Asymmetric cyclopropanation of conjugated cyanosulfones using a novel cupreine organocatalyst : Rapid access to δ^3-amino acids

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General Experimental

All reactions were carried out at room temperature and magnetically stirred unless otherwise stated. Anhydrous solvents were supplied as Sureseal® bottles by Aldrich. All reagents and solvents were purchased commercially or prepared according to literature procedures. Chemicals and solvents were supplied by Sigma-Aldrich and Fisher, and were used as supplied unless otherwise stated. Literature procedures were followed for the synthesis of catalysts **I**[1], **II**[2], **III**[3], **IV**[4], **IX**[5], **X**[4], **XII**[6], **XIII**[5] and **XIV**.[4] Vinyl sulfones **1a-i** were prepared according to literature procedures,[7] as were *O*-acetylhydroquinine[8] and *O*-(1-naphthoyl)quinine.[9] Compound numbering within this supporting information continues from the manuscript.

Chromatography: Thin layer chromatography (TLC) was performed on Merck aluminium backed plates coated with 0.2 mm silica gel 60F254. The spots were visualised using UV light (254 nm) and then permanent staining by solutions of potassium permanganate, ninhydrin or bromocresol green. Flash column chromatography was performed on Sigma-Aldrich silica gel 60Å (230-400 mesh).

NMR data: ^{1}H NMR spectra were recorded using a Bruker DPX 400 (400 MHz) or a Bruker Avance III 400 (400 MHz) spectrometer. Chemical shifts (δ) are quoted in parts per million using the abbreviations: s, singlet; bs, broad singlet; d, doublet; dd, double doublet; t, triplet; tt, triplet triplet; q, quartet; m, multiplet. ^{13}C NMR spectra were recorded at 100 MHz on a Bruker DPX 400 or Bruker Avance III 400. Two-dimensional spectroscopy (COSY, HMQC and HMBC) was used to assist in the assignments.

IR data: Infrared spectra were recorded on a Thermo Scientific Nicolet iS5 FT-IR spectrometer using iD5 ATR accessory. The selected absorptions are quoted in wavenumbers (cm^{-1}).

MS data: High-resolution mass spectra were recorded on a Thermo Scientific LTQ Orbitrap XL using electrospray ionisation (ESI) conditions.

Optical Rotation: Optical rotation readings were taken using a Perkin-Elmer 341 polarimeter. Specific optical rotations ($[\alpha]$) were recorded at the sodium D line (589 nm) in chloroform or methanol and are quoted in units of deg mL g^{-1} dm^{-1}. Solution concentrations (c) are given in the units of 10^{-2} g mL^{-1}. Temperatures (T) are given in degrees Celsius (°C). The prefixes (+) and (–) indicate the sign of the optical rotation.

HPLC Profiles: HPLC analysis was determined on an Agilent Technologies 1200 Series HPLC, using a ratio of HPLC grade hexanes and propan-2-ol as the eluent, using either a Chiralpak AD-H column (0.46 cm ø X 25 cm) or a Chrialcel OD column (0.46 cm ø X 25 cm), and detection by UV at 210 nm or 254 nm.

Single Crystal X-ray: X-ray data was collected on an Oxford Gemini S-ultra diffractometer using Kα (λ = 1.54180 Å) radiation.

