm ID), conditions: *n*-heptane/*i*-PrOH = 95/5,1mL/min, 210 nm; t $_{major}$ =24.472 min, t $_{minor}$ = 26.028 min.




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 21.151 | BV | 0.4444 | 3651.12720 | 126.62154 | 18.6244 |
| 2 | 21.839 | VB | 0.4838 | 3860.59351 | 121.79987 | 19.6929 |
| 3 | 24.746 | BV | 0.5211 | 5858.72607 | 173.42030 | 29.8853 |
| 4 | 26.012 | VB | 0.6045 | 6233.56055 | 158.96889 | 31.7974 |




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 24.472 | BV | 0.5523 | 2.37064e4 | 639.84930 | 81.4157 |
| 2 | 26.028 | VB | 0.6154 | 5411.31299 | 135.93820 | 18.5843 |

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