Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Electronic Supplementary Information

Straightforward Access to Densely Substituted Chiral Succinimides through Enantioselective Organocatalyzed Michael Addition of α-Alkyl-Cyclic Ketones to Maleimides

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[†] Equal contribution to this study.

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Experimental Procedures

1. General Information:

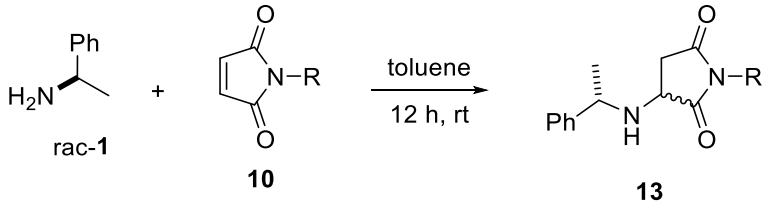
All operations involving air or moisture sensitive materials were performed under a dry argon atmosphere using syringes, oven-dried glassware, and freshly dried solvents (THF, toluene and CH_2Cl_2 were purified by passage through a solvent drying column and stored under argon over 3Å molecular sieves). Air and moisture-sensitive liquids, reagents and solvents were transferred via syringe using standard techniques. All reagents were obtained from commercial sources and used without further purification unless otherwise stated. Organic solutions were concentrated by rotary evaporation (house vacuum, *ca*. 40 Torr) at 30 °C, unless otherwise noted. Analytical thin-layer chromatography (TLC) was performed using glass plates pre-coated with silica gel 60 F254 (0.25 mm thickness) impregnated with a fluorescent indicator (254 nm). TLC plates were visualized by exposure to ultraviolet light (UV), and/or submersion in aqueous ceric ammonium molybdate solution (CAM), acidic *p*-anisaldehyde solution (PAA), followed by brief (*ca*. 30 s) heating on a stream of hot air (*ca*. 300 °C). Flash column chromatography was performed as described by Still et al.[1] employing silica gel (60 Å pore size, 40-63 mm). IR spectra were recorded as thin films for oils and for solids by the reflexion method on a FT IR spectrometer. NMR spectra were run in $CDCl_3$ at 300 or 400 MHz for ^1H and at 75 or 100 MHz for ^{13}C (JMOD experiments) in $CDCl_3$ using as internal standards the residual $CHCl_3$ signal for ^1H NMR (δ = 7.26) and the deuterated solvent signal for ^{13}C NMR (δ = 77.0). Chemical shifts are expressed in ppm downfield from TMS. Data are reported as follows: chemical shift (multiplicity [s: singlet, d: doublet, t: triplet, q: quartet, Q: quintuplet, m: multiplet, br: broad), coupling constants (*J*) in Hertz, integration]. A combination of 2D COSY, HSQC, HMBC and nOe experiments was used to aid assignment and establish the relative stereochemistry when necessary. Low resolution mass spectra were obtained with an ion trap (ESI source) by the FAB method. High resolution mass spectra were realized either by electronic impact (EI) or by electrospray impact (ESI) and atmospheric pressure chemical ionisation (APCI). Melting points were measured on a digital melting point capillary apparatus and were uncorrected. Specific optical rotations were measured in solution using sodium light (D line 589 nm). X-ray data were collected at room temperature on a Rigaku diffractometer constituted

by a MM007 HF rotating-anode generator, delivering Cu-Kα radiation (λ =1.54187 Å) through Osmic CMF confocal optics, and a Rapid II curved Image Plate for Bragg peak detection.

2. Preparation of *aza*-Michael adducts

Aza-Michael adducts detected in the organocatalyzed assisted Michael reactions studied were prepared as authentic samples on large scale using a stoichiometric approach for easier characterizations since they were not described earlier, although some of them are commercialy available.[2] These compounds present characteristic quadruplets (C*H*PhMe) between 3.5 and 4.5 and ppm.

Table S1. Stoichiometric preparation of *aza*-Michael adducts.



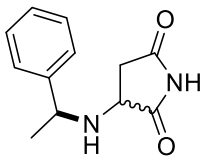
Entry	R	Yield [%]	de[b] [%]
1	H (**13a**)	75%	> 90
2	Me (**13b**)	81%	50
3	cyclohexyl (**13e**)	44%	0
4	Ph (**13f**)	80%	0
5	4-MeOPh (**13g**)	70%	40
6[c]	4-MePh (**13h**)	6%	0
7	4-FPh (**13i**)	69%	0
8	4-ClPh (**13j**)	91%	0

[a] diastereomeric ratios were determined by ^{1}H NMR analysis of the crude reaction mixture. [b] Compound **13g** was isolated from the organocatalyzed pathway.

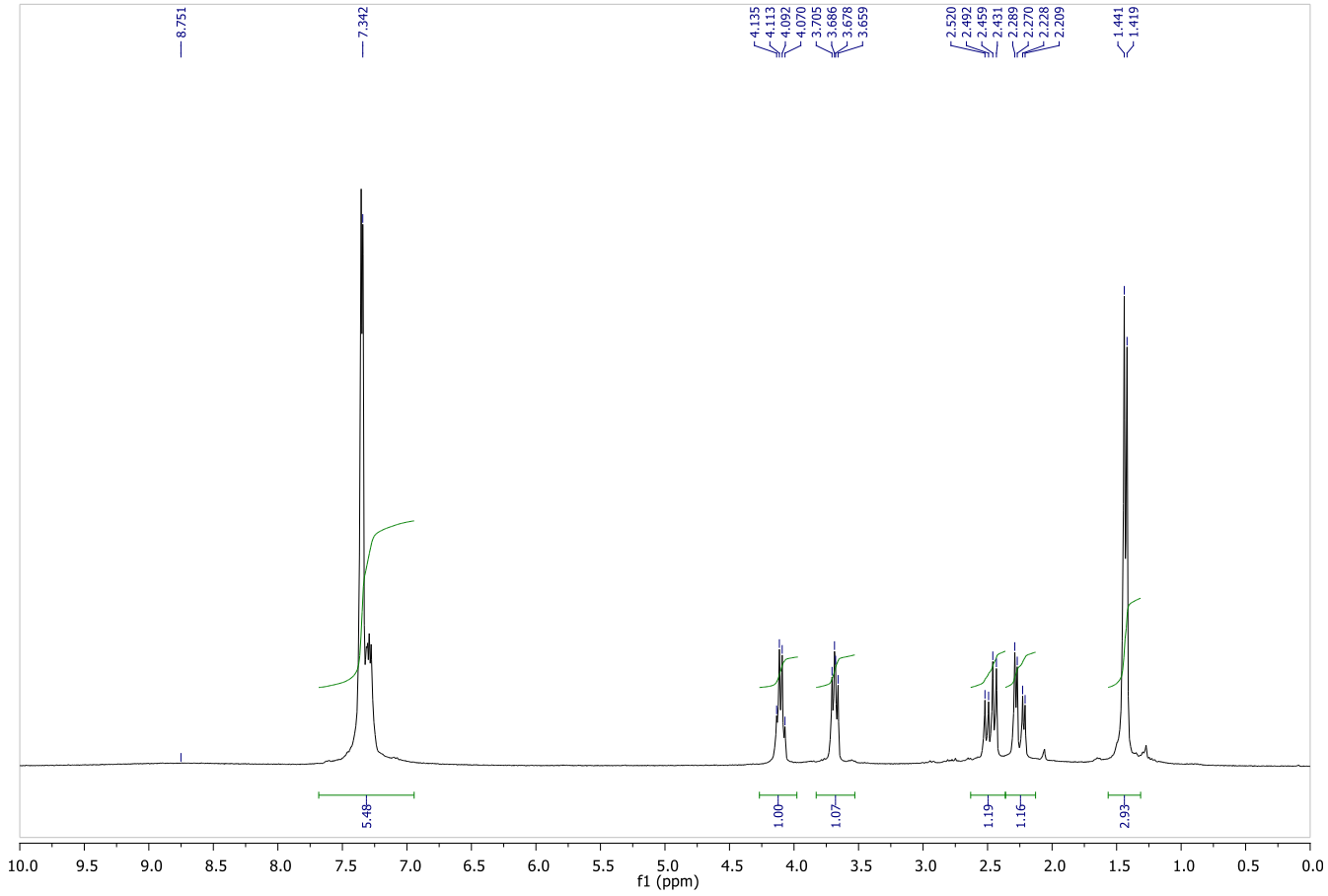
General procedure

A mixture of commercially available maleimides **10** (1 mmol, 1eq) and rac-1-phenylethylamine **1** (1 mmol, 1 eq) in toluene (1 mL) was stirred at room temperature overnight. After complete disappearance of **10** followed by TLC, the reaction mixture was concentrated and the resulting residue chromatographed over silica gel (cyclohexane/ethyl acetate = 1:1) to afford compounds **13**.

3-((1-Phenylethyl)amino) 2,5-pyrrolidinedione 13a



Compound **13a** was synthesized in 75% yield as an oil (de > 90%). **Rf** = 0.1 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.50-7.20 (m, 5 H), 4.10 (q, *J* = 6.4 Hz, 1H), 3.68 (dd, *J* = 8.3, 5.8 Hz, 1H, d), 2.48 (dd, *J* = 18.2, 8.4 Hz, 1H), 2.25 (dd, *J* = 18.2, 5.7 Hz, 1H), 1.43 (d, *J* = 6.4 Hz, 3H);**^{13}C NMR** (75 MHz, $CDCl_3$) δ 179.3, 175.9, 144.3, 128.8, 127.8, 127.2, 58.5, 56.8, 38.8, 24.2. **HRMS (ESI)** m/z calcd for $[C_{12}H_{15}N_2O_2]^+$, 219.1128, found 219.1135; **IR** (neat) 3029, 2955, 2853, 1777, 1709, 1689, 1369, 1242, 1180 cm^{-1}.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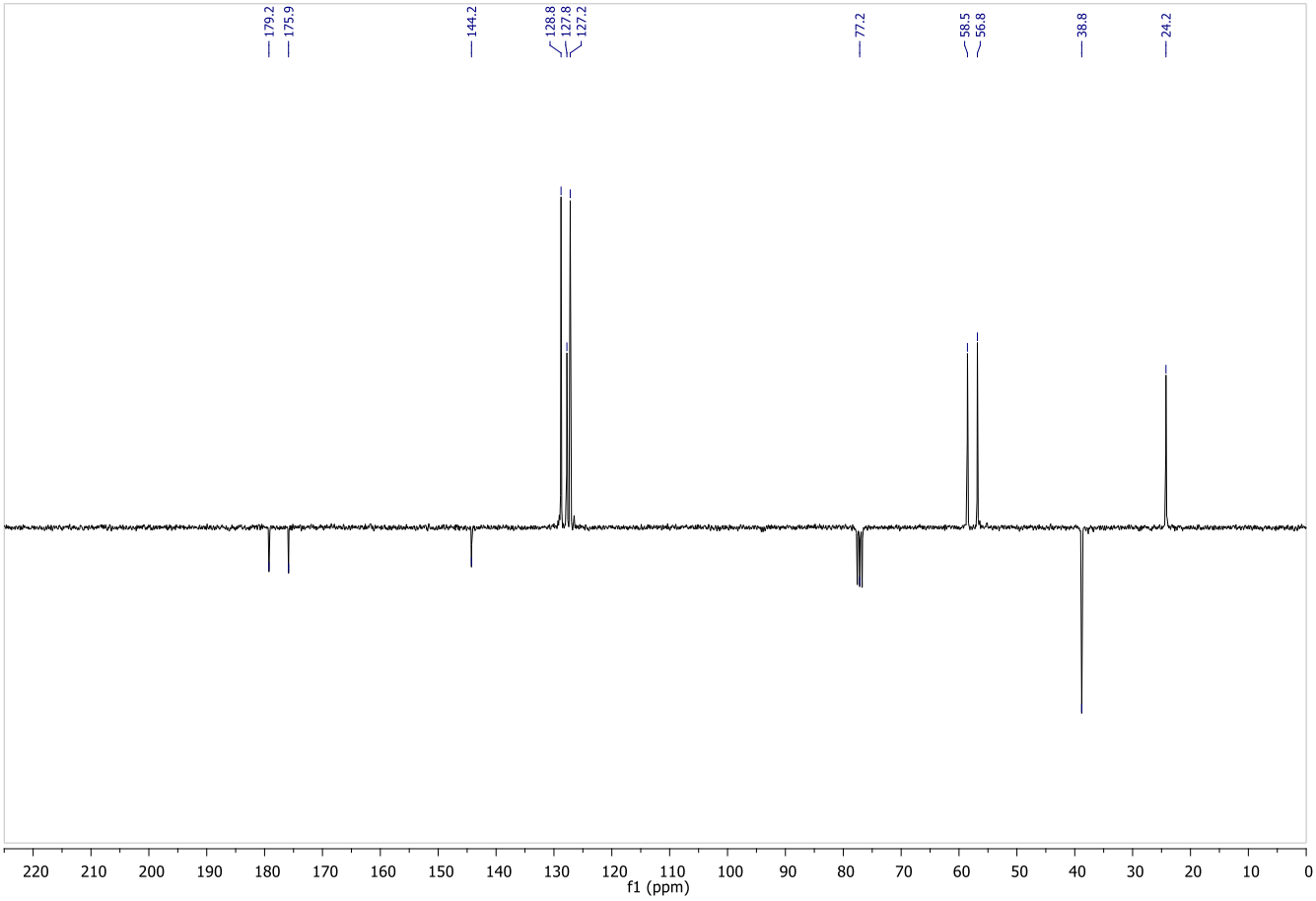
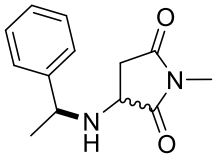
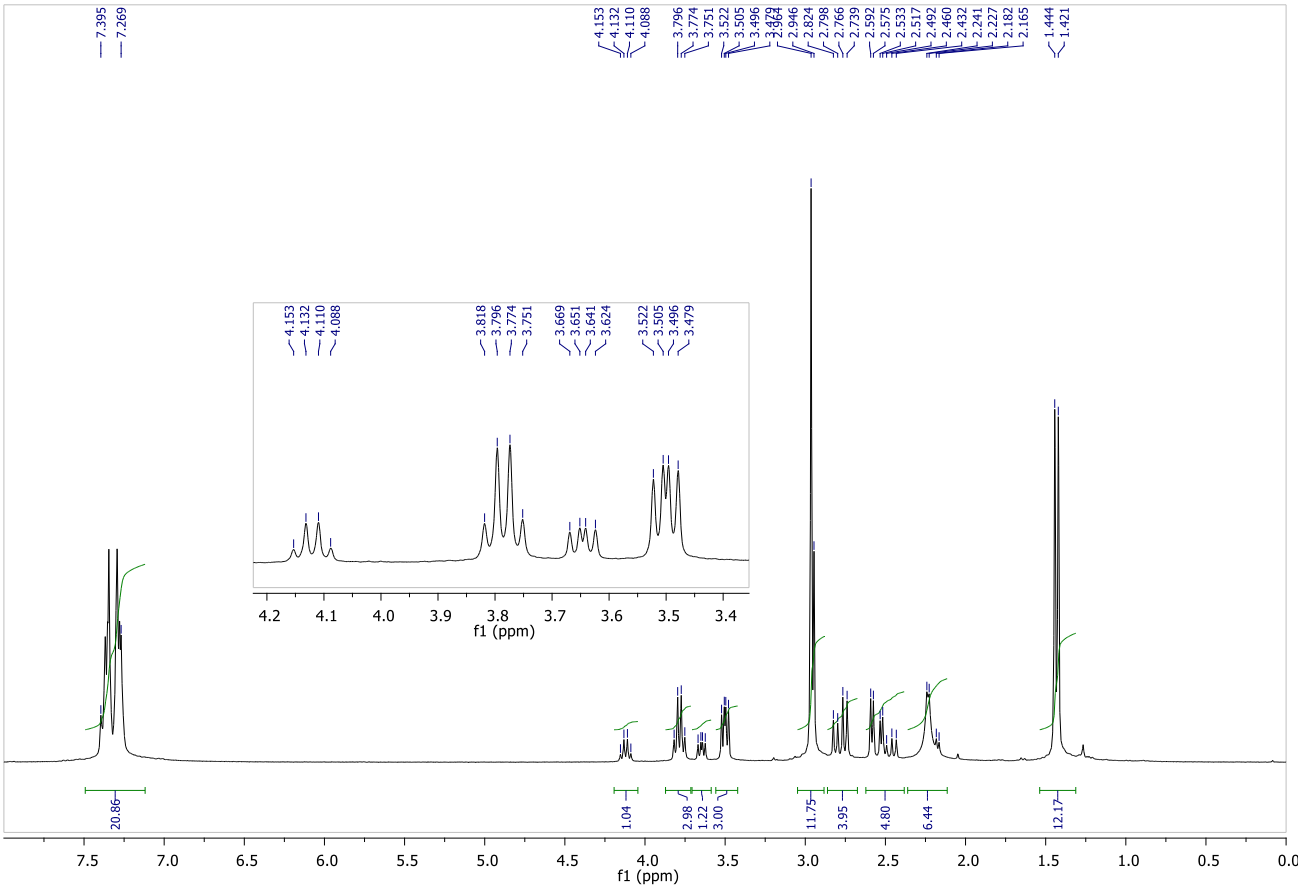
7.342
4.135
4.113
4.092
4.070
3.705
3.686
3.678
3.659
2.520
2.492
2.459
2.431
2.289
2.270
2.228
2.209
1.441
1.419
5.48
1.00
1.07
1.19
1.16
2.93
f1 (ppm)

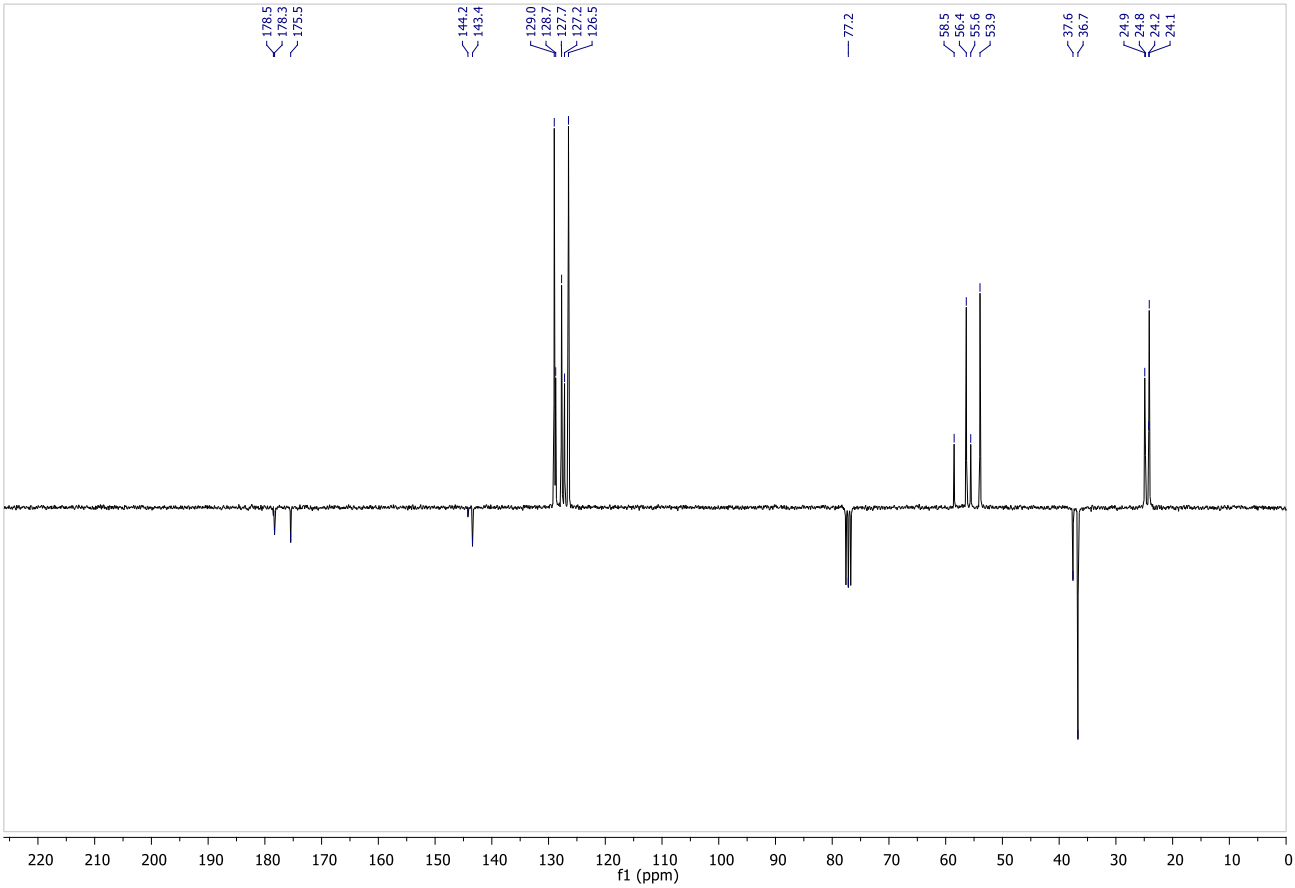

179.2
175.9
144.2
128.8
127.8
127.2
77.2
58.5
56.8
38.8
24.2
f1 (ppm)

1-Methyl-3-((-1-phenylethyl)amino)-2,5-pyrrolidinedione 13b

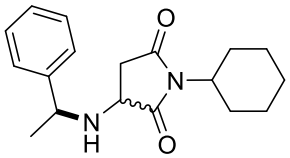


Compound **13b** was synthesized in 81% yield as an oil (inseparable mixture of diastereomers, de = 50%). **Rf** = 0.2 (cyclohexane/EtOAc=1/1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.40–7.12 (m, 5H), 4.11 (q, *J* = 6.4 Hz, 1H, minor), 3.78 (q, *J* = 6.7 Hz, 1H, major), 3.64 (dd, *J* = 8.3, 5.2 Hz, 1H, minor), 3.50 (dd, *J* = 7.9, 5.1 Hz, 1H, major), 2.96 (s, 3H, major), 2.95 (s, 3H, minor), 2.78 (dd, *J* = 17.4, 8.1 Hz, 1H, major + minor), 2.55 (dd, *J* = 17.4, 5.1 Hz, 1H, major), 2.55 (dd, *J* = 18.0, 8.4 Hz, 1H, minor), 2.24-2.16 (m, 1H, minor + major), 1.43 (d, *J* = 6.9 Hz, 3H, minor + major); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 178.5 (minor), 178.3 (major), 175.5 (Cminor + major), 144.2 (minor), 143.4 (major), 129.0 (major), 128.7 (minor), 127.7 (major), 127.2 (minor), 126.5 (minor + major), 58.5 (minor), 56.4 (major), 55.6 (minor), 54.0 (major), 37.6 (minor), 36.7 (major), 24.9 (minor), 24.1 (major). **HRMS (ESI)** m/z calcd for $[C_{13}H_{17}N_2O_2]^+$, 233.1285, found 233.1292; **IR** (neat) 2960, 2932, 2873, 1690, 1401, 1194, 1127, 702 cm^{-1}.

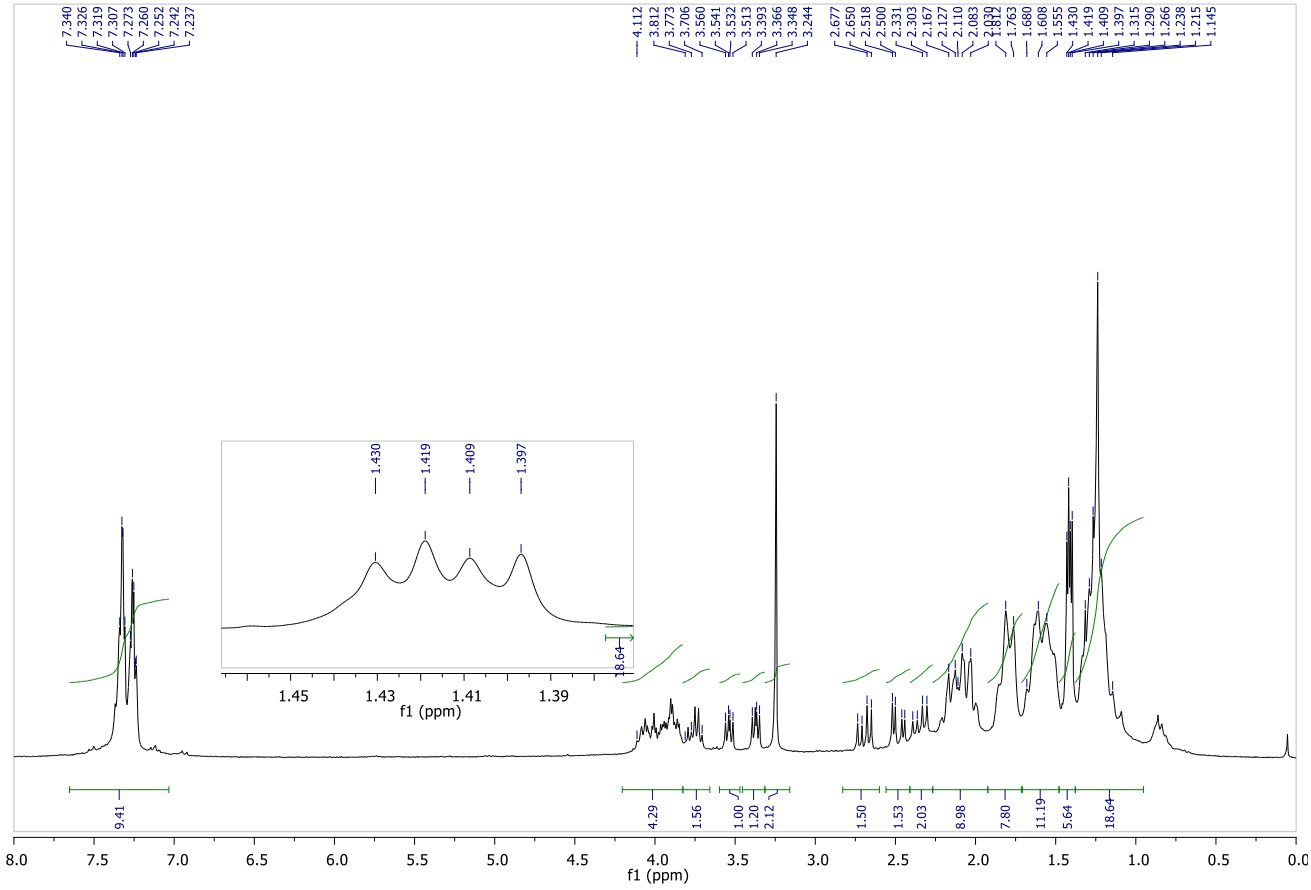




1-Cyclohexyl-3-((1-phenylethyl)amino) -2,5-pyrrolidinedione 13e



Compound **13e** was synthesized in 44% yield as an oil (inseparable mixture of diastereoimers, de = 0%). **Rf** = 0.2 (cyclohexane/EtOAc = 4:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.53-6.97 (m, 10H, major + minor), 4.10-3.60 (m, 2H, major + minor), 3.54 (dd, *J* = 8.3, 5.7 Hz, 1H, minor), 3.37 (dd, *J* = 8.1, 5.5 Hz, 1H, major), 3.24 (s, 2H, major + minor), 2.55 (dd, *J* = 17.5, 8.1 Hz, 1H, c, major), 2.48 (dd, *J* = 17.8, 6.9 Hz, 1H, major), 2.34 (dd, *J* = 17.8, 8.7 Hz, 1H, minor), 2.25-1.80 (m, 9H, major + minor), 1.80-1.45 (m, 19H, major + minor), 1.42 (bd, *J* = 6.3 Hz, 3H, minor), 1.40 (bd, *J* = 6.3 Hz, 3H, major), 1.30-1.00 (m, major + minor); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 178.4 (minor), 178.3 (major), 175.4 (minor), 175.1 (major), 144.1 (minor), 143.5 (major), 129.0 (major), 128.8 (minor or major), 127.7 (minor or major), 127.2 (minor or major), 126.5 (major), 58.8 (minor), 56.4 (major), 55.4 (minor), 53.6 (major), 52.6 (major), 51.8 (minor), 41.3 (major), 37.7 (minor), 36.7 (major), 29.8 (minor), 29.0 (major), 28.7 (minor), 25.9 (minor), 25.1 (CH_2, major), 25.0 (minor), 24.1 (minor); **HRMS (ESI)** m/z calcd for $[C_{18}H_{25}N_2O_2]^+$, 301.1911, found 301.1918; **IR** (neat) 2935, 2920, 2853, 1772, 1702, 1687, 1376, 1201, 1182 cm^{-1}.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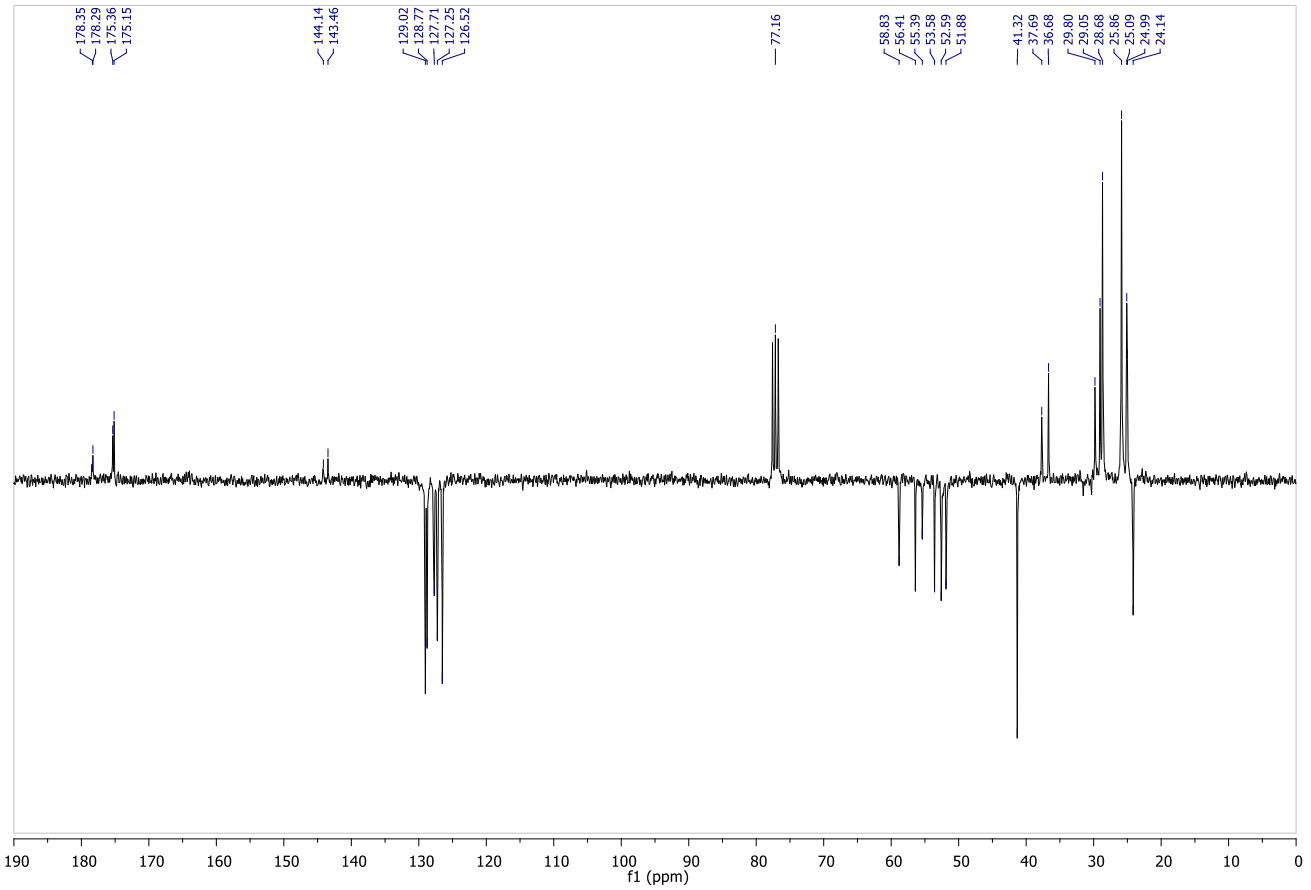
3.706
3.560
3.541
3.532
3.513
3.393
3.366
3.348
3.244
2.677
2.650
2.518
2.500
2.331
2.303
2.167
2.127
2.110
2.083
1.763
1.680
1.608
1.555
1.430
1.419
1.409
1.397
1.315
1.290
1.266
1.238
1.215
1.145
1.430
1.419
1.409
1.397
18.64
1.45
1.43
1.41
1.39
f1 (ppm)
9.41
4.29
1.56
1.00
1.20
2.12
1.50
1.53
2.03
8.98
7.80
11.19
5.64
18.64
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)


178.35
178.29
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175.15
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143.46
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127.25
126.52
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56.41
55.39
53.58
52.59
51.88
41.32
37.69
36.68
29.80
29.05
28.68
25.86
25.09
24.99
24.14
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
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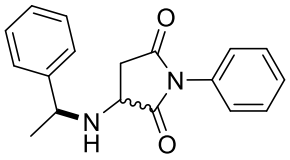
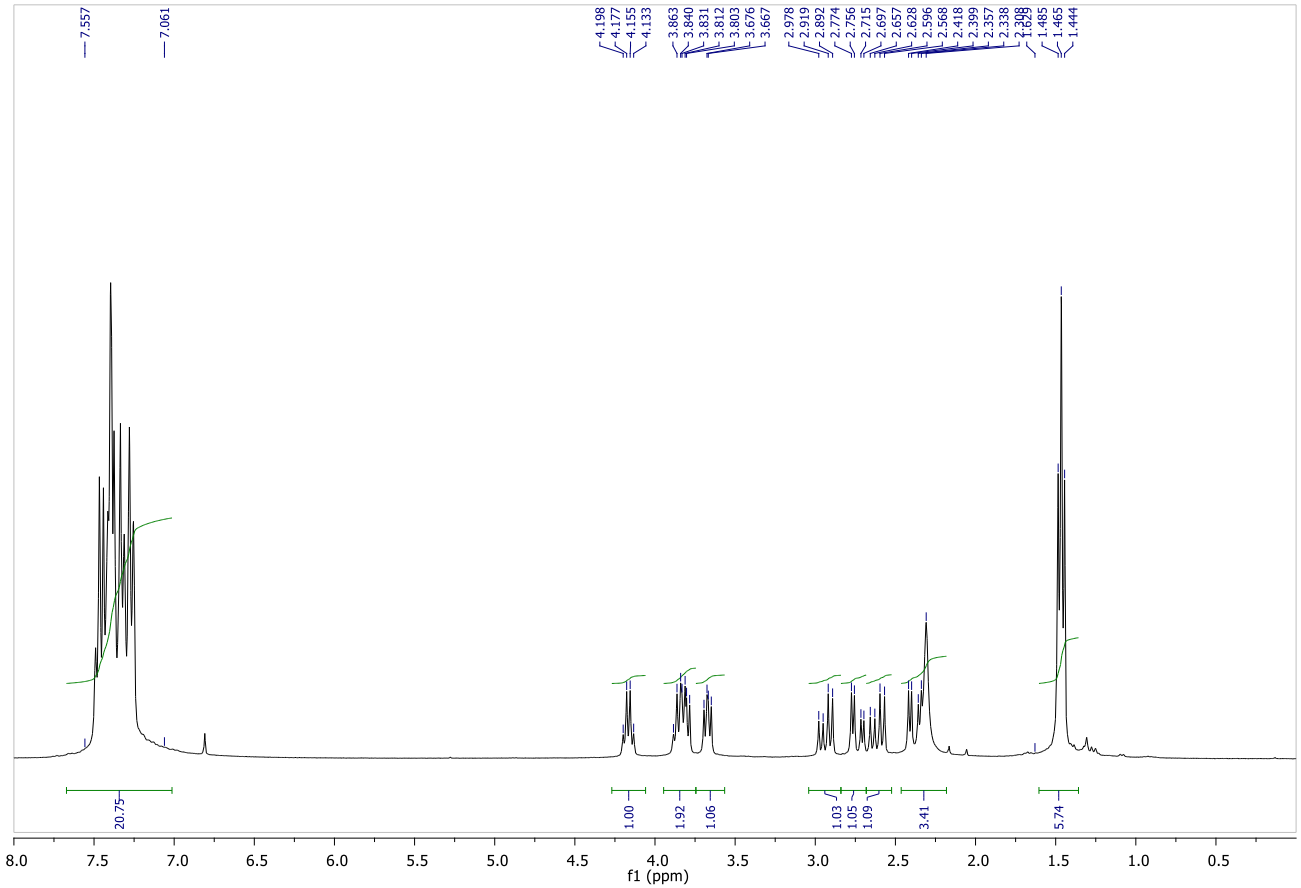
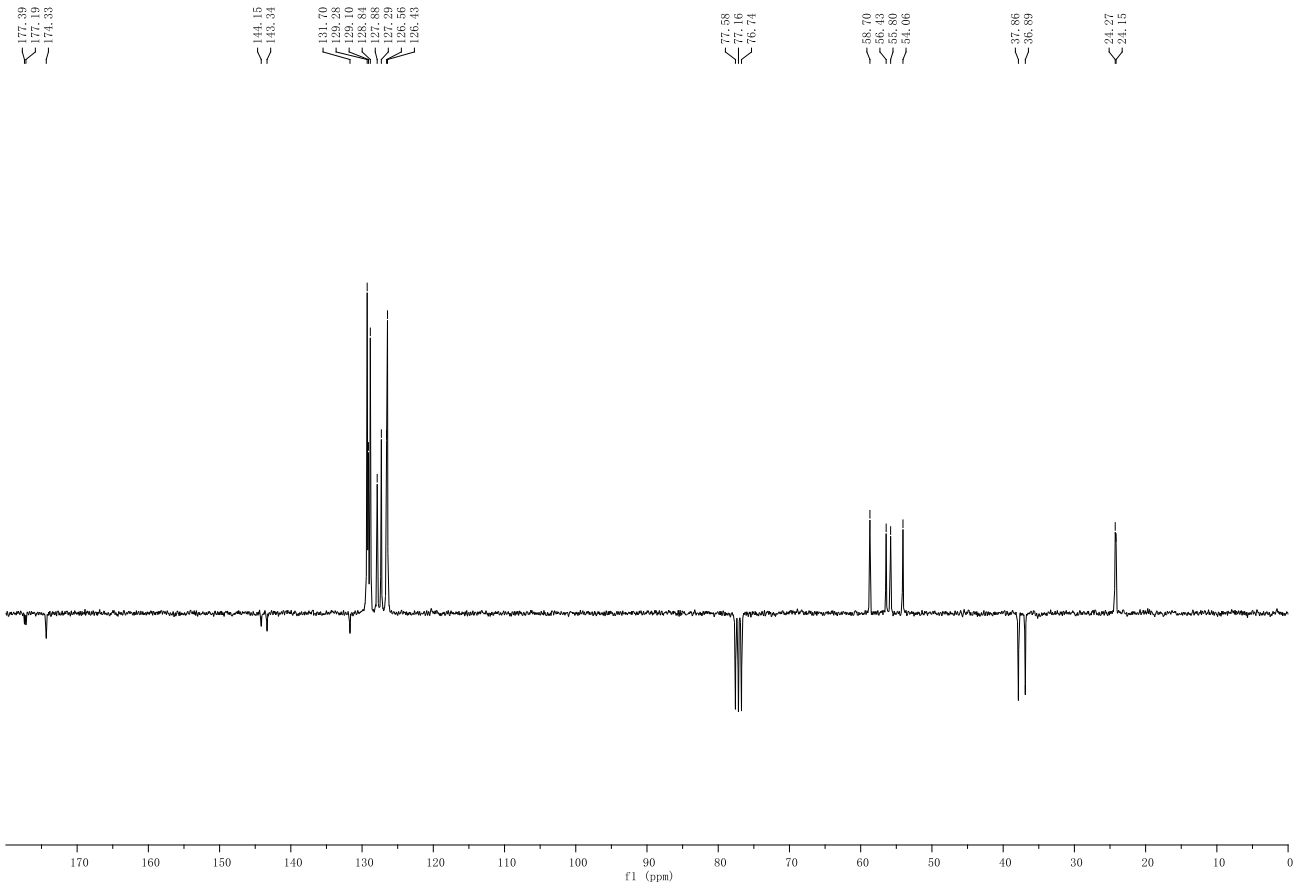
f1 (ppm)

1-Phenyl-3-((1-phenylethyl)amino) -2,5-pyrrolidinedione 13f

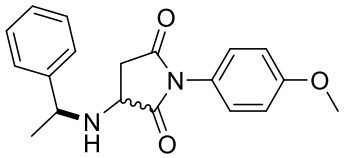


Compound **13f** was synthesized in 80% yield as an oil (inseparable mixture of diastereomers, de = 0%). **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.52-7.20 (m, 20 H), 4.16 (q, *J* = 6.5 Hz, 1H), 3.88-3.78 (m, 2H), 3.66 (dd, *J* = 8.1, 5.4 Hz, 1H), 2.94 (dd, *J* = 17.7, 8.1 Hz, 1H), 2.73 (dd, *J* = 17.7, 5.7 Hz, 1H), 2.61 (dd, *J* = 18.3, 8.7 Hz, 1H), 2.38 (dd, *J* = 18.3, 5.7 Hz, 1H), 2.31 (bs, 2H), 1.47 (d, *J* = 6.0 Hz, 3H), 1.45 (d, *J* = 6.0 Hz, 3H); **^{13}C NMR** (75 MHz, CDCl3) δ 177.4, 177.2, 174.3, 144.2, 143.3, 131.7, 129.3, 129.1, 128.8, 127.9, 127.8, 127.3, 126.6, 126.4, 58.7, 56.4, 55.8, 54.1, 37.9, 36.9, 24.3, 24.2; **HRMS (ESI)** m/z calcd for $[C_{18}H_{19}N_2O_2]^+$ 295.1441, found 295.1443. **IR** (neat) 3030, 2967, 2927, 1781, 1710, 1706, 1598, 1501, 1385, 1183, 908, 760, 729, 699 cm^{-1}.

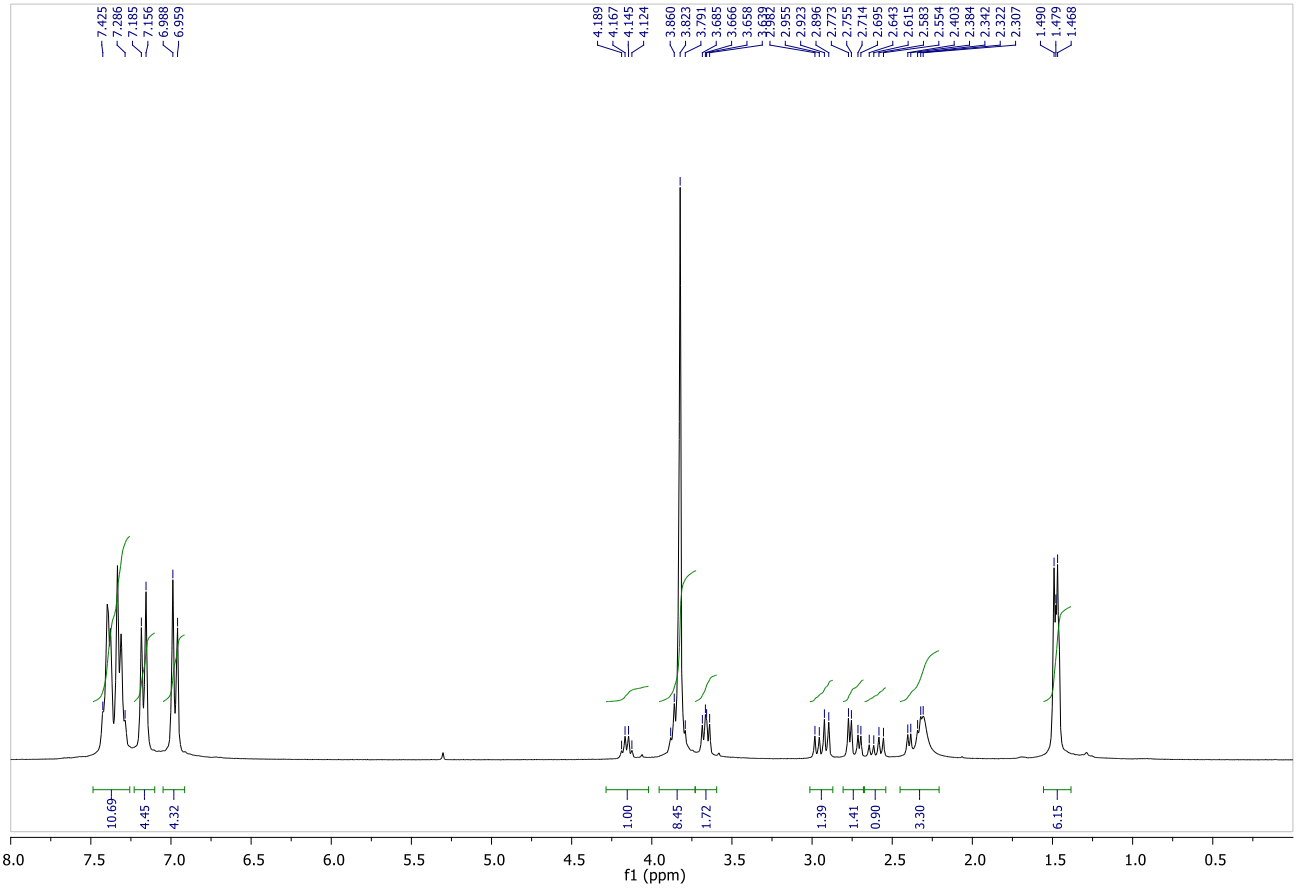




1-(4-Methoxyphenyl)-3-((1-phenylethyl)amino) -2,5-pyrrolidinedione 13g



Compound **13g** was synthesized in 70% yield as an oil (inseparable mixture of diastereomers, de = 40%). **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.50-7.25 (m, 10H, major + minor), 7.17 (d, *J* = 8.7 Hz, 4H, major + minor), 6.97 (d, *J* = 8.8 Hz, 4H, major + minor), 4.15 (q, *J* = 6.4 Hz, 1H, minor), 3.90-3.75 (m, 2H, major + minor), 3.82 (bs, 3H, major + minor), 3.67 (dd, *J* = 8.1, 5.7 Hz, 1H, major), 2.94 (dd, *J* = 17.7, 8.2 Hz, 1H, major), 2.73 (dd, *J* = 17.7, 5.5 Hz, 1Hmajor), 2.60 (dd, *J* = 18.2, 8.5 Hz, 1H, minor), 2.36 (dd, *J* = 18.2, 5.7 Hz, 1H, minor), 2.30 (bs, 2H, major + minor), 1.48 (d, *J* = 6.6 Hz, 3H, major), 1.46 (d, *J* = 6.6 Hz, 3H, minor); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 177.7 (minor), 177.4 (major), 174.6 (major + minor), 159.6 (major + minor), 144.3 (minor), 143.4 (major), 129.0 (major), 128.8 (minor), 127.7 (minor), 127.6 (major), 127.2 (minor), 126.5 (major)), 124.3 (major + minor), 114.6 (major + minor), 58.6 (major + minor), 56.3 (major), 55.8 (minor), 55.5 (major), 54.0 (minor), 37.8 (minor), 36.8 (major), 24.3 (minor), 24.1 (major); **HRMS (ESI)** m/z calcd for $[C_{19}H_{21}N_2O_3]^+$ 325.1547, found 325.1558; **IR** (neat) 2963, 2932, 2838, 1712, 1702, 1512, 1248, 1166, 763, 702 cm^{-1}.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6.959
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4.124
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3.791
3.685
3.666
3.658
2.955
2.923
2.896
2.773
2.755
2.714
2.695
2.643
2.615
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2.307
1.490
1.479
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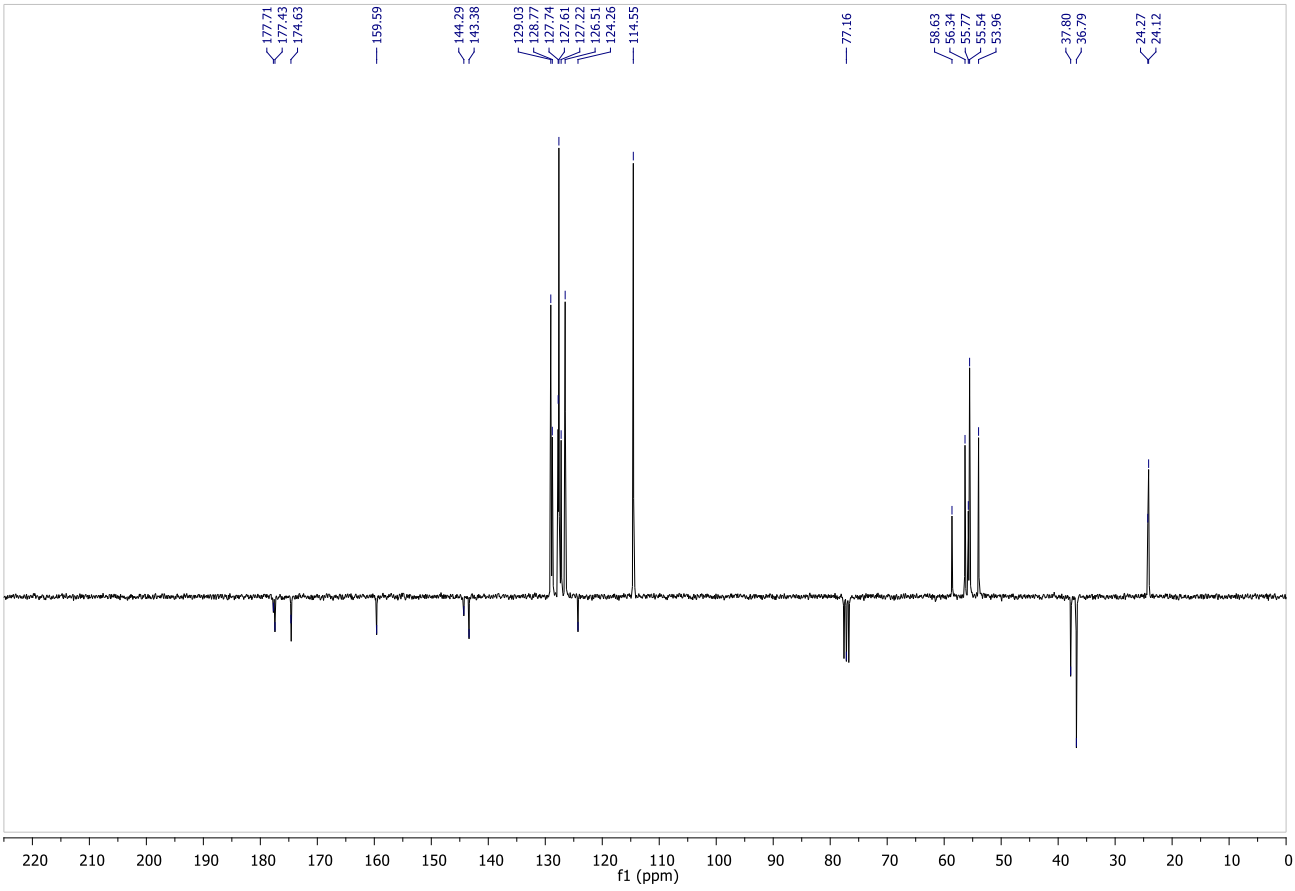
f1 (ppm)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127.22
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124.26
114.55
77.16
58.63
56.34
55.77
55.54
53.96
37.80
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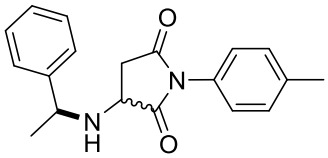
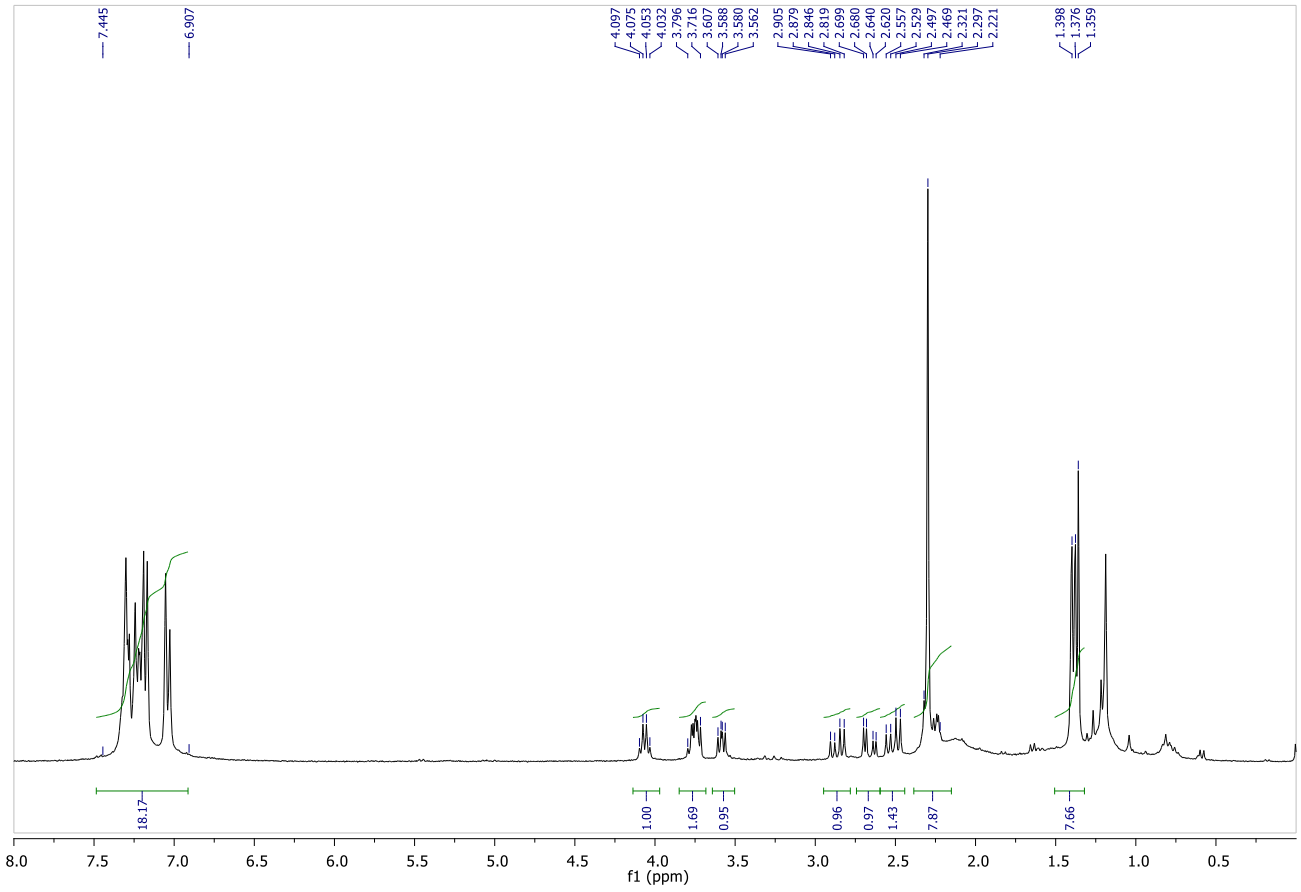
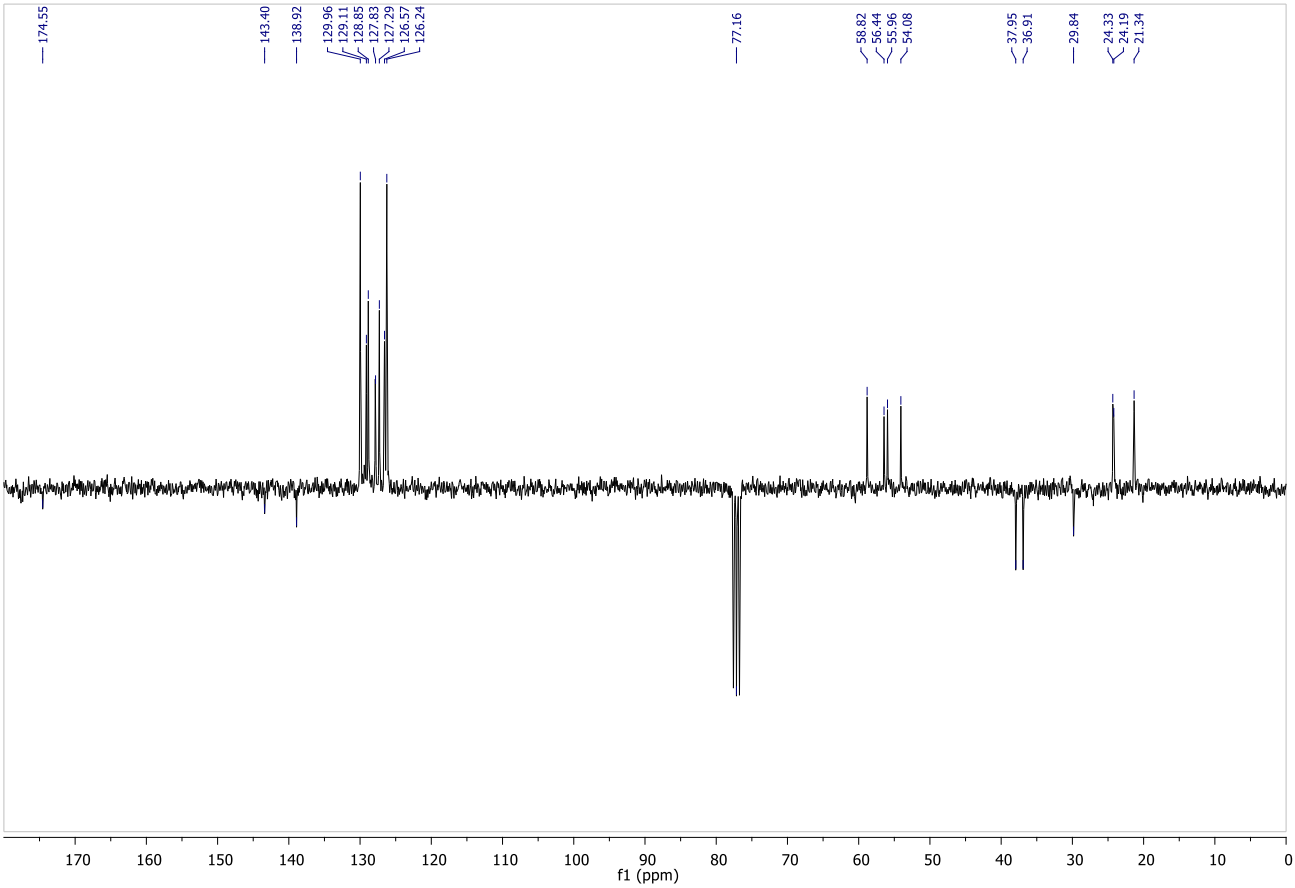
24.12
f1 (ppm)

3-((1-Phenylethyl)amino)-1-(p-tolyl)-2,5-pyrrolidinedione 13h

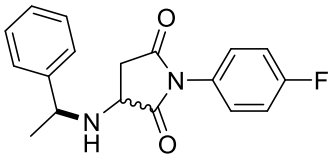


Compound **13h** was isolated from the organocatalyzed reaction in 6% yield as an oil (inseparable mixture of diastereomers, de = 0%). **Rf** = 0.2 (cyclohexane/EtOAc = 4:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.45-6.90 (m, 18 H), 4.06 (q, *J* = 6.6 Hz, 1H), 3.80-3.70 (m, 2H), 3.58 (dd, *J* = 8.1, 5.7 Hz, 1H), 2.86 (dd, *J* = 17.7, 7.8 Hz, 1H), 2.66 (dd, *J* = 17.7, 5.7 Hz, 1H), 2.52 (dd, *J* = 18.0, 8.4 Hz, 1H), 2.30 (bs, 7H), 1.38 (d, *J* = 6.6 Hz, 3H), 1.36 (d, *J* = 5.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 186.3, 174.6, 143.4, 138.9, 130.0, 129.1, 128.9, 127.8, 127.3, 126.6, 126.8, 126.2, 58.8, 56.4, 56.0, 54.1, 38.0, 36.9, 24.3, 24.2, 21.3. **HRMS (ESI)** m/z calcd for $[C_{19}H_{21}N_2O_2]^+$, 309.1598, found 309.1605; **IR** (neat) 2965, 2920, 2850, 1697, 1398, 1344, 1203, 1153, 698 cm^{-1}.



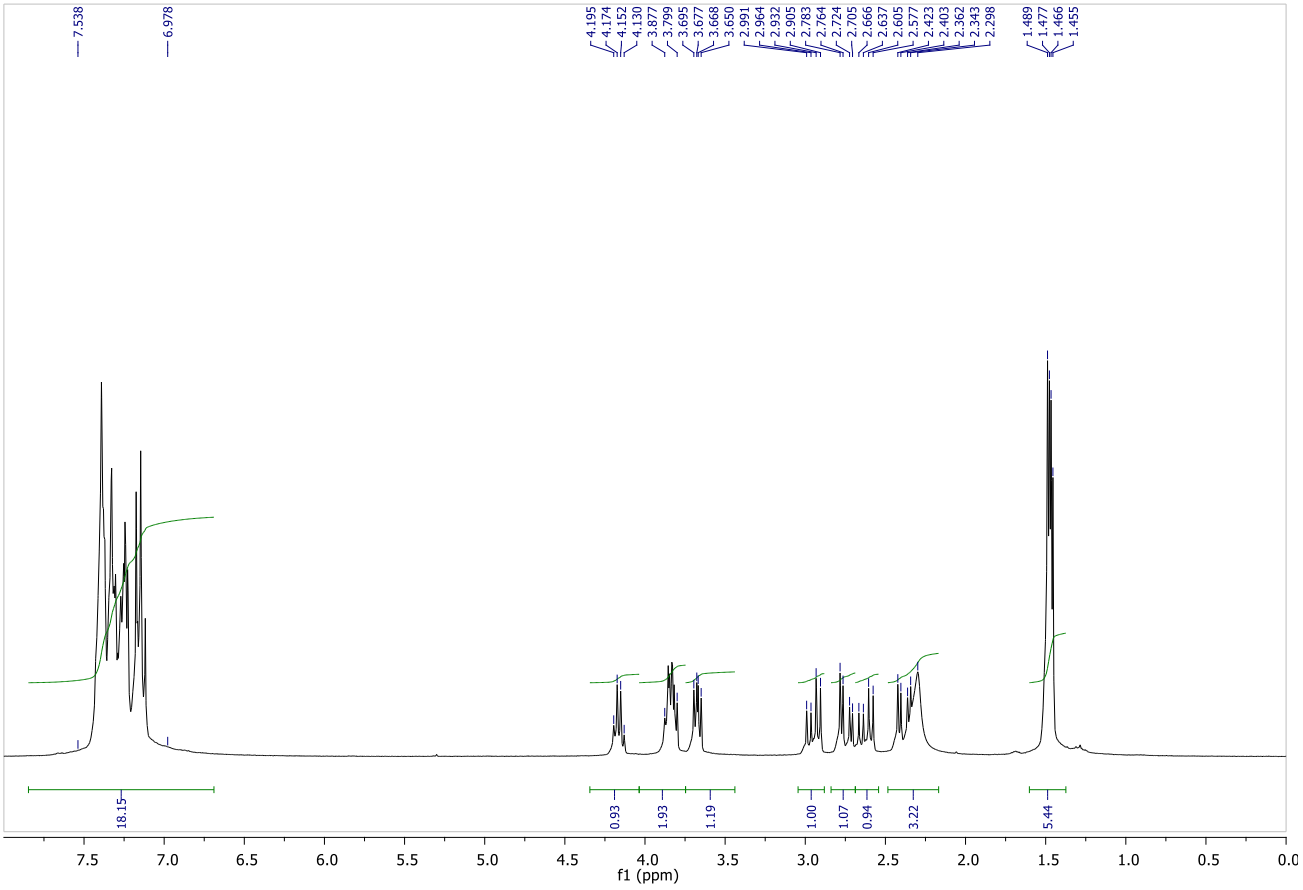


1-(4-Fluorophenyl)-3-((1-phenylethyl)amino) -2,5-pyrrolidinedione 13i



Compound **13i** was synthesized in 69% yield as an oil (inseparable mixture of diastereomers, de = 0%). **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.53-6.98 (m, 18H, major + minor), 4.16 (q, *J* = 6.5 Hz, 1H, minor), 4.00-3.77 (m, 2H, major + major), 3.67 (dd, *J* = 8.1, 5.6 Hz, 1H, major), 2.95 (dd, *J* = 17.8, 8.1 Hz, 1H, major), 2.74 (dd, *J* = 17.8, 5.6 Hz, 1H, minor), 2.61 (dd, *J* = 18.3, 8.7 Hz, 1H, minor), 2.38 (dd, *J* = 17.8, 6.0 Hz, 1H, major), 2.30 (bs, 2H, major + minor), 1.48 (d, *J* = 6.9 Hz, 3H, major), 1.46 (d, *J* = 6.6 Hz, 3H, minor); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 177.4 (minor), 177.1 (major), 174.2 (major + minor), 162.2 (d, *J* = 247.2, major + minor), 144.2 (minor), 143.3 (major), 128.9 (d, *J* = 19.8 Hz, major or minor), 128.2 (d, *J* = 8.5 Hz, major or minor), 127.8 (major + minor), 127.2 (major + minor), 126.5 (major + minor), 116.3 (d, *J* = 22.9 Hz, major + minor), 58.6 (d, minor), 56.4 (major), 55.7 (minor), 54.0 (major), 37.7 (minor), 36.8 (major), 24.3 (minor), 24.1 (major). **HRMS (ESI)** m/z calcd for $[C_{18}H_{18}FN_2O_2]^+$ 313.1347, found 313.1357; **IR** (neat) 3311, 3032, 2961, 1700, 1452, 1356, 1182, 762, 699 cm^{-1}.

.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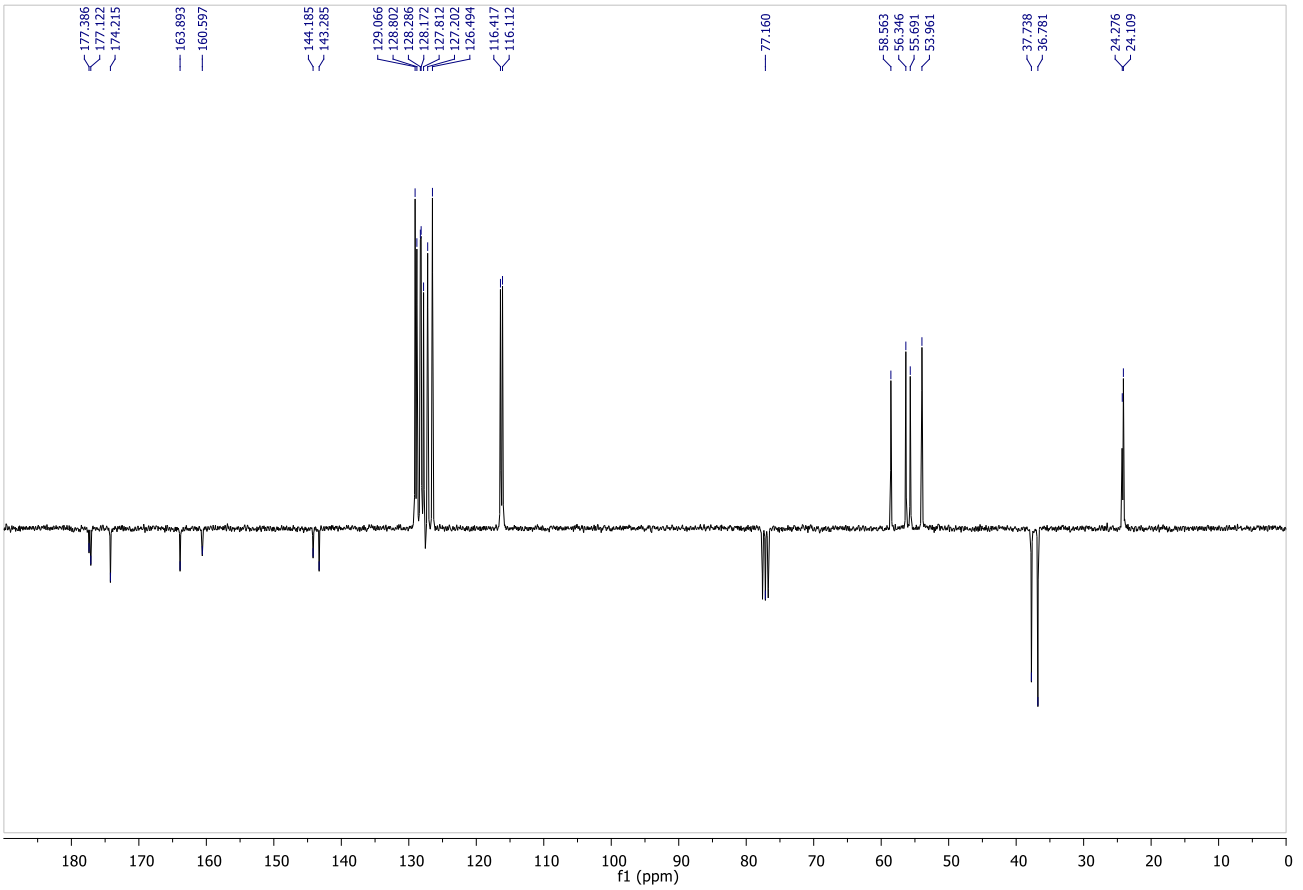
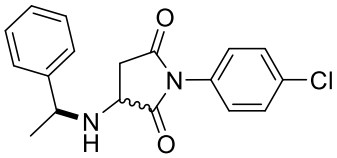
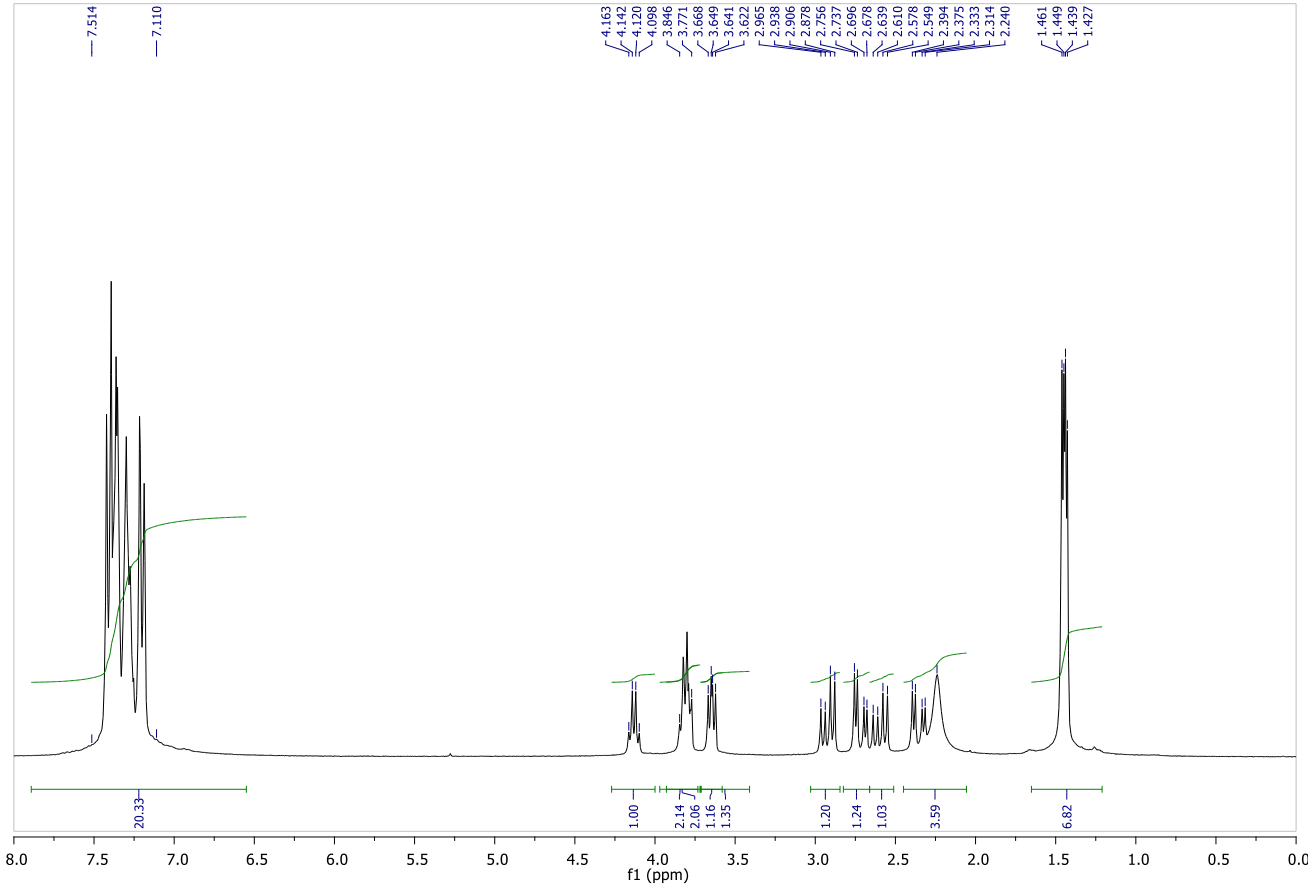
6.978
4.195
4.174
4.152
4.130
3.877
3.799
3.695
3.677
3.668
3.650
2.991
2.964
2.932
2.905
2.783
2.764
2.724
2.705
2.666
2.637
2.605
2.577
2.423
2.403
2.362
2.343
2.298
1.489
1.477
1.466
1.455
18.15
0.93
1.93
1.19
1.00
1.07
0.94
3.22
5.44
f1 (ppm)

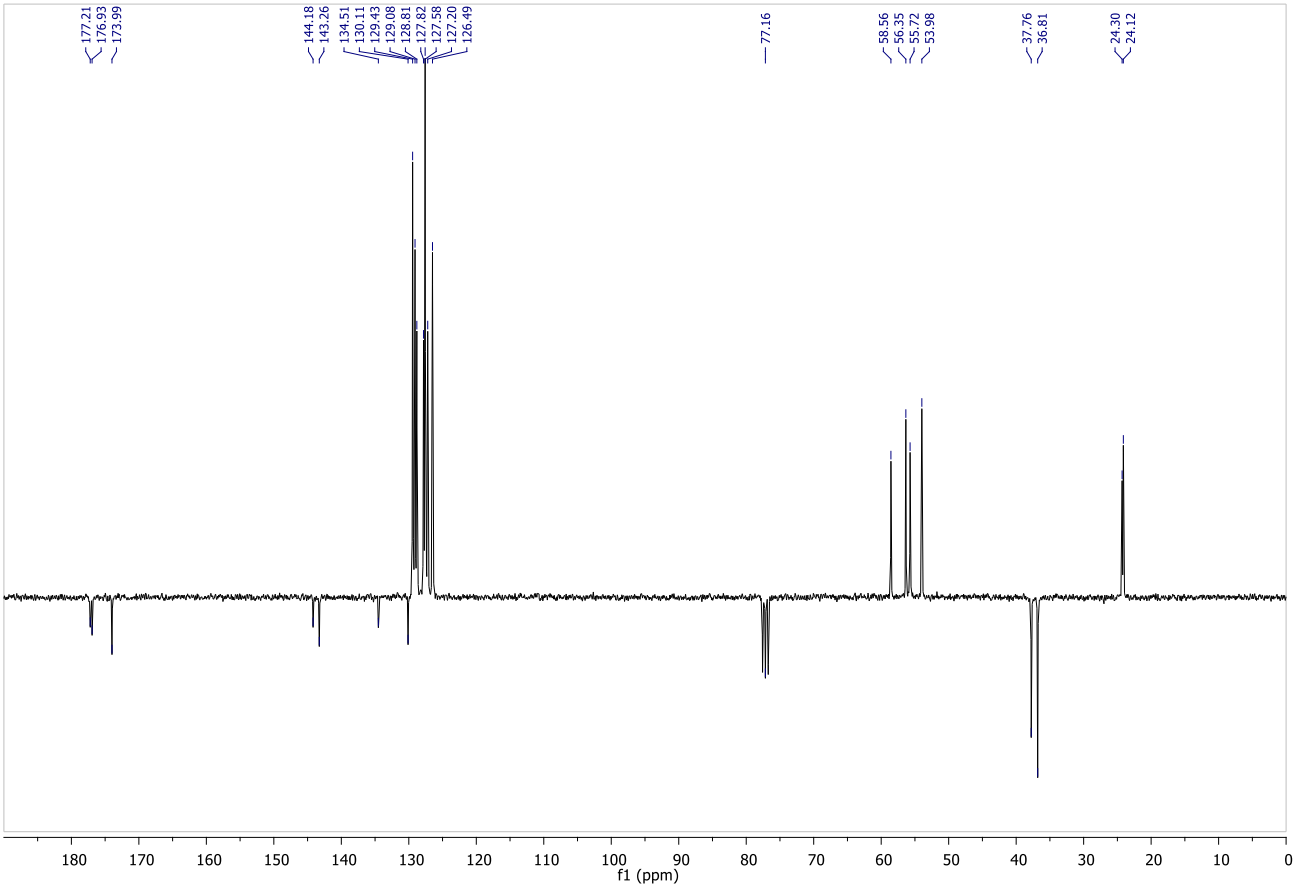

177.386
177.122
174.215
163.893
160.597
144.185
143.285
129.066
128.802
128.286
128.172
127.812
127.202
126.494
116.417
116.112
77.160
58.563
56.346
55.691
53.961
37.738
36.781
24.276
24.109
f1 (ppm)

1-(4-Chlorophenyl)-3-((1-phenylethyl)amino) -2,5-pyrrolidinedione 13j



Compound **13j** was synthesized in 91% yield as an oil (inseparable mixture of diastereomers, de = 0%). **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.51-7.11 (m, 18H, major + minor), 4.14 (q, *J* = 6.5 Hz, 1H, minor), 3.84-3.77 (m, 2H, major + d major), 3.64 (dd, *J* = 8.1, 5.7 Hz, 1H, major), 2.92 (dd, *J* = 17.7, 8.1 Hz, 1H, major), 2.71 (dd, *J* = 17.7, 5.7 Hz, 1H, minor), 2.59 (dd, *J* = 18.3, 8.7 Hz, 1H, minor), 2.35 (dd, *J* = 17.8, 6.0 Hz, 1H, major), 2.40 (bs, 2H, major + minor), 1.45 (d, *J* = 6.6 Hz, 3H, major), 1.43 (d, *J* = 6.6 Hz, 3H, minor); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 177.2 (minor), 176.9 (major), 174.0 (minor + major), 144.2 (minor), 143.3 (major), 134.5 (minor + major), 130.1 (major + minor), 129.4, 129.1, 128.8, 127.8, 127.6, 127.2, 126.5 (major + minor), 58.6 (minor), 56.4 (major), 55.7 (minor), 54.0 (major), 37.8 (minor), 36.8 (major), 24.3 (minor), 24.1 (major); **HRMS (ESI)** m/z calcd for $[C_{18}H_{18}ClN_2O_2]^+$, 329.1051, found 329.1056; **IR** (neat) 3310, 3064, 2955, 2932, 1776, 1717, 1700, 1452, 1159, 791, 699 cm^{-1}.