1. Extended Reaction Screening Data

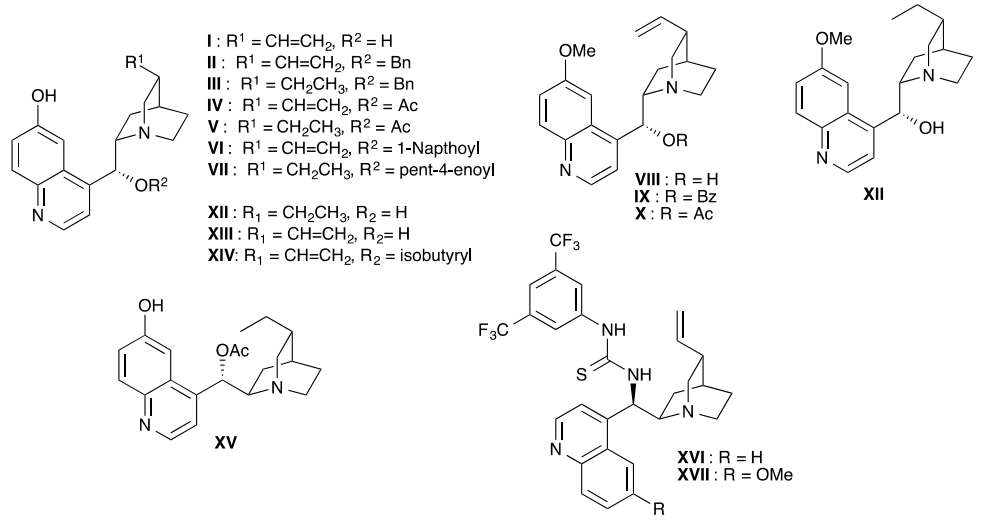
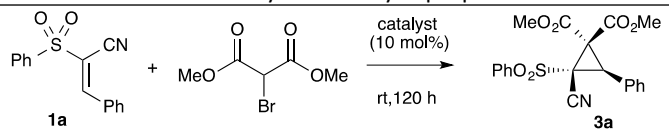


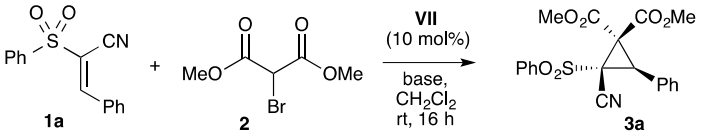
Figure 1 : Complete catalyst screen

Table 1 : Catalyst and Solvent Screen for the asymmetric cyclopropanation



Entry	Cat	Solvent	Yield, %	dr	er
1	**I**	CH_2Cl_2	10	>19:1	68:32
2	**I**	THF	18	>19:1	59:41
3	**I**	$CHCl_3$	7	>19:1	62:38
4	**I**	PhMe	Trace	nd	nd
5	**I**	^{i}PrOH	Trace	nd	nd
6	**II**	CH_2Cl_2	12	>19:1	50:50
7	**III**	CH_2Cl_2	21	>19:1	54.5:45.5
8	**IV**	CH_2Cl_2	17	>19:1	79.5:20.5
9	**V**	CH_2Cl_2	17	>19:1	85:15
10	**VI**	CH_2Cl_2	11	>19:1	83.5:16.5
11	**VII**	CH_2Cl_2	12	>19:1	86:14
12	**VIII**	CH_2Cl_2	31	>19:1	50:50
13	**IX**	CH_2Cl_2	8	>19:1	50:50
14	**X**	CH_2Cl_2	12	>19:1	50:50
15	**XI**	CH_2Cl_2	31	>19:1	50:50
16	**XII**	CH_2Cl_2	7	>19:1	51:49
17	**XIII**	CH_2Cl_2	14	>19:1	64.5:35.5
18	**XIV**	CH_2Cl_2	19	>19:1	84.5:15.5
19	**XV**	CH_2Cl_2	13	>19:1	24.5:75.5
20	**XVI**	CH_2Cl_2	Trace	>19:1	nd
21	**XVII**	CH_2Cl_2	Trace	>19:1	nd
22	**XVIII**	CH_2Cl_2	Trace	>19:1	nd

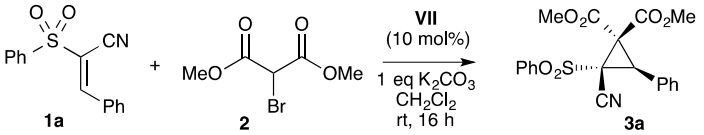
Table 2 : Base Screen for the asymmetric cyclopropanation.



