Supporting information

Asymmetric Michael addition between kojic acid derivatives and unsaturated ketoesters promoted by C_2-symmetric organocatalysts

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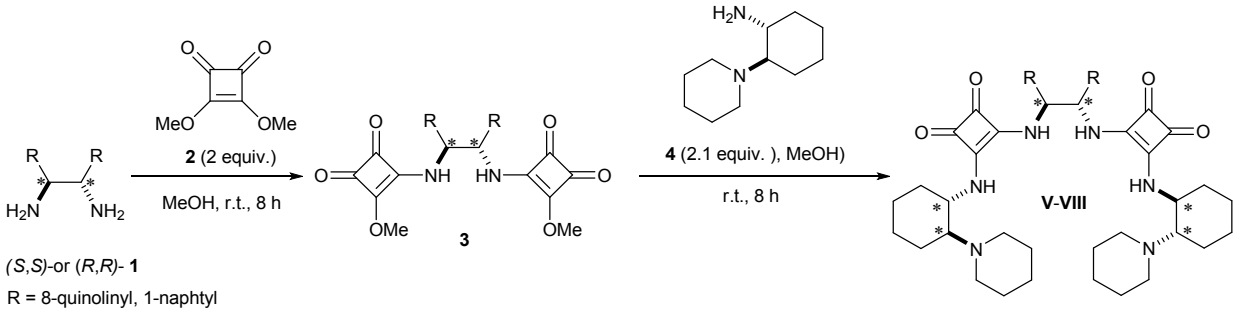
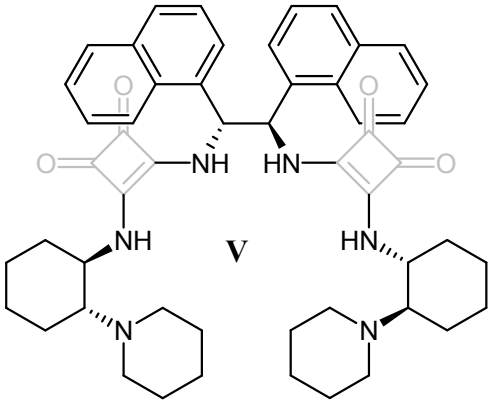
Contents

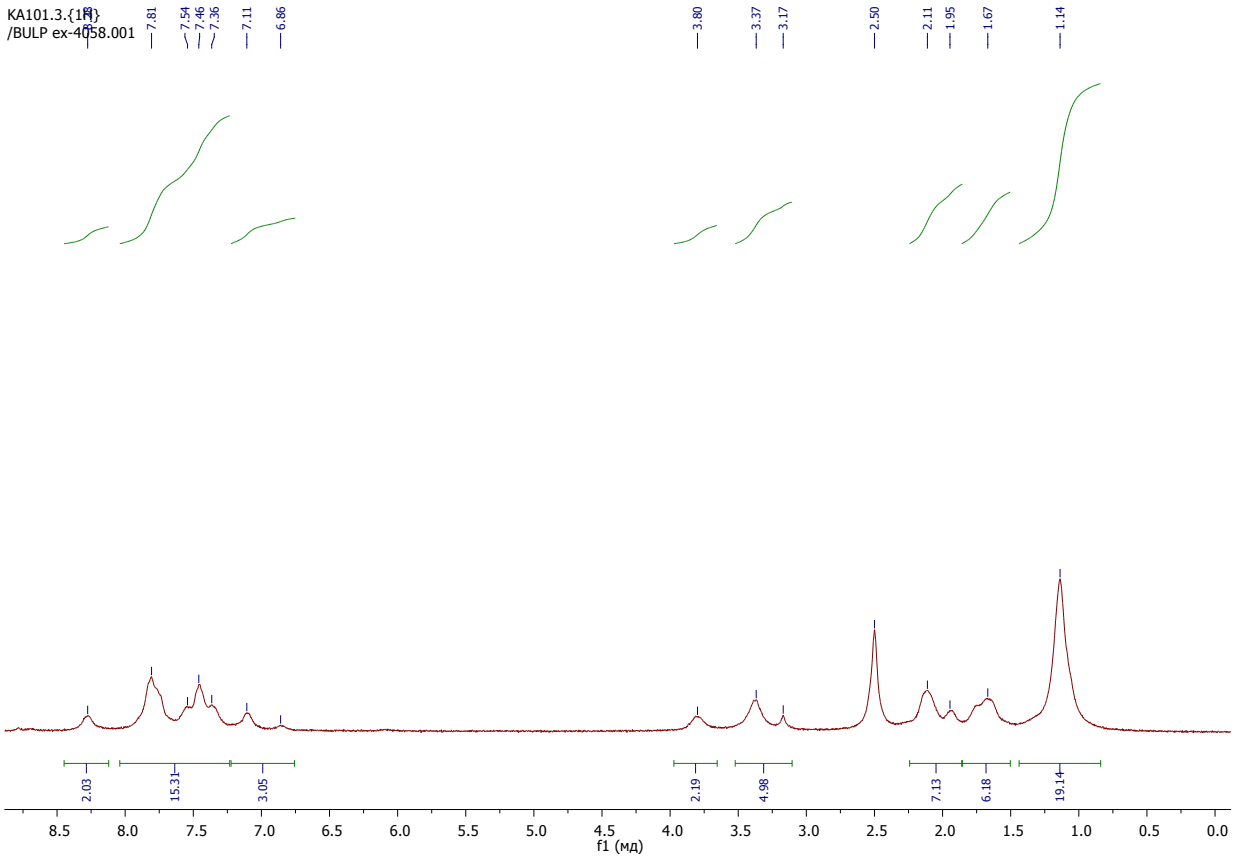
1. Synthesis of catalysts V-VIII (General procedure)



Dimethyl squarate **2** (0.70 g, 4.91 mmol) was added to a solution of corresponding diamine **1** (2.33 mmol) in MeOH (2 mL) in one portion. After 20 h of stirring at ambient temperature, the precipitated product **3** was filtered, washed with Et_2O (3 x 10 mL) and dried in air. Then, it was added without further purification to the solution of 2-(Piperidin-1-yl)cyclohexanamine **4** (0.69 g, 3.77 mmol) in MeOH (2 mL). The reaction mixture was stirred at ambient temperature for 20 h. The precipitate was filtered, washed with Et_2O (3 x 10 mL) and dried under reduced pressure (10 Torr) to afford corresponding catalyst **V**, **VI**, **VII** or **VIII**. Catalysts **III-IV** were prepared by known procedures [1].

(*R,R*)-4,4'-(((1*R*,2*R*)-1,2-Di(naphthalen-1-yl)ethane-1,2-diyl)bis(azanediyl))bis(3-(((1*R*,2*R*)-2-(piperidin-1-yl)cyclohexyl)amino)cyclobut-3-ene-1,2-dione) (V): Yellow solid (0.72 g, 82%). Mp: >230°C dec. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.28 (m, 3H), 8.08 – 6.76 (m, 19H), 3.81 (s, 3H), 3.17 (s, 1H), 2.03 (m, 8H), 1.67 (m, 6H), 1.14 (s, 20H) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ 183.3, 182.6, 168.7, 167.7, 134.9, 133.8, 130.9, 129.1, 127.2, 126.4, 125.8, 122.8, 68.7, 54.3, 49.7, 35.1, 26.5, 25.2, 24.9, 24.8, 24.0 ppm. HRMS (ESI): *m/z* M + H^+ calcd for $C_{52}H_{61}N_6O_4^+$ 833.4748, found 833.4760.

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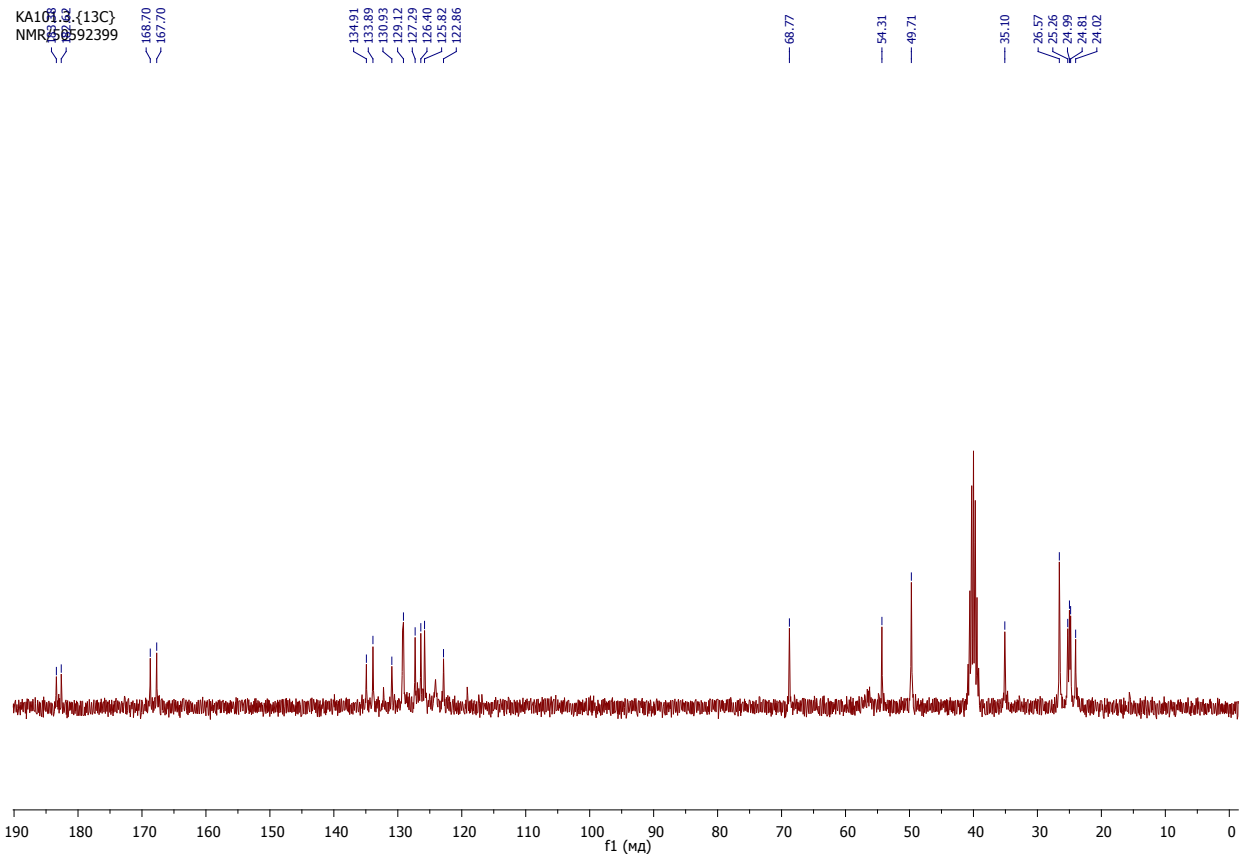
7.81
7.54
7.46
7.36
7.11
6.86
3.80
3.37
3.17
2.50
2.11
1.95
1.67
1.14
2.03
15.31
3.05
2.19
4.98
7.13
6.18
19.14
f1 (мд)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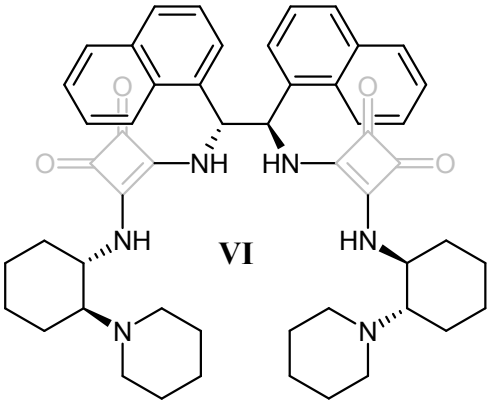
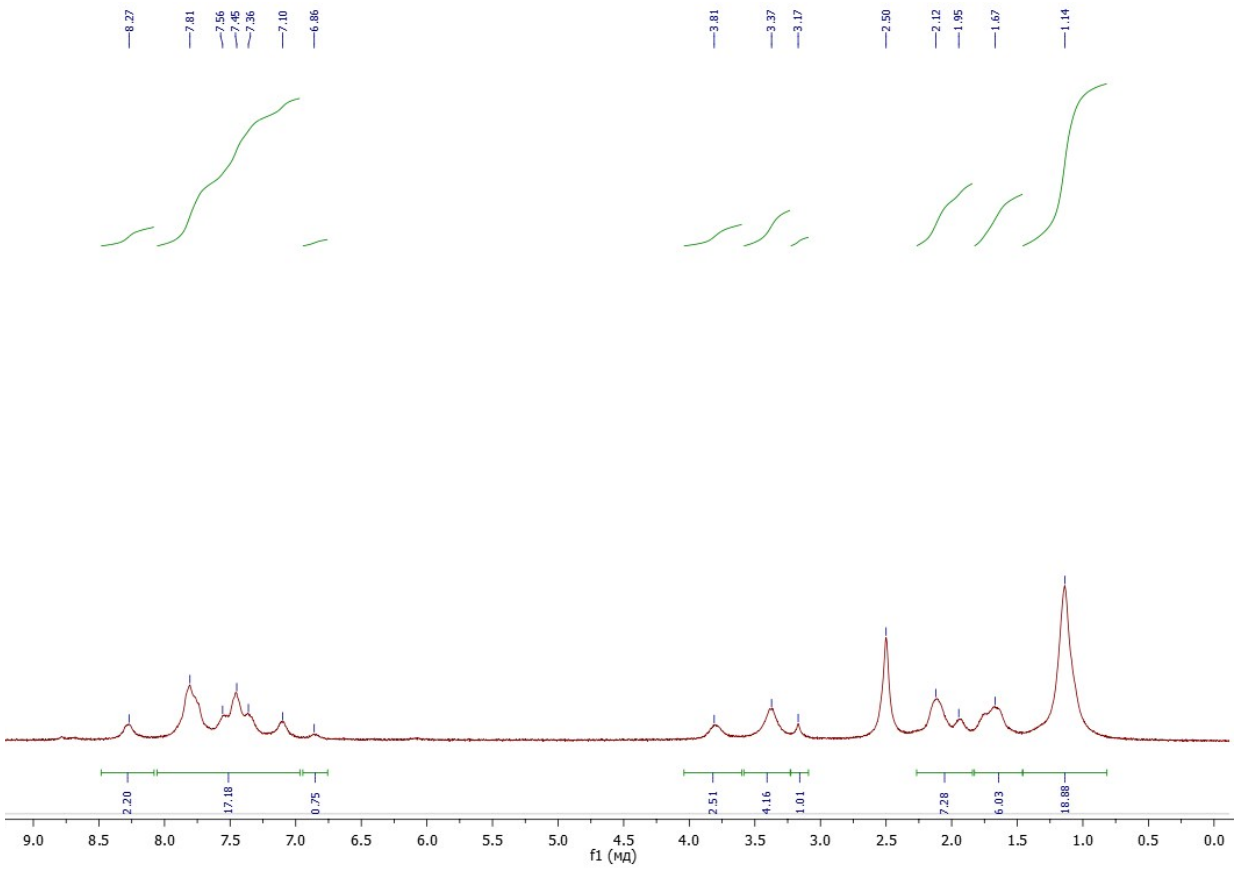
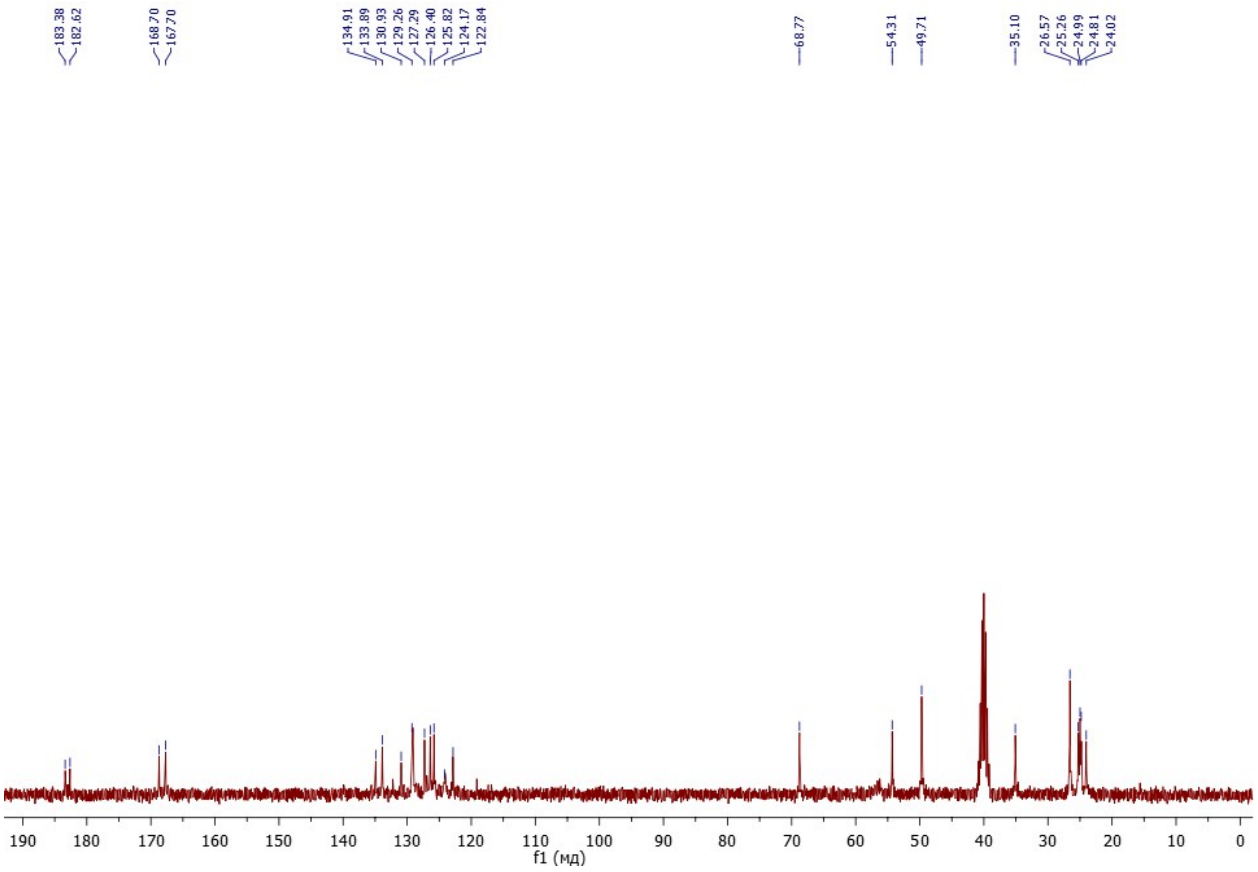
167.70
134.91
133.89
130.93
129.12
127.29
126.40
125.82
122.86
68.77
54.31
49.71
35.10
26.57
25.26
24.99
24.81
24.02
f1 (мд)

(*S*,*S*)-4,4'-(((1*R*,2*R*)-1,2-Di(naphthalen-1-yl)ethane-1,2-diyl)bis(azanediyl))bis(3-(((1*S*,2*S*)-2-(piperidin-1-yl)cyclohexyl)amino)cyclobut-3-ene-1,2-dione) (VI): Yellow solid (0.81 g, 83% yield). Mp: >230°C dec. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.27 (m, 3H), 8.08 – 7.05 (m, 19H), 6.86 (s, 1H), 3.81 (s, 3H), 3.17 (s, 1H), 2.25 – 1.75 (m, 8H), 1.67 (m, 6H), 1.14 (s, 20H) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ 183.3, 182.6, 168.7, 167.7, 134.9, 133.8, 130.9, 129.1, 127.2, 126.4, 125.8, 122.8, 68.7, 54.3, 49.7, 35.1, 26.5, 25.2, 24.9, 24.8, 24.0 ppm. HRMS (ESI): *m/z* M + H^+ calcd for $C_{52}H_{61}N_6O_4^+$ 833.4748, found 833.4741.



VI

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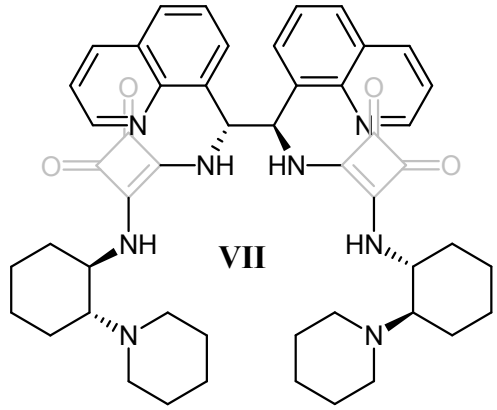
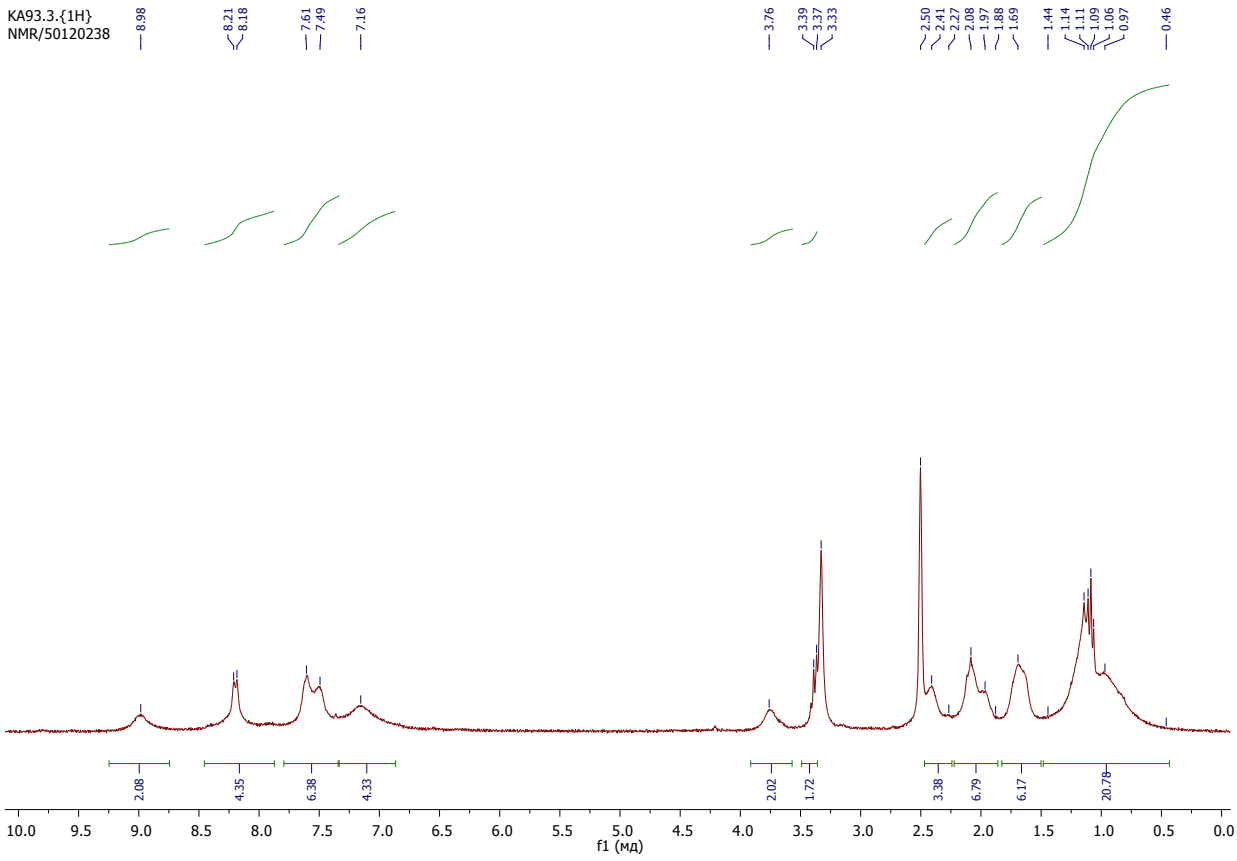
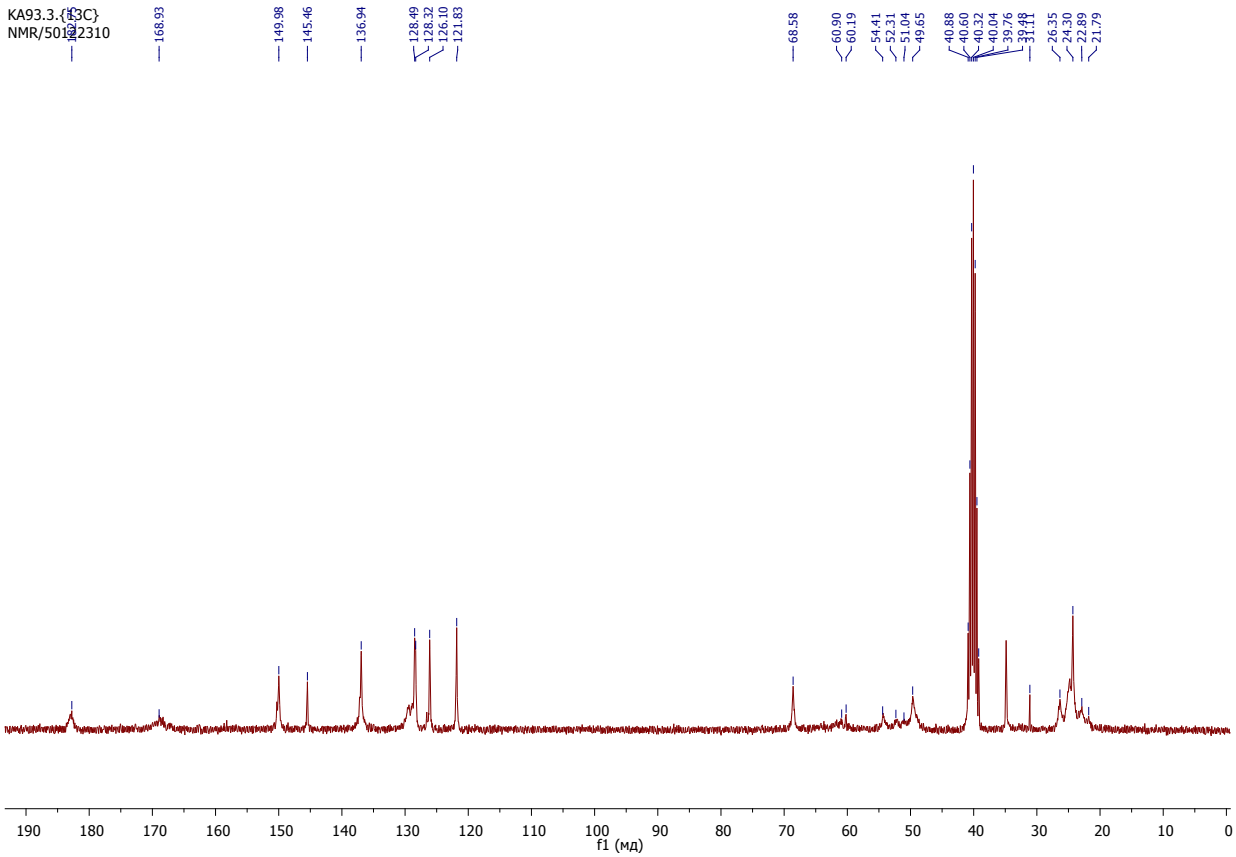
182.62
168.70
167.70
134.91
133.89
130.93
129.26
127.29
126.40
125.82
124.17
122.84
68.77
54.31
49.71
35.10
26.57
25.26
24.99
24.81
24.02
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (мд)

(*R*,*R*)-4,4'-(((1*R*,2*R*)-1,2-Di(quinolin-8-yl)ethane-1,2-diyl)bis(azanediyl))bis(3-(((1*R*,2*R*)-2-(piperidin-1-yl)cyclohexyl)amino)cyclobut-3-ene-1,2-dione) (VII): Yellow solid (0.69 g, 72% yield). Mp 195-197°C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.98 (s, 2H), 8.20 (d, *J* = 8.3 Hz, 4H), 7.55 (m, 6H), 7.16 (s, 4H), 3.76 (s, 2H), 3.38 (d, *J* = 7.2 Hz, 2H), 2.34 (m, 4H), 2.22 – 1.86 (m, 6H), 1.69 (s(br), 3H), 1.48 – 0.43 (m, 20H) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ 182.7, 168.9, 149.9, 145.4, 136.9, 128.4, 128.3, 126.1, 121.8, 68.5, 60.9, 60.1, 54.4, 52.3, 51.0, 49.6, 40.8, 40.6, 40.3, 40.0, 39.7, 39.4, 39.2, 31.1, 26.3, 24.3, 22.8, 21.79.182.7, 168.9, 149.9, 145.4, 136.9, 128.4, 128.3, 126.1, 121.8, 68.5, 60.9, 60.1, 54.4, 52.3, 51.0, 49.6, 40.8, 40.6, 40.3, 40.0, 39.7, 39.4, 39.2, 31.1, 26.3, 24.3, 22.8, 21.7 ppm. HRMS (ESI): *m/z* M + H$^+$ calcd for $C_{50}H_{59}N_8O_4^+$ 835.4654, found 835.4712.