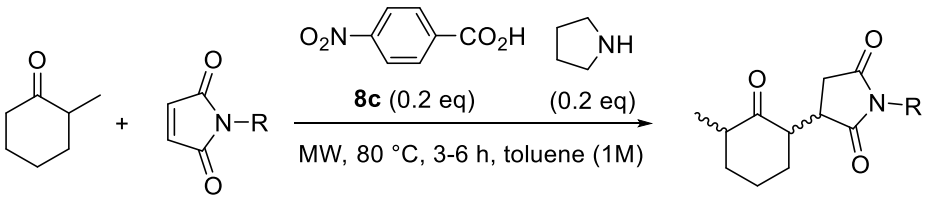




3. Preparation of regioisomers

The organocatalyzed Michael's reaction of α-methylcyclohexanone to maleimides led to the formation of 5-10% of regioisomers **22**. The latter were prepared, when possible, on a larger scale using an organocatalyzed approach, inspired by Stork's work,[2] for easier characterizations. They present characteristic doublets (COCHC*H*$_3$) between 0.9 and 1.2 ppm.

Table S2. Organocatalyzed access to regioisomers **22**.



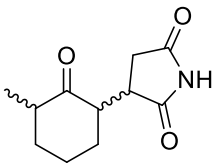
Entry	R	Yield	d.r.[a]
1	H (**22a**)	49%	50/50
2	Me (**22b**)	51%	87/13
3	Ph (**22f**)	65%	nd
4	4-FPh (**22i**)	64%	nd

[a] determined by ^{1}H NMR of the mixture obtained by flash chromatography.

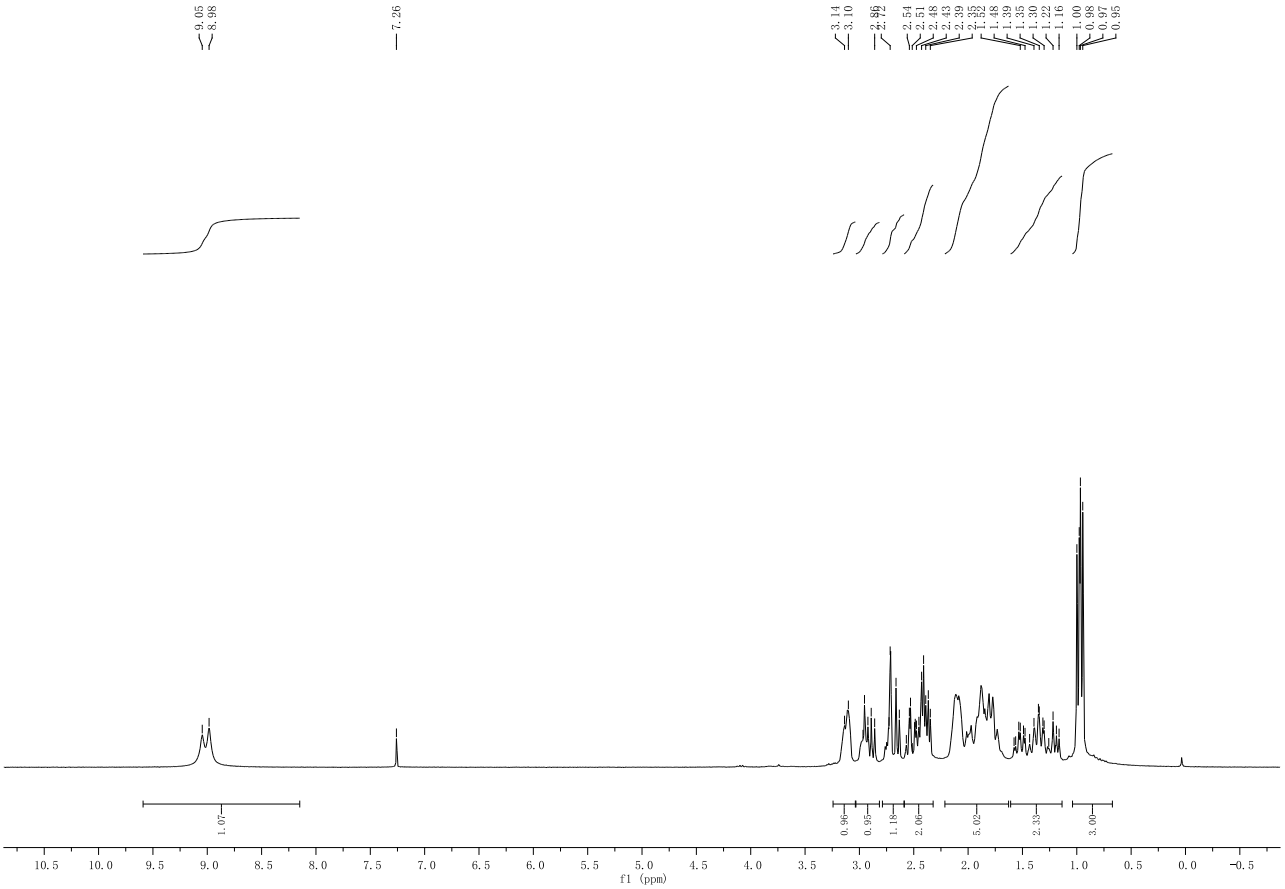
General procedure

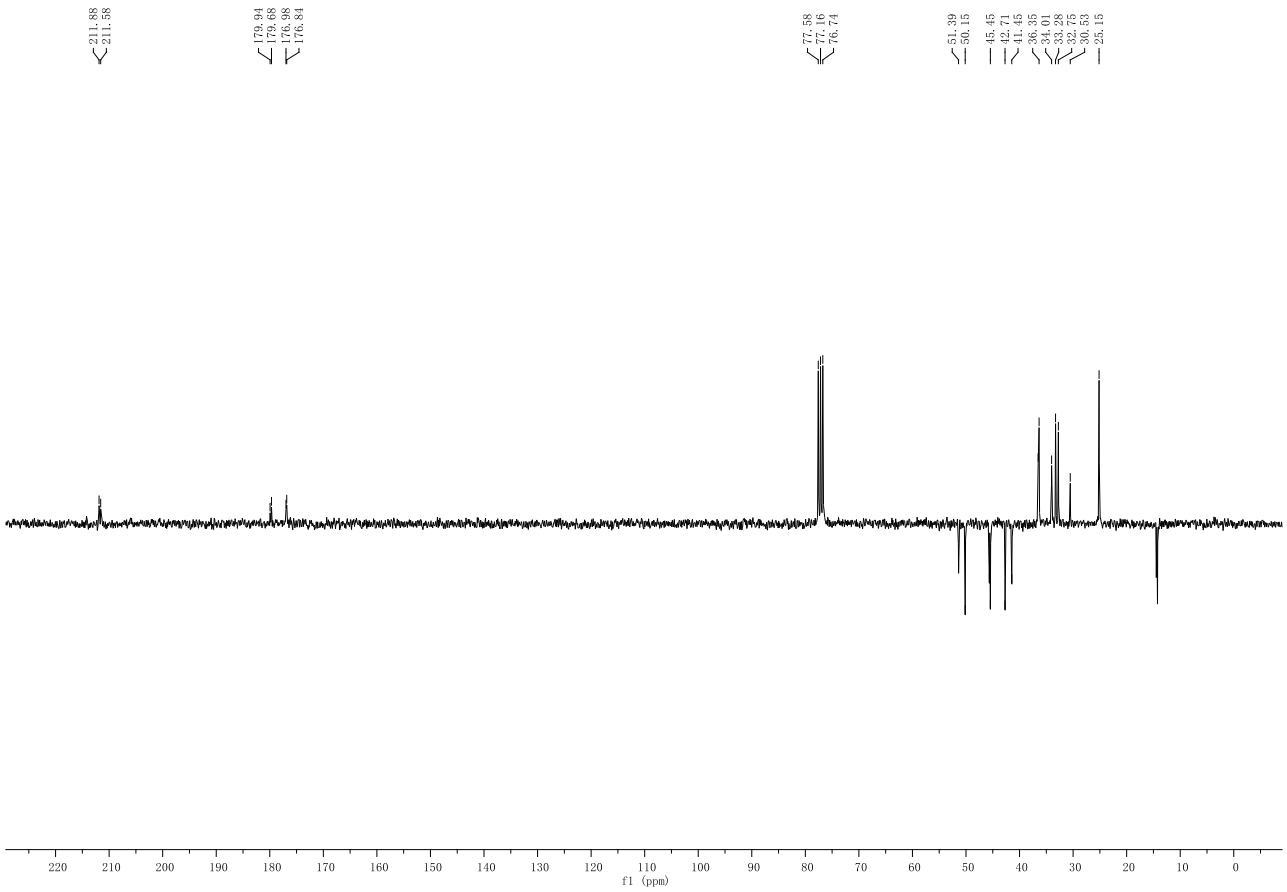
A mixture of α-methyl cyclohexanone **9** (1.3 mmol), maleimides **10** (1 mmol), pyrrolidine (0.2 eq) and 4-nitrobenzoic acid **8c** (0.2 eq) in toluene (1 mL) was stirred for 6 hours at 80 °C under MW irradiation. After complete disappearance of **10** followed by TLC, the reaction mixture was concentrated and the resulting residue chromatographed over silica gel (cyclohexane/ethyl acetate = 5:1) to afford compounds **22** as a mixture of diastereomers.

3-(3-Methyl-2-oxocyclohexyl)pyrrolidine-2,5-dione 22a

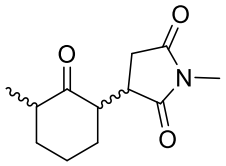


Compound **22a** was synthesized in 49% yield as an oil (inseparble mixture of diastereomers, dr = 1:1). **Rf** = 0.1 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 9.60-8.15 (m, 1H), 3.24-3.04 (m, 1H), 3.03-2.82 (m, 1H), 2.78-2.58 (m, 1H), 2.58-2.33 (m, 2H), 2.21-1.63 (m, 5H), 1.61-1.14 (m, 2H), 0.99 (d, *J* = 6.0 Hz, 3H), 0.96 (d, *J* = 6.0 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 211.9, 211.6, 179.9, 179.7, 177.0, 176.8, 51.4, 50.2, 45.6, 45.5, 42.7, 41.5, 36.5, 36.4, 34.0, 33.3, 32.8, 30.5, 25.2, 14.5, 14.3; **HRMS (ESI)** m/z calcd for $[C_{11}H_{16}NO_3]^+$, 210.1130 found 210.1127; **IR** (neat) 3271, 3070, 2976, 2934, 1768, 1716, 1697, 1459, 1207 cm^{-1}

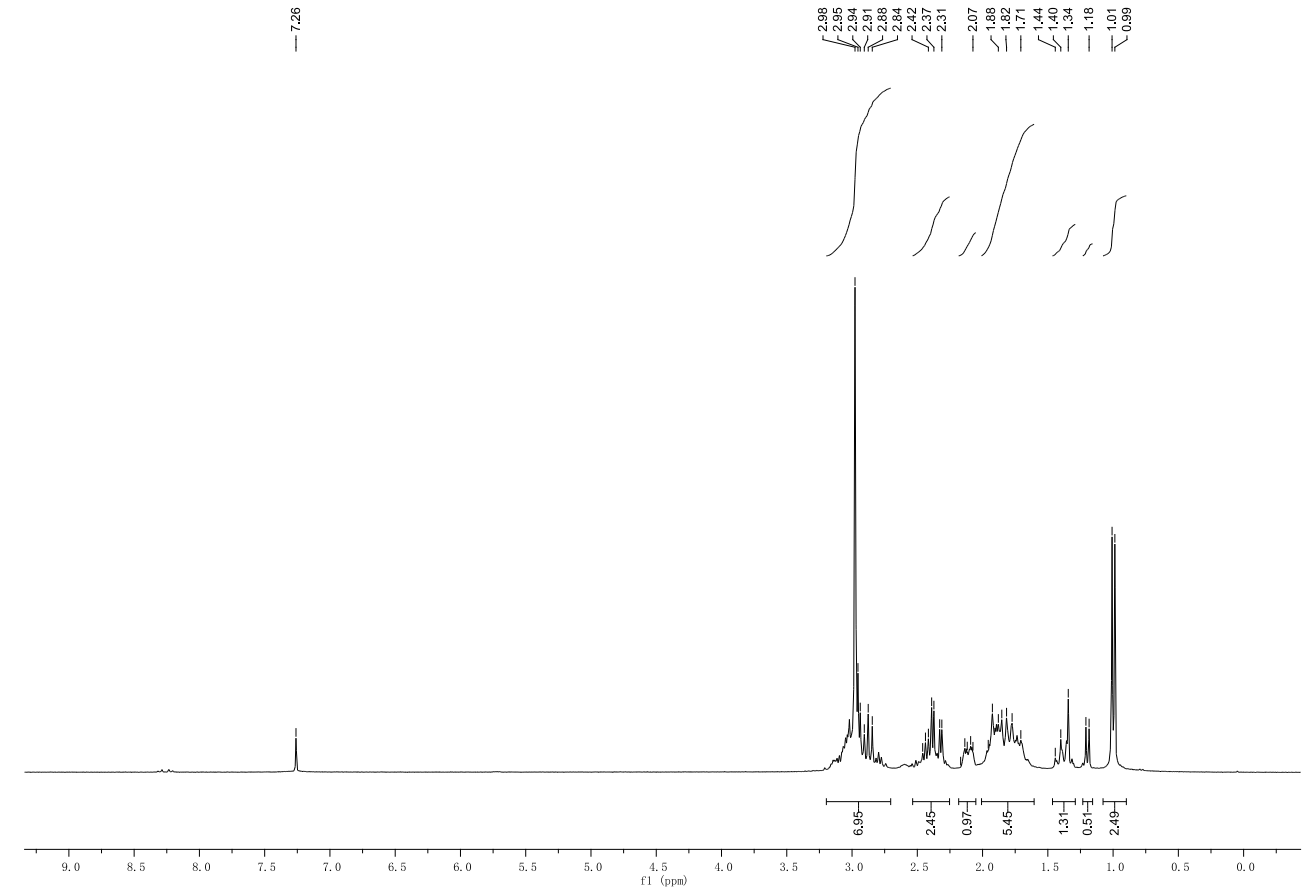




1-Methyl-3-(3-methyl-2-oxocyclohexyl)pyrrolidine-2,5-dione 22b



Compound **22b** was obtained in 51% yield as an oil (inseparable mixture of diastereomers, dr = 87:13). **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.18-2.70 (m, 7H), 2.54-2.25 (m, 2H), 2.18-2.05 (m, 1H), 2.01-1.60 (m, 5H), 1.40-1.29 (m, 1H), 1.19 (d, *J* = 9.0 Hz, 3H, k, minor), 1.00 (d, J = 6.0 Hz, 3H, major); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 211.6, 179.7, 177.0, 51.5, 47.7, 46.7, 45.6, 44.4, 40.1, 38.5, 36.5, 32.9,30.6, 29.0, 27.1, 25.1, 24.8, 22.0, 17.2, 14.4; **HRMS (ESI)** m/z calcd for $[C_{12}H_{18}NNaO_3]^+$ 246.1106, found 246.1106; **IR** (neat) 2855, 1764, 1706, 1690, 1430, 1377, 1279, 1113, 697 cm^{-1}.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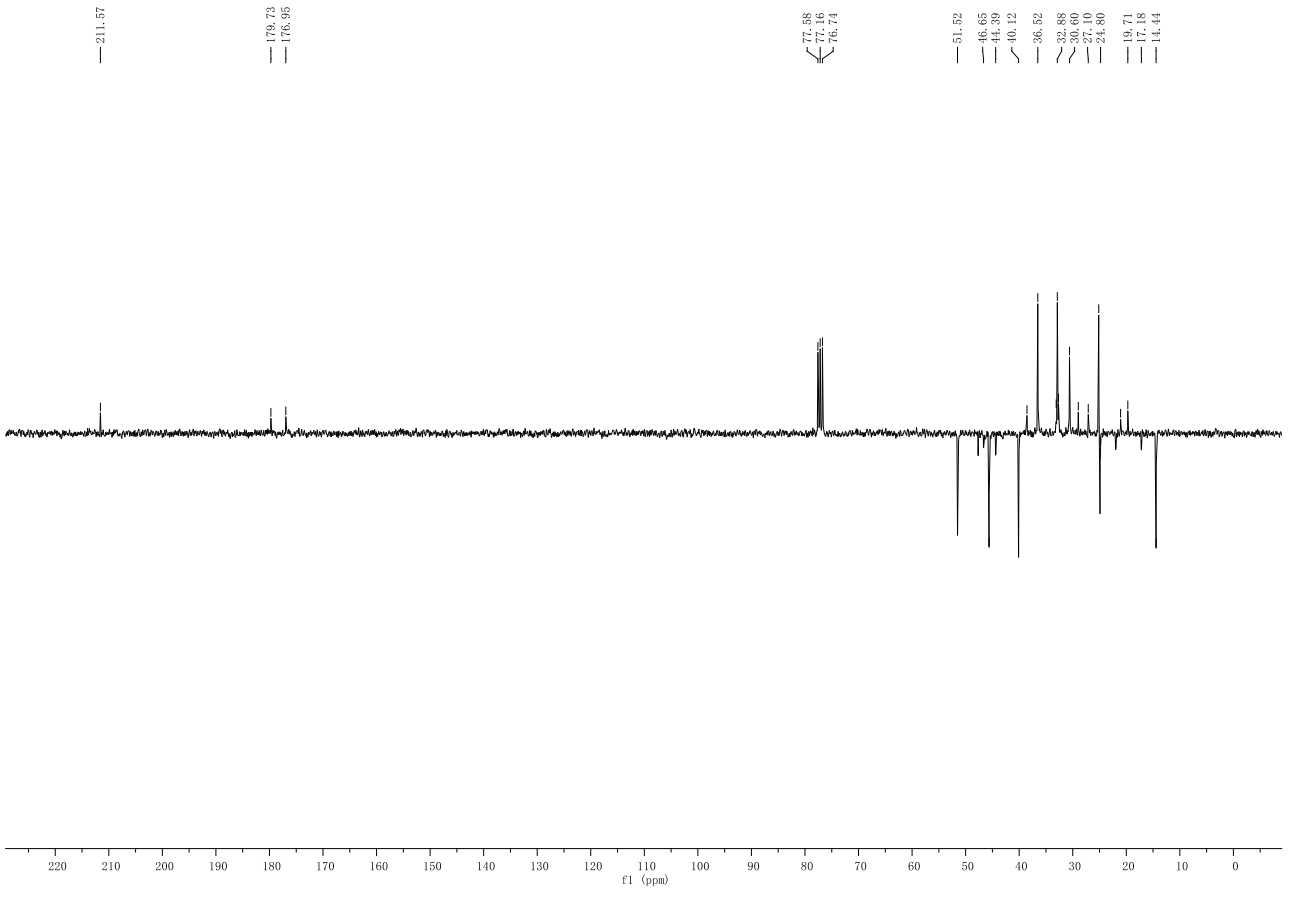
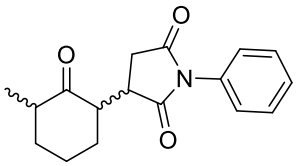
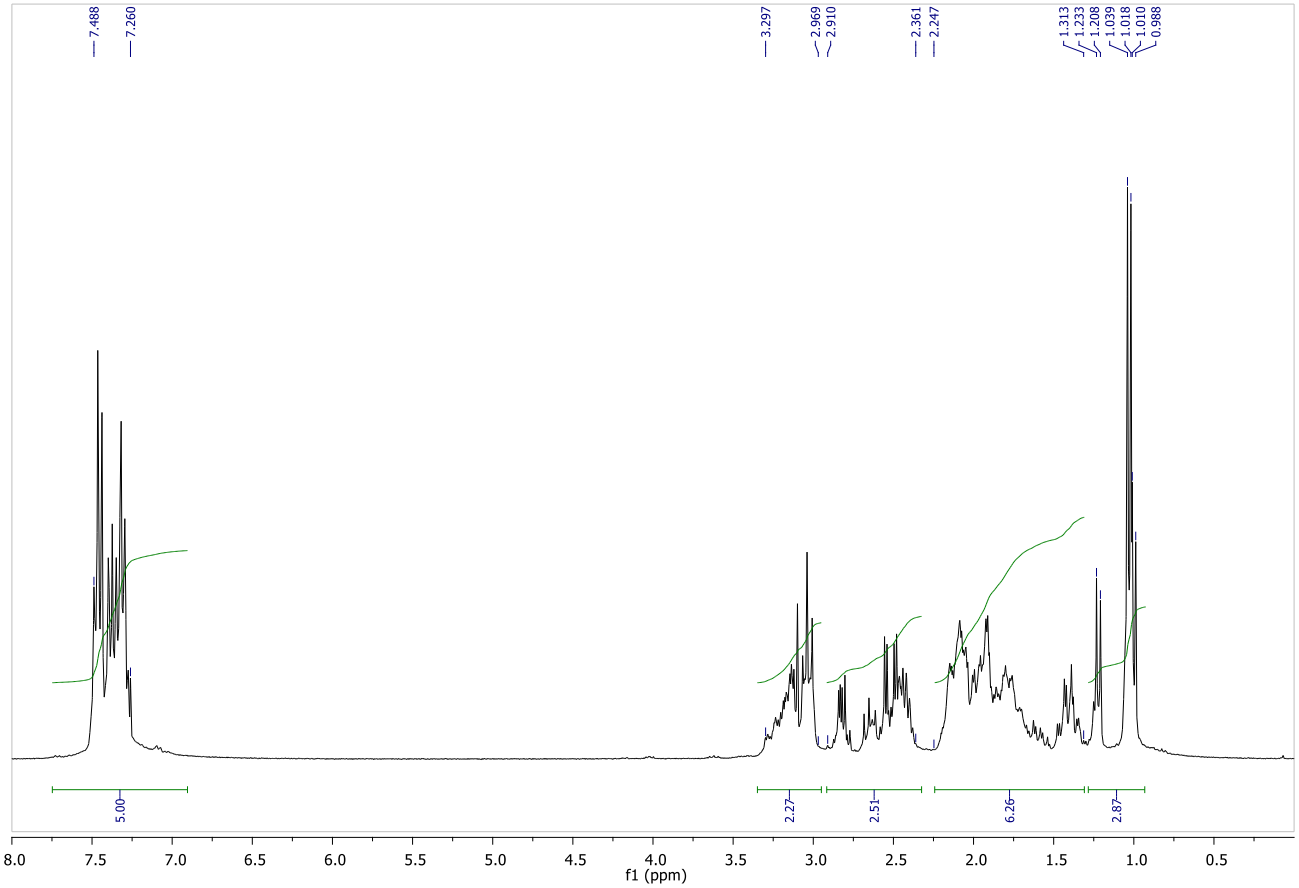
2.98
2.95
2.94
2.91
2.88
2.84
2.42
2.37
2.31
2.07
1.88
1.82
1.71
1.44
1.40
1.34
1.18
1.01
0.99
6.95
2.45
0.97
5.45
1.31
0.51
2.49
f1 (ppm)

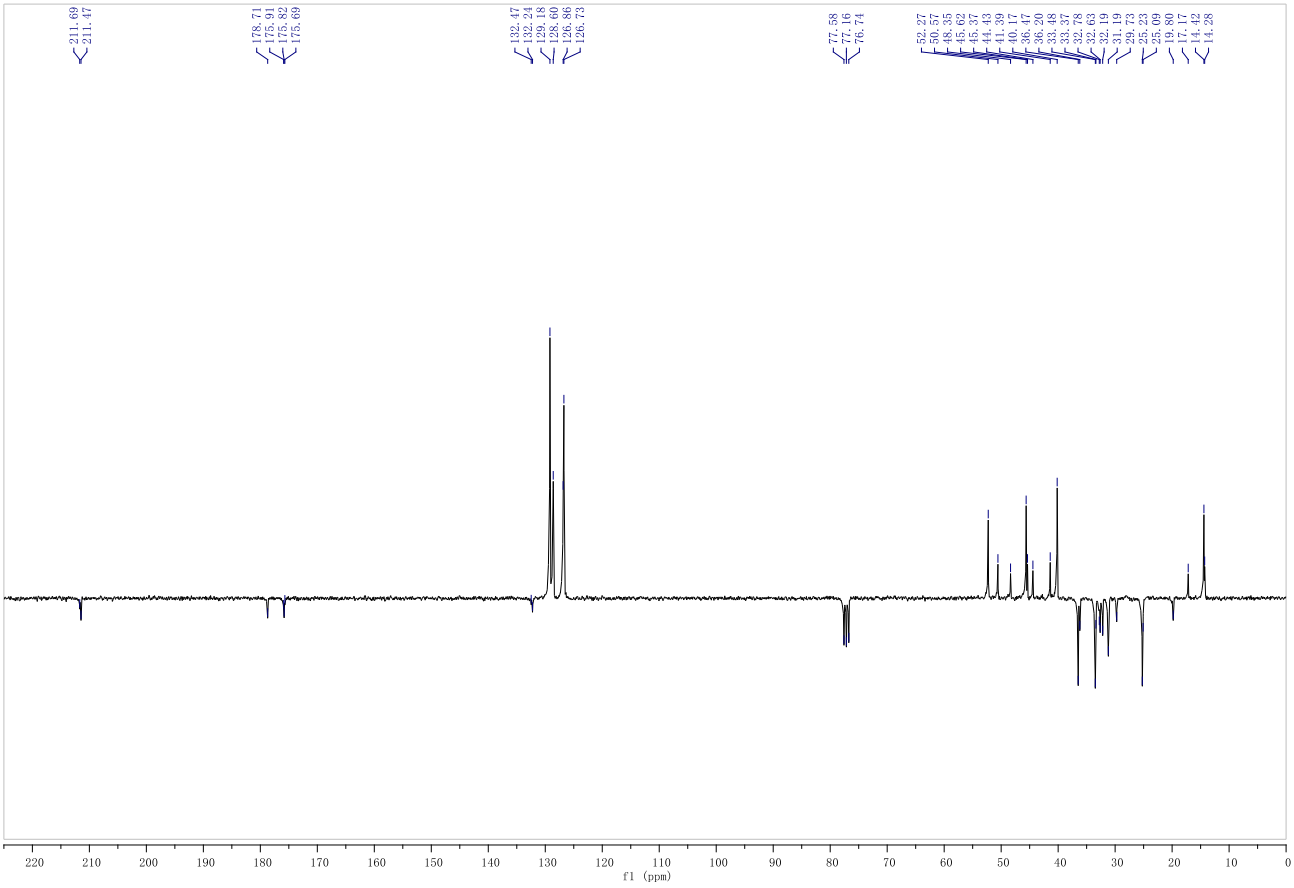

211.57
179.73
176.95
77.58
77.16
76.74
51.52
46.65
44.39
40.12
36.52
32.88
30.60
27.10
24.80
19.71
17.18
14.44
f1 (ppm)

3-(3-Methyl-2-oxocyclohexyl)-1-phenylpyrrolidine-2,5-dione 22f

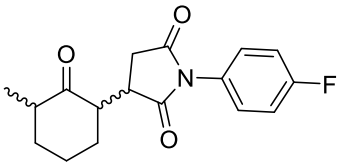


Compound **22f**[4] was synthesized in 65% yield as an oil (mixture of 3 diastereomers, proportions not determined). **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.50-7.20 (m, 5H), 3.29-2.97 (m, 2H), 2.91-1.36 (m, 3H), 2.25-1.31 (m, 6H), 1.22 (d, *J* = 7.5 Hz, 3H, k), 1.22 (d, *J* = 6.3 Hz, 3H, k), 1.22 (d, *J* = 6.6 Hz, 3H, k); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 211.7, 211.5, 178.7, 175.9, 175.8, 175.7, 132.5, 132.2, 129.2, 128.60, 126.9, 126.7, 52.3, 50.6, 48.3, 45.6, 45.4, 44.4, 41.4, 40.2, 36.5, 36.2, 33.5, 33.4, 32.8, 32.6, 32.2, 31.2, 29.7, 25.2, 25.1, 19.80, 17.2, 14.42 17.2, 14.3 17.2 ; **HRMS (ESI)** m/z calcd for $[C_{17}H_{19}NO_3]^+$ 308.1257, found 308.1253; **IR** (neat) 2932, 2859, 1777, 1712, 1696, 730, 694 cm^{-1}.

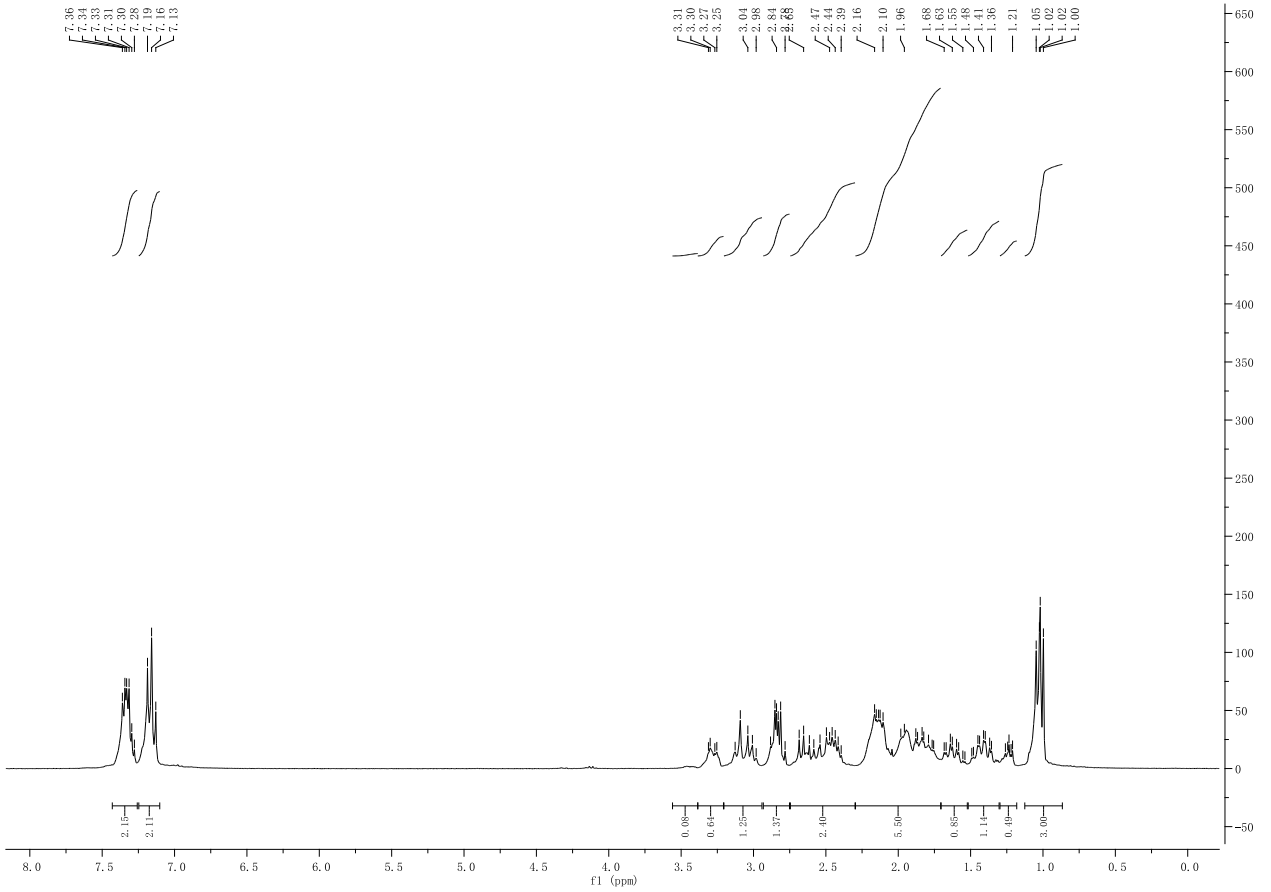


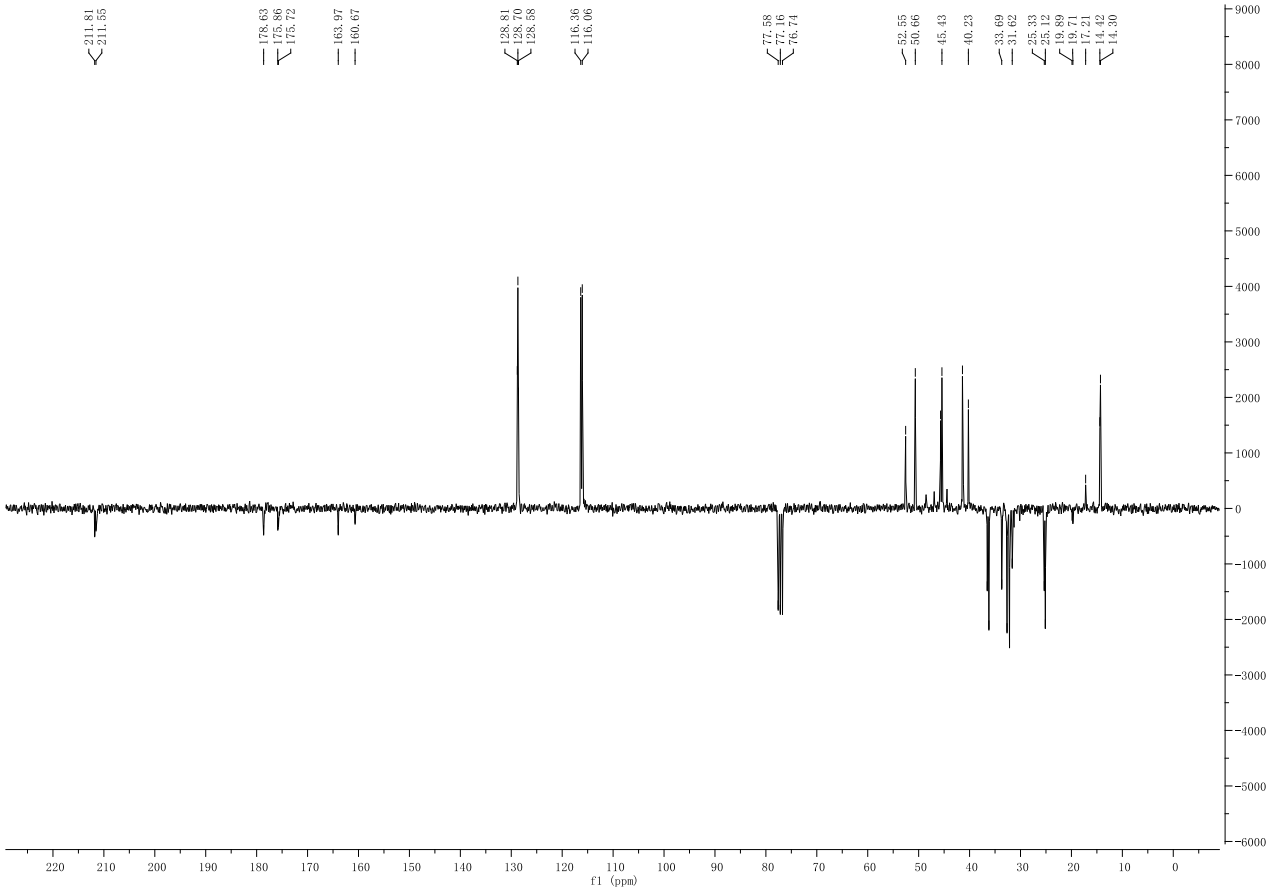


1-(4-Fluorophenyl)-3-(3-methyl-2-oxocyclohexyl)pyrrolidine-2,5-dione 22i

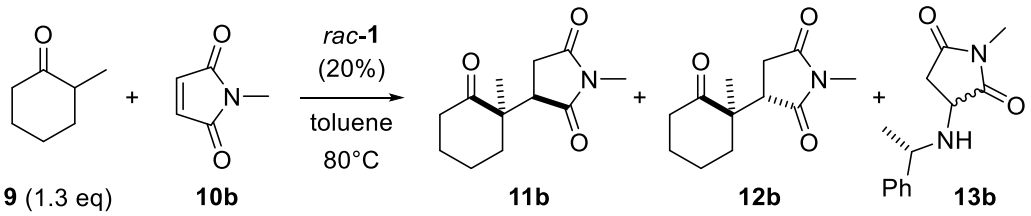


Compound **22i** was synthesized in 64% yield as an oil (mixture of 3 diastereomers, proportions not determined). **Rf** = 0.1 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.43-7.26 (m, 2H), 7.25-7.10 (m, 2H), 3.48-2.95 (m, 2H), 2.95-2.30 (m, 3H), 2.30-1.15 (m, 6H), 1.12-0.87 (m, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 211.8, 211.6, 178.6, 175.9, 175.7, 164.0, 160.7, 128.7 (t, *J* = 8.25), 116.21 (d, *J* = 22.5 Hz), 52.6, 50.7, 45.7, 45.4, 41.4, 40.2, 36.5, 36.2, 33.7, 32.6, 32.2, 31.6, 25.3, 25.1, 14.4, 14.3; **HRMS (ESI)** m/z calcd for $C_{17}H_{18}NO_3FNa$, 326.1168 found 326.1170; **IR** (neat) 2972, 2933, 2861, 1777, 1712, 1696, 1452, 1291, 1178, 1152, 837, 713 cm^{-1}.


7.36
7.34
7.33
7.31
7.30
7.28
7.19
7.16
7.13
3.31
3.30
3.27
3.25
3.04
2.98
2.84
2.47
2.44
2.39
2.16
2.10
1.96
1.68
1.63
1.55
1.48
1.41
1.36
1.21
1.05
1.02
1.02
1.00
2.15
2.11
0.08
0.64
1.25
1.37
2.40
5.50
0.85
1.14
0.49
3.00
f1 (ppm)


211.81
211.55
178.63
175.86
175.72
163.97
160.67
128.81
128.70
128.58
116.36
116.06
77.58
77.16
76.74
52.55
50.66
45.43
40.23
33.69
31.62
25.33
25.12
19.89
19.71
17.21
14.42
14.30
f1 (ppm)

4. Screening of the reaction conditions



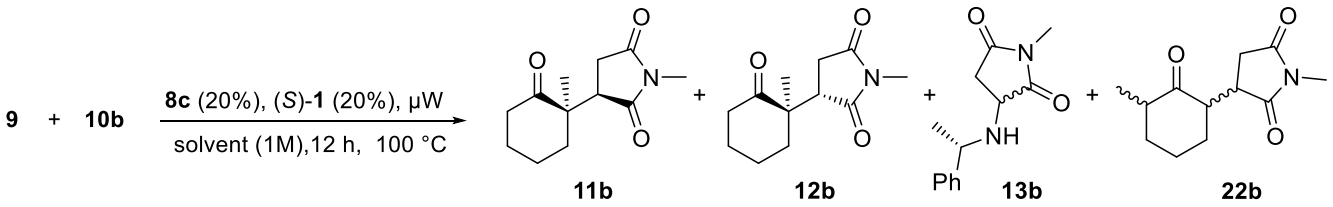
Scheme S1. Screening of the reaction conditions (Table 1).

Thermal conditions (Table 1, entries 1-5), general procedure

A mixture of α-methyl cyclohexanone **9** (1.3 mmol), maleimides **10** (1 mmol), racemic 1-phenylethylamine **1** (0.2 eq) and co-catalyst (or not) (acid **8a-c** or AcOH (0.2 eq)) in toluene (1 mL) was stirred for 24 hours at 80 °C. The reaction mixture was concentrated and the resulting residue chromatographed over silica gel (cyclohexane/ethyl acetate = 5:1) to afford compounds mixtures of products according to table 1 (see text).

Microwave conditions (Table 1, entry 6), see part 6 below (p 24)

Table S3. Effect of the solvent.



Entry	Solvent	Yield (**11b**/**12b**)[a]	de (**11b**/**12b**)[b]	ee (**11b**)[c]	rr[d]	**13b**[e]
1	Toluene	79%	50	87%	91/9	6%
2	Dichloro-1,2-ethane	62%	64	87%	90/10	2%
3	Mesitylene	69%	24	85%	88/12	3%
4	Cyclohexane	65%	56	89%	81/19	3%

[a] Isolated yields after flash chromatography. [b] de corresponding to Michael adducts **11b** and **12b** were determined by ^{1}H NMR analysis. [c] Determined by chiral HPLC. [d] The regioisomeric ratio (**11b** + **12b**/**22b**) were determined by ^{1}H NMR analysis of the chromatographed mixtures. [e] Isolated yields.

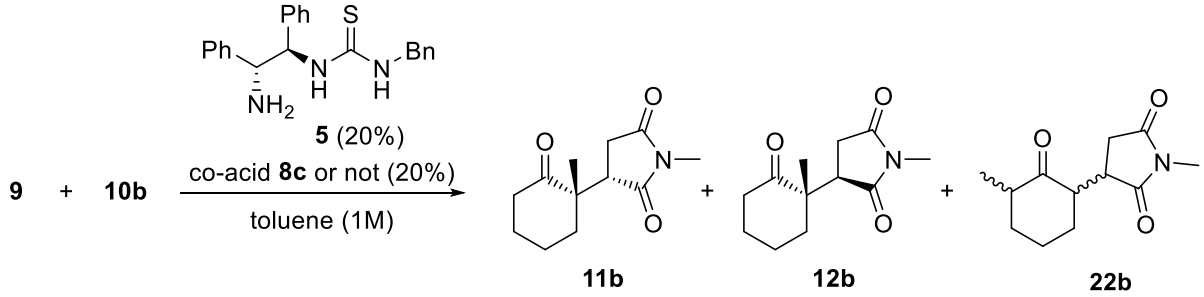
A mixture of α-methyl cyclohexanone **9** (1.3 mmol), maleimide **10b** (1 mmol), (*S*)-1-phenylethylamine **1** (0.2 eq) and co-catalyst acid **8c** (0.2 eq) in the appropriate solvent (1 mL) was stirred for 12 h at 100 °C under microwave irradiation (μW). The reaction mixture was concentrated and the resulting residue chromatographed over silica gel (cyclohexane/ethyl acetate = 5:1) to afford compounds mixtures of products as reported in table S3 (see text).

We focused our attention on nonpolar and nonprotic solvents which are usally used in enantioselective Michael additions. Solvation or hydrogen bonding interactions were indeed evoked[5] to explain loss of both enantioselectivity and yields. Toluene is the most appropriate solvent according to > 10% yield obtained in comparison with other solvents. The lower diastereomeric excess (50%) found for toluene in comparison with dichloro ethane (vs 64% entry 2) is higher working at 80°C (70%, see table 3 in the main text). We found no significant influence of the solvents on enantiomeric excesses which slightly vary (85-89%) as well as on the regiomeric ratio (81/19 to 91/9).

5. Screening the effect of Carter's catalyst

Following the protocol used studying solvent effects (corresponding to Table S3, p22), we screened the effect of various amines as organocatalysts (see Table 2, in the text) and were surprised to find that Carter's catalyst,[6] in our case, led to the formation of enhanced proportion of regioisomers. Here are the corresponding experimental details (Table S4).

Table S4. Effect of Carter's catalyst.

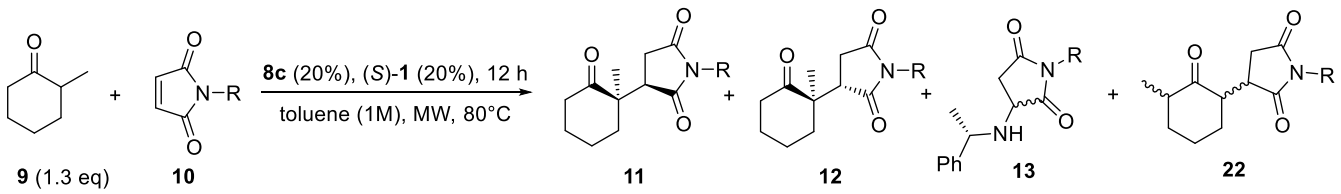


Entry	Conditions	Yield [%][a] **11b**/**12b** (**22b**)	dr [%][b] (**11b**/**12b**)	rr[c] **11b**+**12b**/**22b**
1	Reflux without co-acid, 24 h	0	-	-
2	µW, without co-acid, 100 °C, 12 h	25	nd	nd
3	µW, **8c**, 100 °C, 12 h	50 (27)	97/3	63/37

[a] Isolated yields after flash chromatography. [b] dr of Michael adducts **11b** and **12b** were determined by ^{1}H NMR analysis of the mixture of these compounds isolated by flash chromatography. [c] The regioisomeric ratio (**11b** + **12b**/**22b**) were determined by ^{1}H NMR analysis after chromatography.

Surprisingly, Carter's catalyst without co-acid gave no conversion of starting materials (Table S4, entry 1) after 24 h at toluene reflux. Furthermore, under µW conditions, it allowed the formation of desired product **11b** in poor yield and with an increased proportion of regioisomers **22b** (rr = 63/37, entry 3) when compared with other amines (4-8%).

6. Scope of reaction of α-methyl cyclohexanone 9 with respect to the maleimide

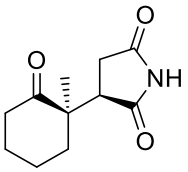


Scheme S2. Scope of reaction of **9** with respect to maleimides, general scheme (Table 3).

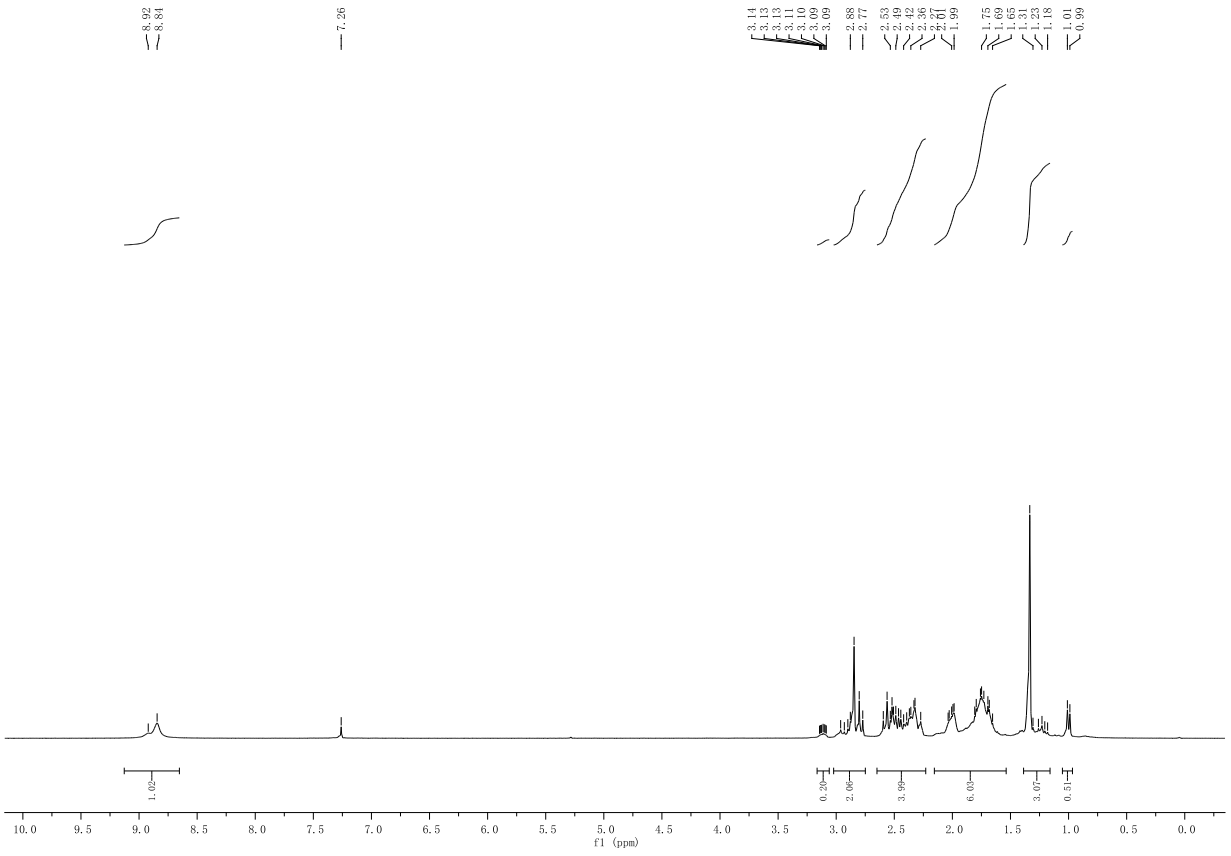
General procedure

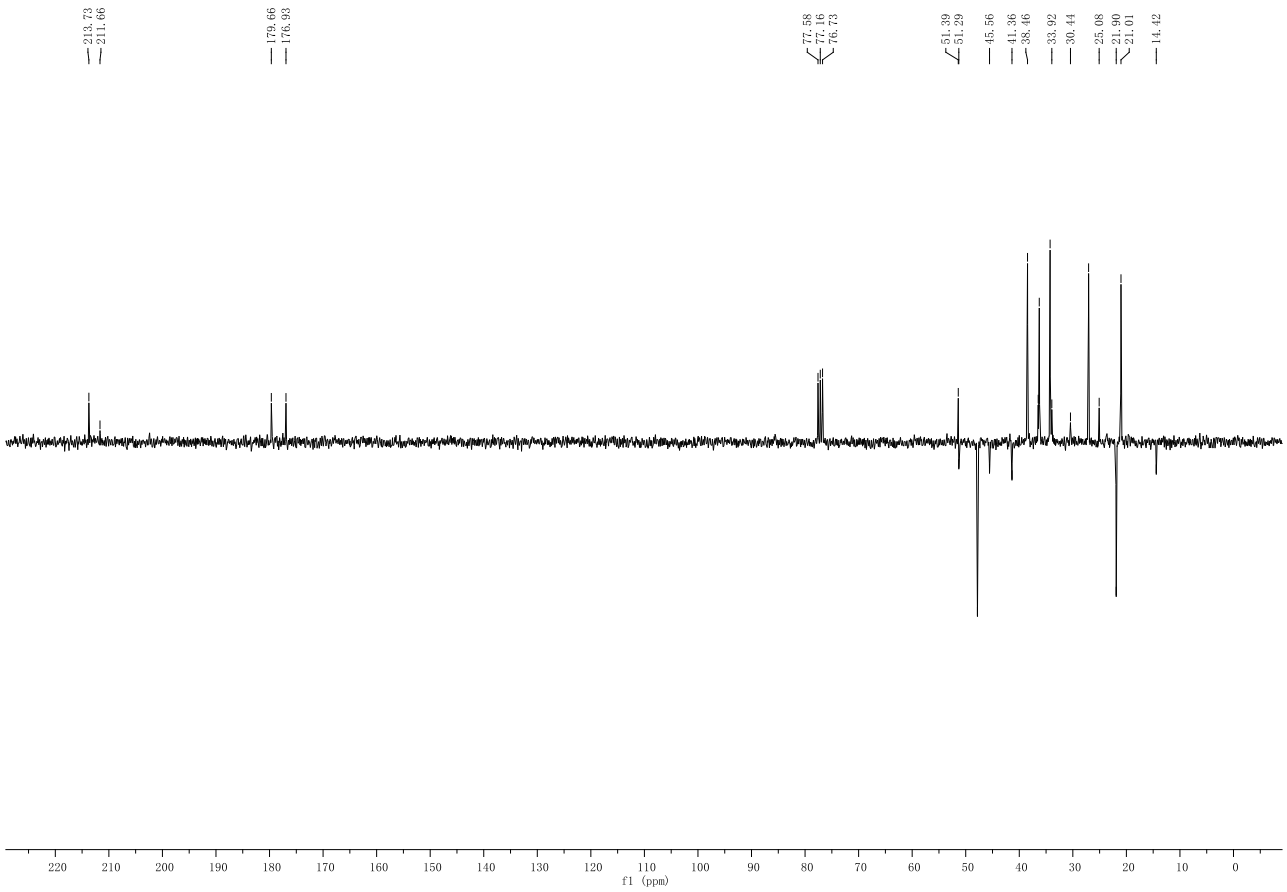
A mixture of α-methyl cyclohexanone **9** (1.3 mmol), maleimide **10** (1 mmol), (*S*)-1-phenylethylamine **1** (0.2 eq) and co-catalyst acid **8c** (0.2 eq)) in toluene (1 mL) was stirred for 12 h at 80 °C under µW irradiation. The reaction mixture was concentrated and the resulting residue chromatographed over silica gel (cyclohexane/ethyl acetate = 5:1) to afford compounds mixtures of products as reôrted in table 3 (see text).

(*R*)-3-((*R*)-1-Methyl-2-oxocyclohexyl)-2,5-pyrrolidinedione 11a



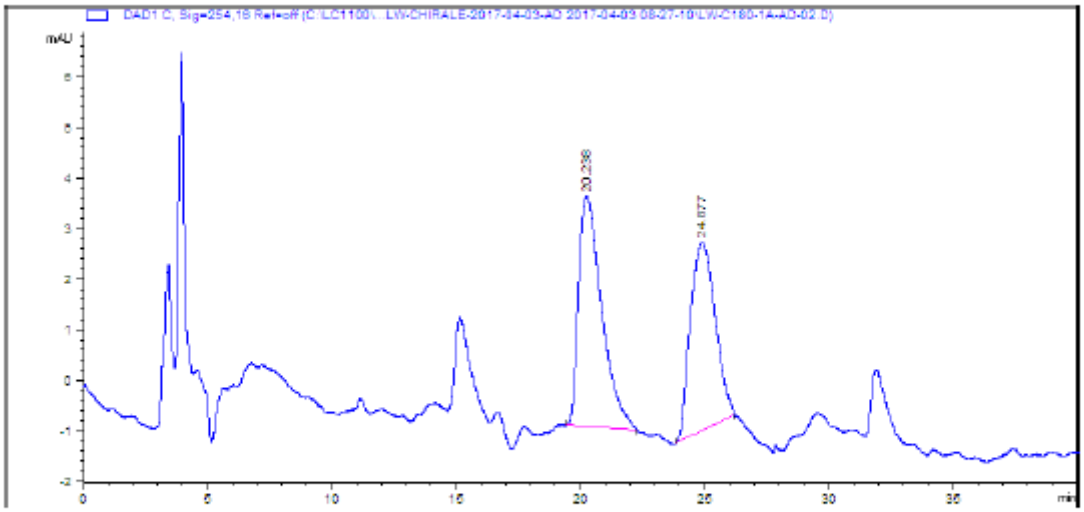
Compound (1*R*,3*R*)-**11a** was obtained in 70% yield (146 mg) as a colorless oil containing an inseparable mixture of regioisomers **22a** (4%) and traces of diastereomer **12a**. 4% (9 mg) of *aza*-Michael adduct **12a** were also isolated. **Rf** = 0.1 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.03-2.75 (m, 2H), 2.65-2.23 (m, 4H), 2.15-1.55 (m, 6H), 1.33 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 213.7, 179.7, 176.9, 51.4, 45.6, 38.5, 36.3, 34.3, 27.1, 21.9, 21.0; **HRMS (ESI)** m/z calcd for $[C_{11}H_{15}N\ NaO_3]^+$, 232.0950 found 232.0956; **IR** (neat) 3154, 3060, 2962, 2932, 1768, 1712, 1696, 1449, 1361 cm^{-1}





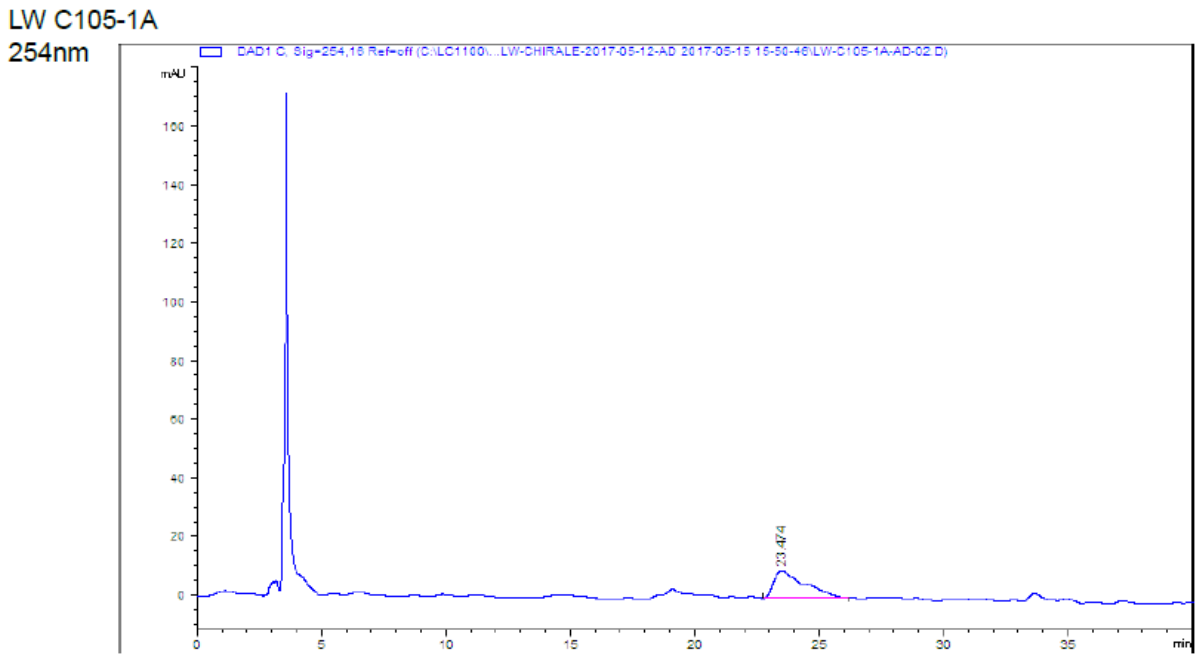
HPLC: (±)-**11a**. Chiralcel AD-H, *i*-PrOH/hexane = 20:80, 1 mL/min, 254 nm, Retention times = 20.238, 24.877 min.

LW 180-1A Hexane / isopropanol 80 : 20
254 nm



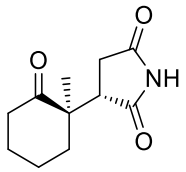
#	Time	Area	Height	Width	Area%	Symme-try
1	20.238	297.7	4.6	0.7708	53.26	0.513
2	24.877	261.3	3.7	0.8232	46.74	0.856

HPLC: (1*R*,3*R*)-**11a**. Chiralcel AD-H, *i*-PrOH/hexane = 20:80, 1 mL/min, 254 nm; 99% ee, retention time = 23.47 min.



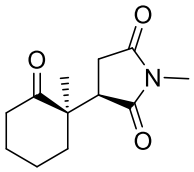
#	Time	Area	Height	Width	Area%	Symmetry
1	23,47	793,20	9,10	1,02	100,00	0,33

(*S*)-3-((*R*)-1-Methyl-2-oxocyclohexyl) -2,5-pyrrolidinedione (1*S*,3*R*)-12a

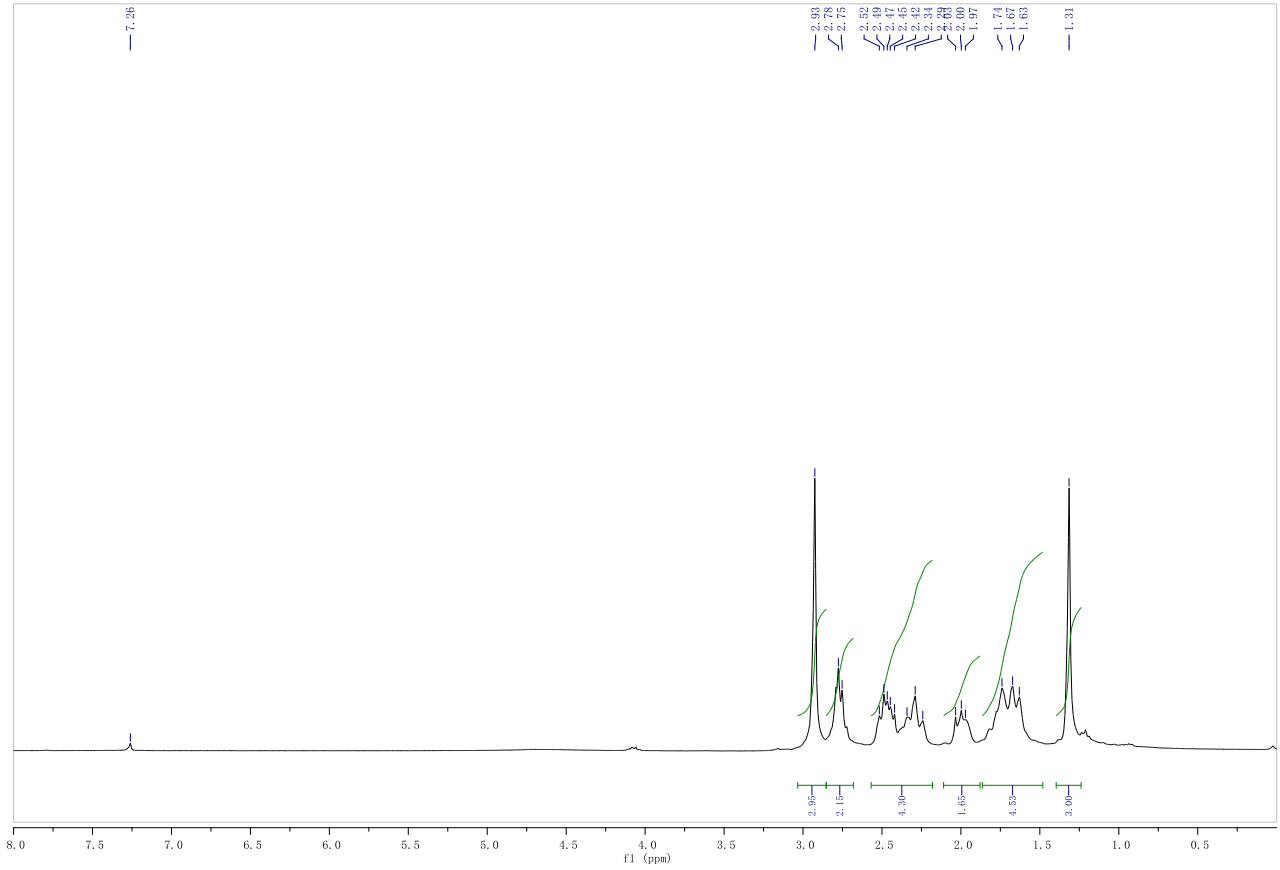


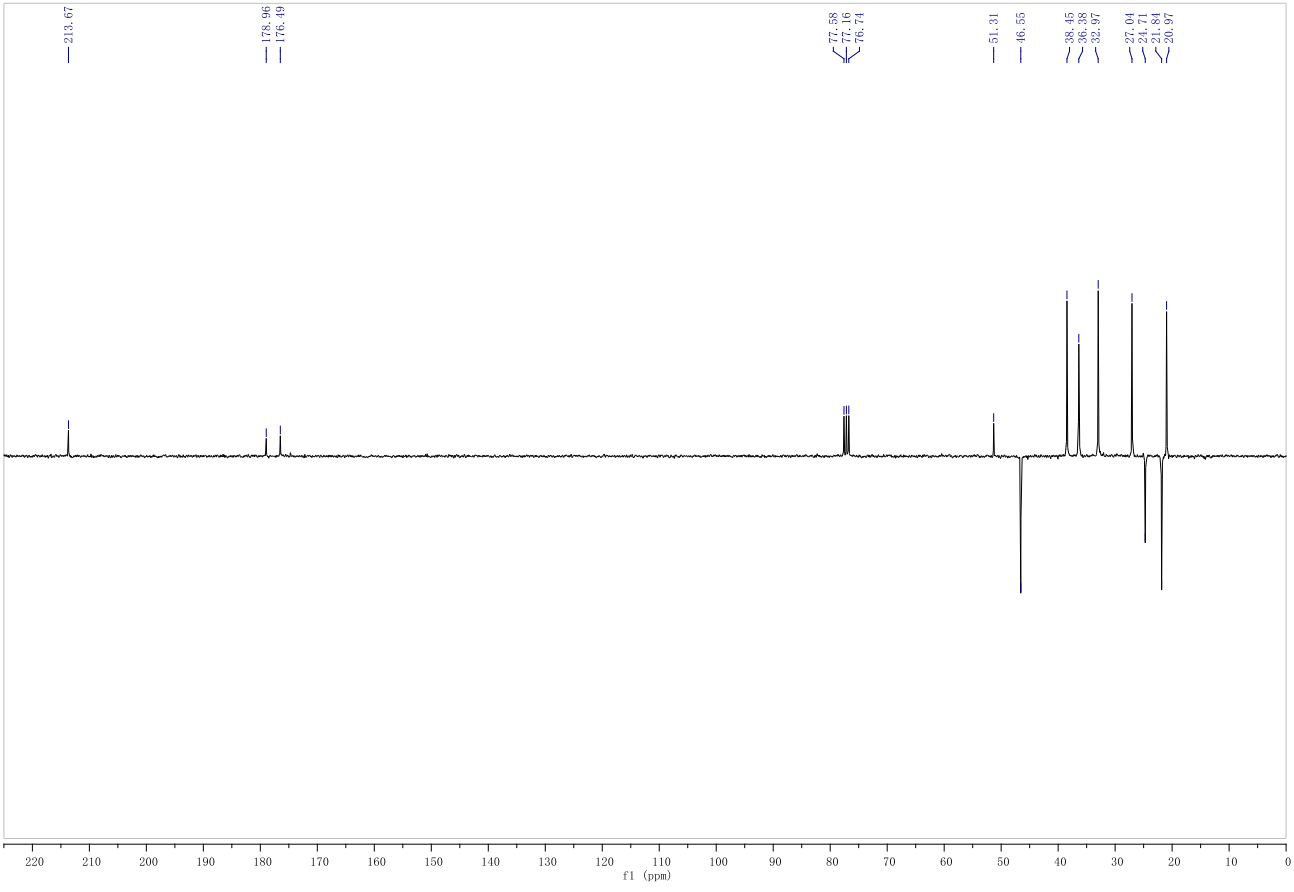
Traces, inseparable.

(*R*)-1-Methyl-3-((*R*)-1-methyl-2-oxocyclohexyl)pyrrolidine-2,5-dione (1*R*,3*R*)-11b



Compound (1*R*,3*R*)-**11b** was obtained in 65% yield (144 mg) as a colorless oil together with 14% (32 mg) of its diastereomer **12b**, 6% of a mixture of regioisomers **22b** (13 mg) and 6% (14 mg) of *aza*-Michael adduct **13b**. **Rf** = 0.1 (cyclohexane/EtOAc = 1:1); **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 2.94 (s, 3H), 2.85-2.70 (m, 2H), 2.58-2.42 (m, 4H), 2.42-2.22 (m, 1H), 2.10-1.94 (m, 1H), 1.90-1.59 (m, 5H), 1.33 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 213.6, 179.0, 176.5, 51.5, 46.6, 38.5, 36.4, 33.0, 27.1, 24.8, 21.8, 21.0; **HRMS (ESI)** m/z calcd for $[C_{12}H_{18}NO_3]^+$ 224.1281, found 224.1288; **IR** (neat) 2933, 2868, 1772, 1689, 1682, 1434, 1383, 1280, 1116, 695 cm^{-1}.

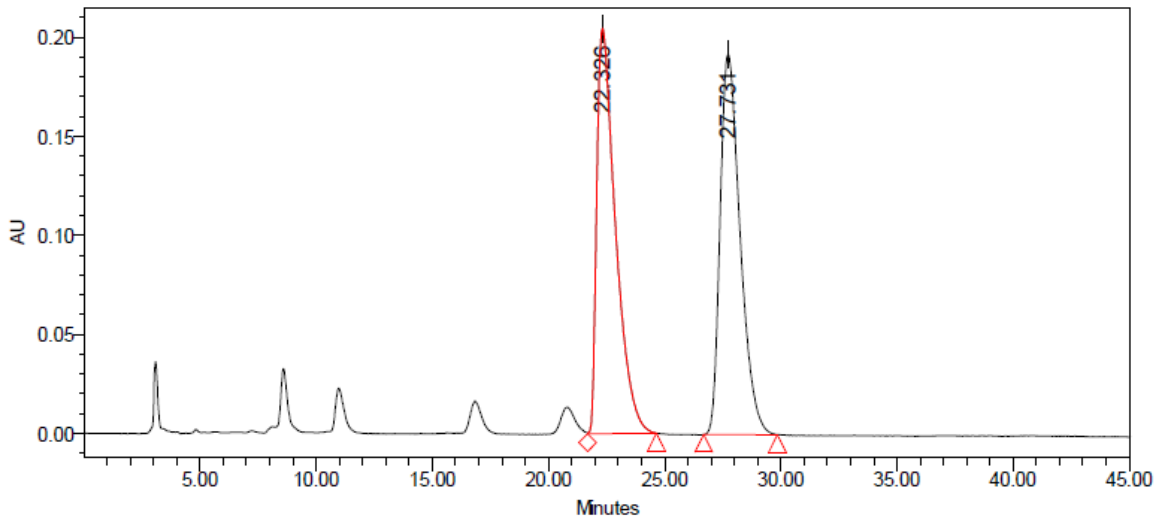

7.26
2.93
2.78
2.75
2.52
2.49
2.47
2.45
2.42
2.34
2.29
2.00
1.97
1.74
1.67
1.63
1.31
2.95
2.15
4.30
1.65
4.53
3.00
f1 (ppm)


213.67
178.96
176.49
77.58
77.16
76.74
51.31
46.55
38.45
36.38
32.97
27.04
24.71
21.84
20.97
f1 (ppm)

HPLC: (±)-**11b**. Chiralpal AD, Solvent: Hexane/i-PrOH = 90:10, Flow Speed 1.0 mL/min , UV: 215nm, retention times: 23.326, 27.731.

Colonne CHIRALCEL AD Hexane / isopropanol 90 : 10
215 nm

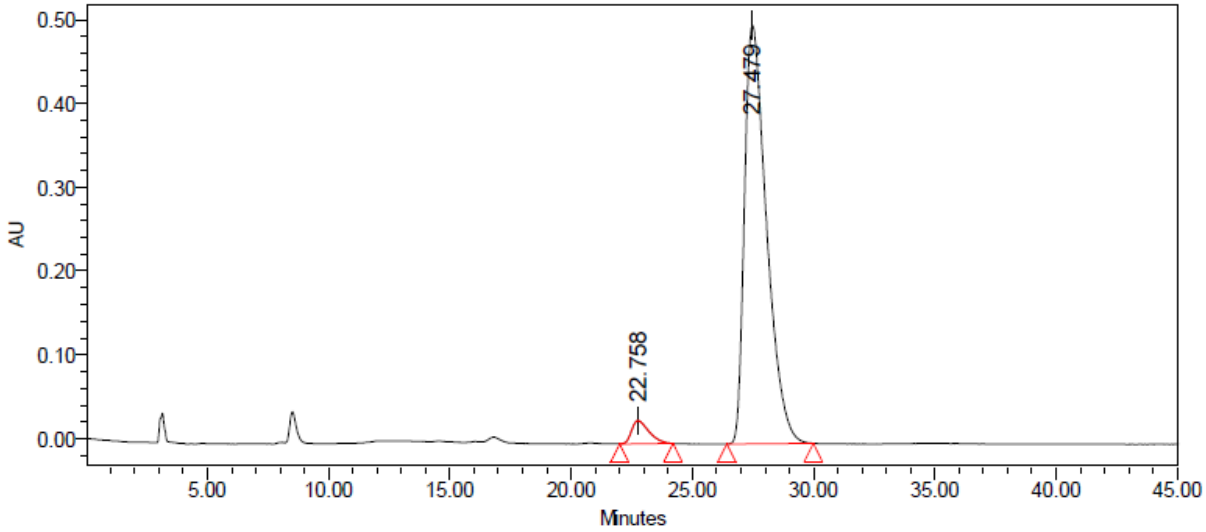
LW C-25-1A



	Retention Time	Area	% Area	Height	Int Type	Start Time	End Time	% Height	Width
1	22.326	11478178	49.94	204539	VB	21.680	24.647	51.58	178.000
2	27.731	11503970	50.06	192022	BB	26.680	29.847	48.42	190.000

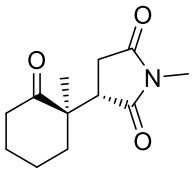
HPLC: (*R*,*R*)-**11b**. Chiralpal AD, Solvent: Hexane/i-PrOH = 90:10, Flow Speed 1.0 mL/min , UV: 215nm, 92% ee, retention time: 27.479.