Entry	Base	Eq	Yield, %	dr	er
1	K_2CO_3	1	86	>19:1	80.5:19.5
2	Cs_2CO_3	1	94	>19:1	50:50
3	$Ba(OH)_2$	1	90	>19:1	65:35
4	LiOH	1	81	>19:1	53.5:46.5
5	KO^tBu	1	87	>19:1	50:50
6	Et_3N	1	75	>19:1	56.5:43.5
7	Pyridine	1	30	>19:1	50:50
8	K_2CO_3 (oven dried)	1	90	>19:1	85:15
9	Na_2CO_3 (oven dried)	1	92	>19:1	85:15
10	Cs_2CO_3 (oven dried)	1	86	>19:1	53.5:46.5
11	K_2CO_3 (oven dried)	0.5	88	>19:1	86:14
12	K_2CO_3 (oven dried)	2	92	>19:1	84.5:15.5
13	K_2CO_3 (oven dried)	4	90	>19:1	83.5:16.5
14*	Hünig's Base	1	>99%	>19:1	56:44
15*	DBU	1	81%	>19:1	53.5:46.5

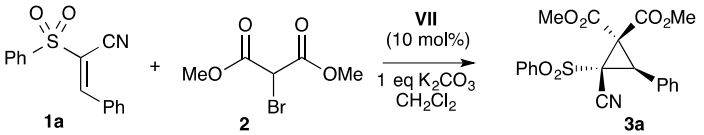
*conducted after peer-review

Table 3 : Catalyst loading screen.



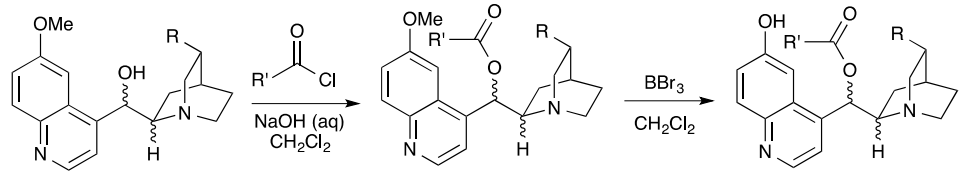
Entry	Loading of VII	Yield	dr	er
1	0.02 eq.	53	>19:1	80:20
2	0.05 eq.	85	>19:1	82.5:17.5
3	0.1 eq.	89	>19:1	86:14
4	0.2 eq.	89	>19:1	85:15

Table 4 : Temperature screen

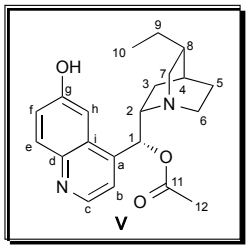


Entry	Temperature	Reaction time	Yield	dr	er
1	21°C	16h	53	>19:1	86:14
2	1°C	96h	85	>19:1	87:13
3	-10°C	120h	89	>19:1	88:12