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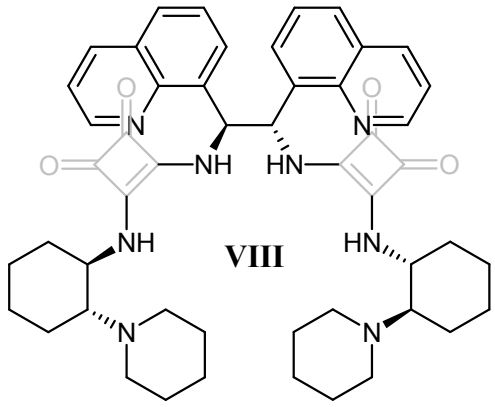
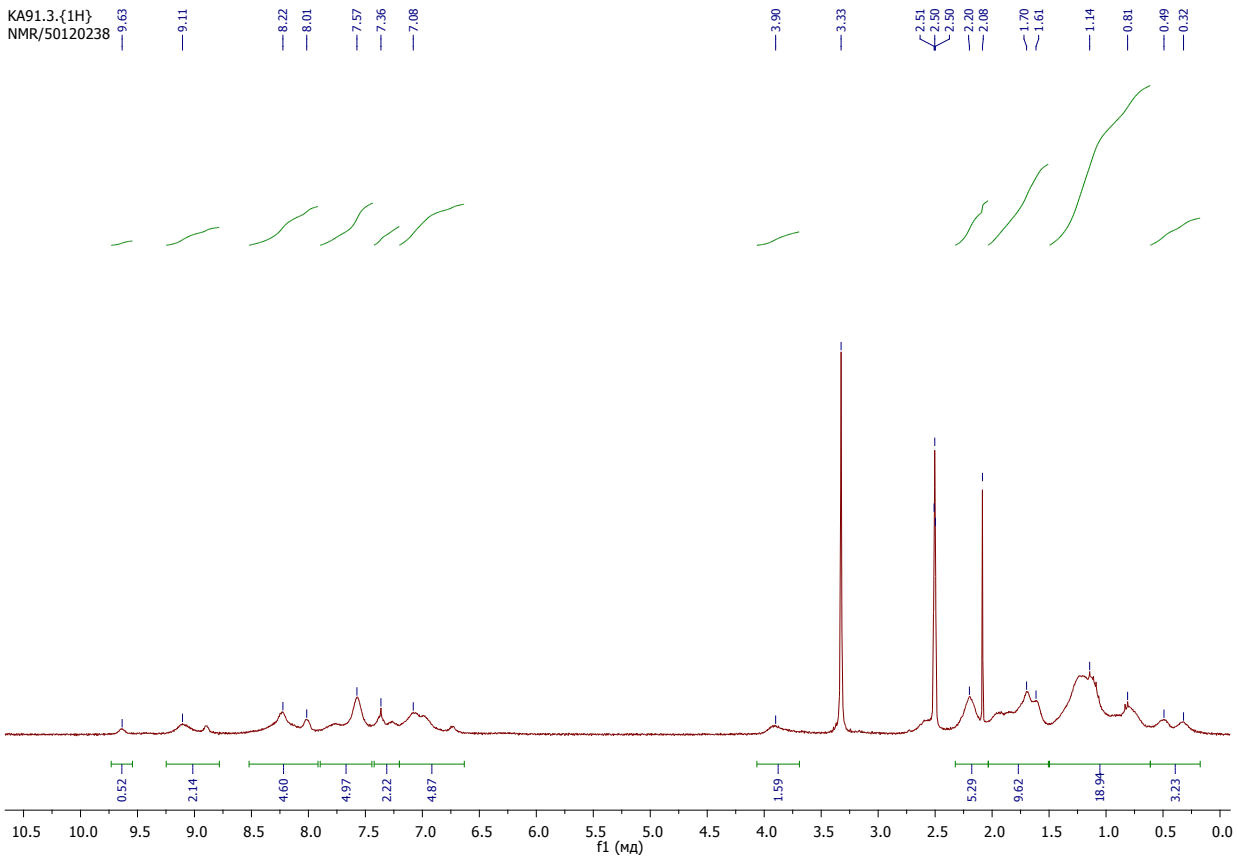
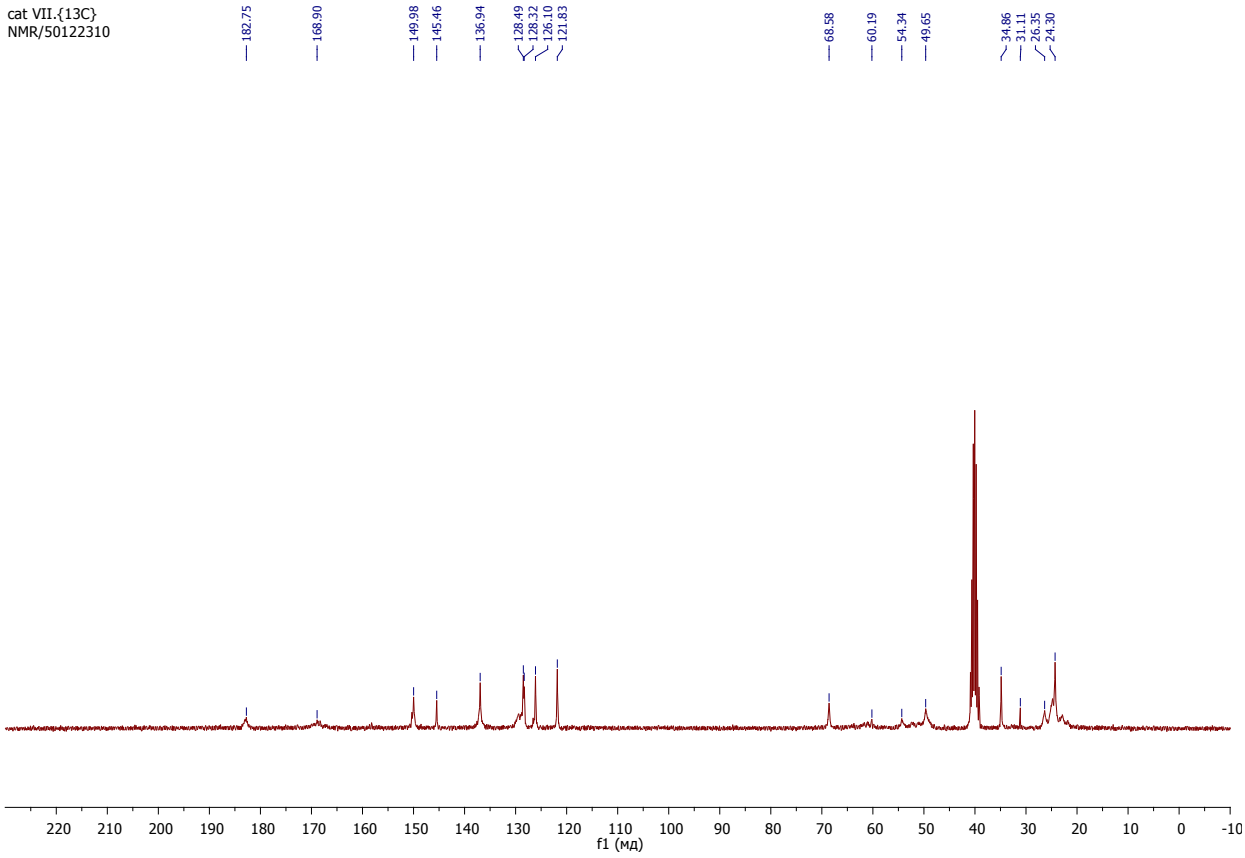
168.93
149.98
145.46
136.94
128.49
128.32
126.10
121.83
68.58
60.90
60.19
54.41
52.31
51.04
49.65
40.88
40.60
40.32
40.04
39.76
39.48
31.11
26.35
24.30
22.89
21.79
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)

(*R*,*R*)-4,4'-(((1*S*,2*S*)-1,2-Di(quinolin-8-yl)ethane-1,2-diyl)bis(azanediyl))bis(3-(((1*R*,2*R*)-2-(piperidin-1-yl)cyclohexyl)amino)cyclobut-3-ene-1,2-dione) (VIII): Yellow solid (0.74 g, 77% yield). Mp 191-193°C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.63 (s, 1H), 9.20-8.82 (m, 2H), 8.30-8.03 (m, 5H), 7.99-7.40 (m, 5H), 7.37-7.22 (m, 2H), 7.18-6.68 (m, 5H), 3.90 (s(br), 2H), 2.25-2.06 (m, 5H), 2.04-1.58 (m, 10H), 1.50-0.68 (m, 19H), 0.67-0.30 (m, 3H) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ 182.7, 168.9, 149.9, 145.4, 136.9, 128.4, 128.3, 126.1, 121.8, 68.5, 60.1, 54.3, 49.6, 34.8, 31.1, 26.3, 24.3 ppm. HRMS (ESI): *m/z* M + H^+ calcd for $C_{50}H_{59}N_8O_4^+$ 835.4654, found 835.4776.



VIII

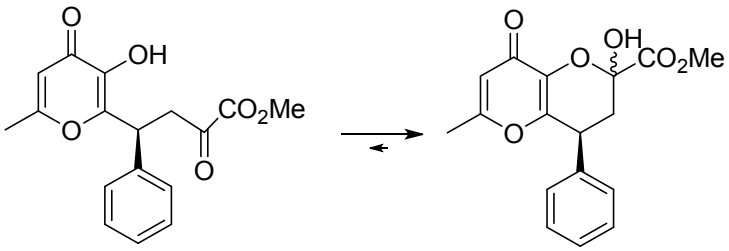


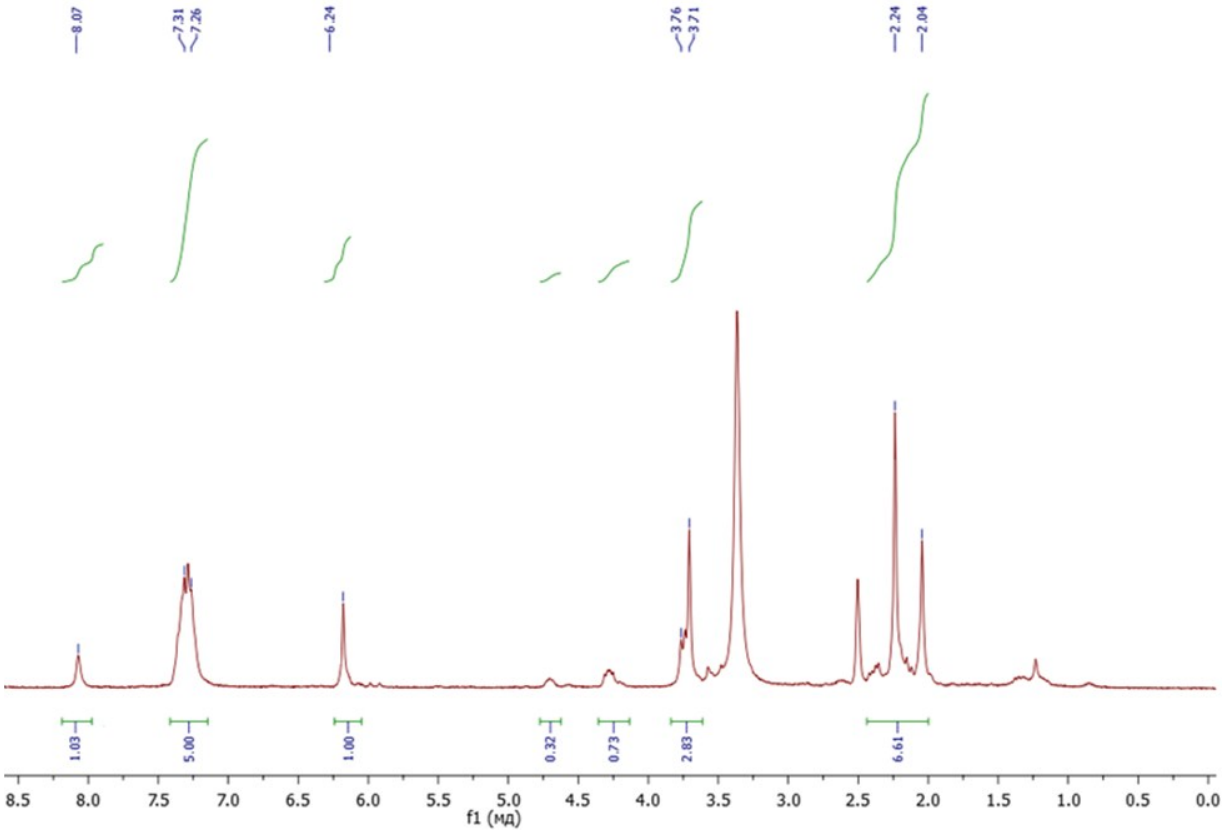

cat VII.{13C}
NMR/50122310
182.75
168.90
149.98
145.46
136.94
128.49
128.32
126.10
121.83
68.58
60.19
54.34
49.65
34.86
31.11
26.35
24.30
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (мд)

2. Catalytic Michael reaction between 6 and 7 (General Procedure)

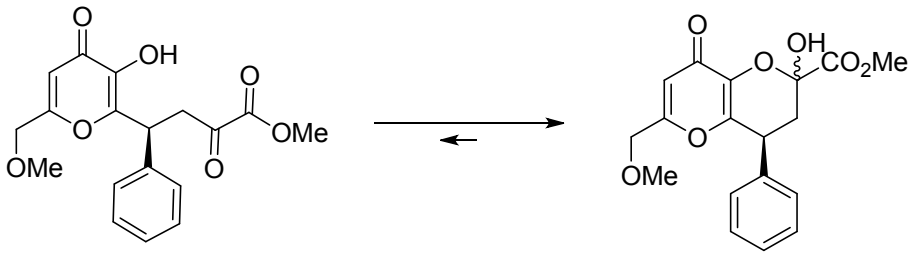
Kojic acid derivative **6** (0.12 mmol) and β,γ-unsaturated α-ketoester **7** (0.12 mmol) were added to a mixture of catalyst **V** (1 mg, 0.0012 mmol) and DCM (0.1 mL). After stirring at room temperature for 8 h, the solvent was evaporated under reduced pressure (10 Torr). The residue was extracted with MeOH (2 × 4 mL). The combined extracts were filtered through silica gel to afford pure **8**.

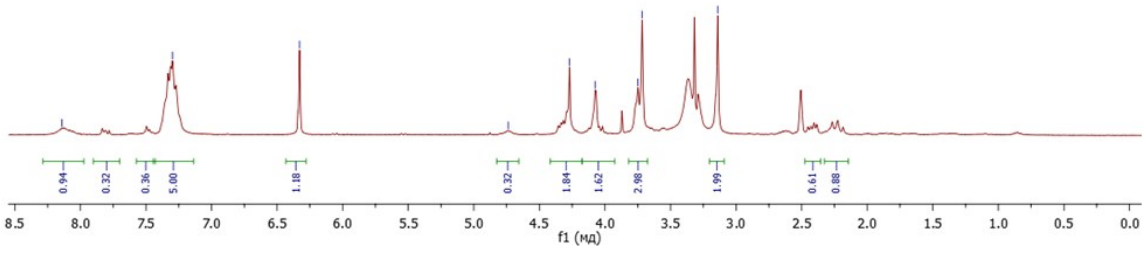
(*S*)-Methyl 2-hydroxy-6-methyl-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8aa): Yellow oil. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.94 (brs, 1.29H), 8.07 (brs, 1.03H), 7.29 (m, 5H), 6.24 (s, 1.00H), 4.70 (m, 0.32H), 4.30 (m, 0.73H), 3.74 (m, 2.83H), 2.14 (m, 6.61H) ppm. [2,3]

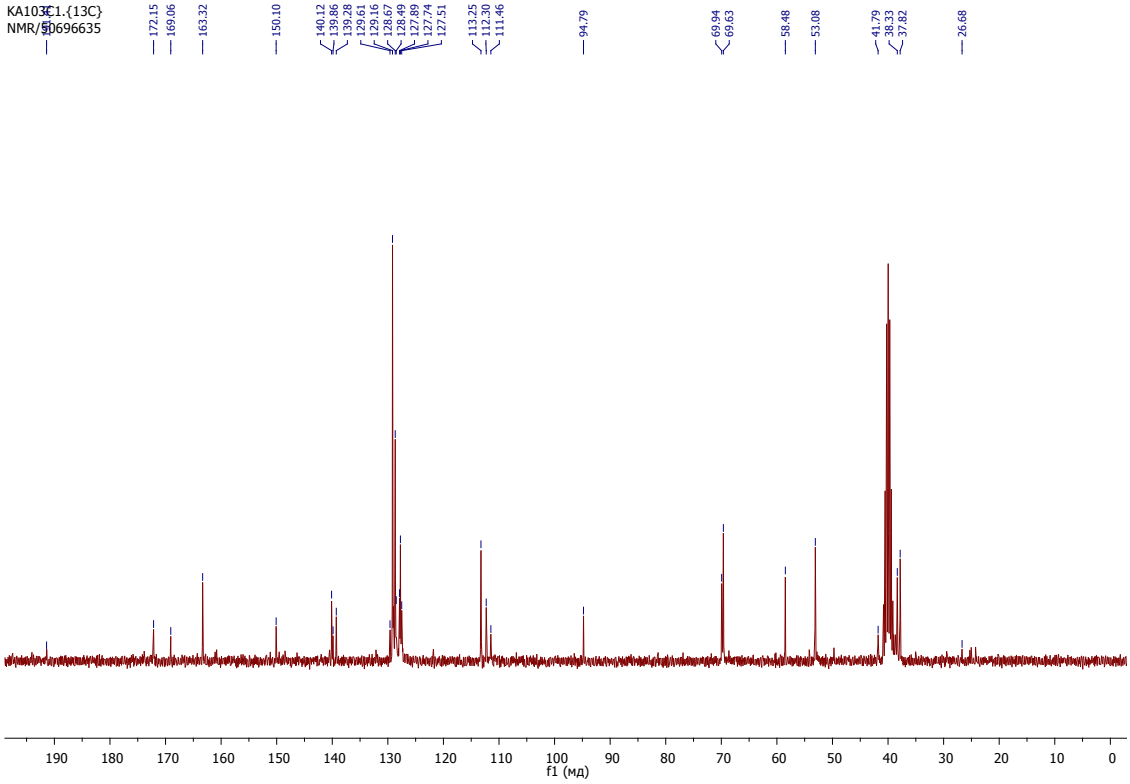




(*S*)-Methyl 2-hydroxy-6-(methoxymethyl)-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano-[3,2-b]pyran-2-carboxylate (8ba): Yellow oil. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.17 (brs, 0.87H), 8.10 (m, 0.94H), 7.83-7.78 (m, 0.32H), 7.50 (m, 0.36H), 7.30 (m, 5.14H), 6.39-6.33 (m, 1.18H), 4.74 (s, 0.33H), 4.35 – 4.19 (m, 1.87H), 4.07 (s, 1.7H), 3.79 – 3.67 (m, 3H), 3.19 – 3.09 (s, 2H), 2.43 (m, 0.61H), 2.23 (m, 0.88H) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ 191.4, 172.1, 169.0, 163.3, 150.1, 140.1, 139.8, 139.2, 129.6, 129.1, 128.6, 128.4, 127.8, 127.7, 127.5, 113.2, 112.3, 111.4, 94.7, 69.9, 69.6, 58.4, 53.0, 41.7, 38.3, 37.8 ppm. HRMS (ESI): *m/z* M + H^+ calcd for $C_{18}H_{19}O_7^+$ 347.1125, found 347.1185.



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163.32
150.10
140.12
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139.28
129.61
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128.67
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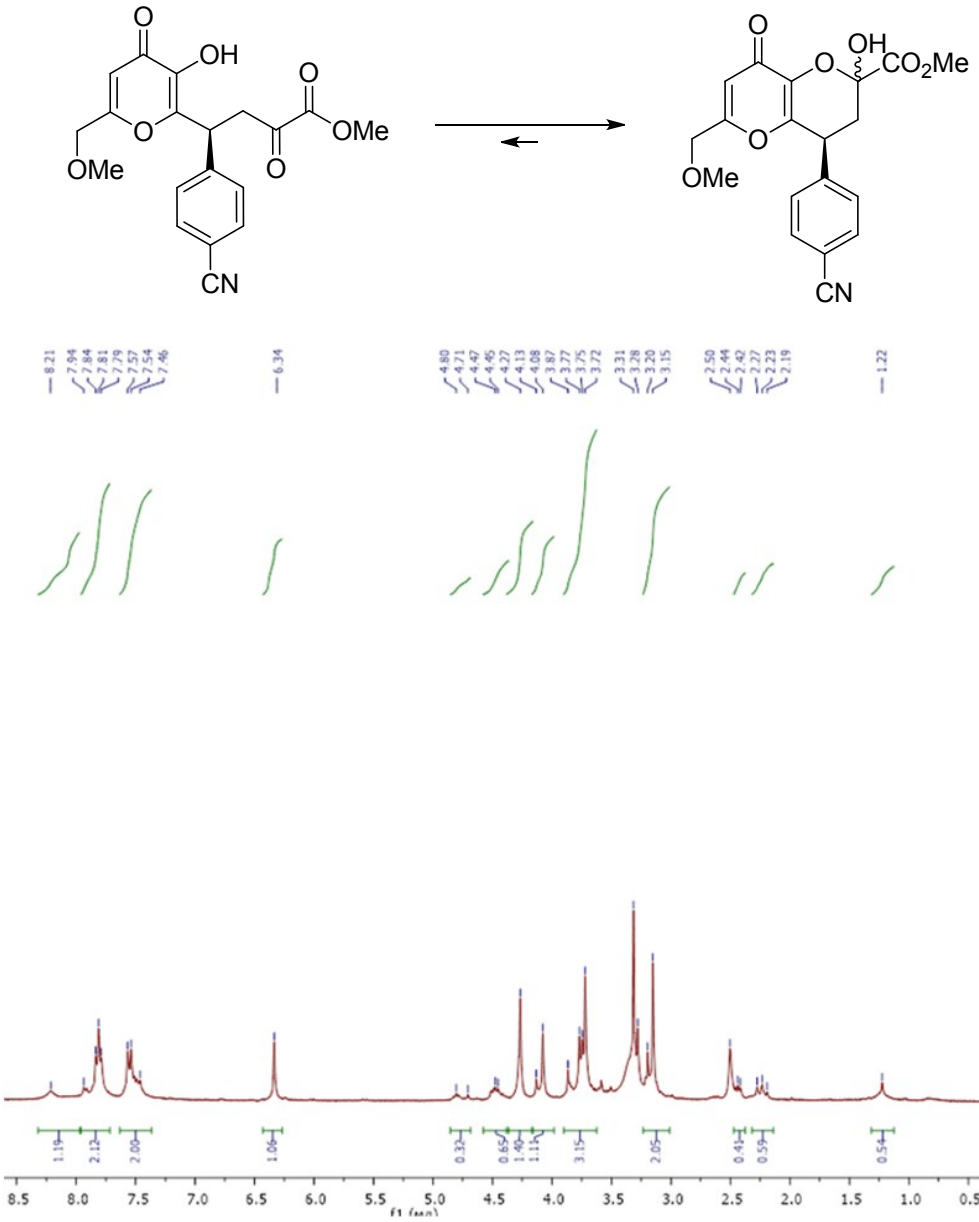
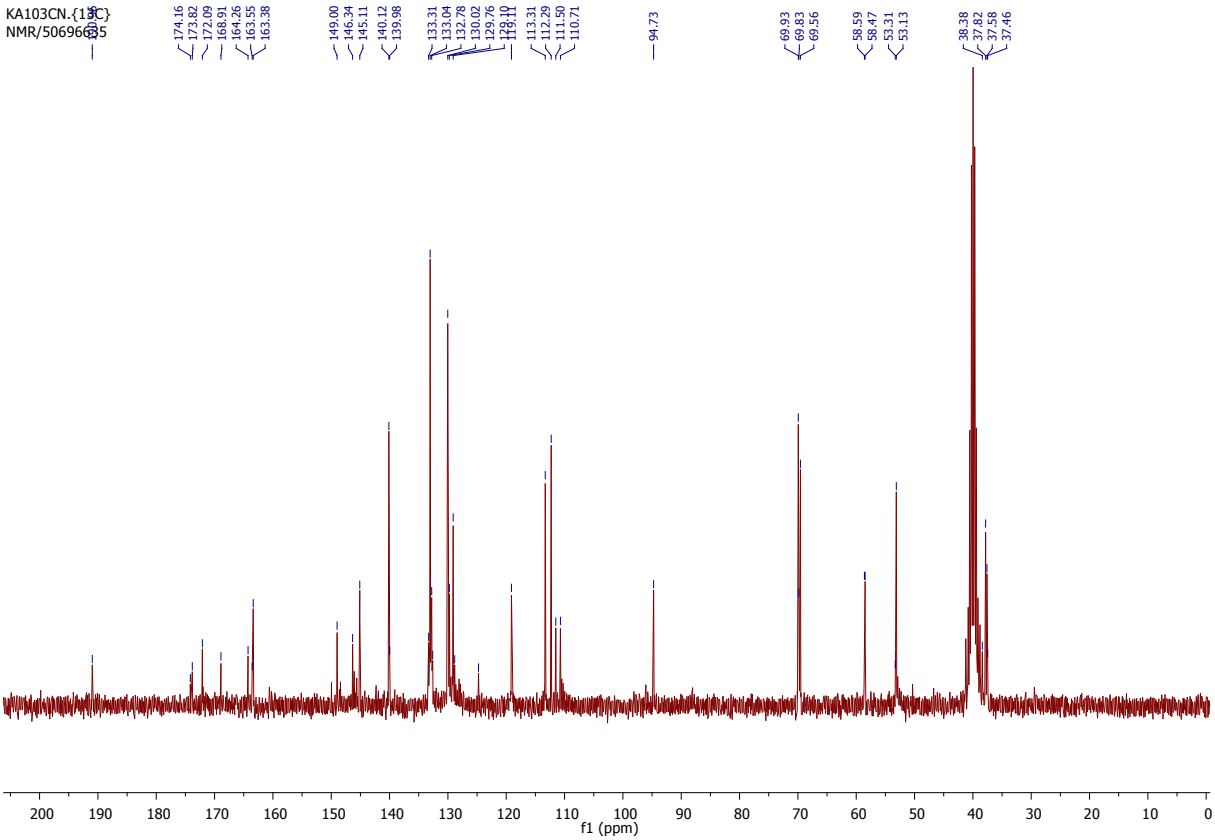
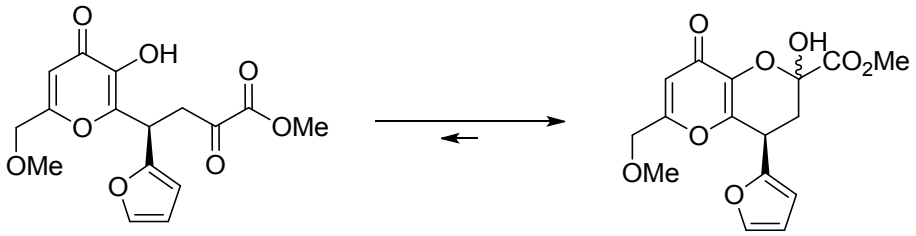
127.74
127.51
113.25
112.30
111.46
94.79
69.94
69.63
58.48
53.08
41.79
38.33
37.82
26.68
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)