LW C38-2A

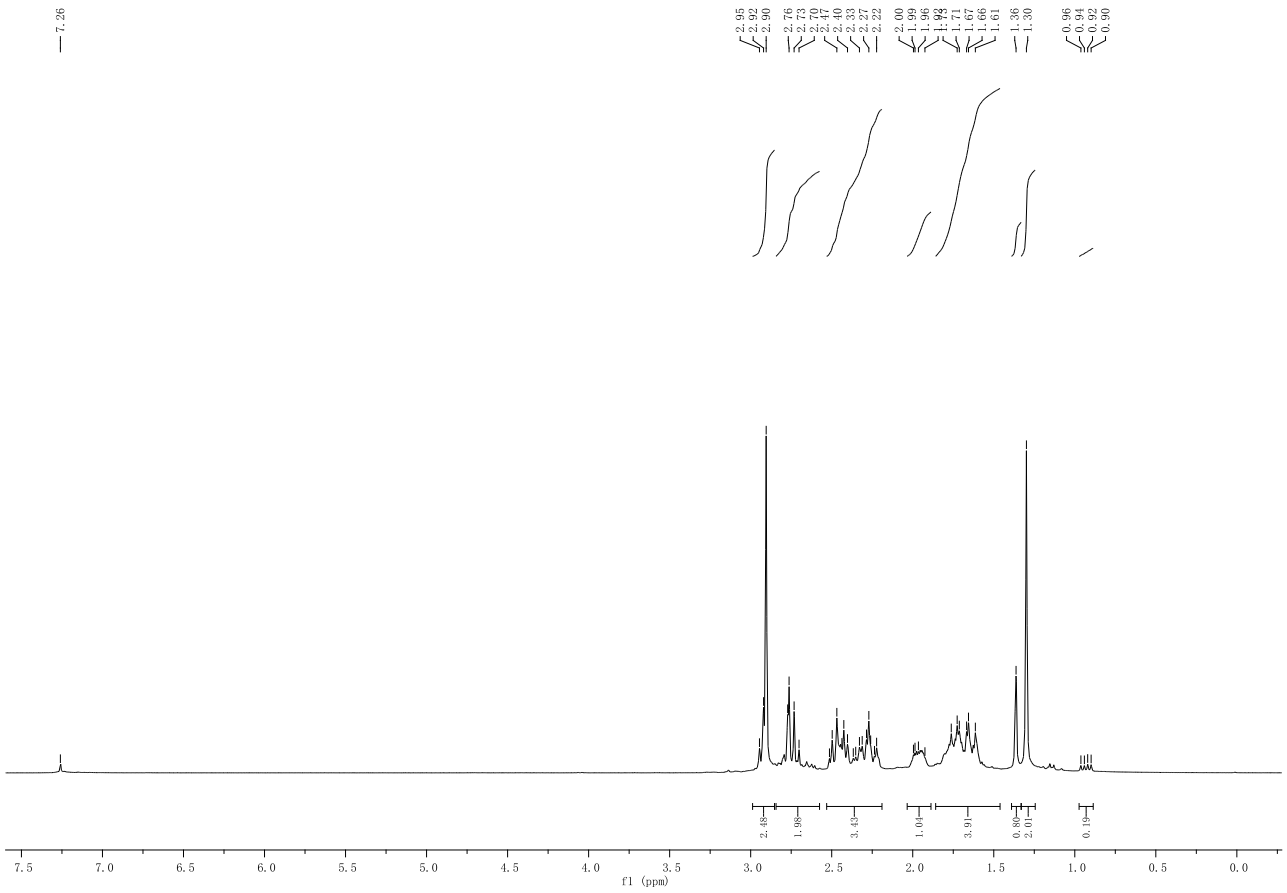


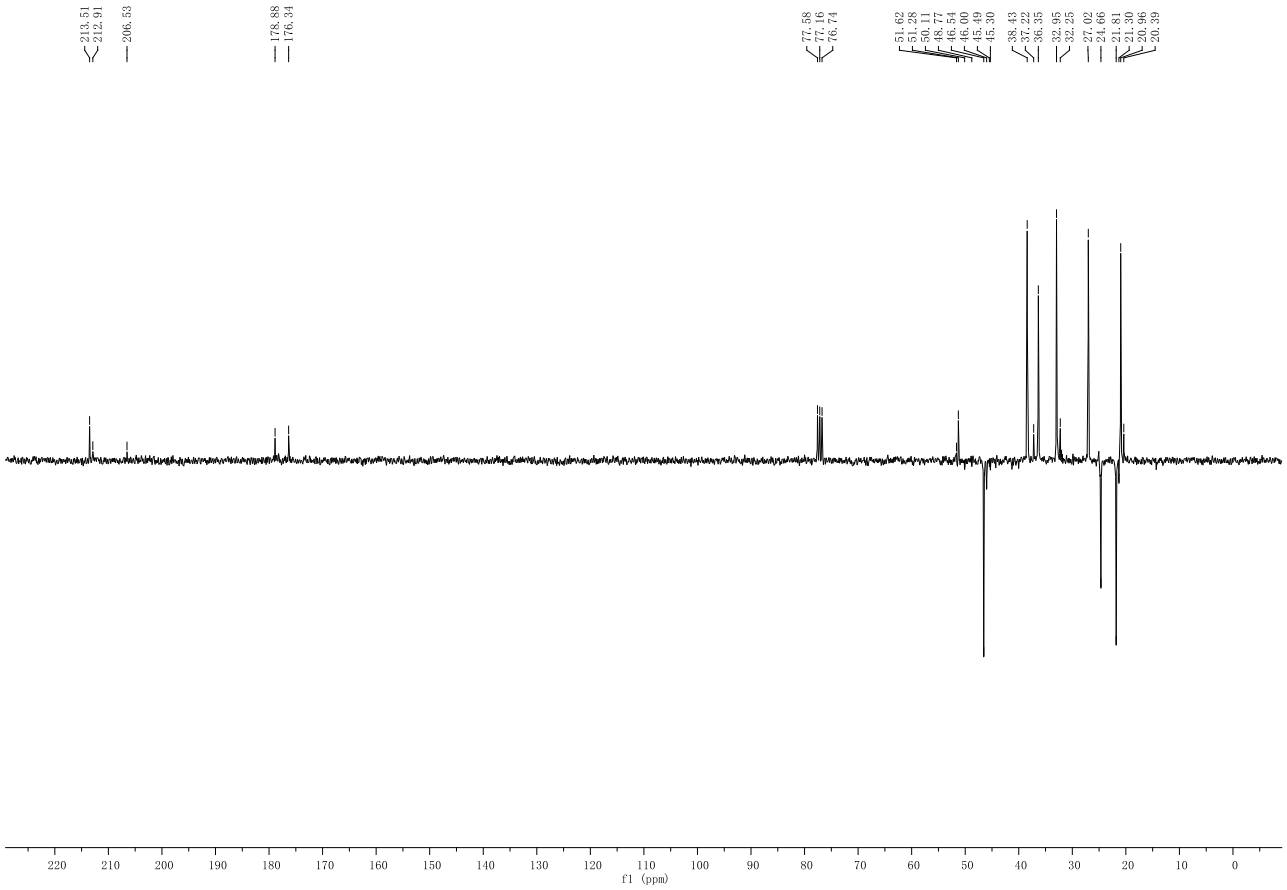
	Retention Time	Area	% Area	Height	Int Type	Start Time	End Time	% Height	Width
1	22.758	1372202	4.16	27451	BB	21.998	24.198	5.21	132.000
2	27.479	31574406	95.84	499250	BB	26.415	29.982	94.79	214.000

(*S*)-1-Methyl-3-((*R*)-1-methyl-2-oxocyclohexyl)-2,5-pyrrolidinedione (1*R*,3*S*)-12b

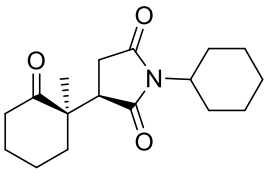


NMR spectra shows the presence of inseparable diastereomer **11b** (27%) and traces of regioisomers **22b**. **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 2.99-2.85 (m, 3H), 2.85-2.58 (m, 2H), 2.53-2.18 (m, 4H), 2.04-1.88 (m, 1H), 1.86-1.46 (m, 4H), , 1.30 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 213.5, 212.9, 178.9, 176.3, 51.3, 46.5, 38.4, 33.0, 27.0, 24.7, 21.8, 21.0; **HRMS (ESI)** m/z calcd for $[C_{12}H_{18}NO_3]^+$ 224.1281, found 224.1288; **IR** (neat) 2933, 2868, 1772, 1689, 1682, 1434, 1383, 1280, 1116, 695 cm^{-1}.

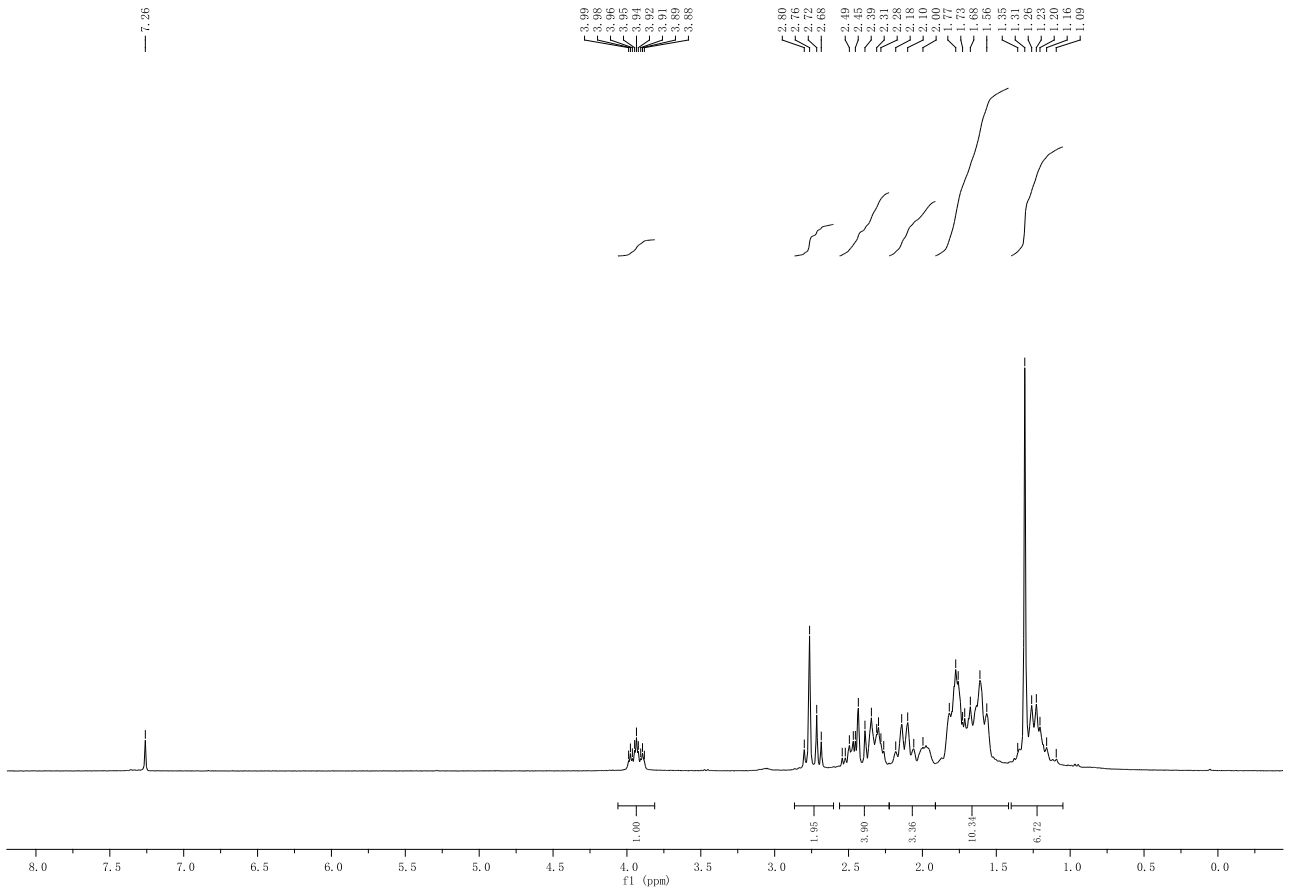


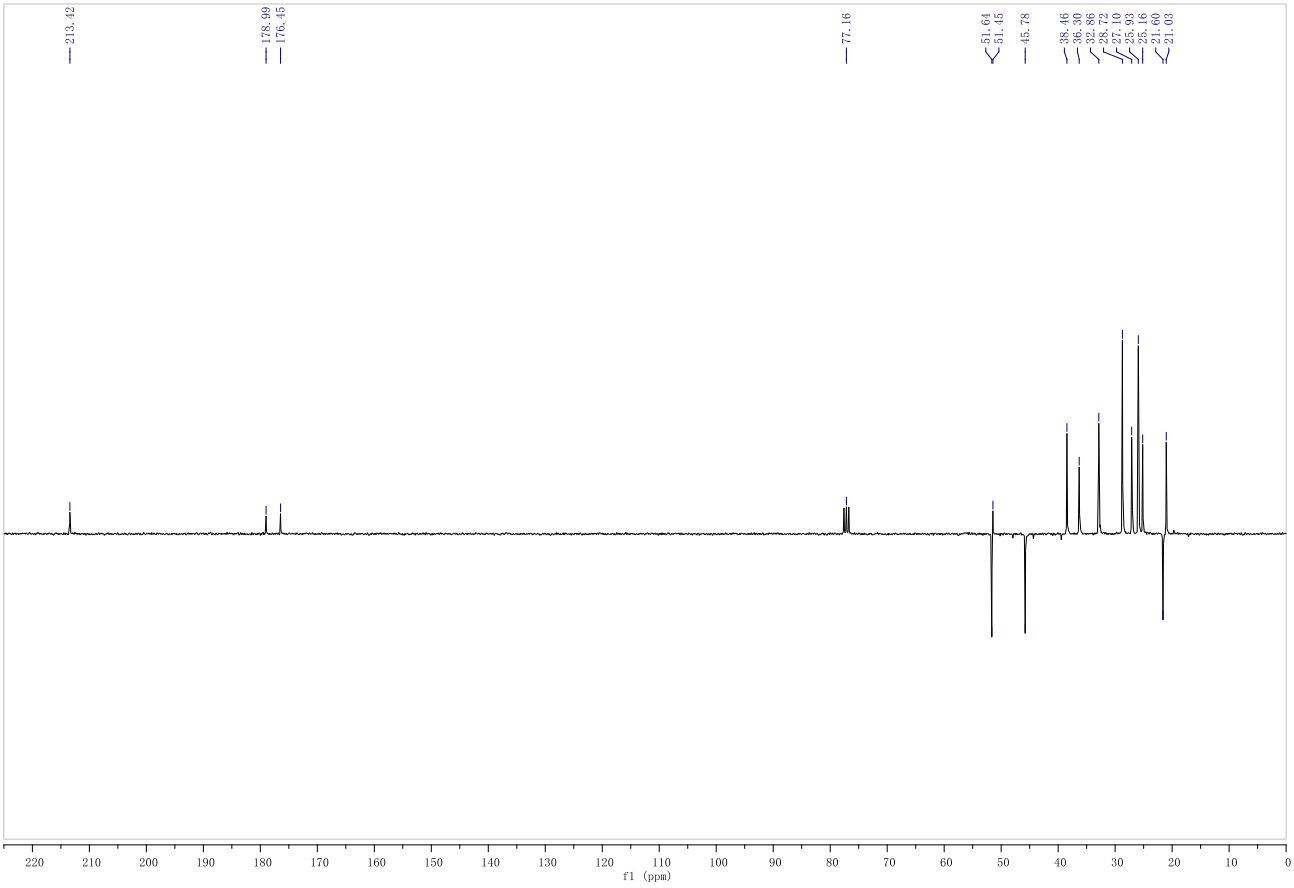


(*R*)-1-Cyclohexyl-3-((*R*)-1-methyl-2-oxocyclohexyl)pyrrolidine-2,5-dione (1*R*,3*R*)-11e



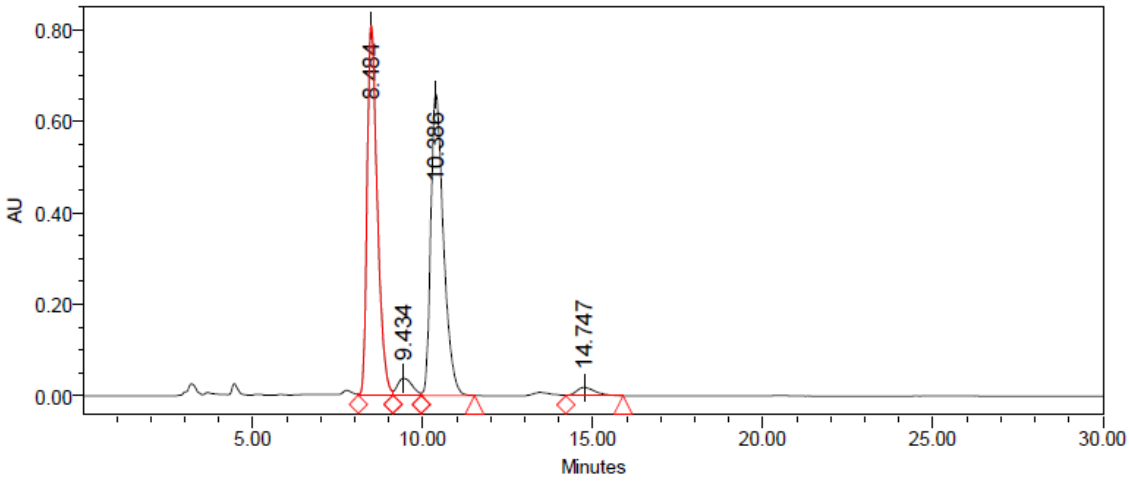
Compound (1*R*,3*R*)-**11e** was obtained in 77% yield (224 mg) as a colorless oil. Its diastereomer **12e** and regioisomers **22e** were not detected. *aza*-Michael adducts **13e** (15 mg, 5%) were also isolated. **Rf** = 0.15 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.91 (tt, *J* = 12.3, 3.7 Hz, 1H), 2.85-2.61 (m, 2H), 2.56-2.22 (m, 3H), 2.20-1.89 (m, 3H), 1.85-1.49 (m 10H), 1.28 (s, 3H), 1.34-1.04 (m, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 213.4, 179.0, 176.5, 51.6, 51.5, 45.8, 38.5, 36.3, 32.9, 28.7, 27.1, 25.9, 25.2, 21.6, 21.0; **IR** (neat) 1769, 1711, 1681, 1450, 1401, 1378 cm^{-1}; **HRMS (ESI)** m/z calcd for $C_{17}H_{25}NO_3Na$, 314.1732 found 314.1724; **IR** (neat) 2850, 1711, 1681, 1450, 1401, 1378, 1277, cm^{-1}.


7.26
3.99
3.98
3.96
3.95
3.94
3.92
3.91
3.89
3.88
2.80
2.76
2.72
2.68
2.49
2.45
2.39
2.31
2.28
2.18
2.10
2.00
1.77
1.73
1.68
1.56
1.35
1.31
1.26
1.23
1.20
1.16
1.09
1.00
1.95
3.90
3.36
10.34
6.72
f1 (ppm)


213.42
178.99
176.45
77.16
51.64
51.45
45.78
38.46
36.30
32.86
28.72
27.10
25.93
25.16
21.60
21.03
f1 (ppm)

HPLC: (±)-**11e**. Chiralpal AD, Solvent: Hexane/*i*-PrOH = 80:20, Flow Speed 1.0 mL/min, UV: 215nm, retention times: 8.484, 10.386 min.

LW C101-1B
215 nm

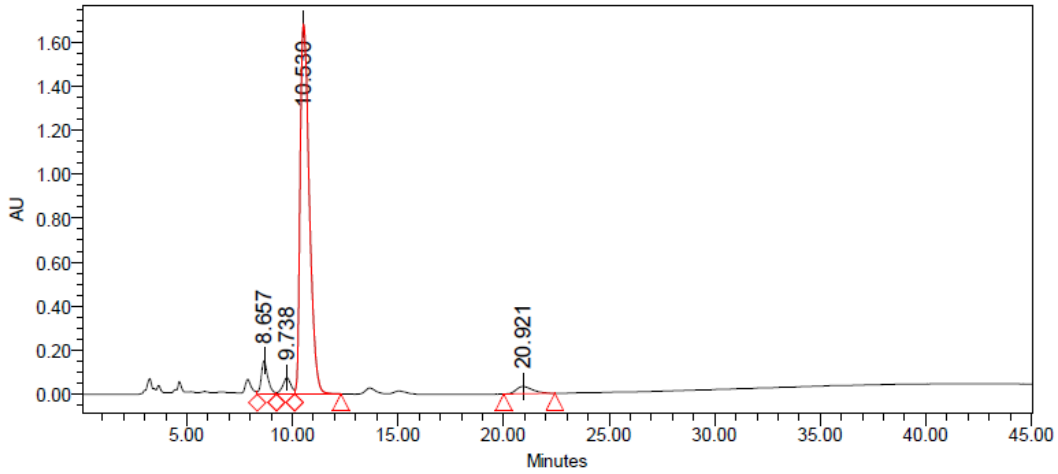


	Retention Time	Area	% Area	Height	Int Type	Start Time	End Time	% Height	Width
1	8.484	16903244	47.15	809150	VV	8.107	9.123	53.13	61.000
2	9.434	1115984	3.11	36823	VV	9.123	9.957	2.42	50.000
3	10.386	17110453	47.73	658382	VB	9.957	11.523	43.23	94.000
4	14.747	721098	2.01	18480	VB	14.207	15.890	1.21	101.000

HPLC. (1*R*,3*R*)-**11g**. Chiralpal AD, Solvent: Hexane/i-PrOH = 80:20, Flow Speed 1.0 mL/min, UV: 215nm, 93% ee, retention time: 10.530 min.

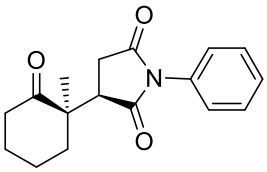
Colonne CHIRALCEL AD Hexane / isopropanol 80 : 20

LW C100-1A
215 nm

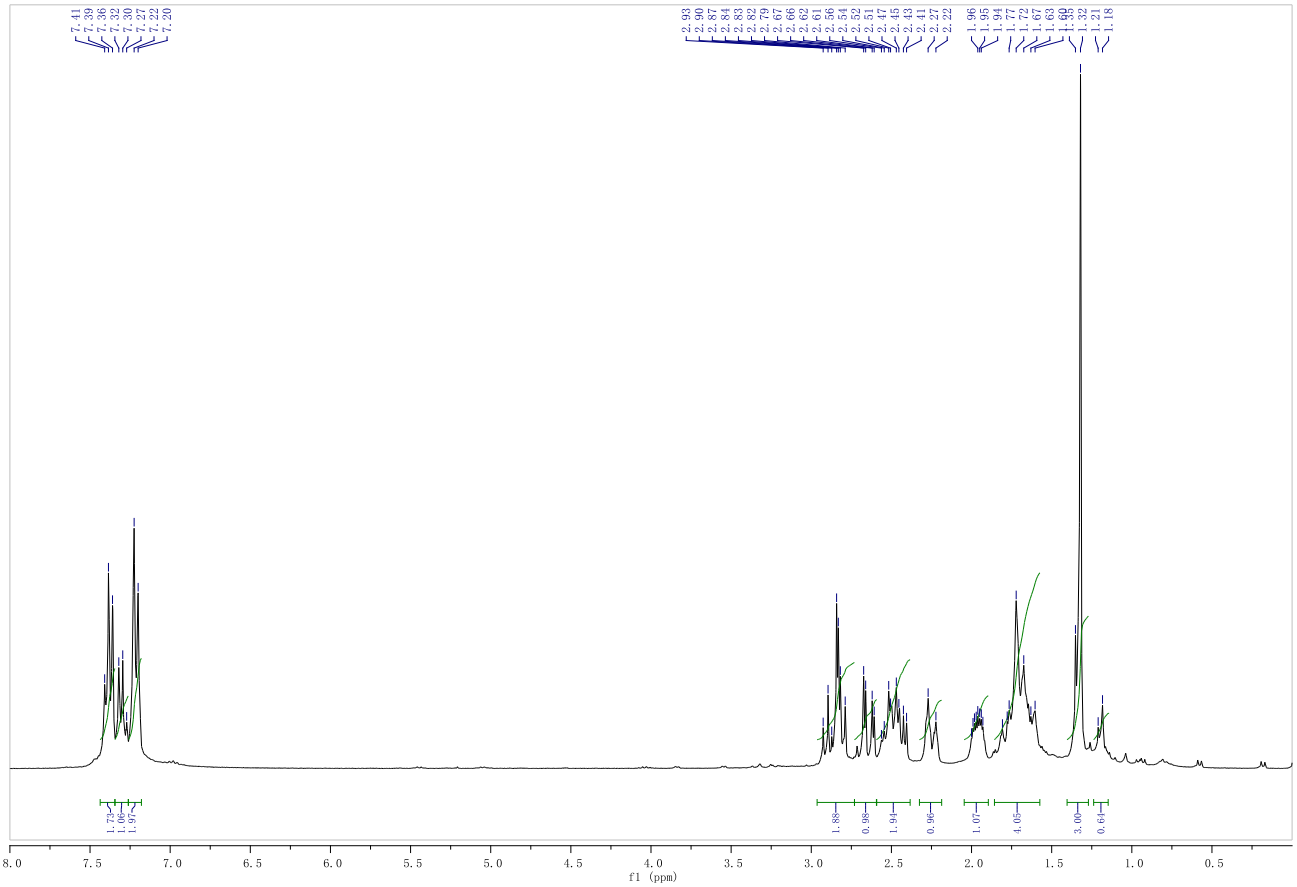


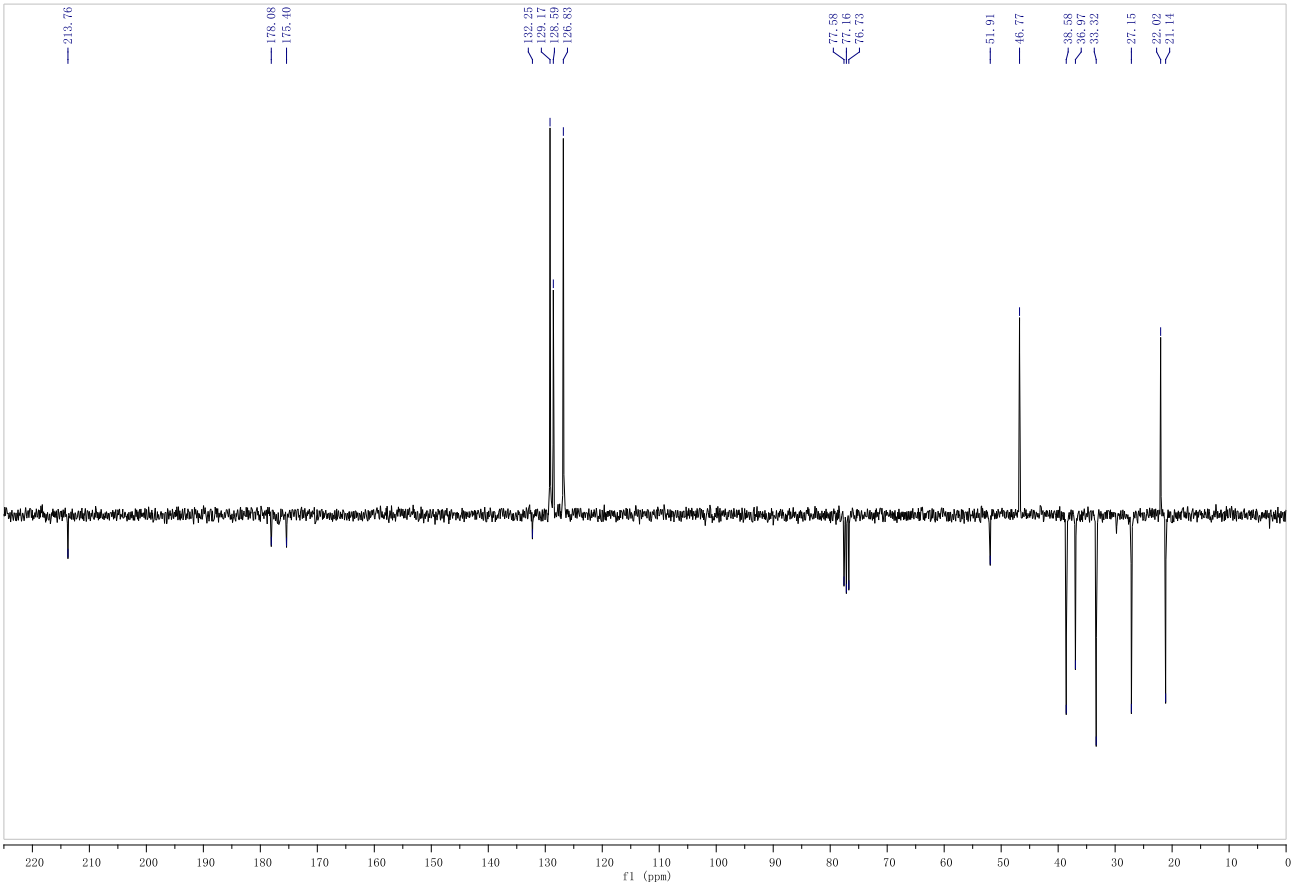
	Retention Time	Area	% Area	Height	Int Type	Start Time	End Time	% Height	Width
1	8.657	3283192	5.66	151424	VV	8.327	9.243	7.80	55.000
2	9.738	2006042	3.46	74980	VV	9.243	10.110	3.86	52.000
3	10.530	50904978	87.82	1681779	VB	10.110	12.293	86.64	131.000
4	20.921	1773481	3.06	32860	BB	20.010	22.427	1.69	145.000

(*R*)-3-((*R*)-1-Methyl-2-oxocyclohexyl)-1-phenylpyrrolidine-2,5-dione (1*R*,3*R*)-11f

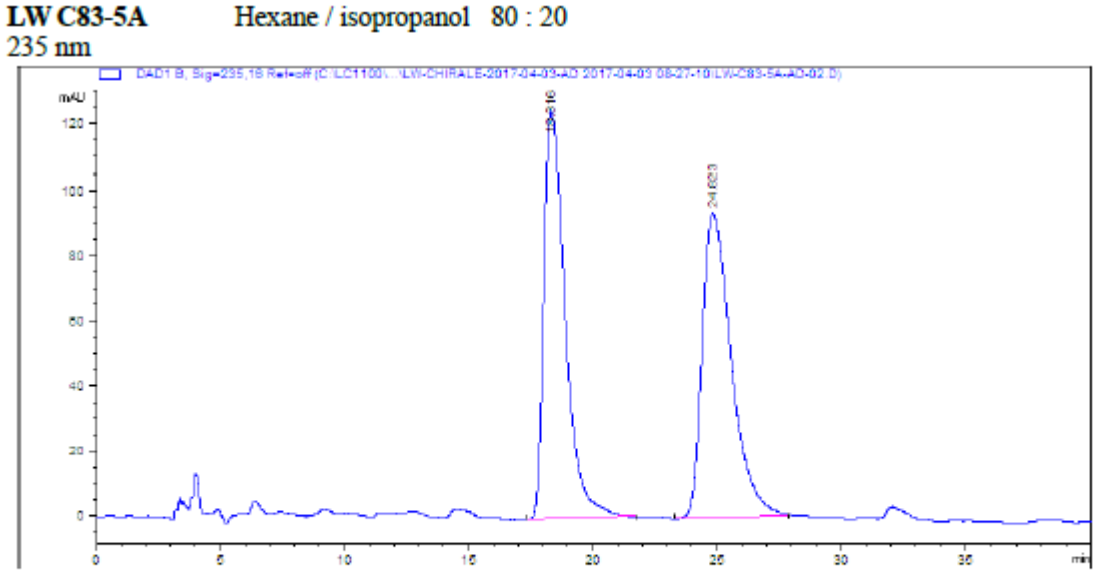


Compound (1*R*,3*R*)-**11f** was obtained in 67% yield (149 mg) as a colorless oil containing inseparable traces of its regioisomers **22f**. Its diastereomer **12f** was not detected. *aza*-Michael adducts **13f** (18 mg, 6%) were also isolated. **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.62-7.20 (m, 5H), 2.96-2.77 (m, 2H), 2.64 (dd, *J* = 15.9, 3.8 Hz, 1H), 2.60-2.36 (m, 2H), 2.32-2.18 (m, 1H), 2.05-1.90 (m, 1H), 1.86-1.57 (m, 4H), 1.32 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 213.8, 178.0, 175.4, 132.2, 129.2, 128.6, 126.8, 51.9, 46.8, 38.6, 37.0, 33.3, 27.1, 22.0, 21.1; **HRMS (ESI)** m/z calcd for $[C_{17}H_{19}NNaO_3]^+$, 308.1257, found 308.1259; **IR** (neat) 1769, 1696, 1596, 1494, 760, 701 cm^{-1}.



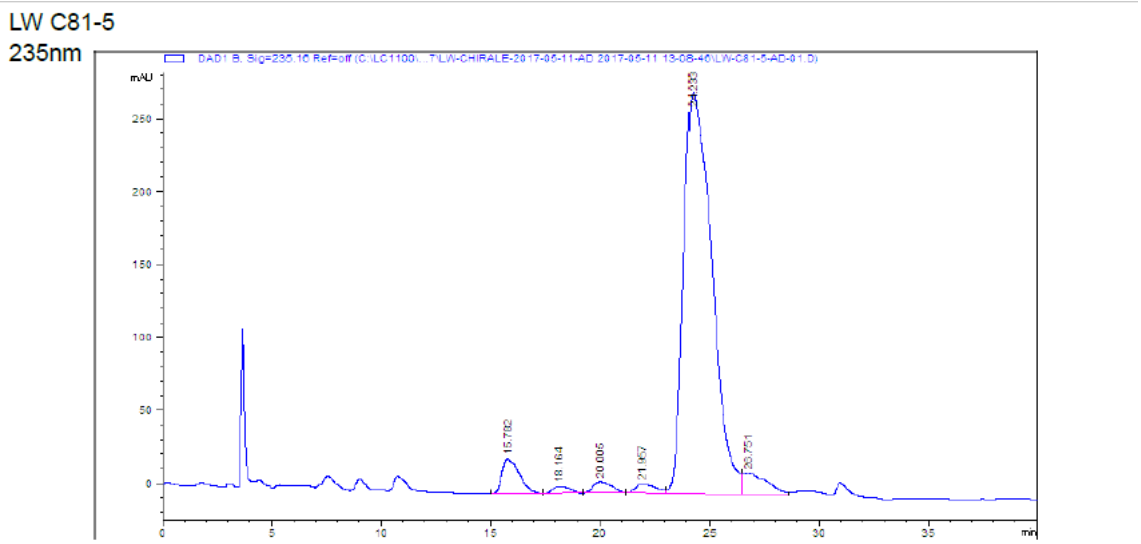


HPLC: (±)-**11f**. Chiralcel AD-H, *i*-PrOH/hexane = 20:80, 1 mL/min, 235 nm, retention times: 18.316, 24.823 min.



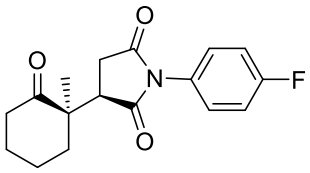
#	Time	Area	Height	Width	Area%	Symme-try
1	18.316	7468.6	124.7	0.7069	49.314	0.519
2	24.823	7676.4	93.8	0.962	50.686	0.563

HPLC. (1*R*,3*R*)-**11h**. Chiralcel AD-H, *i*-PrOH/hexane = 20:80, 1 mL/min, 235 nm; 98% ee, retention time: 18.16, 24.23 min.

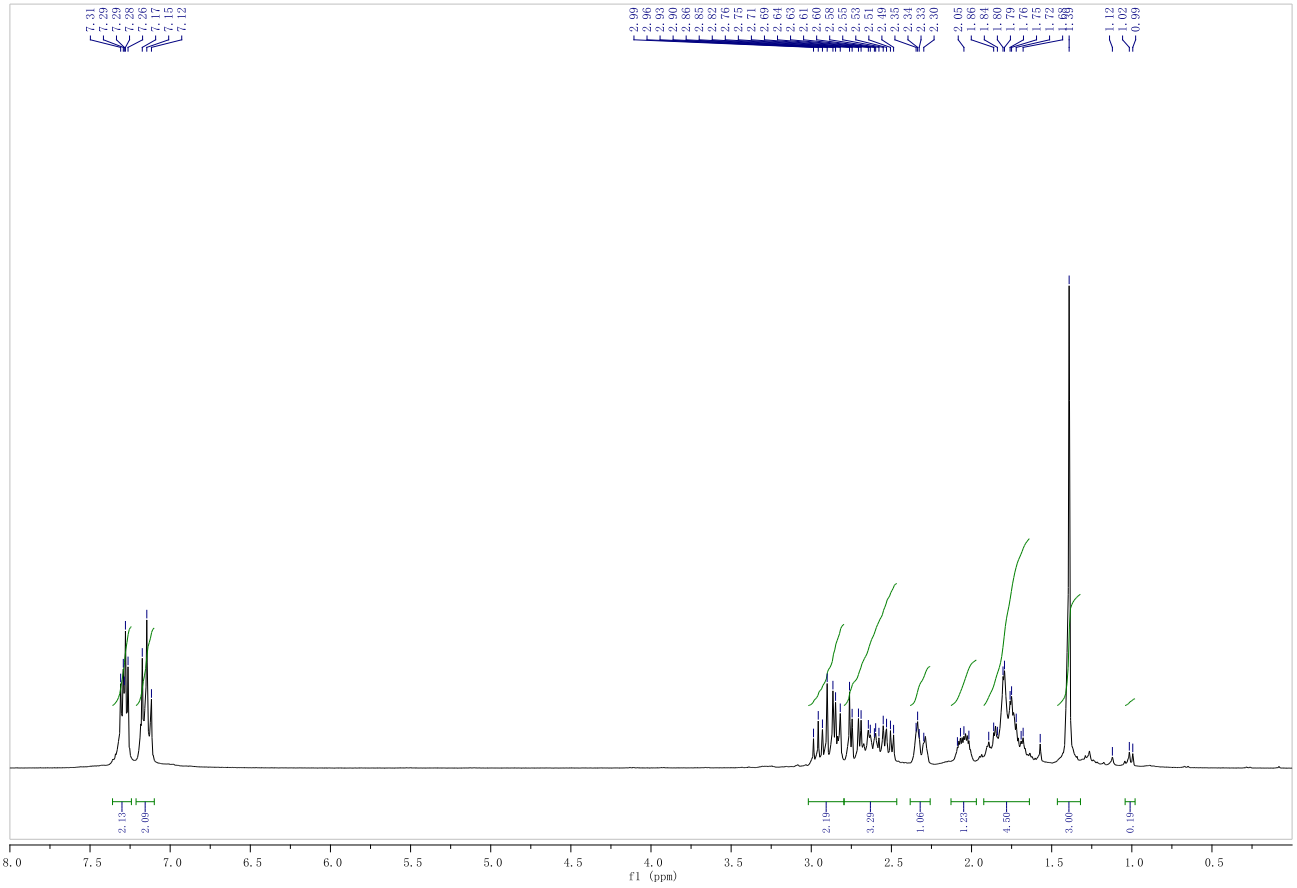


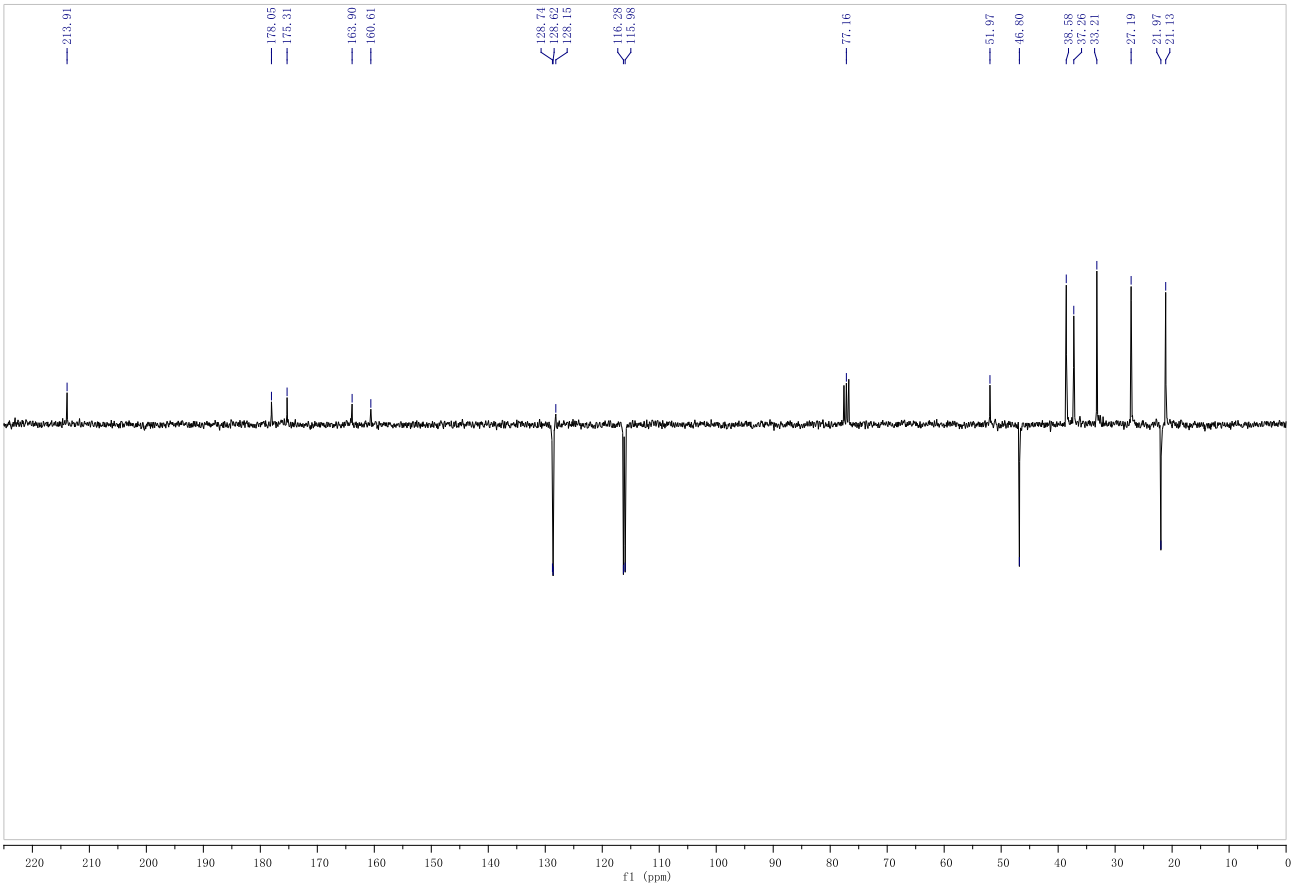
#	Time	Area	Height	Width	Area%	Symmetry
1	15,78	1300,20	23,70	0,77	4,69	0,46
2	18,16	253,50	4,50	0,67	0,92	0,62
3	20,01	451,60	7,70	0,70	1,63	0,57
4	21,96	401,20	6,10	0,79	1,45	0,48
5	24,23	24140,00	275,30	1,22	87,11	0,47
6	26,75	1165,30	15,00	0,93	4,21	0,23

(*R*)-1-(4-Fluorophenyl)-3-((*R*)-1-methyl-2-oxocyclohexyl)-2,5-pyrrolidinedione (1*R*, 3*R*)-11i



Compound (1*R*,3*R*)-**11i** was obtained in 70% yield (212 mg) as a colorless oil containing inseparable traces of its regioisomers **22i**. Its diastereomer **12i** was not detected. *aza*-Michael adducts **13i** (16 mg, 5%) were also isolated. **Rf** = 0.1 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.31-7.12 (m, 4H), 3.00-2.80 (m, 2H), 2.80-2.45 (m, 3H), 2.35-2.30 (m, 1H), 2.10-2.00 (m, 1H), 1.90-1.60 (m, 4H), 1.39 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 213.9, 178.0, 175.3, 162.2 (d, *J* = 246.7 Hz), 128.6 (d, *J* = 9 Hz), 128.1, 116.1 (d, *J* = 22.5 Hz), 52.0, 46.8, 38.6, 37.3, 33.2, 27.2, 22.0, 21.1; **HRMS (ESI)** m/z calcd for $C_{17}H_{18}NO_3FNa$, 326.1168 found 326.1161; **IR** (neat) 1770, 1696, 1506, 769 cm^{-1}.

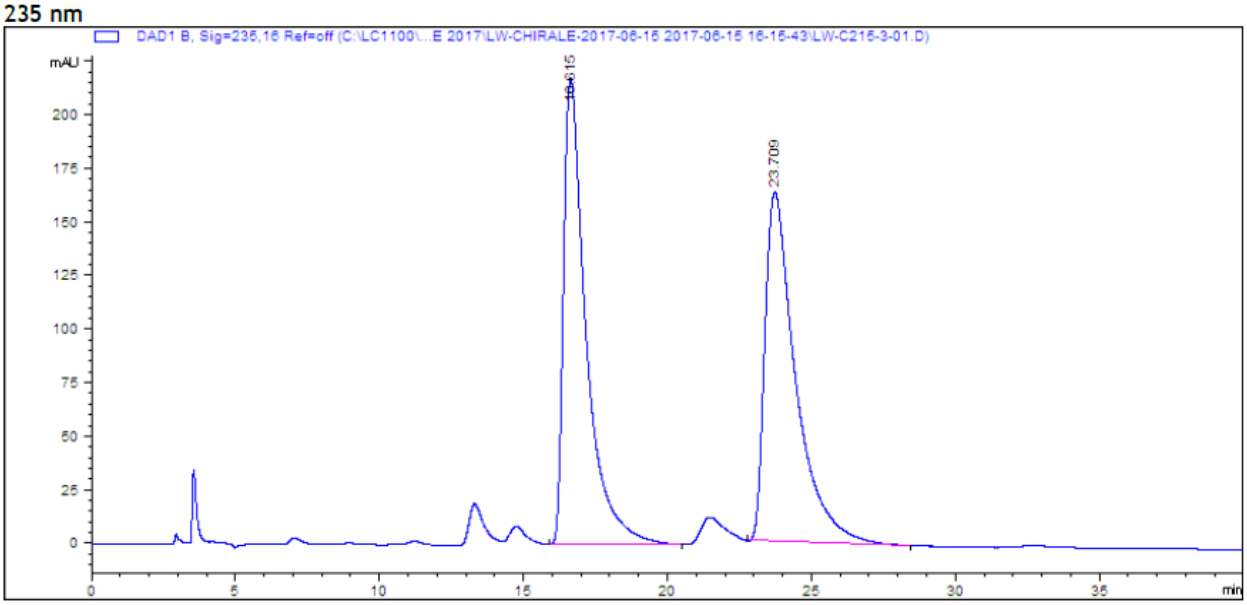

7.31
7.29
7.29
7.28
7.28
7.26
7.17
7.15
7.12
2.99
2.96
2.93
2.90
2.86
2.85
2.82
2.76
2.75
2.71
2.68
2.64
2.63
2.61
2.60
2.58
2.55
2.53
2.51
2.49
2.35
2.34
2.33
2.30
2.05
1.86
1.84
1.80
1.79
1.76
1.75
1.72
1.12
1.02
0.99
2.13
2.09
2.19
3.29
1.06
1.23
4.56
3.00
0.19
f1 (ppm)


213.91
178.05
175.31
163.90
160.61
128.74
128.62
128.15
116.28
115.98
77.16
51.97
46.80
38.58
37.26
33.21
27.19
21.97
21.13
f1 (ppm)

HPLC: (±)-**11i**. Chiralcel AD-H, *i*-PrOH/hexane = 20:80, 1 mL/min, 235 nm; retention times: 16.615, 23.709 min.

Colonne CHIRALCEL AD

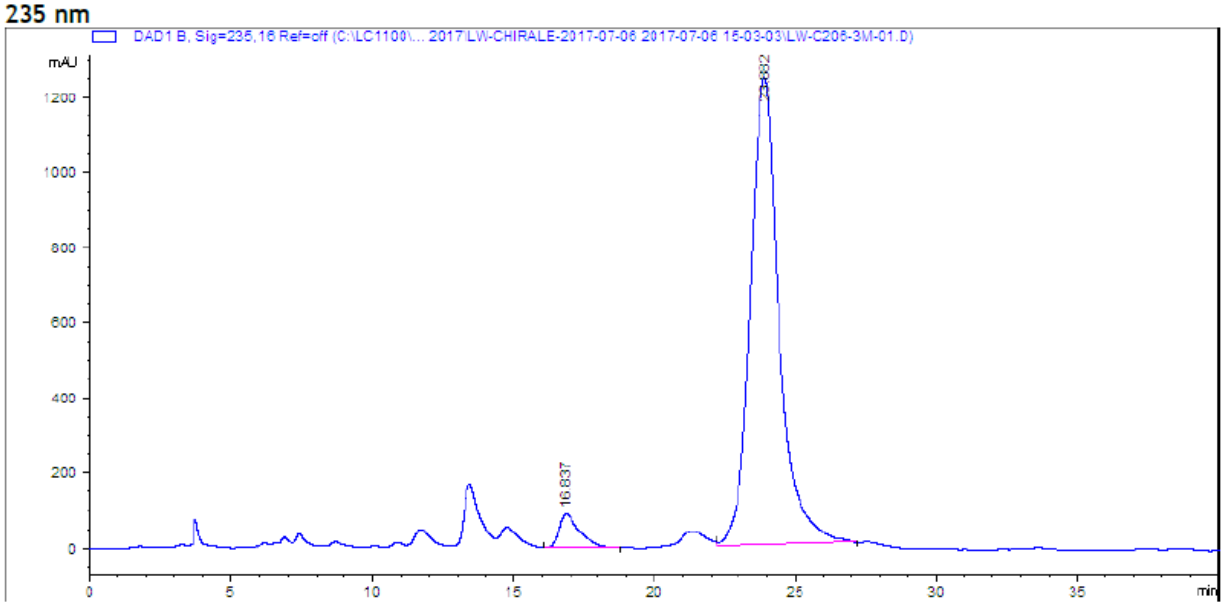
LW C215-3 **hexane / isopropanol 80 : 20**
235 nm



#	Time	Area	Height	Width	Area%	Symmetry
1	16.615	11852.9	217.4	0.77	49.423	0.411
2	23.709	12129.5	163	1.03	50.577	0.441

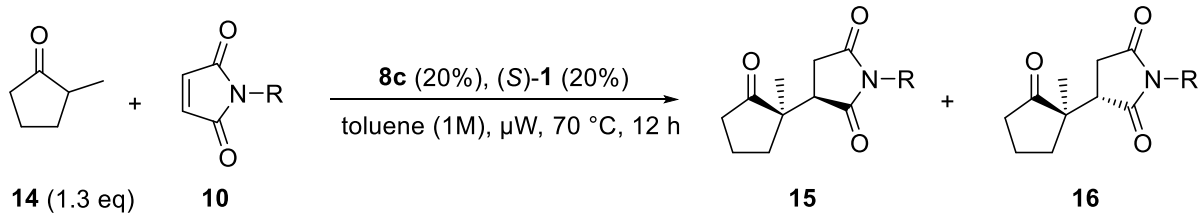
HPLC: (1*R*, 3*R*)-**11k**. Chiralcel AD-H, *i*-PrOH/hexane = 20:80, 1 mL/min, 235 nm; 91% ee, Retention time: 23.882 min.

LW C206-3M **hexane / isopropanol 80 : 20**
235 nm



#	Time	Area	Height	Width	Area%	Symmetry
1	16.837	4397.4	88.8	0.654	4.719	0.473
2	23.882	88779.7	1243	0.8403	95.281	0.922

7. Scope of reaction of α-methyl cyclopentanone 14 with respect to the maleimide

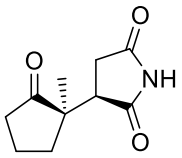


Scheme S3. Scope of reaction of **14** with respect to maleimides, general scheme (Table 4, see text).

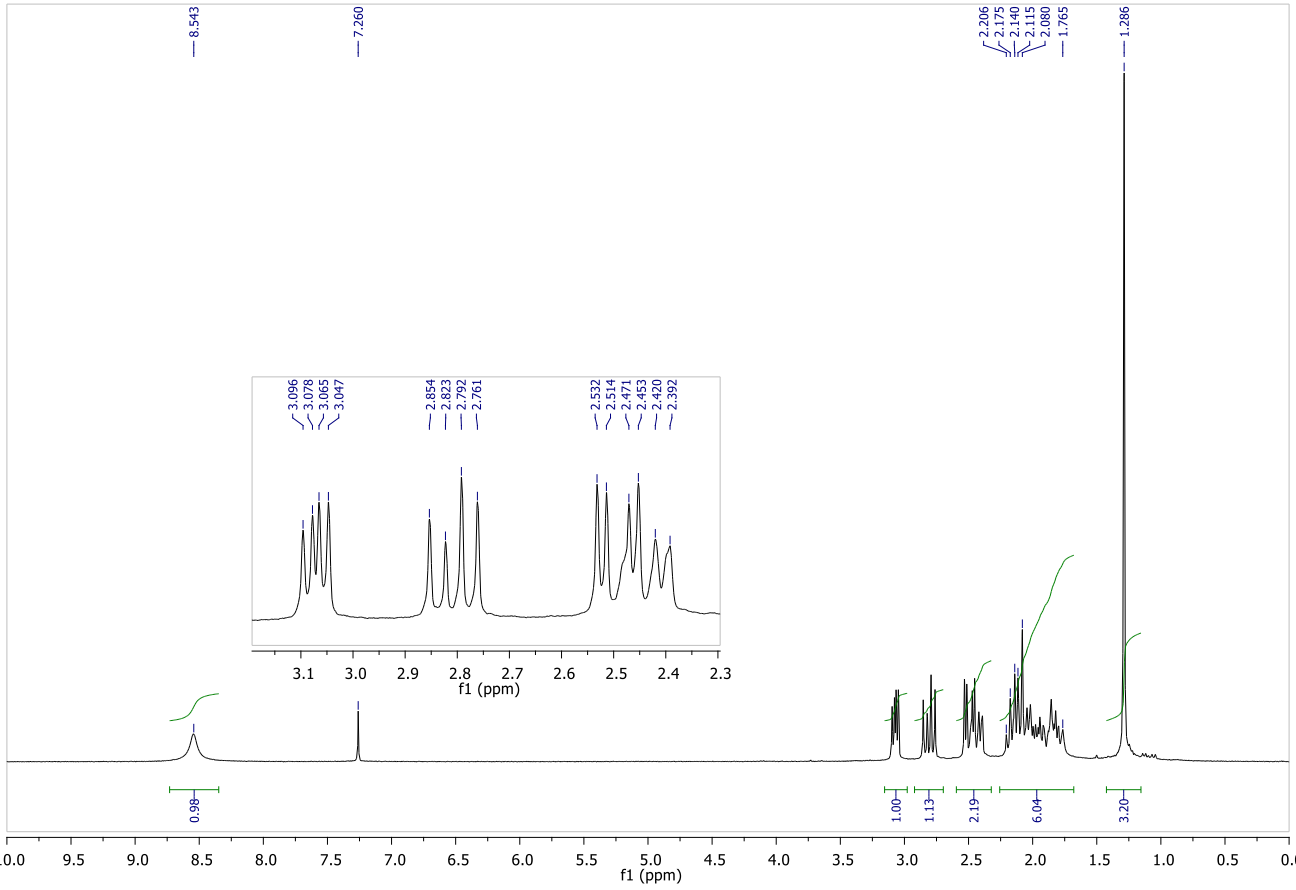
General procedure:

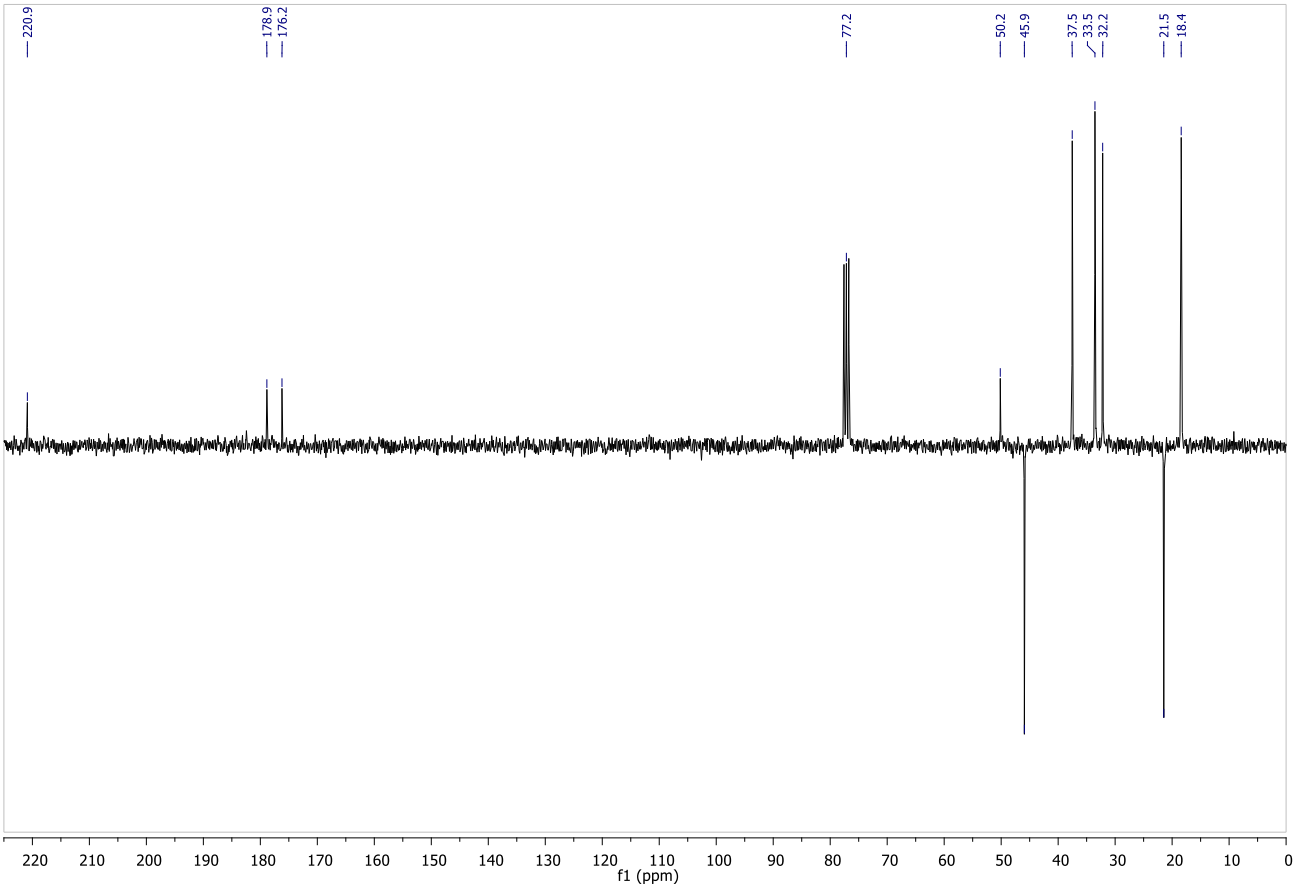
A mixture of α-methyl cyclopentanone **14** (1.3 mmol), maleimides **10** (1 mmol), (*S*)-1-phenylethylamine **1** (0.2 eq) and co-catalyst acid **8c** (0.2 eq) in toluene (1 mL) was stirred for 12 h at 70 °C under μW irradiation. The reaction mixture was concentrated and the resulting residue chromatographed over silica gel (cyclohexane/ethyl acetate = 5:1) to afford compounds and mixtures of products as reported in table 4 (see text).

(*R*)-3-((*R*)-1-Methyl-2-oxocyclopentyl)pyrrolidine-2,5-dione (1*R*,3*R*)-**15a**



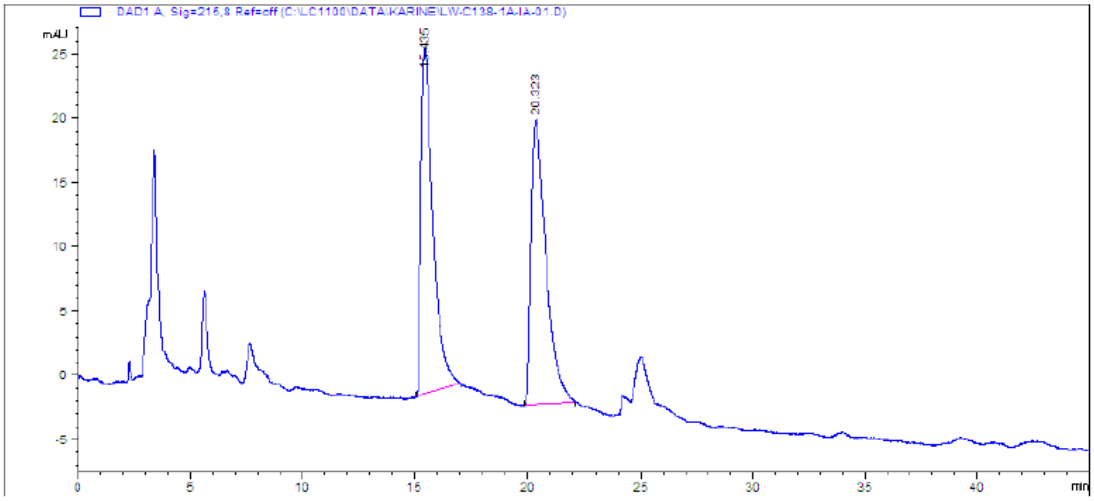
Compound (1*R*,3*R*)-**15a** was obtained in 47% yield (92 mg) as a white solid. Its diastereomer **16a** was isolated in 20% yield (39 mg) as a colorless oil. **Rf** = 0.1 (cyclohexane/EtOAc = 1:1); **m.p.** = 123.1 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.54 (bs, 1H), 3.07 (dd, *J* = 9.3, 5.4 Hz, 1H), 2.81 (dd, *J* = 18.4, 9.3 Hz, 1H), 2.49 (dd, *J* = 18.4, 9.3 Hz, 1H), 2.44 (bdd, *J* = 18.0, 8.4 Hz, 1H), 2.21-1.76 (m, 6H), 1.29 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 220.9, 178.9, 176.2, 50.2, 45.9, 37.5, 33.5, 32.2, 21.5, 18.4; **HRMS (ESI)** m/z calcd for $[C_{10}H_{14}NO_3]^+$ 196.0968, found 196.0970; **IR** (neat) 2970, 1765, 1733, 1701, 1353, 1195 cm^{-1}; **$[\alpha]^{18}_D$** = + 28.6 (c = 2.60, $CHCl_3$).


8.543
7.260
2.206
2.175
2.140
2.115
2.080
1.765
1.286
3.096
3.078
3.065
3.047
2.854
2.823
2.792
2.761
2.532
2.514
2.471
2.453
2.420
2.392
f1 (ppm)
0.98
1.00
1.13
2.19
6.04
3.20
f1 (ppm)


220.9
178.9
176.2
77.2
50.2
45.9
37.5
33.5
32.2
21.5
18.4
f1 (ppm)

HPLC: (±)-**15a**. Chiralcel AD-H, *i*-PrOH/hexane = 20:80, 1 mL/min, 215 nm; retention times: 15.44, 20.32 min.

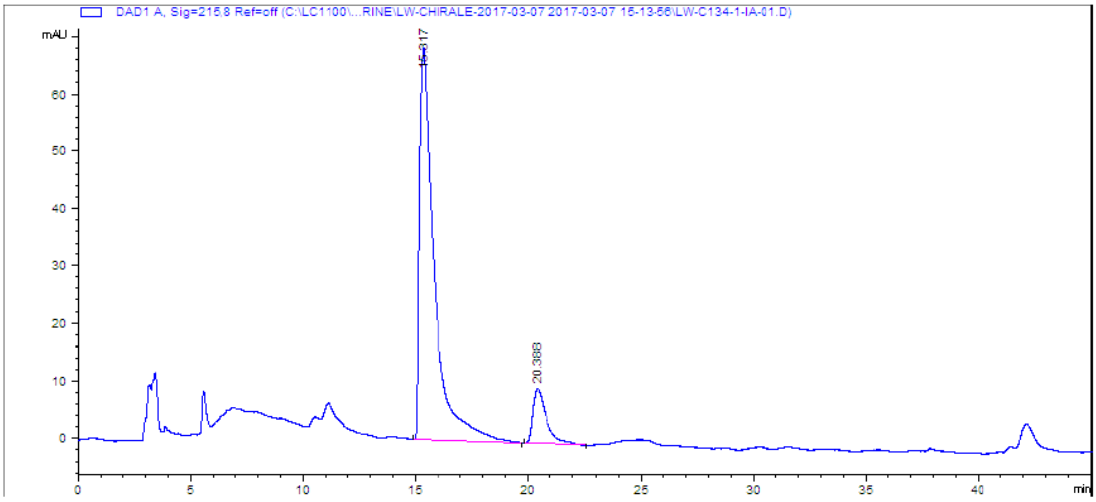
LW C138-1A **Hexane / isopropanol 80 : 20**
215 nm



MeasRetTime	CorrExpRetTime	IntPeakType	Area	Height	Width	Symmetry
15.44	0.00	BB	1006.06	26.95	0.46	0.45
20.32	0.00	BB	1024.61	22.21	0.55	0.47

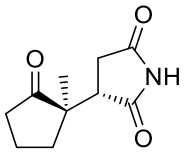
HPLC: (1*R*, 3*R*)-**15a**. Chiralcel AD-H, *i*-PrOH/hexane = 20:80, 1 mL/min, 215 nm; 77% ee, retention time: 15.32, min.

LW C134-1A Hexane / isopropanol 80 : 20
215 nm

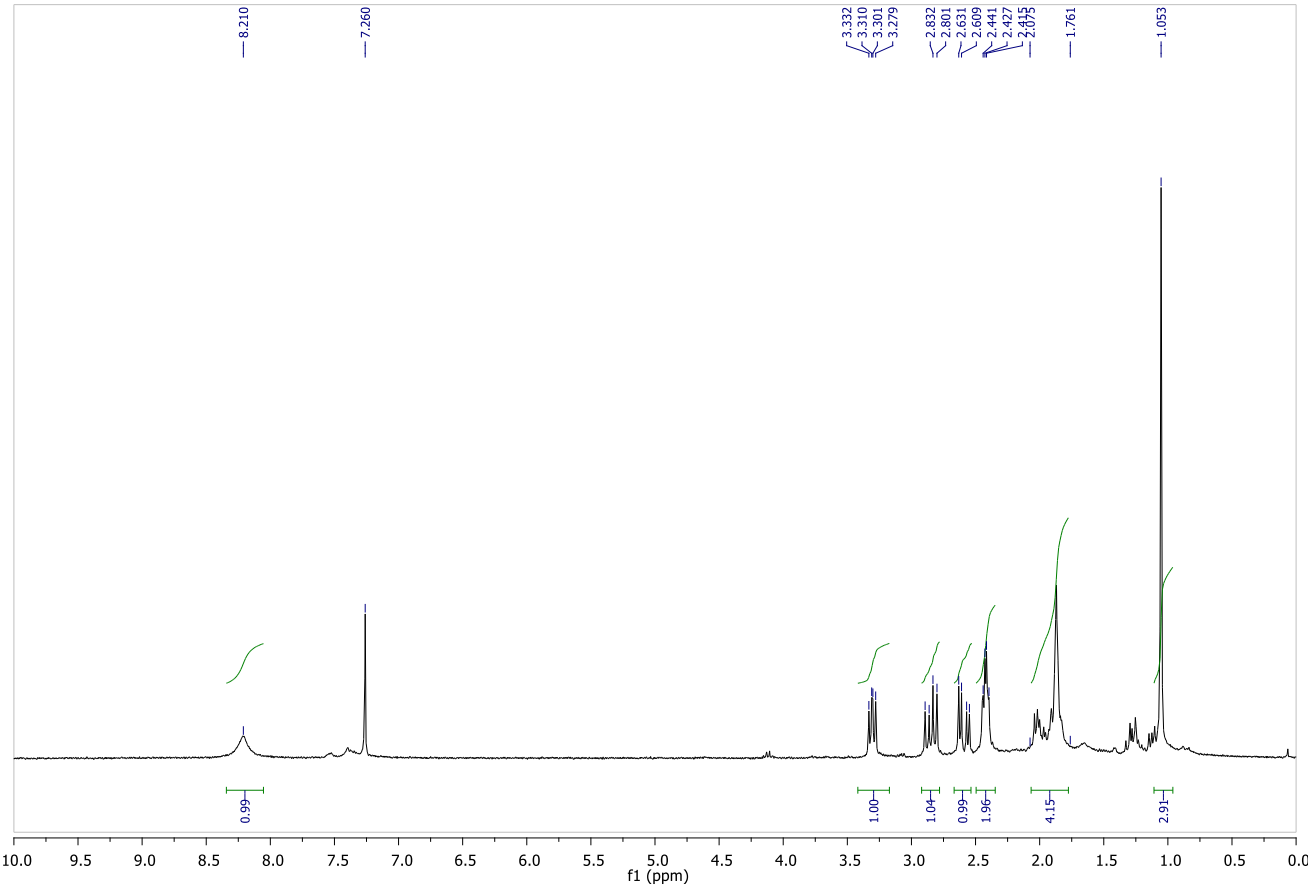


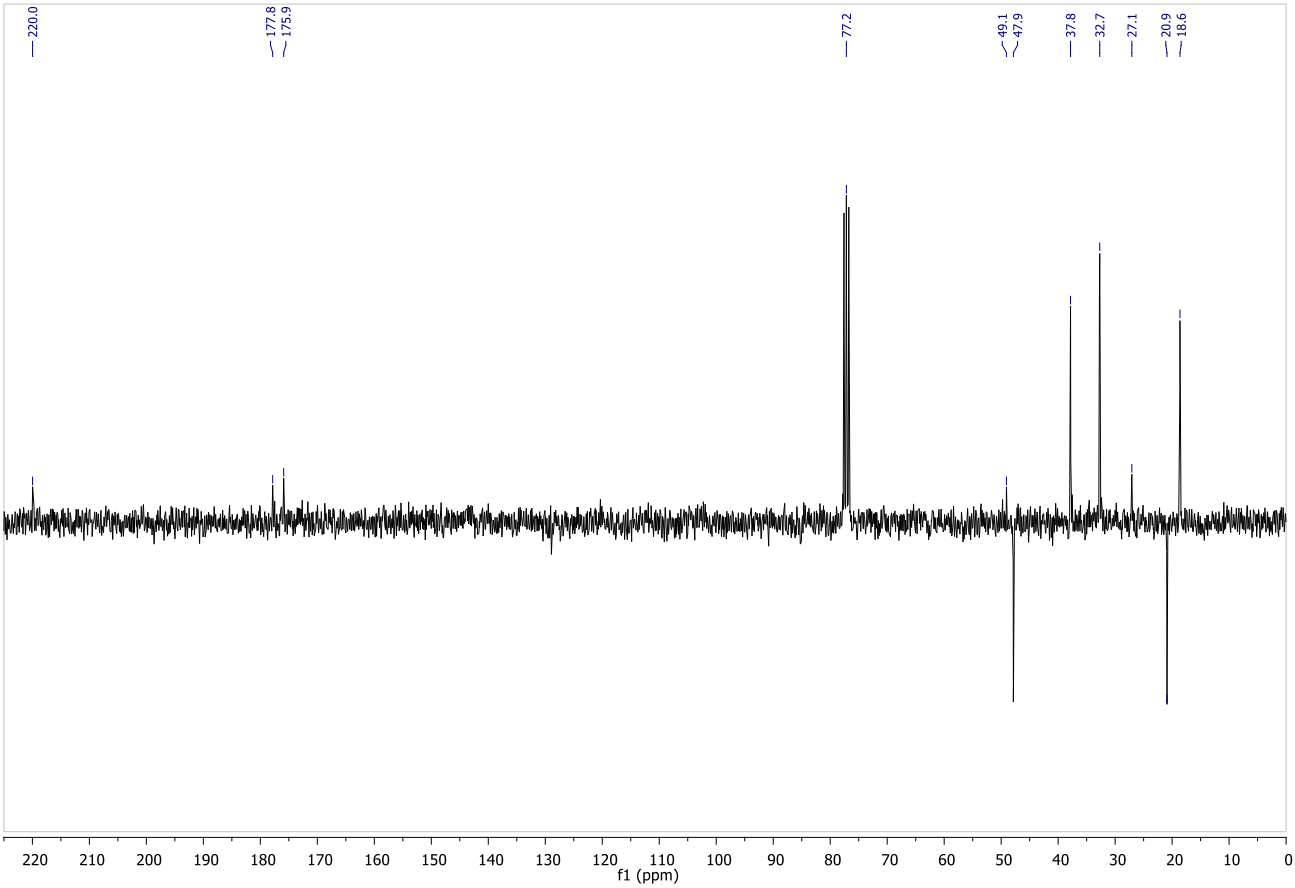
MeasRetTime	CorrExpRetTime	IntPeakType	Area	Height	Width	Symmetry
15.32	0.00	BB	3175.56	68.22	0.66	0.33
20.39	0.00	BB	409.24	9.51	0.59	0.49

(*S*)-3-((*R*)-1-Methyl-2-oxocyclopentyl)pyrrolidine-2,5-dione (1*R*,3*S*)-**16a**

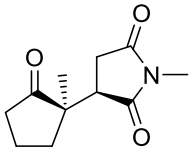


20% yield. White solid. It was not possible to obtain pure (1*R*,3*S*)-**16a**. Consequently, its NMR spectra contain traces of other impurities. **Rf** = 0.1 (cyclohexane/EtOAc = 1:1); **m.p.** not determined due to presence of impurities; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.21 (s, 1H), 3.30 (dd, *J* = 9.0, 6.6 Hz, 1H), 2.85 (dd, *J* = 18.3, 9.4 Hz, 1H), 2.59 (dd, *J* = 18.3, 6.7 Hz, 1H), 2.48-2.38 (m, 2H), 2.06-1.80 (m, 4H), 1.05 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 220.0, 177.8, 175.9, 49.1, 47.9, 37.8, 32.8, 27.1, 20.9, 18.6; **HRMS (ESI)** m/z calcd for $[C_{10}H_{14}NO_3]^+$ 196.0968, found 196.0970; **IR** (neat) 2961, 1772, 1737, 1709, 1697, 1346, 1188 cm^{-1}.