2. Preparation of New Organocatalysts

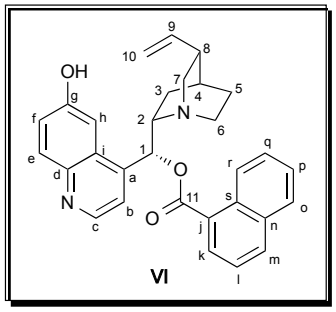


Scheme 1 : General procedure for catalyst synthesis



V

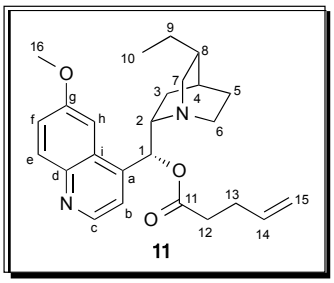
(*R*)-((1*S*,2*S*,4*S*,5*R*)-5-ethylquinuclidin-2-yl)(6-hydroxyquinolin-4-yl)methyl acetate V. *O*-acetylhydroquinine (1.22 g, 3.32mmol) was dissolved in dichloromethane (40 mL) and stirred under nitrogen at -78 °C. To this was added 1M BBr_3 solution in heptane (13.5 mL, 13.5 mmol) and the reaction allowed to warm to room temperature. It was then heated to 40 °C for 1h, before being cooled and quenched with 30% NH_4OH solution (15 mL) and stirred for a further 30 min. The reaction was then diluted with dichloromethane (100 mL) and water (80 mL) and the organic phase isolated. The aqueous phase was then extracted with DCM (50 mL) and the combined organic extracts were dried over $MgSO_4$, filtered and removed under reduced pressure to yield the title compound as a yellow solid (975mg, 83%). MPt = 159-161°C. $[a]_D^{20} =$ -139 (c = 0.1, $CHCl_3$). IR (neat, cm^{-1}) 2926.5, 1744.1, 1468.4, 1233.5, 853.0. ^{1}H NMR ($CDCl_3$, 400MHz) δ 8.66 (d, 1H, H-c), 7.96 (d, 1H, H-e), 7.61 (s, 1H, H-h), 7.30-7.6 (m, 2H, H-f + H-b), 6.59 (1H, H-1), 3.27-3.14 (m, 2H, H-2 + H-6), 3.00 (t, 1H, H-7), 2.71 (quintet, 1H, H-6), 2.25 (d, 1H, H-7), 2.15 (s, 3H, H-12), 1.80-1.44 (m, 6H, H-3 + H-4 + H-5 + H-8), 1.32-1.6 (quintet, 2H, H-9), 0.71 (t, 3H, H-10). ^{13}C NMR ($CDCl_3$, 100MHz) δ 169.47 (C-12), 157.32 (C-g) , 146.16 (C-c), 143.62 (C-d), 142.46 (C-a), 131.62 (C-e), 126.81 (C-i), 123.15 (C-h), 117.51 (C-f), 104.87 (C-b), 73.48 (C-1), 58.31 (C-2), 57.92 (C-7), 42.87 (C-6), 36.66 (C-8), 29.03 (C-5), 27.45 (C-3), 27.19 (C-9), 25.08 (C-4), 21.20 (C-11), 11.78 (C-10). HRMS required for $C_{21}H_{27}O_3N_2$ $[M+H]^+$ is 355.2016, found 355.2015.



VI

(*R*)-(6-hydroxyquinolin-4-yl)((1*S*,2*S*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl-1-naphthoate VI. *O*-(1-naphthoyl)quinine (500 mg, 1.04mmol) was dissolved in dry dichloromethane (20 mL) and stirred under nitrogen at -78°C. To this solution was added 1M BBr_3 in heptane (4 mL, 4mmol) and the reaction allowed to warm to room temperature. It was then heated to 40°C for 1h, before being cooled and quenched with 30% NH_4OH solution (10 mL) and stirred for 30 min. The reaction was then diluted with water (50 mL) and the aqueous layer washed with dichloromethane (2 x 30 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure to give the crude residue, which was purified by column chromatography (9:1 EtOAc:Hexane) to yield the title compound as a white solid (332 mg, 68%). MPt = 212°C (at which decomposition occurs) $[a]_D^{20} =$ +50 (c = 0.1, $CHCl_3$). IR (neat, cm^{-1}) 2920.7, 1699.5, 1614.0, 1468.4, 1247.1, 1192.7, 1126.7, 1004.4. ^{1}H NMR ($CDCl_3$, 400MHz) δ 8.85 (d, 1H, H-r), 8.67 (d, 1H, H-c), 8.34 (d, 1H, H-k), 8.05 (d, 1H, H-m), 8.00 (d, 1H, H-e), 7.88-7.84 (m, 2H, Hq + Ho). 7.58-7.33 (m, 5H, H-b + H-f + H-h + H-l + H-p), 6.95 (d, 1H, H-1) 5.69 (septet, 1H, H-9), 4.93-4.88 (m, 2H, H-10), 3.44, (m, 1H, H-2) 3.30 (m, 1H, H-6), 2.96 (t, 1H, H-7), 2.71 (quintet, 1H, H-6), 2.56 (d, 1H, H-7), 2.24 (m, 1H, H-8), 1.92-1.78 (m, 4H, H-5 + H-4 + H-3), 1.54 (m, 1H, H-5). ^{13}C NMR ($CDCl_3$, 100MHz) 165.63 (C-11), 157.13 (C-g), 146.19 (C-c), 143.58 (C-a), 142.85 (C-d), 140.47