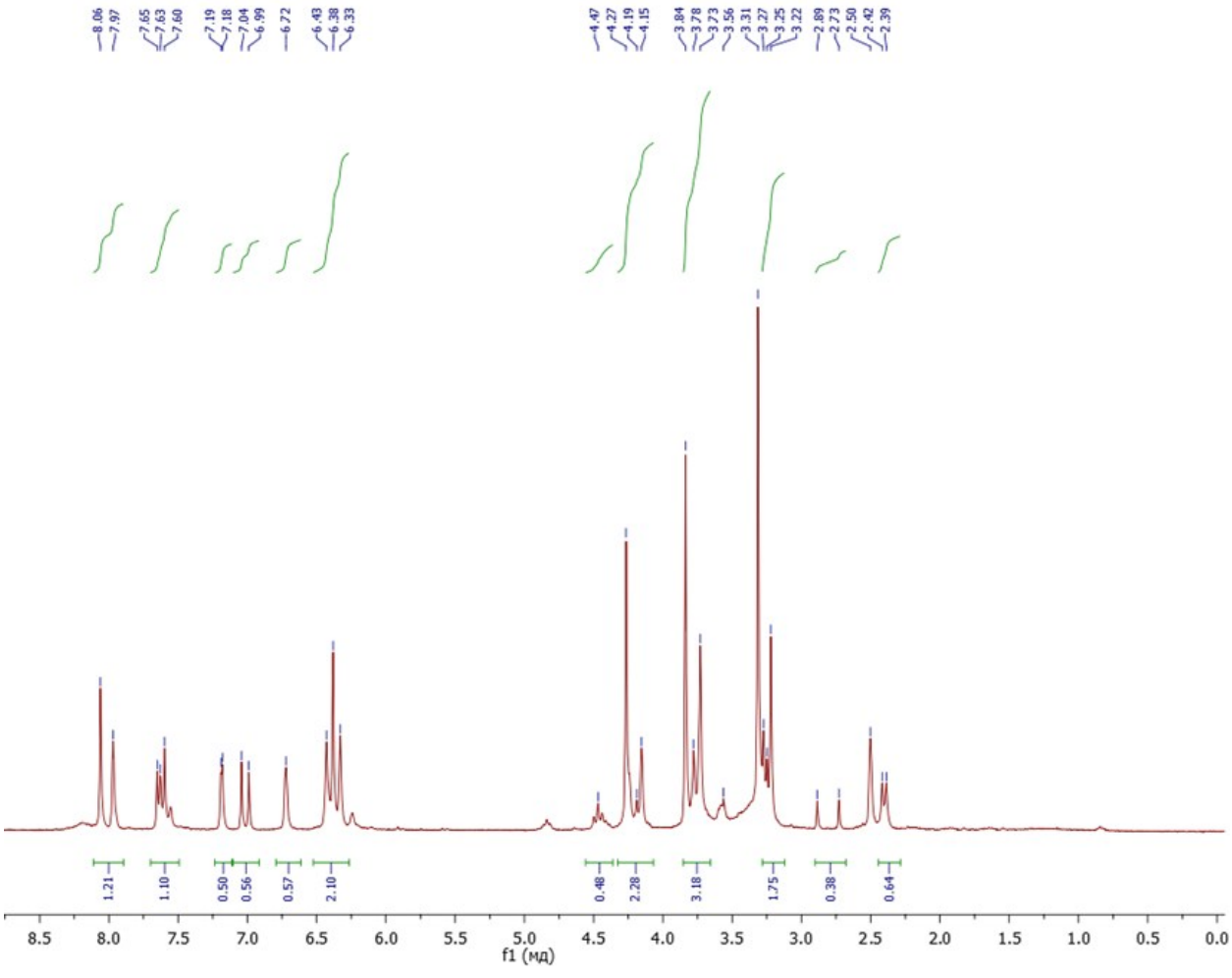
(*S*)-Methyl 4-(4-cyanophenyl)-2-hydroxy-6-(methoxymethyl)-8-oxo-2,3,4,8-tetrahydro-pyrano[3,2-b]pyran-2-carboxylate (**8bb**): Yellow oil. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.15 (brs, 0.87H), 8.32 – 7.97 (m, 1.19H), 7.84 (m, 2.12H), 7.63 – 7.36 (m, 2H), 6.36 (m, 1H), 4.76 (m, 0.32H), 4.46 (m, 0.36H), 4.27 (s, 1.40H), 4.10 (m, 1.11H), 3.78 (m, 3.15H), 3.17 (m, 2.05H), 2.43 (m, 0.41H), 2.32 – 2.14 (m, 0.59H) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ 190.9, 172.0, 164.2, 163.3, 149.0, 146.3, 145.1, 140.1, 133.0, 132.7, 130.0, 129.7, 129.1, 119.1, 113.3, 112.2, 111.5, 110.7, 94.7, 69.9, 69.8, 69.5, 58.5, 58.4, 53.1, 38.3, 37.8, 37.5 ppm. HRMS (ESI): *m/z* M + H^+ calcd for $C_{19}H_{18}NO_7^+$ 371.1005, found 371.1018.

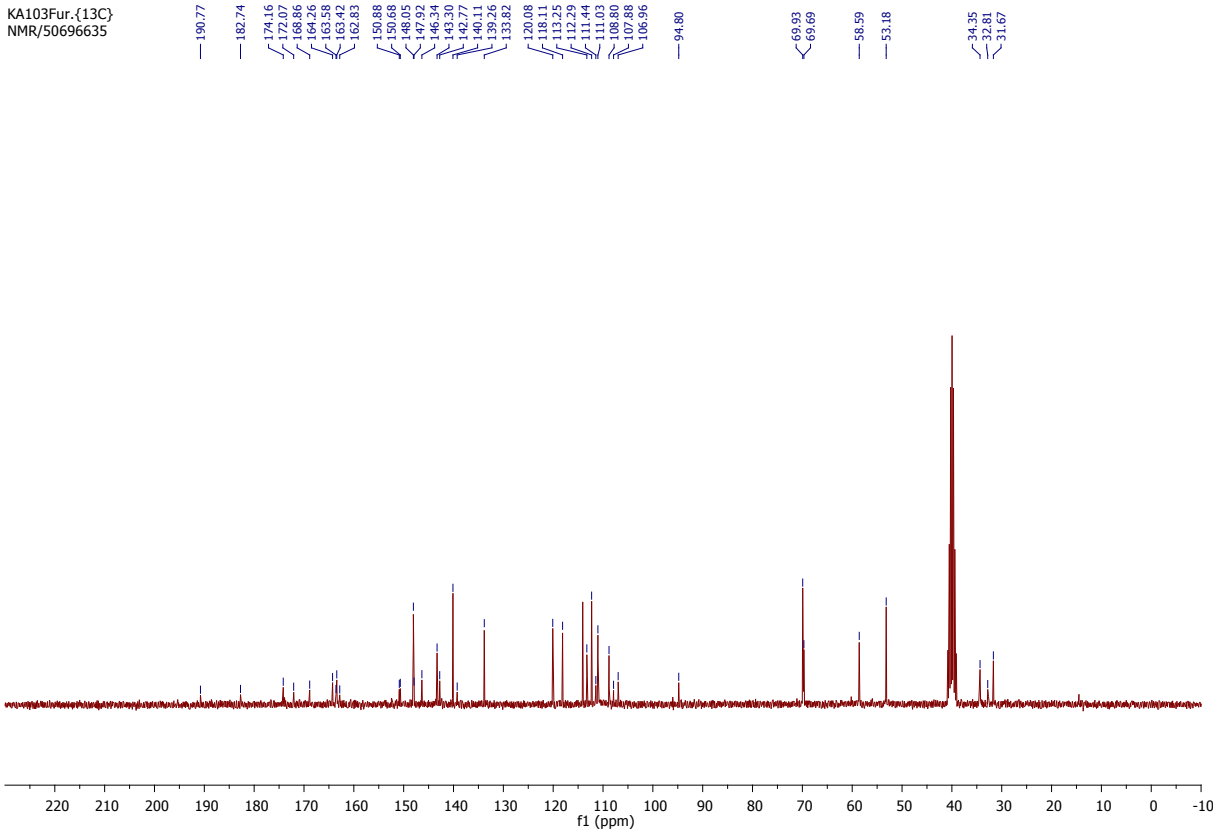



KA103CN.{13C}
NMR/50696635
174.16
173.82
172.09
168.91
164.26
163.55
163.38
149.00
146.34
145.11
140.12
139.98
133.31
133.04
132.78
130.02
129.76
94.73
69.93
69.83
69.56
58.59
58.47
53.31
53.13
38.38
37.82
37.58
37.46
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

(*S*)-Methyl 4-(furan-2-yl)-2-hydroxy-6-(methoxymethyl)-8-oxo-2,3,4,8-tetrahydro-pyrano[3,2-b]pyran-2-carboxylate (8bc): Yellow oil. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.20 (s, 0.83H), 8.01 (m, 1.21H), 7.61 (m, 1.10H), 7.19 (m, 0.50H), 7.02 (m, 0.56H), 6.72 (s, 0.57H), 6.38 (m, 2H), 4.47 (t, *J* = 8.8 Hz, 1H), 4.33 – 4.07 (m, 2.28H), 3.85 – 3.66 (m, 3.18H), 3.28 – 3.12 (m, 1.75H), 2.81 (m, 0.38H), 2.40 (d, *J* = 8.8 Hz, 0.64H) ppm. ^{13}C NMR (75 MHz, DMSO-d6) δ 190.7, 182.7, 174.1, 164.2, 163.4, 150.6, 148.0, 147.9, 146.3, 143.3, 142.7, 140.1, 133.8, 120.0, 118.1, 114.0, 113.2, 112.2, 111.4, 111.0, 108.8, 106.9, 94.8, 69.9, 69.6, 58.5, 53.1, 34.3, 31.6 ppm. HRMS (ESI): *m*/*z* M + H$^+$ calcd for $C_{16}H_{17}O_8^+$ 337.0918, found 337.0922.



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NMR/50696635
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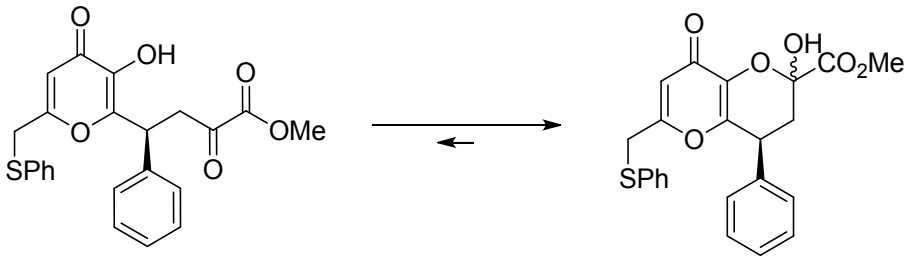
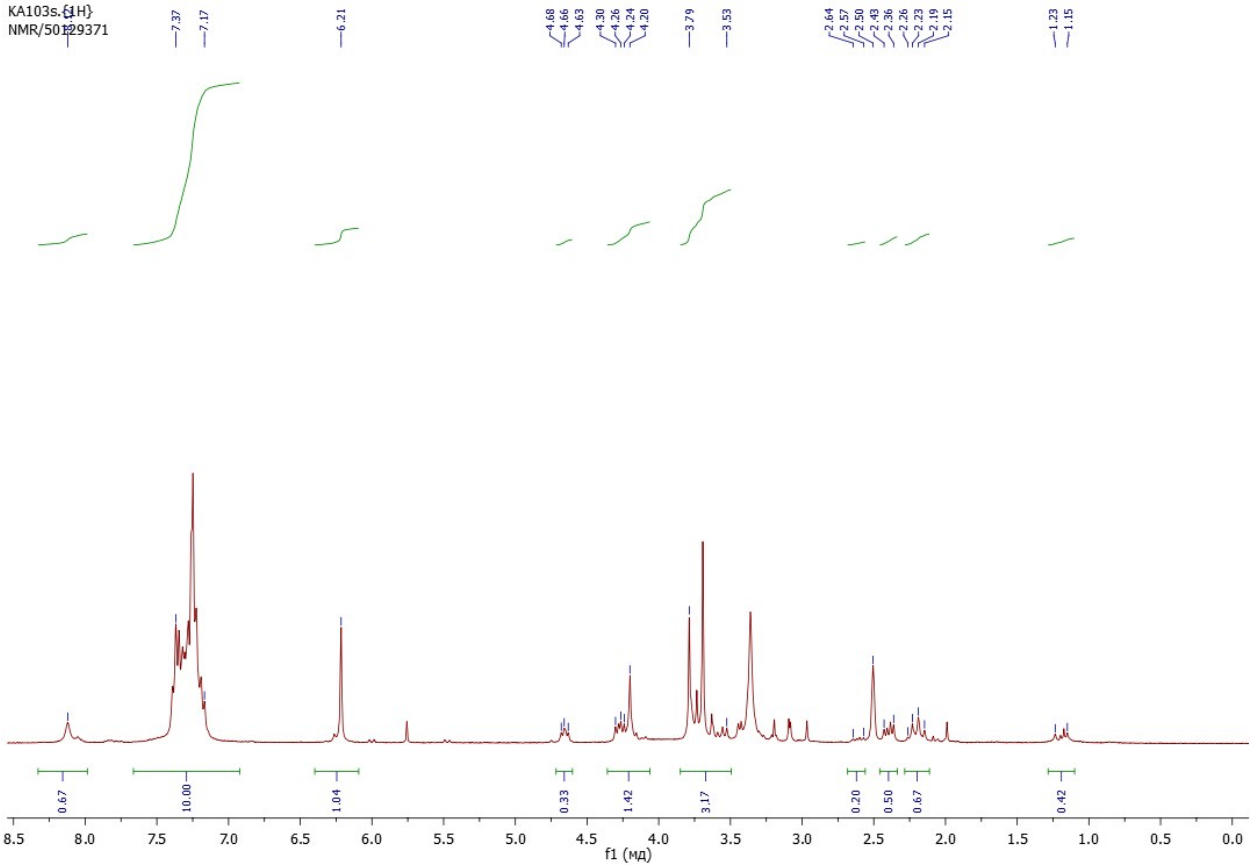
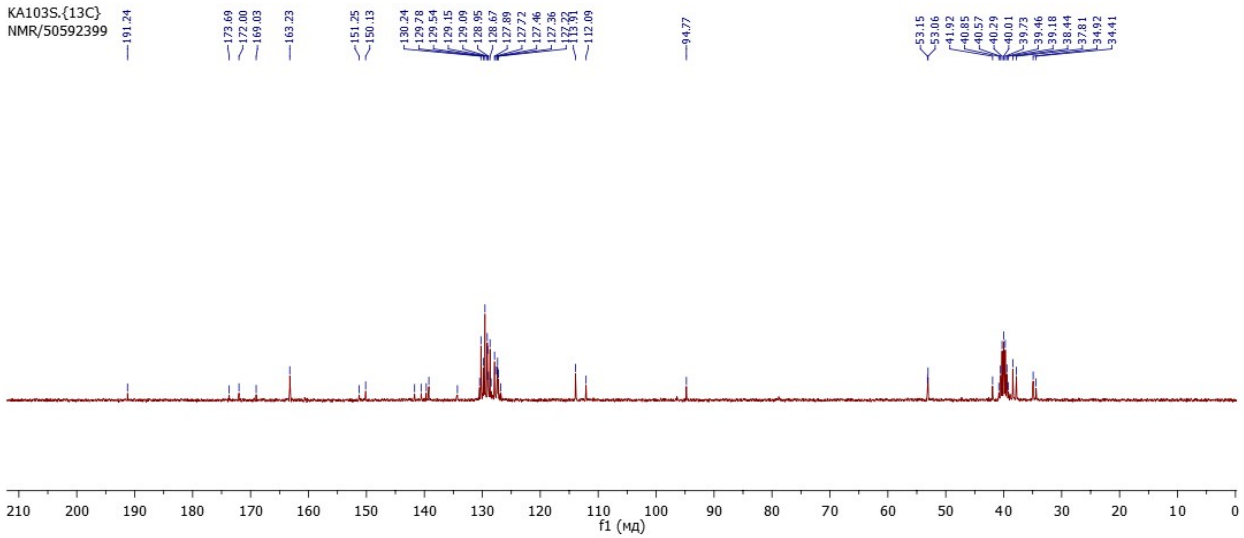
182.74
174.16
172.07
168.86
164.26
163.58
163.42
162.83
150.88
150.68
148.05
147.92
146.34
143.30
142.77
140.11
139.26
133.82
120.08
118.11
113.25
112.29
111.44
111.03
108.80
107.88
106.96
94.80
69.93
69.69
58.59
53.18
34.35
32.81
31.67
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

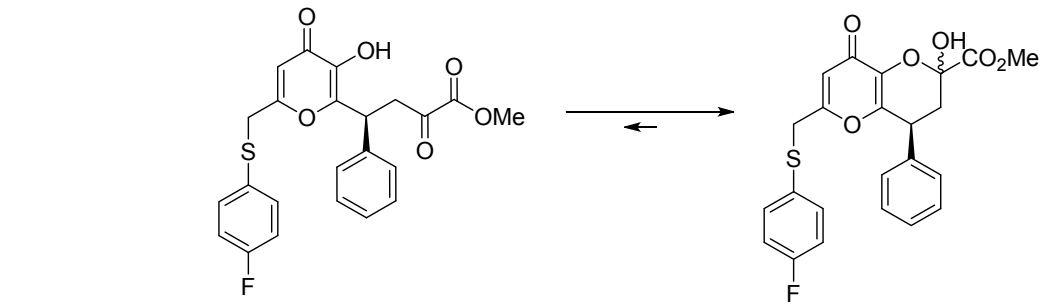
(*S*)-Methyl 2-hydroxy-8-oxo-4-phenyl-6-((phenylthio)methyl)-2,3,4,8-tetrahydro-pyrano[3,2-b]pyran-2-carboxylate (8ca): Yellow oil. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.05 (brs, 0.45H), 8.12 (m, 0.67H), 7.47 – 7.08 (m, 10H), 6.21 (m, 1.1H), 4.72 – 4.57 (m, 0.38H), 4.29 – 4.15 (m, 1.1H), 4.06 – 3.92 (m, 1.15H), 3.71 (m, 3.12H), 3.59 – 3.48 (m, 0.42H), 2.40 (m, 0.53H), 2.19 (m, 0.73H) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ 191.2, 172.0, 163.2, 150.1, 141.6, 140.5, 139.6, 139.2, 130.4, 130.2, 129.7, 129.5, 129.1, 129.0, 128.9, 128.6, 128.4, 127.8, 127.7, 127.4, 127.3, 127.2, 126.8, 113.9, 112.0, 94.7, 53.1, 53.0, 41.9, 38.4, 37.8, 34.9, 34.4 ppm. HRMS (ESI): *m/z* M + H$^+$ calcd for $C_{23}H_{21}O_6S^+$ 425.1053, found 425.1062.

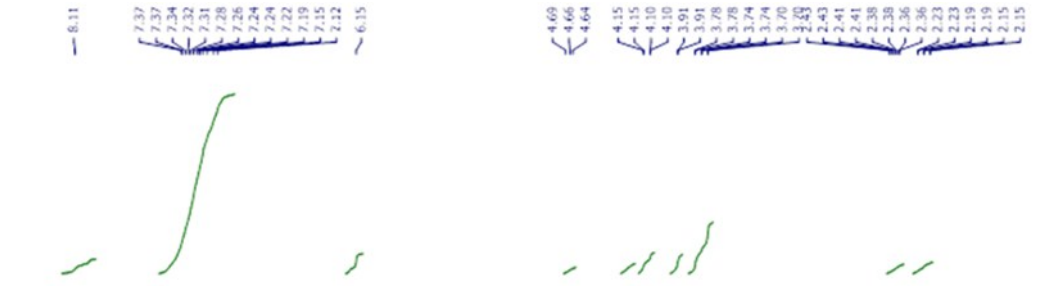


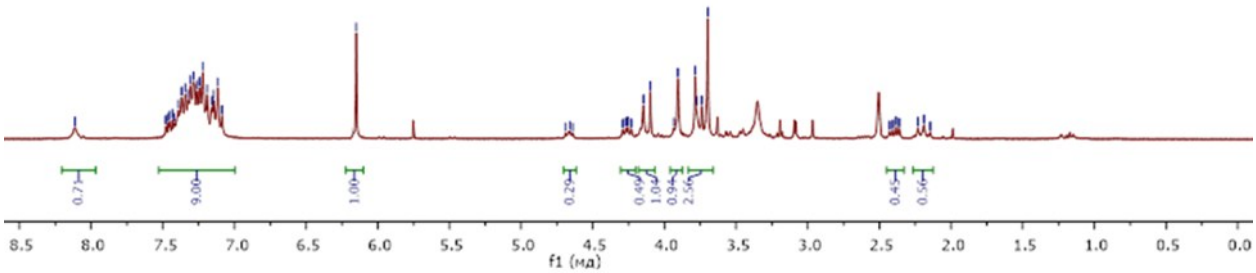


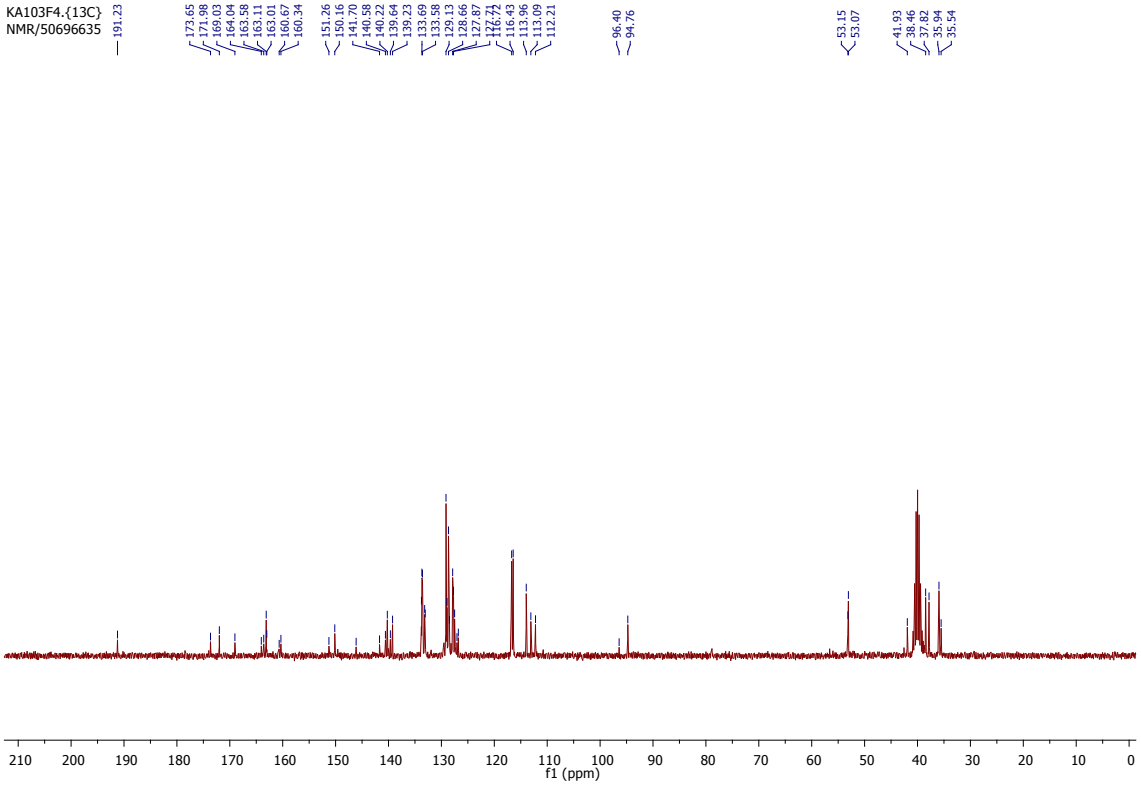

KA103S.{13C}
NMR/50592399
191.24
173.69
172.00
169.03
163.23
151.25
150.13
130.24
129.78
129.54
129.15
129.09
128.95
128.67
127.89
127.72
127.46
127.36
94.77
112.09
53.15
53.06
41.92
40.85
40.57
40.29
40.01
39.73
39.46
39.18
38.44
37.81
34.92
34.41
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (мд)

(*S*)-Methyl 6-(((4-fluorophenyl)thio)methyl)-2-hydroxy-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8da): Yellow oil. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.08 (s, 0.48H), 8.21 – 7.97 (m, 71H), 7.53 – 7.00 (m, 9.00H), 6.17 (m, 1.00H), 4.70 – 4.62 (m, 0.29H), 4.18 – 4.07 (m, 1.04H), 3.92 (m, 0.94H), 3.83 – 3.66 (m, 2.56H), 2.45 – 2.33 (m, 0.36H), 2.27 – 2.13 (m, 0.56H) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ 191.2, 173.6, 171.9, 169.0, 163.1, 160.3, 150.1, 140.5, 140.2, 139.6, 139.2, 133.7, 133.6, 133.5, 133.1, 133.0, 129.1, 128.9, 128.6, 128.4, 127.8, 127.7, 127.5, 126.8, 116.8, 116.7, 116.5, 116.4, 113.9, 113.4 (d, $J_{C\text{-}F}$ = 66.6 Hz), 94.7, 53.1, 53.0, 41.9, 38.4, 37.8, 35.9, 35.5 ppm. HRMS (ESI): *m/z* M + H^+ calcd for $C_{23}H_{20}FO_6S^+$ 443.0959, found 443.0941.