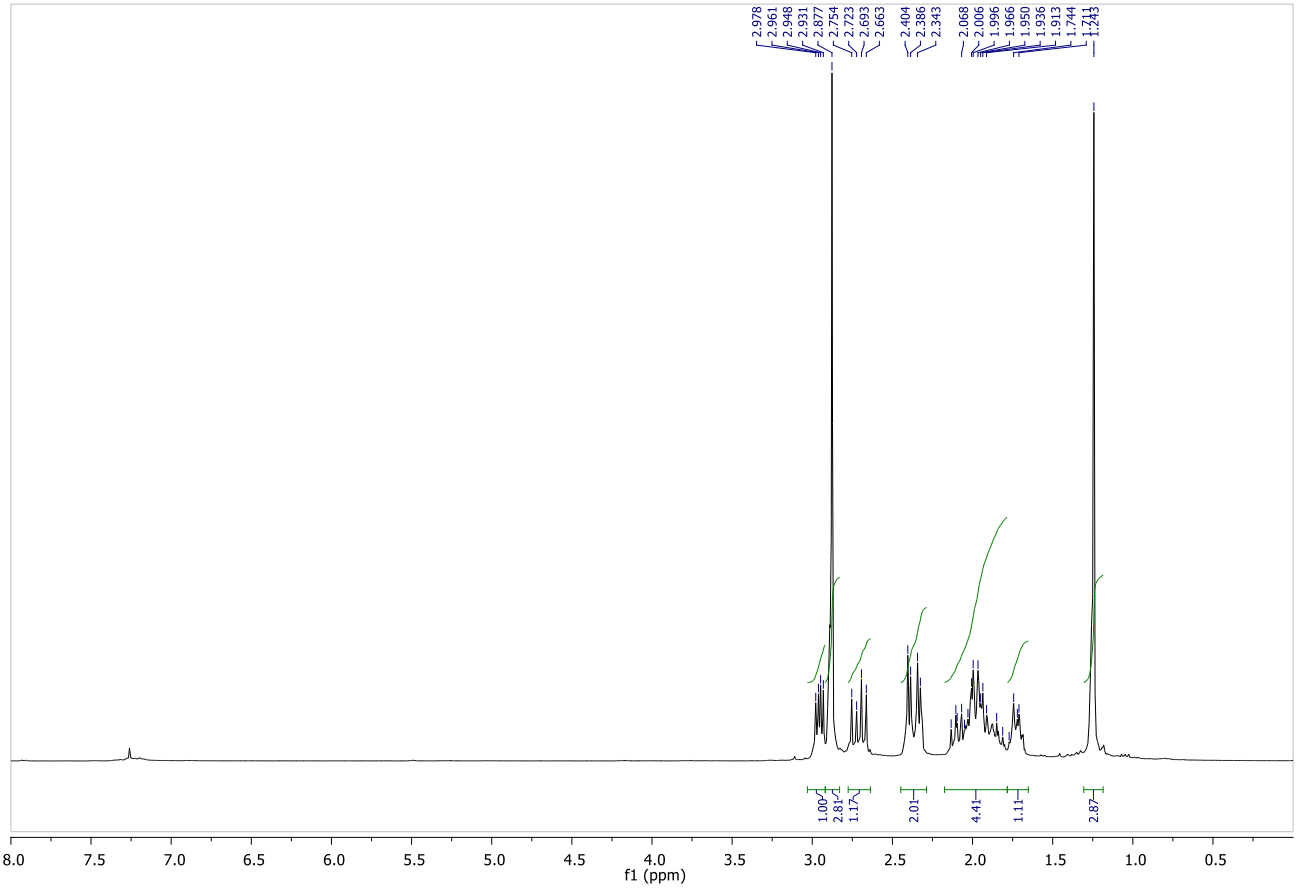


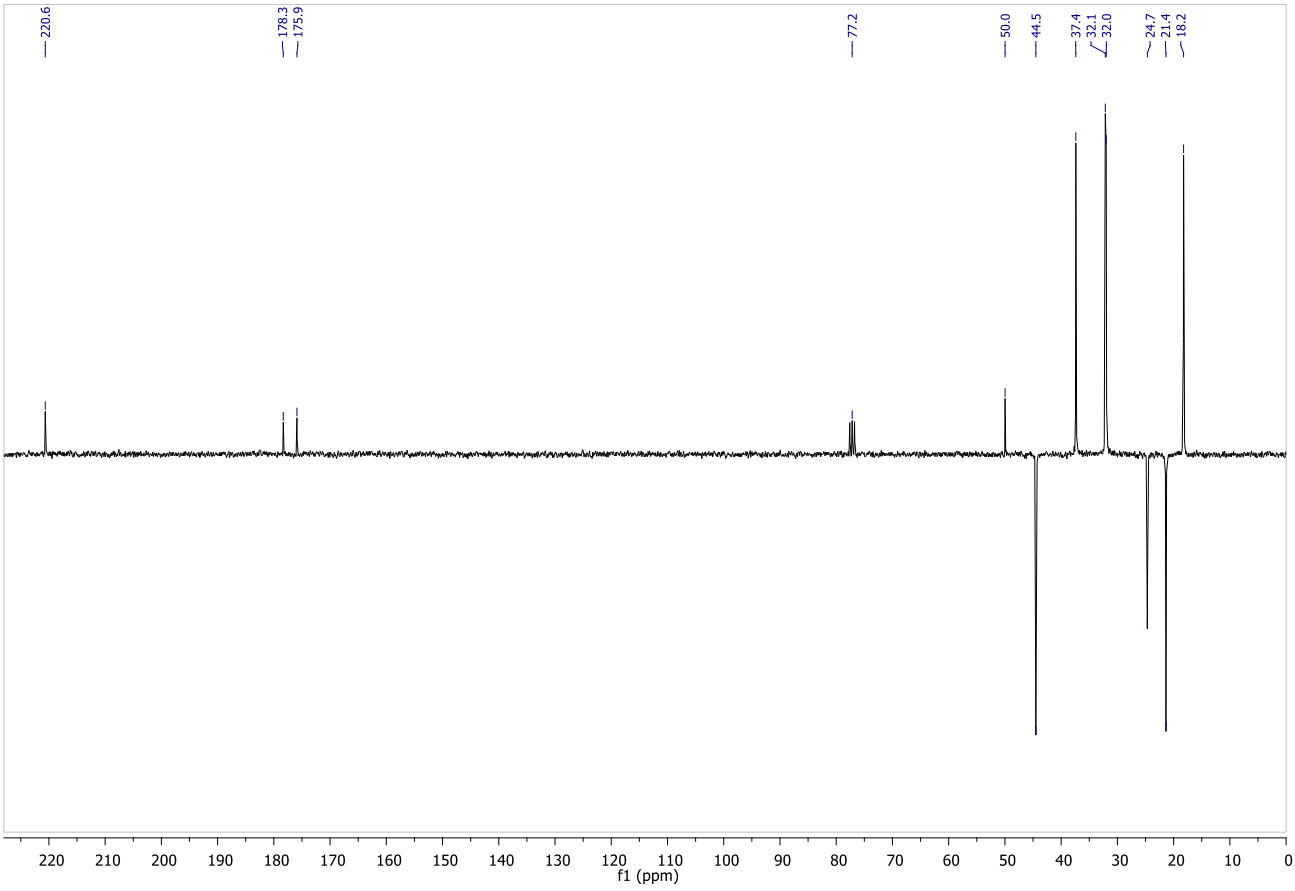
(*R*)-1-Methyl-3-((*R*)-1-methyl-2-oxocyclopentyl)-2,5-pyrrolidinedione (1*R*, 3*R*)-15b



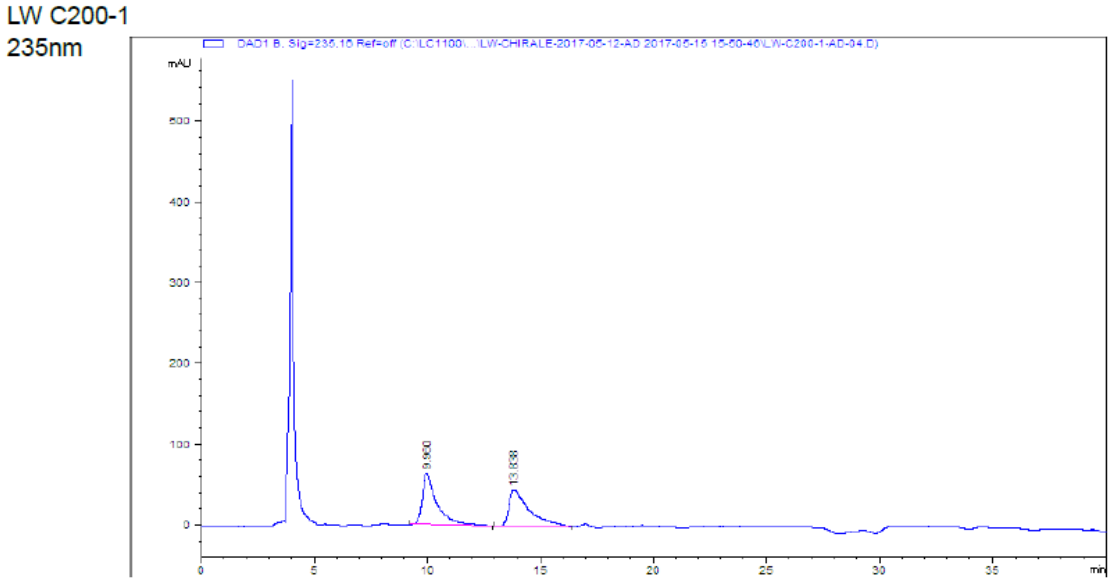
Compound (1*R*,3*R*)-**15b** was obtained as a white solid in 52% yield (109 mg) (dr = 78:22, ee = 92%). Its diastereomer **16b** was isolated in 15% yield (31 mg). Minor quantities of *aza*-Michael adducts and regioisomers were detected by ^{1}H NMR analysis of the crude reaction mixtures but not isolated.

(1*R*,3*R*)-**15b** : **m.p.** 65.3 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 2.95 (dd, *J* = 9.1, 5.3 Hz, 1H), 2.88 (s, 3H), 2.70 (dd, *J* = 18.2, 9.1 Hz, 1H), 2.40-2.30 (m, 1H), 2.35 (dd, *J* = 18.2, 5.3 Hz, 1H), 2.10–1.70 (m, 5H), 1.24 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 220.6, 178.3, 175.9, 50.0, 44.5, 37.4, 32.1, 32.0, 24.7, 21.4, 18.2; **HRMS (ESI)** m/z calcd for $[C_{11}H_{15}NNaO_3]^+$ 232.0950, found 232.0953; **IR** (neat) 2966, 1765, 1734, 1693 cm^{-1}; $[\alpha]^{29}_{D}$ = + 126.5 (c = 8.45, $CHCl_3$).


2.978
2.961
2.948
2.931
2.877
2.754
2.723
2.693
2.663
2.404
2.386
2.343
2.068
2.006
1.996
1.966
1.950
1.936
1.913
1.744
1.711
1.243
1.00
2.81
1.17
2.01
4.41
1.11
2.87
f1 (ppm)

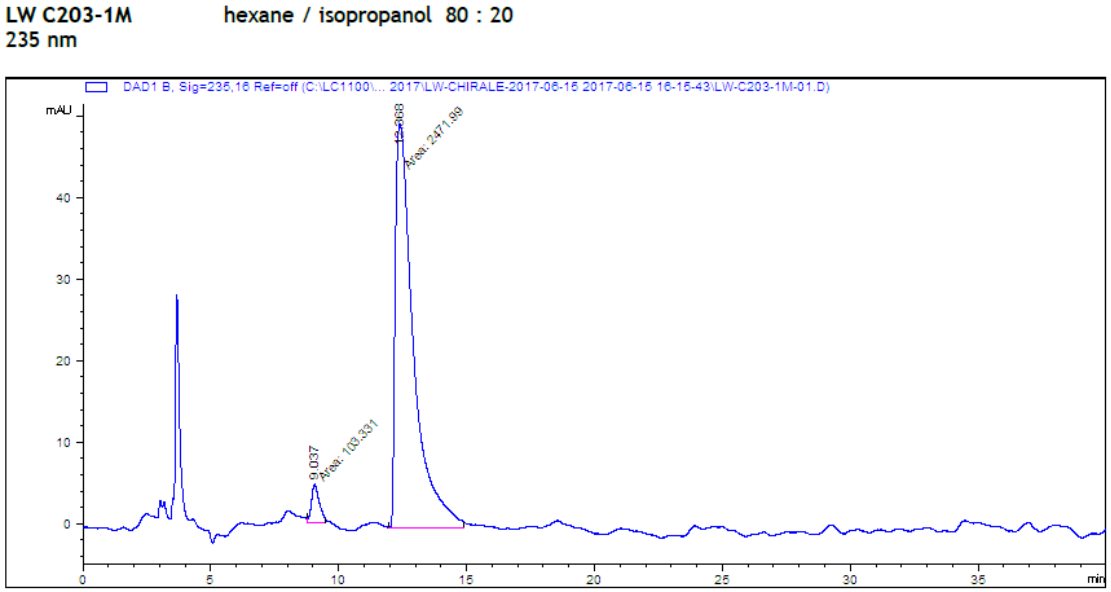

220.6
178.3
175.9
77.2
50.0
44.5
37.4
32.1
32.0
24.7
21.4
18.2
f1 (ppm)

HPLC: (±)-**15b**. Chiralcel AD-H, *i*-PrOH/hexane = 20:80, 1 mL/min, 235 nm, Flow Speed 1.0 mL/min, UV: 254 nm, retention times: 9.96, 13.84.



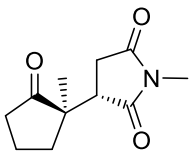
#	Time	Area	Height	Width	Area%	Symmetry
1	9,96	2902,30	63,70	0,60	50,39	0,38
2	13,84	2857,10	44,70	0,83	49,61	0,32

HPLC: (+)-(1*R*, 3*R*)-**15b**. Chiralpal AD, Solvent: Hexane/i-PrOH = 80:20, Flow Speed 1.0 mL/min, UV: 235nm, 92% ee, retention time: 12.368 min.

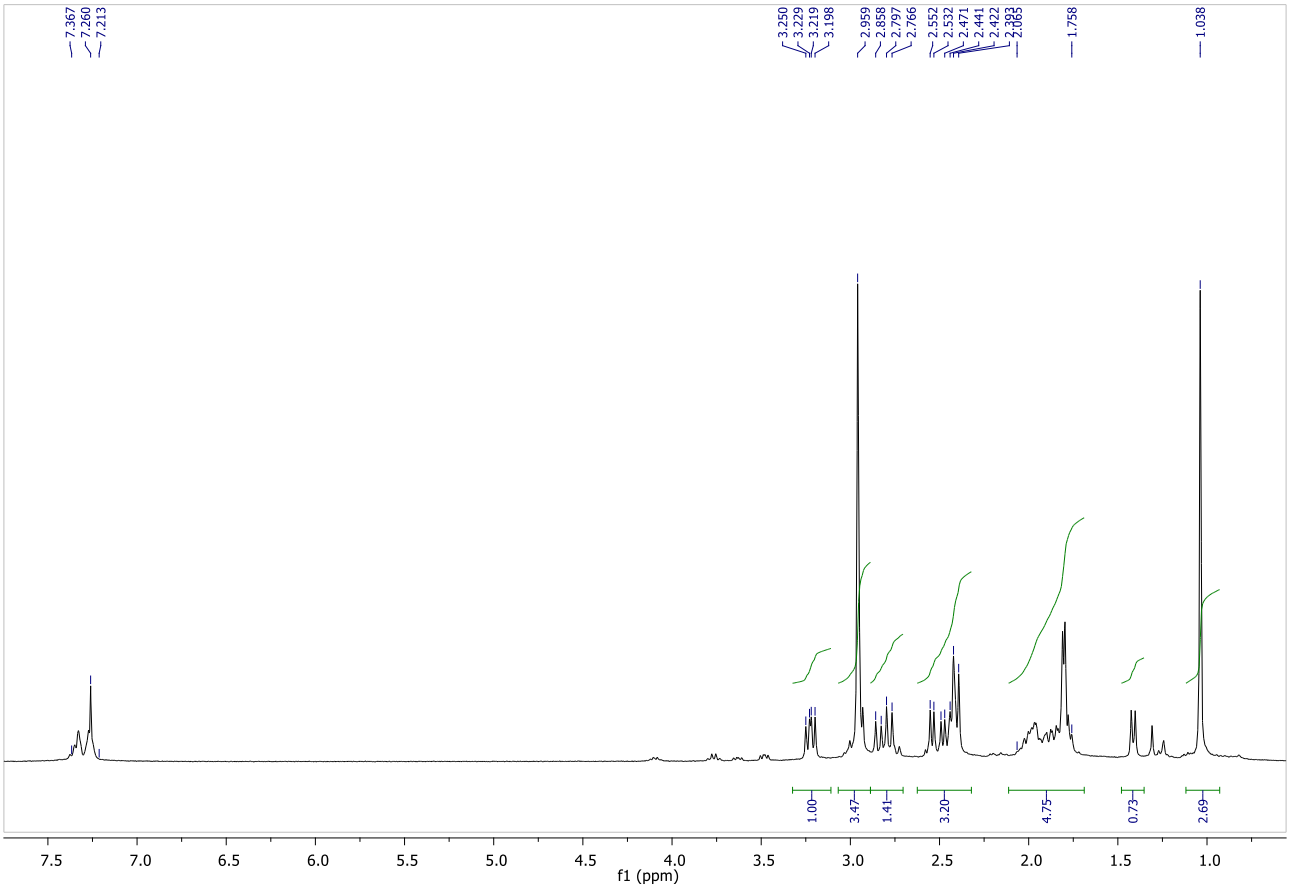


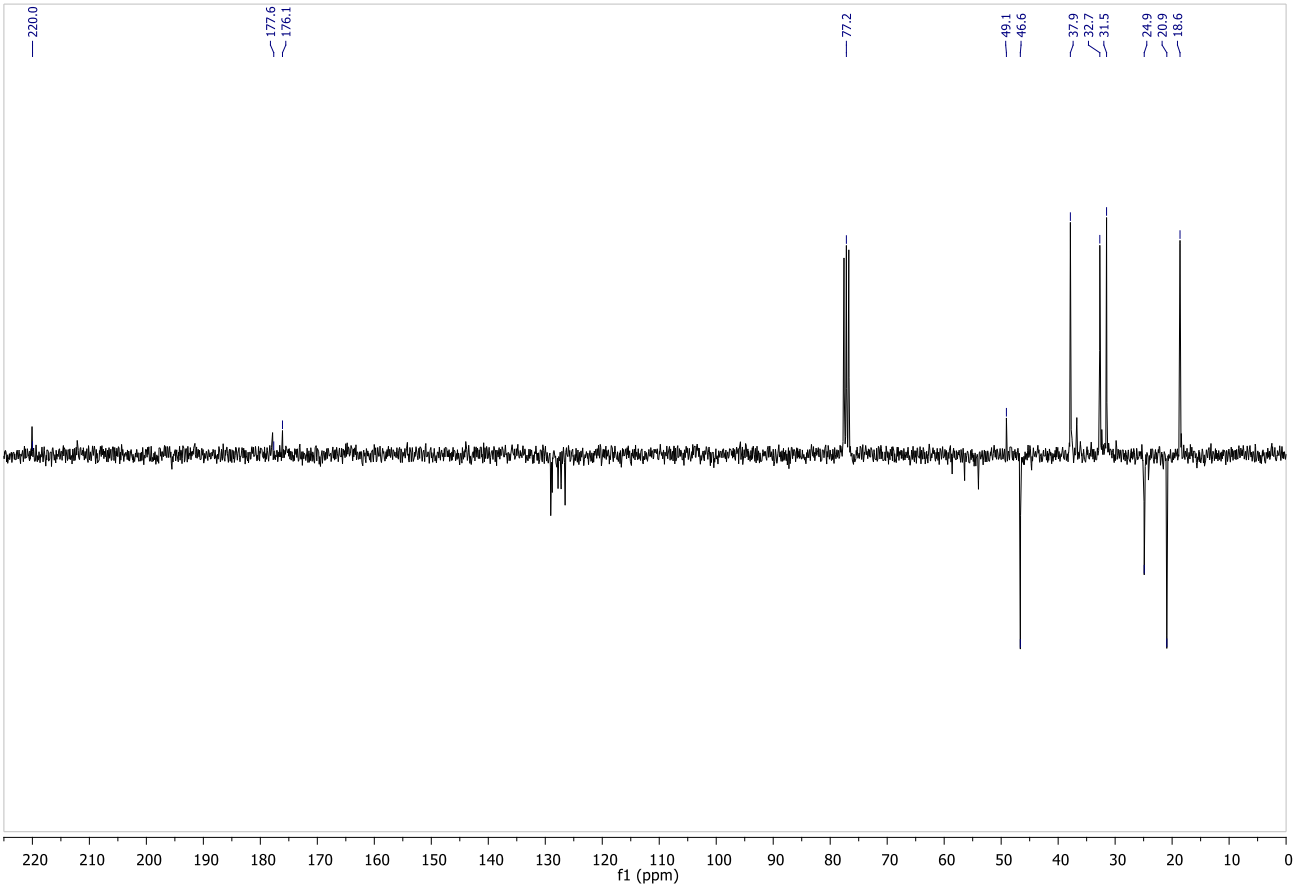
#	Time	Area	Height	Width	Area%	Symmetry
1	9.037	103.3	4.8	0.3612	4.012	0.638
2	12.368	2472	49.6	0.8309	95.988	0.311

(*S*)-1-Methyl-3-((*R*)-1-methyl-2-oxocyclopentyl)pyrrolidine-2,5-dione 16b

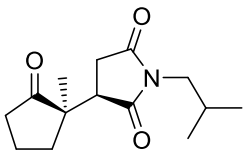


16b: 15% yield as a white solid. **m. p.** not determined due to the presence of trace impurities. It was not possible to obtain pure compound (1*R*,3*S*)-**16b** which is inseparable from small amounts of compound **13b** and other impurities. **Rf** = 0.2 (cyclohexane/EtOAc = 4:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.22 (dd, *J* = 9.2, 6.3 Hz, 1H), 2.96 (s, 3H), 2.81 (dd, *J* = 18.3, 9.3 Hz, 1H), 2.50 (dd, *J* = 18.3, 6.3 Hz, 1H), 2.50–2.32 (m, 2H), 2.06-1.76 (m, 4H), 1.04 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 220.0, 177.6, 176.1, 49.1, 46.6, 37.9, 32.7, 31.5, 24.9, 20.9, 18.6; **HRMS (ESI)** m/z calcd for $[C_{11}H_{15}NaNO_3]^+$ 232.0944, found 232.0950; **IR** (neat) 2964, 2874, 1774, 1734, 1690, 1435, 1382, 1291, 1122, 734 cm^{-1}.

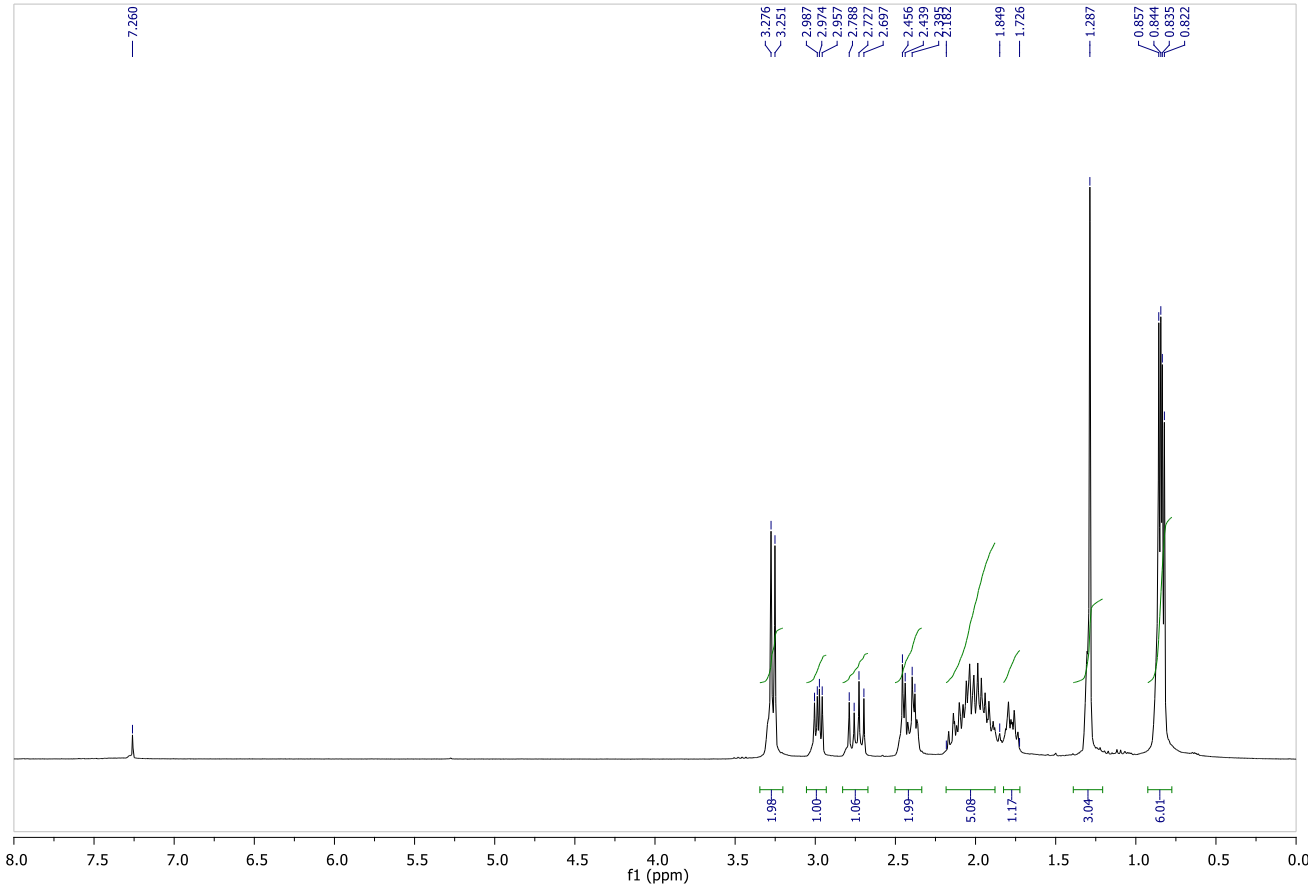


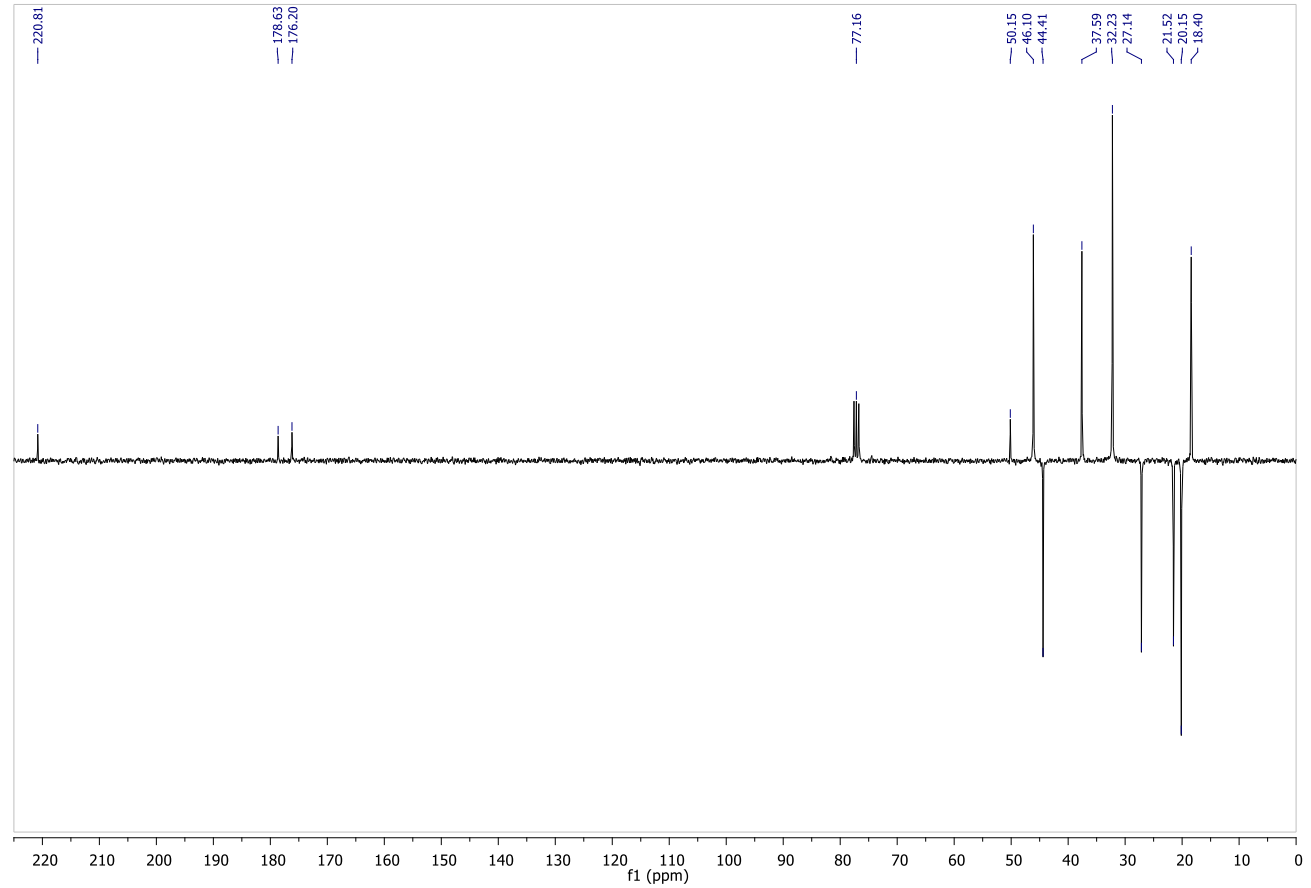


(*R*)-1-*iso*Butyl-3-((*R*)-1-methyl-2-oxocyclopentyl)-2,5-pyrrolidinedione (1*R*, 3*R*)-15c



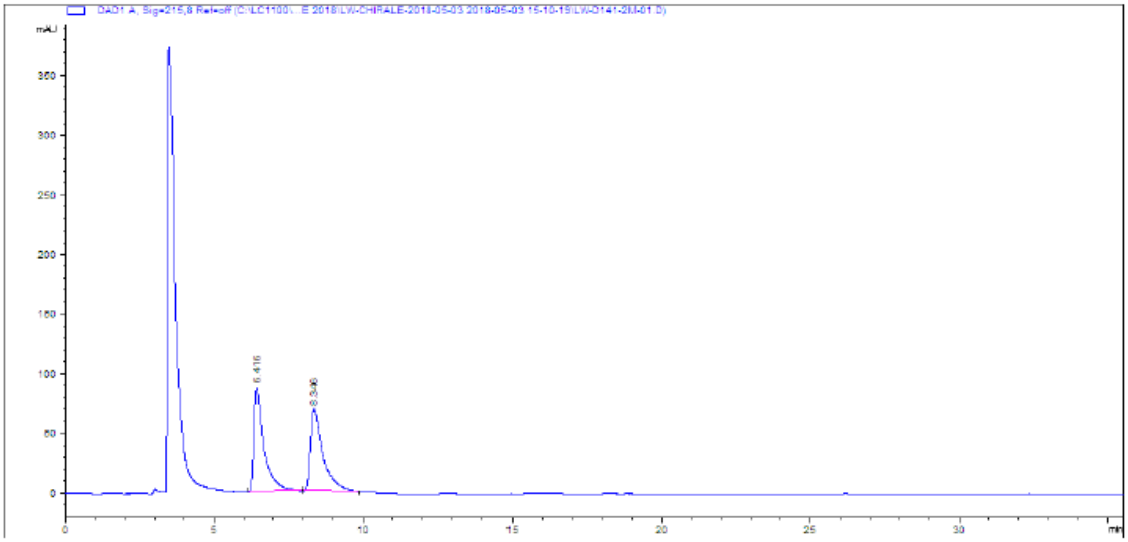
Compound (1*R*,3*R*)-**15c** was obtained in 55% yield (139 mg) as a colorless oil. Its diastereomer **16c** was isolated as a white solid in 10% yield (25 mg). **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.27 (d, *J* = 7.5 Hz, 2H), 2.97 (dd, *J* = 9.3, 5.2 Hz, 1H), 2.74 (dd, *J* = 18.3, 9.3 Hz, 1H), 2.42 (dd, *J* = 18.3, 5.2 Hz, 1H), 2.50-2.35 (m, 1H), 2.18-1.85 (m, 5H), 1.85-1.73 (m, 1H), 1.29 (s, 3 H), 0.84 (d, *J* = 6.6 Hz, 3H), 0.83 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 220.8, 178.6, 176.2, 50.1, 46.1, 44.4, 37.6, 32.2, 27.1, 21.5, 20.1, 18.4; **HRMS (ESI)** m/z calcd for $[C_{14}H_{21}NaNO_3]^+$ 274.1414, found 274.1425; **IR** (neat) 2963, 2933, 2874, 1773, 1735, 1690, 1402 cm^{-1}; **$[\alpha]^{25}_D$** = + 45.2 (5.4, $CHCl_3$)


7.260
3.276
3.251
2.987
2.974
2.957
2.788
2.727
2.697
2.456
2.439
2.295
2.182
1.849
1.726
1.287
0.857
0.844
0.835
0.822
1.98
1.00
1.06
1.99
5.08
1.17
3.04
6.01
f1 (ppm)


220.81
178.63
176.20
77.16
50.15
46.10
44.41
37.59
32.23
27.14
21.52
20.15
18.40
f1 (ppm)

HPLC: Racemic (±)-**15c**. Chiralpal AD, Solvent: Hexane/i-PrOH = 80:20, Flow Speed 1.0 mL/min, UV: 215nm, retention times: 6.416, 8.346 min.

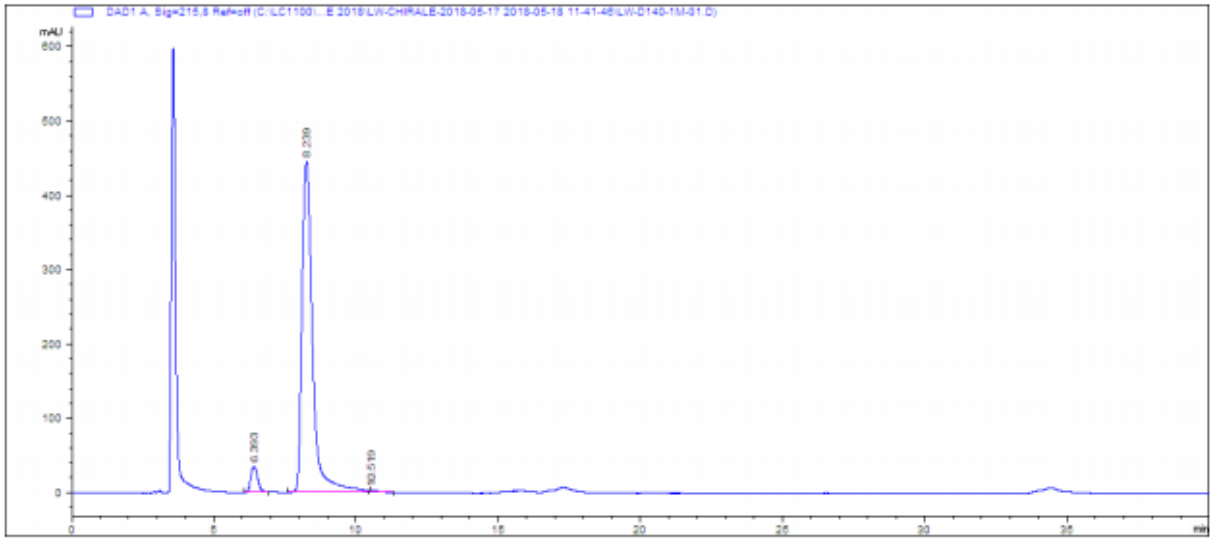
LW D141-2M **Hexane / Isopropanol 80 : 20**
215nm



#	Time	Area	Height	Width	Area%	Symmetry
1	6.416	2062.2	87.9	0.3308	50.138	0.347
2	8.346	2050.9	68.5	0.4343	49.862	0.368

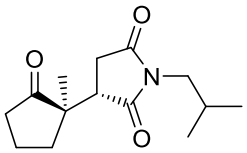
HPLC: (1*R*,3*R*)-**15c**. Chiralpal AD, Solvent: Hexane/i-PrOH = 80:20, Flow Speed 1.0 mL/min, UV: 215nm, 90% ee, retention time: 8.239 min.

LW D140-1M **Hexane / Isopropanol 80 : 20**
215nm

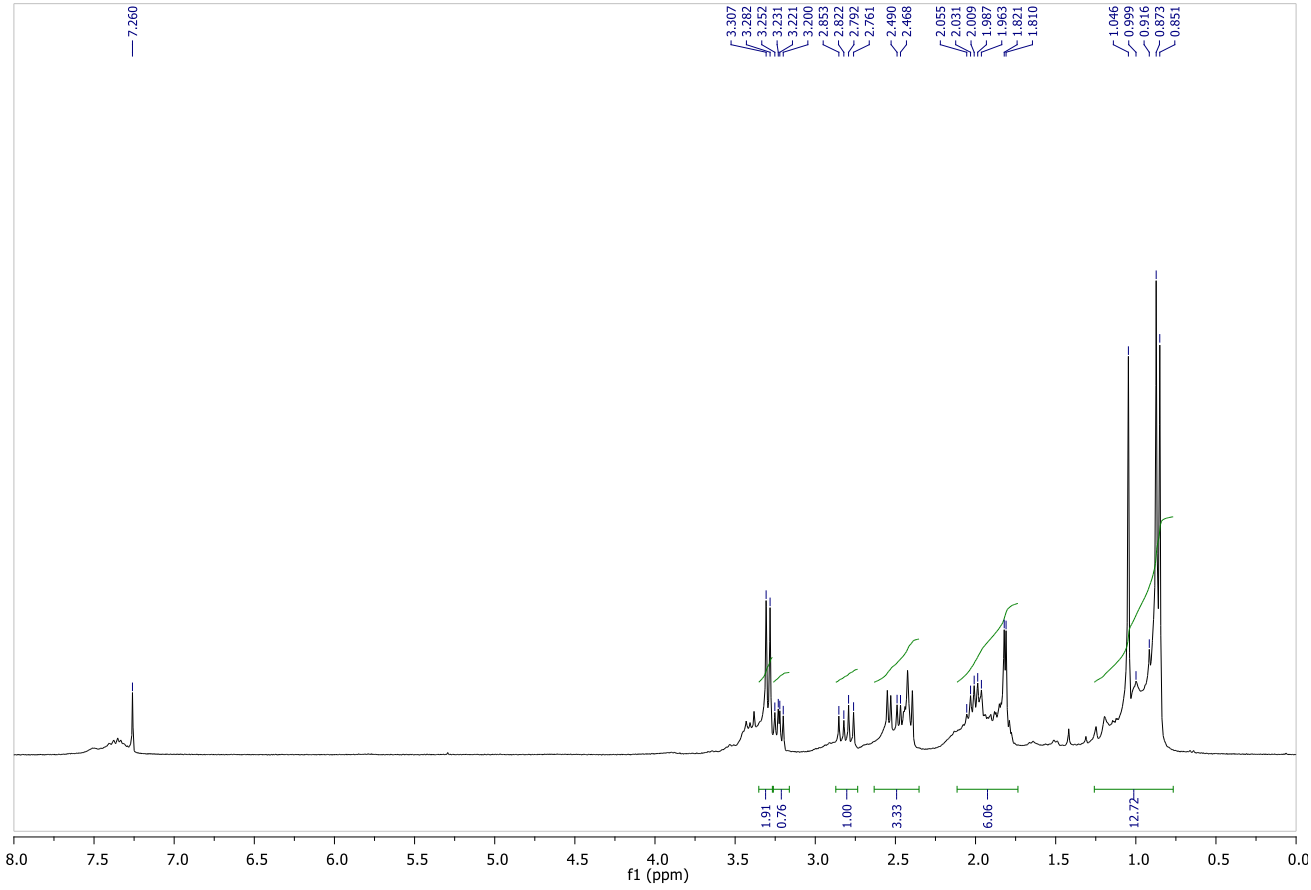


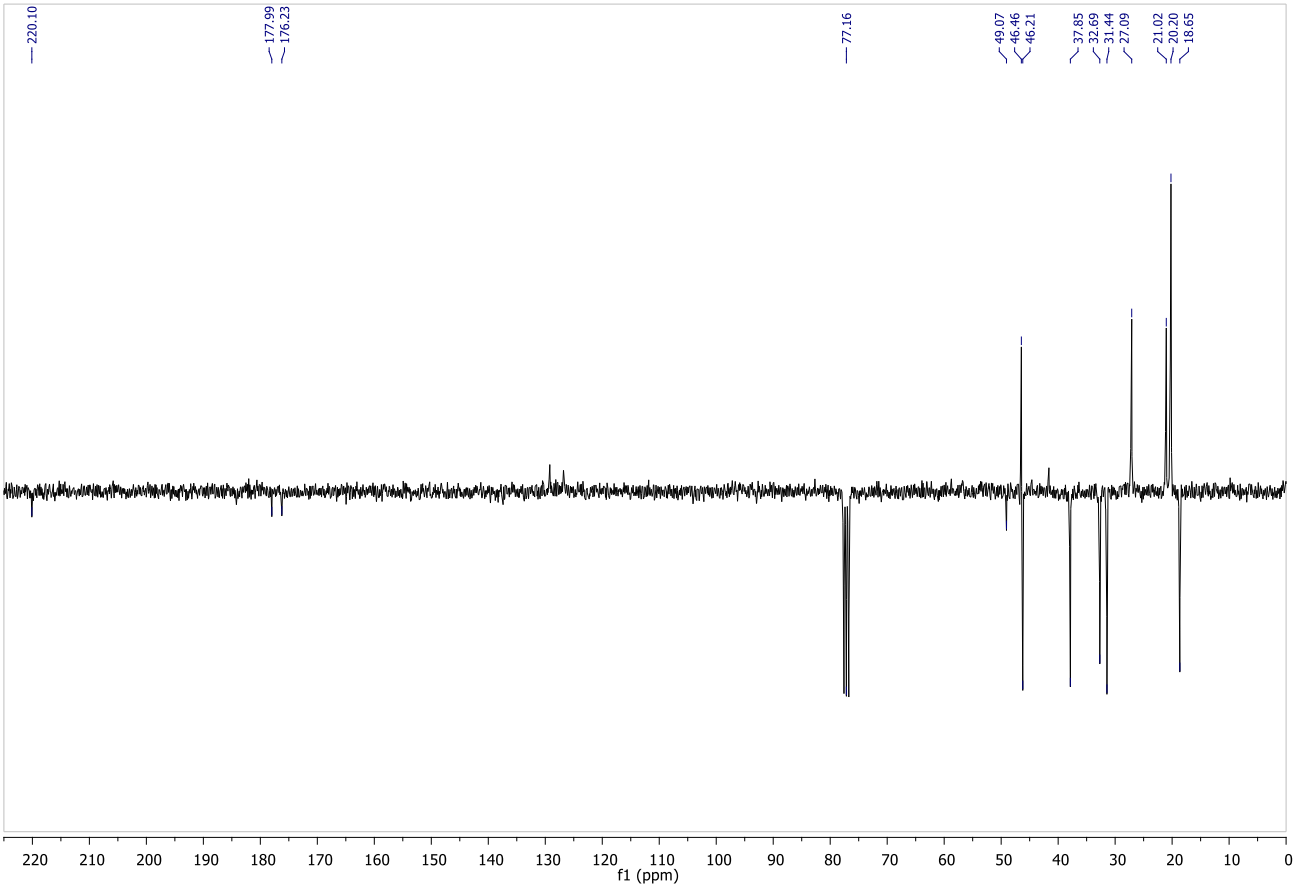
#	Time	Area	Height	Width	Area%	Symmetry
1	6.393	612	34.7	0.275	4.977	0.812
2	8.239	11623.1	445.5	0.4054	94.513	0.651
3	10.519	62.8	2.8	0.2728	0.511	5.96E-2

(*S*)-1-*iso*Butyl-3-((*R*)-1-methyl-2-oxocyclopentyl)pyrrolidine-2,5-dione (1*R*,3*S*)-16c

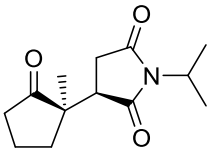


16c: It was not possible to separate compound (1*R*,3*S*)-**16c** from impurities. White solid, 10% yield. **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.29 (d, *J* = 9.0 Hz, 2H), 3.23 (dd, *J* = 6.0 , 9.0 Hz, 1H), 2.81 (dd, J = 18.0, 9.0 Hz, 1H), 2.62-2.38 (m, 3H), 2.12-1.76 (m, 5H), 1.05 (s, 3H), 0.86 (d, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 220.1, 178.0, 176.2, 49.1, 46.5, 46.2, 37.8, 32.7, 31.4, 27.1, 21.0, 20.2, 18.6; **HRMS (ESI)** m/z calcd for $[C_{14}H_{21}NaNO_3]^+$ 274.1419, found 274.1427; **IR** (neat) 2966, 2934, 2874, 1743, 1697 cm^{-1}.

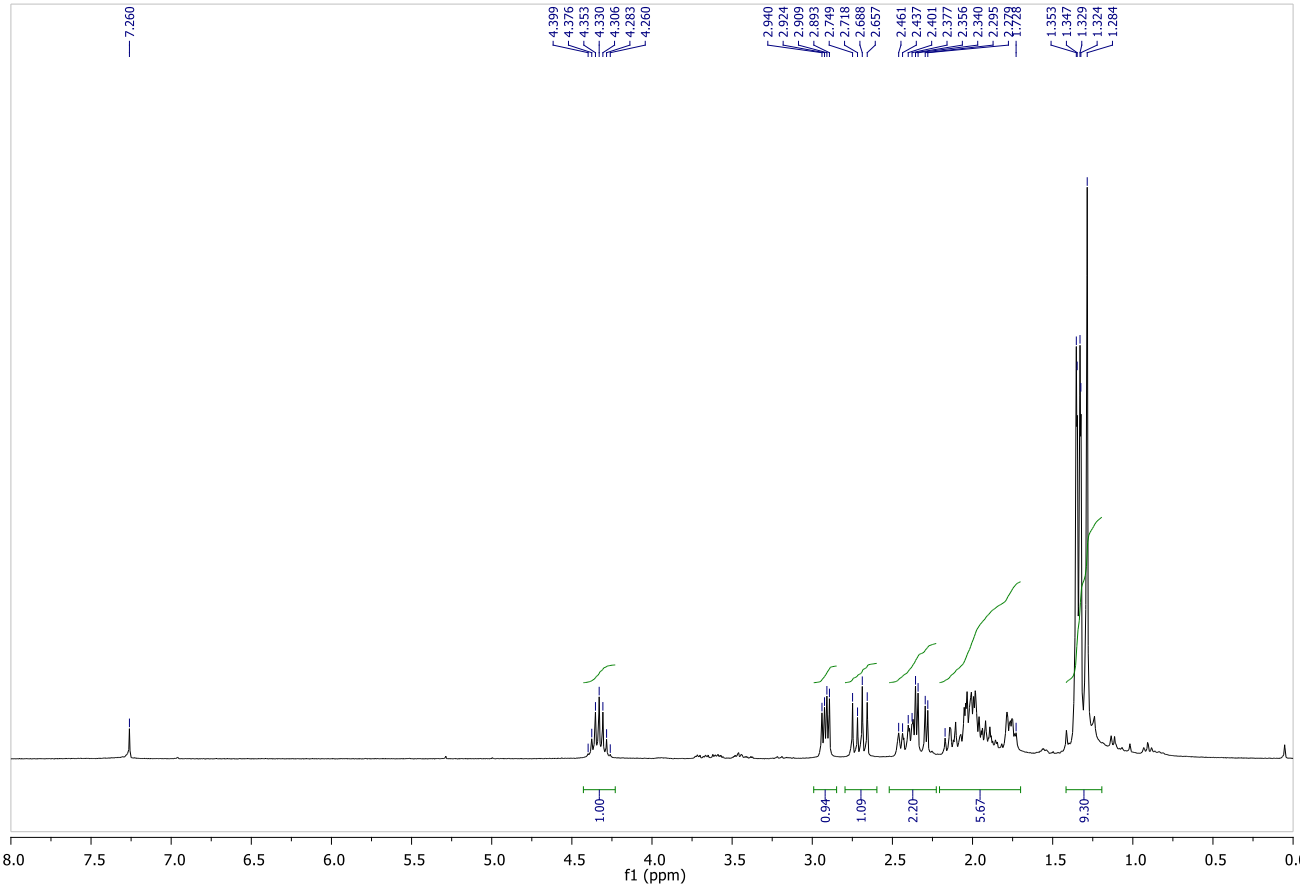


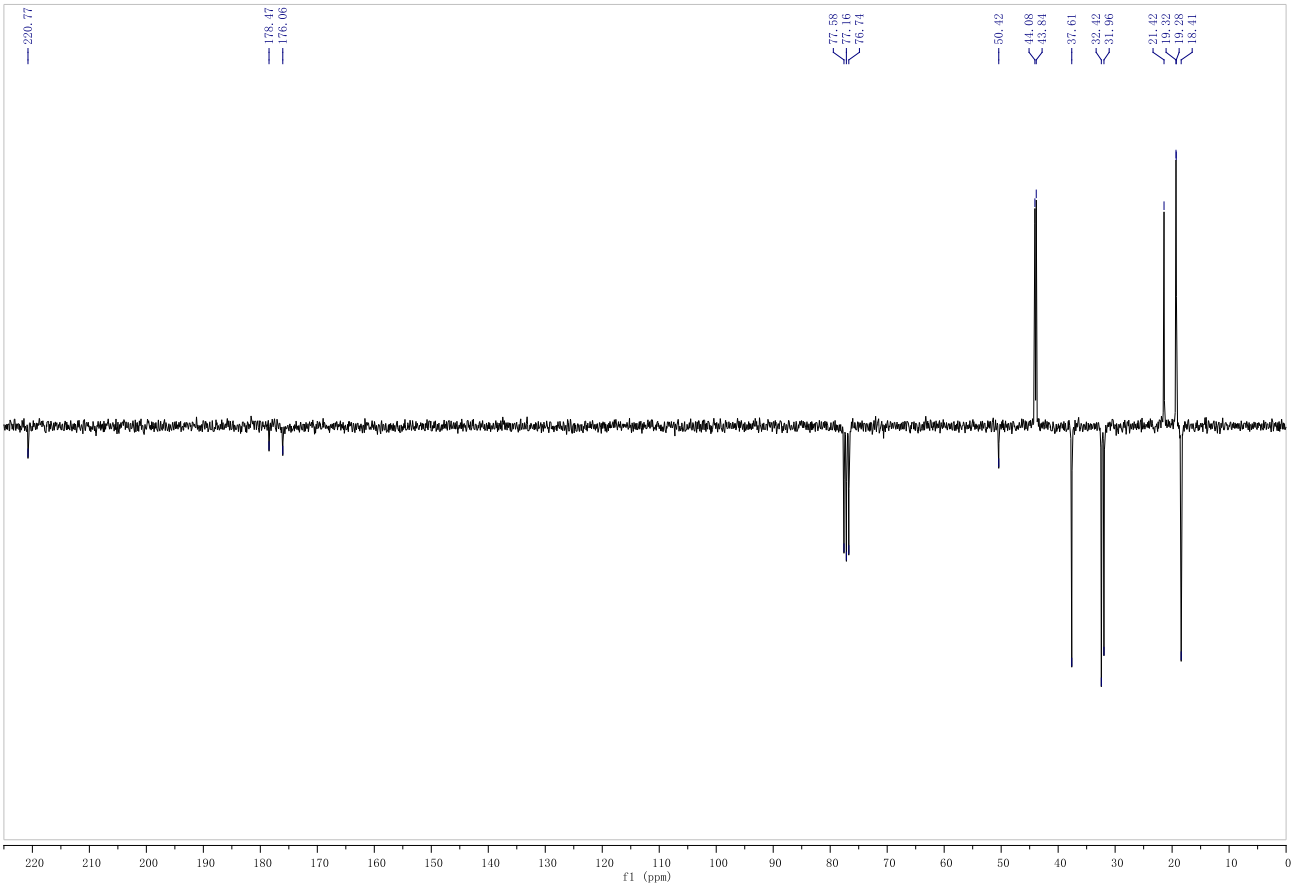


(*R*)-1-*iso*Propyl-3-((*R*)-1-methyl-2-oxocyclopentyl)-2,5-pyrrolidinedione 15d



Compound (1*R*,3*R*)-**15d** was obtained as a colorless oil in 61% (145 mg) yield (de > 96%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 4.33 (sept, *J* = 6.9 Hz, 1H), 2.92 (dd, *J* = 9.2, 4.8 Hz, 1H), 2.70 (dd, *J* = 18.2, 9.3 Hz, 1H), 2.42 (bdd, *J* = 18.0, 7.2 Hz, 1H), 2.32 (dd, *J* = 18.2, 4.8 Hz, 1H), 2.17-1.73 (m, 5H), 1.34 (dd, *J* = 6.9 Hz, 3H), 1.33 (dd, *J* = 6.9 Hz, 3H), 1.28 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 220.8, 178.5, 176.1, 50.4, 44.1, 43.8, 37.6, 32.4, 32.0, 21.4, 19.32, 19.28, 18.4; **HRMS (ESI)** m/z calcd for $[C_{13}H_{19}NaNO_3]^+$ 260.1257, found 260.1272; **IR** (neat) 2972, 1769, 1735, 1690, 1462, 1400, 1366 cm^{-1}; **$[\alpha]^{25}_D$** = + 67.6 (4.66, $CHCl_3$).

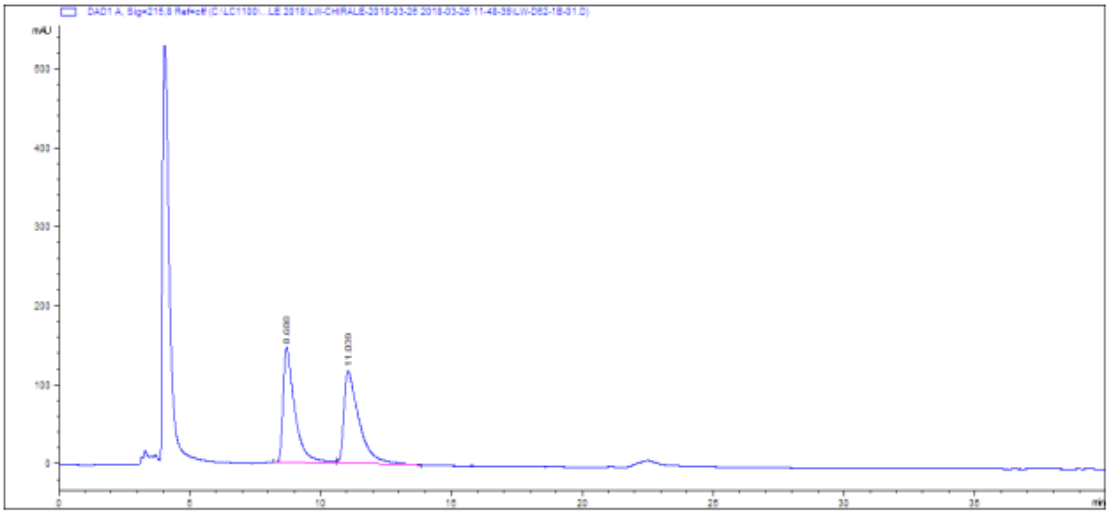

7.260
4.399
4.376
4.353
4.330
4.306
4.283
4.260
2.940
2.924
2.909
2.893
2.749
2.718
2.688
2.657
2.461
2.437
2.401
2.377
2.356
2.340
2.295
2.278
2.228
1.353
1.347
1.329
1.324
1.284
1.00
0.94
1.09
2.20
5.67
9.30
f1 (ppm)


220.77
178.47
176.06
77.58
77.16
76.74
50.42
44.08
43.84
37.61
32.42
31.96
21.42
19.32
19.28
18.41
f1 (ppm)

HPLC: (±)-**15d**. Chiralpal AD, Solvent: Hexane/i-PrOH = 80:20, Flow Speed 1.0 mL/min, UV: 215nm, retention times: 8.688, 11.039 min.

Colonne CHIRALCEL AD

LW D 62-1B hexane / isopropanol 90 : 10
215 nm

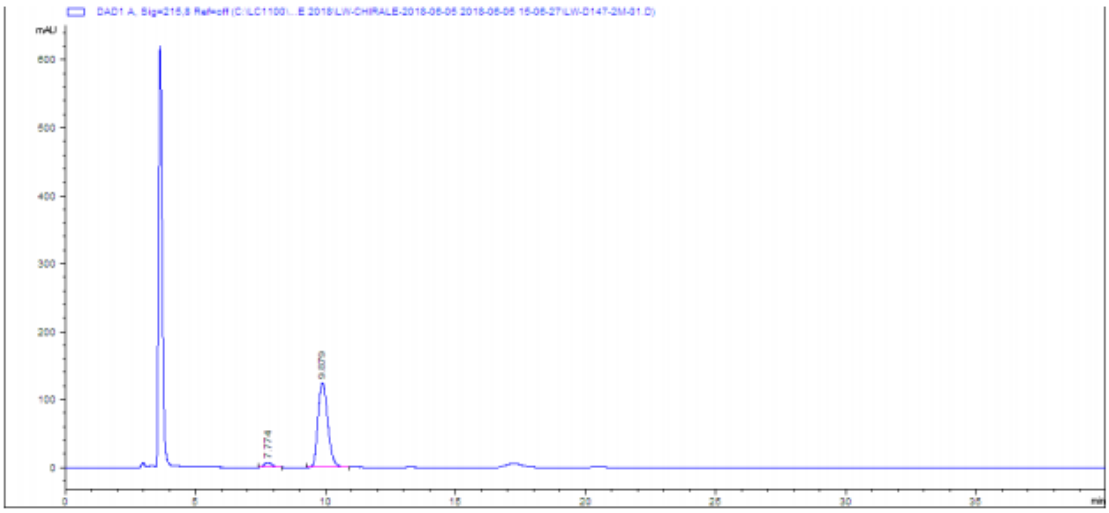


#	Time	Area	Height	Width	Area%	Symmetry
1	8.688	4602	146	0.4328	48.953	0.393
2	11.039	4798.8	118.2	0.5545	51.047	0.361

HPLC: (1*R*,3*R*)-**15d**. Chiralpal AD, Solvent: Hexane/i-PrOH = 80:20, Flow Speed 1.0 mL/min, UV: 215nm, 90 %ee retention time: 9.879 min.

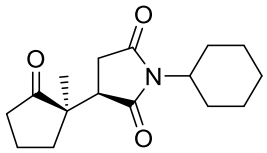
Colonne CHIRALCEL AD

LW D147-2 **Hexane / Isopropanol 90 : 10**
215 nm

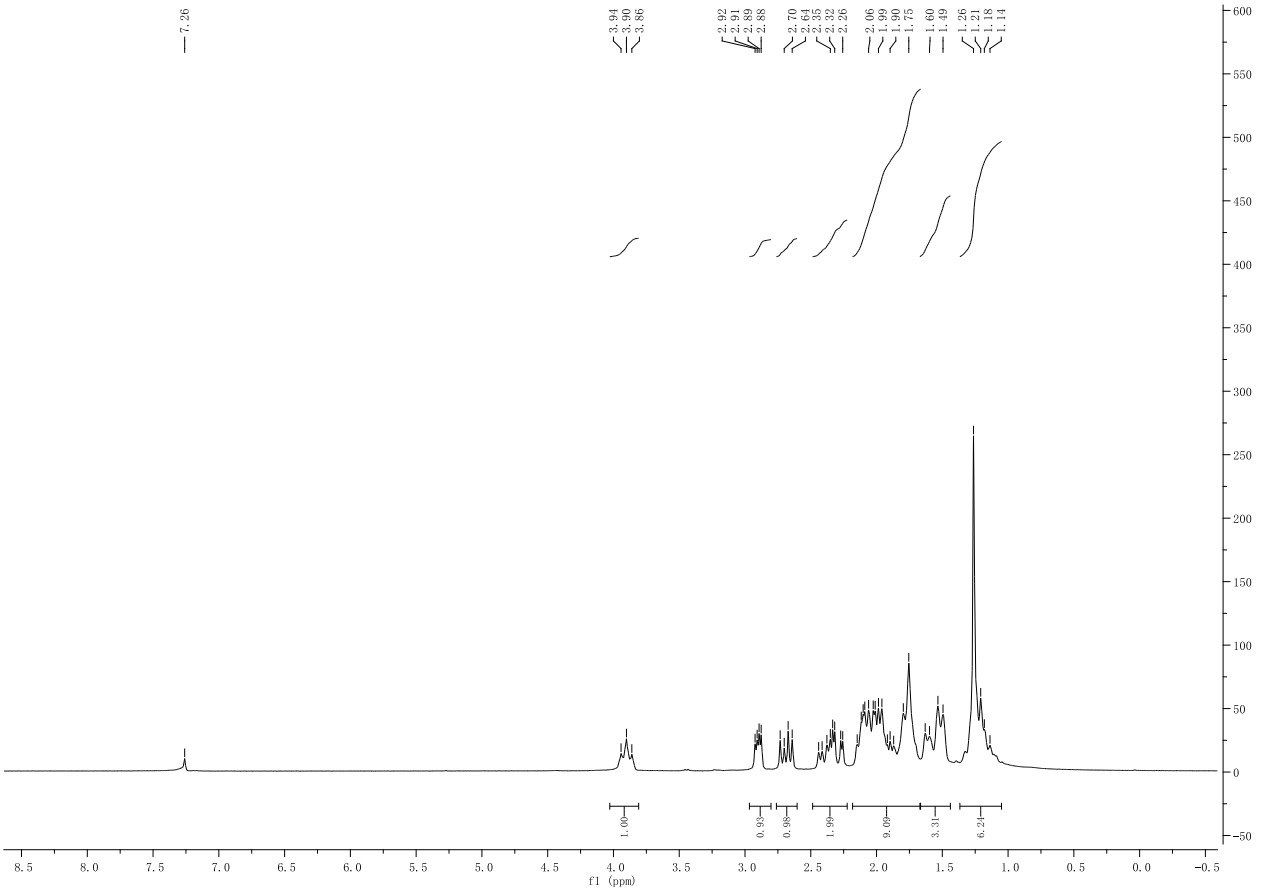


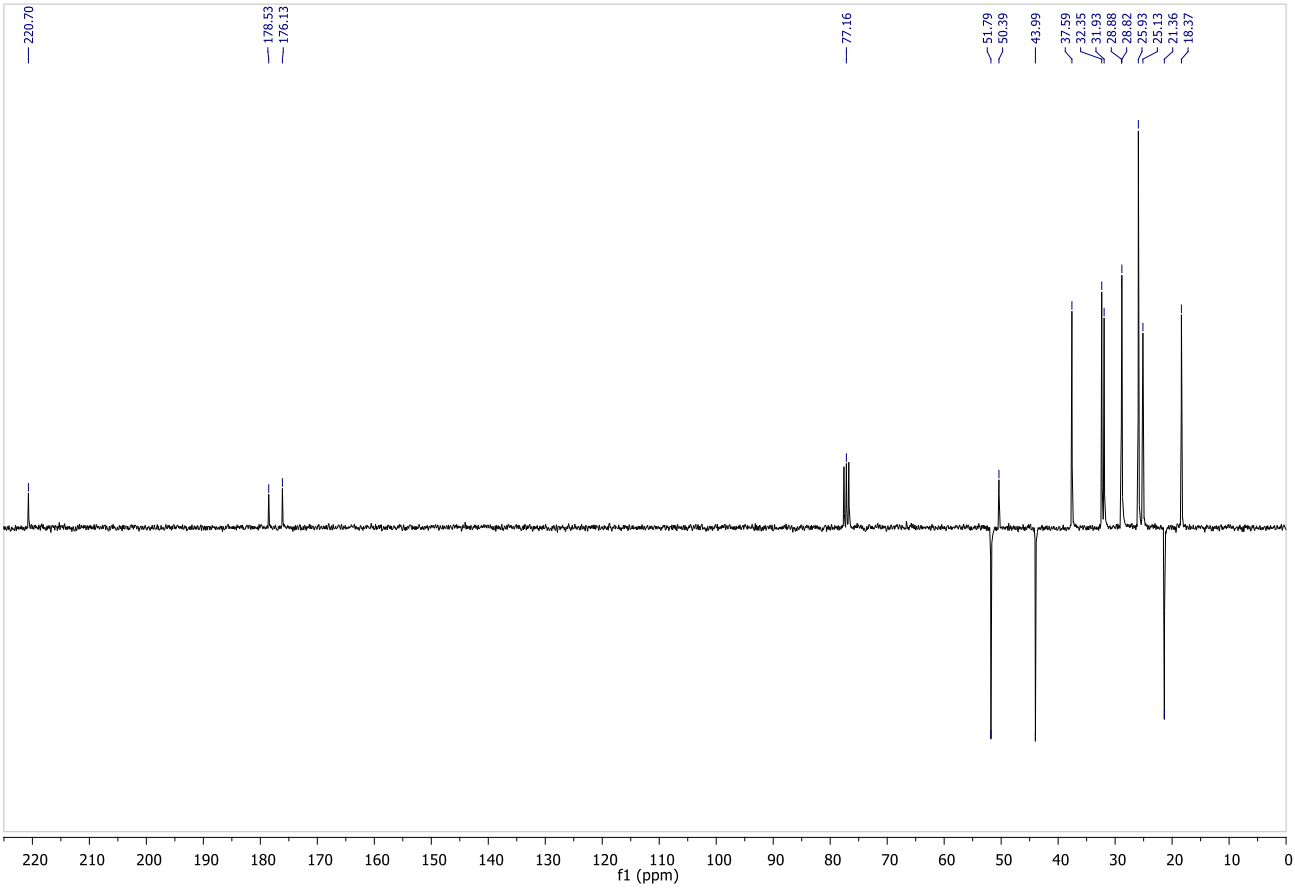
#	Time	Area	Height	Width	Area%	Symmetry
1	7.774	169.8	7.7	0.2633	4.933	0.816
2	9.879	3271.9	124.4	0.4138	95.067	0.829

(*R*)-1-Cyclohexyl-3-((*R*)-1-methyl-2-oxocyclopentyl)-2,5-pyrrolidinedione 15e



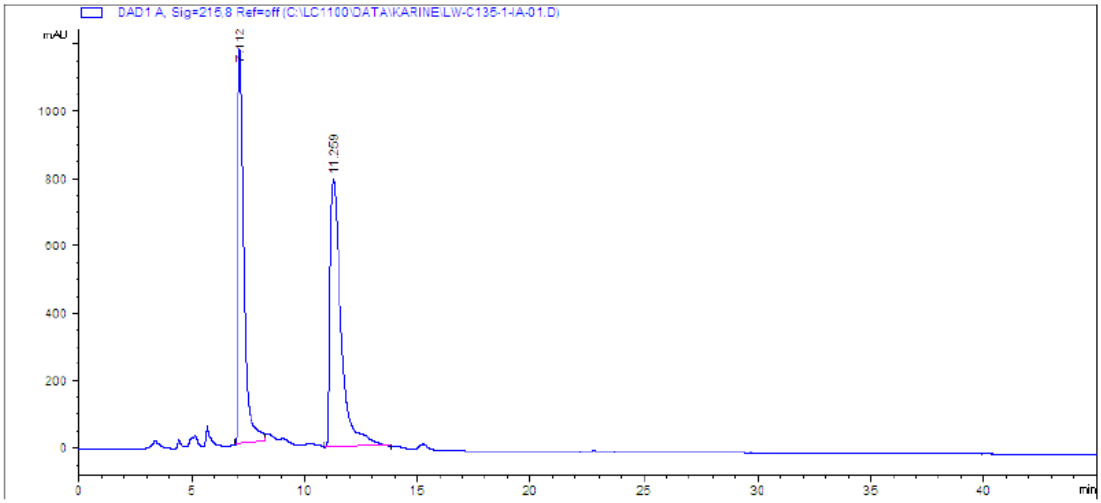
Succinimide (1*R*,3*R*)-**15e** was obtained in 46% yield (127 mg) as a white solid (dr = 73:27, ee = 98%). The corresponding diastereomer **16e** was obtained in 17% yield (47 mg). **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **m.p.** 85.7 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.90 (tt, *J* = 12.3, 3.7 Hz, 1H), 2.90 (dd, *J* = 9.3, 4.8 Hz, 1H), 2.68 (dd, *J* = 18.2, 9.3 Hz, 1H), 2.39 (bdd, *J* = 18.3, 7.5 Hz, 1H), 2.29 (dd, *J* = 18.2, 4.8 Hz, 1H), 2.20–1.46 (m, 13H), 1.33–1.90 (m, 2H), 1.26 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 220.7, 178.5, 176.1, 51.8, 50.4, 44.0, 37.6, 32.3, 31.9, 28.9, 28.8, 25.1, 21.4, 18.4; **HRMS (ESI)** m/z calcd for $[C_{16}H_{24}NO_3]^+$ 278.1751, found 278.1750; **IR** (neat) 2934, 2856, 1769, 1736, 1691, 1398, 1375, 1346, 1197, 1145, 907, 730 cm^{-1}; **$[\alpha]^{28}_D$** = + 17 (c = 0.13, $CHCl_3$).





HPLC: **(±)-15e**. Chiralpal AD, Solvent: Hexane/i-PrOH = 80:20, Flow Speed 1.0 mL/min, UV: 215nm, retention times: 7.11, 11.26 min.

LW C135-1 **Hexane / isopropanol 80 : 20**
215 nm

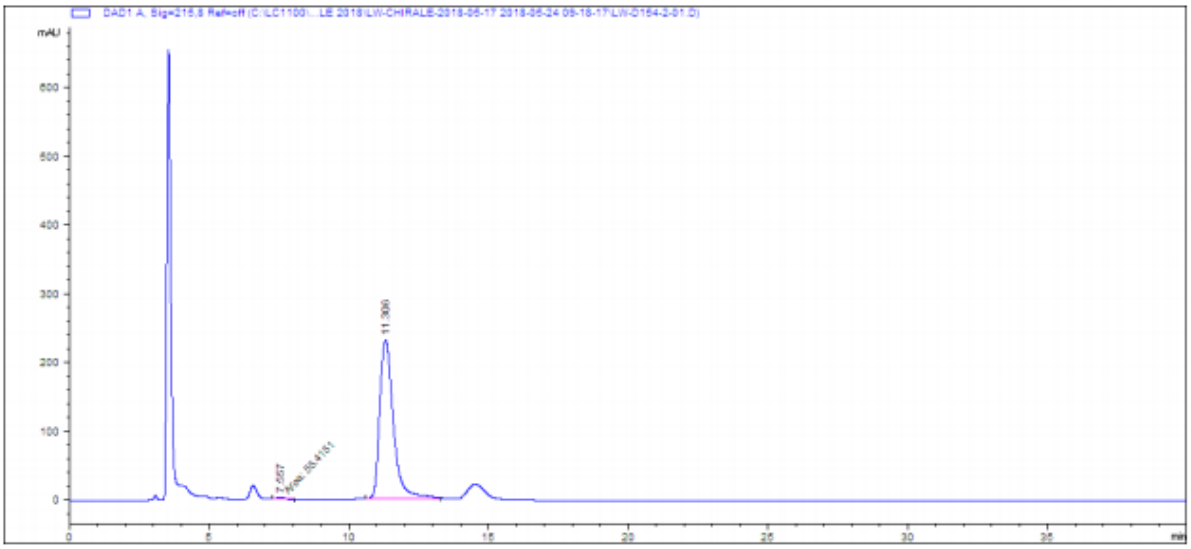


MeasRetTime	CorrExpRetTime	IntPeakType	Area	Height	Width	Symmetry
7.11	0.00	BV	21772.82	1175.93	0.28	0.37
11.26	0.00	BB	26773.45	794.93	0.48	0.39

HPLC: (1*R*,3*R*)-**15e** Chiralpal AD, Solvent: Hexane/i-PrOH = 80:20, Flow Speed 1.0 mL/min , UV: 215nm, 98% ee, retention time 11.30 min.

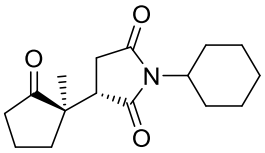
Colonne CHIRALCEL AD

LW D154-2 **Hexane / Isopropanol 80 : 20**
215 nm

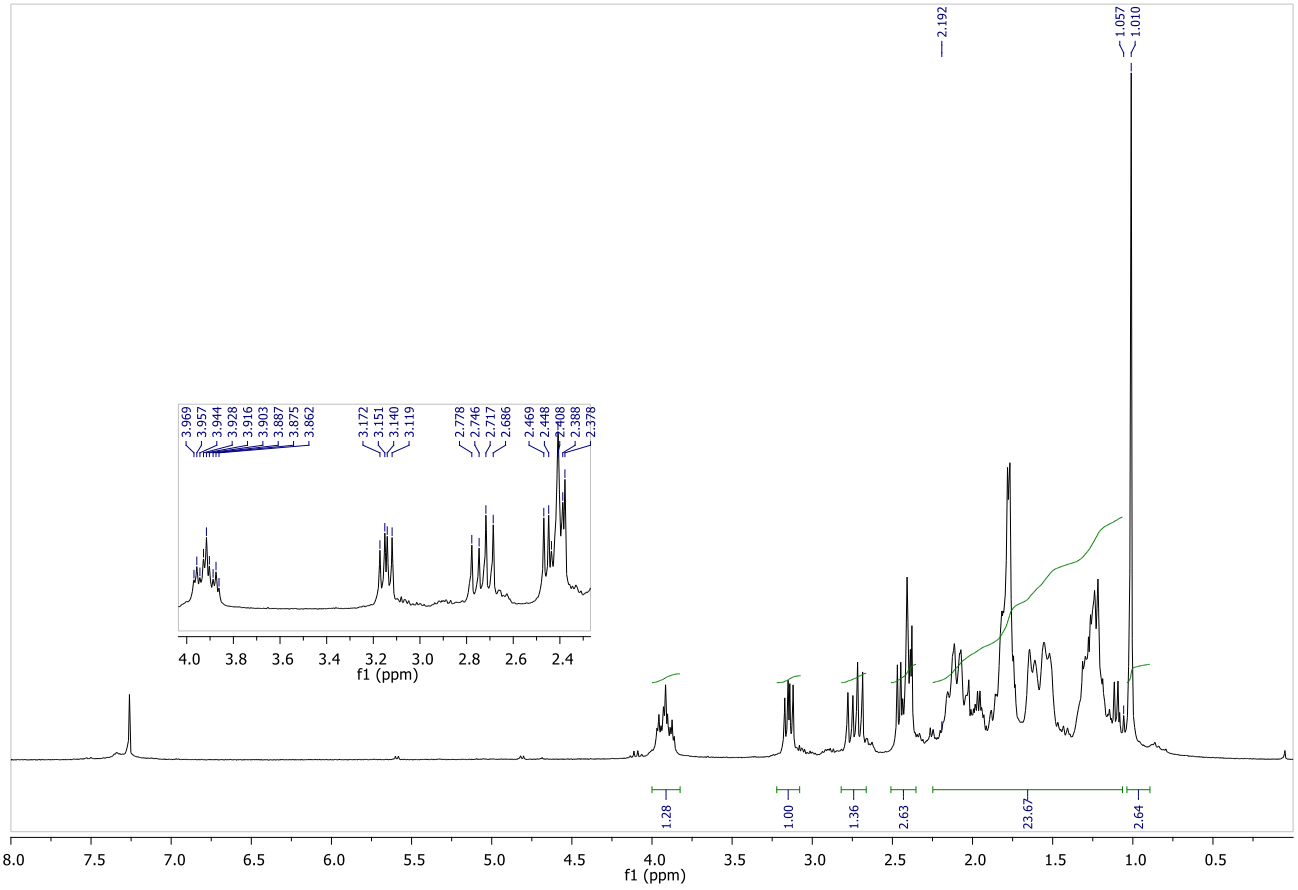


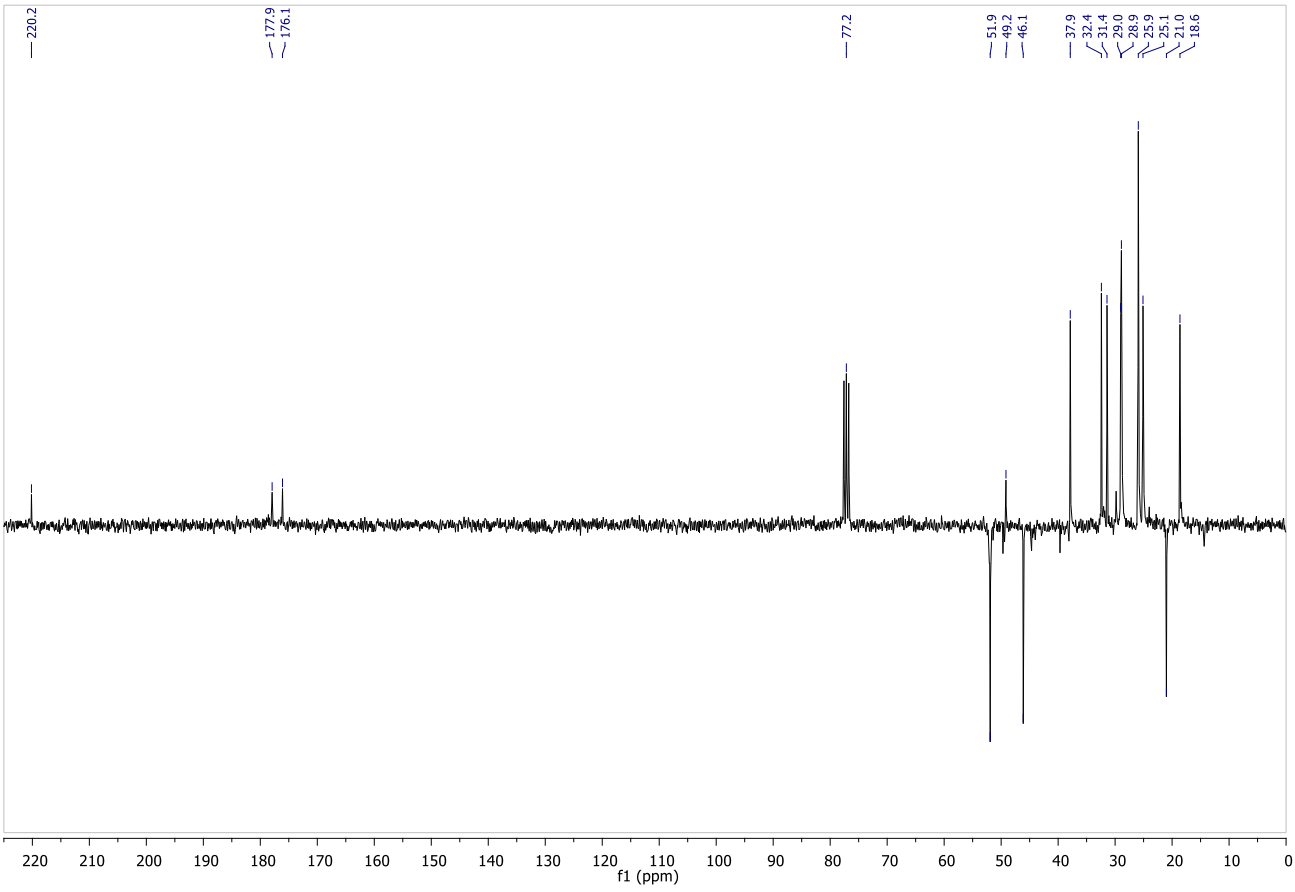
#	Time	Area	Height	Width	Area%	Symmetry
1	7.557	55.4	2.8	0.3351	0.698	0.878
2	11.306	7885.2	230.9	0.5263	99.302	0.67

(*S*)-1-Cyclohexyl-3-((*R*)-1-methyl-2-oxocyclopentyl)-2,5-pyrrolidinedione 16e

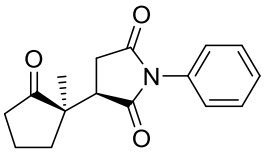


Compound (1*R*,3*S*)-**16e**: 17% yield; white solid; contains traces of its corresponding diastereomer (1*R*,3*R*)-**15e**. **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.92 (tt, *J* = 12.4, 3.8 Hz, 1H), 3.15 (dd, *J* = 9.4, 6.3 Hz, 1H), 2.72 (dd, *J* = 18.3, 9.6 Hz, 1H), 2.47-2.30 (m, 3H), 2.20-1.00 (m, 14H), 1.01 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 220.2, 177.9, 176.1, 51.9, 49.2, 46.1, 37.9, 32.4, 31.4, 29.0, 28.9, 25.1, 21.0, 18.6; **HRMS (ESI)** m/z calcd for $[C_{16}H_{24}NaNO_3]^+$ 300.1576, found 300.1577; **IR** (neat) 2961, 2932, 2854, 1769, 1737, 1690, 1453, 1398, 1374, 1201, 1188, 1144 cm^{-1}.