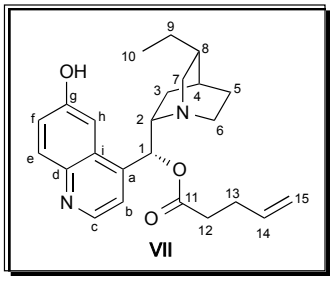
(C-9), 134.24 (C-m), 133.91 (C-n), 131.53 (C-o), 131.13 (C-s), 130.02 (C-k), 128.69 (C-e), 128.25 (C-p), 127.20 (C-j), 126.91 (C-q), 126.52 (C-r), 125.97 (C-l), 125.58 (C-f), 124.52 (C-b), 123.14 (C-i), 114.88 (C-10), 101.46 (C-h). HRMS required for $C_{30}H_{29}O_3N_2$ $[M+H]^+$ is 465.2173, found 465.2172.



11

(*R*)-((1*S*,2*S*,4*S*,5*R*)-5-ethylquinuclidin-2-yl)(6-methoxyquinolin-4-yl)methylpent-4-enoate 11. Hydroquinine (500 mg, 1.53mmol) was dissolved in dry dichloromethane (20 mL) and stirred at 20 ^oC. To this was added neat 4-pentenoyl chloride (0.51 mL, 4.61mmol) drop-wise, followed by NaOH (1.5 mL of 30% aq. solution) and the reaction mixture stirred for 4h. After this time, the reaction was quenched with water (70 mL) and extracted with DCM (100 mL). The aqueous phase was extracted with a further 50 mL of dichloromethane, and the combined organic extracts were washed with saturated aqueous $NaHCO_3$ solution (100 mL). The combined organic extracts were dried over $MgSO_4$, filtered and removed under reduced pressure to yield the title compound as a colourless oil (620mg, 99%).

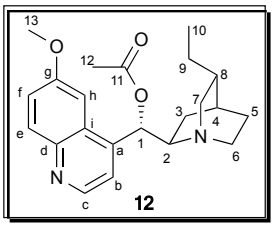
$[a]_D^{20} =$ -13 (c = 0.1, $CHCl_3$) ^{1}H NMR 400MHz, ($CDCl_3$) δ = 8.73 (d, 1H, H-c), 8.01 (d, 1H, H-e), 7.44 (s, 1H, H-h), 7.37-7.34 (m, 2H, H-f + H-b), 6.50 (d, 1H, H-1), 5.78 (octet, 1H, H-14), 5.03-4.95 (m, 2H, H-15), 3.95 (s, 3H, H-16), 3.35 (q, 1H, H-2), 3.38-2.99 (m, 2H, H-6 + H-7), 2.63 (t, 1H, H-6), 2.50 (t, 2H, H-12), 2.44-2.30 (m, 3H, H-13 + H-7), 1.81-1.69 (m, 3H, H-5 + H-4 + H-3), 1.48-1.30 (d, 5H, H-9 + H-5 + H-8 + H-3), 0.88 (t, 3H, H-10). ^{13}C NMR ($CDCl_3$, 100MHz) δ 171.90 (C-11), 158.47 (C-g), 147.37 (C-c), 144.84 (C-a), 143.20 (C-d), 136.21 (C-14), 131.77 (C-e), 126.93 (C-i), 122.26 (C-f), 118.76 (C-b), 115.89 (C-15), 101.43 (C-h), 73.39 (C-1), 58.81 (C-2), 58.02 (C-7), 56.07 (C-16), 42.61 (C-6), 37.18 (C-8), 33.64 (C-12), 28.65 (C-13), 27.83 (C-3), 27.60 (C-9), 25.19 (C-4), 23.56 (C-5), 12.04 (C-10) HRMS required for $C_{25}H_{33}O_3N_2$ $[M+H]^+$ is 409.2491, found 409.2489.