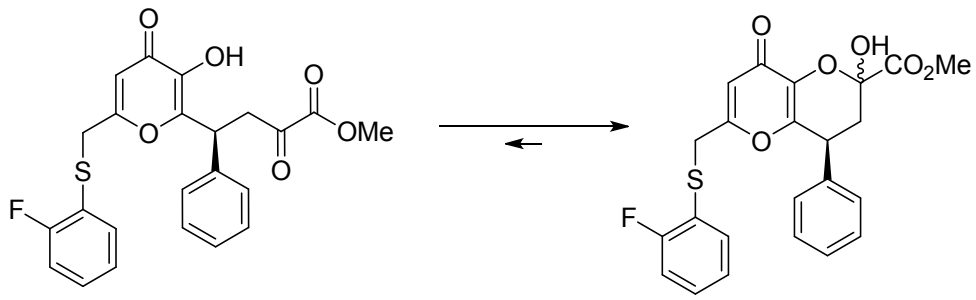


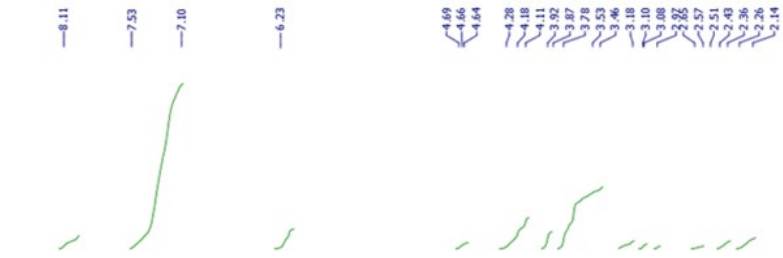


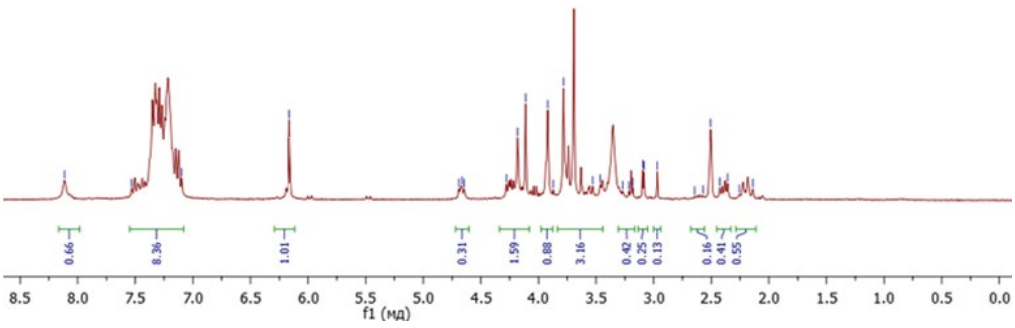


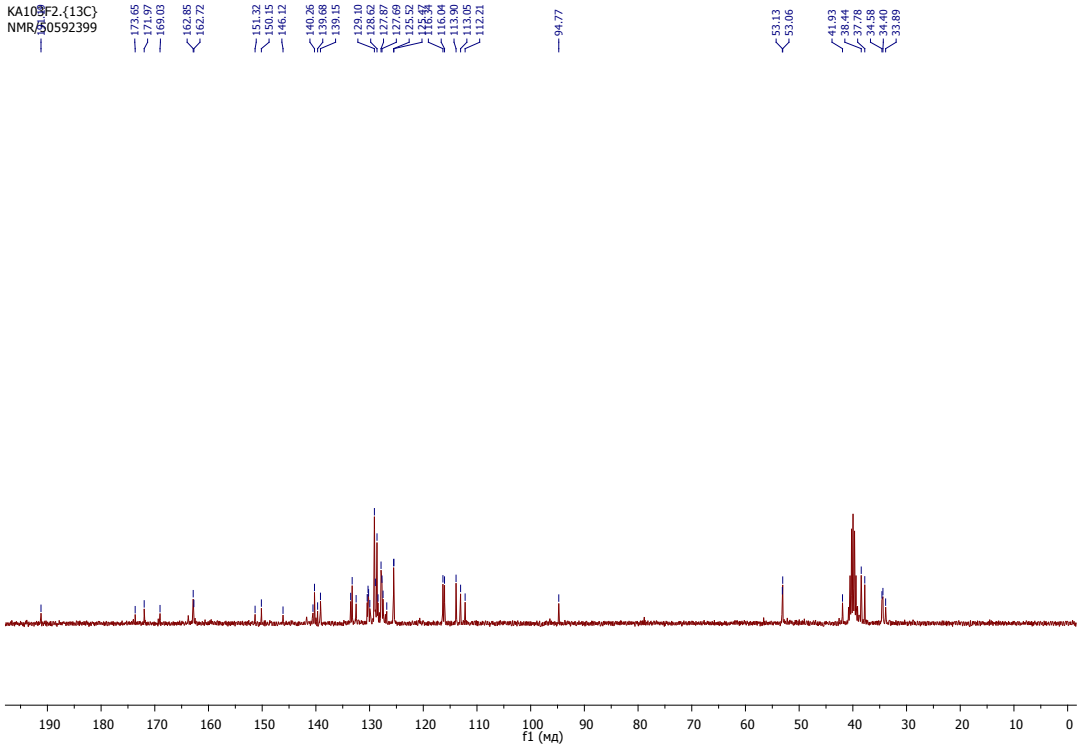

KA103F4.{13C}
NMR/50696635
191.23
173.65
171.98
169.03
164.04
163.58
163.11
161.01
160.67
160.34
151.26
150.16
141.70
140.58
140.22
139.64
139.23
133.69
133.58
129.13
128.66
127.87
127.71
116.72
116.43
113.96
113.09
112.21
96.40
94.76
53.15
53.07
41.93
38.46
37.82
35.94
35.54
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

(*S*)-Methyl 6-(((2-fluorophenyl)thio)methyl)-2-hydroxy-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8ea): Yellow oil. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.09 (s, 0.53H), 8.06 (m, 0.66H), 7.57 – 7.03 (m, 8.36H), 6.20 (m, 1.01H), 4.79 – 4.55 (m, 0.31H), 4.35 – 4.08 (m, 1.59H), 3.92 (s, 0.88H), 3.82 – 3.65 (m, 3.16H), 3.12 (m, 0.42H), 2.43-2.36 (m, 0.41H), 2.22-2,14 (m, 0.55H) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ 191.1, 173.6, 171.9, 169.0, 162.8, 162.7, 151.3, 150.1, 146.1, 140.5, 140.2, 139.6, 139.1, 133.5, 133.2, 132.5, 130.4, 130.2, 130.1, 129.9, 129.1, 128.9, 128.6, 128.4, 127.8, 127.6, 127.4, 126.8, 125.5, 125.4, 116.3, 116.0, 113.9, 113.6 (d, $J_{C\text{-}F}$ = 63.6 Hz), 94.7, 53.1, 53.0, 41.9, 38.4, 37.7, 34.5, 34.4, 33.8 ppm. HRMS (ESI): *m/z* M + H$^+$ calcd for $C_{23}H_{20}FO_6S^+$ 443.0959, found 443.0948.

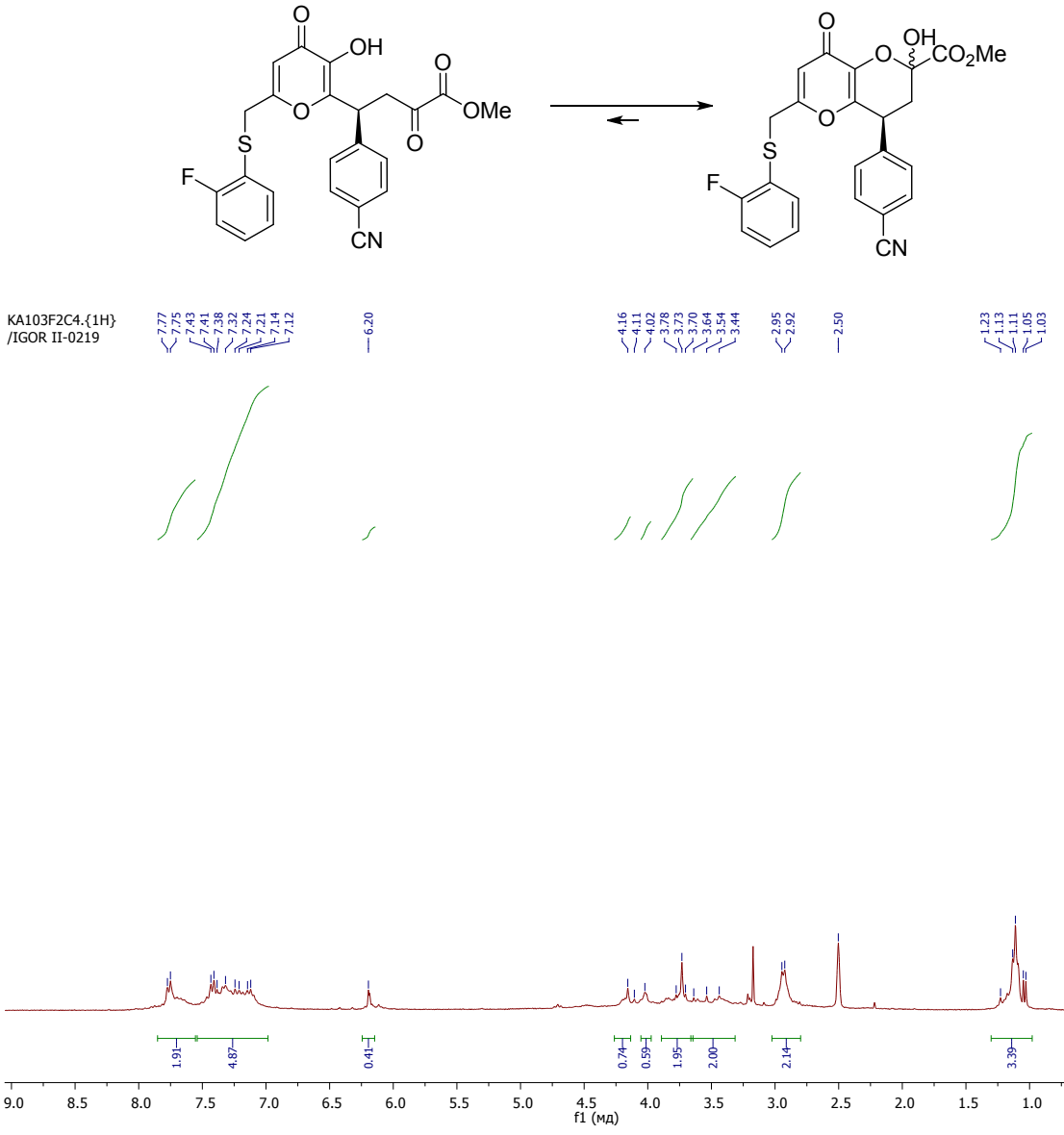


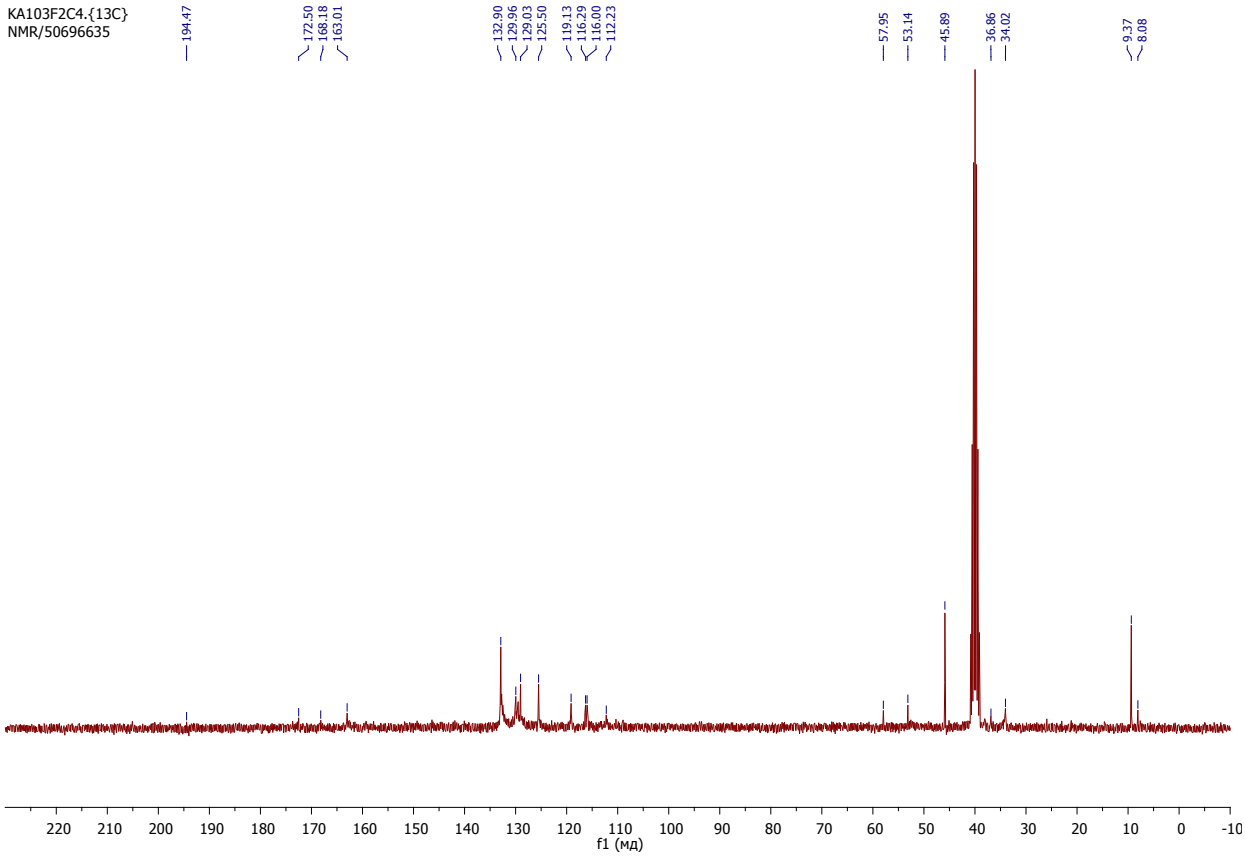




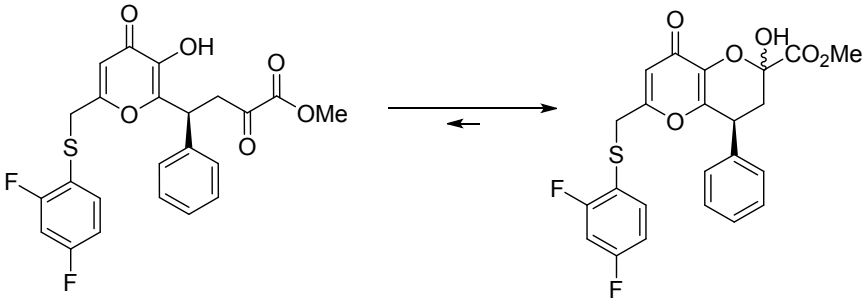

KA103F2.{13C}
NMR/50592399
173.65
171.97
169.03
162.85
162.72
151.32
150.15
146.12
140.26
139.68
139.15
129.10
128.62
127.87
127.69
125.52
116.04
113.90
113.05
112.21
94.77
53.13
53.06
41.93
38.44
37.78
34.58
34.40
33.89
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)

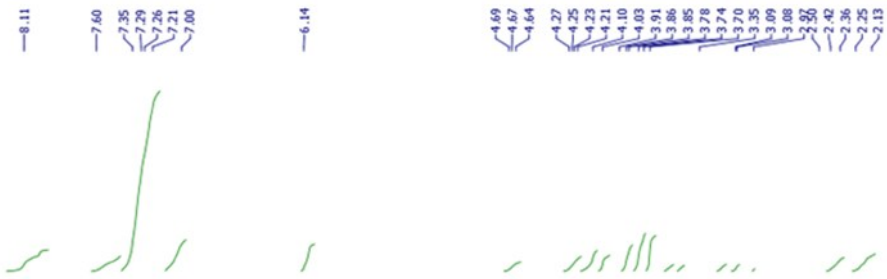
(*S*)-Methyl 4-(4-cyanophenyl)-6-(((2-fluorophenyl)thio)methyl)-2-hydroxy-8-oxo-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8eb): Yellow oil. ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.76 (m, 1.91H), 7.28 (m, 4.87H), 6.20 (s, 0.41H), 4.16 (m, 0.74H), 4.02 (m, 0.59H), 3.74 (m, 1.95H), 3.66 – 3.31 (m, 2H), 2.93 (m, 2H), 1.23 – 1.03 (m, 3.39H) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ 194.5, 172.5, 168.2, 163.0, 140.2, 133.4, 132.9, 131.9, 131.4, 129.8, 129.5, 129.3, 128.9, 119.1, 113.9, 113.5 (d, $J_{C\text{-}F}$ = 60.2 Hz), 110.6, 94.7, 68.6, 53.1, 37.8, 37.6, 34.8, 34.4 ppm. HRMS (ESI): *m/z* M + H$^+$ calcd for $C_{24}H_{19}FNO_6S^+$ 468.0912, found 468.0915.

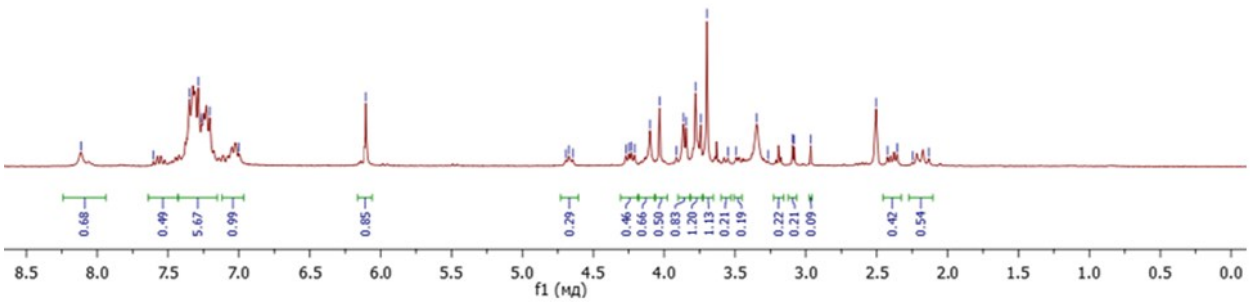


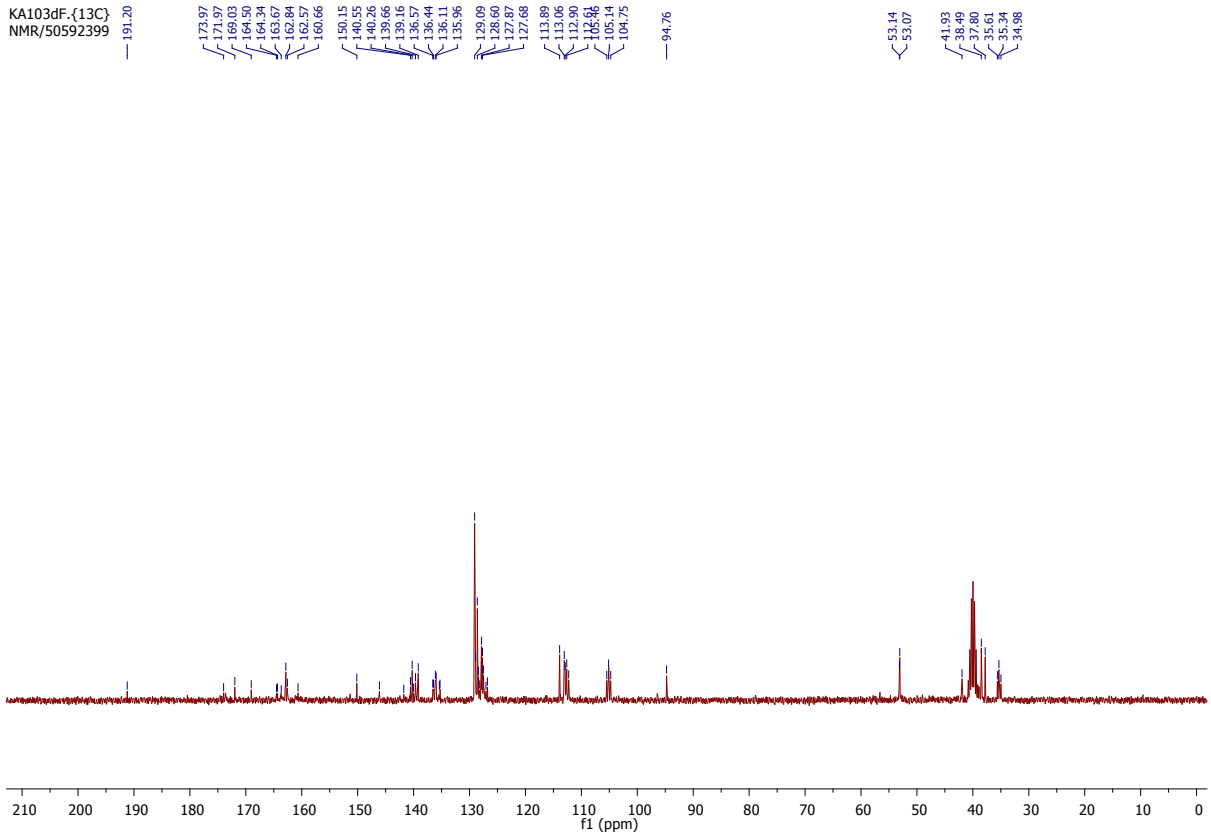

KA103F2C4.{13C}
NMR/50696635
194.47
172.50
168.18
163.01
132.90
129.96
129.03
125.50
119.13
116.29
116.00
112.23
57.95
53.14
45.89
36.86
34.02
9.37
8.08
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (мд)

(*S*)-Methyl 6-(((2,4-difluorophenyl)thio)methyl)-2-hydroxy-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8fa): Yellow oil. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.09 (s, 0.51H), 8.06 (m, 0.68H), 7.47 – 7.12 (m, 7.16H), 6.12 (m, 0.85H), 4.67 (m, 0.29H), 4.24 (m, 0.46H), 4.07 (m, 0.66H), 3.85 (m, 0.83H), 3.78 (s, 1.20H), 3.70 (m, 1.13H), 3.09 (m, 0.21H), 3.09 (s, 0.221H), 2.39 (m, 0.42H), 2.17 (m, 0.54H) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ 191.2, 173.9, 171.9, 169.0, 162.8, 162.5, 150.1, 140.2, 139.6, 139.1, 136.1, 135.9, 129.0, 128.9, 128.6, 128.4, 127.8, 127.6, 127.5, 113.8, 113.0, 112.9, 112.6, 112.2, 105.4, 105.1, 104.7, 94.7, 53.0, 41.9, 38.4, 37.8, 35.6, 35.3, 34.9 ppm. HRMS (ESI): *m/z* M + H^+ calcd for $C_{23}H_{19}F_2O_6S^+$ 461.0865, found 461.0843.

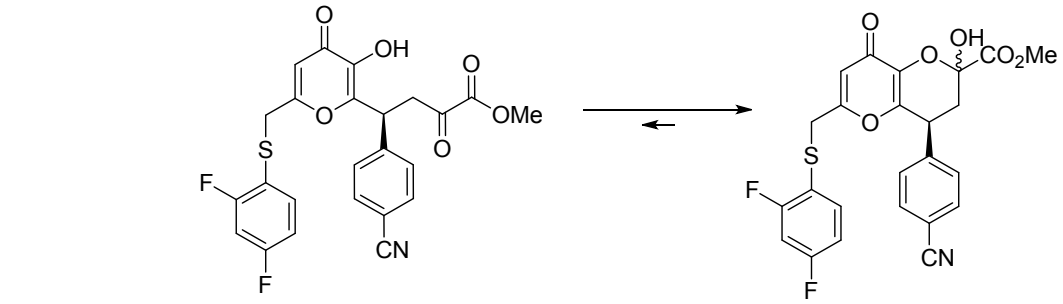


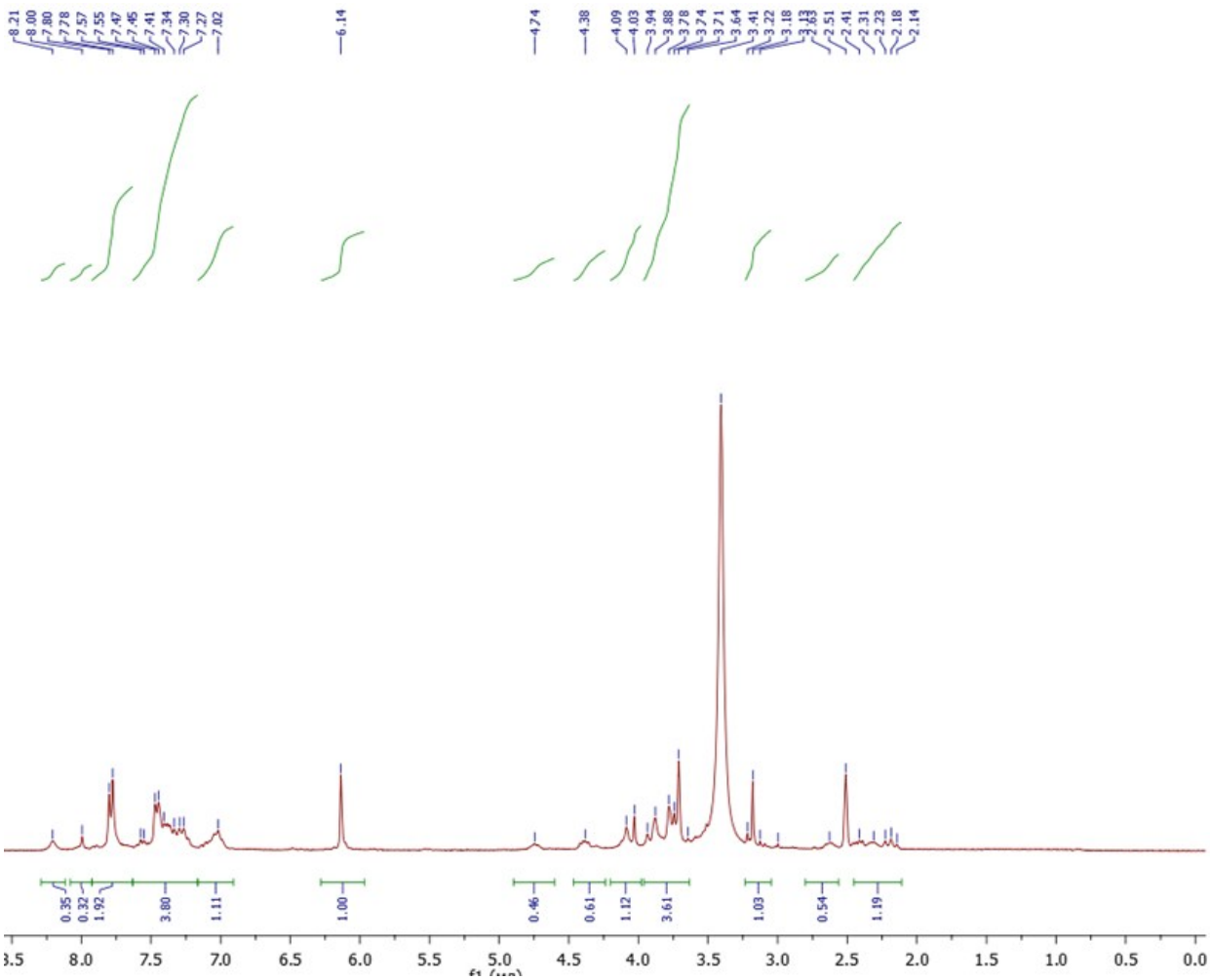


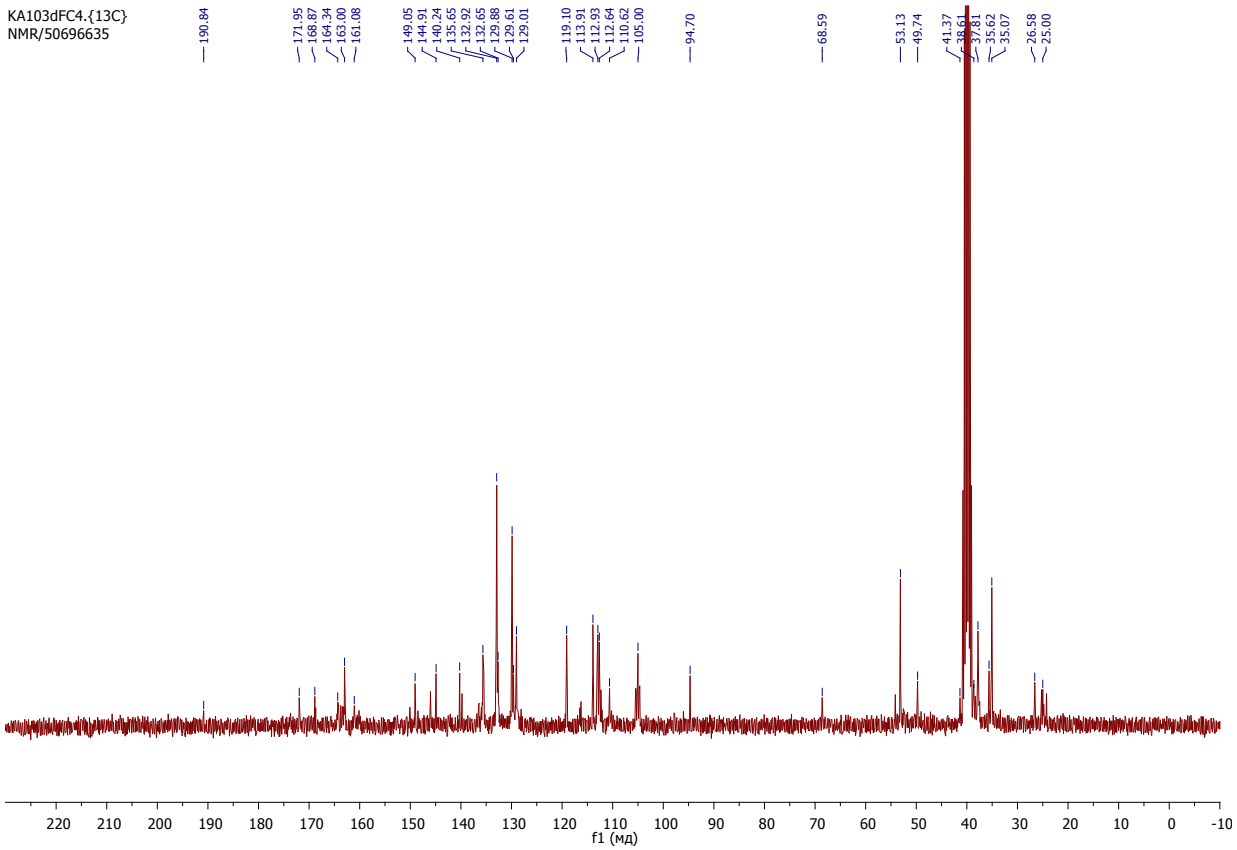



KA103dF.{13C}
NMR/50592399
191.20
173.97
171.97
169.03
164.50
164.34
163.67
162.84
162.57
160.66
150.15
140.55
140.26
139.66
139.16
136.57
136.44
136.11
135.96
129.09
128.60
127.87
127.68
113.89
113.06
112.90
105.14
104.75
94.76
53.14
53.07
41.93
38.49
37.80
35.61
35.34
34.98
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