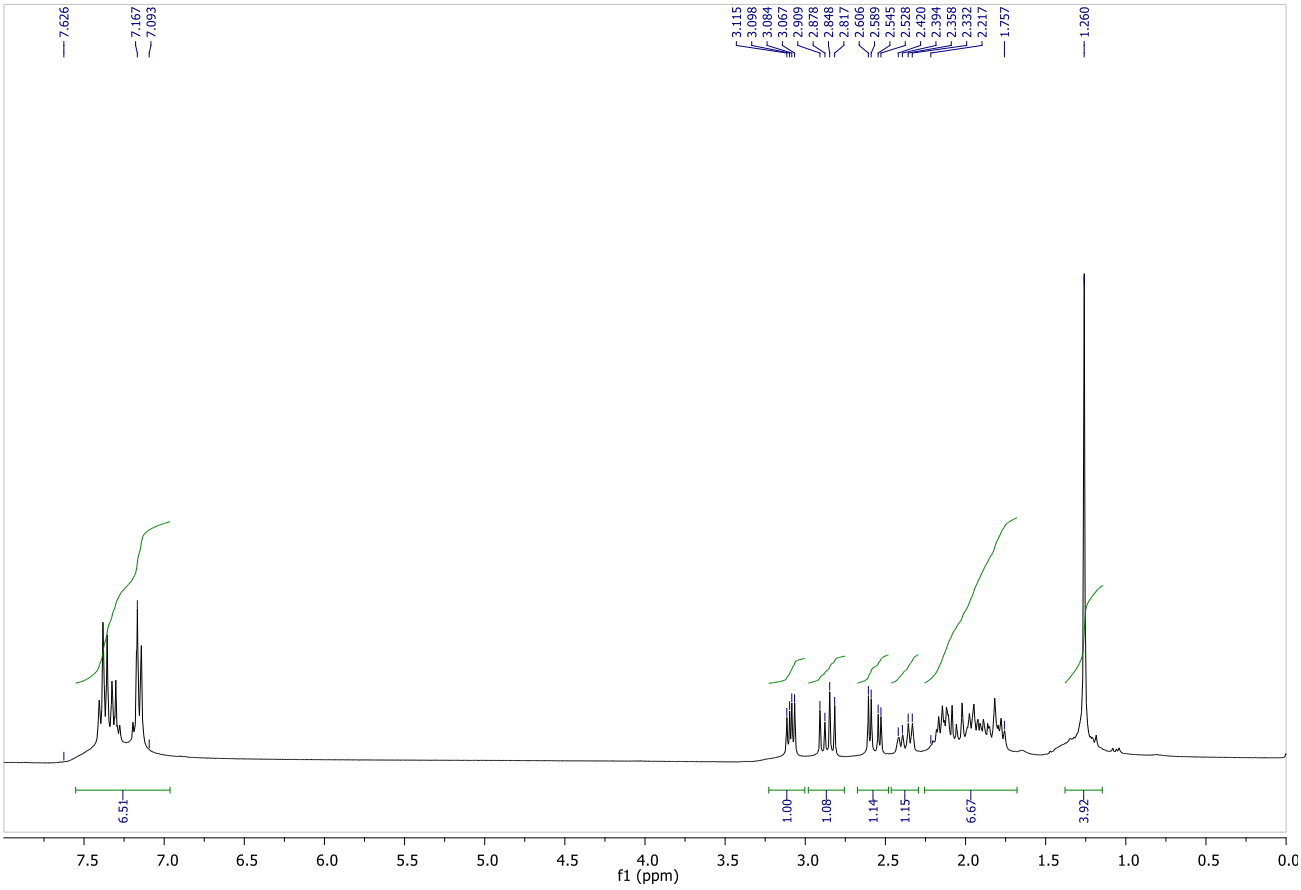

2.192
1.057
1.010
3.969
3.957
3.944
3.928
3.916
3.903
3.887
3.875
3.862
3.172
3.151
3.140
3.119
2.778
2.746
2.717
2.686
2.469
2.448
2.408
2.388
2.378
4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4
f1 (ppm)
1.28
1.00
1.36
2.63
23.67
2.64
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

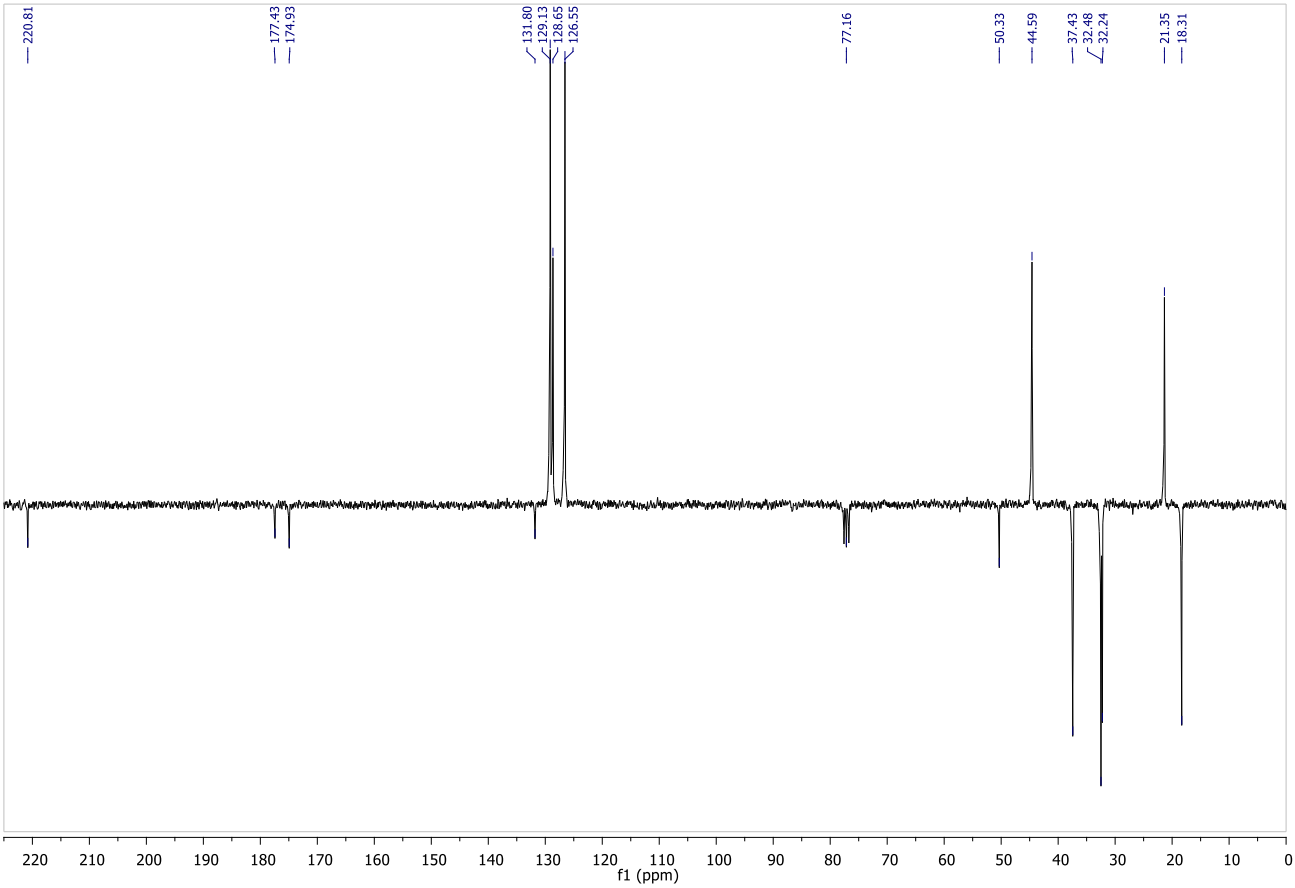

220.2
177.9
176.1
77.2
51.9
49.2
46.1
37.9
32.4
31.4
29.0
28.9
25.9
25.1
21.0
18.6
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

(*R*)-3-((*R*)-1-Methyl-2-oxocyclopentyl)-1-phenyl-2,5-pyrrolidinedione 15f



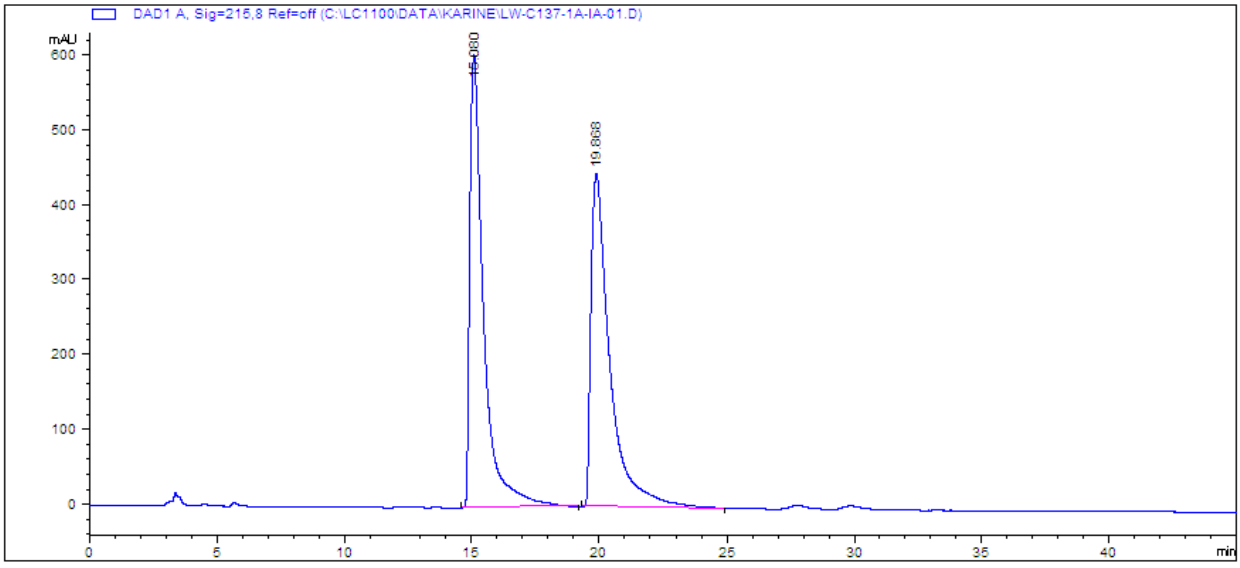
Compound (1*R*,3*R*)-**15f** was obtained in 69% yield (187 mg), dr = 89:11, 83% ee, as a white solid. Itsdiastereomer **16f** was obtained in 8% yield (22 mg). **Rf** = 0.1 (cyclohexane/EtOAc = 1:1; **m.p.** 102.0 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.62-7.09 (m, 5H), 3.09 (dd, *J* = 9.3, 5.2 Hz, 1H), 2.86 (dd, *J* = 18.3, 9.3 Hz, 1H), 2.57 (dd, *J* = 18.3, 5.2 Hz, 1H), 2.38 (dd, *J* = 19.5, 8.6 Hz, 1H), 2.25-1.71 (m, 5H), 1.26 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 220.8, 177.4, 174.9, 131.8, 129.1, 128.7, 126.6, 50.3, 44.6, 37.4, 32.5, 32.2, 21.0, 18.3; **HRMS (ESI)** m/z calcd for $[C_{16}H_{18}NO_3]^+$ 272.1281, found 272.1284; **IR** (neat) 2957, 2161, 1777, 1734, 1701, 1394, 1194, 750, 698 cm^{-1}; **$[\alpha]^{18}_D$** = + 42 (c = 6.8, EtOH).





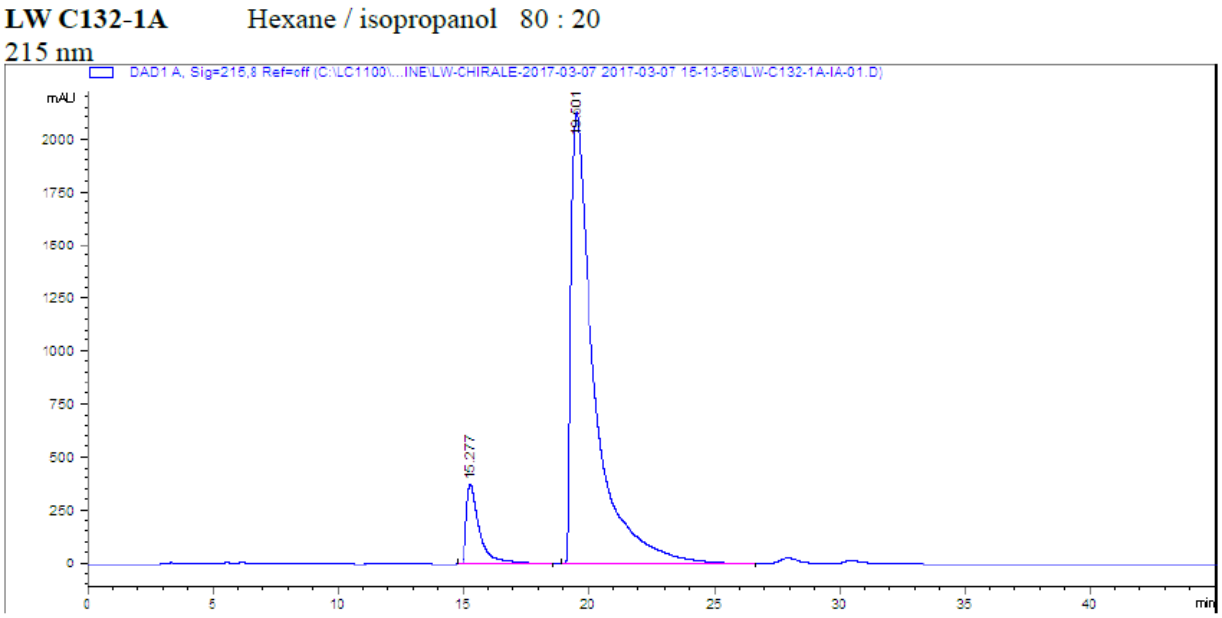
HPLC: (±)-**15f**.:Chiralcel AD-H, *i*-PrOH/hexane = 20:80, 1 mL/min, 215 nm, retention times: 15.08, 19.87 min.

LW C137-1A **Hexane / isopropanol 80 : 20**
215 nm



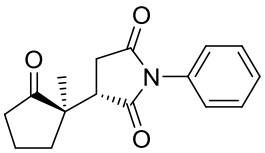
MeasRetTime	CorrExpRetTime	IntPeakType	Area	Height	Width	Symmetry
15.08	0.00	BB	22876.72	604.45	0.54	0.38
19.87	0.00	BB	22898.26	445.70	0.72	0.36

HPLC: (1*R*,3*R*)-**15f**. Chiralcel AD-H, *i*-PrOH/hexane = 20:80, 1 mL/min, 215 nm, 82 % ee, retention time: 19.50 min.

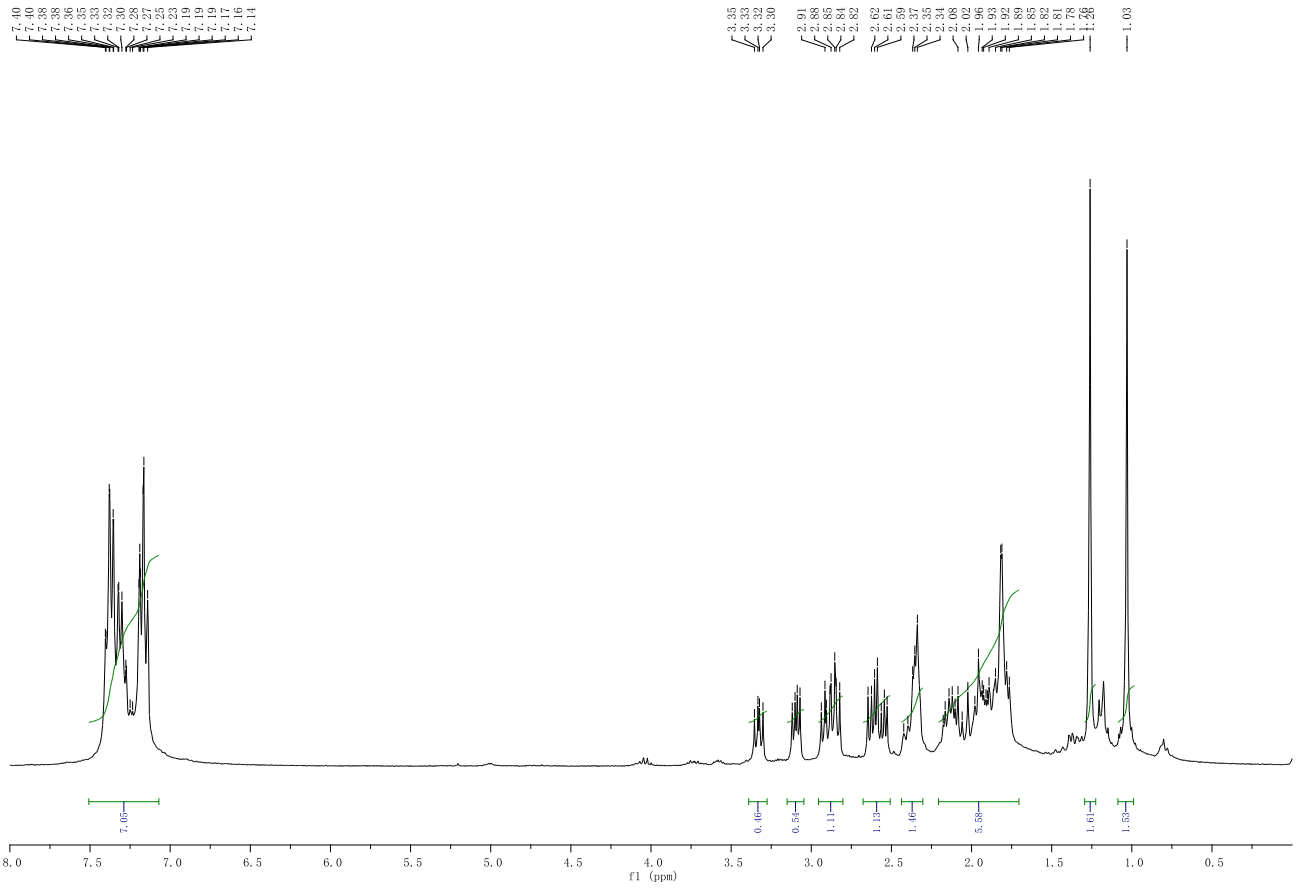


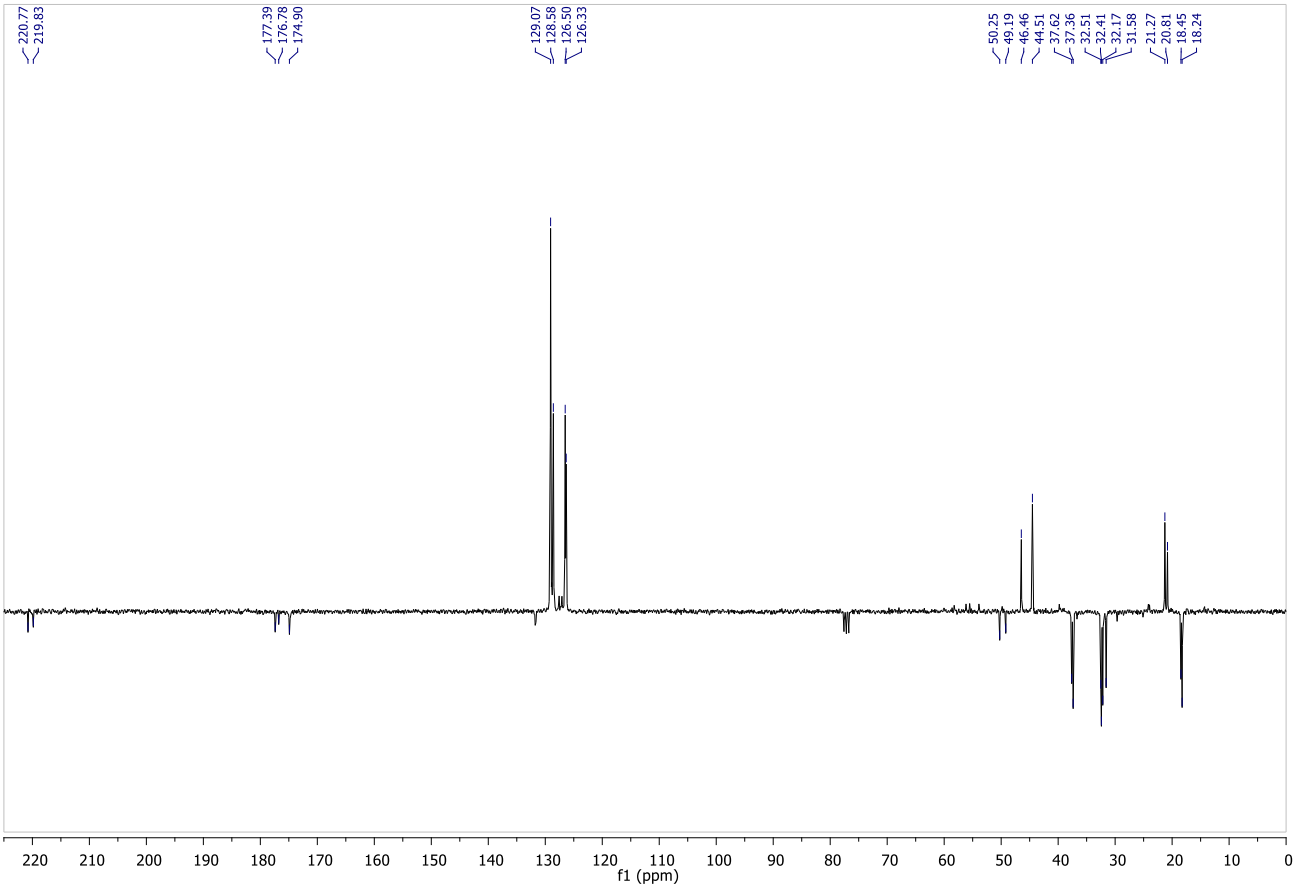
MeasRetTime	CorrExpRetTime	IntPeakType	Area	Height	Width	Symmetry
15.28	0.00	BB	13416.59	370.09	0.52	0.40
19.50	0.00	BB	136491.75	2121.61	0.75	0.31

(*S*)-3-((*R*)-1-Methyl-2-oxocyclopentyl)-1-phenyl-2,5-pyrrolidinedione 16f

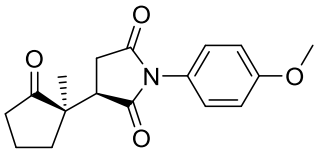


Compound (1*R*,3*S*)-**16f** (8% yield) was obtained as an inseparable mixture of diastereomers **15f/16f** in the respective ratio 54/46**. Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.64-7.01 (m, 5H), 3.33 (dd, *J* = 9.4, 6.5 Hz, 1H), 2.95-2.80 (m, 1H), 2.72-2.50 (m, 1H), 2.45-2.30 (m, 1H), 2.23-1.69 (m, 5H), 1.26 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 220.9, 177.5, 175.0, 131.9, 129.2, 128.8, 126.6, 50.4, 44.7, 37.5, 32.6, 32.3, 21.0, 18.3; **HRMS (ESI)** m/z calcd for $[C_{16}H_{18}NaNO_3]^+$ 294.1106, found 294.1102; **IR** (neat) 2968, 2254, 1778, 1736, 1710, 1707, 1383, 1186, 1166, 905, 727, 697, 648, 621 cm^{-1}.

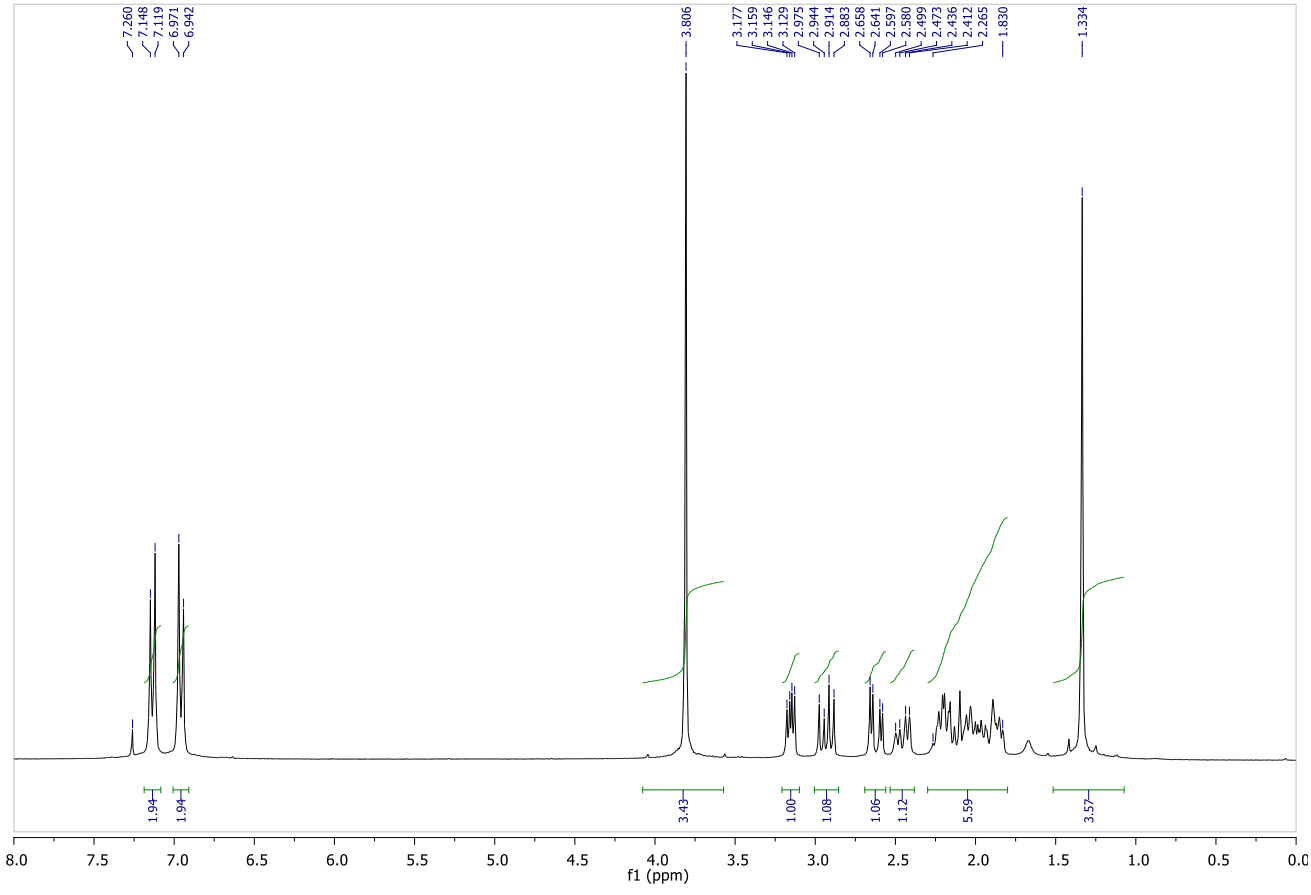

7.40
7.40
7.38
7.38
7.36
7.35
7.33
7.32
7.30
7.28
7.27
7.25
7.23
7.19
7.19
7.19
7.17
7.16
7.14
3.35
3.33
3.32
3.30
2.91
2.88
2.85
2.84
2.82
2.62
2.61
2.59
2.37
2.35
2.34
2.08
2.02
1.96
1.93
1.92
1.89
1.85
1.82
1.81
1.78
1.26
1.03
7.05
0.46
0.54
1.11
1.13
1.46
5.58
1.61
1.53
f1 (ppm)

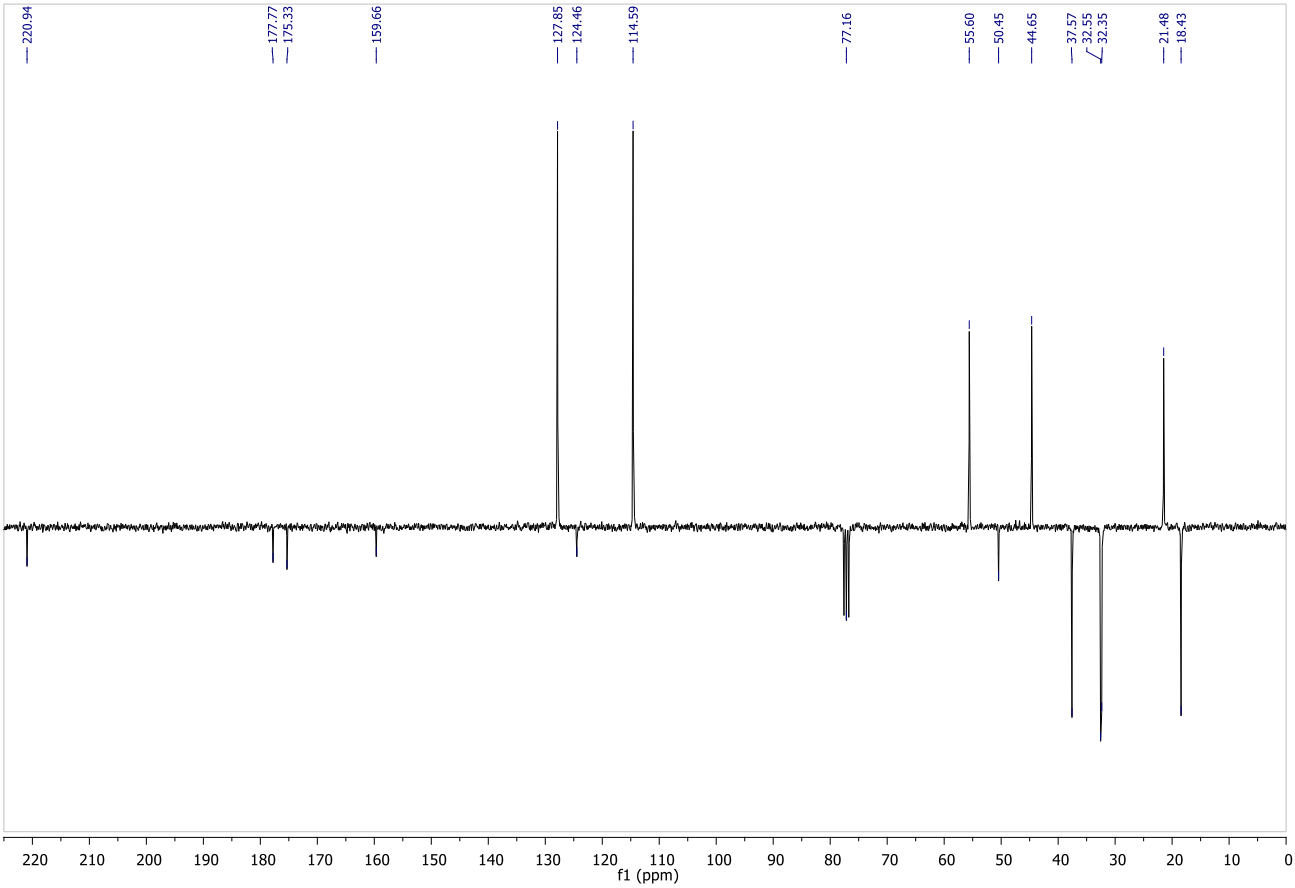

220.77
219.83
177.39
176.78
174.90
129.07
128.58
126.50
126.33
50.25
49.19
46.46
44.51
37.62
37.36
32.51
32.41
32.17
31.58
21.27
20.81
18.45
18.24
f1 (ppm)

(*R*)-1-(4-Methoxyphenyl)-3-((*R*)-1-methyl-2-oxocyclopentyl)-2,5-pyrrolidinedione 15g



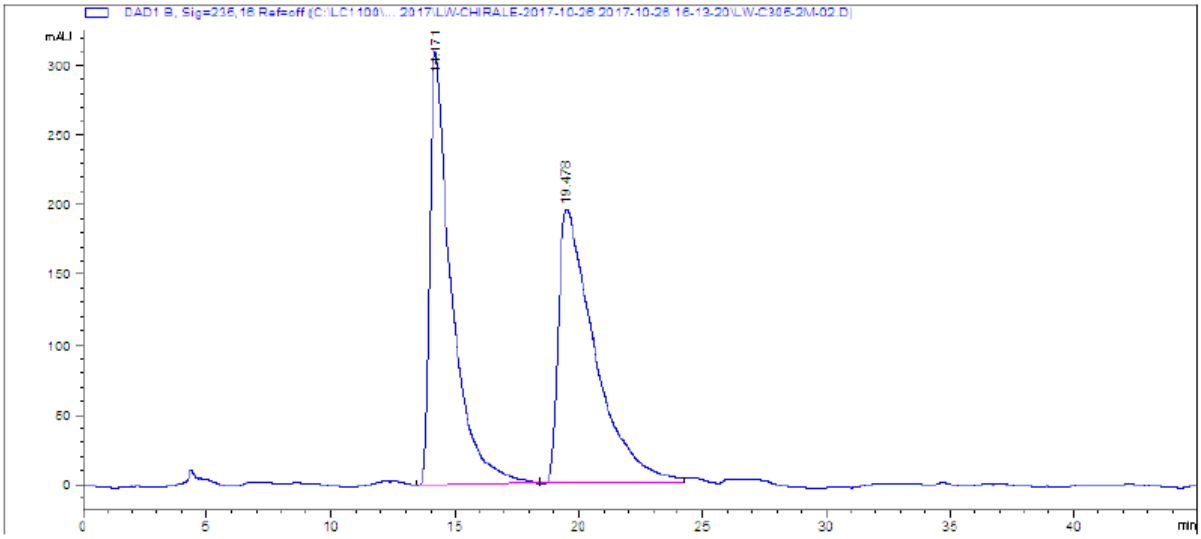
Compound (1*R*,3*R*)-**15g** was obtained in 48% (145 mg) yield (dr = 80:00, 88% ee) as a white solid. The corresponding diastereomer **16g** was obtained in 12% (36 mg) yield. **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **m.p.**: 140.4 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.13 (d, *J* = 8.8 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 2H), 3.81 (s, 3H), 3.15 (dd, *J* = 9.2, 5.2 Hz, 1H), 2.93 (dd, *J* = 18.3, 9.3 Hz, 1H), 2.62 (dd, *J* = 18.3, 5.1 Hz, 1H), 2.45 (dd, *J* = 18.4, 7.5 Hz, 1H), 2.31-1.78 (m, 5H), 1.33 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 220.9, 177.8, 175.3, 159.7, 127.9, 124.5, 114.6, 55.6, 50.5, 44.7, 37.6, 32.6, 32.4, 21.5, 18.4; **HRMS (ESI)** m/z calcd for $[C_{17}H_{19}NNaO_4]^+$ 324.1206, found 324.1205; **IR** (neat) 2972, 2841, 1776, 1733, 1702, 1510, 766 cm^{-1}; **$[\alpha]^{21}_D$** = + 64 (c = 7.25, EtOH).





HPLC: (±)-**15g**. Chiralcel AD-H, *i*-PrOH/hexane = 30/70, 1 mL/min, 235 nm, retention times: 14.171, 19.478 min.

LW C305-2M **hexane / isopropanol 70 : 30**
235 nm

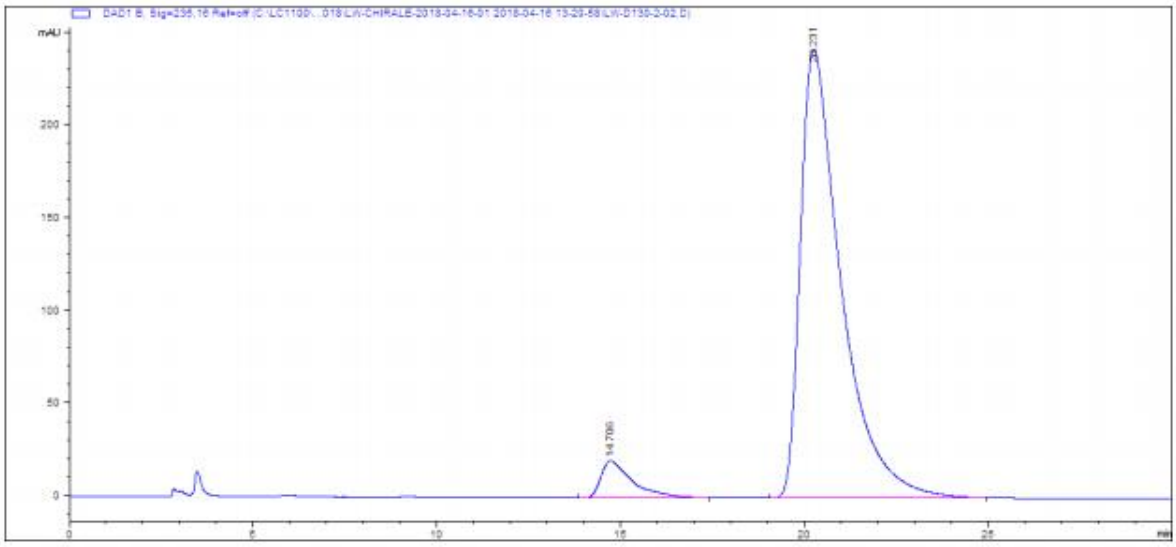


#	Time	Area	Height	Width	Area%	Symmetry
1	14.171	18849.6	310.7	0.8758	48.428	0.304
2	19.478	20073.6	195.9	1.3713	51.572	0.27

HPLC: (1*R*,3*R*)-**15g**. Chiralcel AD-H, *i*-PrOH/hexane = 30/70, 1 mL/min, 235 nm; 88% ee, retention time: 20.231 min.

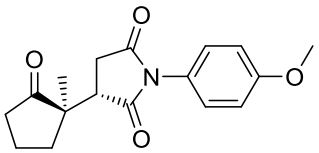
LW 130-2
235nm

Hexane / Isopropanol 70 : 30

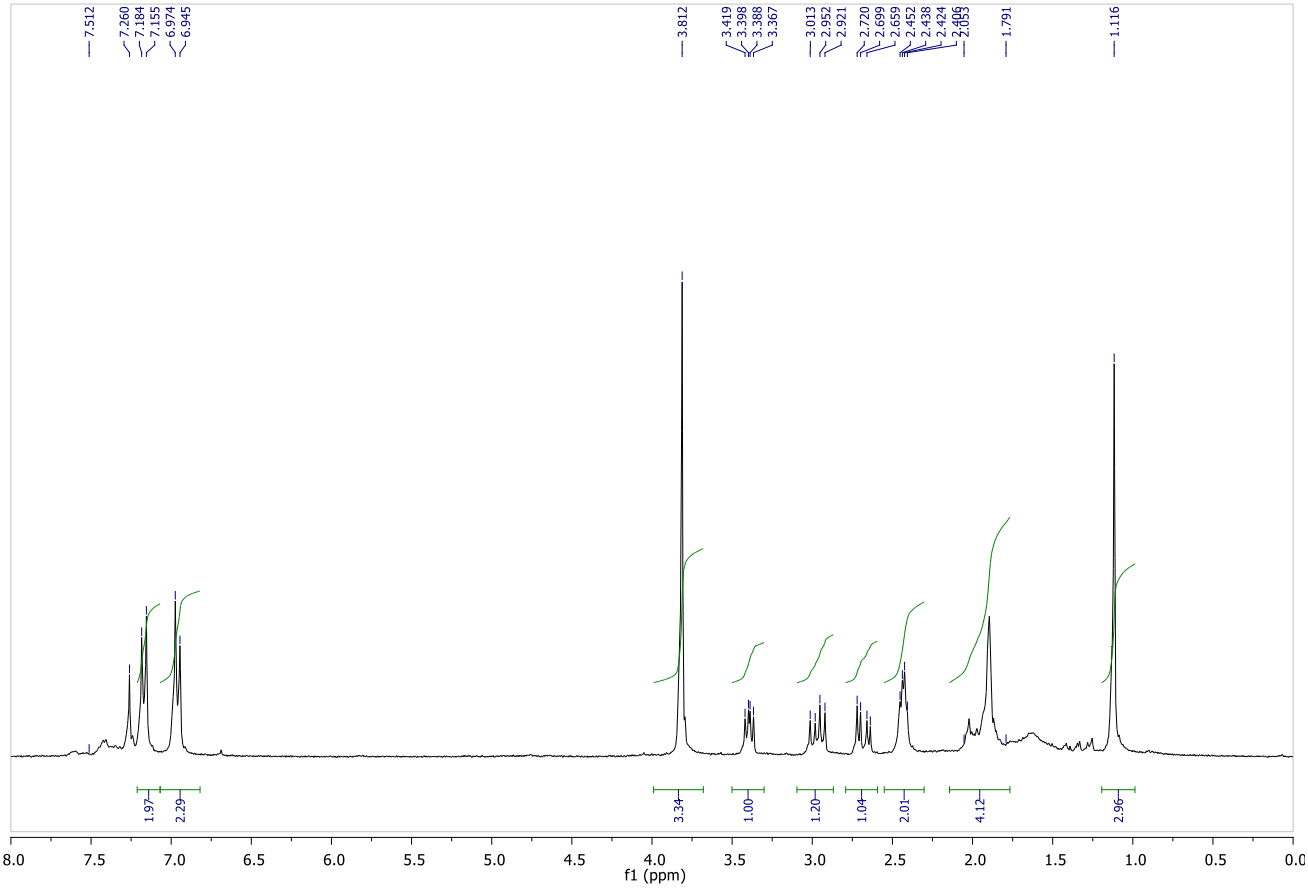


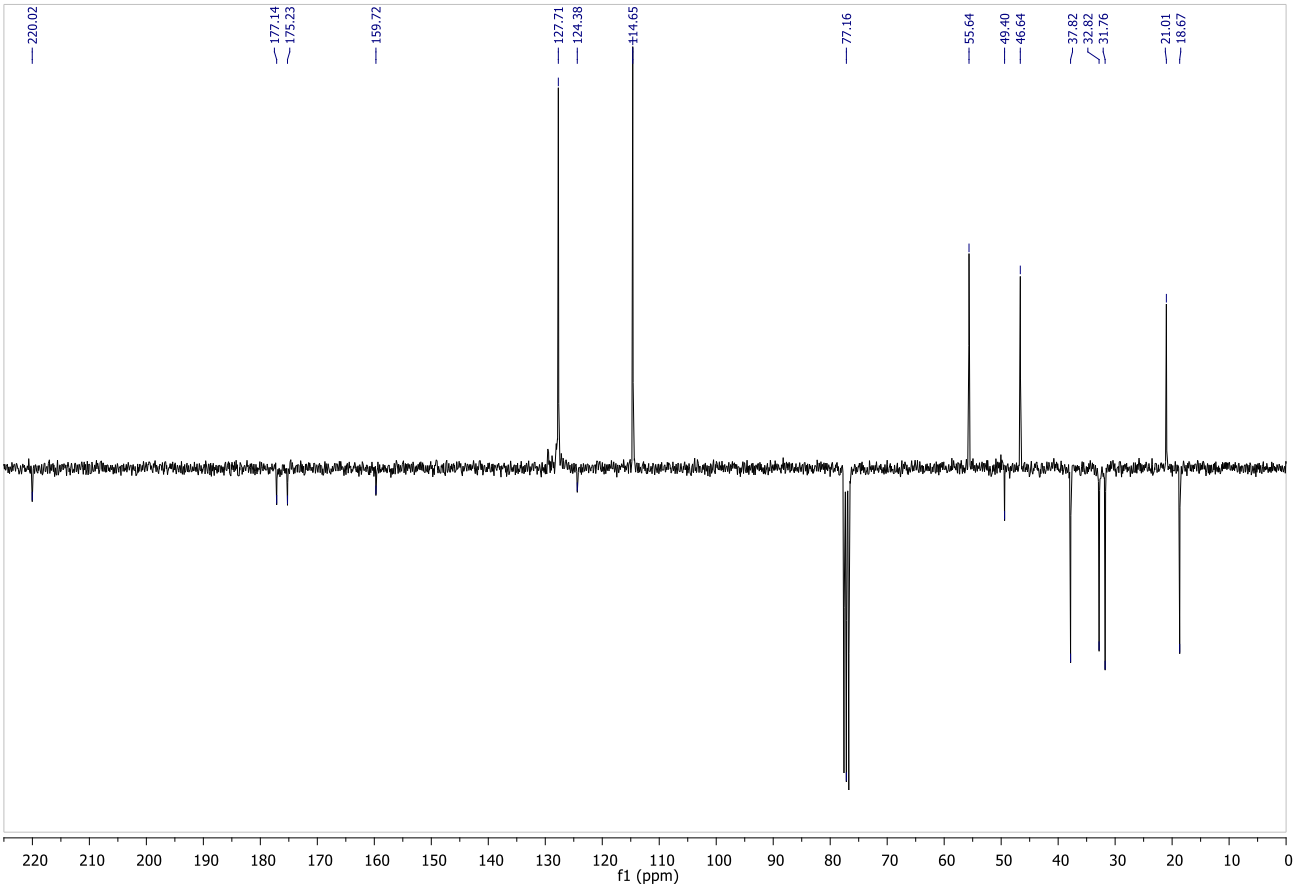
#	Time	Area	Height	Width	Area%	Symmetry
1	14.706	1169.2	19.9	0.7732	5.912	0.415
2	20.231	18607.3	241.8	1.0767	94.088	0.447

(*S*)-1-(4-Methoxyphenyl)-3-((*R*)-1-methyl-2-oxocyclopentyl)-2,5-pyrrolidinedione 16g

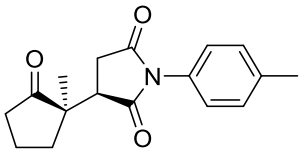


Rf = 0.2 (cyclohexane/EtOAc = 1:1); **m.p.**: undetermined because of trace impurities; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.9 Hz, 1H), 6.96 (d, *J* = 8.8 Hz, 1H), 3.81 (s, 3H), 3.39 (dd, *J* = 9.4, 6.4 Hz, 1H), 2.97 (dd, *J* = 18.2, 9.4 Hz, 1H), 2.68 (dd, *J* = 18.2, 6.4 Hz, 1H), 2.52-2.35 (m, 2H), 2.09-1.80 (m, 4H), 1.12 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 220.0, 177.1, 175.2, 159.7, 127.7, 124.4, 114.7, 55.6, 49.4, 46.6, 37.8, 32.8, 31.8, 21.0, 18.7; **HRMS (ESI)** m/z calcd for $[C_{17}H_{19}NNaO_4]^+$ 324.1206, found 324.1205; **IR** (neat) 2960, 2933, 2933, 2838, 1777, 1730, 1701, 1344, 1194, 774, 731 cm^{-1}.

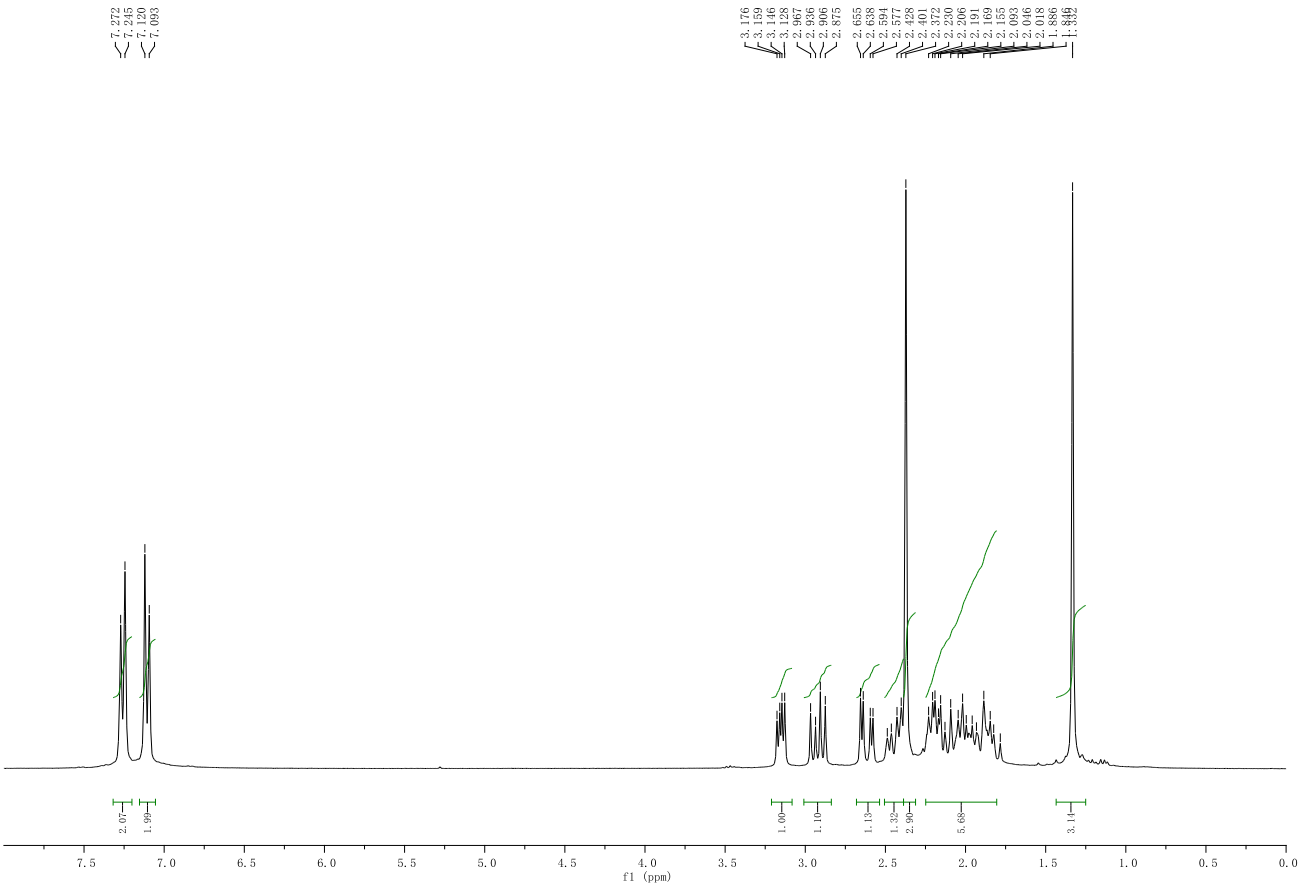

7.512
7.260
7.184
7.155
6.974
6.945
3.812
3.419
3.398
3.388
3.367
3.013
2.952
2.921
2.720
2.699
2.659
2.452
2.438
2.424
2.406
2.053
1.791
1.116
1.97
2.29
3.34
1.00
1.20
1.04
2.01
4.12
2.96
f1 (ppm)

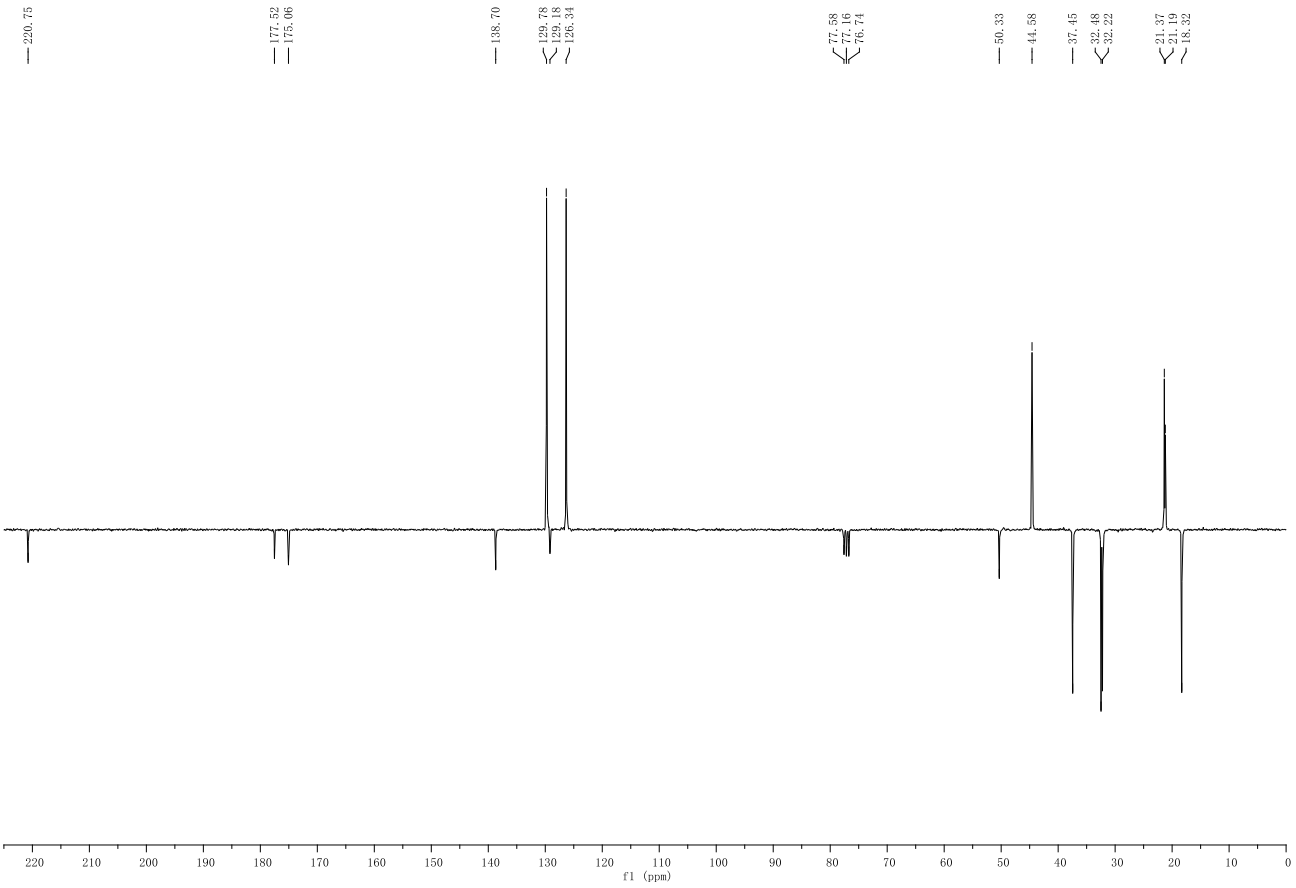

220.02
177.14
175.23
159.72
127.71
124.38
114.65
77.16
55.64
49.40
46.64
37.82
32.82
31.76
21.01
18.67
f1 (ppm)

(*R*)-3-((*R*)-1-Methyl-2-oxocyclopentyl)-1-(p-tolyl)-2,5-pyrrolidinedione 15h



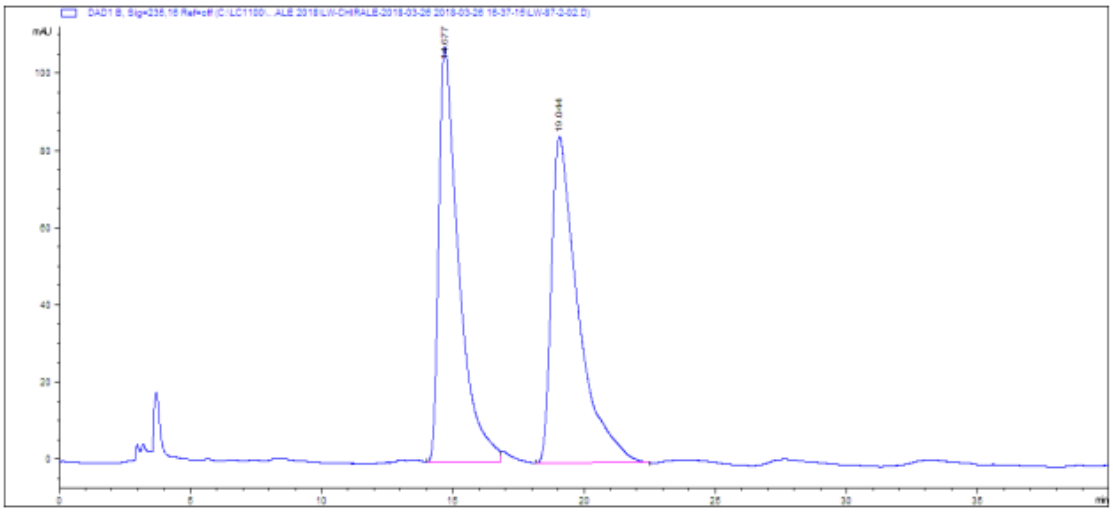
Compound (1*R*,3*R*)-**15h** was obtained as a white solid in 57% yield (163 mg), with dr = 74:26, rr > 20:1, 89% ee. The corresponding diastereomer **16h** was obtained in 20% yield (57 mg). **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **m.p.** 153.2°C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.1 Hz, 2H), 7.11 (d, *J* = 8.1 Hz, 2H), 3.15 (dd, *J* = 8.4, 5.1 Hz, 1H), 2.92 (dd, *J* = 18.3, 8.4 Hz, 1H), 2.62 (dd, *J* = 18.3, 5.1 Hz, 1H), 2.45 (dd, *J* = 18.0, 7.5 Hz, 1H), 2.37 (s, 3H), 2.30-1.75 (m, 5H), 1.33 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 220.8, 177.5, 175.1, 138.7, 129.8, 129.2, 126.3, 50.3, 44.6, 37.5, 32.5, 32.2, 21.4, 21.2, 18.3; **HRMS (ESI)** m/z calcd for $[C_{17}H_{20}NO_3]^+$ 286.1438, found 286.1443; **IR** (neat) 2972, 2923, 1777, 1734, 1702, 1458, 1444, 1397, 1377, 1199, 839, 818, 719 cm^{-1}; **$[\alpha]^{21}_D$** = + 46 (c = 5.0, EtOH).





HPLC: (±)-**15h**. Chiralpal AD, Solvent: hexane/i-PrOH = 80:20, Flow Speed 1.0 mL/min , UV: 235nm, retention times: 14.677, 19.044 min.

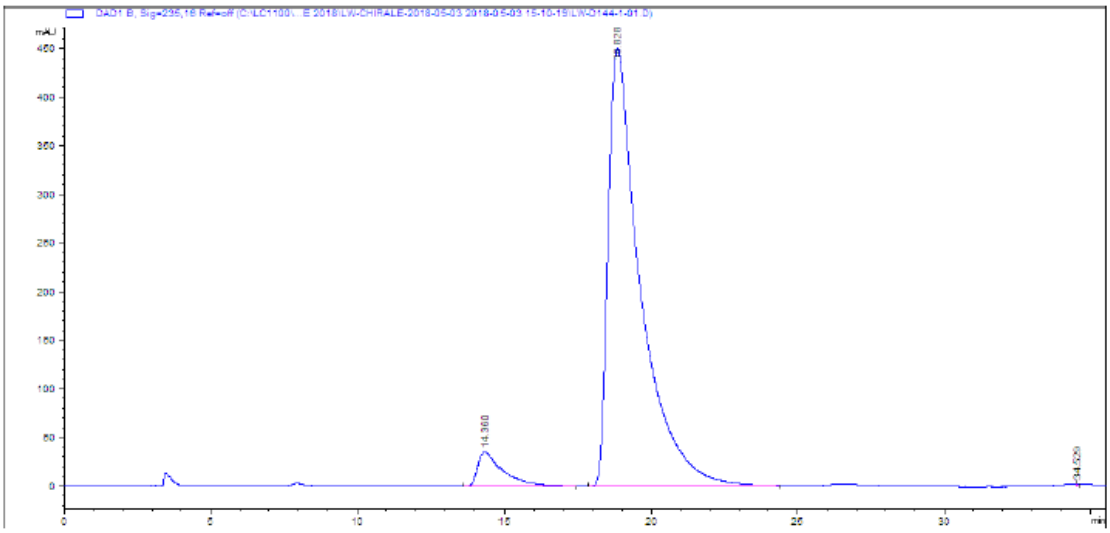
LW D87-2 hexane / isopropanol 80 : 20
235 nm



#	Time	Area	Height	Width	Area%	Symmetry
1	14.677	5711.4	107.6	0.712	48.744	0.399
2	19.044	6005.7	84.6	0.935	51.256	0.397

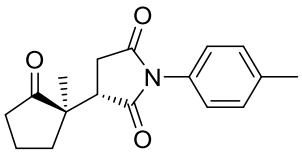
HPLC: (1*R*,3*R*)-**15h**. Chiralpal AD, Solvent: hexane/i-PrOH = 80:20, Flow Speed 1.0 mL/min, UV: 235nm, 89% ee, retention time: 18.828 min.

LW D144-1 **Hexane / Isopropanol 80 : 20**
235nm

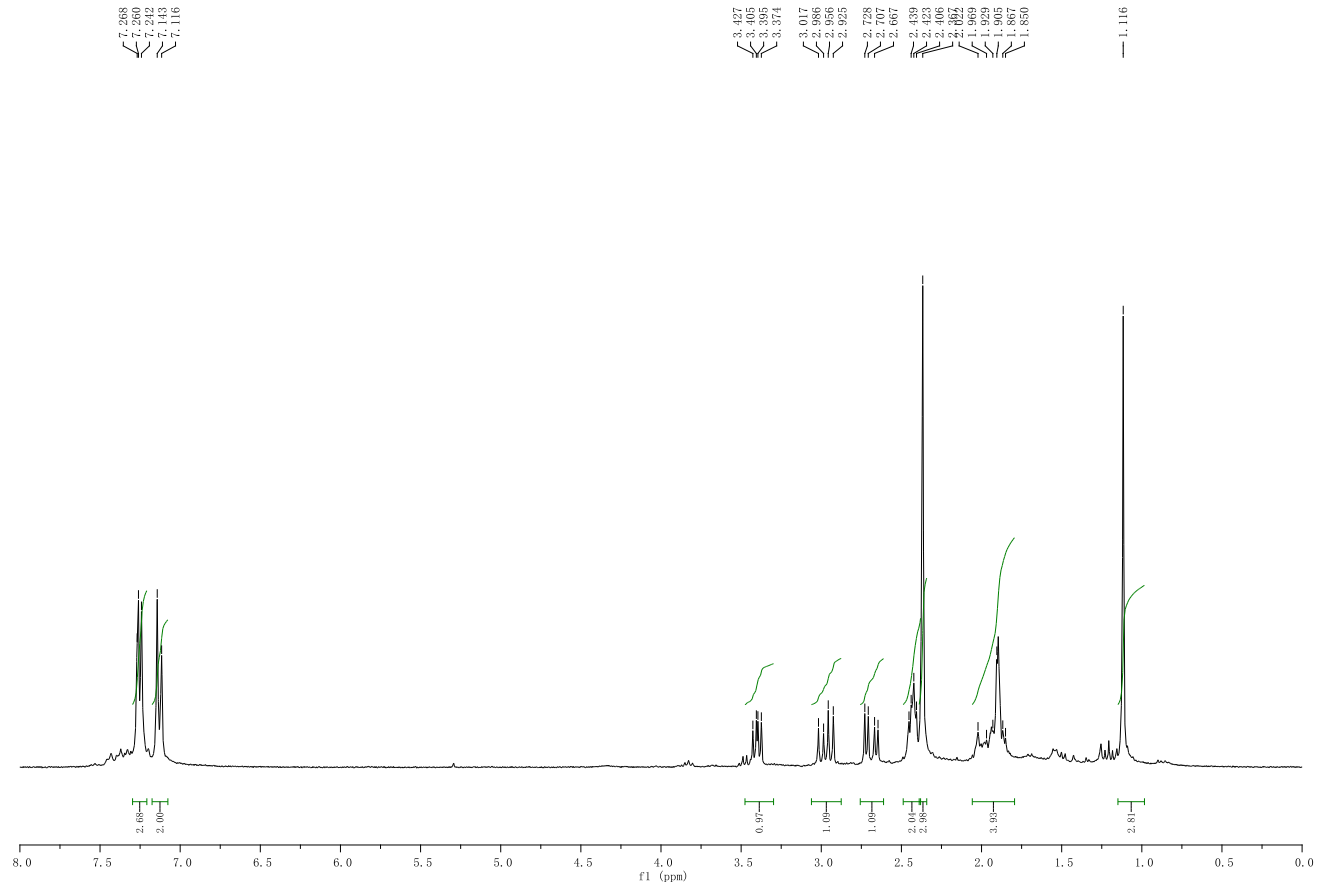


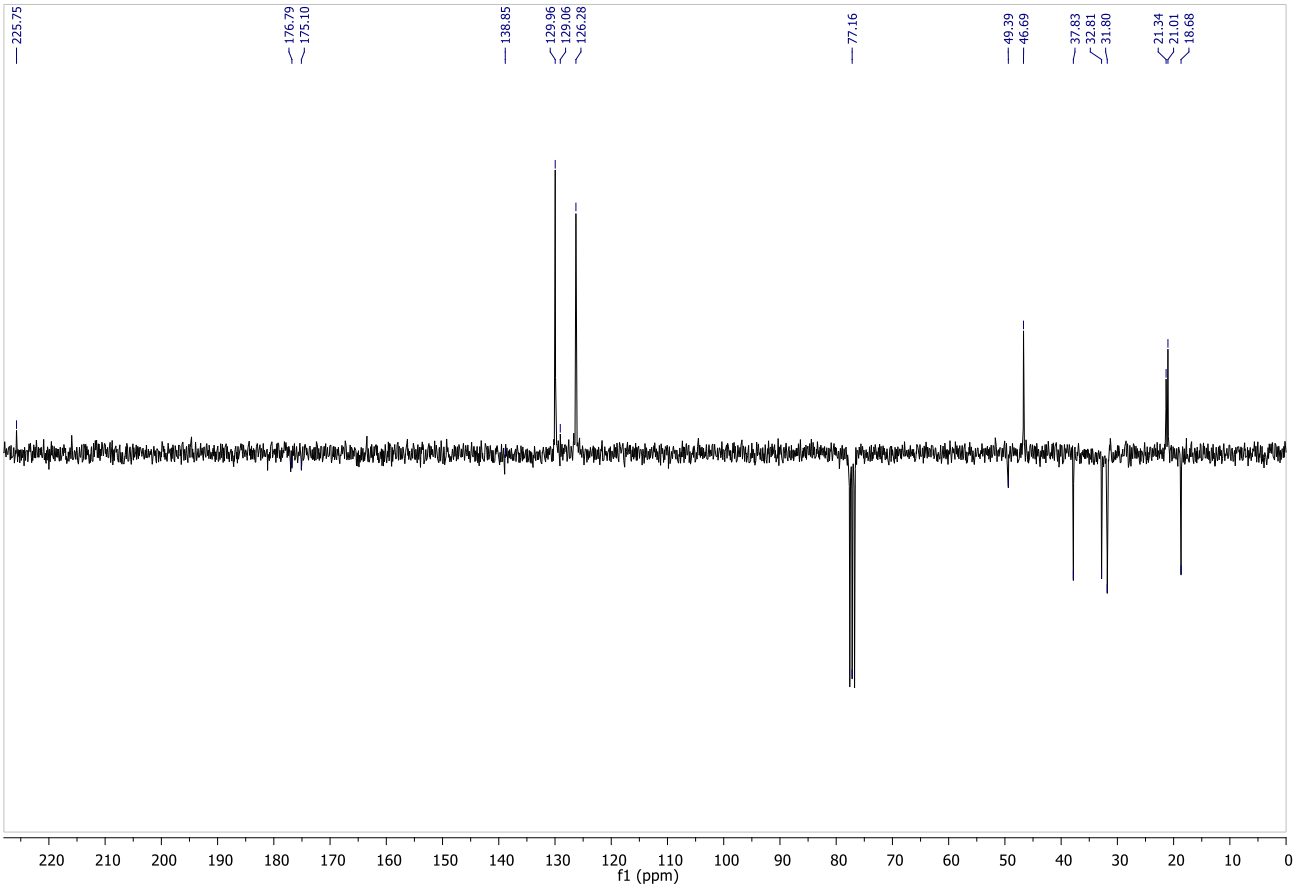
#	Time	Area	Height	Width	Area%	Symmetry
1	14.36	2090.4	35.6	0.7868	5.682	0.377
2	18.828	34687.1	450.3	1.0717	94.282	0.366
3	34.529	13.2	2.2	0.0756	0.036	0.257

(*S*)-3-((*R*)-1-Methyl-2-oxocyclopentyl)-1-(p-tolyl)pyrrolidine-2,5-dione 16h

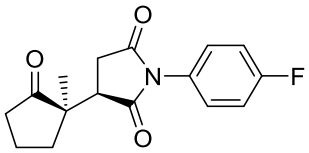


16h: 20% yield; **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); White solid, **m.p.** 204.0 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 8.1 Hz, 2H), 3.40 (dd, *J* = 9.6, 6.6 Hz, 1H), 2.97 (dd, *J* = 18.3, 9.6 Hz, 1H), 2.69 (dd, *J* = 18.3, 6.6 Hz, 1H), 2.43 (m, *J* = 2H), 2.37 (s, 3H), 2.06-1.82 (m, 4H), 1.12 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 225.8, 176.8, 175.1, 139.0, 130.0, 129.1, 126.3, 49.4, 46.7, 37.8, 32.8, 31.8, 21.3, 21.0, 18.7; **HRMS (ESI)** m/z calcd for $[C_{17}H_{19}NNaO_3]^+$ 308.1257, found 308.1261; **IR** (neat) 2972, 2923, 1777, 1734, 1702, 1458, 1444, 1397, 1377, 1199, 839, 818, 719 cm^{-1}.