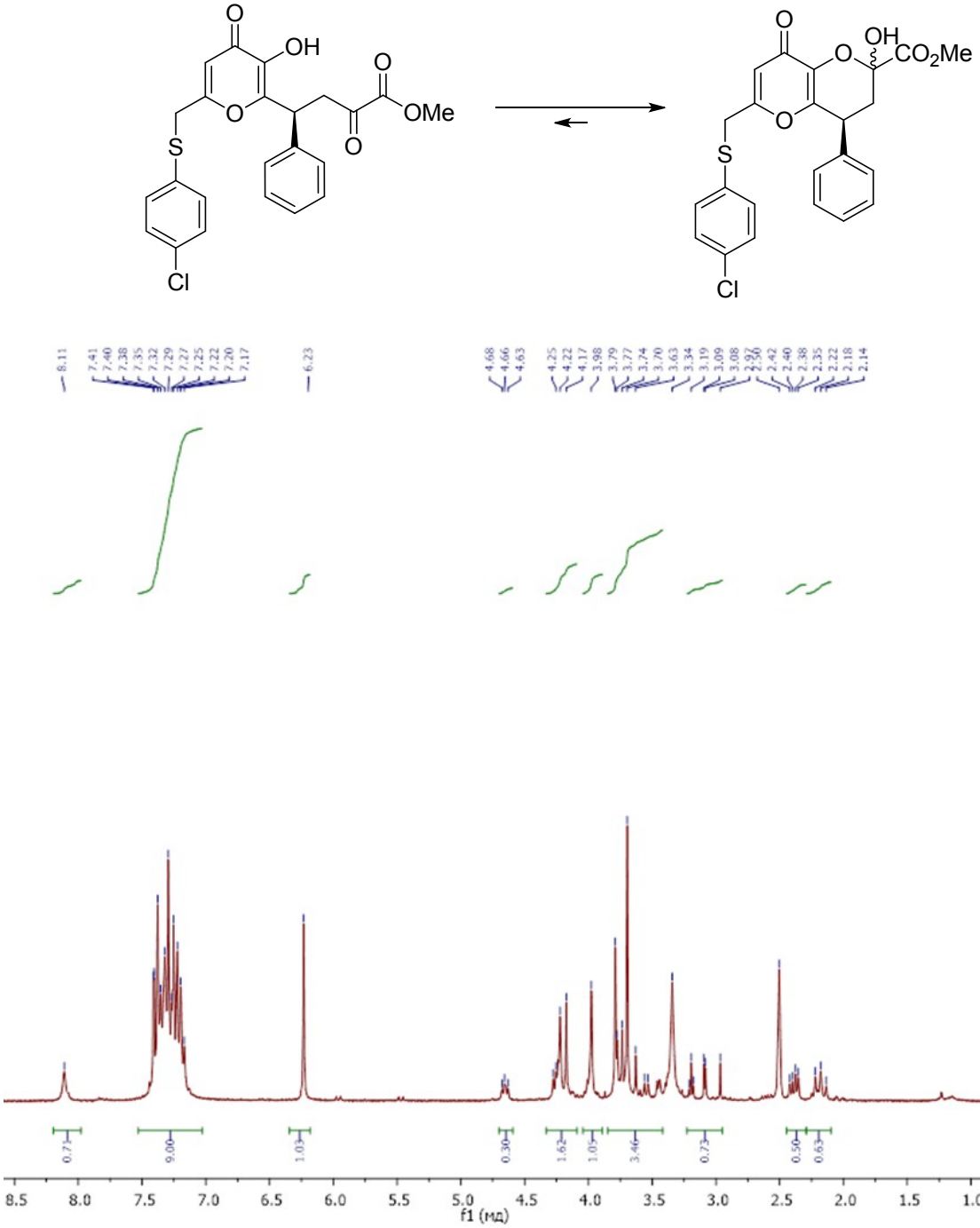
(*S*)-Methyl 4-(4-cyanophenyl)-6-(((2,4-difluorophenyl)thio)methyl)-2-hydroxy-8-oxo-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8fb): Yellow oil. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.73 – 8.67 (m, 0.78H), 8.21 (s, 0.35H), 8.00 (s, 0.32H), 7.78 (m, 1.92H), 7.34 (m, 3.80H), 7.02 (m ,1.11H), 6.14 (s, 1.00H), 4.74 (m, 0.46H), 4.38 (m, 0.61H), 4.17 – 3.60 (m, 4.76H), 3.22 (m, 1.03H), 2.63 (m, 0.54H), 2.28 (m, 1.19H) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ 190.8, 171.9, 168.8, 164.3, 163.0, 161.0, 149.0, 144.9, 140.2, 135.6, 132.9, 132.6, 129.8, 129.6, 129.0, 119.1, 113.9, 112.9, 112.6, 110.6, 105.0, 94.7, 68.5, 53.1, 49.7, 41.3, 38.6, 37.8, 35.6, 35.0, 26.5, 25.0 ppm. HRMS (ESI): *m/z* M + H^+ calcd for $C_{24}H_{18}F_2NO_6S^+$ 486.0817, found 486.0841.

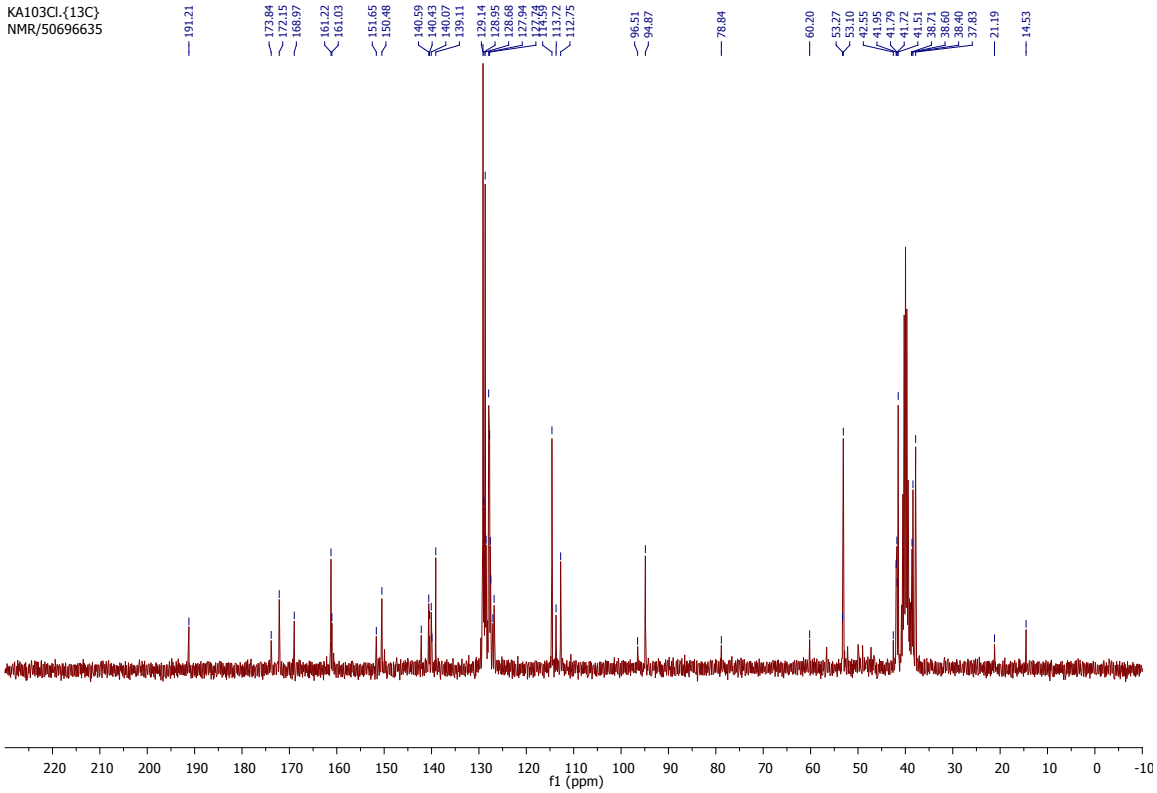




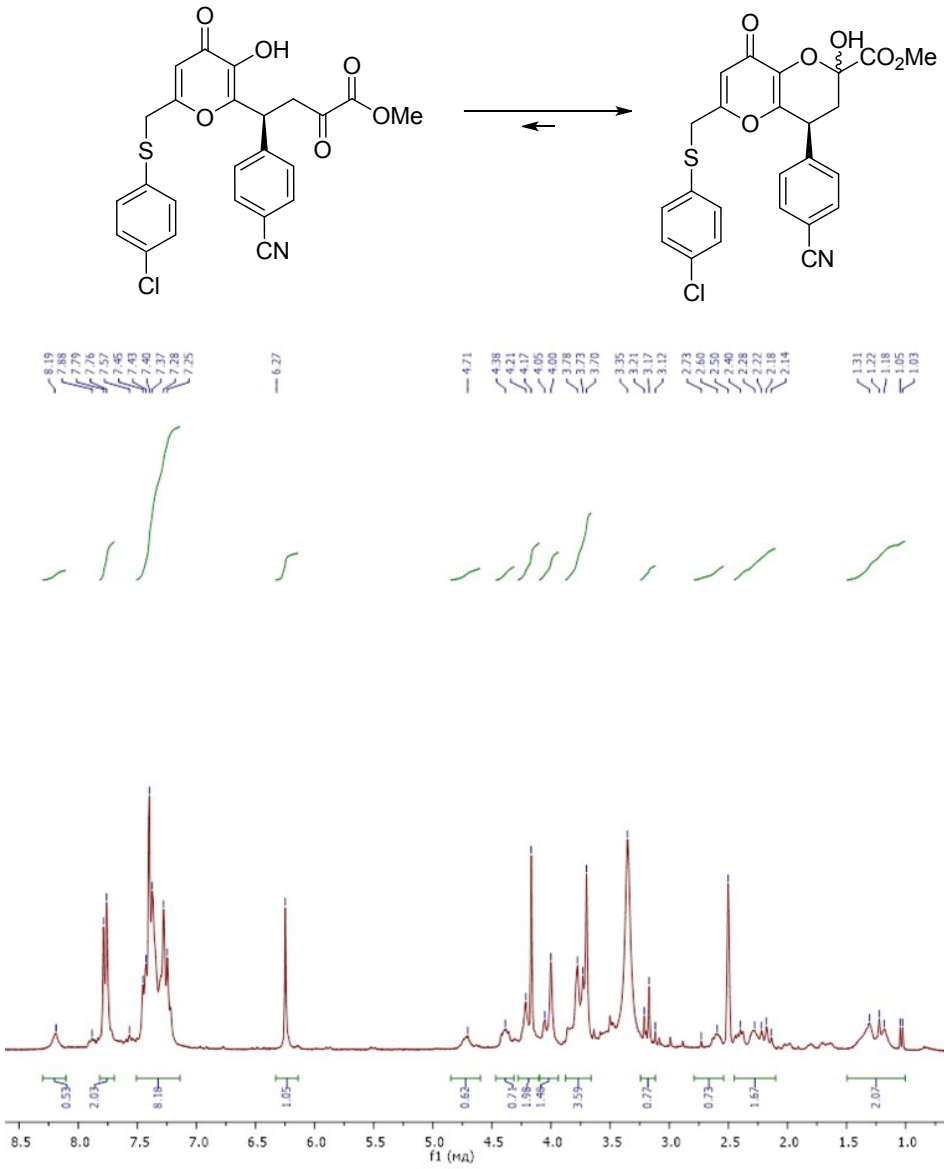

KA103dFC4.{13C}
NMR/50696635
190.84
171.95
168.87
164.34
163.00
161.08
149.05
144.91
140.24
135.65
132.92
132.65
129.88
129.61
129.01
119.10
113.91
112.93
112.64
110.62
105.00
94.70
68.59
53.13
49.74
41.37
38.61
37.81
35.62
35.07
26.58
25.00
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (мд)

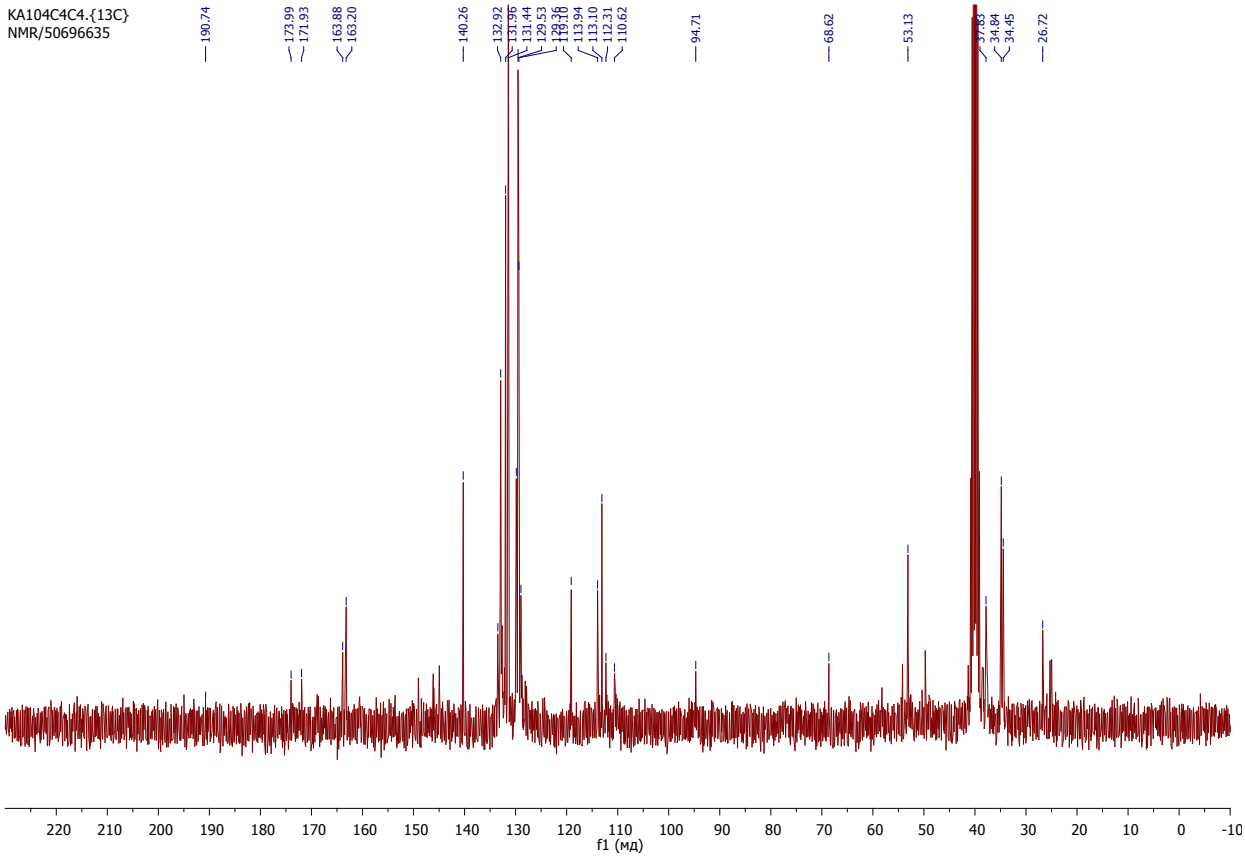
(*S*)-Methyl 6-(((4-chlorophenyl)thio)methyl)-2-hydroxy-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8ga): Yellow oil. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.08 (brs, 0.62H), 8.06 (m, 0.71H), 7.53 – 7.03 (m, 9.00H), 6.26 (m, 1.03H), 4.70 – 4.59 (m, 0.30H), 4.23 (m, 1.62H), 3.98 (s, 1.05H), 3.85 – 3.42 (m, 3.46H), 3.23 – 2.95 (m, 0.73H), 2.39 (m, 0.50H), 2.29 – 2.10 (m, 0.63H) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ 191.1, 171.9, 163.0, 150.1, 140.2, 139.2, 132.0, 131.9, 131.4, 129.5, 129.4, 129.4, 129.1, 128.9, 128.6, 128.4, 127.8, 127.6, 127.4, 113.9, 113.1, 112.2, 94.7, 53.1, 53.0, 41.9, 38.4, 37.8, 34.8, 34.3 ppm. HRMS (ESI): *m/z* M + H$^+$ calcd for $C_{23}H_{20}ClO_6S^+$ 459.0664, found 459.0678.



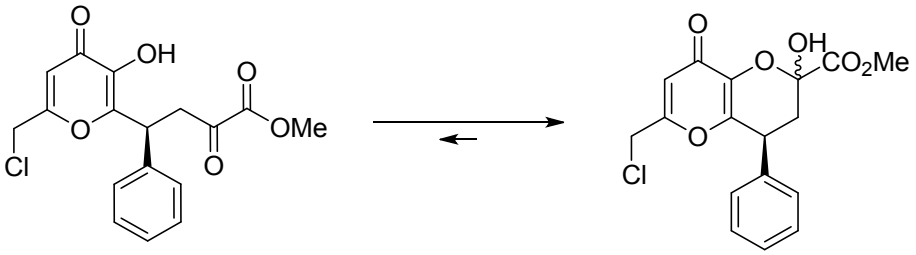

KA103Cl.{13C}
NMR/50696635
191.21
173.84
172.15
166.97
161.22
161.03
151.65
150.48
140.59
140.43
140.07
139.11
129.14
128.95
128.68
127.94
114.59
113.72
112.75
96.51
94.87
78.84
60.20
53.27
53.10
42.55
41.95
41.79
41.72
41.51
38.71
38.60
38.40
37.83
21.19
14.53
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

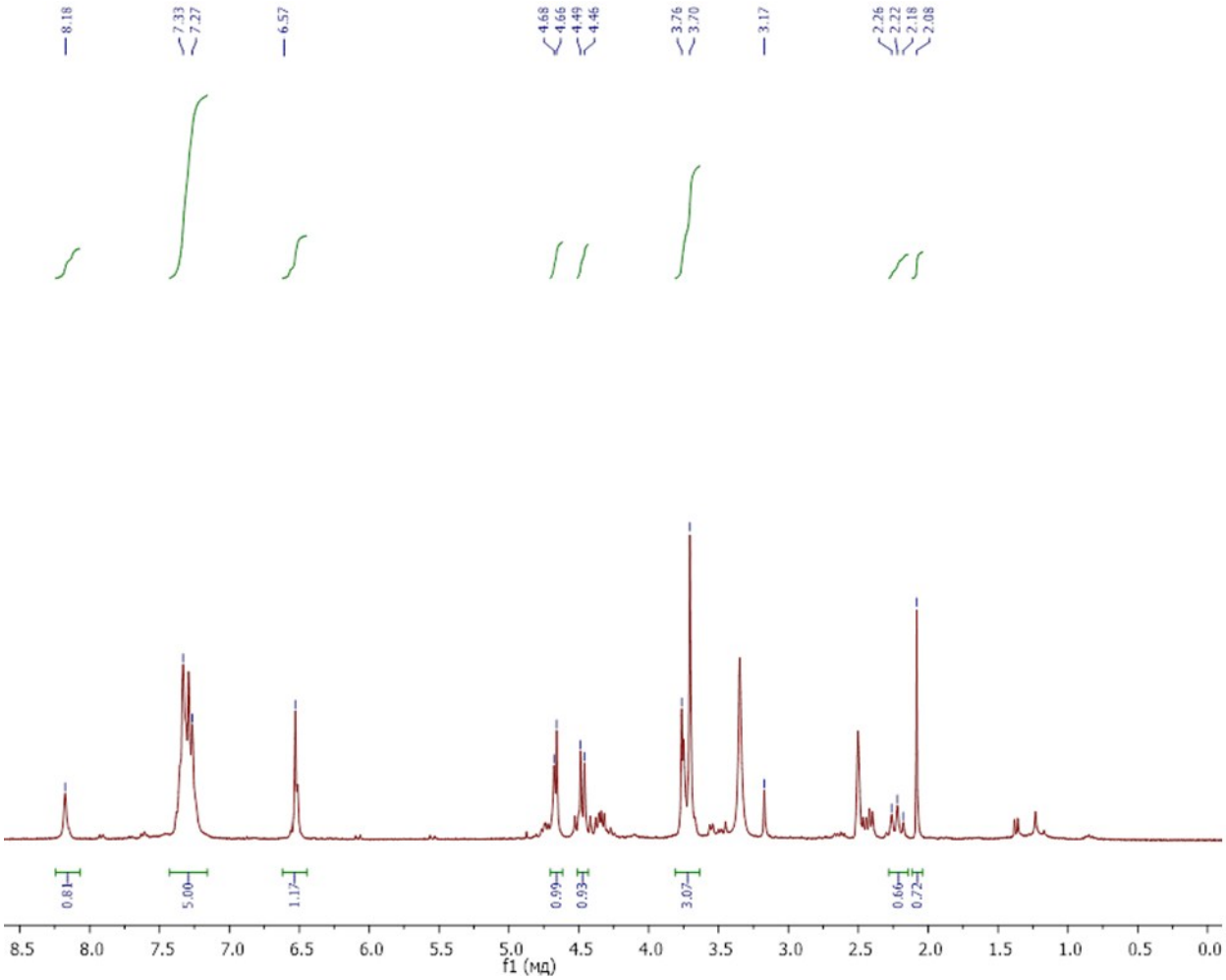
(*S*)-Methyl 6-(((4-chlorophenyl)thio)methyl)-4-(4-cyanophenyl)-2-hydroxy-8-oxo-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8gb): Yellow oil. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.18 (s, 1H), 8.19 (brs, 0.53H), 8.01 (s, 0.55H), 7.77 (m, 2.03H), 7.51 – 7.14 (m, 8.18H), 6.26 (m, 1.05H), 4.71 (m, 0.62H), 4.38 (m, 0.71H), 4.19 (m, 1.98H), 4.03 (m, 1.48H), 3.88 – 3.66 (m, 3.59H), 3.19 (m, 0.77H), 2.66 (m, 0.73H), 2.45 – 2.10 (m, 1.67H), 1.50 – 1.00 (m, 2.07H) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ 190.7, 173.9, 171.9, 163.8, 163.2, 140.2, 133.4, 132.9, 131.9, 131.4, 129.8, 129.5, 129.3, 128.9, 119.1, 113.9, 113.1, 112.3, 110.6, 94.7, 68.6, 53.1, 37.8, 37.6, 34.8, 34.4, 26.7, 24.9 ppm. HRMS (ESI): *m/z* M + H^+ calcd for $C_{24}H_{19}ClNO_6S^+$ 484.0616, found 484.0664.

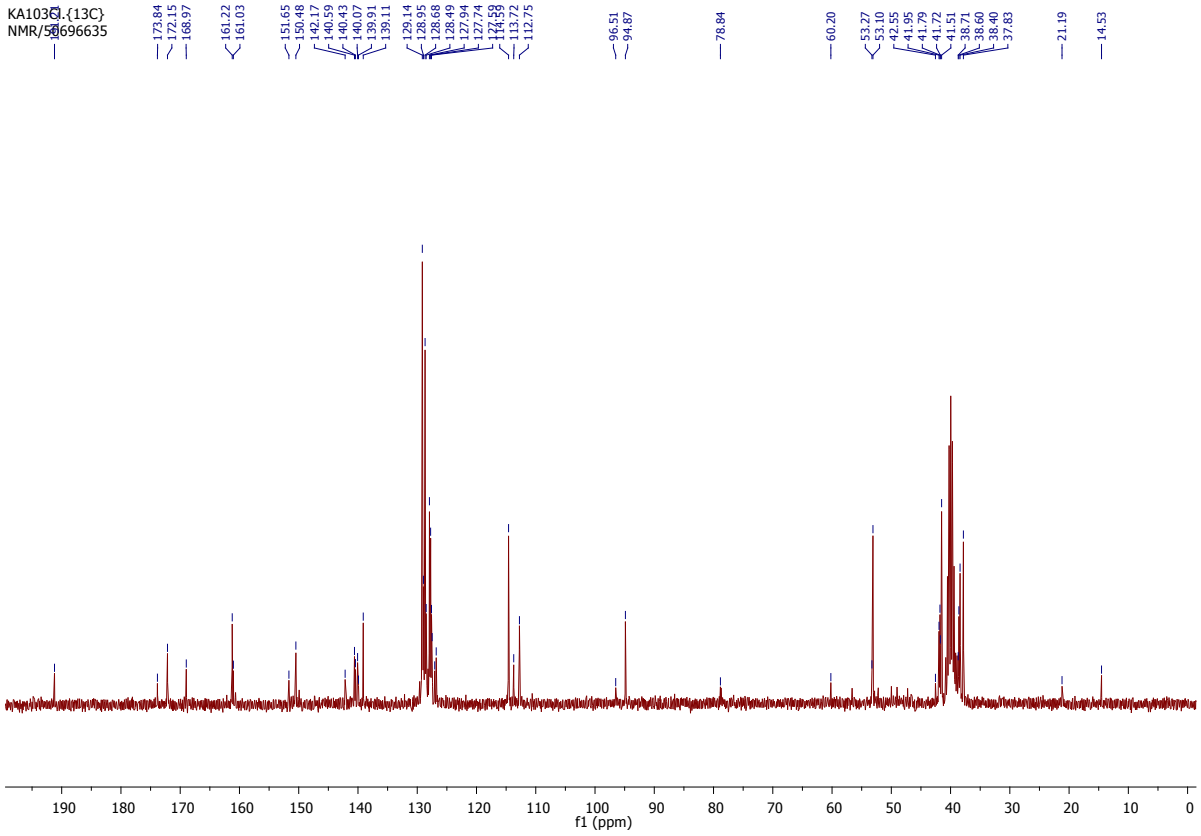



KA104C4C4.{13C}
NMR/50696635
190.74
173.99
171.93
163.88
163.20
140.26
132.92
131.96
131.44
129.53
113.94
113.10
112.31
110.62
94.71
68.62
53.13
37.83
34.84
34.45
26.72
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (мд)

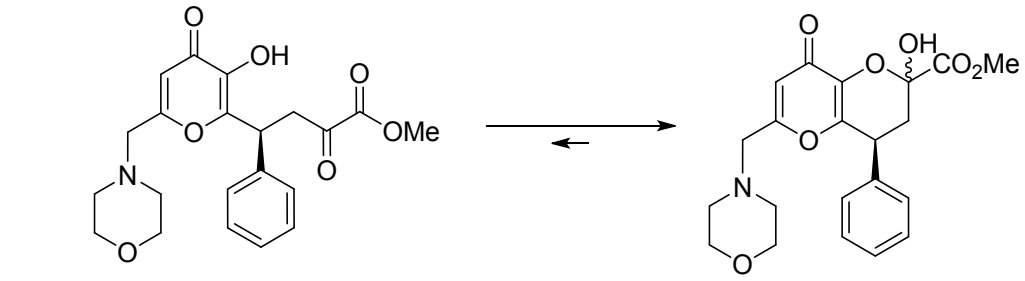
(*S*)-Methyl 6-(chloromethyl)-2-hydroxy-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8ha): Yellow oil. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.27 (s, 0.59H), 8.15 (m, 0.81H), 7.30 (m, 5.00H), 6.55 (m, 1.17H), 4.67 (m, 0.99H), 4.47 (m, 0.93H), 3.73 (m, 3.07H), 2.22 (m, 0.66H), 2.08 (s, 0.72H) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ 191.2, 172.1, 168.9, 161.2, 161.0, 150.4, 140.5, 140.4, 140.0, 139.1, 129.1, 128.9, 128.6, 128.4, 128.1, 127.9, 127.7, 127.5, 127.4, 127.0, 126.8, 114.5, 113.7, 112.7, 94.8, 53.1, 41.9, 41.7, 41.5, 38.6, 38.4, 37.8, 14.5 ppm. HRMS (ESI): *m/z* M + H$^+$ calcd for $C_{17}H_{16}ClO_6^+$ 351.0630, found 351.0635

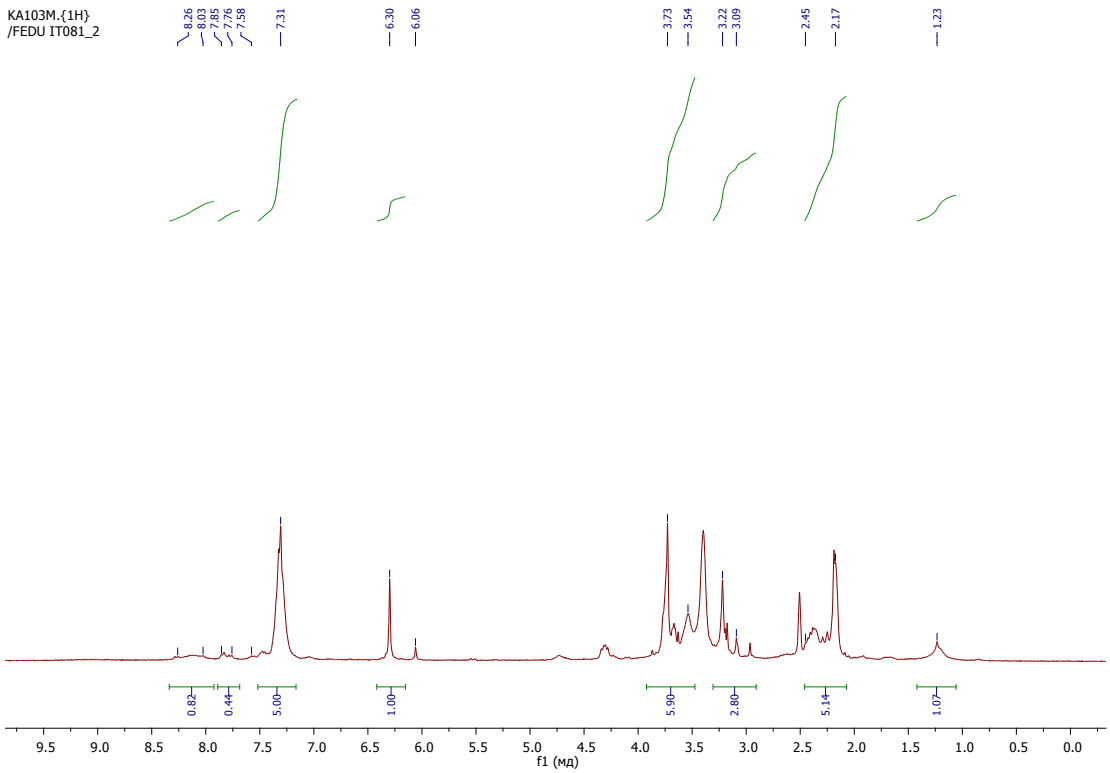


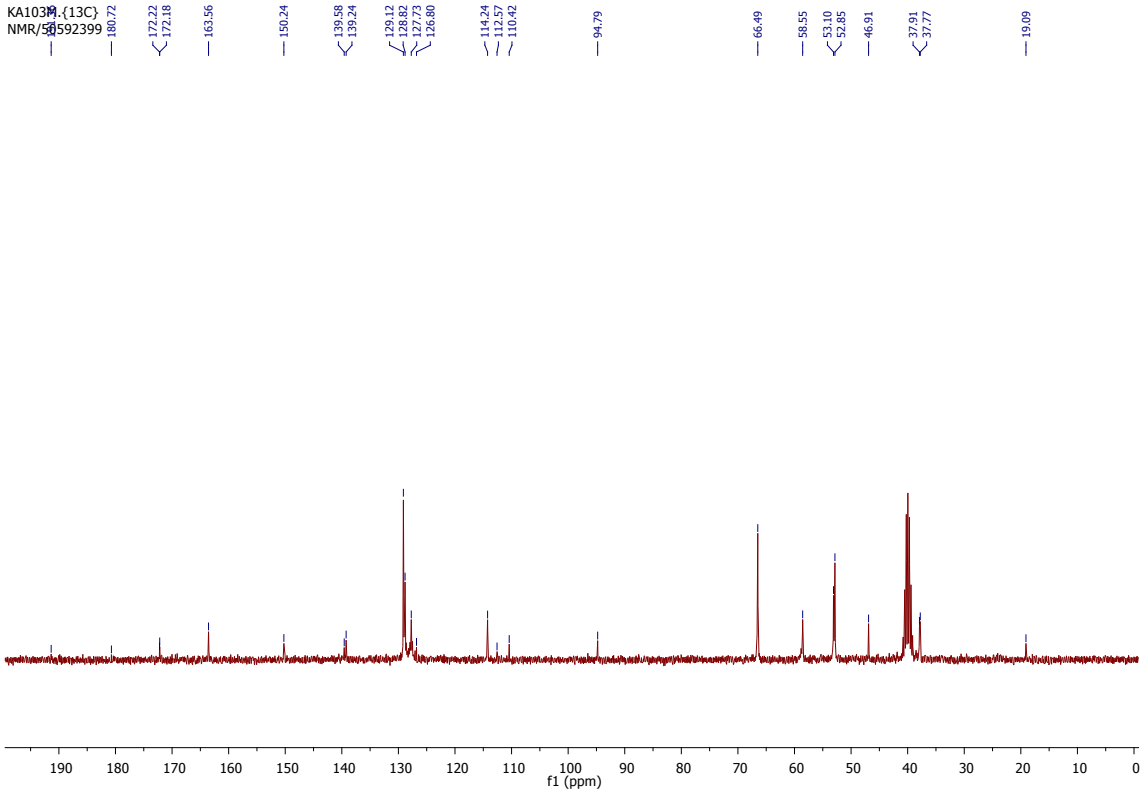



KA1036.{13C}
NMR/5/20696635
173.84
172.15
168.97
161.22
161.03
151.65
150.48
142.17
140.59
140.43
140.07
139.91
139.11
129.14
128.95
128.68
128.49
127.94
127.74
114.59
113.72
112.75
96.51
94.87
78.84
60.20
53.27
53.10
42.55
41.95
41.79
41.72
41.51
38.71
38.60
38.40
37.83
21.19
14.53
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

(*S*)-Methyl 2-hydroxy-6-(morpholinomethyl)-8-oxo-4-phenyl-2,3,4,8-tetrahydro-pyrano[3,2-b]pyran-2-carboxylate (8ia): Yellow oil. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.14 (m, 0.82H), 7.81 (m, 0.44H), 7.31 (m, 5.00H), 6.30 (s, 1.00H), 3.73-3.54 (m, 5.90H), 3.22-3.09 (m, 2.80H), 2.45-2.17 (m, 5.14H), 1.23 (m, 1.07H) ppm. ^{13}C NMR (75 MHz, DMSO-d_6): δ 172.2, 163.6, 150.2, 139.6, 139.2, 129.1, 128.8, 128.0, 127.5, 126.8, 124.2, 112.6, 110.4, 94.8, 66.5, 58.6, 53.1, 52.9, 46.9, 37.9, 37.8 ppm. HRMS (ESI): *m/z* M + H^+ calcd for $C_{21}H_{24}NO_7^+$ 402.1547, found 402.1584.





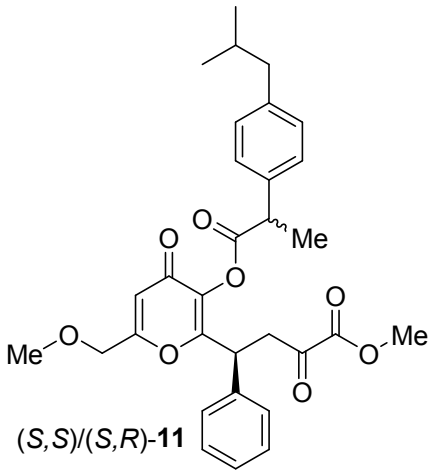

KA1038.{13C}
NMR/5859239
180.72
172.22
172.18
163.56
150.24
139.58
139.24
129.12
128.82
127.73
126.80
114.24
112.57
110.42
94.79
66.49
58.55
53.10
52.85
46.91
37.91
37.77
19.09
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

3. Synthesis of esters 11 and 12 (general procedure).

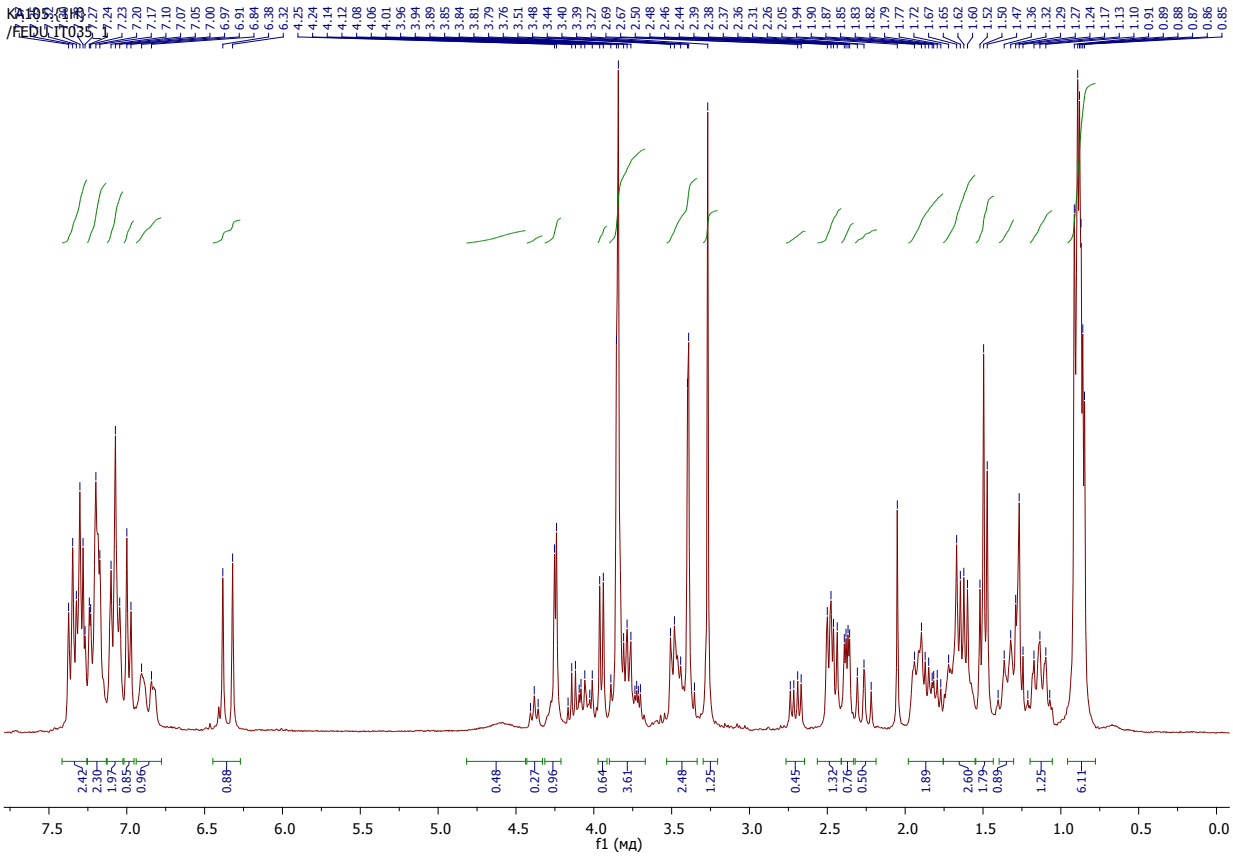
Synthesis of 11. DMAP (*cat*) was added with stirring to a solution of DCC (22.7 mg, 0.11 mmol), **8ba** (34.6 mg, 0.1 mmol) and *rac*-**9** or (*S*)-**9** (20.7 mg, 0.1 mmol) in DCM (3 ml). The reaction mixture was stirred at ambient temperature for 10 h and then washed with water (2 x 1 mL). The organic phase was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure (10 Torr). The residue was purified by flash chromatography (*n*-hexane/EtOAc 2:1) to afford compound **(*S,S*)/(*S,R*)-11** or **(*S,S*)-11** as colorless oil.

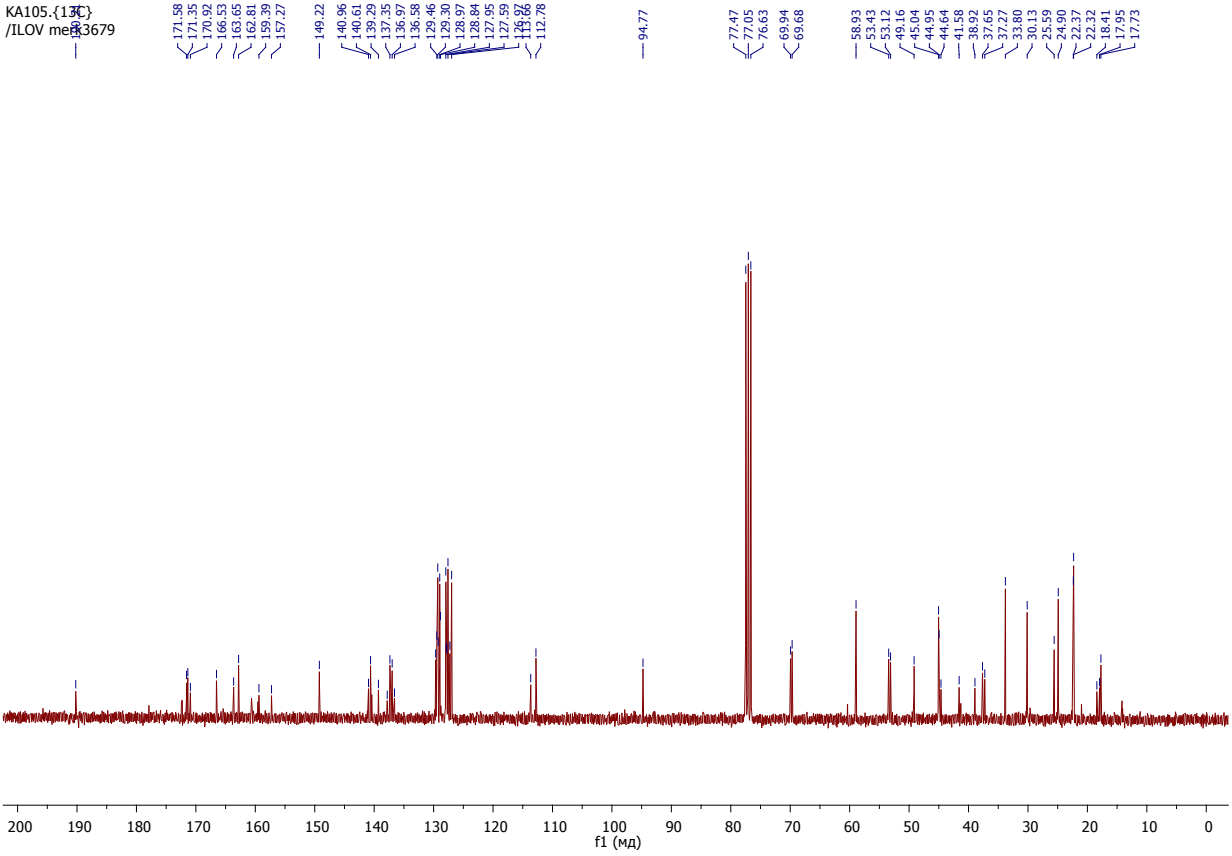
Synthesis of 12. DMAP (*cat*) was added with stirring to a solution of DCC (22.7 mg, 0.11 mmol), **8ha** (35 mg, 0.1 mmol) and **10** (18.4 mg, 0.1 mmol) in DCM (3 ml). The reaction mixture was stirred at ambient temperature for 10 h. Product **12** was isolated as colorless oil similar to aforementioned procedure.

Methyl 4-(3-((2-(4-isobutylphenyl)propanoyl)oxy)-6-(methoxymethyl)-4-oxo-4H-pyran-2-yl)-2-oxo-4-phenylbutanoate ((*S,S*)/(*S,R*)-11). Colorless oil (37.8 mg, 70% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 2.4H), 7.21 (m, 2.3H), 7.07 (m, 2H), 6.99 (m, 1H), 6.87 (m, 1H), 6.37 (m, 1H), 4.58 (s, 1H), 4.38 (m, 0.3H), 4.25 (m, 1H), 3.95 (m, 0.6H), 3.90 – 3.67 (m, 3.6H), 3.53 – 3.34 (m, 2.5H), 3.27 (s, 1H), 2.70 (m, 0.5H), 2.47 (m, 1.3H), 2.37 (m, 0.8H), 2.32 – 2.19 (m, 0.5H), 1.85 (m, 1.9H), 1.76 – 1.55 (m, 2.6H), 1.50 (m, 1.8H), 1.34 (m, 1H), 1.12 (m, 1.3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.2, 171.5, 171.3, 170.9, 166.5, 163.6, 162.8, 159.3, 157.2, 149.2, 140.9, 140.6, 139.2, 137.8, 137.3, 136.9, 136.5, 129.6, 129.4, 129.3, 129.2, 128.9, 128.8, 127.9, 127.8, 127.7, 127.5, 127.2, 126.9, 113.6, 112.7, 94.7, 69.9, 69.6, 58.9, 53.4, 53.1, 49.1, 45.0, 44.9, 44.6, 41.5, 38.9, 37.6, 37.2, 33.8, 30.1, 25.5, 24.9, 22.3, 22.3, 18.4, 17.9, 17.7 ppm. HRMS (ESI): m/z M + Na^+ calcd for $C_{31}H_{33}O_8Na^+$ 557.2146, found 557.2146.

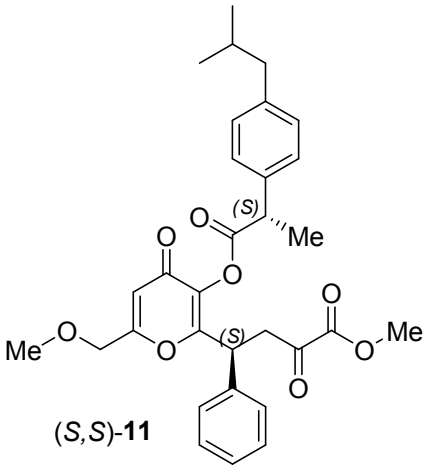


(*S,S*)/(*S,R*)-**11**

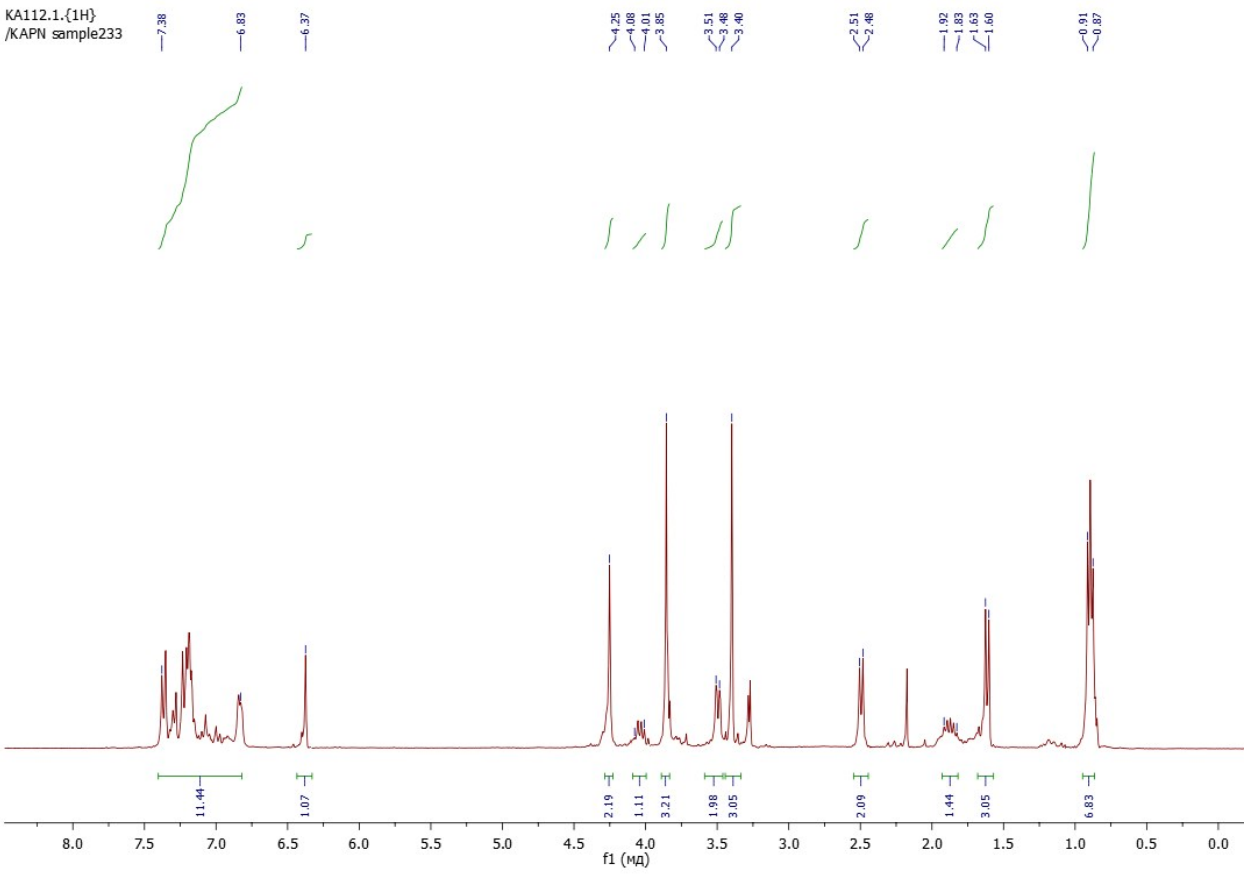

KA105.{1H}
/FEDU1T035_1
f1 (мд)

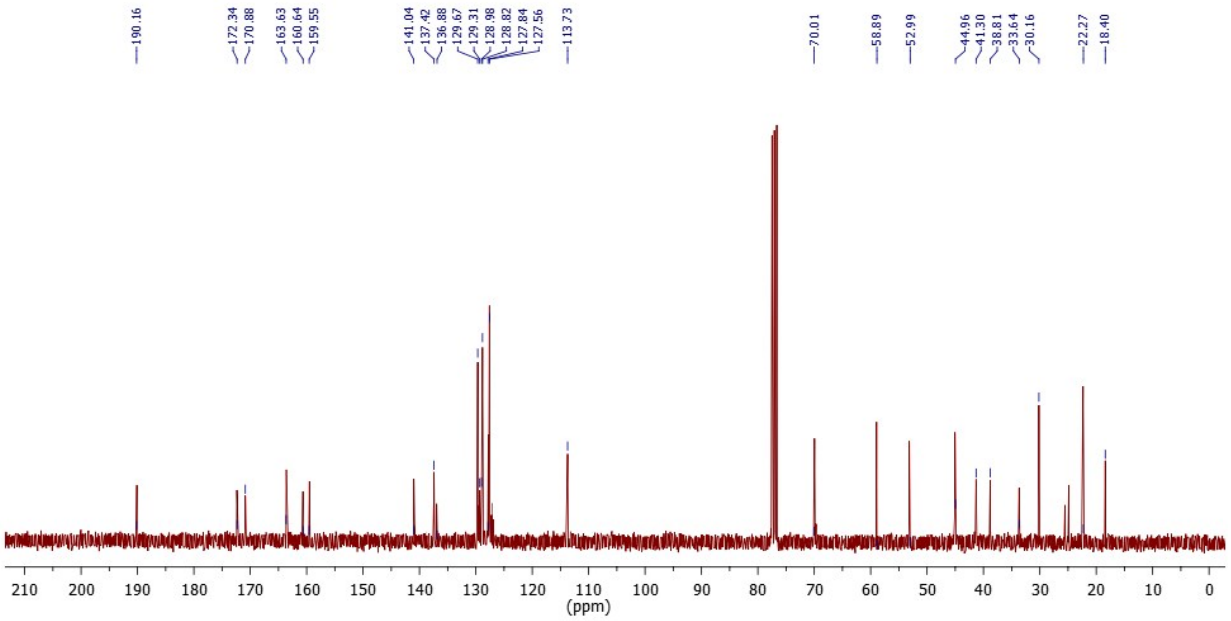

KA105.{13C}
/ILOV me3679
f1 (мд)

(*S*)-methyl 4-(3-(((*S*)-2-(4-isobutylphenyl)propanoyl)oxy)-6-(methoxymethyl)-4-oxo-4H-pyran-2-yl)-2-oxo-4-phenylbutanoate ((*S*,*S*)-11). Colorless oil (43.3 mg, 81% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 - 6.84 (m, 9H (*Ar*)), 6.37 (s, 1H), 4.25 (s, 2H), 4.08-4.01 (m, 1H), 3.85 (s, 3H), 3.51-3.48 (m, 2H), 3.40 (s, 3H), 2.51-2.48 (d, *J* = 7.0 Hz, 2H), 1.92 - 1.83 (m, 1H), 1.63-1.60 (d, *J* = 7.0 Hz, 3H), 0.91-0.87 (m, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.1, 172.3, 170.9, 163.6, 160.6, 159.6, 141.0, 137.4, 136.9, 129.7 - 127.0 (*Ar*), 113.7, 70.0, 58.9, 53.0, 45.0, 41.3, 38.8, 33.6, 30.2, 22.3, 18.4 ppm.