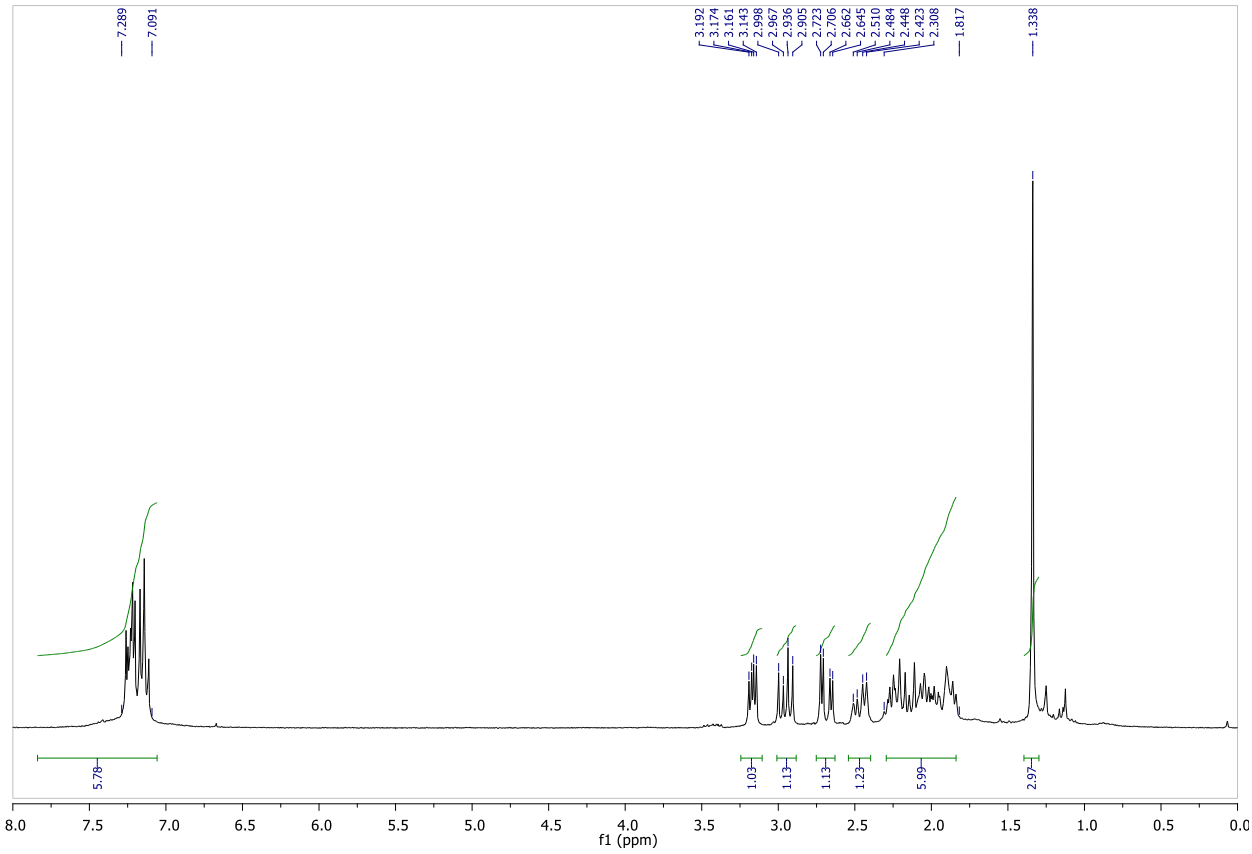

7.268
7.260
7.242
7.143
7.116
3.427
3.405
3.395
3.374
3.017
2.986
2.956
2.925
2.728
2.707
2.667
2.439
2.423
2.406
1.969
1.929
1.905
1.867
1.850
1.116
2.68
2.00
0.97
1.09
1.09
2.04
2.98
3.93
2.81
f1 (ppm)

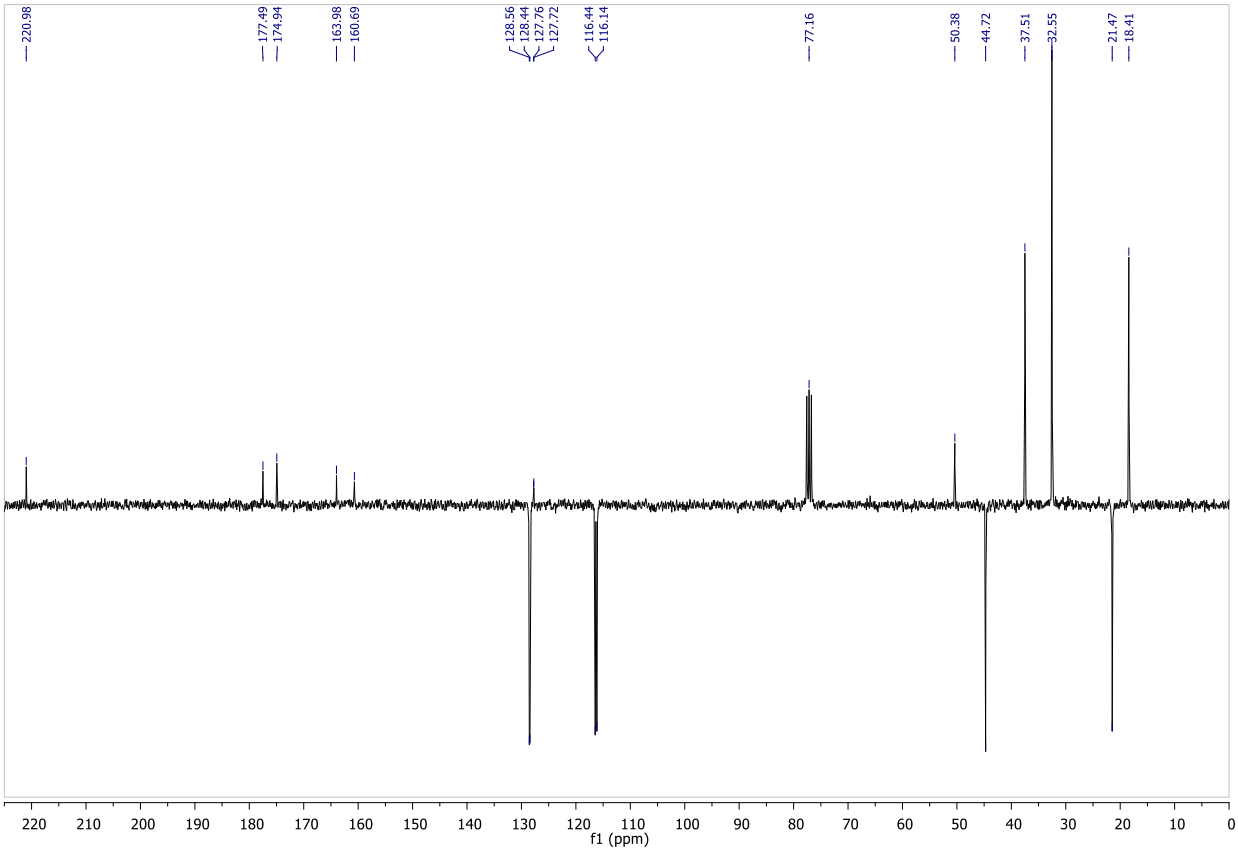

225.75
176.79
175.10
138.85
129.96
129.06
126.28
77.16
49.39
46.69
37.83
32.81
31.80
21.34
21.01
18.68
f1 (ppm)

(*R*)-1-(4-Fluorophenyl)-3-((*R*)-1-methyl-2-oxocyclopentyl)-2,5-pyrrolidinedione 15i



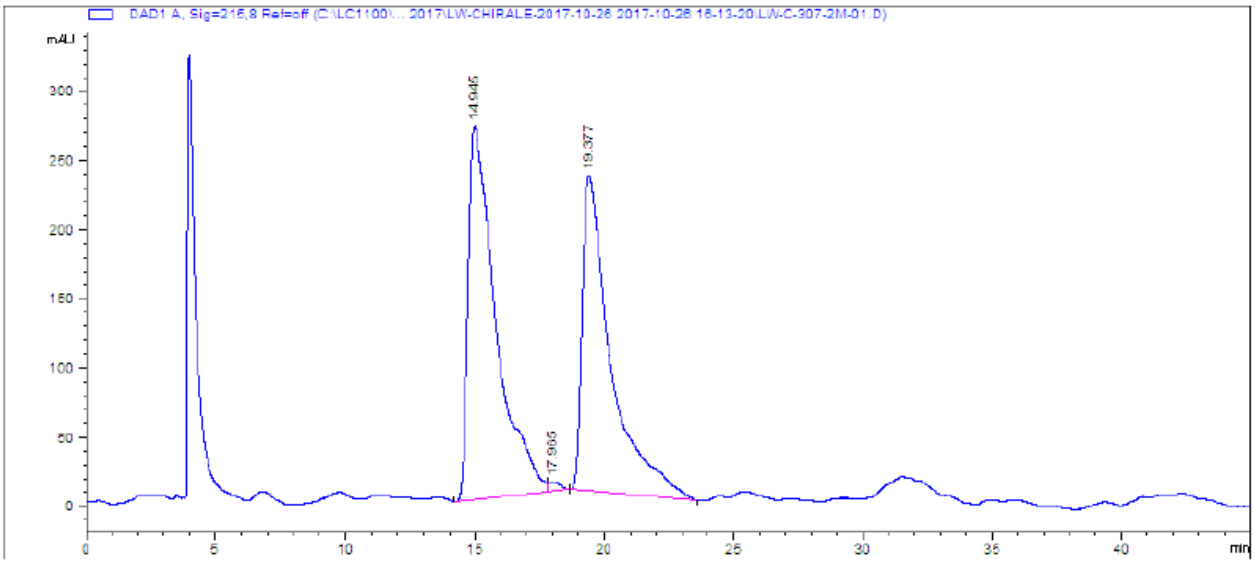
Compound (1*R*,3*R*)-**15i** was obtained in 46% (134 mg) yield as a white solid (d.r. 70/30, 87% ee). The corresponding diastereomer **16i** was obtained in 21% yield (61 mg). **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **m.p.** 104.7 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.29-7.00 (m, 4H), 3.16 (dd, *J* = 9.3, 5.4 Hz, 1H), 2.95 (dd, *J* = 18.3, 9.3 Hz, 1H), 2.68 (dd, *J* = 18.3, 5.4 Hz, 1H), 2.46 (bdd, *J* = 18.6, 7.5 Hz, 1H), 2.30-1.82 (m, 5H), 1.34 (s, 3H); **^{13}C NMR** (75 MHz, CDCl3) δ 221.0, 177.5, 174.9, 164.0 (d, *J* = 246.7 Hz), 128.5 (d, *J* = 9 Hz), 127.7 (d, *J* = 3.0 Hz), 116.3 (d, *J* = 22.5 Hz), 50.4, 44.7, 37.5, 32.6, 21.5, 18.4; **HRMS (ESI)** m/z calcd for $[C_{16}H_{16}FNNaO_3]^+$ 312.1006, found 312.1002; **IR** (neat) 2968, 1779, 1736, 1710, 1511, 1392, 1223, 1180, 836 cm^{-1}; **$[\alpha]^{25}_D$** = + 47.7 (c = 5.9, $CHCl_3$).





HPLC: (±)-**15i**. Chiralcel AD-H, *i*-PrOH/hexane = 10/90, 1 mL/min, 215 nm; retention times: 14.945, 19.377 min.

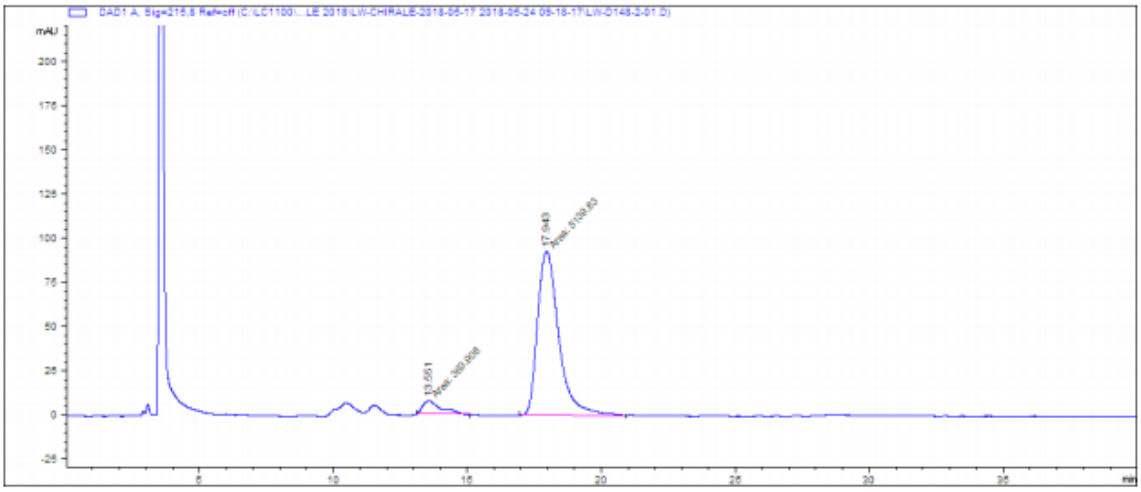
LW C307-2M **hexane / isopropanol 80 : 20**
215 nm



#	Time	Area	Height	Width	Area%	Symmetry
1	14.945	20144.1	270.3	0.9815	53.531	0.277
2	19.377	17486.9	228.3	1.0537	46.469	0.285

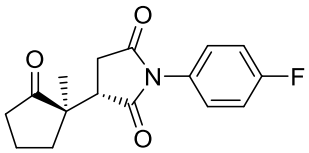
HPLC: (1*R*,3*R*)-**15i**. Chiralcel AD-H, *i*-PrOH/hexane = 20/80, 1 mL/min, 215 nm; 87% ee, retention time: 17.943 min.

LW D148-2 **Hexane / Isopropanol 80 : 20**
215 nm

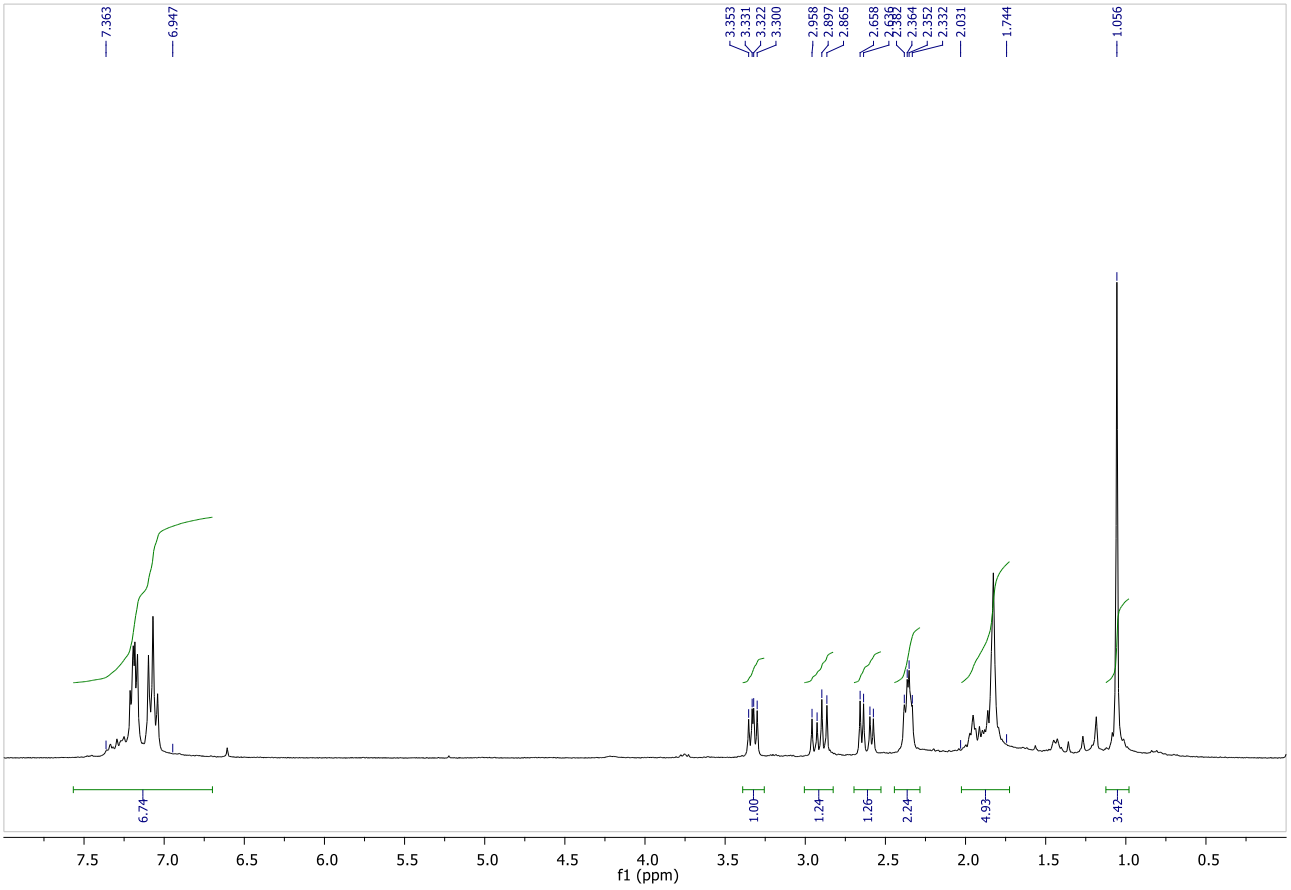


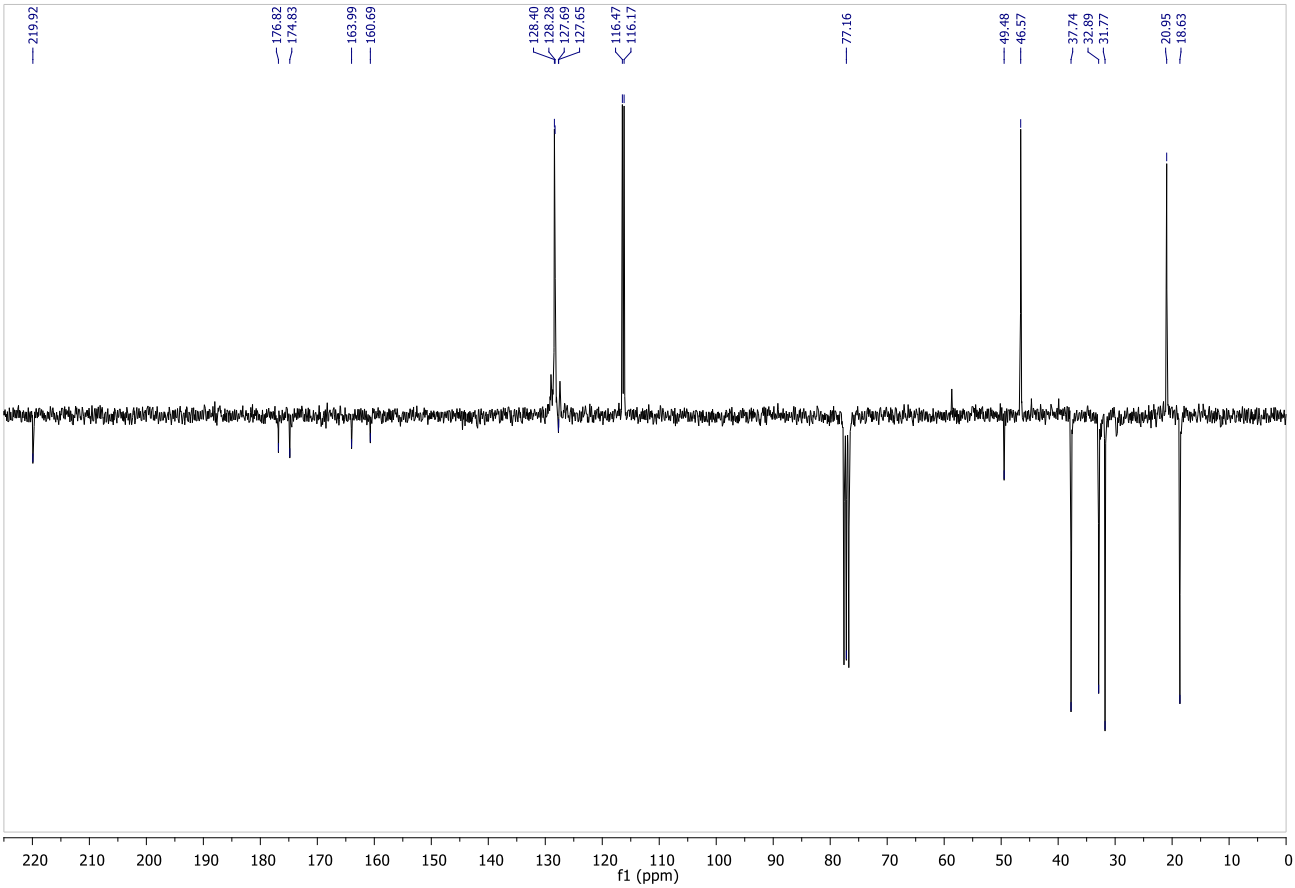
#	Time	Area	Height	Width	Area%	Symmetry
1	13.551	363.9	7.6	0.8033	6.612	0.494
2	17.943	5139.8	92.8	0.9234	93.388	0.71

(*S*)-1-(4-Fluorophenyl)-3-((*R*)-1-methyl-2-oxocyclopentyl)-2,5-pyrrolidinedione (1*R*,3*S*)-16i

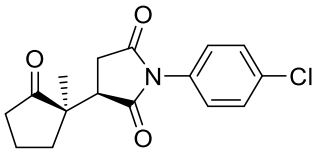


16i: 21% yield; White solid, **m.p.** 186.2 °C; **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.36-6.95 (m, 4H), 3.33 (dd, *J* = 9.4, 6.5 Hz, 1H), 2.91 (dd, *J* = 18.4, 9.5 Hz, 1H), 2.62 (dd, *J* = 18.4, 6.5 Hz, 1H), 2.36 (dd, *J* = 9.2, 5.7 Hz, 2H), 2.03-1.74 (m, 4H), 1.06 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 219.9, 176.8, 174.8, 162.3 (d, *J* = 247.5 Hz), 128.3 (d, *J* = 9 Hz), 127.7 (d, *J* = 3.0 Hz), 116.3 (d, *J* = 22.5 Hz), 49.5, 46.6, 37.7, 32.9, 32.9, 20.9, 18.6; **HRMS (ESI)** m/z calcd for $[C_{16}H_{16}FNNaO_3]^+$ 312.1006, found 312.1006; **IR** (neat) 2969, 1780, 1737, 1708, 1511, 1391, 1223, 1186, 1168, 1157, 879, 730 cm^{-1}.

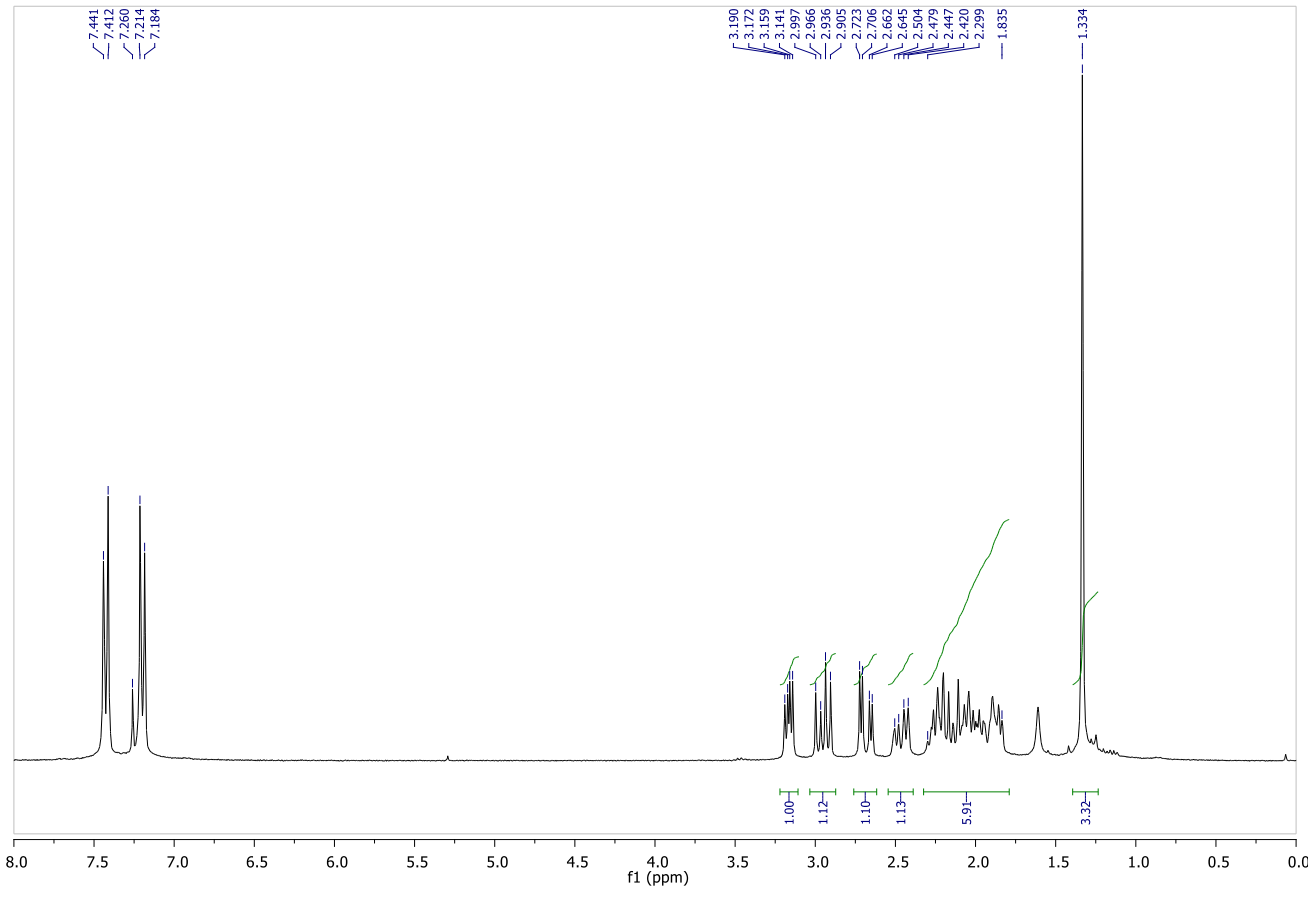

7.363
6.947
3.353
3.331
3.322
3.300
2.958
2.897
2.865
2.658
2.364
2.352
2.332
2.031
1.744
1.056
6.74
1.00
1.24
1.26
2.24
4.93
3.42
f1 (ppm)

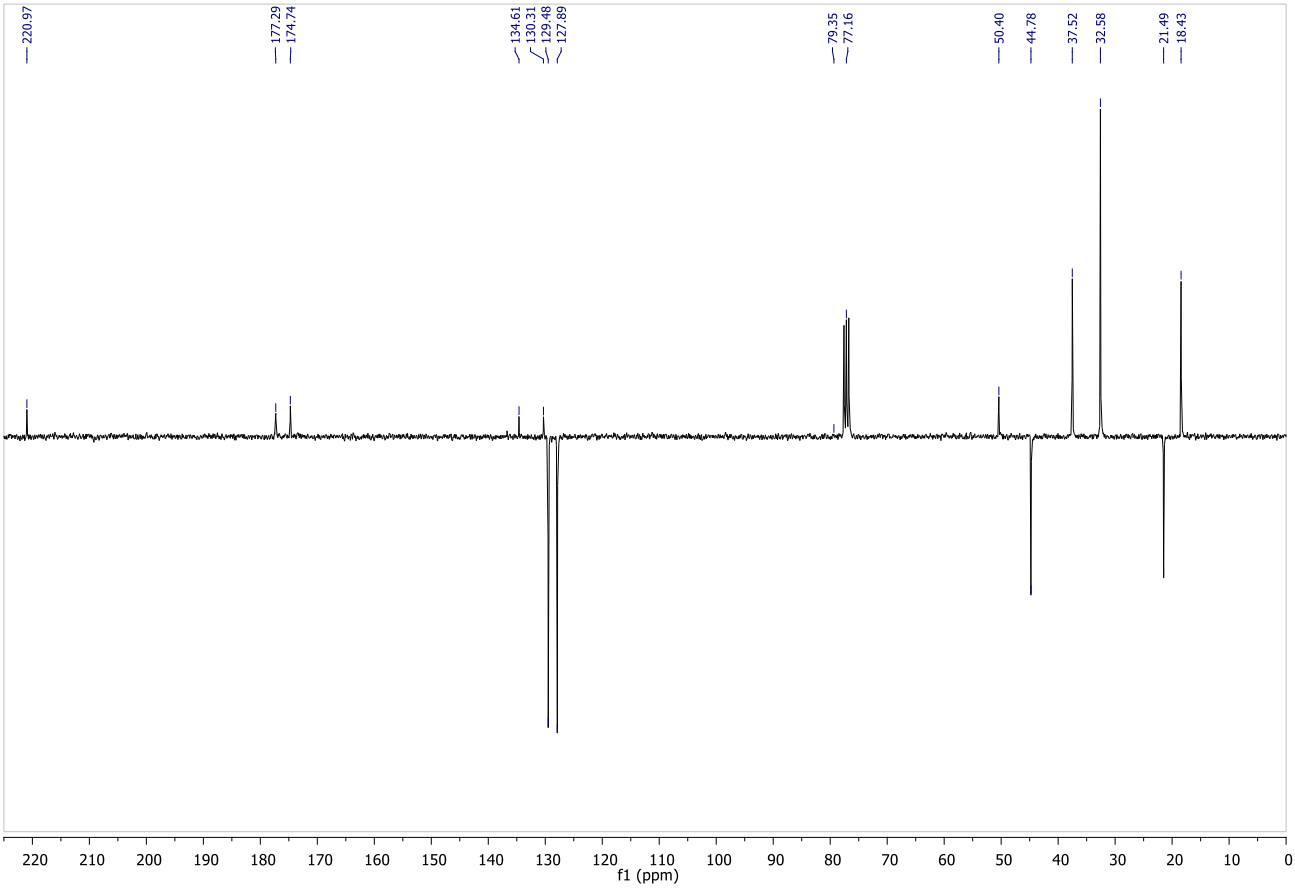

219.92
176.82
174.83
163.99
160.69
128.40
128.28
127.69
127.65
116.47
116.17
77.16
49.48
46.57
37.74
32.89
31.77
20.95
18.63
f1 (ppm)

(*R*)-1-(4-Chlorophenyl)-3-((*R*)-1-methyl-2-oxocyclopentyl)-2,5-pyrrolidinedione 15j



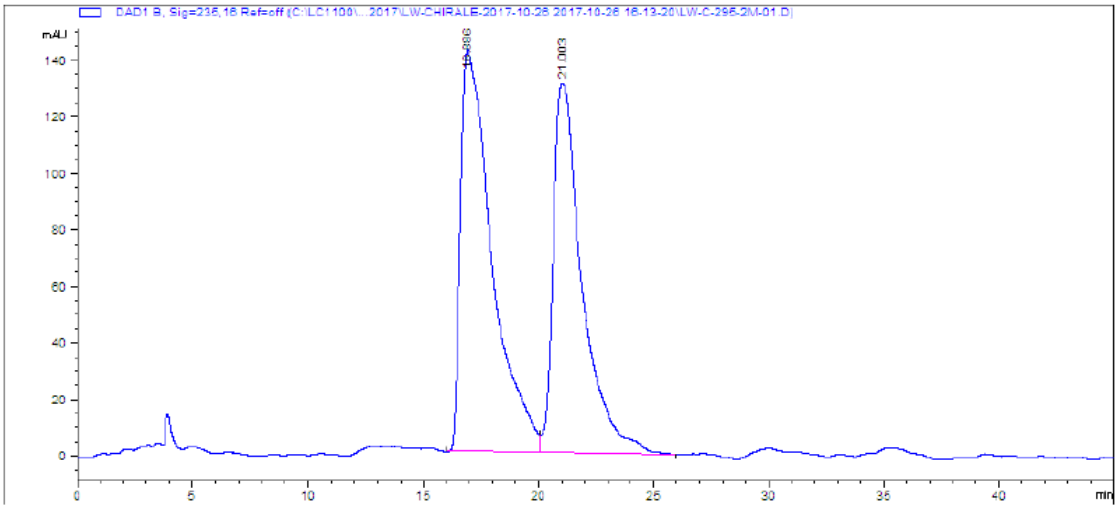
Compound (1*R*,3*R*)-**15j** was obtained as a white solid in 40% yield (122 mg) with dr = 72:28, 88% ee. The corresponding diastereomer was obtained in 18% yield (55 mg) as a white solid. **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **m.p.** 155.8 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.7 Hz, 2 H), 7.20 (d, *J* = 8.7 Hz, 2 H), 3.17 (dd, *J* = 9.3, 5.3 Hz, 1H), 2.95 (dd, *J* = 18.3, 9.3 Hz, 1H), 2.68 (dd, *J* = 18.3, 5.4 Hz, 1H), 2.46 (dd, *J* = 18.1, 8.4 Hz, 1H), 2.30-1.80 (m, 5H), 1.33 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 221.0, 177.3, 174.7, 134.6, 130.3, 129.5, 127.9, 50.4, 44.8, 37.5, 32.6, 21.5, 18.4; **HRMS (ESI)** m/z calcd for $[C_{16}H_{16}ClNNaO_3]^+$ 328.0711, found 328.0718; **IR** (neat) 3098, 2972, 2949, 1776, 1734, 1702, 766, 695 cm^{-1}; **$[\alpha]^{24}_D$** = + 43 (c = 5.90, EtOH).





HPLC: (±)-**15j**. Chiralpal AD, Solvent: Hexane/i-PrOH = 80:20, Flow Speed 1.0 mL/min, UV: 235nm, retention times: 16.886, 21.003 min.

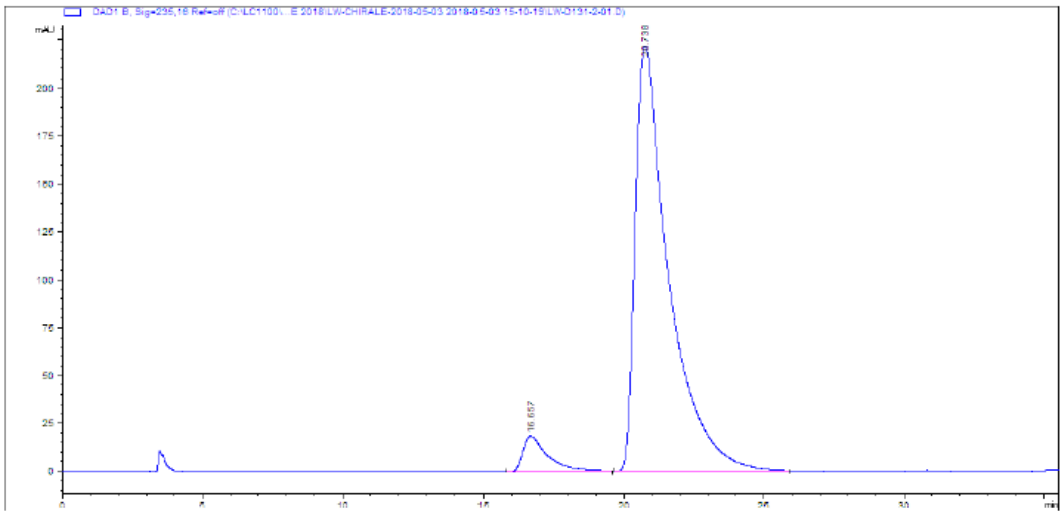
Waters
LW C295-2M **hexane / isopropanol 80 : 20**
235 nm



#	Time	Area	Height	Width	Area%	Symmetry
1	16.886	13567.3	142.6	1.262	54.289	0.276
2	21.003	11423.8	130.5	1.2371	45.711	0.423

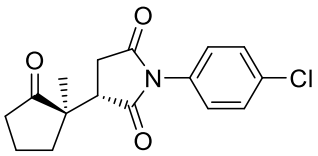
HPLC: (1*R*,3*R*)**-15j**. Chiralpal AD, Solvent: Hexane/i-PrOH = 80:20, Flow Speed 1.0 mL/min , UV: 235nm 88% ee, retention time 20.738 min.

LW D131-2 **Hexane / Isopropanol 80 : 20**
235nm

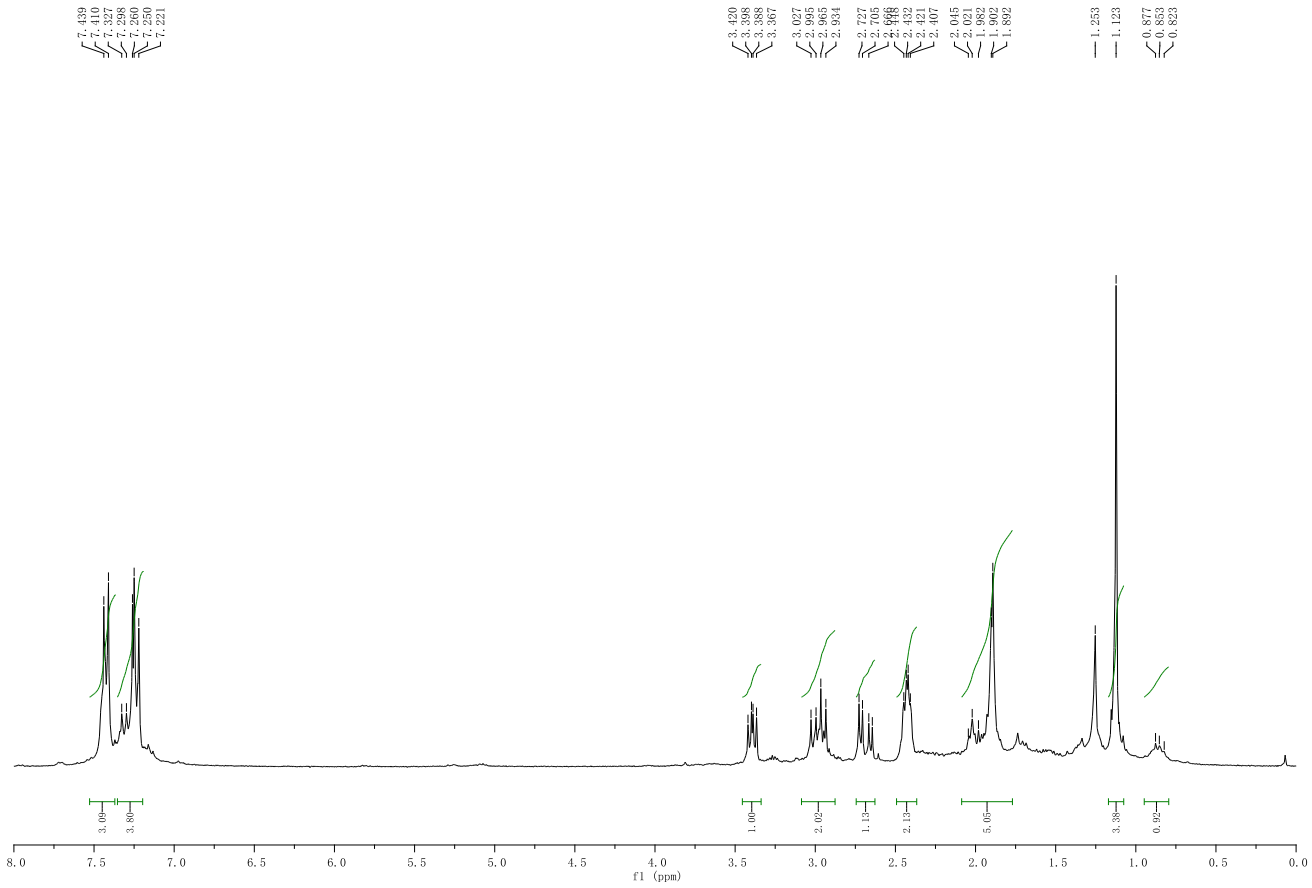


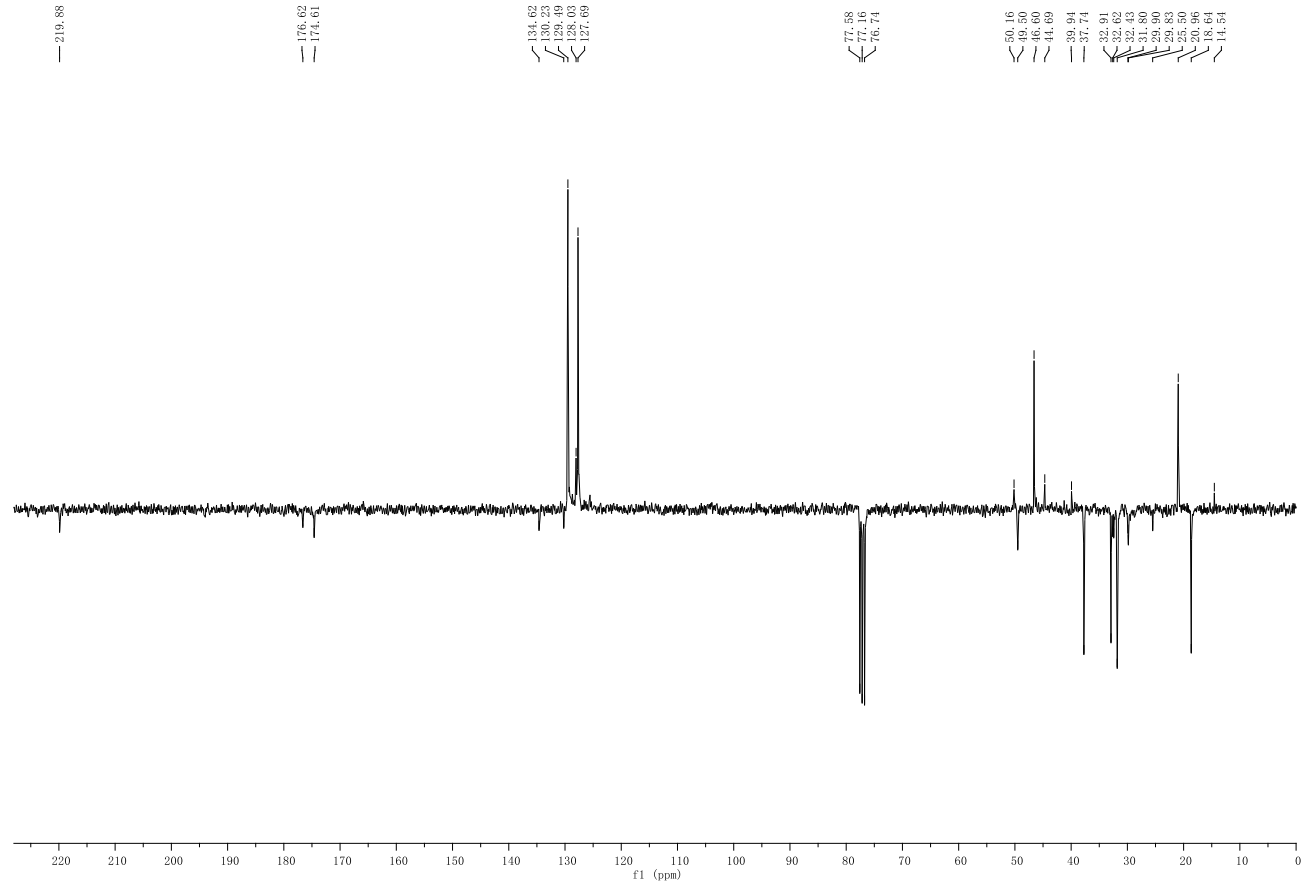
#	Time	Area	Height	Width	Area%	Symmetry
1	16.657	1161.8	18.8	0.7821	5.894	0.42
2	20.738	18550.9	221.5	1.142	94.106	0.381

(*S*)-1-(4-Chlorophenyl)-3-((*R*)-1-methyl-2-oxocyclopentyl)pyrrolidine-2,5-dione 16j

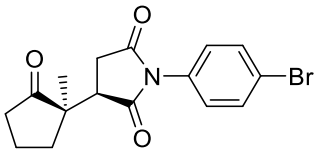


16j: 18% yield; white solid; **m.p.** 179.1 °C; **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.43 (d, *J* = 9.0 Hz, 2H), 7.23 (d, *J* = 8.7 Hz, 1H), 3.40 (dd, *J* = 9.6, 6.6 Hz, 1H), 2.99 (dd, *J* = 18.6, 9.6 Hz, 1H), 2.69 (dd, *J* = 18.6, 6.6 Hz, 1 H), 2.49-2.37 (m, 2H), 2.10-1.80 (m, 4H), 1.12 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 219.9, 176.6, 174.6, 134.6, 130.2, 129.5, 127.7, 49.5, 46.6, 39.9, 37.7, 32.9, 32.6, 31.8, 29.9, 29.8, 25.5, 21.0, 18.6; **HRMS (ESI)** m/z calcd for $[C_{16}H_{16}ClNNaO_3]^+$ 328.0711, found 328.0717; **IR** (neat) 2932, 2121, 1778, 1738, 1712, 1493, 1384, 1185, 829, 777, 722 cm^{-1}.

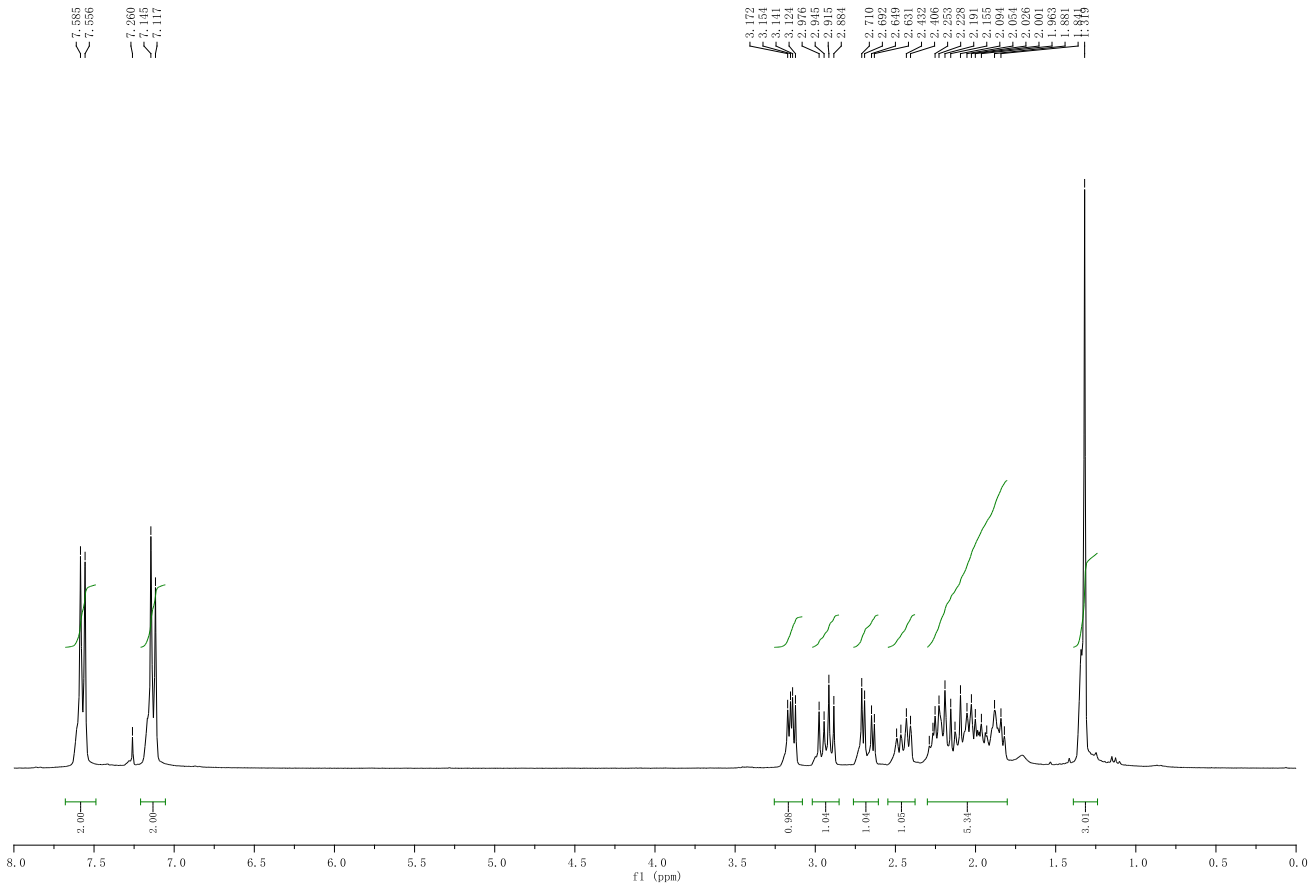

7.439
7.410
7.327
7.298
7.260
7.250
7.221
3.420
3.398
3.388
3.367
3.027
2.995
2.965
2.934
2.727
2.705
2.432
2.421
2.407
2.045
2.021
1.982
1.902
1.892
1.253
1.123
0.877
0.853
0.823
3.09
3.80
1.00
2.02
1.13
2.13
5.05
3.38
0.92
f1 (ppm)

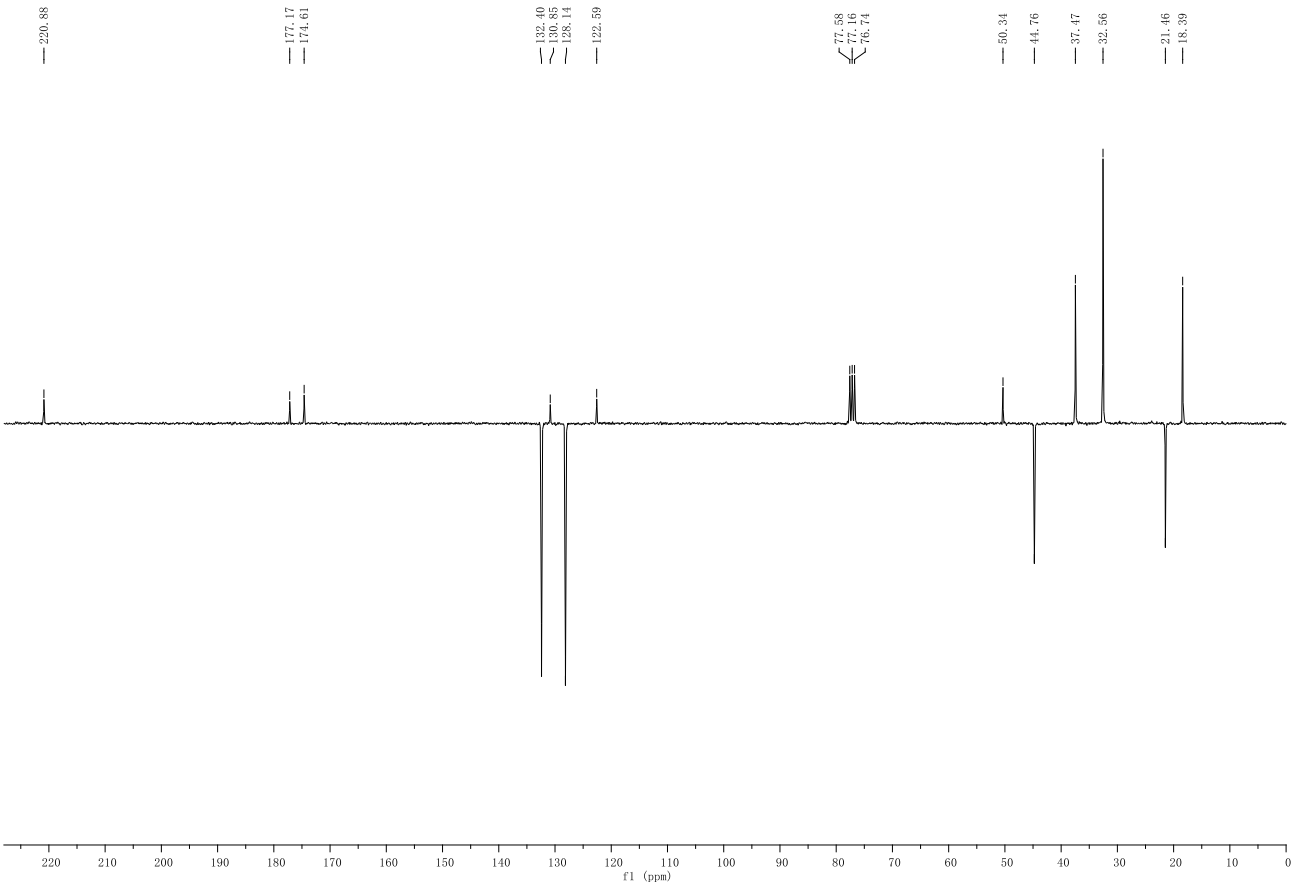

219.68
176.62
174.61
134.62
130.23
129.49
128.03
127.69
77.58
77.16
76.74
50.16
49.50
46.60
44.69
39.94
37.74
32.91
32.62
32.43
31.80
29.90
29.83
25.50
20.96
18.64
14.54
f1 (ppm)

(*R*)-1-(4-Bromophenyl)-3-((*R*)-1-methyl-2-oxocyclopentyl)-2,5-pyrrolidinedione 15k



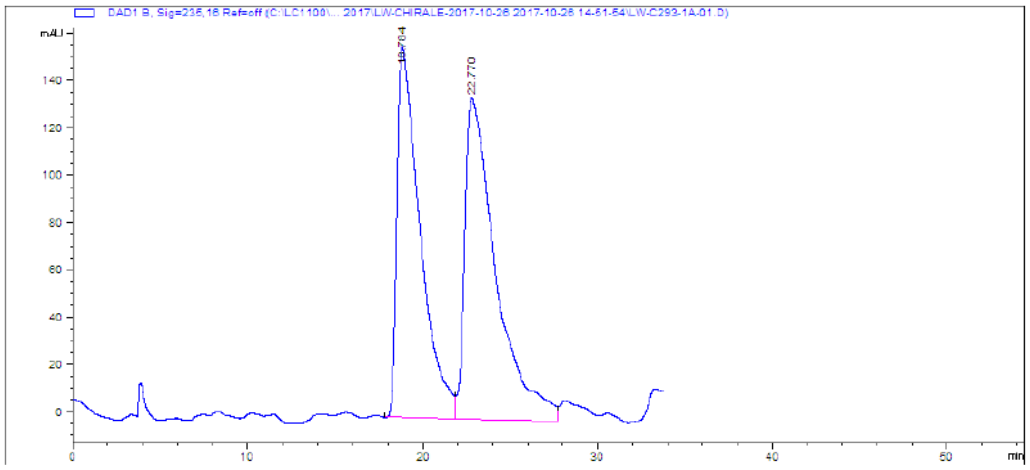
Compound (1*R*,3*R*)-**15k** was synthesized as a white solid in 52% yield (182 mg) with dr = 73:27 and 87% ee. The corresponding diastereomer **16k** was obtained in 19% yield (66 mg) as a white solid. **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **m.p.**171.1 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.7 Hz, 2H), 7.13 (d, *J* = 8.7 Hz, 2H), 3.15 (dd, *J* = 9.3, 5.4 Hz, 1H), 2.93 (dd, *J* = 18.3, 9.3 Hz, 1H), 2.67 (dd, *J* = 18.3, 5.4 Hz, 1H), 2.45 (dd, *J* = 18.3, 8.1 Hz, 1H), 2.30-1.80 (m, 5H), 1.32 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 220.9, 177.2, 174.6, 132.4, 130.9, 128.1, 122.6, 50.3, 44.8, 37.5, 32.6, 21.5, 18.4; **HRMS (ESI)** m/z calcd for $[C_{15}H_9NO_6Br]^+$ 350.0392, found 350.0389; **IR** (neat) 2972, 1776, 1736, 1704, 1488, 1392, 1199, 1180, 1164, 716 cm^{-1}; **$[\alpha]^{21}_D$** = + 52 (c = 8.2, EtOH).





HPLC: (±)-**15k**. Chiralpal AD, Solvent: Hexane/i-PrOH = 80:20, Flow Speed 1.0 mL/min, UV: 235nm retention times: 18.784, 22.77 min.

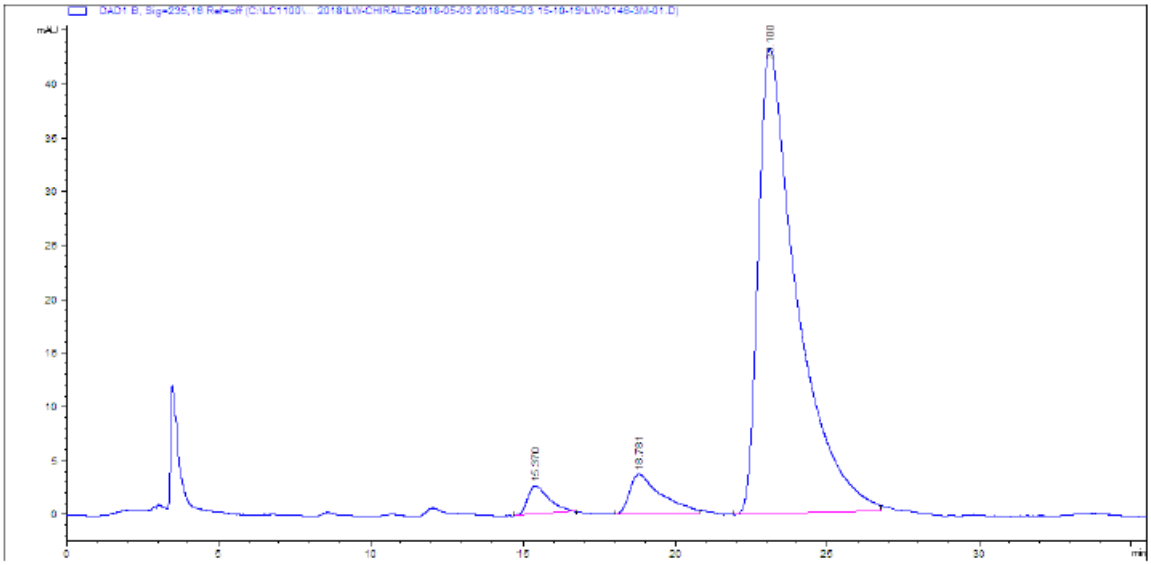
LW C293-1A **hexane / isopropanol 80 : 20**
235 nm



#	Time	Area	Height	Width	Area%	Symmetry
1	18.784	14407.5	157	1.2188	46.235	0.283
2	22.77	16754.2	135.7	1.592	53.765	0.28

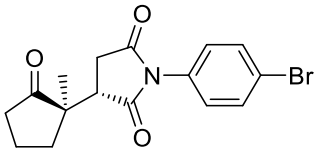
HPLC: (1*R*,3*R*)-**15k**. Chiralpal AD, Solvent: Hexane/i-PrOH = 80:20, Flow Speed 1.0 mL/min , UV: 235nm 87 % ee, retention time: 23.1 min.

LW D146-3M **Hexane / Isopropanol 80 : 20**
235nm

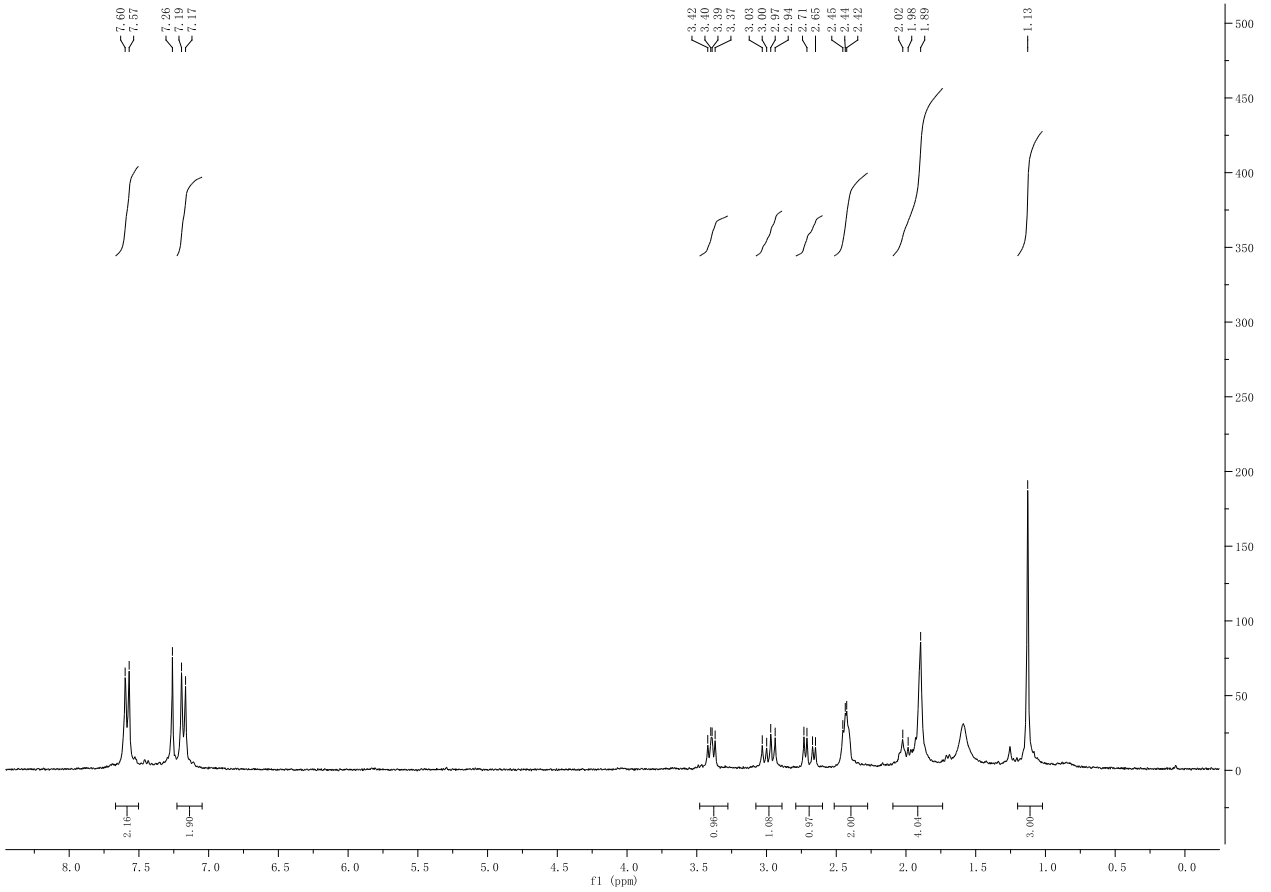


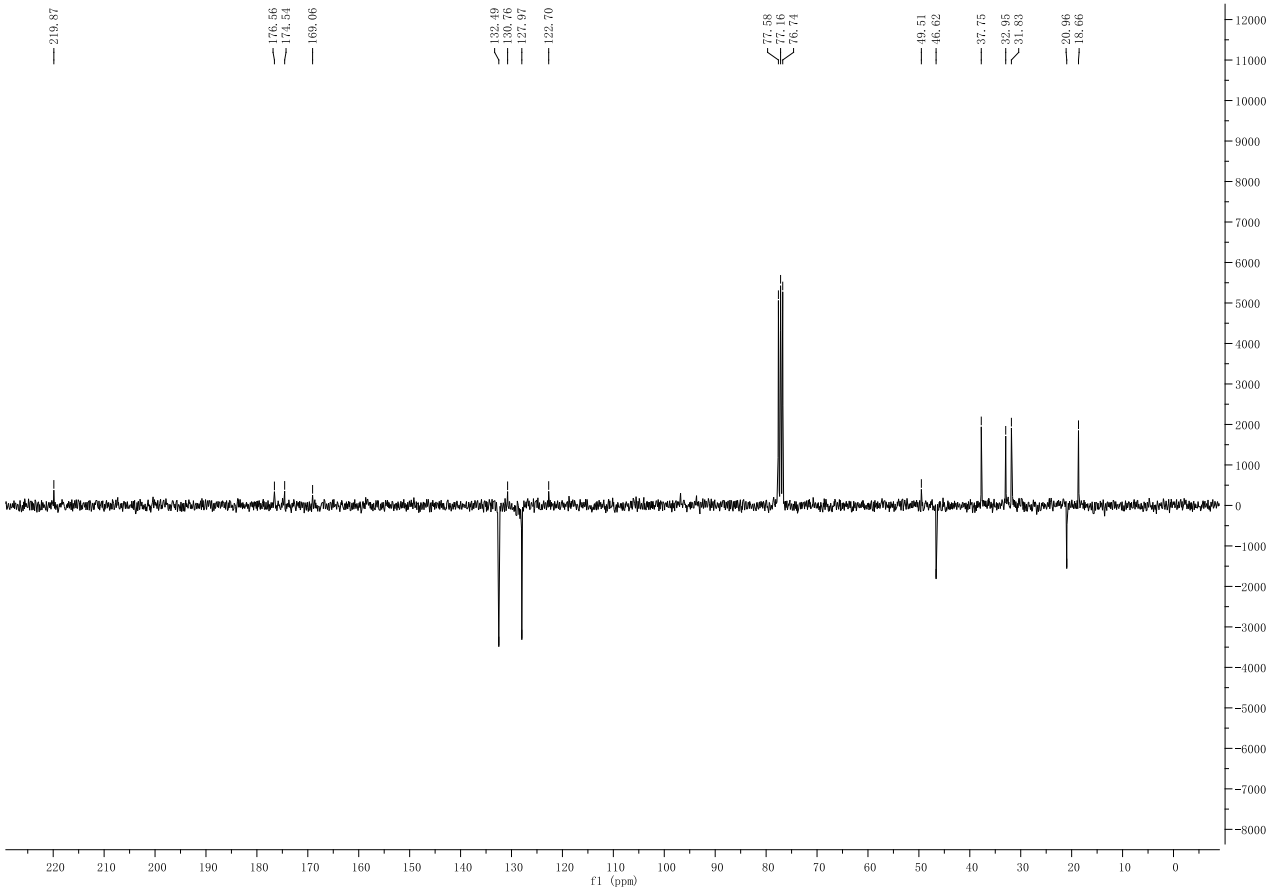
#	Time	Area	Height	Width	Area%	Symmetry
1	15.37	131.8	2.6	0.59	3.100	0.539
2	18.781	277.7	3.8	0.8664	6.531	0.385
3	23.1	3843.3	43.3	1.0561	90.369	0.421

(*S*)-1-(4-Bromophenyl)-3-((*R*)-1-methyl-2-oxocyclopentyl)-2,5-pyrrolidinedione 16k

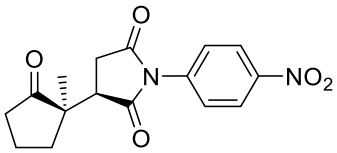


(1*R*,3*S*)-**16k**: 19% yield, white solid; **m.p.** 193.7 °C; **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.7 Hz, 2H), 7.18 (d, *J* = 8.7 Hz, 2H), 3.40 (dd, *J* = 9.3, 6.6 Hz, 1H), 2.99 (dd, *J* = 18.6, 9.3 Hz, 1H), 2.69 (dd, *J* = 18.6, 6.6 Hz, 1H), 2.43 (dd, *J* = 9.3, 6.0 Hz, 2H), 2.10-1.79 (m, 4H), 1.13 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 219.9, 176.6, 174.5, 132.5, 130.8, 128.0, 122.7, 49.5, 46.6, 37.8, 33.0, 31.8, 21.0, 18.7; **HRMS (ESI)** m/z calcd for $[C_{15}H_9NO_6Br]^+$ 350.0392, found 350.0399; **IR** (neat) 2962, 2927, 1778, 1736, 1707, 1491, 1403, 1381, 1186, 1166, 735, 717 cm^{-1}.

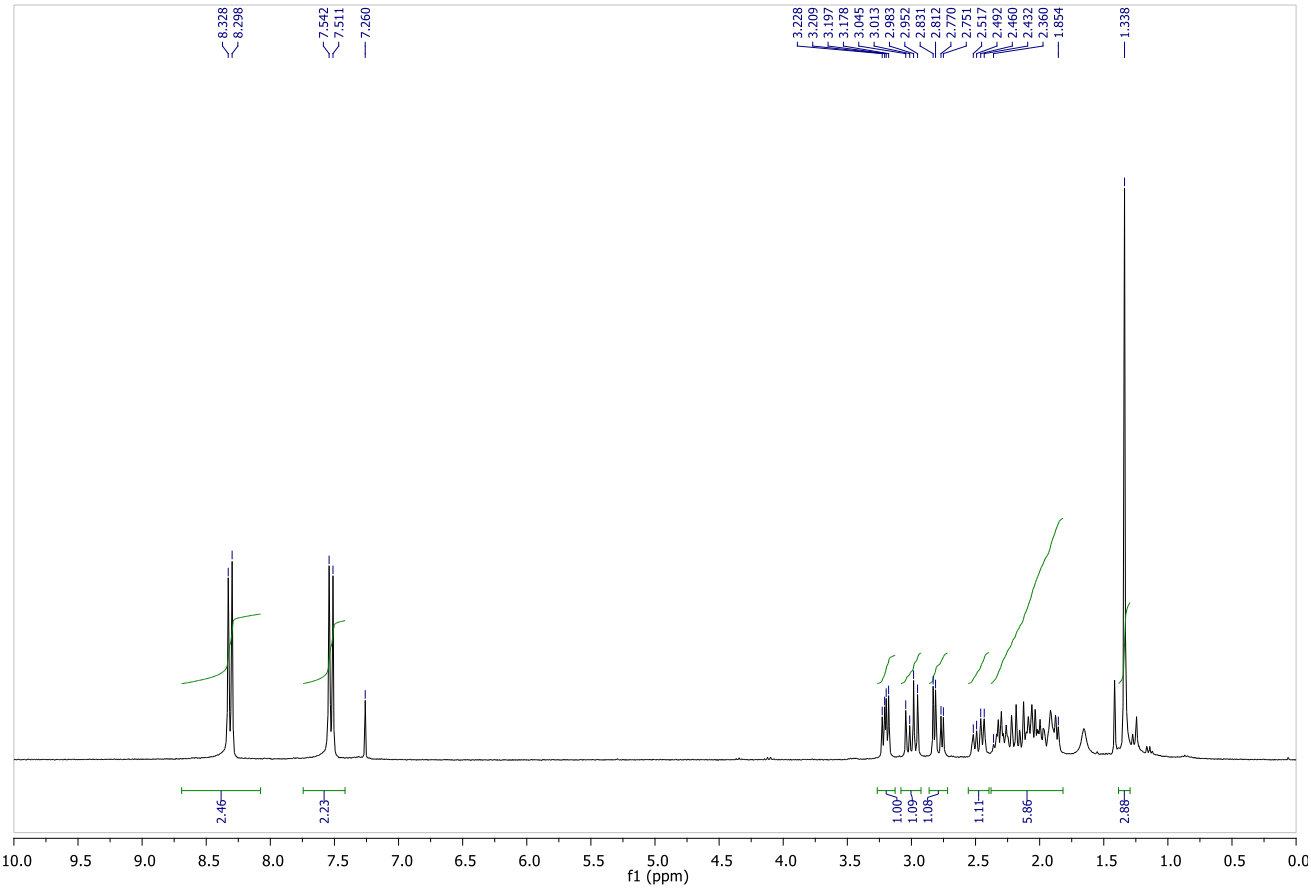

7.60
7.57
7.26
7.19
7.17
3.42
3.40
3.39
3.37
3.03
3.00
2.97
2.94
2.71
2.65
2.45
2.44
2.42
2.02
1.98
1.89
1.13
2.16
1.90
0.96
1.08
0.97
2.00
4.04
3.00
f1 (ppm)

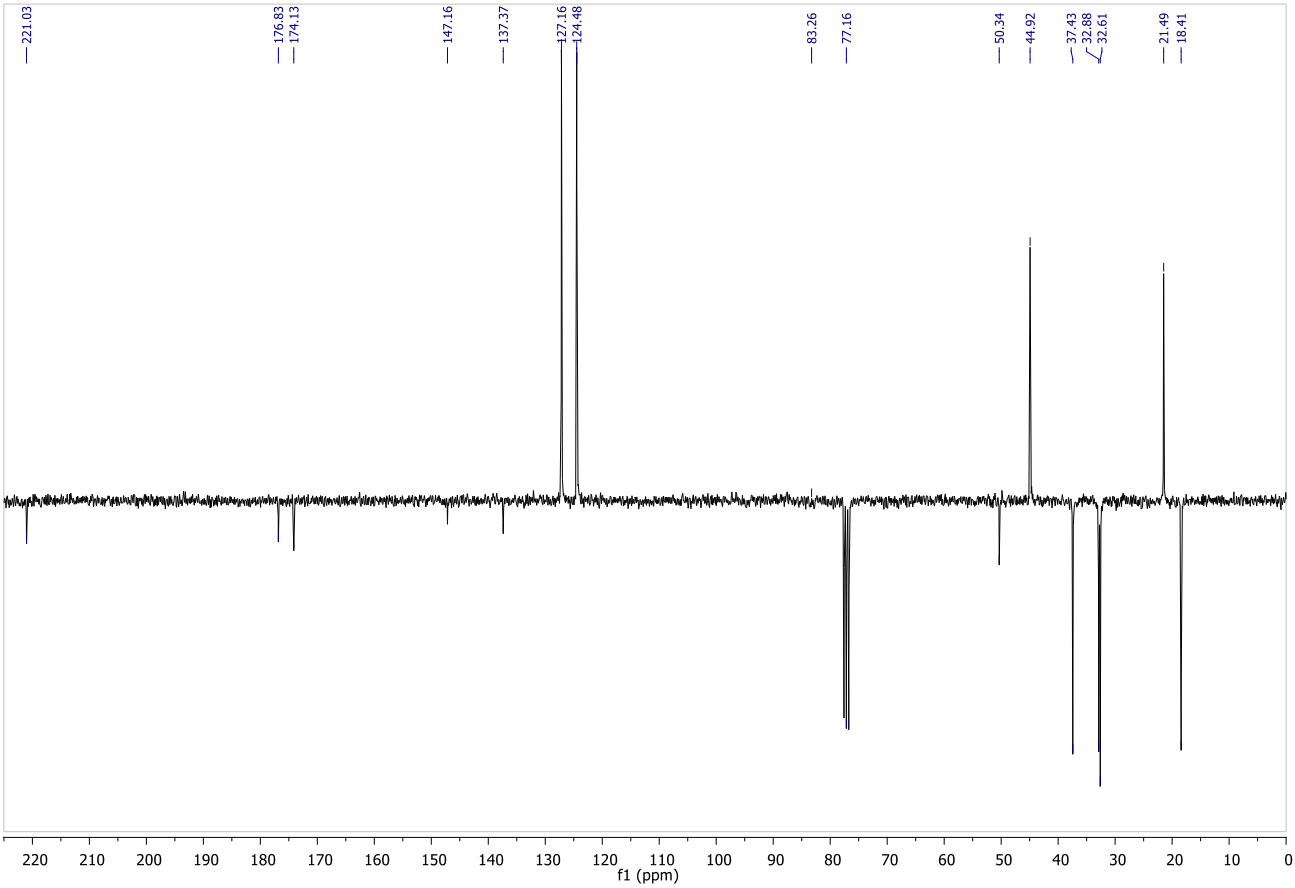

219.87
176.56
174.54
169.06
132.49
130.76
127.97
122.70
77.58
77.16
76.74
49.51
46.62
37.75
32.95
31.83
20.96
18.66
f1 (ppm)

(*R*)-3-((*R*)-1-Methyl-2-oxocyclopentyl)-1-(4-nitrophenyl)pyrrolidine-2,5-dione 15l



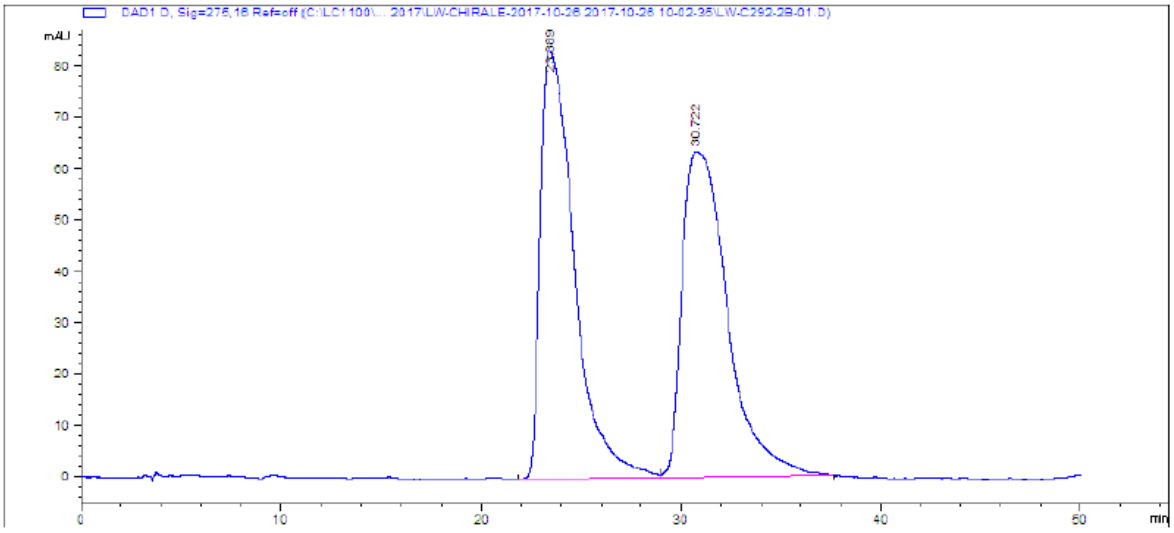
Compound (1*R*,3*R*)-**15l** was obtained in 48% yield (152 mg) as a white solid with dr = 71:29 and 75% ee. The corresponding diastereomer **16l** was obtained in 19% yield (60 mg). **Rf** = 0.1 (cyclohexane/EtOAc = 1:1); **m.p.**: 194.8 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.31 (d, *J* = 9.1 Hz, 2 H), 7.53 (d, *J* = 9.1 Hz, 2 H), 3.20 (dd, *J* = 9.3, 5.7 Hz, 1H), 3.00 (dd, *J* = 18.4, 9.3 Hz, 1H), 2.79 (dd, *J* = 18.3, 5.6 Hz, 1H), 2.48 (dd, *J* = 17.6, 8.0 Hz, 1H), 2.39-1.79 (m, 5H), 1.34 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 221.0, 176.8, 174.1, 147.2, 137.4, 127.2, 124.5, 50.3, 44.9, 37.4, 32.9, 32.6, 21.5, 18.41; **HRMS (ESI)** m/z calcd for $[C_{16}H_{16}N_2NaO_5]^+$ 339.0951, found 339.0955; **IR** (neat) 2967, 1780, 1735, 1707, 768, 751 cm^{-1}; **$[\alpha]^{21}_D$** = + 28 (c = 5.2, EtOH).