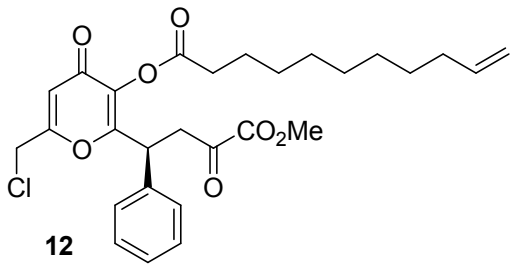
(*S*,*S*)-**11**



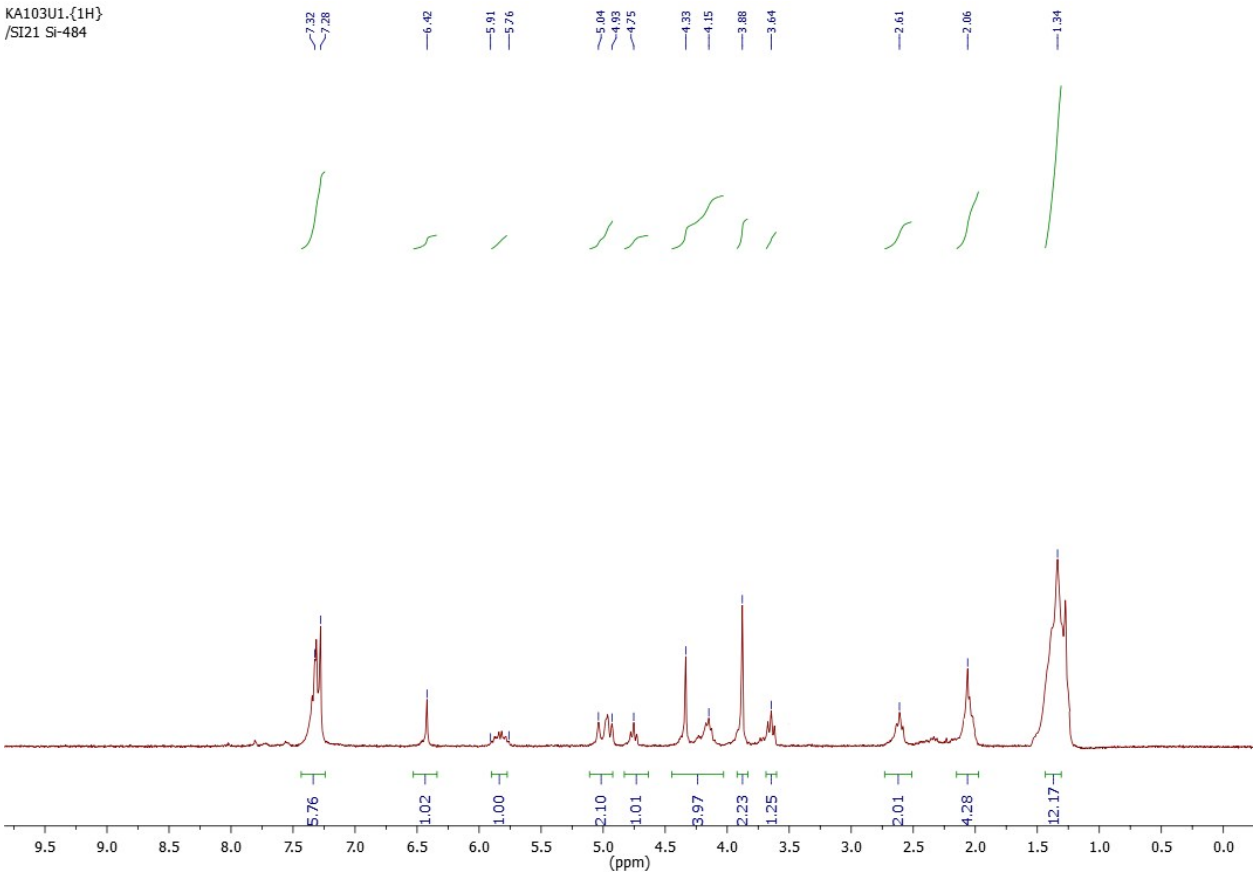


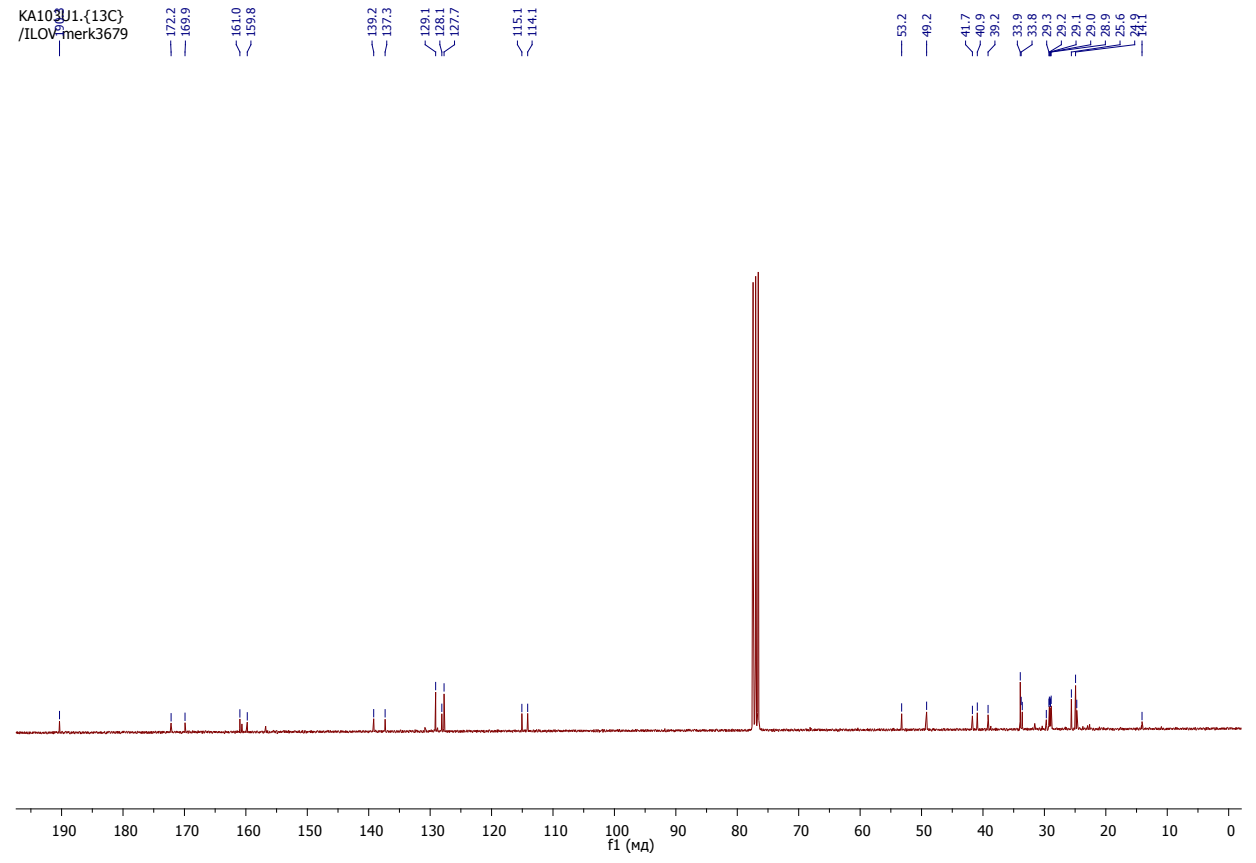
(*S*)-6-(Chloromethyl)-2-(4-methoxy-3,4-dioxo-1-phenylbutyl)-4-oxo-4H-pyran-3-yl undec-10-enoate (12): Colorless oil (41.8 mg, 85% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 – 7.28 (m, 5H), 6.42 (m, 1H), 5.91 – 5.76 (m, 1H), 5.04 – 4.93 (m, 2H), 4.75 (m, 1H), 4.33 – 4.15 (m, 4H), 3.88 (m, 2H), 3.64 (t, *J* = 7.8 Hz, 1H), 2.61 (m, 2H), 2.06 (m, 4H), 1.34 (m, 12H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.3, 172.1, 169.9, 160.9, 159.7, 139.1, 137.3, 129.1, 128.1, 127.7, 115.0, 114.1, 53.2, 49.1, 41.7, 40.9, 39.1, 33.9, 33.7, 33.6, 29.6, 29.2, 29.1, 29.0, 29.0, 28.9, 25.6, 24.9, 24.7, 14.1 ppm. HRMS (ESI): m/z M + NH_4^+ calcd for $C_{28}H_{33}ClO_7NH_4^+$ 534.2254, found 534.2243.

.



12

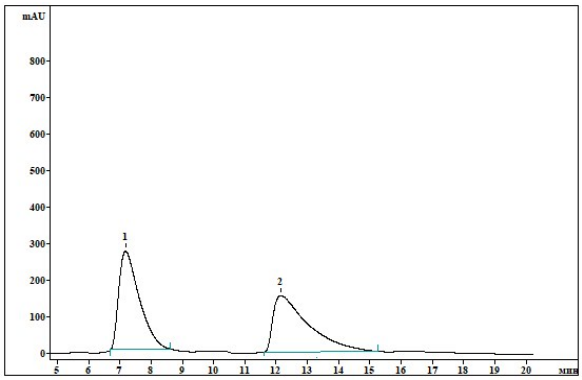

KA103U1.{1H}
/SI21 Si-484
7.32
7.28
6.42
5.91
5.76
5.04
4.93
4.75
4.33
4.15
3.88
3.64
2.61
2.06
1.34
5.76
1.02
1.00
2.10
1.01
3.97
2.23
1.25
2.01
4.28
12.17
(ppm)


KA103U1.{13C}
/ILOVmerk3679
172.2
169.9
161.0
159.8
139.2
137.3
129.1
128.1
127.7
115.1
114.1
53.2
49.2
41.7
40.9
39.2
33.9
33.8
29.3
29.2
29.1
29.0
28.9
25.6
24.9
14.1
f1 (мд)

4. HPLC data for adducts 8

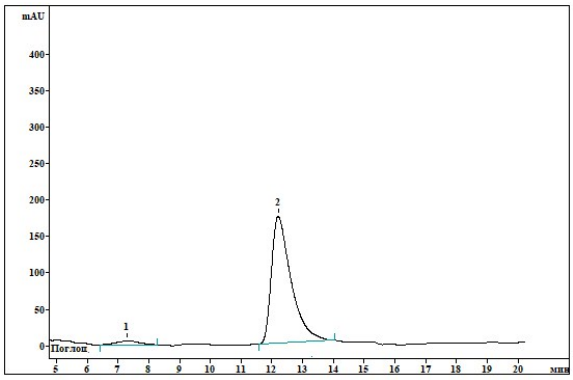
(*S*)-Methyl 2-hydroxy-6-methyl-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8aa): CHIRALPAC OD-H, *n*-hexane-^{i}PrOH 90/10, 1 mL/min, 220 nm, t_{major} = 7.3 min, t_{minor} = 12.1 min

Rac *Chiral **8aa***



РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

Пик	Время мин	Площадь mAU*сек	Площадь %
1	7.31	12314.24	50.48
2	12.1	12078.93	49.52
2	19.41	24393.17	100.00

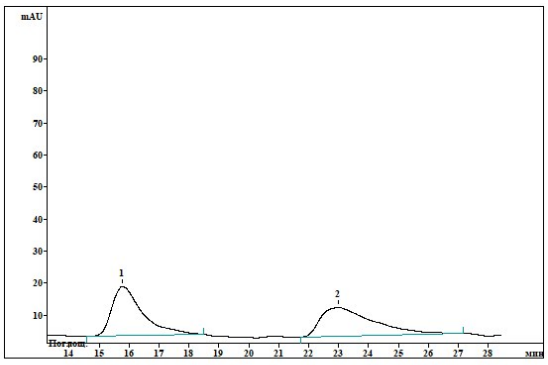


РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

Пик	Время мин	Площадь mAU*сек	Площадь %
1	7.38	450.82	3.84
2	12.36	11275.07	96.16
2	19.74	11725.89	100.00

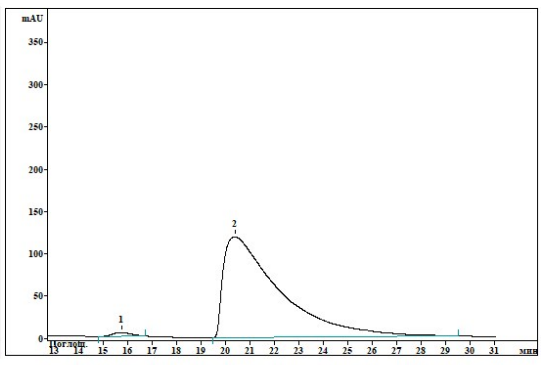
(*S*)-Methyl 2-hydroxy-6-(methoxymethyl)-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8ba): CHIRALPAC OD-H, *n*-hexane-^{i}PrOH 90/10, 1 mL/min, 220 nm, t_{minor} = 15.8 min, t_{major} = 23.0 min.

Rac *Chiral **8ba***



РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

Пик	Время мин	Площадь mAU*сек	Площадь %
1	15.79	1104.04	50.18
2	22.97	1096.05	49.82
2	29.08	2200.09	100.00

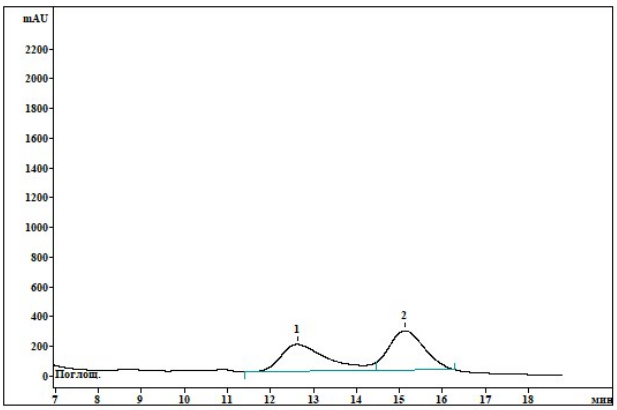


РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

Пик	Время мин	Площадь mAU*сек	Площадь %
1	15.74	245.40	1.27
2	20.39	19082.85	98.73
2	32.21	19328.25	100.00

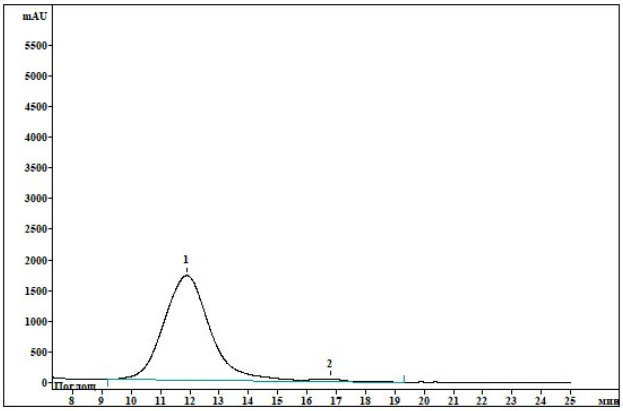
(*S*)-Methyl 4-(4-cyanophenyl)-2-hydroxy-6-(methoxymethyl)-8-oxo-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8bb): CHIRALPAC OJ-H, *n*-hexane-^{i}PrOH 70/30, 1 mL/min, 220 nm, t_{major} = 12.6 min, t_{minor} = 15.1 min

Rac *Chiral **8bb***



РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

Пик	Время мин	Площадь mAU*сек	Площадь %
1	12.62	14185.37	48.13
2	15.13	15286.58	51.87
2	18.83	29471.95	100.00

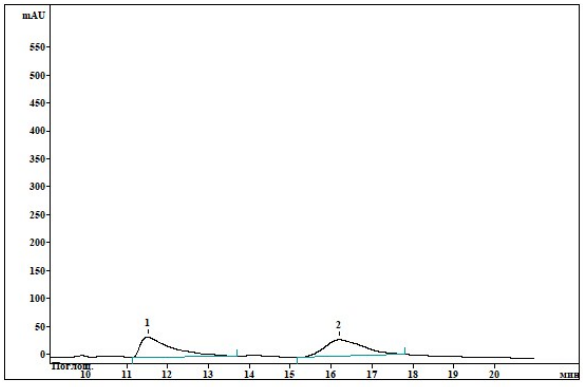


РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

Пик	Время мин	Площадь mAU*сек	Площадь %
1	11.9	187055.83	98.29
2	16.8	3261.52	1.71
2	34.79	190317.35	100.00

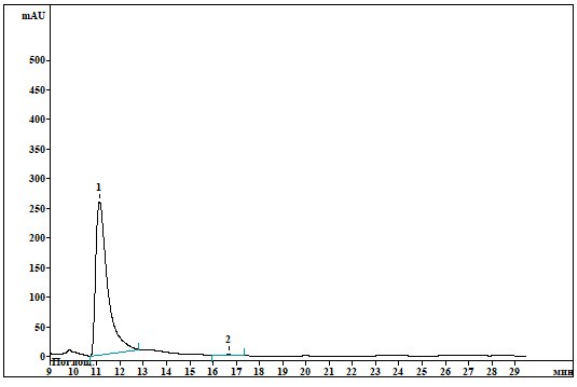
(*S*)-Methyl 4-(furan-2-yl)-2-hydroxy-6-(methoxymethyl)-8-oxo-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8bc): CHIRALPAC OJ-H, *n*-hexane-^{i}PrOH 70/30, 1 mL/min, 220 nm, t_{major} = 11.5 min, t_{minor} = 16.2 min

Rac *Chiral **8bc***



РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

Пик	Время мин	Площадь mAU*сек	Площадь %
1	11.52	1922.63	49.49
2	16.19	1962.64	50.51
2	32.55	3885.28	100.00

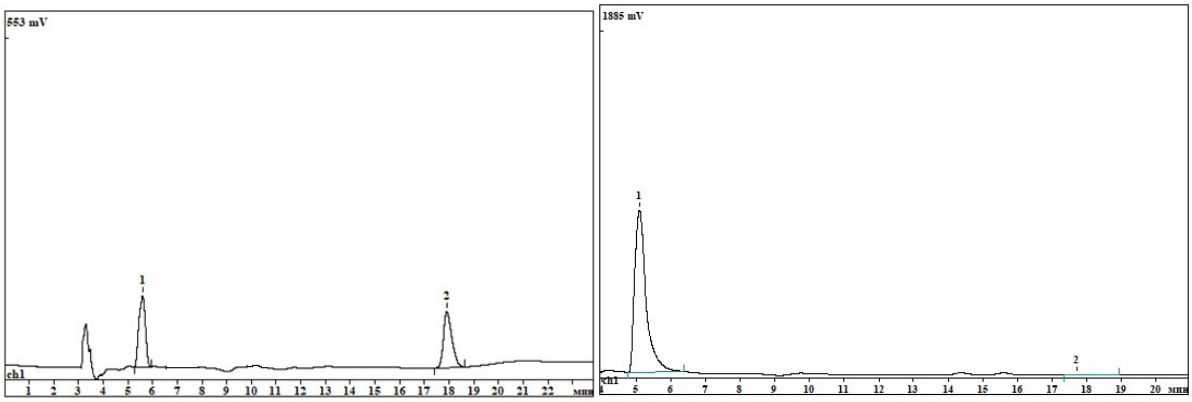


РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

Пик	Время мин	Площадь mAU*сек	Площадь %
1	11.11	9157.14	99.49
2	16.68	47.30	0.51
2	29.83	9204.44	100.00

(*S*)-Methyl 2-hydroxy-8-oxo-4-phenyl-6-((phenylthio)methyl)-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8ca): CHIRALPAC OJ-H, *n*-hexane-^{i}PrOH 70/30, 1 mL/min, 220 nm, t_{major} = 5.6 min, t_{minor} = 17.9 min

Rac *Chiral **8ca***



Quantitation method: Заказной

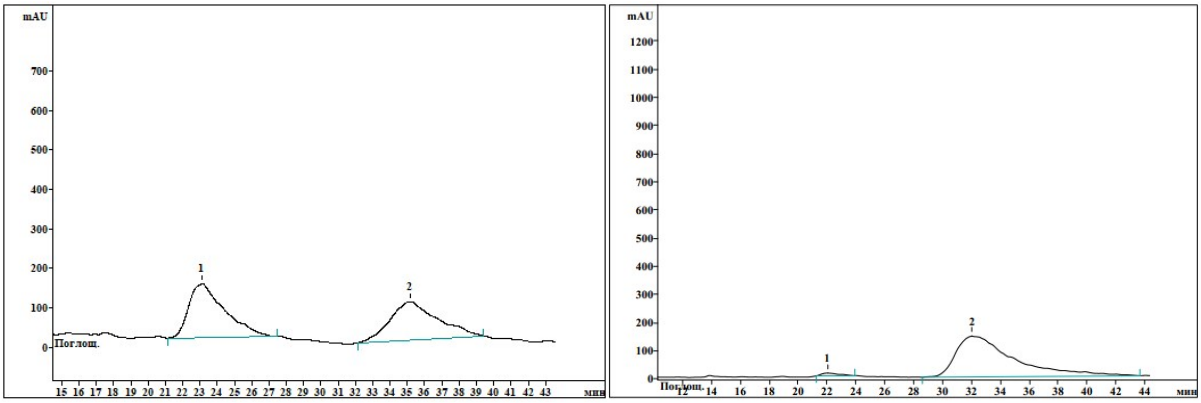
Peak	Retention мин	Area mV*сек	Area %
1	5.60	2110.125	49.87
2	17.91	2121.197	50.13
2	23.85	4231.322	100.00

Quantitation method: Заказной

Peak	Retention мин	Area mV*сек	Area %
1	5.08	20290.746	99.95
2	17.77	9.389	0.05
2	27.45	20300.134	100.00

(*S*)-Methyl 6-(((4-fluorophenyl)thio)methyl)-2-hydroxy-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8da): CHIRALPAC OJ-H, *n*-hexane-^{i}PrOH 70/30, 1 mL/min, 220 nm, t_{minor} = 23.1 min, t_{major} = 35.1 min

Rac *Chiral **8da***



РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

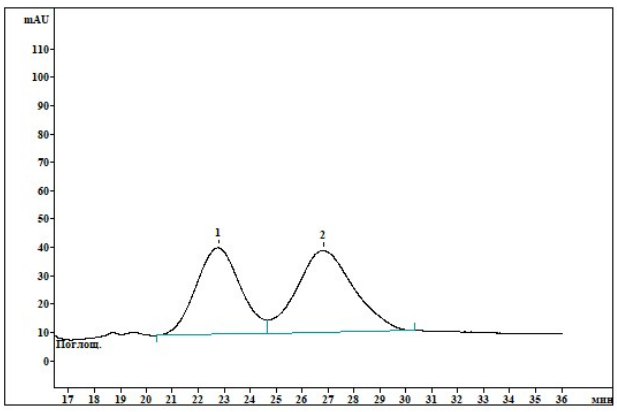
Пик	Время мин	Площадь mAU*сек	Площадь %
1	23.13	19568.20	51.69
2	35.14	18289.66	48.31
2	44.18	37857.86	100.00

РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

Пик	Время мин	Площадь mAU*сек	Площадь %
1	22.01	772.95	1.88
2	32.02	40307.24	98.12
2	49.99	41080.19	100.00

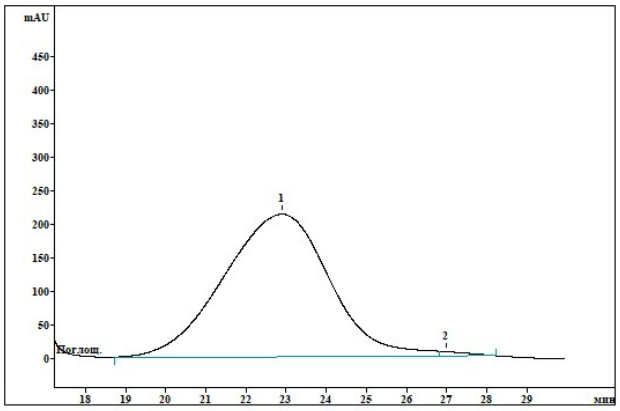
(*S*)-Methyl 6-(((2-fluorophenyl)thio)methyl)-2-hydroxy-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8ea): CHIRALPAC OJ-H, *n*-hexane-*i*PrOH 70/30, 1 mL/min, 220 nm, t_{major} = 22.8 min, t_{minor} = 26.8 min

Rac *Chiral **8ea***



РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

Пик	Время мин	Площадь mAU*сек	Площадь %
1	22.76	3607.88	44.96
2	26.8	4416.30	55.04
2	36.12	8024.18	100.00

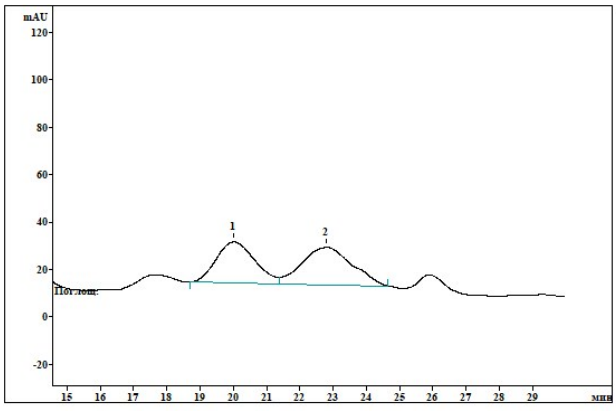


РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

Пик	Время мин	Площадь mAU*сек	Площадь %
1	22.89	38869.10	99.21
2	26.98	311.09	0.79
2	29.98	39180.19	100.00

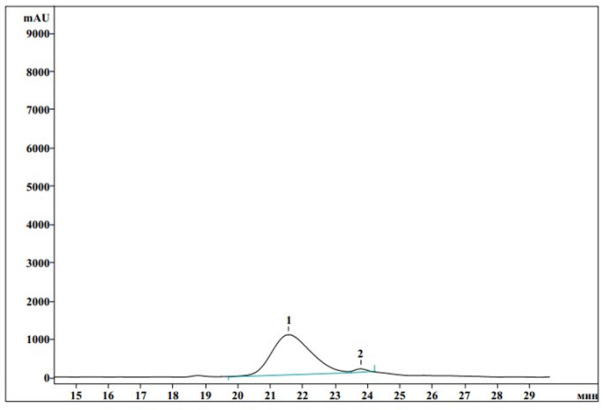
(*S*)-Methyl 4-(4-cyanophenyl)-6-(((2-fluorophenyl)thio)methyl)-2-hydroxy-8-oxo-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8eb): CHIRALPAC OJ-H, *n*-hexane-*i*PrOH 70/30, 1 mL/min, 220 nm, t_{major} = 20.0 min, t_{minor} = 22.8 min

Rac *Chiral **8eb***



РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

Пик	Время мин	Площадь mAU*сек	Площадь %
1	20.01	1413.90	46.29
2	22.81	1640.28	53.71
2	49.98	3054.18	100.00

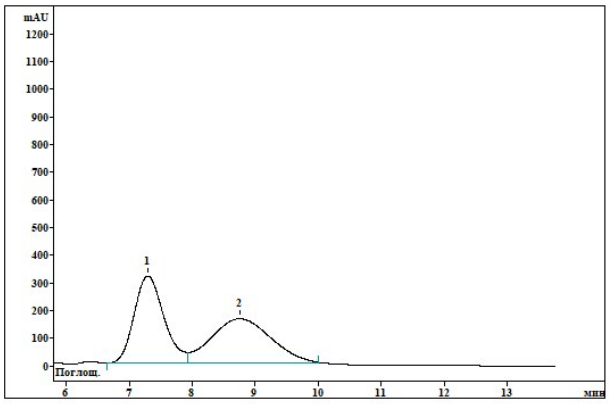


РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

Пик	Время мин	Площадь mAU*сек	Площадь %
1	21.55	103015.66	97.29
2	23.79	2871.99	2.71
2	49.98	105887.65	100.00

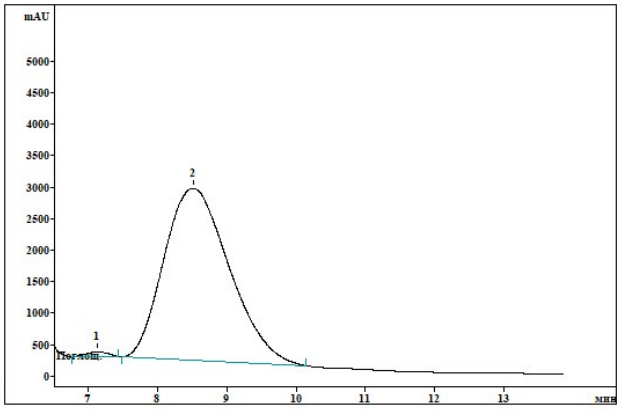
(*S*)-Methyl 6-(((2,4-difluorophenyl)thio)methyl)-2-hydroxy-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8fa): CHIRALPAC OJ-H, *n*-hexane-^{i}PrOH 70/30, 1 mL/min, 220 nm, t_{minor} = 7.3 min, t_{major} = 8.8 min

Rac *Chiral **8fa***



РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

Пик	Время мин	Площадь mAU*сек	Площадь %
1	7.292	10256.92	50.04
2	8.754	10239.56	49.96
2	13.89	20496.48	100.00