HPLC: (±)-**15l**. Chiralpal AD, Solvent: Hexane/i-PrOH = 60:40, Flow Speed 0.8 mL/min , UV: 275nm, retention times: 23.389, 28.413 min.

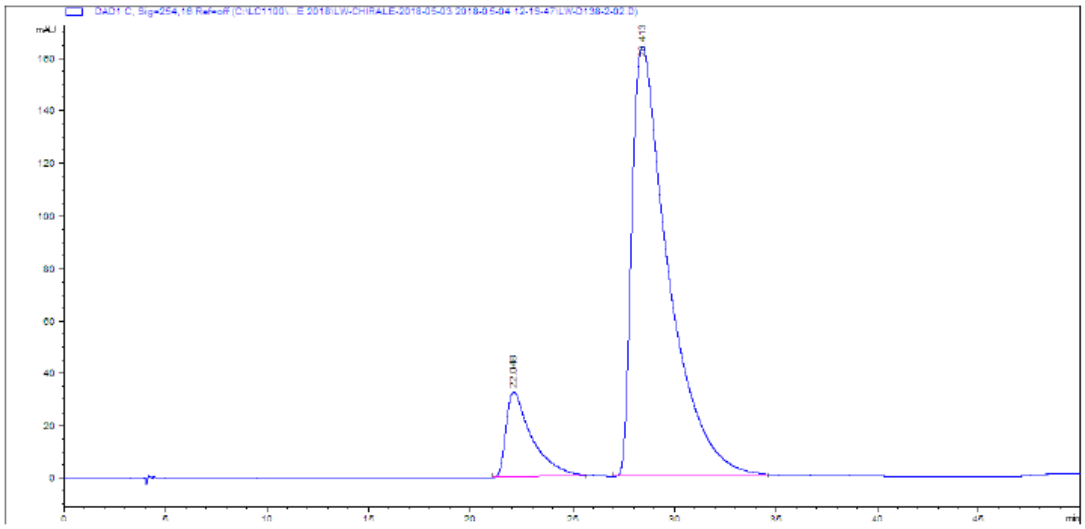
LW C292-2B hexane / isopropanol 70 : 30
275 nm



#	Time	Area	Height	Width	Area%	Symmetry
1	23.389	9861.9	83.3	1.6044	49.553	0.365
2	30.722	10039.7	63.5	2.0338	50.447	0.41

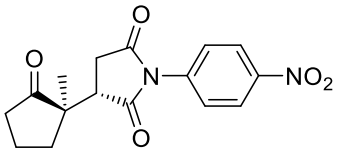
HPLC: (1*R*,3*R*)-**15l** Column: Chiralpal AD, Solvent: Hexane/i-PrOH = 60:40, Flow Speed 0.8 mL/min , UV: 254nm, 75% ee, retention time: 28.413 min.

LW D138-2 **Hexane / Isopropanol 60 : 40** **0.8 mL /min**
254nm

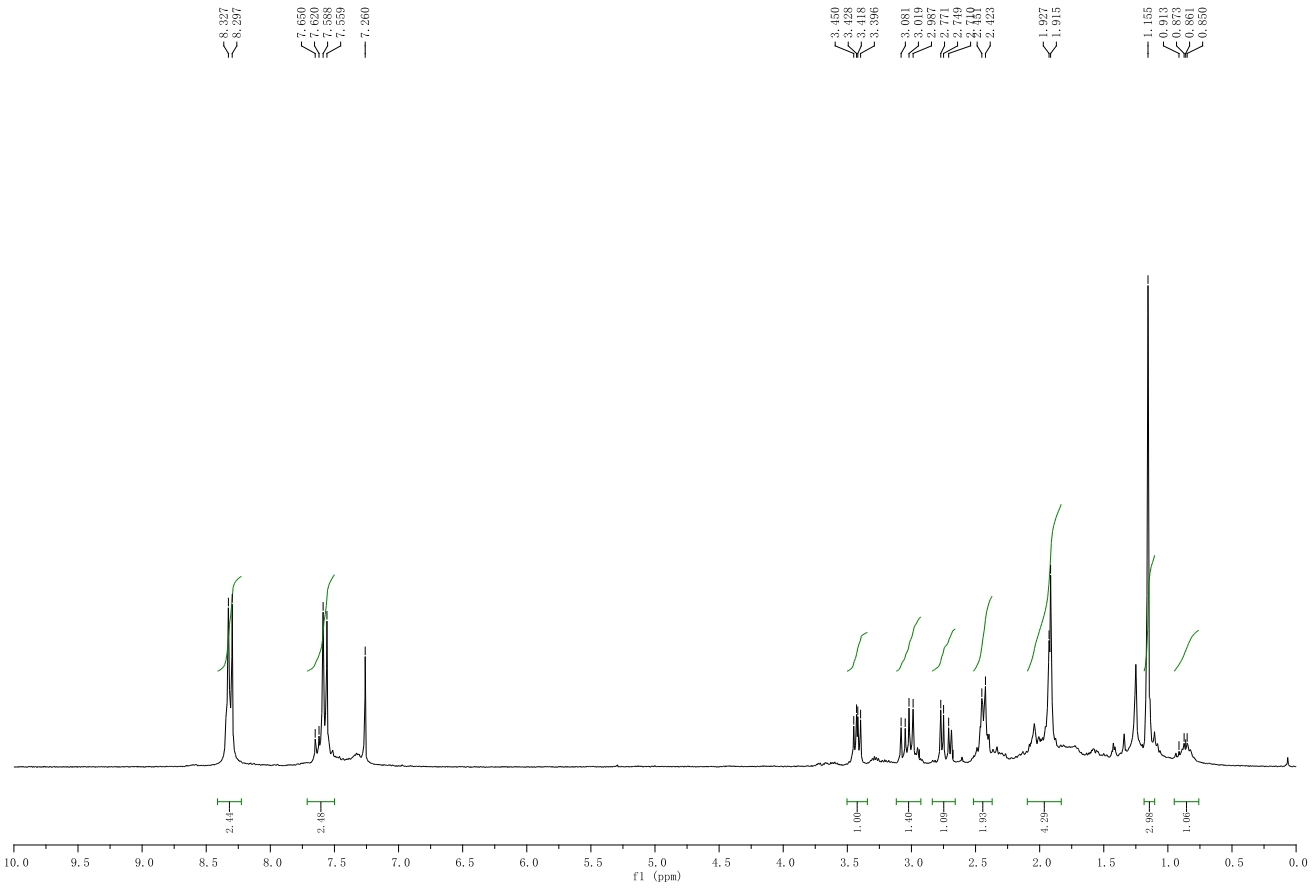


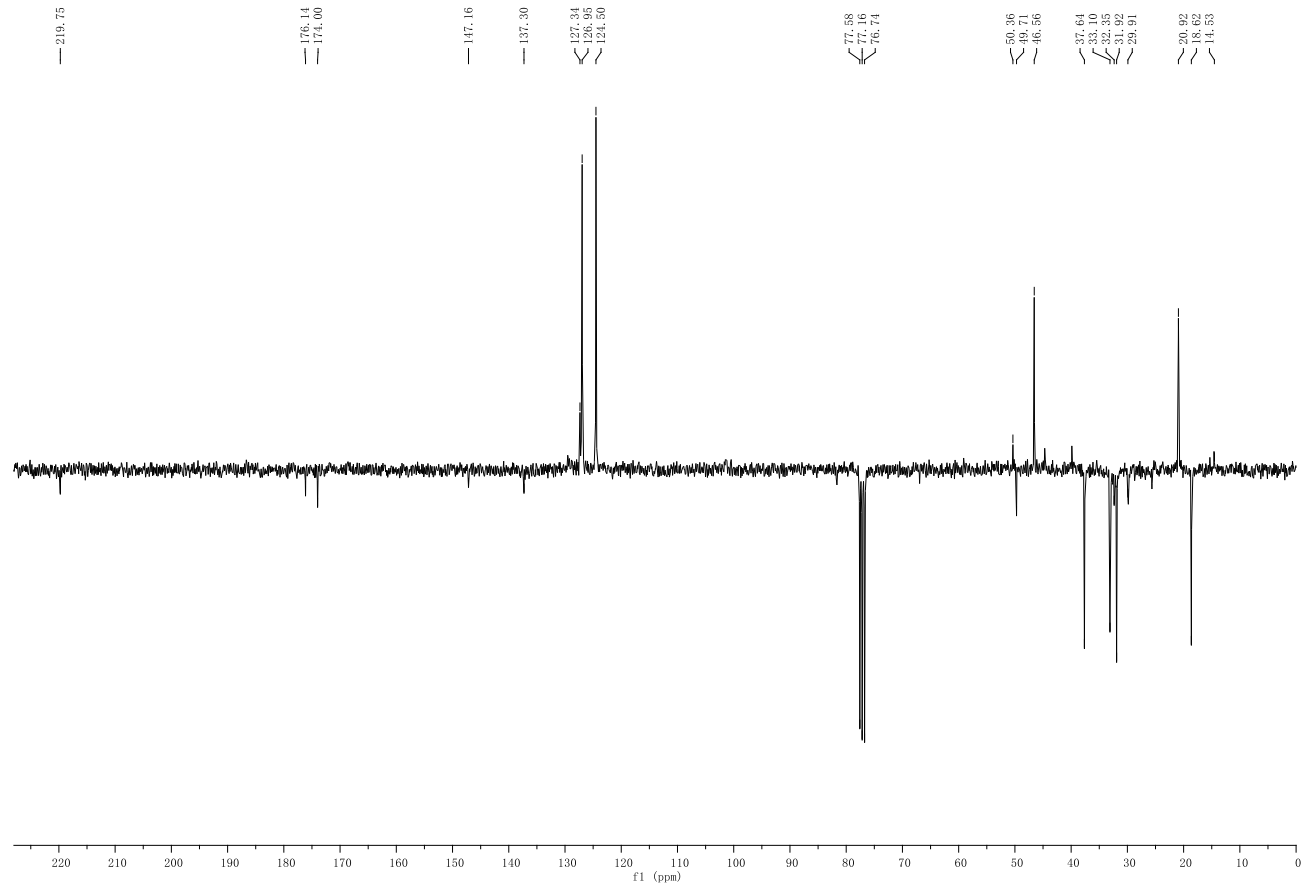
#	Time	Area	Height	Width	Area%	Symmetry
1	22.048	2942.6	32.9	1.1109	12.581	0.368
2	28.413	20445.5	164.2	1.4671	87.419	0.392

(*S*)-3-((*R*)-1-Methyl-2-oxocyclopentyl)-1-(4-nitrophenyl)-2,5-pyrrolidinedione 16l

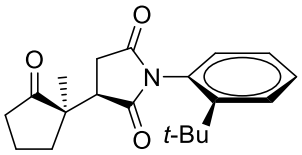


(1*R*,3*S*)-**16l**: 19% yield; **m.p.** not determined because of trace impurities; **Rf** = 0.1 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.31 (d, *J* = 9.0 Hz, 2H), 7.57 (d, *J* = 9.0 Hz, 2H), 3.43 (dd, *J* = 9.6, 6.6 Hz, 1H), 3.03 (dd, *J* = 18.6, 9.6 Hz, 1H), 2.74 (dd, *J* = 18.6, 6.6 Hz, 1H), 2.52-2.40 (m, 2H), 2.10-1.75 (m, 4H), 1.15 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 219.7, 176.1, 174.0, 147.2, 137.3, 126.9, 124.5, 49.7, 46.6, 37.6, 33.1, 31.9, 20.9, 18.6; **HRMS (ESI)** m/z calcd for $[C_{16}H_{16}N_2NaO_5]^+$ 339.0951, found 339.0952; **IR** (neat) 2965, 2917, 2850, 1710, 1705, 1526, 1345, 711 cm^{-1}.


8.327
8.297
7.650
7.620
7.588
7.559
7.260
3.450
3.428
3.418
3.396
3.081
3.019
2.987
2.771
2.749
2.145
2.423
1.927
1.915
1.155
0.913
0.873
0.861
0.850
2.44
2.48
1.00
1.40
1.09
1.93
4.29
2.08
1.00
f1 (ppm)

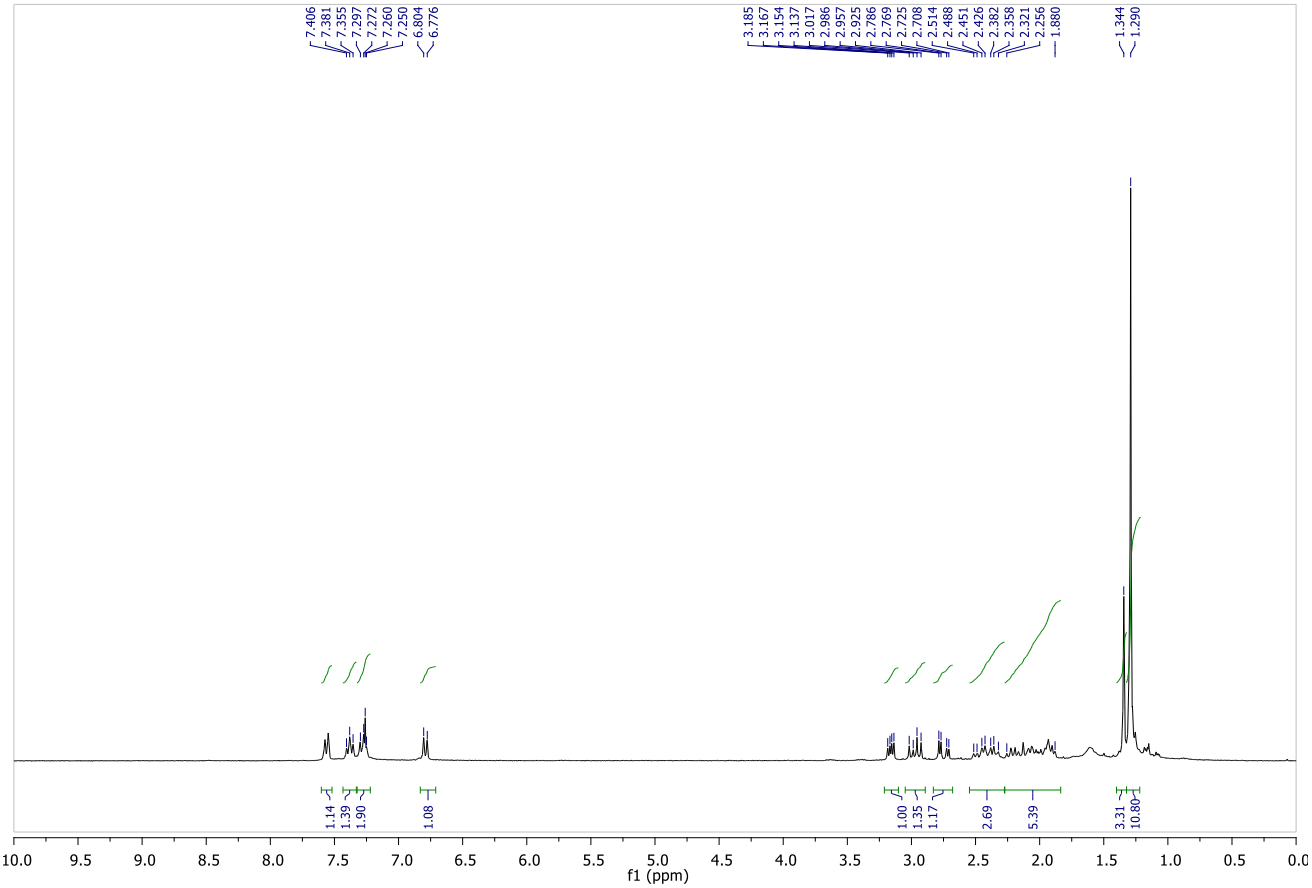

219.75
176.14
174.00
147.16
137.30
127.34
126.95
124.50
77.58
77.16
76.74
50.36
49.71
46.56
37.64
33.10
32.35
31.92
29.91
20.92
18.62
14.53
f1 (ppm)

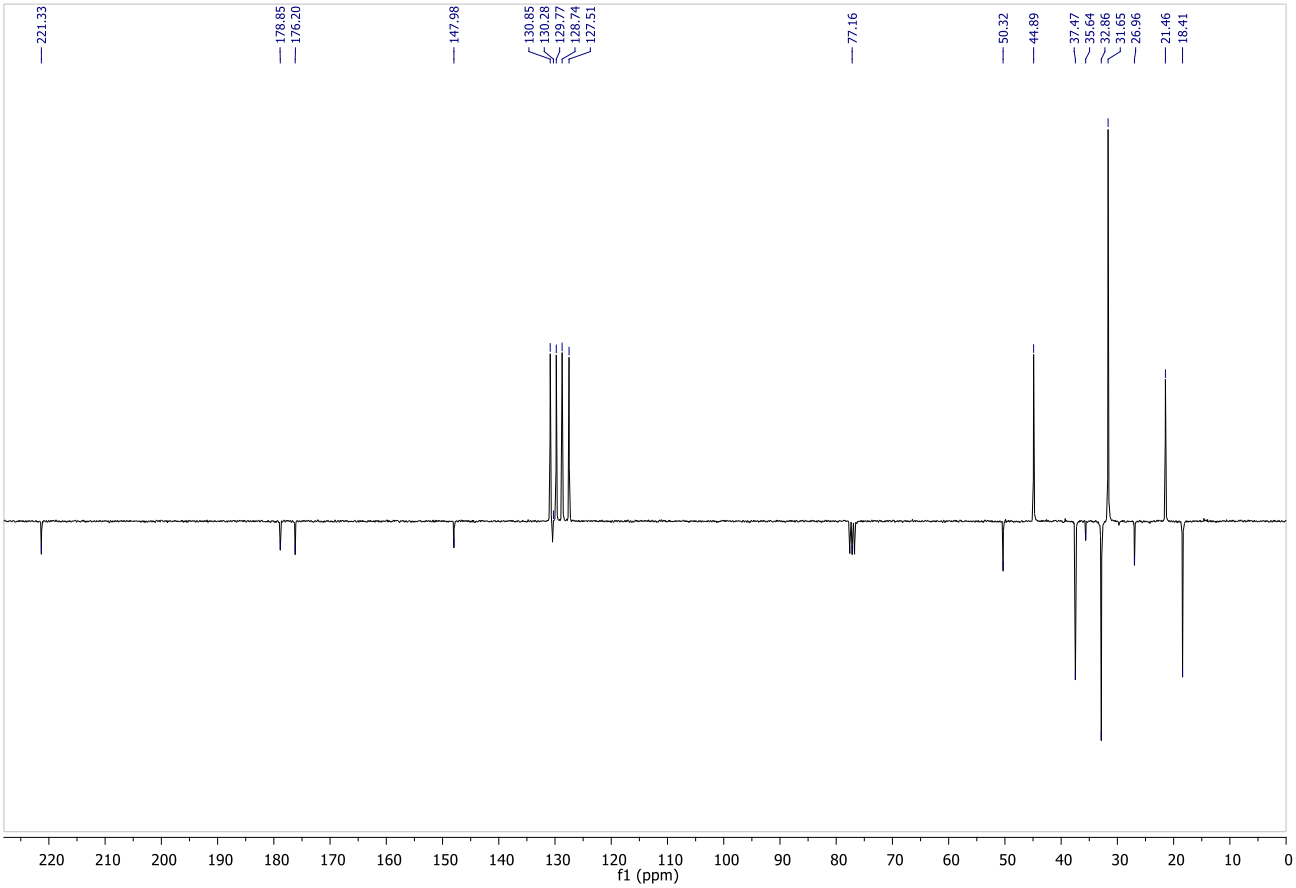
(*M*)-(*R*)-1-(2-(*tert*-Butyl)phenyl)-3-((*R*)-1-methyl-2-oxocyclopentyl)-2,5-pyrrolidinedione 15ma



Compound (*M*)-(1*R*,3*R*)-**15ma** was obtained in 56% yield (183 mg) as a white solid (dr = 65:35, 98% ee). The corresponding diastereomer **16m** was not detected but the corresponding rotamer **15mb** was isolated in 30% yield (98 mg) as a white solid.

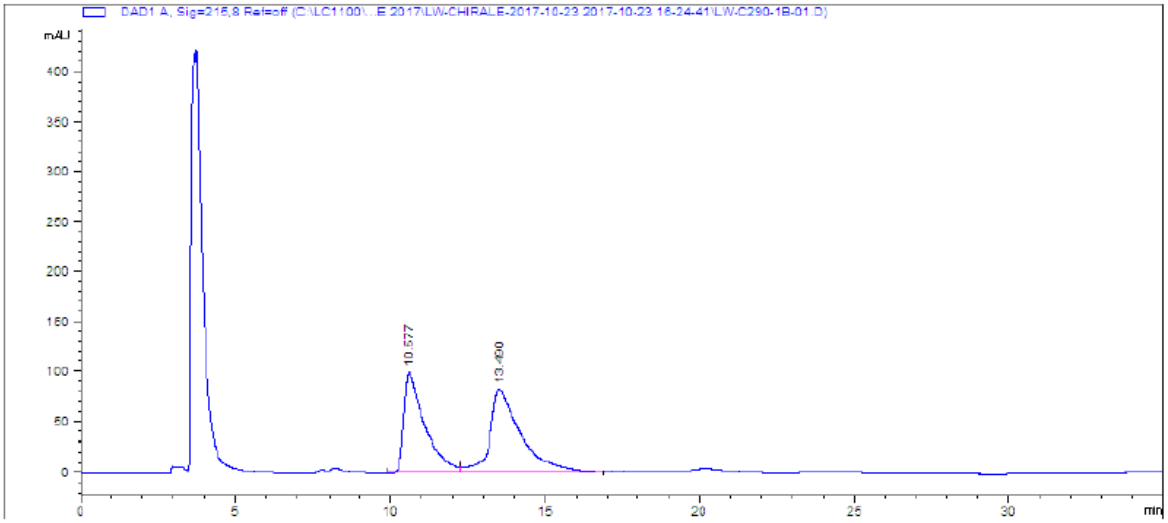
(*M*)-(1*R*,3*R*)-**15ma**: **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **m.p.** 137.2 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.56 (bd, *J* = 7.6 Hz, 1H), 7.38 (t, *J* = 7.7 Hz, 1H), 7.27-7.25 (m, 1H), 6.79 (d, *J* = 7.7 Hz, 1H), 3.16 (dd, *J* = 9.3, 5.2 Hz, 1H), 2.97 (dd, *J* = 18.3, 9.5 Hz, 1H), 2.75 (dd, *J* = 18.3, 5.1 Hz, 1H), 2.53-2.28 (m, 2H), 2.28-1.85 (m, 4H), 1.34 (s, 3H), 1.29 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 221.4, 178.9, 176.3, 148.0, 130.9, 130.5, 129.9, 128.9, 127.6, 50.5, 45.0, 35.8, 37.6, 33.0, 31.7, 21.2, 18.7; **HRMS (ESI)** m/z calcd for $[C_{20}H_{25}NNaO_3]^+$ 350.1727, found 350.1737; **IR** (neat) 2962, 2973, 1779, 1735, 1705, 763, 703 cm^{-1}; **$[\alpha]^{25}_D$** = + 35.0 (c = 5.23, $CHCl_3$).





HPLC : (±)-**15ma**. Chiralcel AD-H, *i*-PrOH/hexane = 10:90, 1 mL/min, 215 nm; retention times: 10.577, 13.49.

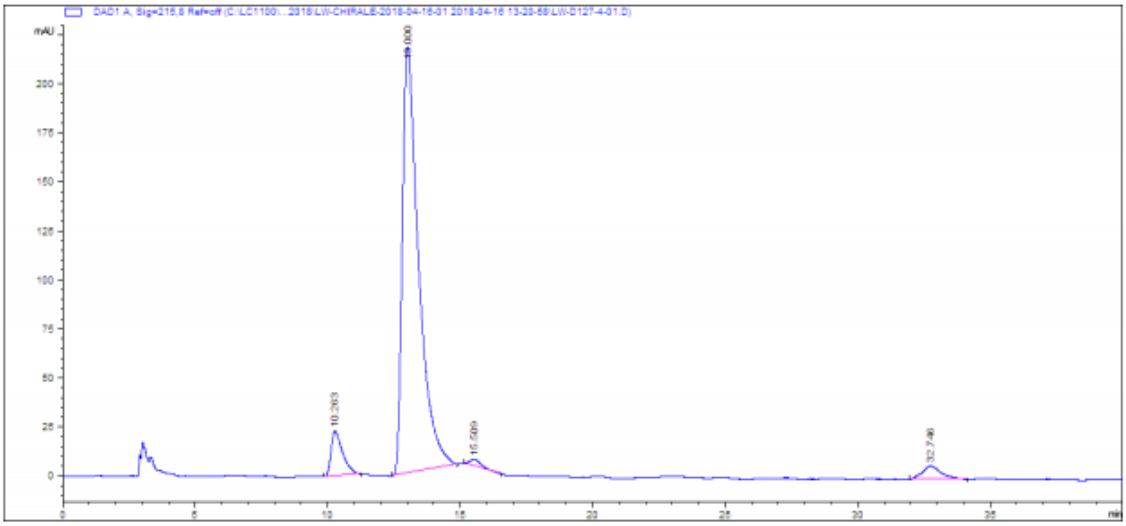
LW C290-1B **hexane / isopropanol 90 : 10**
215 nm



#	Time	Area	Height	Width	Area%	Symmetry
1	10.577	4743.2	100.4	0.6471	44.455	0.329
2	13.49	5926.3	83.2	0.9833	55.545	0.441

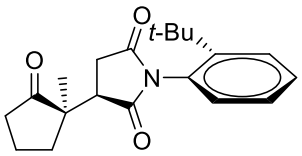
HPLC:(*P*)-(1*R*,3*R*)-**15ma**. Chiralcel AD-H, *i*-PrOH/hexane = 10/90, 1 mL/min, 215 nm, 98%ee, retention times: 13.000 min.

LW 127-4 **Hexane / Isopropanol 90 : 10**
215nm

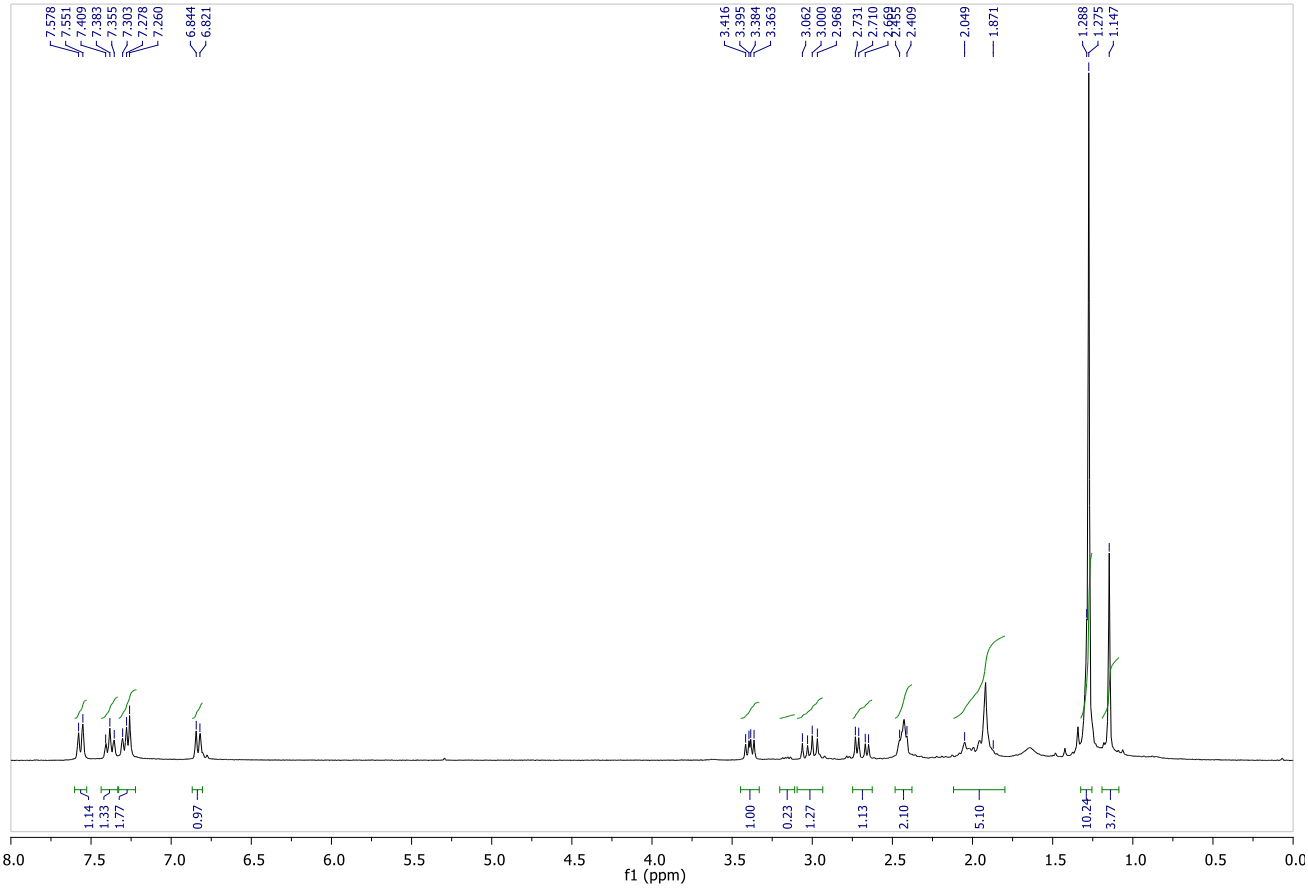


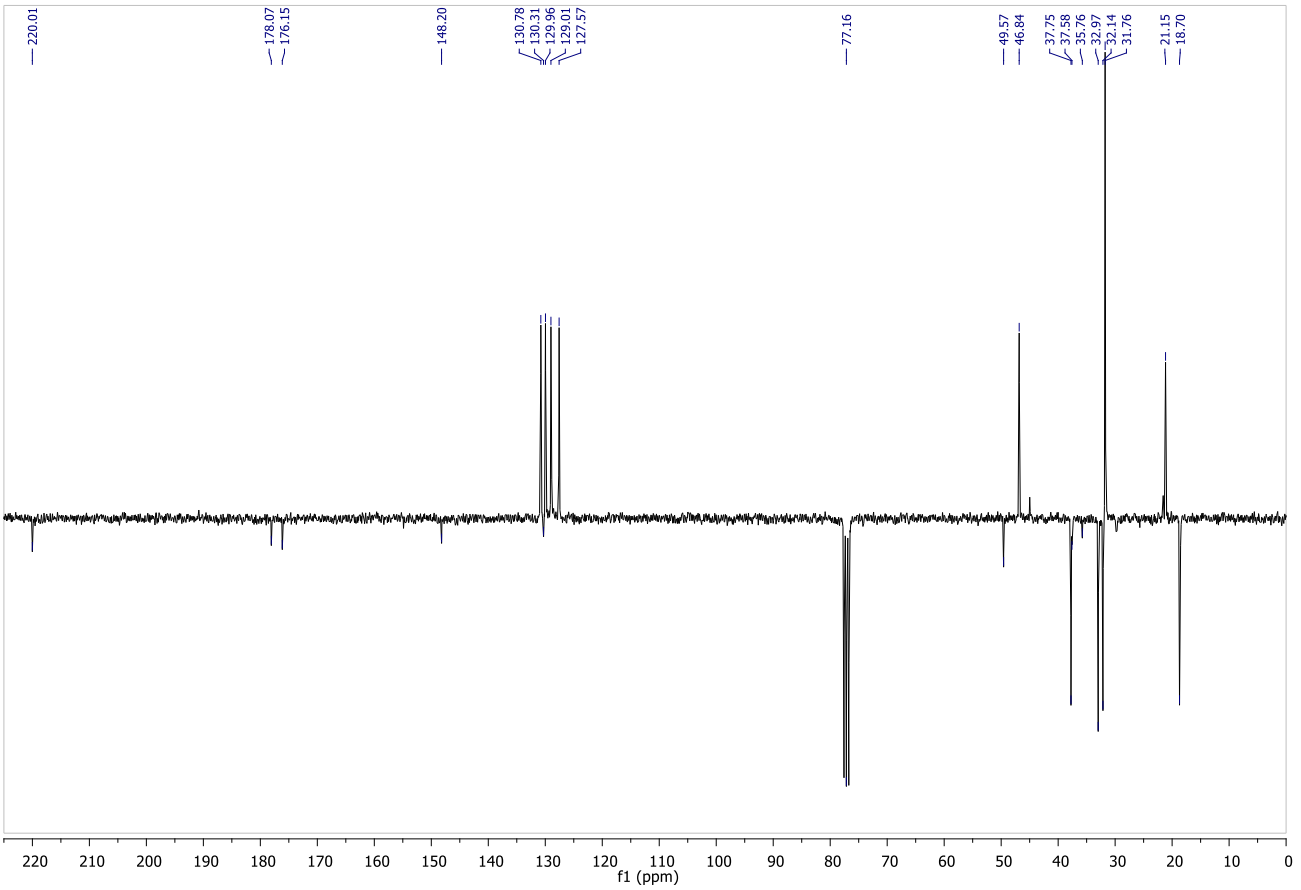
#	Time	Area	Height	Width	Area%	Symmetry
1	10.263	695	23	0.3843	6.632	0.488
2	13	9325.8	217.5	0.6012	88.986	0.445
3	15.509	109.8	3.4	0.3819	1.048	0.484
4	32.746	349.4	6.9	0.5959	3.334	0.788

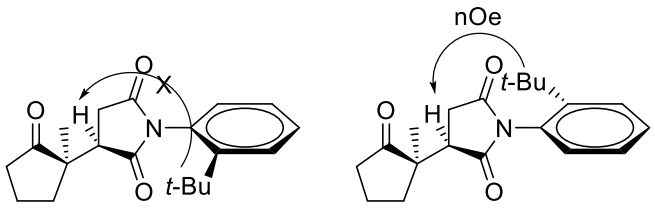
(*P*)-(*R*)-1-(2-(*tert*-Butyl)phenyl)-3-((*R*)-1-methyl-2-oxocyclopentyl)-2,5-pyrrolidinedione 15mb



(*P*)-(1*R*,3*R*)-**15mb**: 30% yield, white solid; **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **m.p** 132.8 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.56 (bd, *J* = 8.0 Hz, 1H), 7.45-7.35 (m, 1H), 7.35-7.23 (m, 1H), 6.83 (bd, *J* = 6.9 Hz, 1H), 3.39 (dd, *J* = 9.5, 6.2 Hz, 1H), 3.01 (dd, J = 18.4, 9.6 Hz, 1H), 2.69 (dd, J = 18.5, 6.2 Hz, 1H), 2.51-2.38 (m, 2H), 2.05-1.85 (m, 4H), 1.27 (s, 9H), 1.15 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 220.0, 178.1, 176.2, 148.2, 130.8, 130.3, 130.0, 129.0, 127.6, 49.6, 46.8, 37.8, 35.8, 33.0, 32.1, 31.8, 21.1, 18.7; **HRMS (ESI)** m/z calcd for $[C_{20}H_{25}NNaO_3]^+$ 350.1727, found 350.1737; **IR** (neat) 2968, 1778, 1739, 1705, 1384, 1167, 1084, 761, 707 cm^{-1}; **$[\alpha]^{25}_D$** = + 9.4 (c = 5.10, $CHCl_3$).

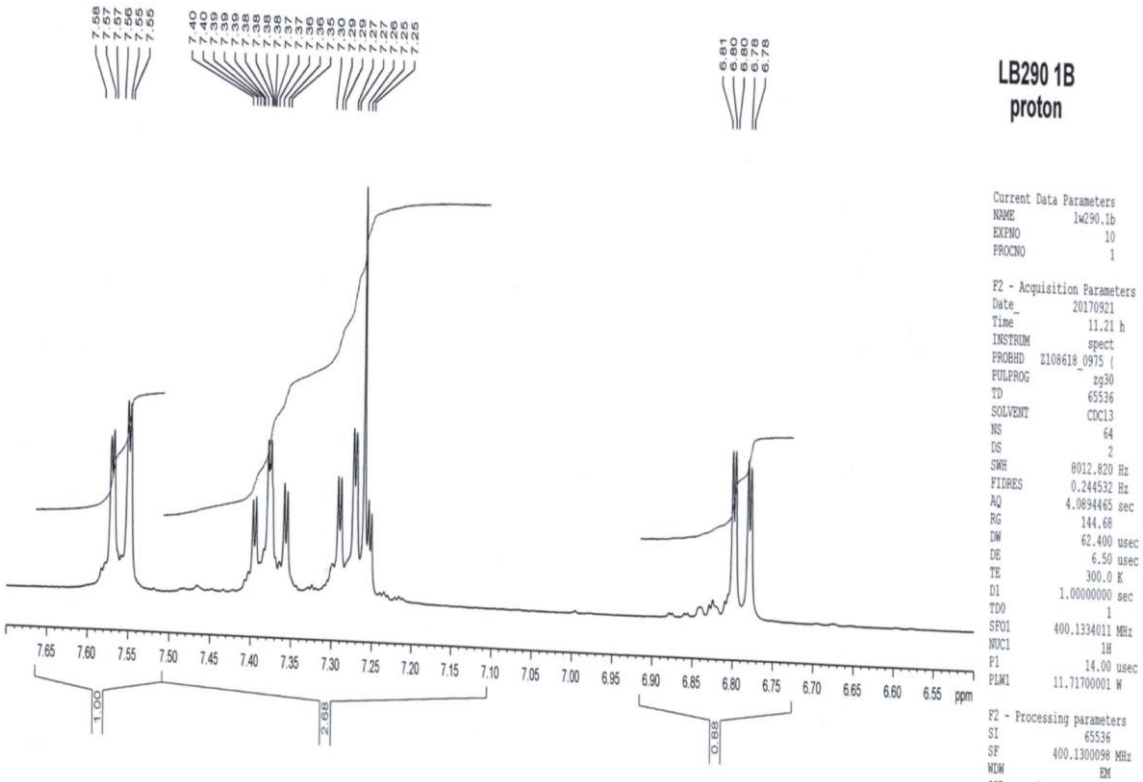

7.578
7.551
7.409
7.383
7.355
7.303
7.278
7.260
6.844
6.821
3.416
3.395
3.384
3.363
3.062
3.000
2.968
2.731
2.710
2.669
2.655
2.409
2.049
1.871
1.288
1.275
1.147
1.14
1.33
1.77
0.97
1.00
0.23
1.27
1.13
2.10
5.10
10.24
3.77
f1 (ppm)

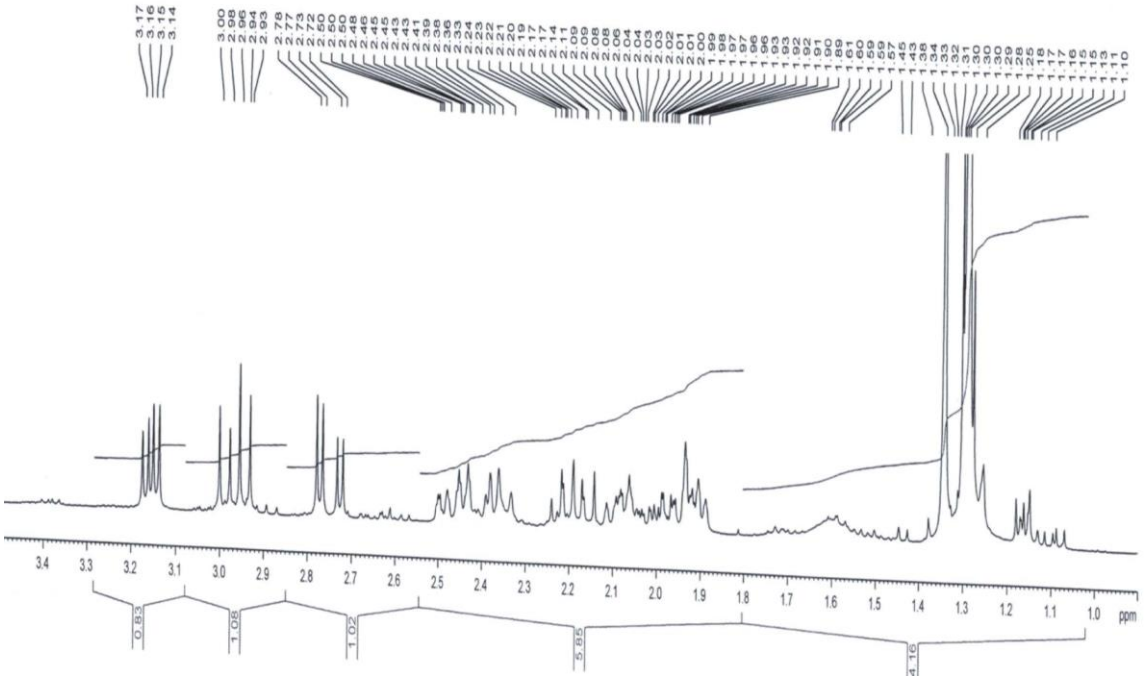

220.01
178.07
176.15
148.20
130.78
130.31
129.96
129.01
127.57
77.16
49.57
46.84
37.75
37.58
35.76
32.97
32.14
31.76
21.15
18.70
f1 (ppm)



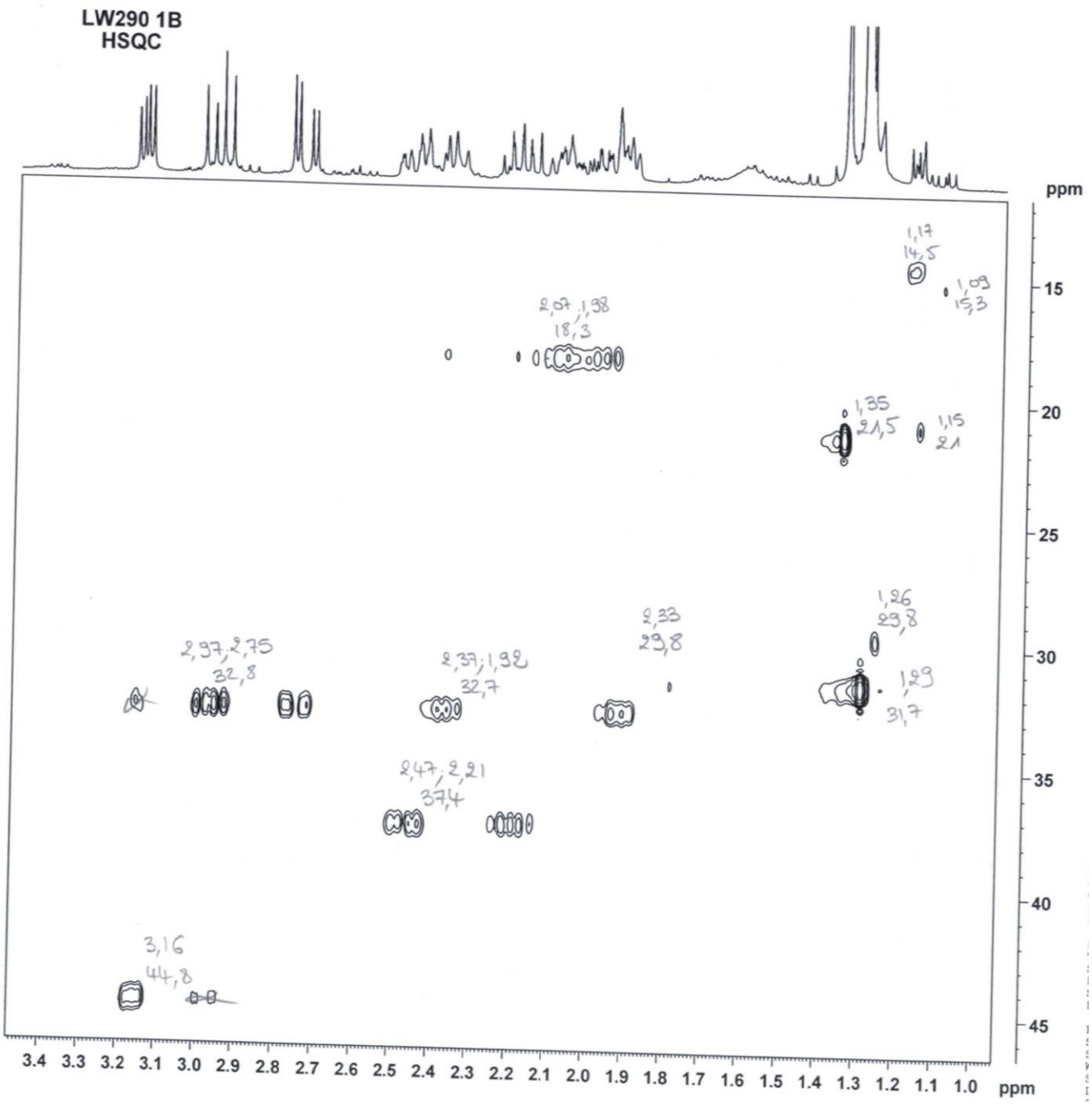
15ma (LW290-1B) **15mb** (LW290-1C)

(*M*)-(1*R*,3*R*)-**15ma**

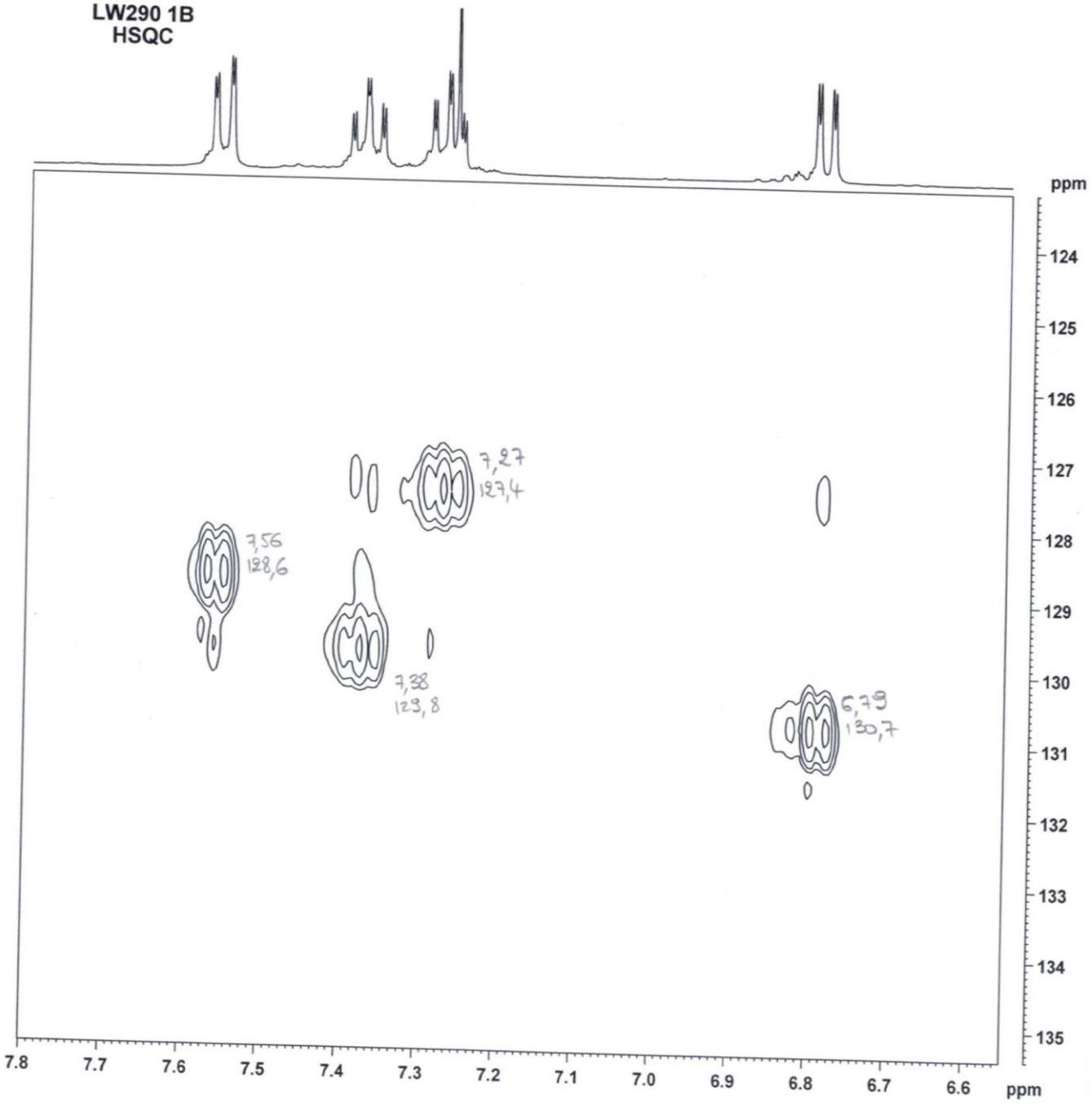




(*M*)-(1*R*,3*R*)-**15ma**

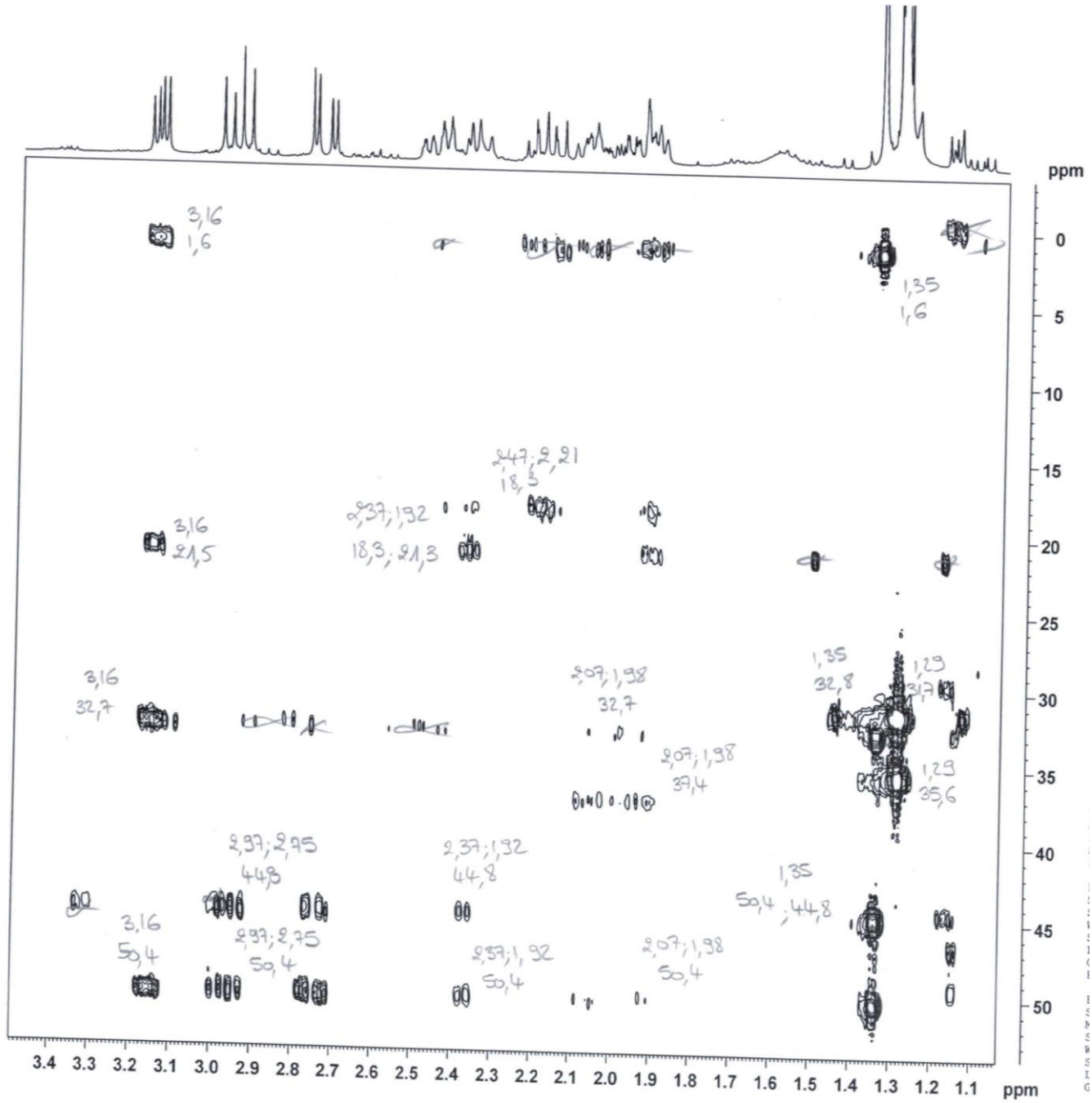

LW290 1B
HSQC
ppm
1,17
14,5
1,09
15,3
2,07; 1,98
18,3
1,35
21,5
1,15
21
1,26
29,8
2,33
29,8
2,97; 2,75
32,8
2,39; 1,98
32,7
1,29
31,7
2,47; 2,21
37,4
3,16
44,8
3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 ppm
15 20 25 30 35 40 45

(*M*)-(1*R*,3*R*)-**15ma**


LW290 1B
HSQC
ppm
124
125
126
127
128
129
130
131
132
133
134
135
7,27
127,4
7,56
128,6
7,38
129,8
6,79
130,7
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
6.6
ppm

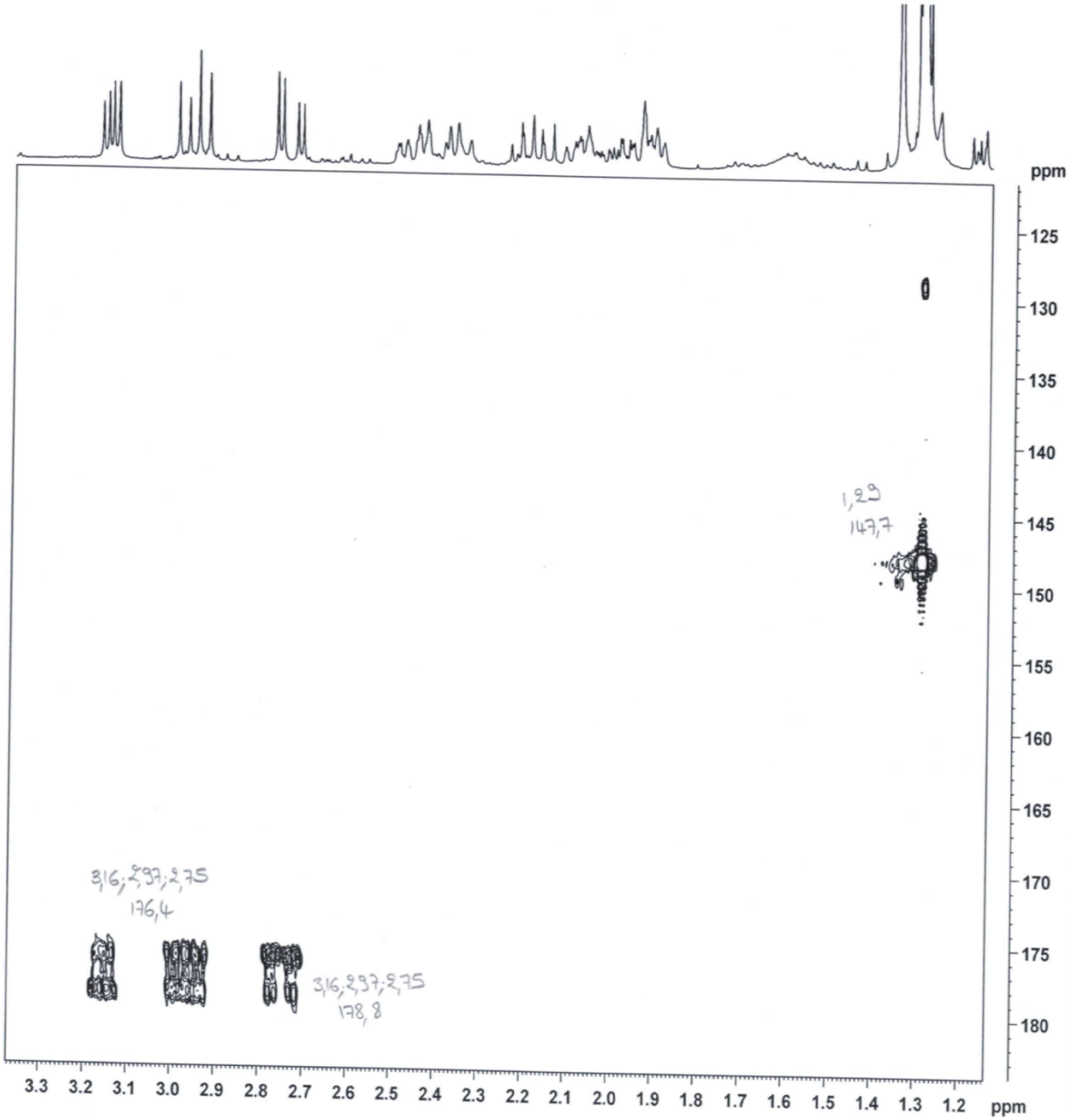
(*M*)-(1*R*,3*R*)-**15ma** (**LW 290 1-B)**

HMBC



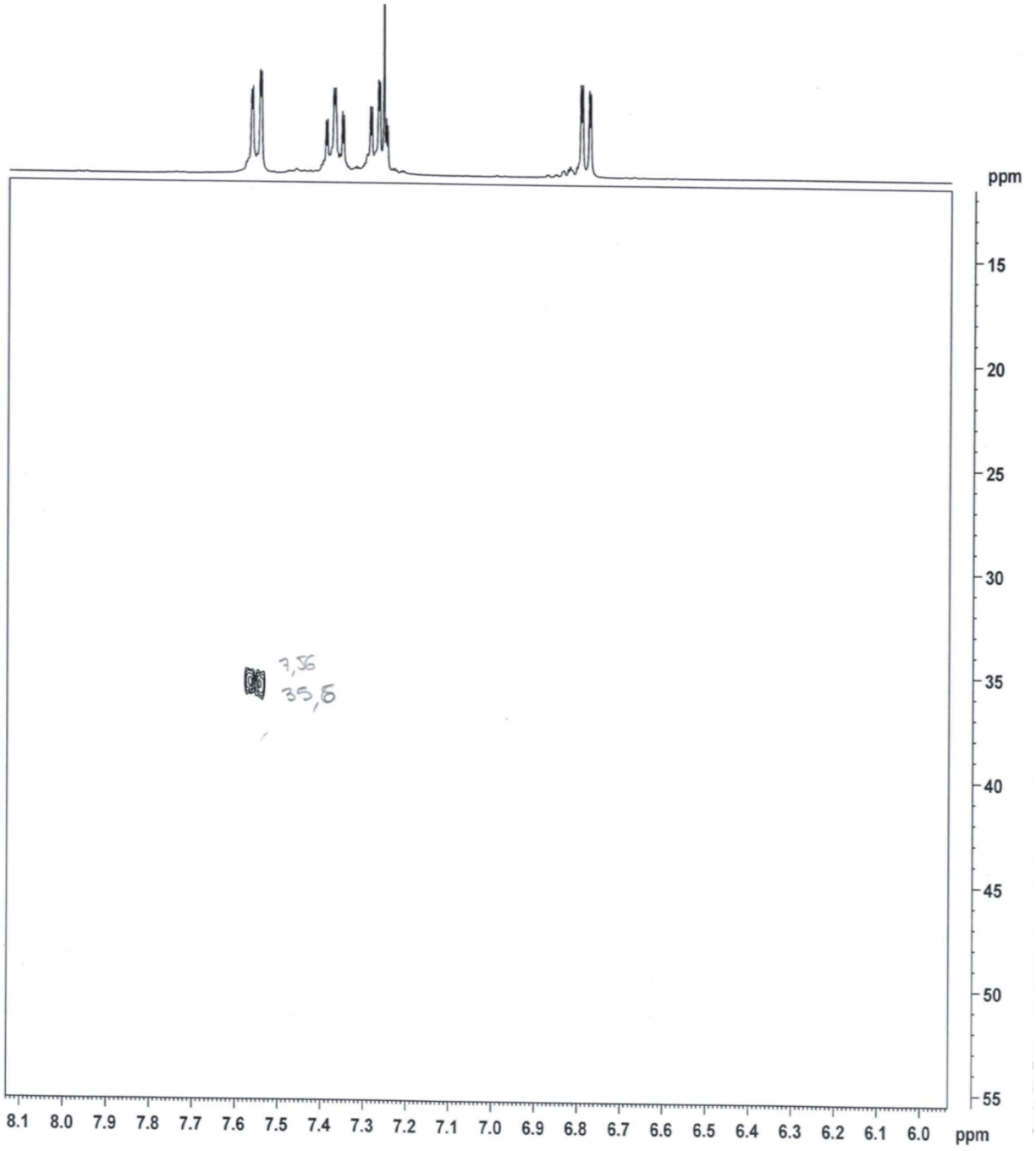
(*M*)-(1*R*,3*R*)-**15ma** (**LW 290 1-B**)

HMBC



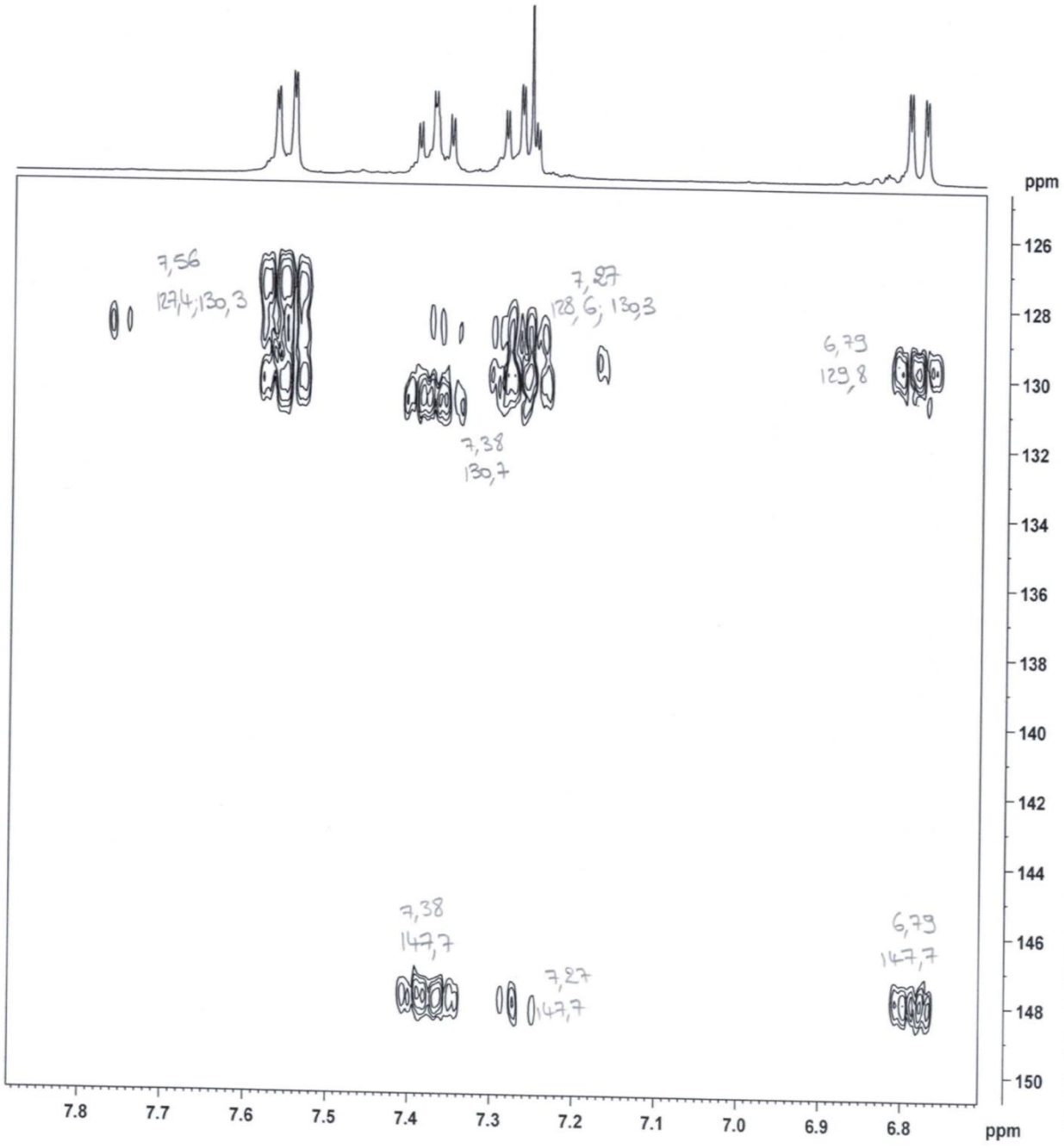
(*M*)-(1*R*,3*R*)-**15ma** (**LW 290 1-B**)

HMBC



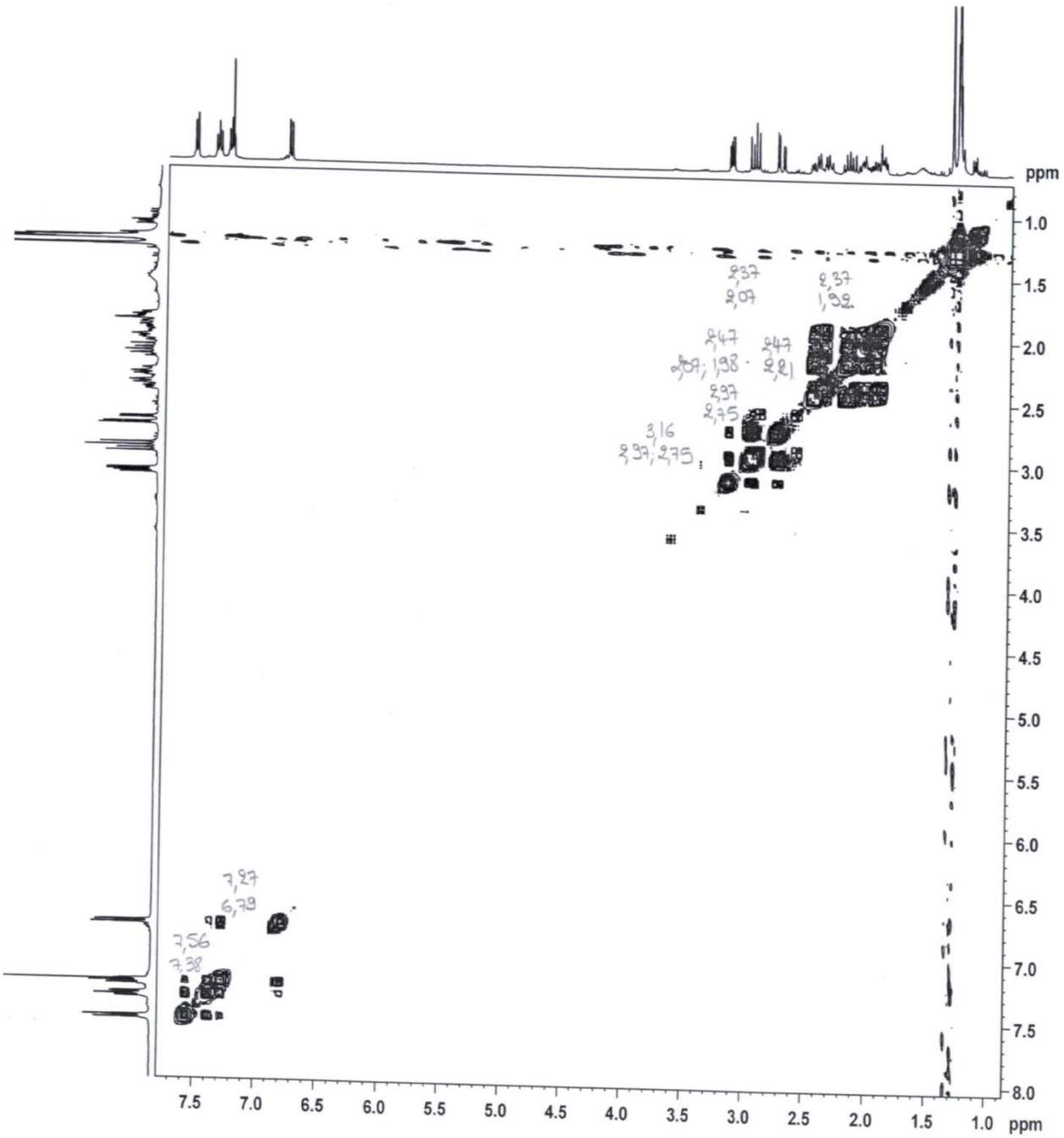
(*M*)-(1*R*,3*R*)-**15ma** (**LW 290 1-B**)

HMBC



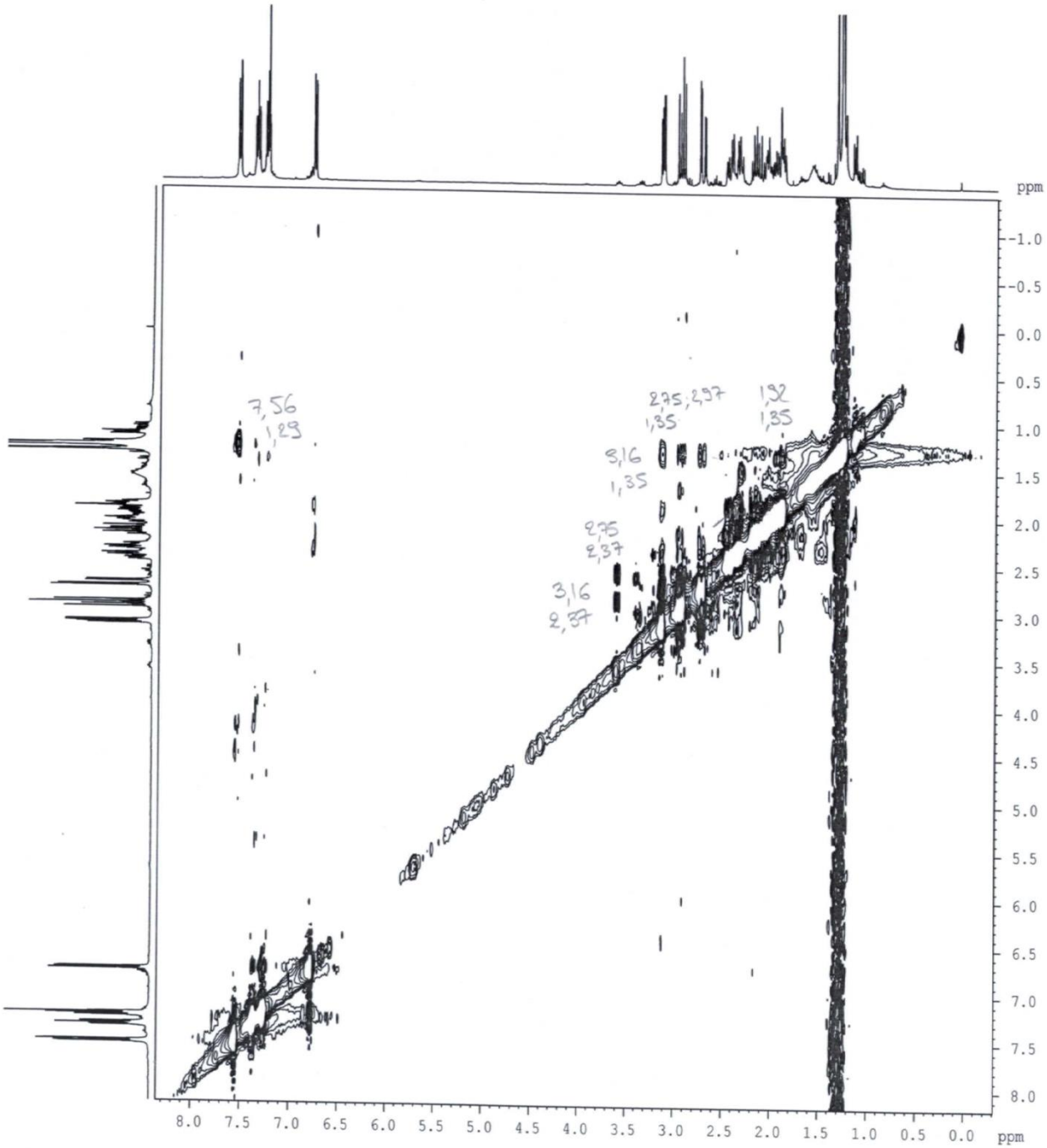
(*M*)-(1*R*,3*R*)-**15ma** (**LW 290 1-B**)

COSY

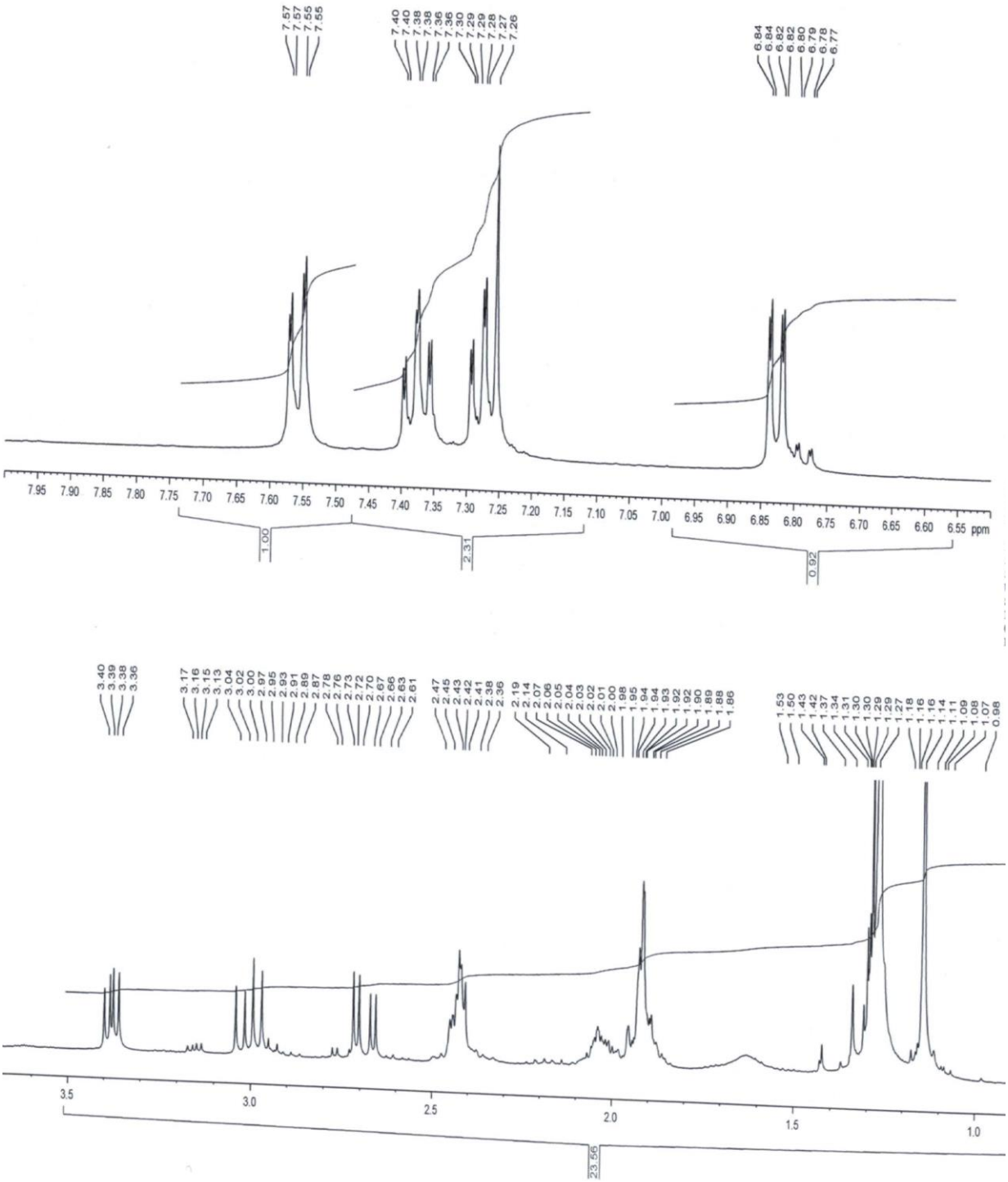


(*M*)-(1*R*,3*R*)-**15ma** (**LW 290 1-B**)

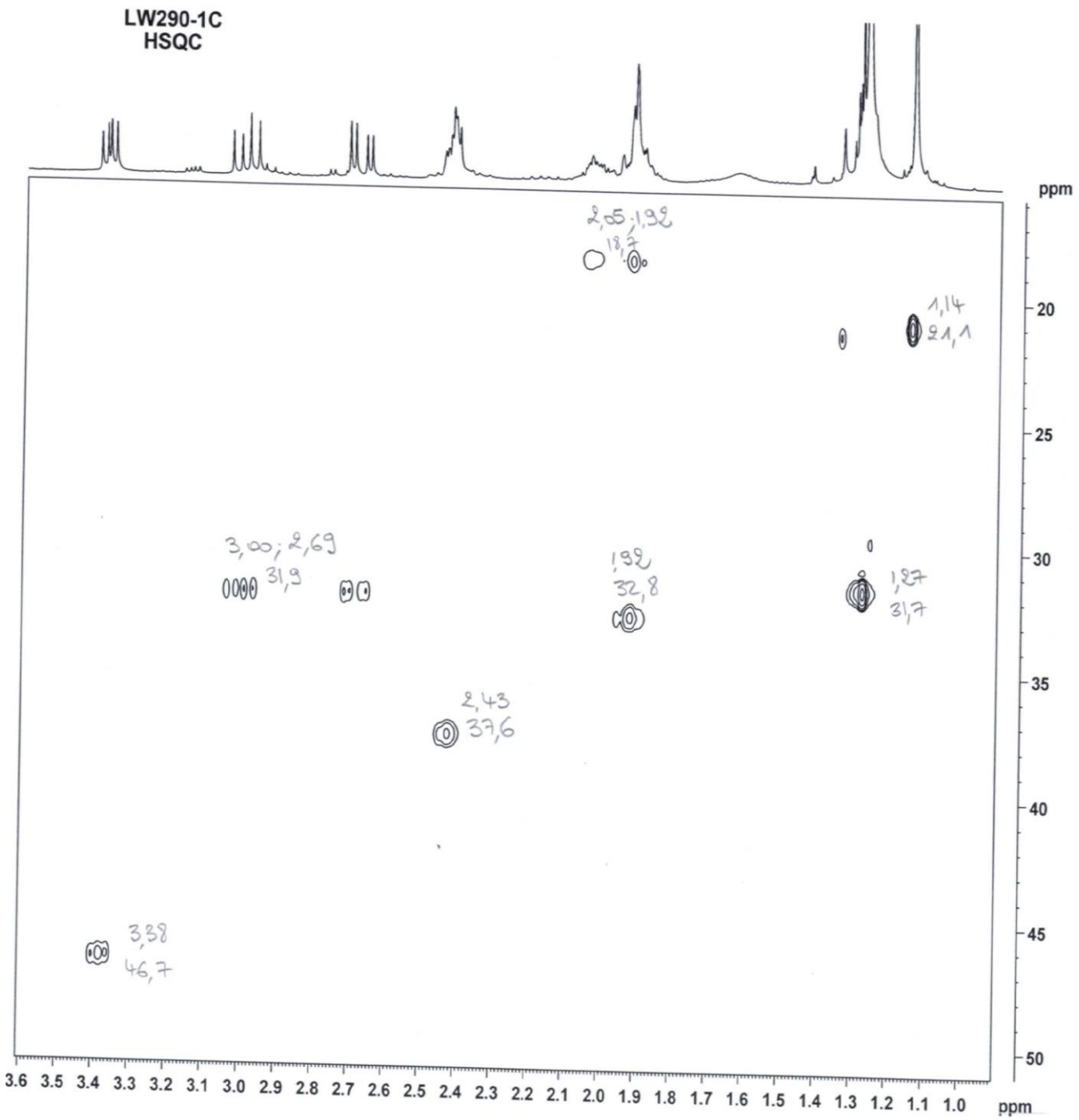
NOESY



(*P*)-(1*R*,3*R*)-**15mb** (**LW 290 1-C**)

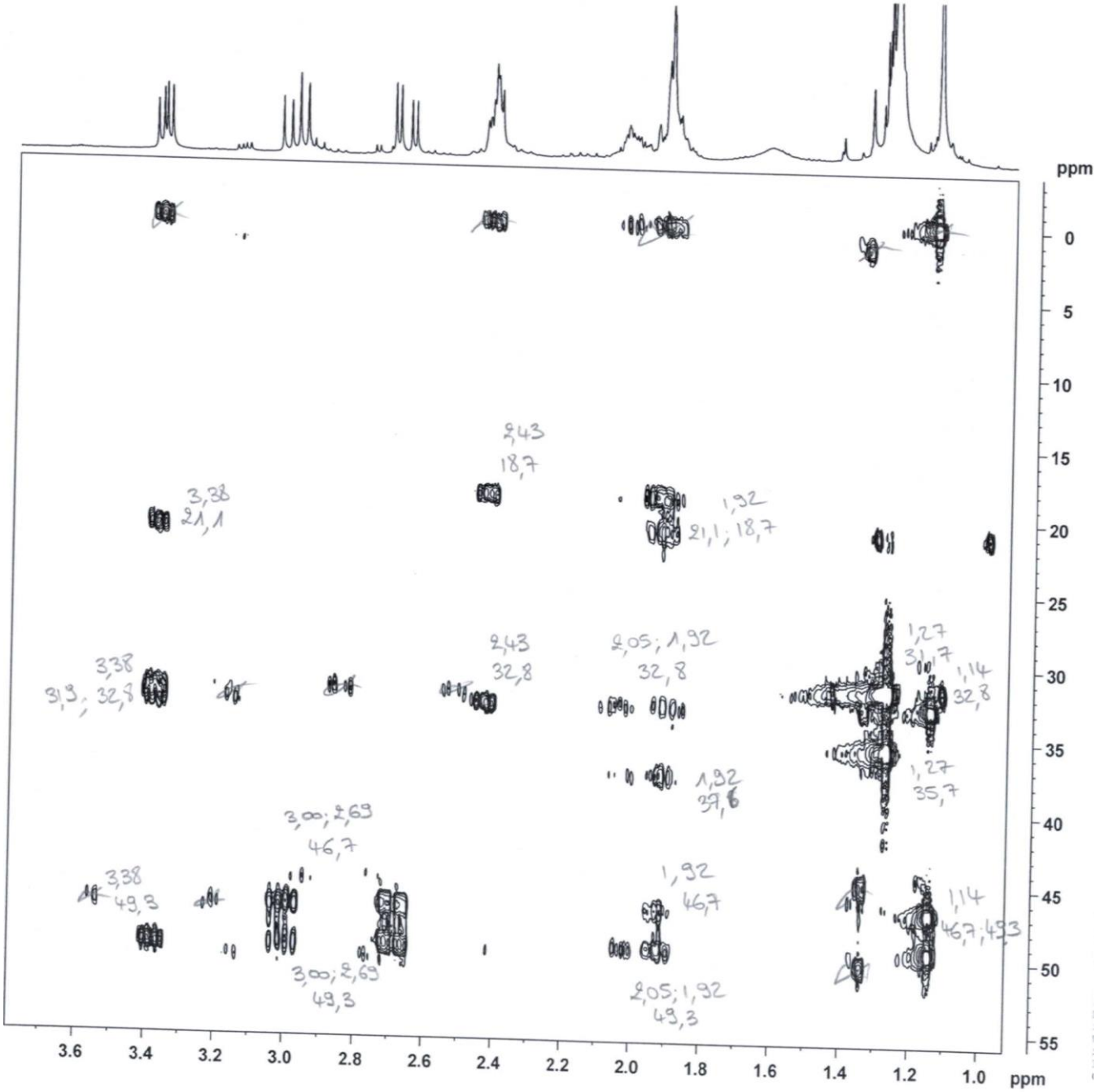


(*P*)-(1*R*,3*R*)-**15mb**


LW290-1C
HSQC
2,05; 1,98
18,7
1,14
21,1
3,00; 2,69
31,9
1,98
32,8
1,87
31,7
2,43
37,6
3,38
46,7
ppm
20
25
30
35
40
45
50
3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0
ppm

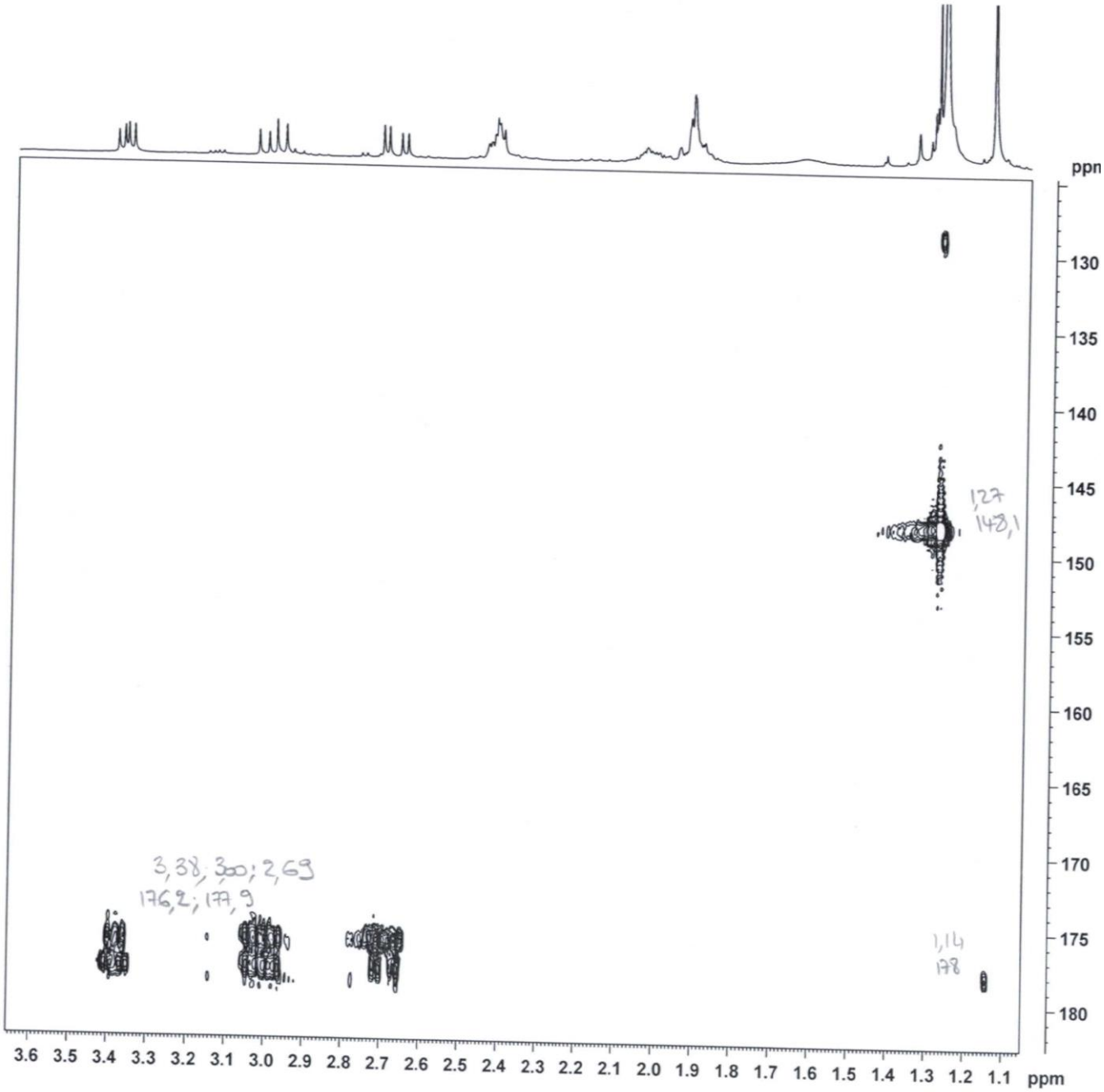
(*P*)-(1*R*,3*R*)-**15mb** (**LW 290 1-C**=

HMBC



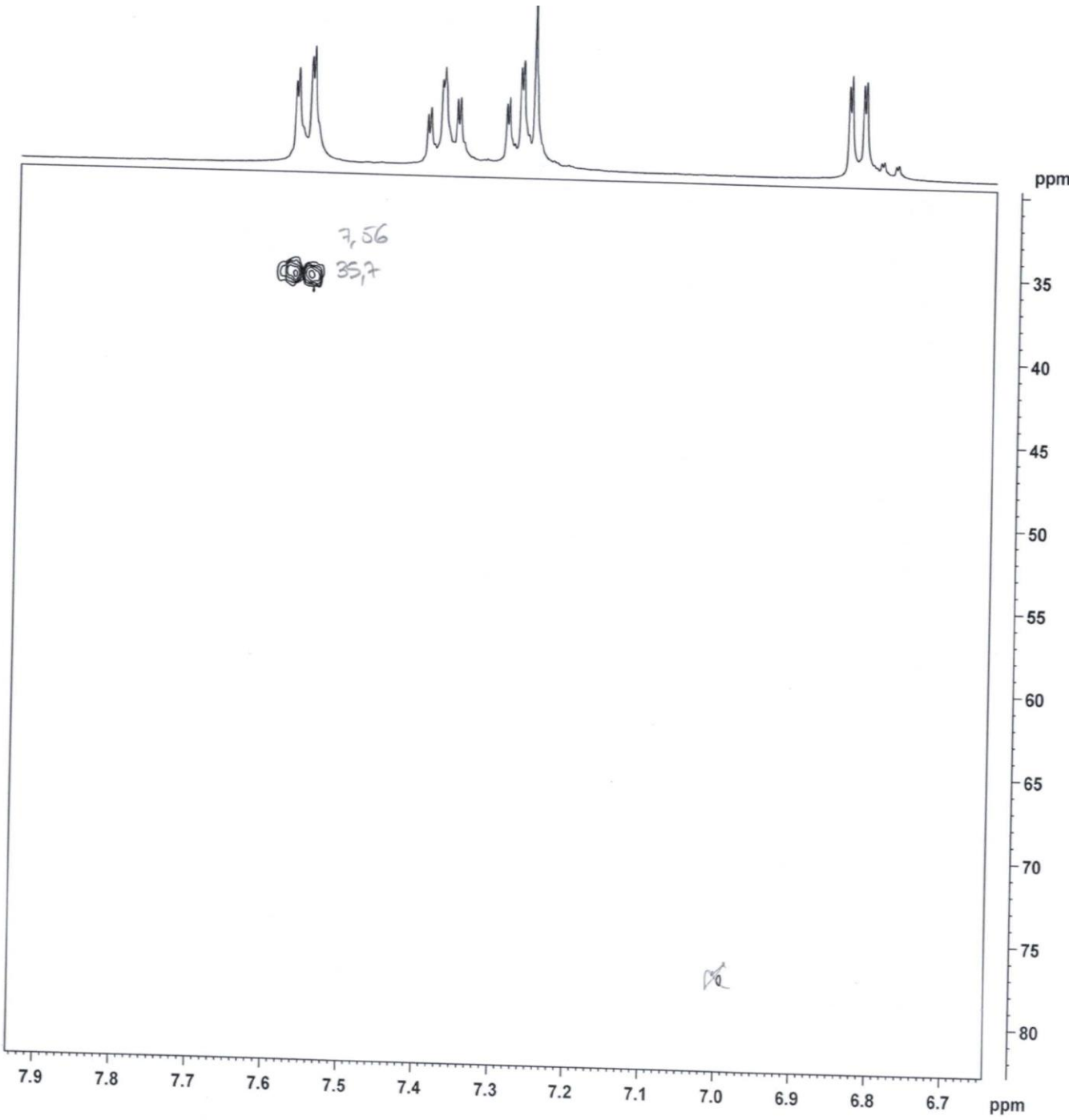
(*P*)-(1*R*,3*R*)-**15mb** (**LW 290 1-C**)

HMBC



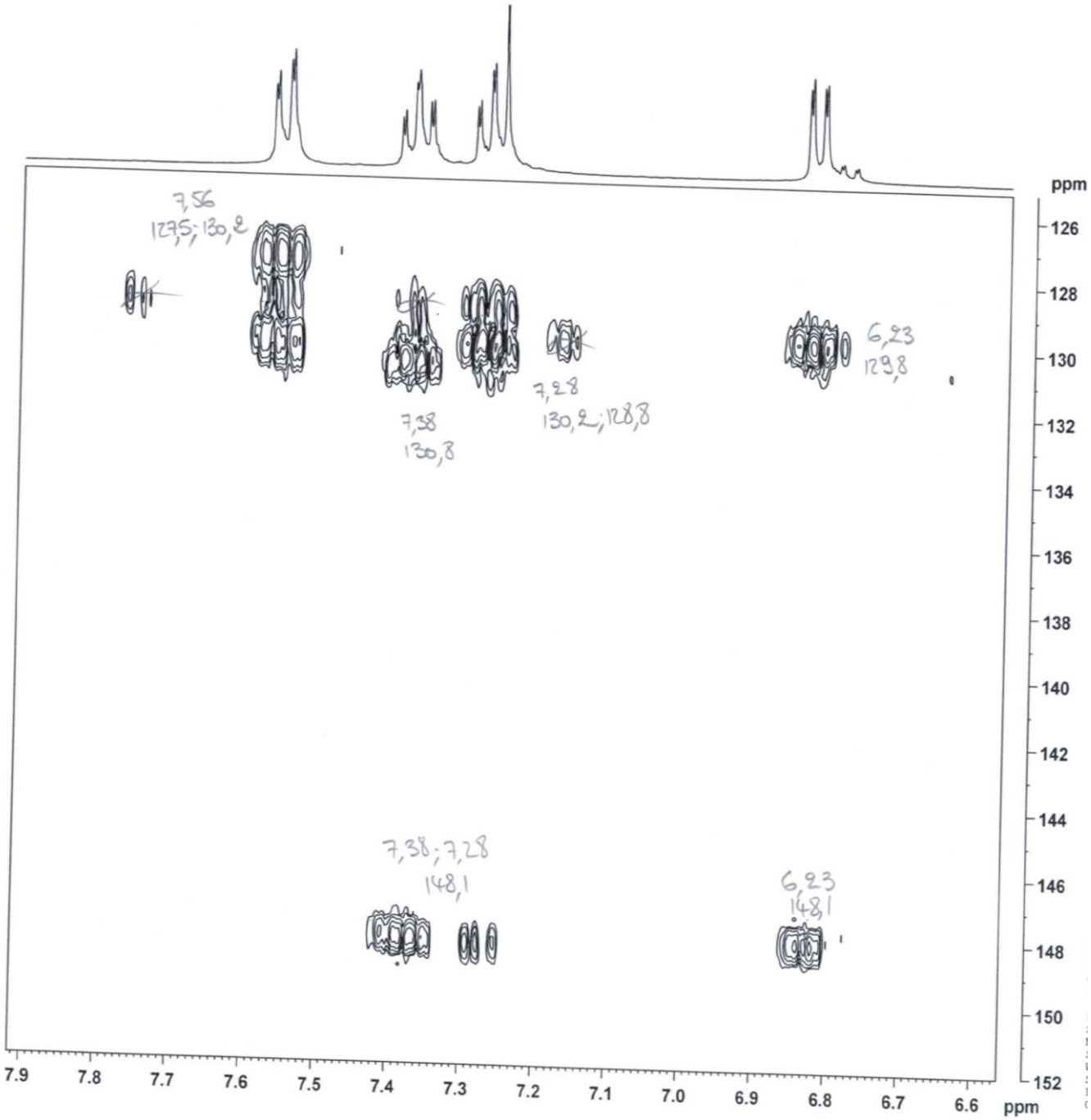
(*P*)-(1*R*,3*R*)-**15mb** (**LW 290 1-C**)

HMBC



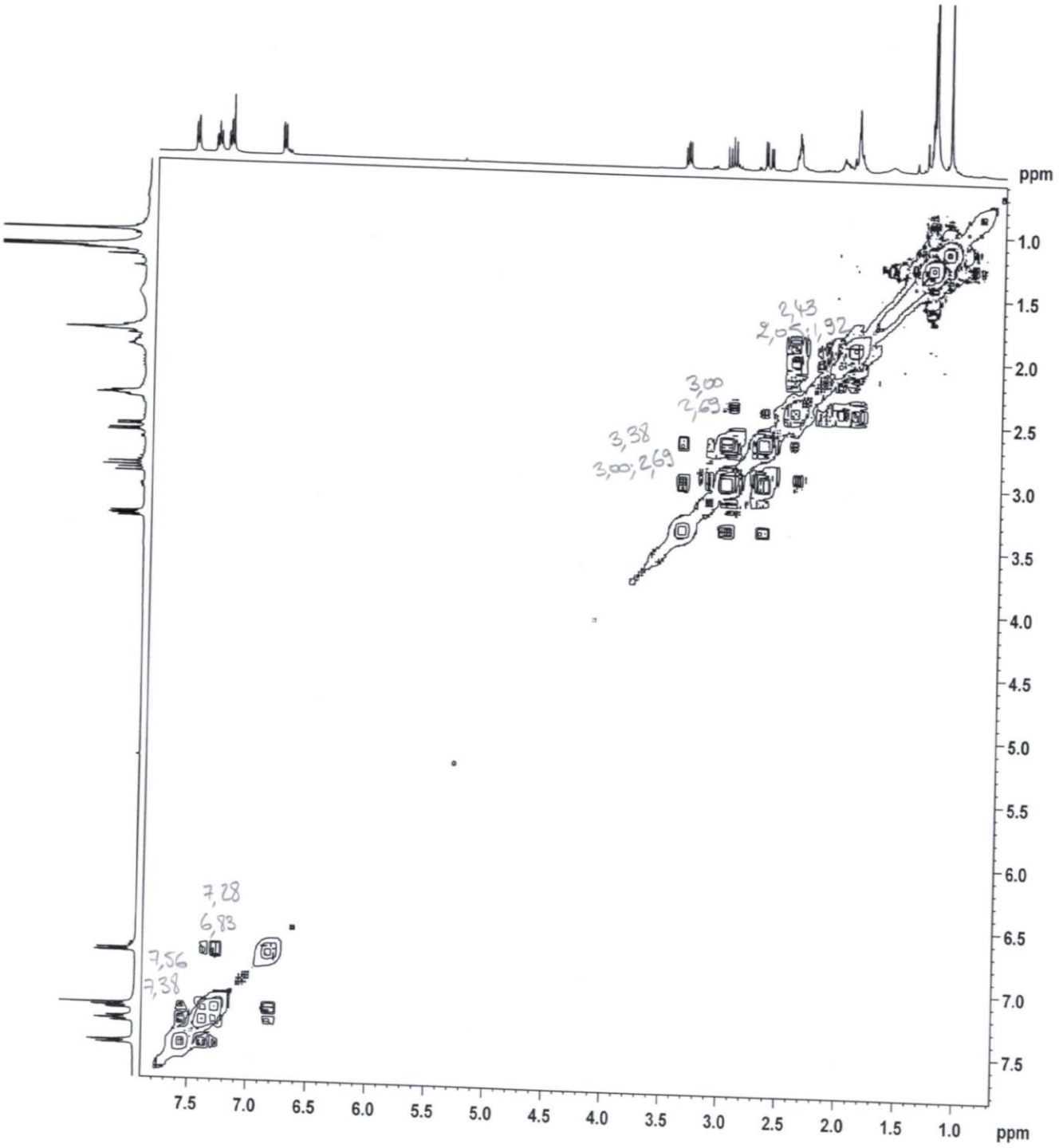
(*P*)-(1*R*,3*R*)-**15mb** (**LW 290 1-C**)

HMBC



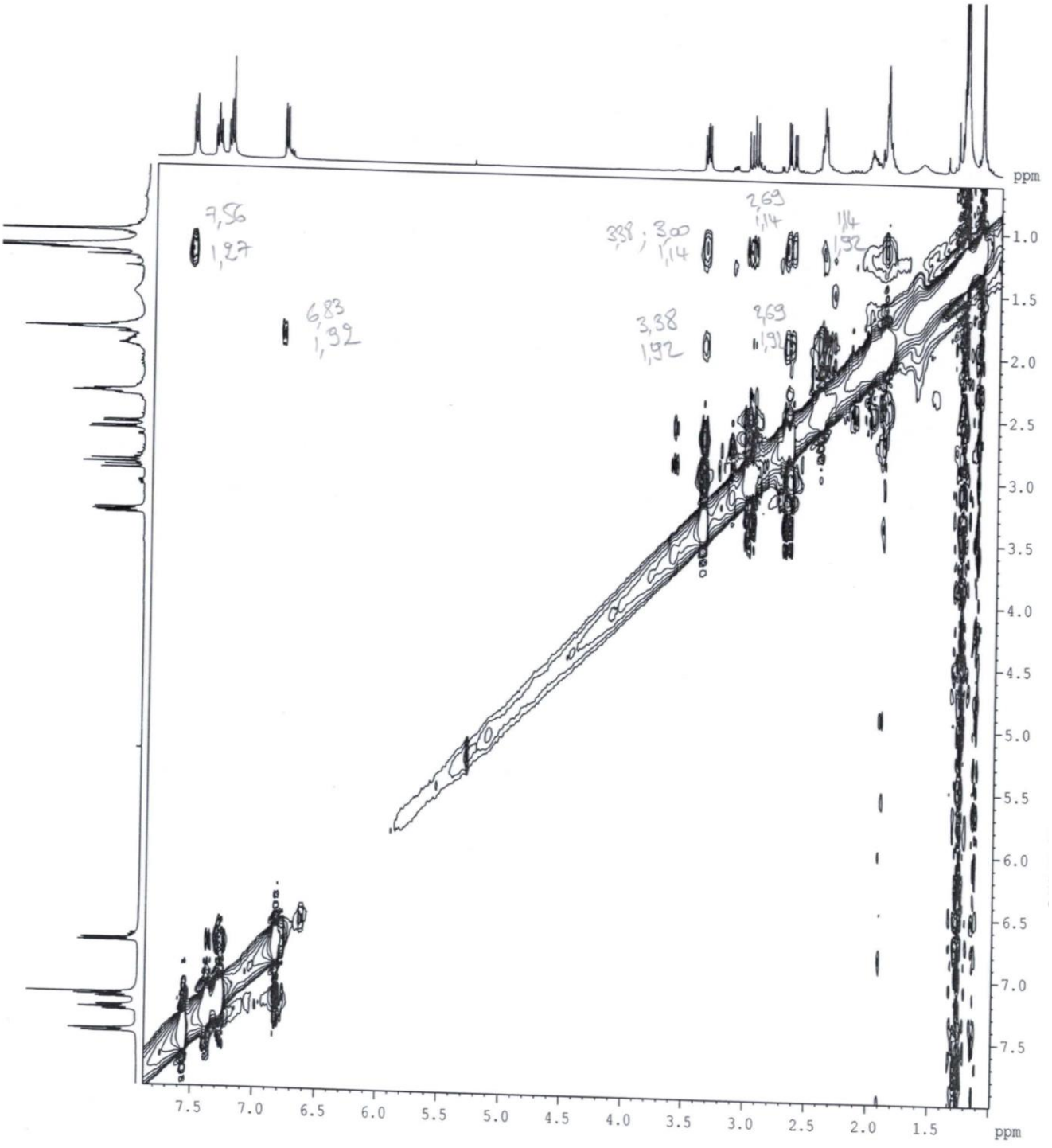
(*P*)-(1*R*,3*R*)-**15mb** (**LW 290 1-C**)

COSY

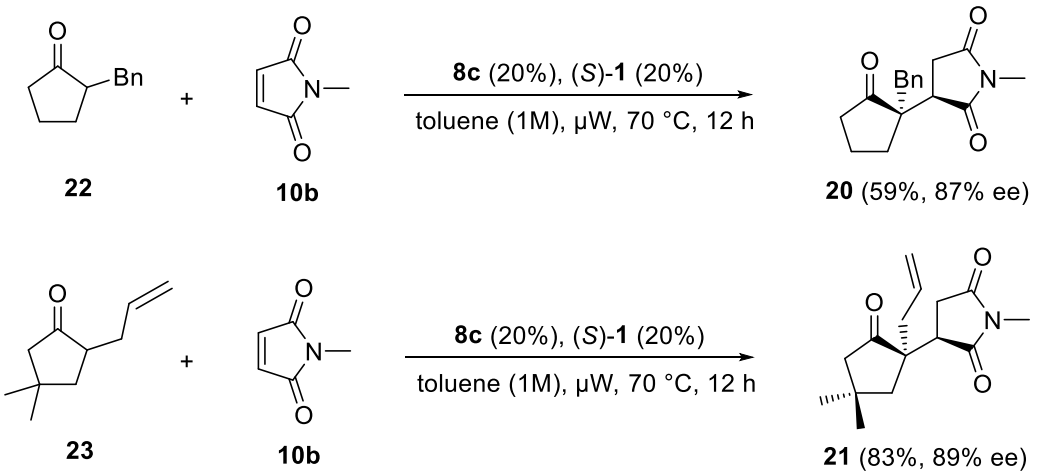


(*P*)-(1*R*,3*R*)-**15mb** (**LW 290 1-C**)

NOESY



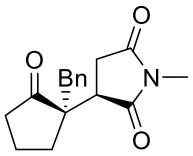
8. Synthesis of succinimides 20 and 21



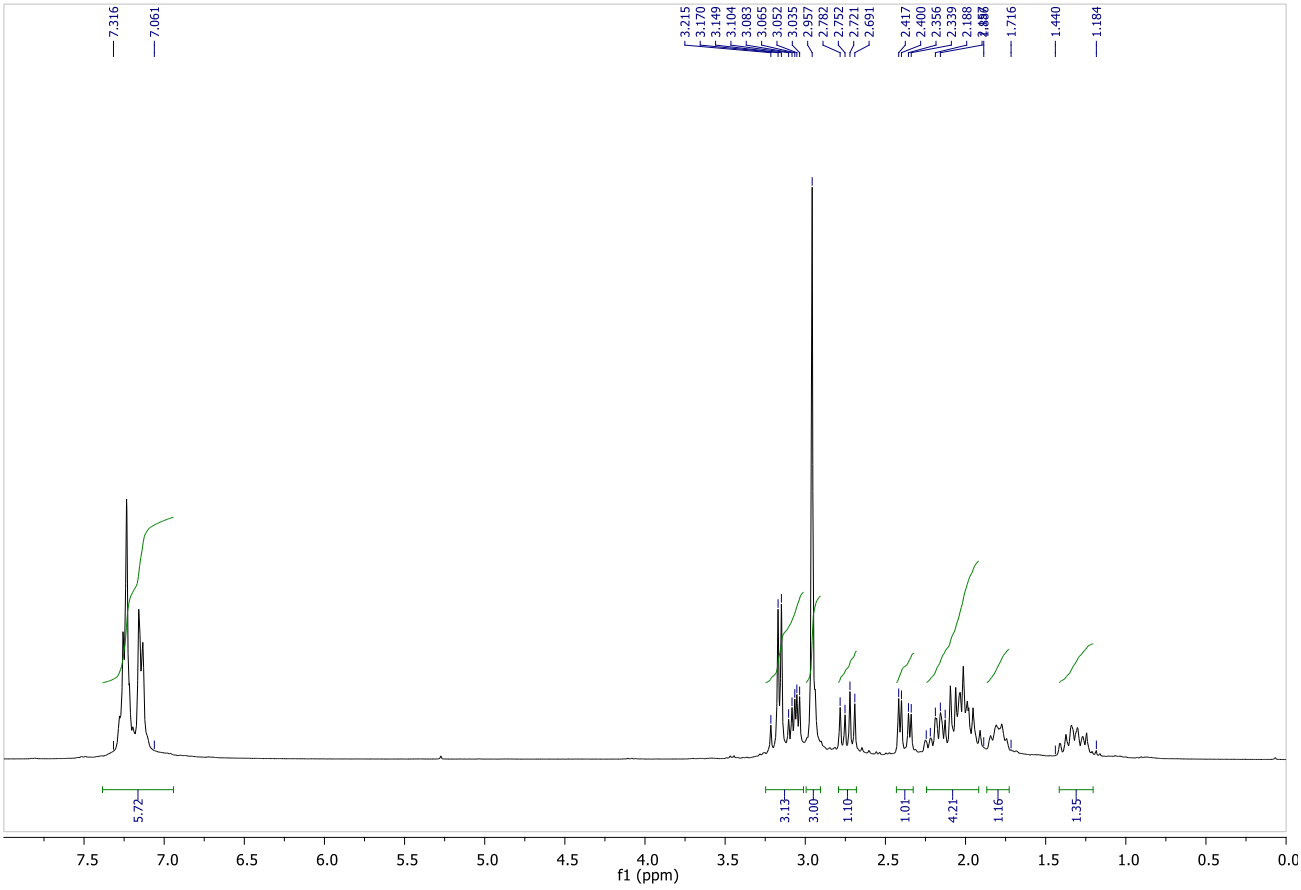
Scheme S4. Synthesis of succinimdes **20** and **21**.

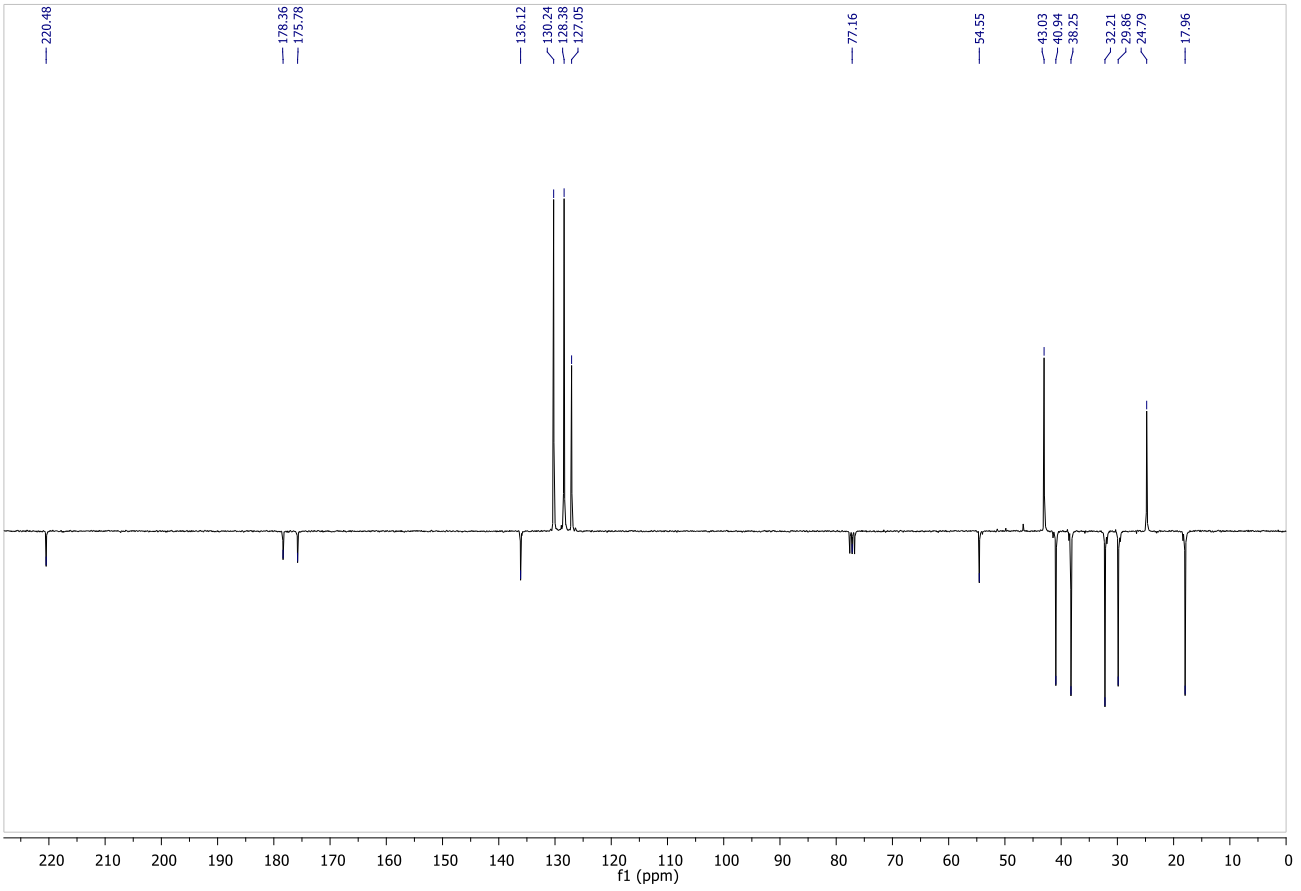
Compounds **20** (59%) and **21** (83%) were synthesized respectively from cyclopentanones **22**[7] and **23**[8] following the general procedure described for compounds **15** (see p S38). No regio- or diastereomers were isolated in these reactions.

(*R*)-3-((*S*)-1-Benzyl-2-oxocyclopentyl)-1-methyl-2,5-pyrrolidinedione 20



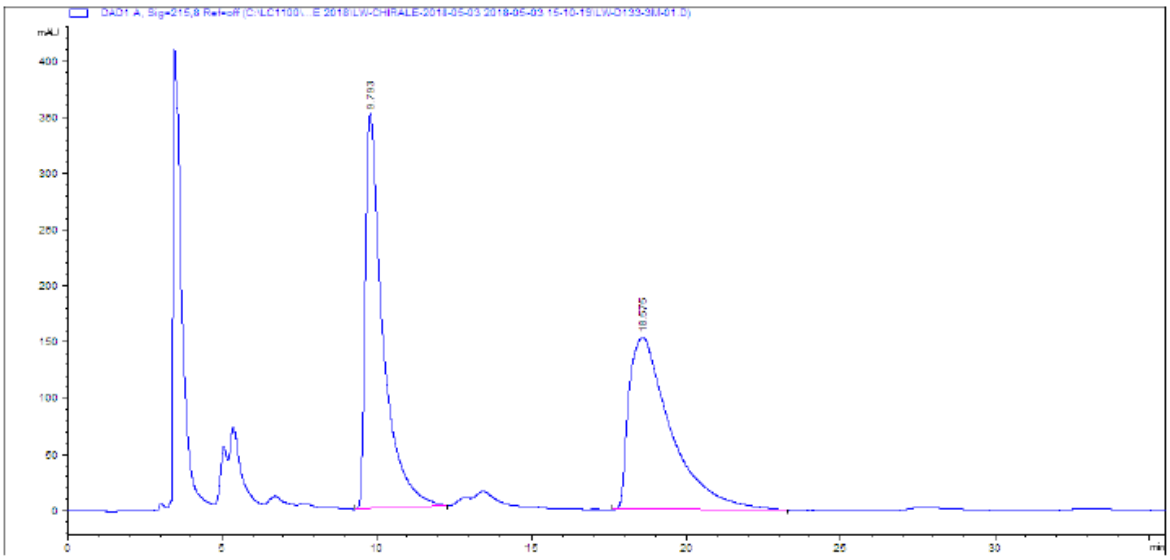
(1*S*,3*R*)-**20**: **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.32-7.06 (m, 5H), 3.19 (d, *J* = 13.5 Hz, 1H), 3.12 (d, *J* = 13.5 Hz, 1H), 3.05 (dd, *J* = 9.0, 5.1 Hz, 1H), 2.96 (s, 3H), 2.74 (dd, *J* = 18.3, 9.0 Hz, 1H), 2.38 (dd, *J* = 18.3, 5.1 Hz, 1H), 2.25-1.84 (m, 4H), 1.84-1.72 (m, 1H), 1.44-1.18 (m, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 220.5, 178.4, 175.8, 136.1, 130.2, 128.4, 127.0, 54.5, 43.0, 40.9, 38.2, 32.2, 29.9, 24.8, 17.8; **HRMS (ESI)** m/z calcd for $[C_{17}H_{19}NNaO_3]^+$ 308.1257, found 308.1262; **IR** (neat) 2961, 1773, 1731, 1690, 1454, 1435, 1383, 1280, 1126, 751, 704, 691 cm^{-1}; **$[\alpha]^{24}_D$** = + 1.2 (c = 0.87, $CHCl_3$).


7.316
7.061
3.215
3.170
3.149
3.104
3.083
3.065
3.052
3.035
2.957
2.782
2.752
2.721
2.691
2.417
2.400
2.356
2.339
2.188
1.716
1.440
1.184
5.72
3.13
3.00
1.10
1.01
4.21
1.16
1.35
f1 (ppm)


220.48
178.36
175.78
136.12
130.24
128.38
127.05
77.16
54.55
43.03
40.94
38.25
32.21
29.86
24.79
17.96
f1 (ppm)

HPLC: (±)-**20**. Chiralpal AD, Solvent: Hexane/i-PrOH = 80:20, Flow Speed 1.0 mL/min , UV: 215nm, retention times: 9.793, 18.575.

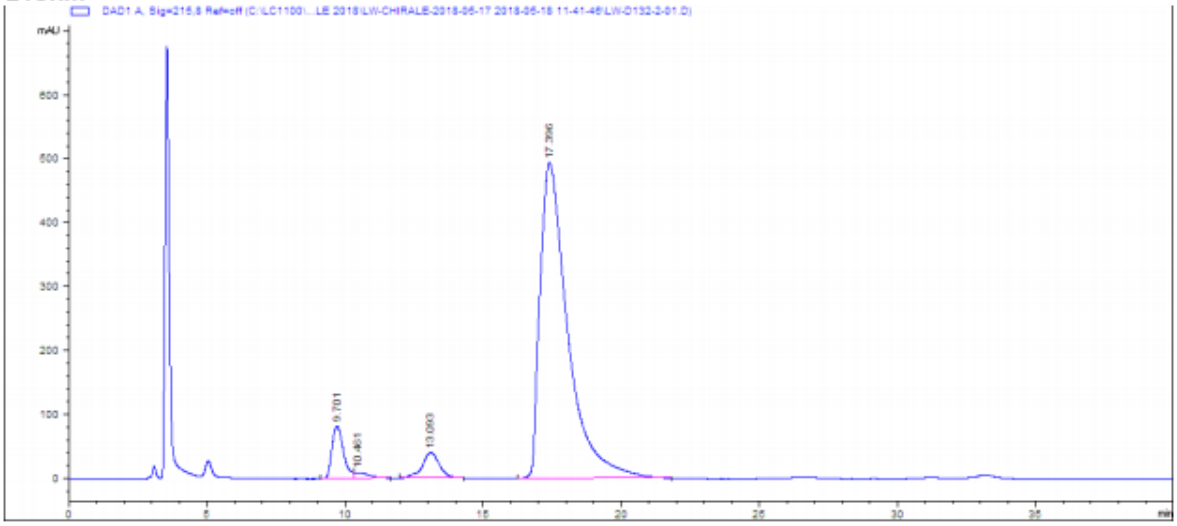
LW D133-3M **Hexane / Isopropanol 80 : 20**
215nm



#	Time	Area	Height	Width	Area%	Symmetry
1	9.793	13875.4	351.8	0.5642	48.895	0.351
2	18.575	14502.5	153.9	1.1243	51.105	0.458

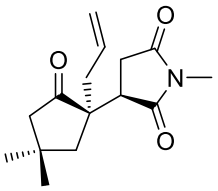
HPLC:(1*S*,3*R*)-**20**. Chiralpal AD, Solvent: Hexane/i-PrOH = 80:20, Flow Speed 1.0 mL/min , UV: 215nm, 87%ee, retention time: 17.396.

LW D132-2 **Hexane / Isopropanol 80 : 20**
215nm

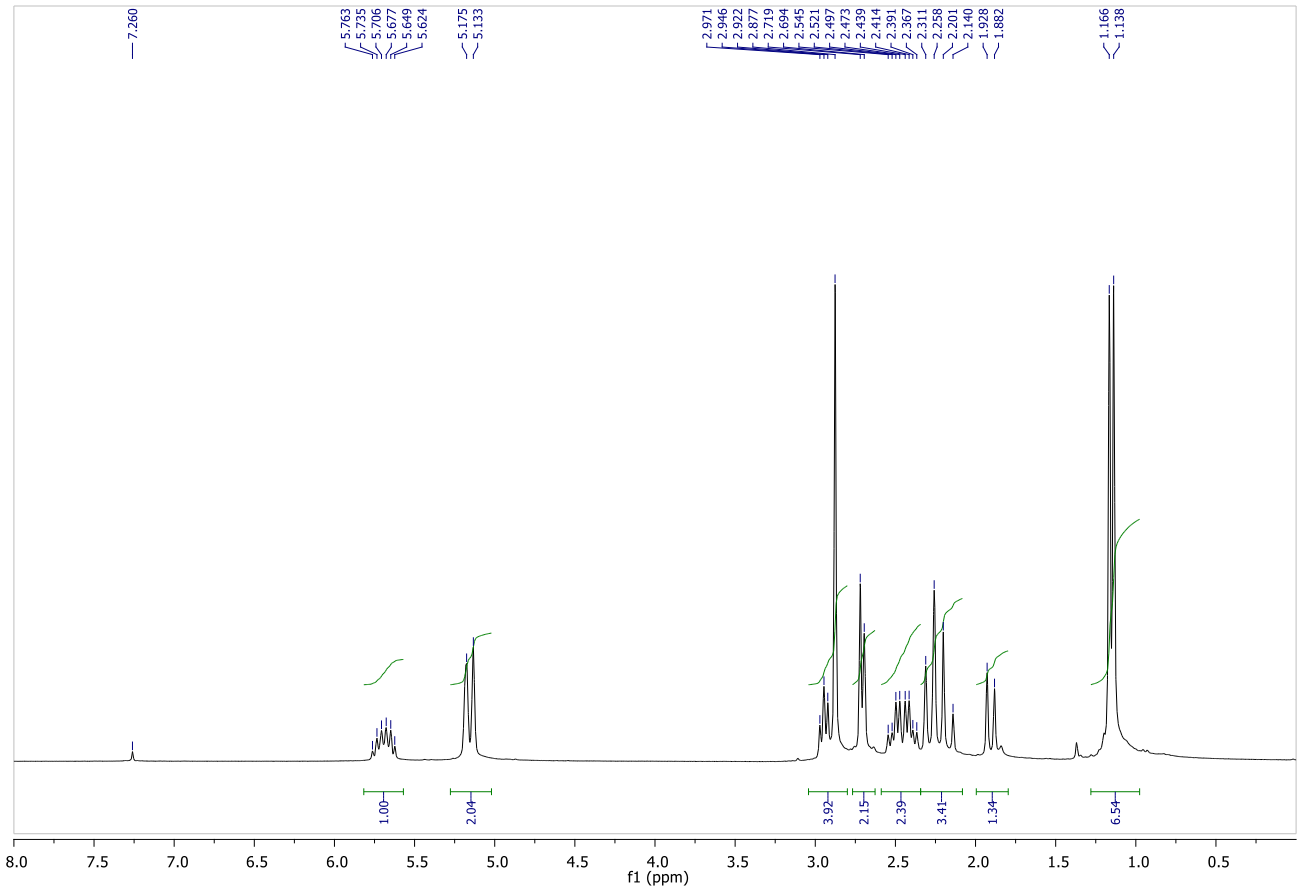


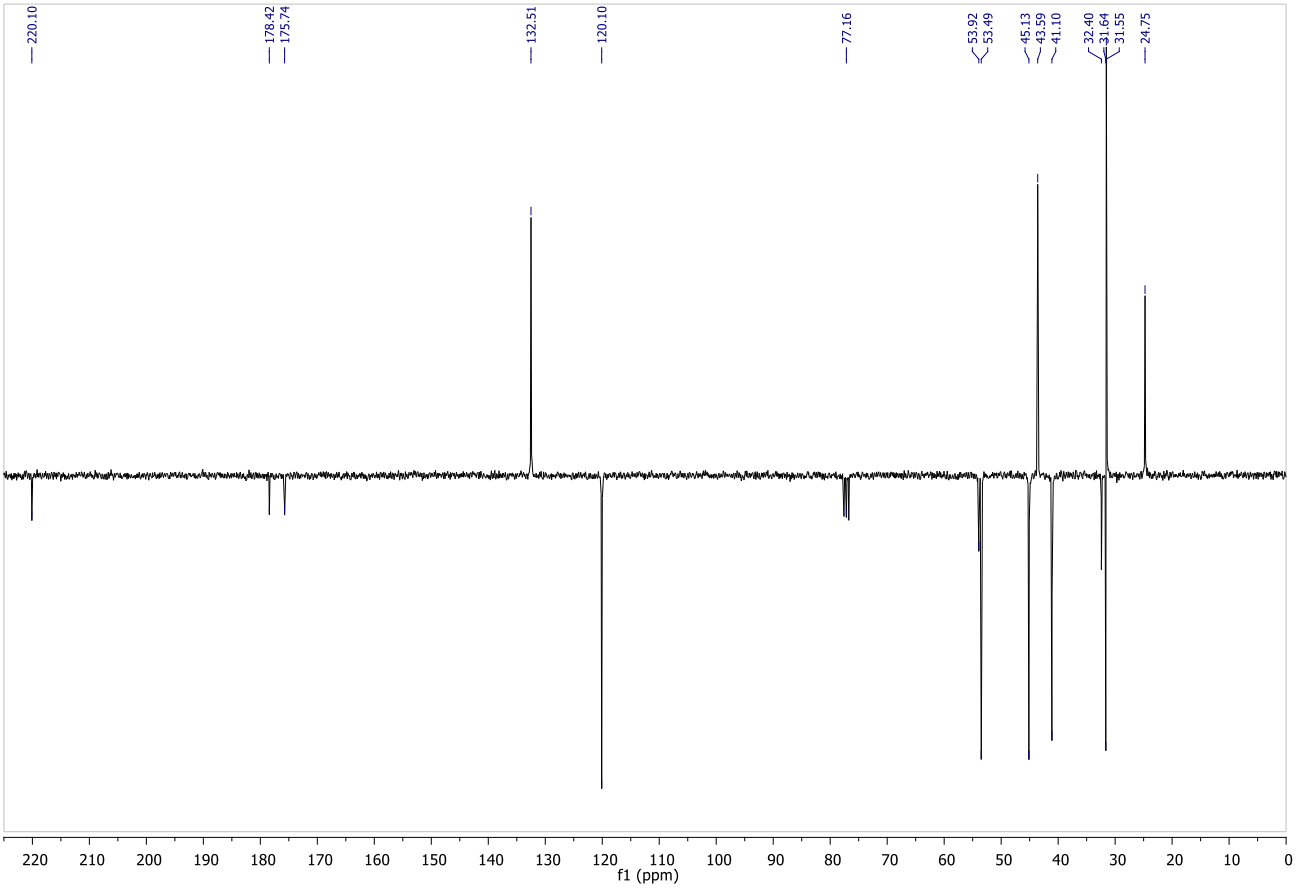
#	Time	Area	Height	Width	Area%	Symmetry
1	9.701	2406.4	82.5	0.4494	6.159	0.735
2	10.461	356.3	9.5	0.4434	0.912	0.232
3	13.093	1786.1	40.1	0.533	4.571	0.946
4	17.396	34522.5	493.7	0.9228	88.358	0.474

(*R*)-3-((*R*)-1-Allyl-4,4-dimethyl-2-oxocyclopentyl)-1-methyl-2,5-pyrrolidinedione (1*R*,3*R*)-21



(1*R*,3*R*)-**21**: white solid; **m.p.**: 77.3 °C; **Rf** = 0.2 (cyclohexane/EtOAc = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 5.85-5.55 (m, 1H), 5.17 (bs, 1H), 5.13 (bs, 1H), 2.95 (bt, *J* = 7.4, Hz, 1H), 2.88 (s, 3H), 2.72 (bs, 1H), 2.69 (bs, 1H), 2.50 (dd, *J* = 14.4, 7.3 Hz, 1H), 2.40 (dd, *J* = 14.4, 7.3 Hz, 1H), 2.28 (bd, *J* = 15.9 Hz, 2H), 2.17 (bd, *J* = 18.3 Hz, 1H), 1.90 (bd, *J* = 13.9 Hz, 1H), 1.17 (s, 3H), 1.14 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 220.1, 178.4, 175.7, 132.5, 120.1, 53.9, 53.5, 45.1, 43.6, 41.1, 32.4, 31.6, 31.6, 24.8; **HRMS (ESI)** m/z calcd for $[C_{15}H_{21}NNaO_3]^+$, 286.1414, found 286.1413; **IR** (neat) 2951, 2924, 2866, 2359, 2325, 1726, 1693, 1457, 1293, 1275 cm^{-1}; **$[\alpha]^{15}_D$** = + 8.7 (c = 6.35, $CHCl_3$).

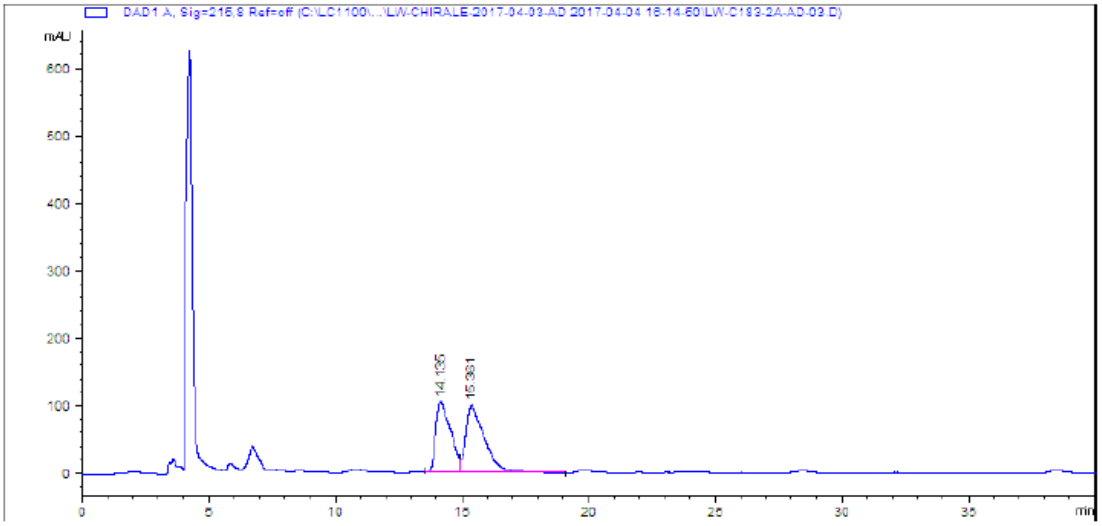




HPLC: (±)-**21**. Chiralpal AD, Solvent: Hexane/i-PrOH = 95:5, Flow Speed 1.0 mL/min, UV: 215nm, retention times: 14.135, 15.361 min.

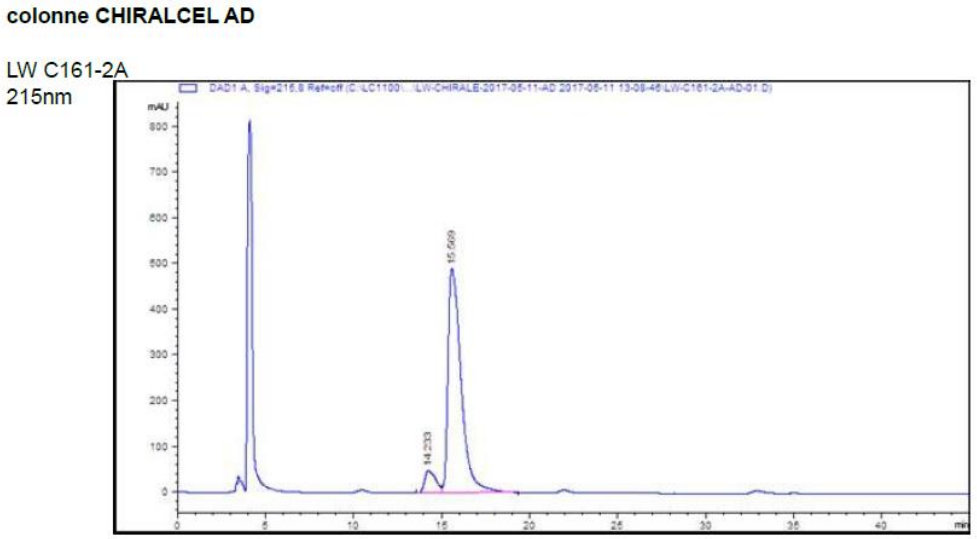
Colonne CHIRALCEL AD

LW C183-2A hexane / isopropanol 95 : 05
215 nm



#	Time	Area	Height	Width	Area%	Symme-try
1	14.135	4308.4	104.5	0.5812	45.266	0.446
2	15.361	5209.5	100.5	0.7149	54.734	0.396

HPLC: (1*R*,3*R*)-**21**. Chiralpal AD, Solvent: Hexane/i-PrOH = 95:5, Flow Speed 1.0 mL/min , UV: 215nm, 85%ee, retention time: 14.23, 15.57 (min.

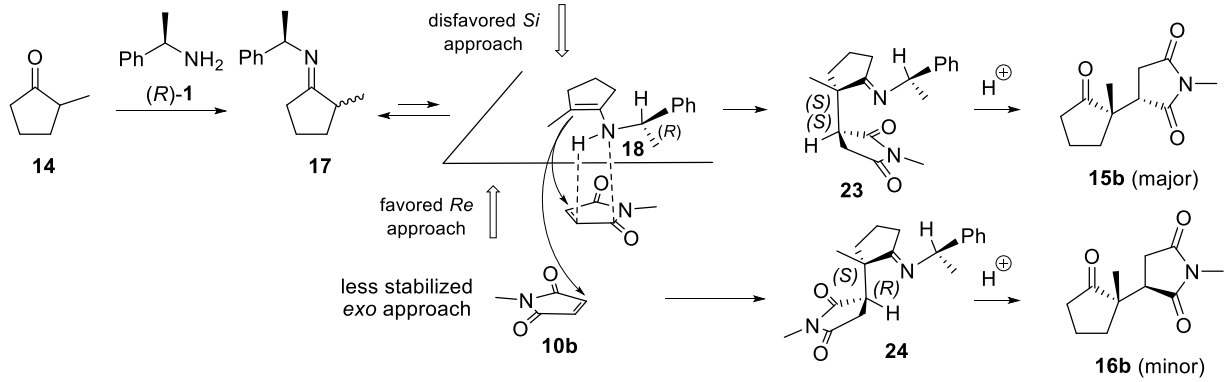


#	Time	Area	Height	Width	Area%	Symmetry
1	14,23	2143,40	49,50	0,58	7,77	0,49
2	15,57	25433,80	491,20	0,71	92,23	0,39

Results and Discussion

1. Model for determination of the stereochemical course of the reaction

The stereochemical outcome of the stoichiometric addition of enamines to Michael acceptors is well established since the nineties.[9] It can be extended to the present organocatalyzed approach involving the transient formation of imine **17** (Scheme S4), in equilibrium with its reacting enamine tautomer **18**. The regioselectivity of this alkylation in favor of the Cα more hindered position, in such a case, is the consequence of a favored concerted but non synchronous proton transfer which was supported by theoretical calculations giving a good agreement with the observed experimental results.[10] According to our empirical model (Scheme S4), Michael addition of the enamine **18**, tautomer of **17**, to maleimide **10b** should arise through the *Re* face, via an *endo* approach, giving the major Michael adduct **23**. The *exo* approach lacking an extra secondary N-C stabilization explains the formation of the minor imine **24**.



Scheme S5. Proposed model for stereoselectivity determination using (*R*)-phenylethylamine **1** as catalyst. Compound **14** was chosen as the pre-nucleophile and maleimide **10b** as the electrophile because stereochemistry of the resulting product **15b** was ascertained by X-ray crystallographic analysis (see bellow). As exemplified for the stoichiometric corresponding reaction, this model may nevertheless be extended to the other substrates used in this study.

After hydrolysis, major and minor products **15b** and **16b** are obtained. The proton transfer from the NH of the enamine to the C2 position of the acceptor is a concerted process with the creation of the C-C bond.

The presence of the opposite enantiomers of **15b** and **16b** (when ee < 100%) is explained by a disfavored *Si* approach of the enamine face by the maleimide. An X-ray diffraction analysis of the major product **15b** confirmed its relative and absolute configurations (Figure S1).

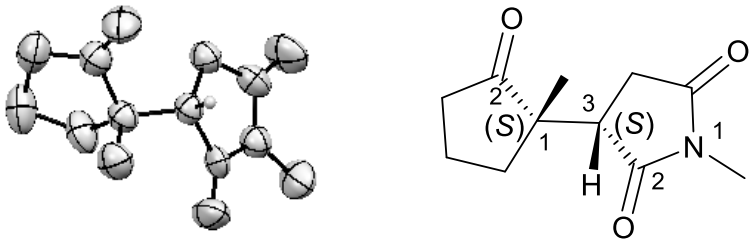


Figure S1: Thermal ellipsoid plot (left) of the molecular structure of (3*S*)-1-methyl-3-[(1*S*)-1-methyl-2-oxocyclopentyl]-2,5-pyrrolidinedione **15b** (right). Most of the H atoms have been omitted for clarity. The ellipsoids enclose 50% of the electronic density. Figure S1 left was drawn with the Mercury program[11] in the ORTEP style.[12]

X-ray analysis of (*S*)-1-methyl-3-((*S*)-1-methyl-2-oxocyclopentyl)-2,5-pyrrolidinedione (1*S*,3*S*)-**15b**

X-ray Crystallographic Data. Hexagonal space group, $P6_1$, a = 14.9300(18) Å, b = 14.9300(18) Å, c = 9.2555(7) Å, V = 1786.7(5) Å^3, Z = 6, D_x = 1.340 Mg/m^3, μ(Cu Kα) = 0.766 mm^{-1}, and F(000) = 780 e−. Crystal dimensions: 0.35 x 0.28 x 0.14 mm^3. A total of 13001 reflections were measured with 2276 independent reflections (R_{int} = 0.0375). Final R_1 = 0.0438, wR_2 = 0.1011 for 1477 $I > 2\sigma(I)$. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (deposit No. CCDC 1847461). Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0)223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

Colourless crystal suitable for single-crystal X-ray analysis was obtained from slow evaporation of anhydrous solution of in a hexane/ethyl acetate mixture. The data were collected on a Rigaku diffractometer constituted by a MM007 HF rotating-anode generator, delivering Cu-Kα radiation (λ =1.54187 Å) through Osmic CMF confocal optics, and a Rapid II curved Image Plate for Bragg peak detection, at room temperature. The crystal-to-detector distance was 127.40 mm, and in accordance with the IP detector area, allowed us to record large (20°)-oscillation frames in the range of $6 \leq 2\theta \leq 142.7°$ with 15 seconds of exposure per degree of oscillation. The ω-scan strategy aimed at optimizing the Bijvoet pair measurement with a 95% coverage. Data reduction and scaling were carried out with an empirical absorption correction, as well as a treatment for Lorentz and polarization effects using the program *Fs_Process*.[13] Compound (1*S*,3*S*)-**15b** was assigned to the chiral space group P 6_1 (n° 169), based upon systematic absences, *E*-statistics, agreement factors for equivalent reflections, successful solution by phasing intrinsic methods (SHELXT),[14] and refinement of the corresponding structure with the correct absolute configuration (see below). The refinement step was performed by full matrix least squares on F^2 using SHELXL. Anisotropic thermal parameters were used for all non-hydrogen atoms and if the H atoms were located in residual maps they all were refined using a riding model with U_{eq} values set at 1.2U_{eq} (parent atom) (1.5 for the methyl groups). Solvent accessible infinite tunnels making cavity of 211 Å per unit cell run along the six-fold helicoidal axis in the direction of the crystallographic ***c*** axis. Residual electron density inside the cavity was estimated by the SQUEEZE function of *PLATON*[15] to a

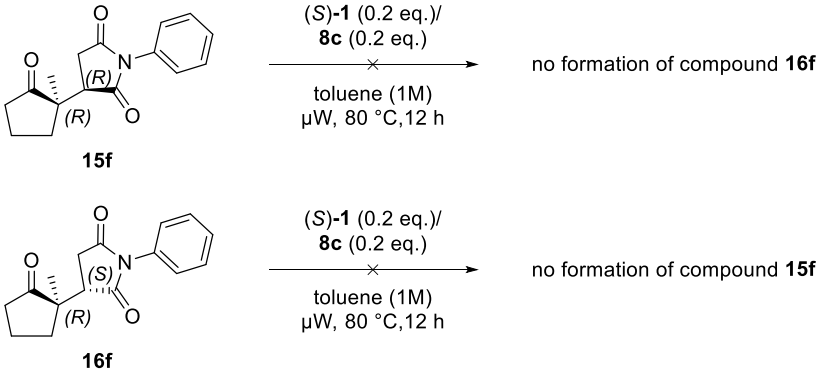
value of 18 electrons per unit cell, which might correspond to 0.36 solvent molecules of disordered, linear hexane. Squeeze procedure back–Fourier transform into A (discrete) and B (solvent) contributions to F(calc) to be used for subsequent *L.S.* refinement of the solvent-free model. The number of solvent electrons was included in the formula, formula weight, calculated density, μ and F(000). Despite the weak anomalous scattering contribution enhanced however by the copper radiation, post-refinement Bijvoet analysis delivered Bayesian statistics[16] (P2(true) and P3(true) = 1.000 and 0.998) convincing enough to support the modest inversion-distinguishing power of the Flack parameter,[17] z = 0.11(7) determined using 529 quotients[18], and the Hooft[16] parameter y = 0.16(9) to claim the enantiopure (1*S*,3*S*)-**15b** compound as C2*S*, C7*S* (numbering corresponding to crystallographic analysis) enantiomer.

Table S5. Crystal data and structure refinement for compound (1*S*,3*S*)-**15b**.

Identification code	**lw-2-105-1** (**15b**)	
Empirical formula	C_{11} H_{15} N O_3 , 0.36 [C_6 H_{14}]	
Formula weight	240.26	
Temperature	293(2) K	
Wavelength	1.54187 Å	
Crystal system	Hexagonal	
Space group	P 6_1	
Unit cell dimensions	*a* = 14.9300(18) Å	*α* = 90°.
	b = 14.9300(18) Å	*β* = 90°.
	c = 9.2555(7) Å	*γ* = 120°.
Volume	1786.7(5) Å^3	
Z	6	
Density (calculated)	1.340 Mg/m^3	
Absorption coefficient	0.766 mm^{-1}	
F(000)	780	
Crystal size	0.350 x 0.280 x 0.140 mm^3	
Theta range for data collection	7.624 to 71.931°.	
Index ranges	-17 ≤ h ≤ 17, -17 ≤ k ≤ 18, -10 ≤ l ≤ 11	
Reflections collected	13001	
Independent reflections	2676 [R(int) = 0.0375]	
Completeness to □ = 67.687°	98.9%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.000 and 0.688	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2266 / 1 / 139	
Goodness-of-fit on F^2	1.121	
Final R indices [I>2□(I)]	R1 = 0.0438, wR2 = 0.1011	
R indices (all data)	R1 = 0.0717, wR2 = 0.1380	
Absolute structure parameter	0.11(7)	
Largest diff. peak and hole	0.138 and -0.168 e.Å^{-3}	

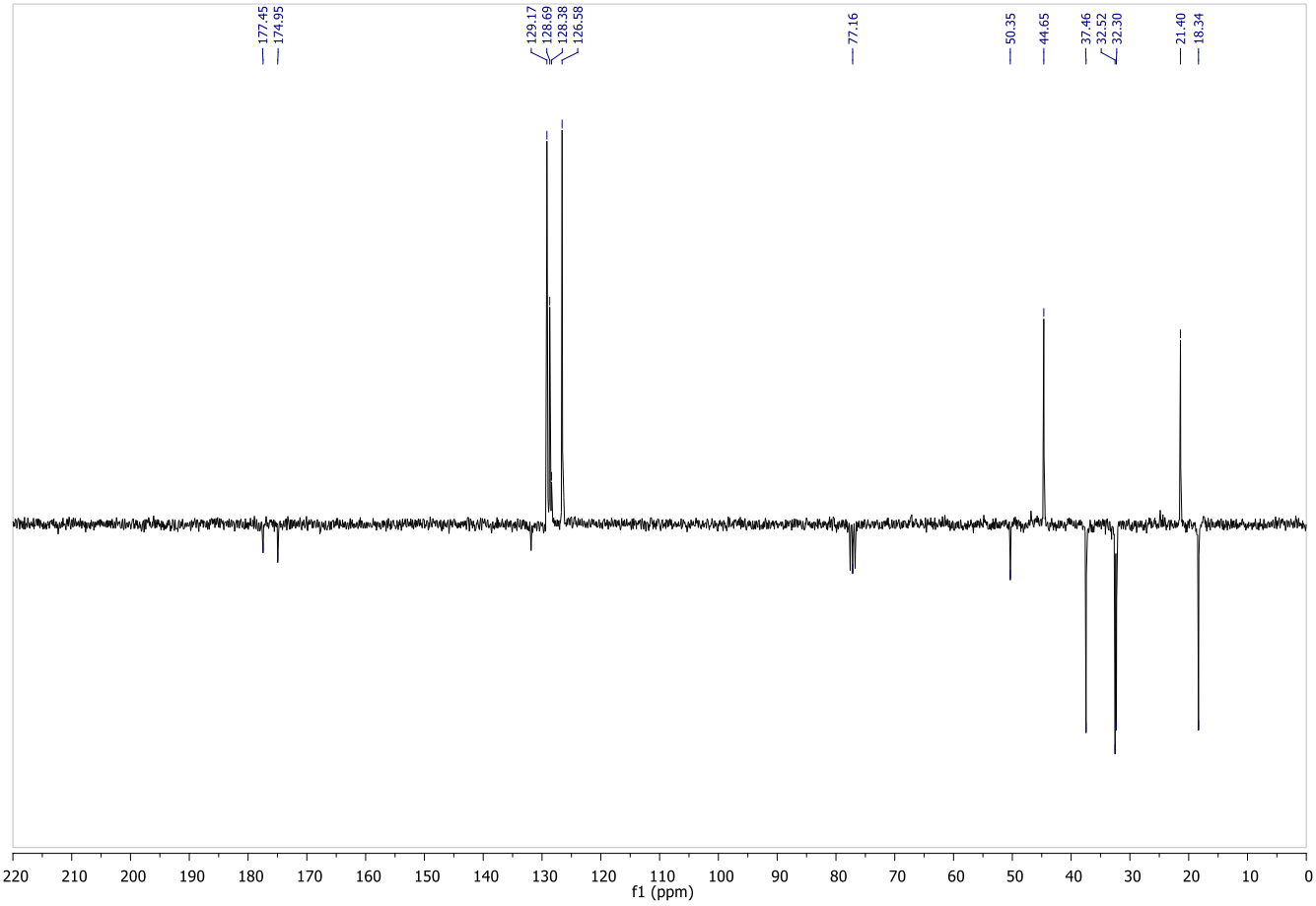
2. Thermodynamic study

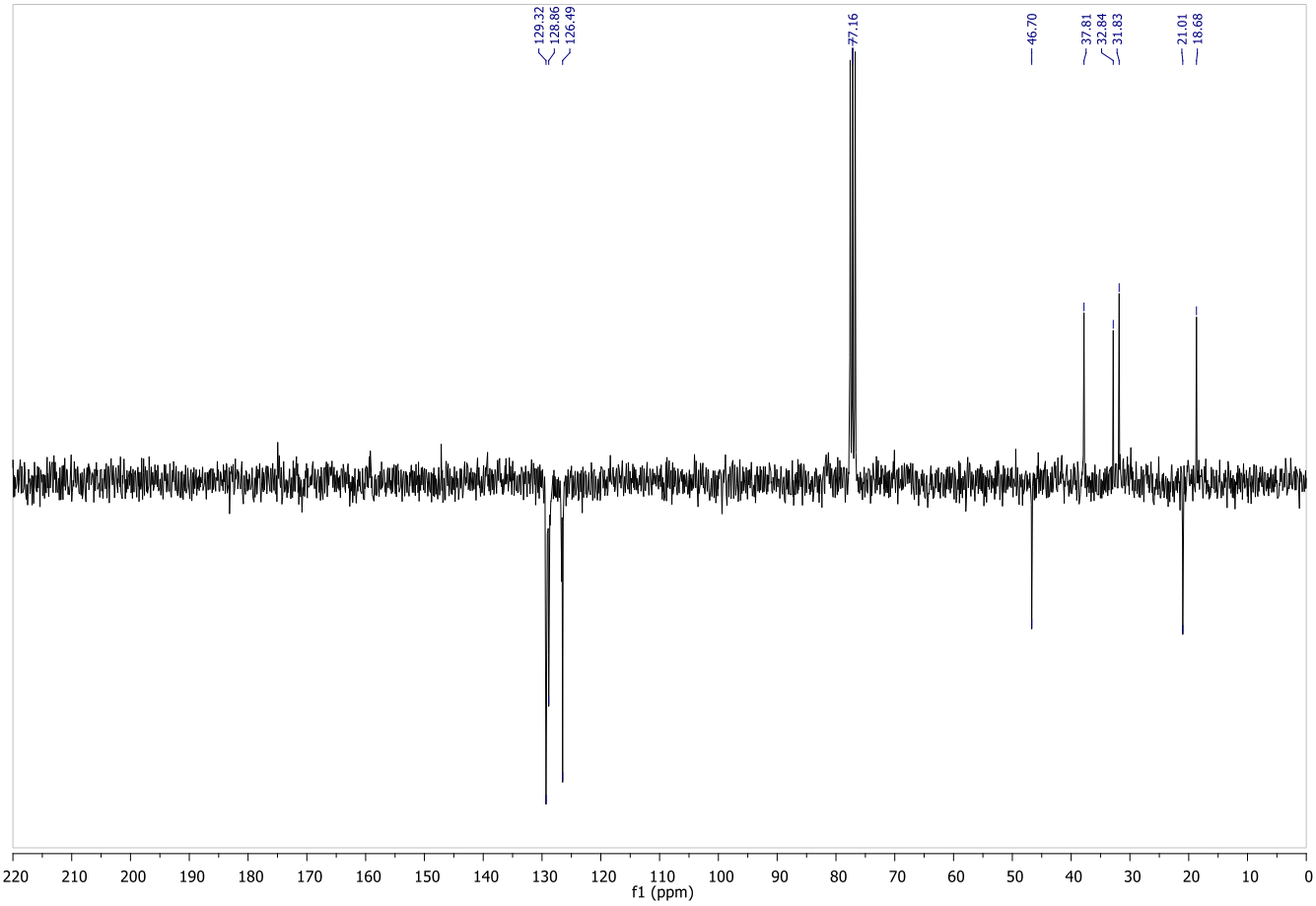
Retro-Michael reaction is a well-known process encountered with many donors such as oxo,[19] *aza*,[20] thio[21] or C[22-24] nucleophiles that could be responsible for racemization of products. Moreover, the proton on the TCC position in our products **15f** or **16f** is prone to epimerization due to its acidic nature. Although it is in the familiar chemist's mind that QCC are not prone to racemization, such retro-Michael process was already observed and linked to acidic carbonyl compounds.[25,26] To test this hypothesis, we chose separable diastereomers **15f** and **16f** obtained in the Michael reaction in poor diastereoselectivity (Table 20, 54% de, entry 9) and submit them to the reaction conditions (80 °C, microwave, 12 h) used in their syntheses (Scheme 85).



Scheme S6. Thermodynamic study on diastereomers **15f** and **16f**.

As can be seen on the following ^{13}C JMOD spectra, after elimination of the organocatalyst by filtration over silica gel, this reaction did not deliver mixture of diastereomers **15f**/**16f** starting from either pure **15f** or **16f**, excluding the possibility of a retro Michael process or an epimerization leading to equilibration of these bicyclic molecules in the studied reaction conditions.


177.45
174.95
129.17
128.69
128.38
126.58
77.16
50.35
44.65
37.46
32.52
32.30
21.40
18.34
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


129.32
128.86
126.49
77.16
46.70
37.81
32.84
31.83
21.01
18.68
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

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