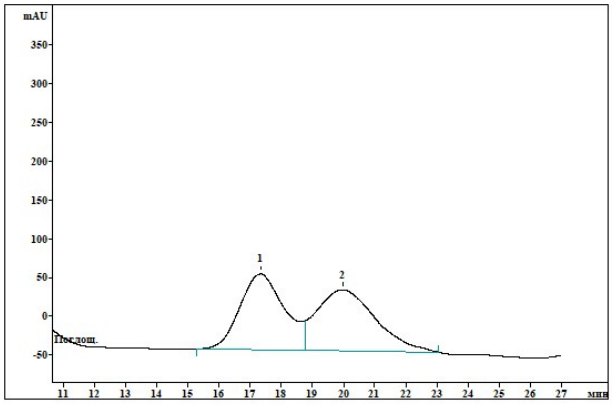


РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

Пик	Время мин	Площадь mAU*сек	Площадь %
1	7.133	1603.76	0.89
2	8.508	179016.15	99.11
2	13.87	180619.91	100.00

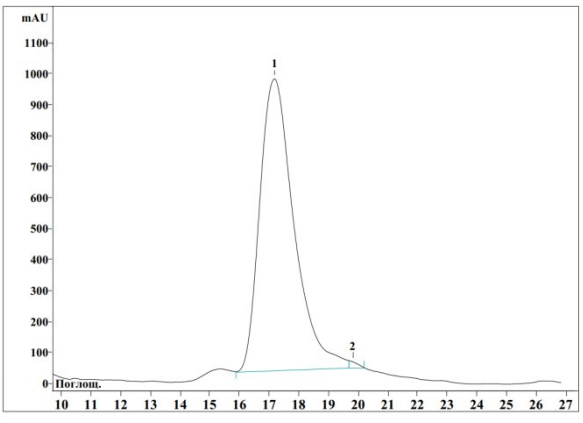
(*S*)-Methyl 4-(4-cyanophenyl)-6-(((2,4-difluorophenyl)thio)methyl)-2-hydroxy-8-oxo-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8fb): CHIRALPAC OJ-H, *n*-hexane-^{i}PrOH 70/30, 1 mL/min, 220 nm, t_{major} = 17.3 min, t_{minor} = 20.0 min

Rac *Chiral **8fb***



РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

Пик	Время мин	Площадь mAU*сек	Площадь %
1	17.33	9804.42	48.74
2	19.97	10312.13	51.26
2	37.97	20116.55	100.00

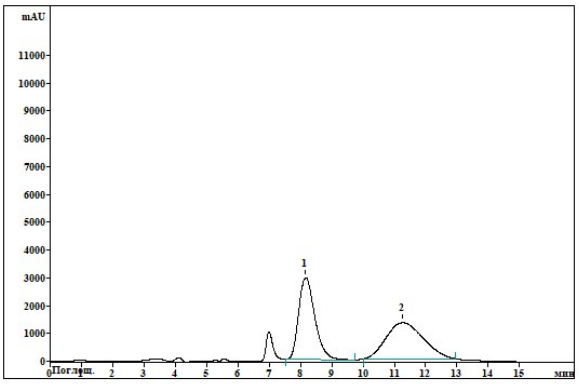


РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

Пик	Время мин	Площадь mAU*сек	Площадь %
1	17.27	71125.69	99.47
2	19.88	378.76	0.53
2	37.97	71504.45	100.00

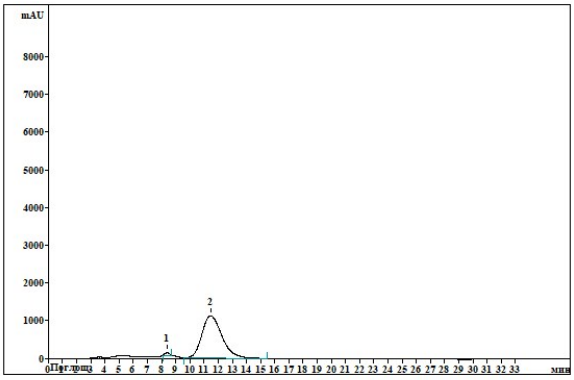
(*S*)-Methyl 6-(((4-chlorophenyl)thio)methyl)-2-hydroxy-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8ga): CHIRALPAC OJ-H, *n*-hexane-*i*PrOH 70/30, 1 ml/min, 220 nm, t_{minor} = 8.2 min, t_{major} = 11.3 min

Rac *Chiral **8ga***



РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

Пик	Время мин	Площадь mAU*сек	Площадь %
1	8.167	106171.03	49.72
2	11.28	107367.42	50.28
2	15.27	213538.45	100.00

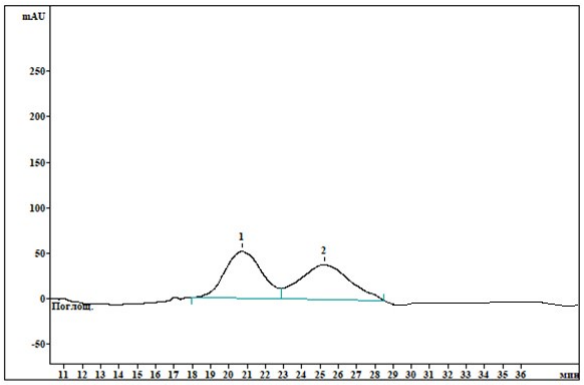


РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

Пик	Время мин	Площадь mAU*сек	Площадь %
1	8.385	1412.60	1.28
2	11.47	109188.51	98.72
2	33.79	110601.11	100.00

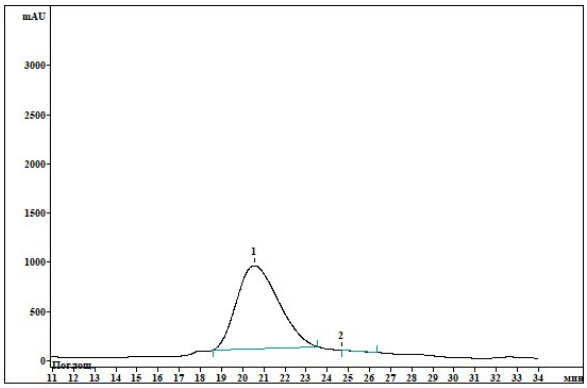
(*S*)-Methyl 6-(((4-chlorophenyl)thio)methyl)-4-(4-cyanophenyl)-2-hydroxy-8-oxo-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8gb): CHIRALPAC OJ-H, *n*-hexane-*i*PrOH 70/30, 1 mL/min, 220 nm, t_{major} = 20.7 min, t_{minor} = 25.2 min

Rac *Chiral **8gb***



РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

Пик	Время мин	Площадь mAU*сек	Площадь %
1	20.71	7355.44	50.16
2	25.2	7309.30	49.84
2	37.63	14664.74	100.00

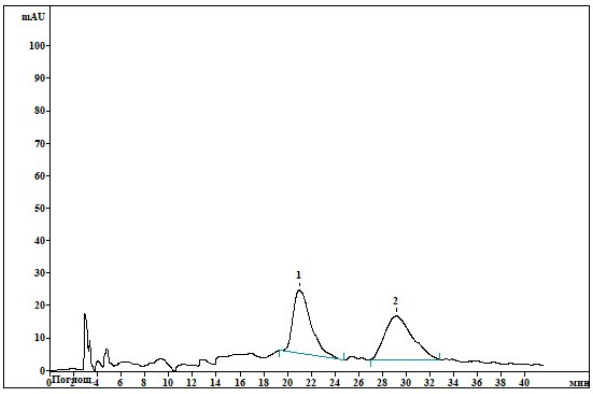


РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

Пик	Время мин	Площадь mAU*сек	Площадь %
1	20.54	115748.07	99.92
2	24.7	94.57	0.08
2	34.37	115842.64	100.00

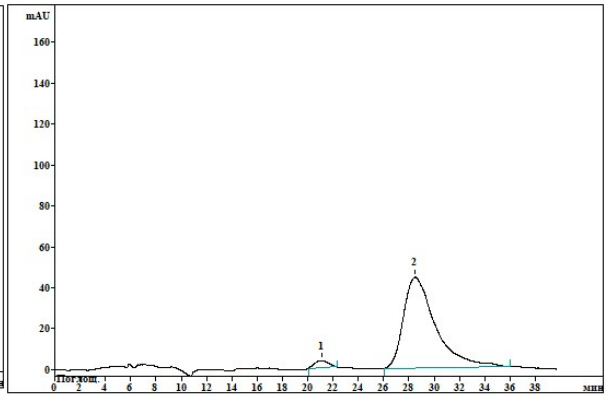
(*S*)-Methyl 6-(chloromethyl)-2-hydroxy-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8ha): CHIRALPAC OD-H, *n*-hexane-^{i}PrOH 90/10, 1 mL/min, 220 nm, t_{minor} = 21.0 min, t_{major} = 29.2 min

Rac *Chiral **8ha***



РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

Пик	Время мин	Площадь mAU*сек	Площадь %
1	21	2059.60	49.02
2	29.16	2141.93	50.98
2	41.62	4201.53	100.00

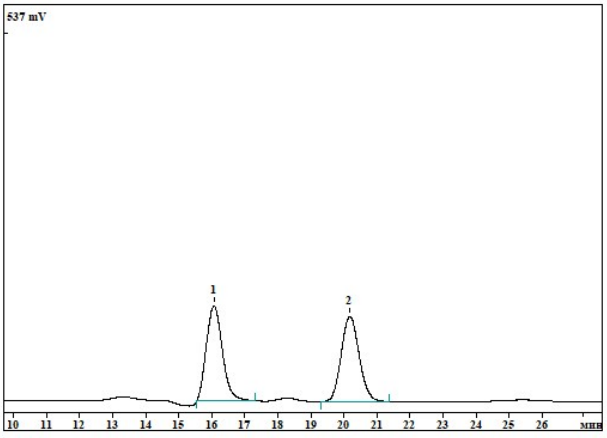


РЕЗУЛЬТАТЫ РАСЧЕТА
Метод расчета: Нормировка отклика
Стандарт: Нет

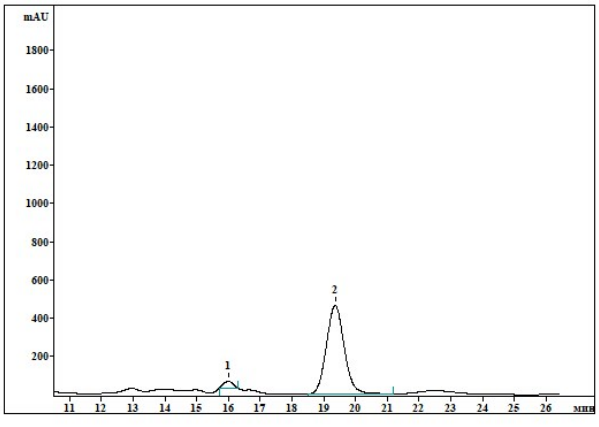
Пик	Время мин	Площадь mAU*сек	Площадь %
1	21.09	264.04	3.28
2	28.5	7794.71	96.72
2	39.75	8058.75	100.00

(*S*)-Methyl 2-hydroxy-6-(morpholinomethyl)-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8ia): CHIRALPAC OD-H, *n*-hexane-^{i}PrOH 90/10, 1 mL/min, 220 nm, t_{minor} = 16.1 min, t_{major} = 20.2 min

Rac *Chiral **8ha***



Peak	Retention мин	Area mV*сек	Area %
1	16.09	2249.834	50.13
2	20.22	2237.728	49.87
2	36.31	4487.562	100.00



Пик	Время мин	Площадь mAU*сек	Площадь %
1	15.99	406.38	4.02
2	19.26	9694.55	95.98
2	35.25	10100.93	100.00

5. HRMS pictures of catalyst V and compounds 11 and 12

Freshly prepared catalyst **V**

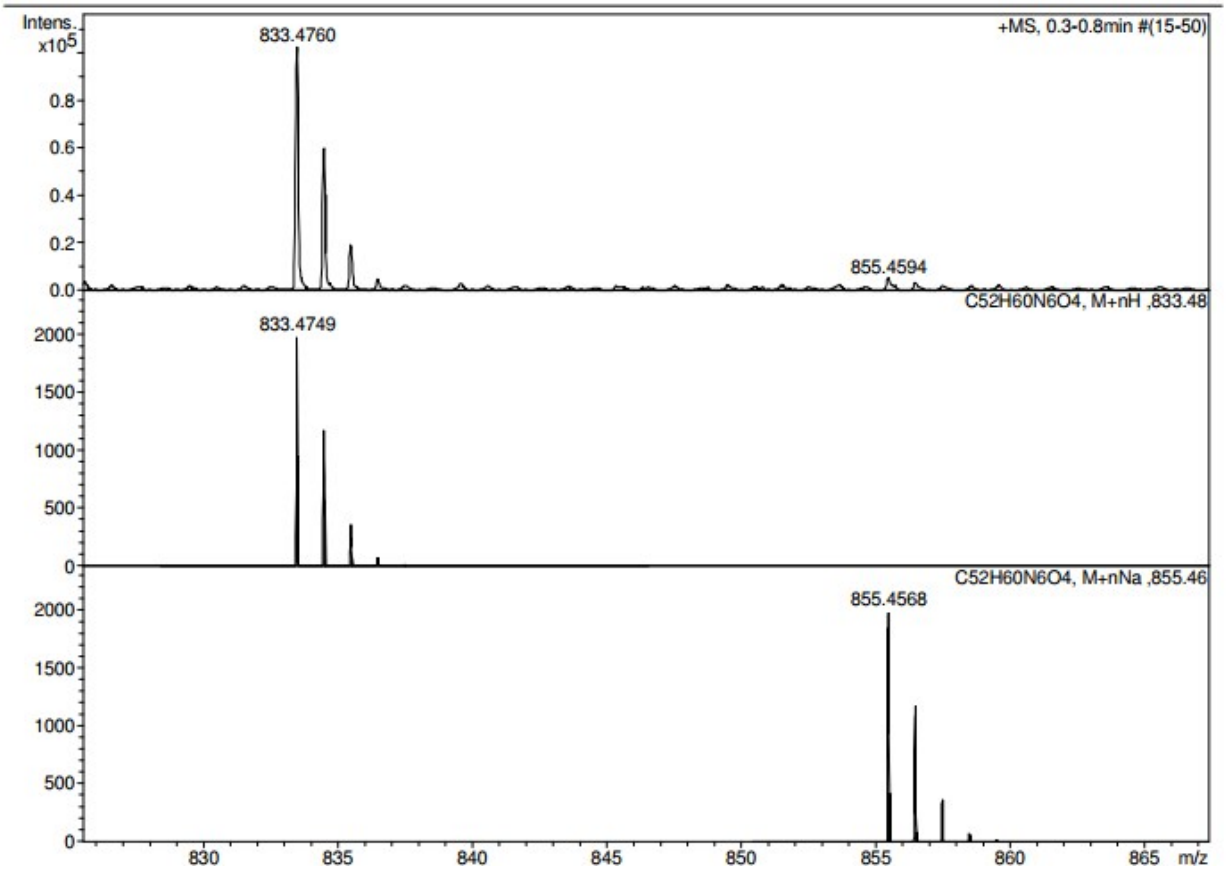
Display Report

Analysis Info

Analysis Name	D:\Data\Kolotyrkina\2018\Kostenko\0808007.d	Acquisition Date	08.08.2018 13:24:58
Method	tune_wide.m	Operator	BDAL@DE
Sample Name	/ZSGN KA103Reg	Instrument / Ser#	micrOTOF 10248
Comment	C52H60N6O4 mH 833.4748 clb added		

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active			Set Dry Heater	180 °C
Scan Begin	50 m/z	Set Capillary	4500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set End Plate Offset	-500 V	Set Divert Valve	Waste



Catalyst **V** after regeneration

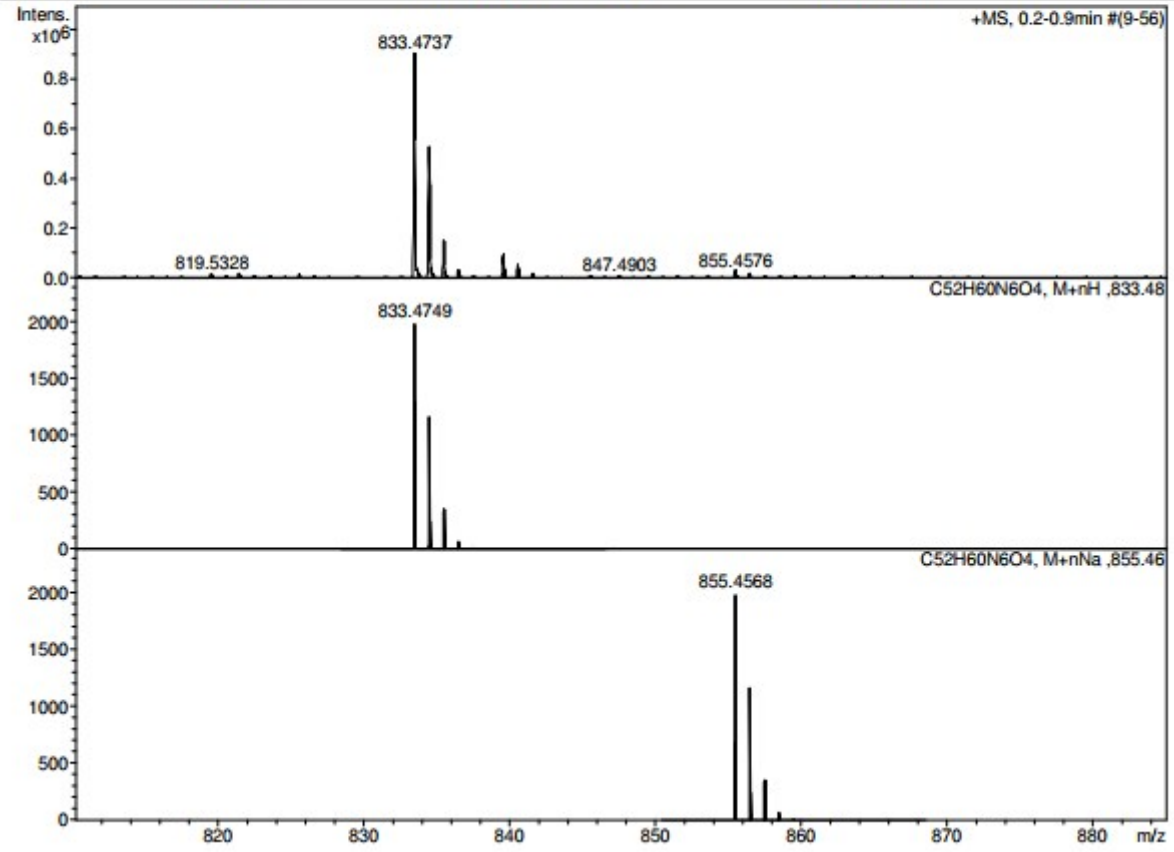
Display Report

Analysis Info

Analysis Name	D:\Data\Kolotyrkina\2018\Kostenko\0808006.d	Acquisition Date	08.08.2018 13:15:52
Method	tune_wide.m	Operator	BDAL@DE
Sample Name	/ZSGN KA103cat	Instrument / Ser#	micrOTOF 10248
Comment	C52H60N6O4 mH 833.4748 clb added		

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active			Set Dry Heater	180 °C
Scan Begin	50 m/z	Set Capillary	4500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set End Plate Offset	-500 V	Set Divert Valve	Waste



HRMS data for compound **11**

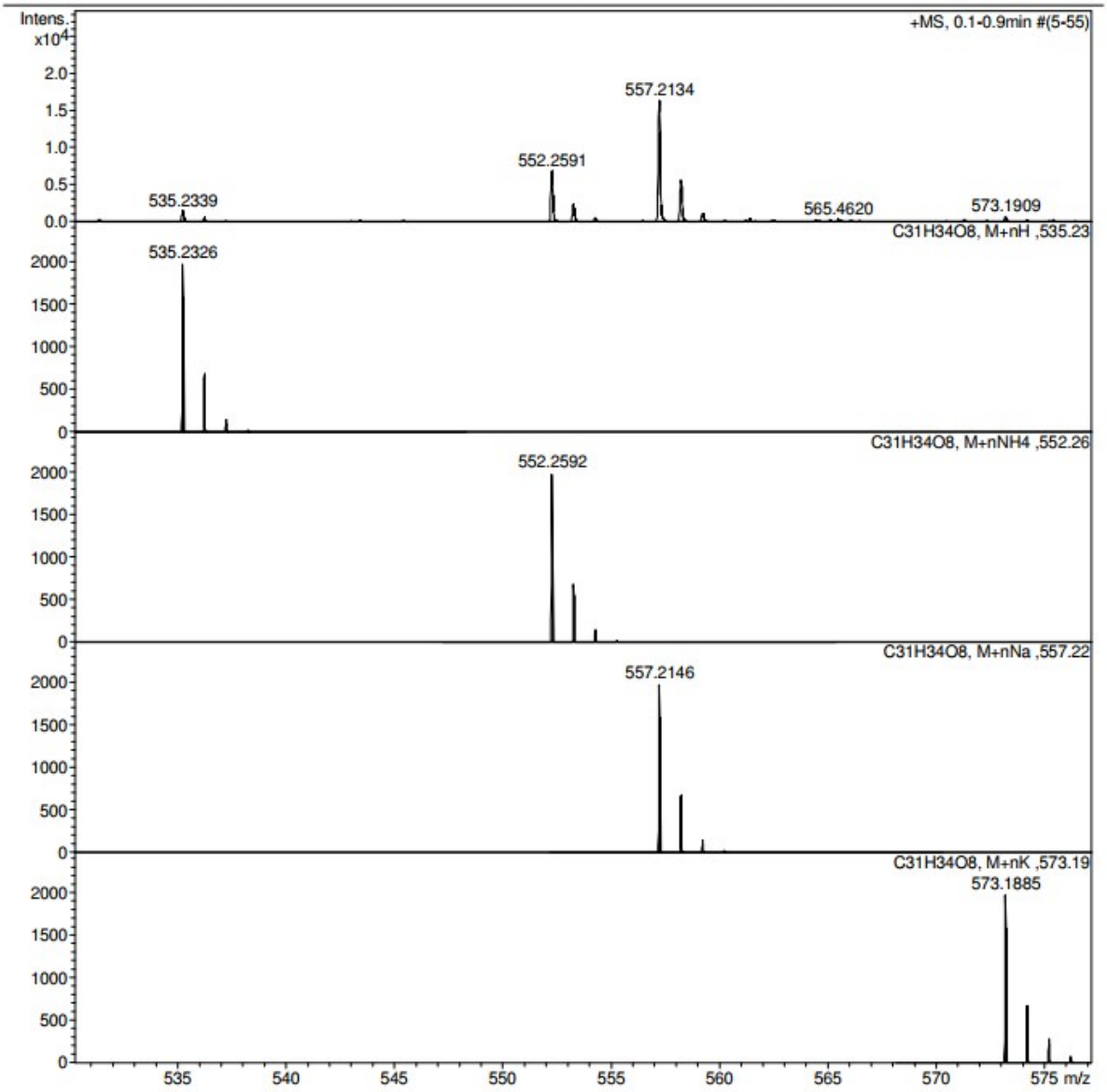
Display Report

Analysis Info

Analysis Name	D:\Data\Kolotyrkina\2018\Kostenko\0904017.d	Acquisition Date	05.09.2018 10:04:10
Method	tune_50-1600.m	Operator	BDAL@DE
Sample Name	/ZSGN KA103IB	Instrument / Ser#	micrOTOF 10248
Comment	C31H34O8 mH 535.2326 calibrant added		

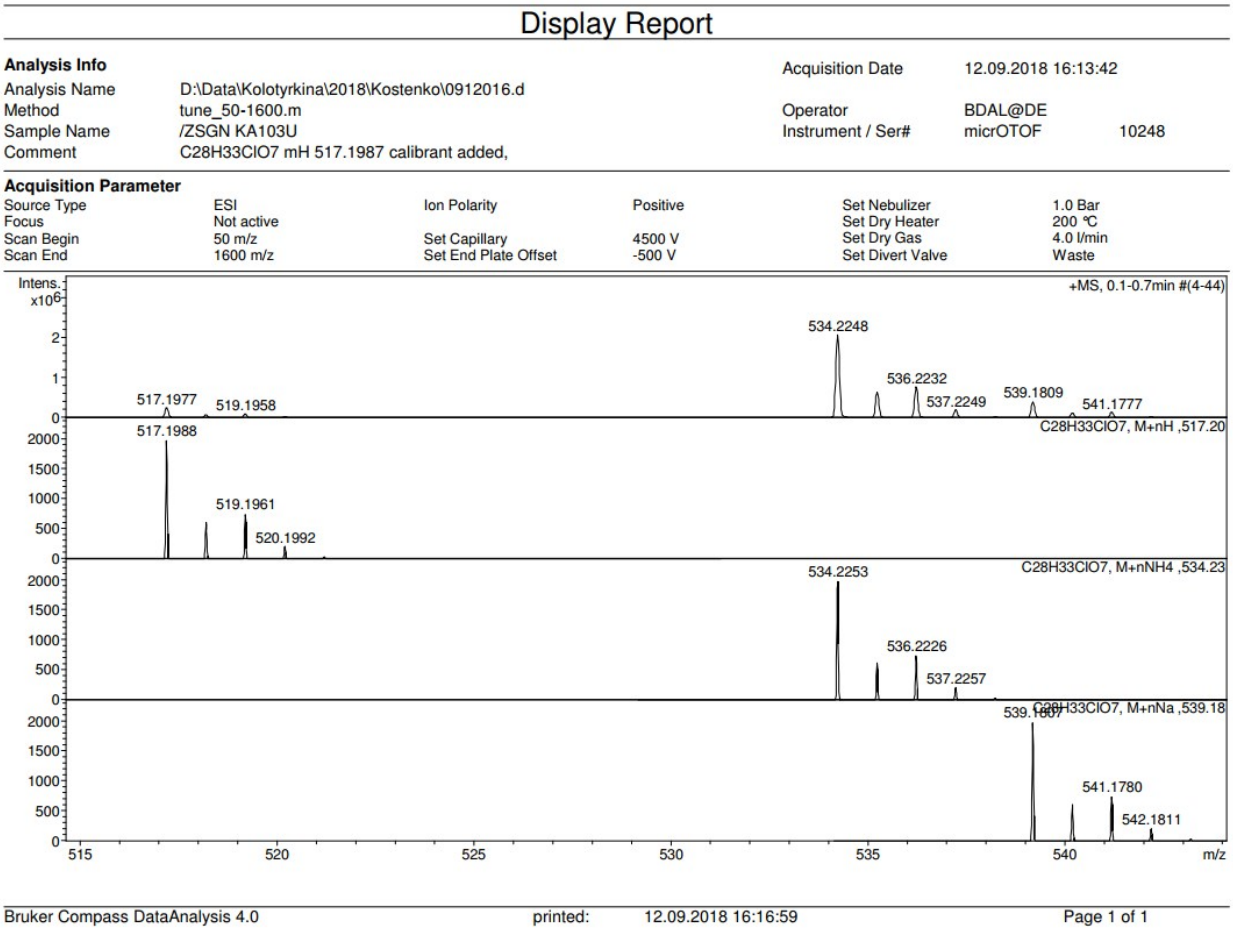
Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Not active			Set Dry Heater	200 °C
Scan Begin	50 m/z	Set Capillary	4500 V	Set Dry Gas	4.0 l/min
Scan End	1600 m/z	Set End Plate Offset	-500 V	Set Divert Valve	Waste



Bruker Compass DataAnalysis 4.0 printed: 05.09.2018 10:07:54 Page 1 of 1

HRMS data for compound **12**



6. Literature

1. A. A. Kostenko, A. S. Kucherenko, S. G. Zlotin, *Tetrahedron*, 2018, **74**, 4769.

2. Y. Liu, Q. Wang, Y. Wang, H. Song, Z. Zhou, *ChemCatChem*, 2014, **6**, 2298.

3. B. V. S. Reddy, M. Swain, S. M. Reddy, J. S. Yadav, B. Sridhar, *RSC Adv.*, 2014, **4**, 42299.