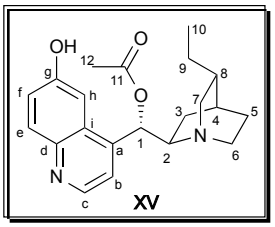
VII

(*R*)-((1*S*,2*S*,4*S*,5*R*)-5-ethylquinuclidin-2-yl)(6-hydroxyquinolin-4-yl)methyl pent-4-enoate VII. (*R*)-((1*S*,2*S*,4*S*,5*R*)-5-ethylquinuclidin-2-yl)(6-methoxyquinolin-4-yl)methylpent-4-enoate **11** (500mg, 1.22mmol) was dissolved in dichloromethane (20 mL) and stirred under nitrogen at -78^{o}C. To this was added 1M BBr_3 solution in heptane (5 mL, 5mmol), and the reaction mixture allowed to warm to room temperature. It was then heated to 40^{o}C for 1h before being cooled and quenched with 30% NH_4OH solution (10 mL) and stirred for a further 30 min. The reaction was then diluted with water (50 mL) and the aqueous phase washed with dichloromethane (2 x 30 mL). The combined organic layers were then dried over $MgSO_4$, filtered and removed under reduced pressure to give the crude residue, which was purified by column chromatography (100% EtOAc) to yield the title compound as a pink solid (380 mg, 79%). $[a]_D^{20} =$ -27 (c = 0.1, $CHCl_3$). MPt = 180-182^{o}C. ^{1}H NMR 400MHz, ($CDCl_3$) δ = 8.66 (s, 1H, H-c), 7.96 (d, 1H, H-e), 7.67 (s, 1H, H-h), 7.35 (d, 1H, H-f), 7.31 (d, 1H, H-b), 6.74 (s, 1H, H-1), 5.81 (octet, 1H, H-14), 5.29-4.91 (m, 2H, H-15), 3.30 (m, 1H, H-2), 3.21 (t, 1H, H-6), 3.12 (t, 1H, H-7), 2.73 (t, 1H, H-6), 2.52 (t, 2H, H-12), 2.36 (m, 3H, H-13 + H-7), 1.84-1.67 (m, 4H, H-3 + H-4 + H-5), 1.57 (d, 2H, H-3 + H-8), 1.29 (s, 2H, H-9), 0.88 (t, 3H, H-10). ^{13}C NMR ($CDCl_3$, 100MHz) δ 171.51 (C-11), 156.52 (C-g), 146.40 (C-c), 144.06 (C-a), 142.70 (C-d), 136.28 (C-14), 131.60 (C-e), 126.93 (C-i), 122.84 (C-f), 117.81 (C-b), 116.03 (C-15), 105.71 (C-h), 73.56 (C-1), 58.60 (C-2), 57.84 (C-7), 42.83 (C-6), 36.73 (C-8), 33.67 (C-12), 28.62 (C-13), 27.41 (C-3),

27.21 (C-9), 25.11 (C-4), 22.05 (C-5), 11.87 (C-10). HRMS required for $C_{26}H_{35}O_3N_2$ $[M+H]^+$ is 395.2329, found 395.2333.

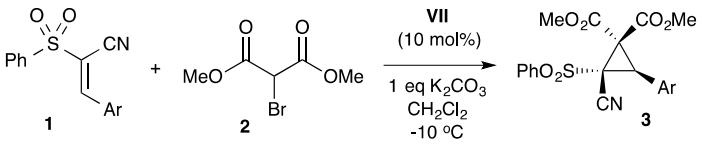


(*S*)-[(1*S*,2*R*,4*S*,5*R*)-5-ethylquinuclidin-2-yl)(6-methoxyquinolin-4-yl)methyl acetate 12. Hydroquinidine (650mg, 2.01mmol) was dissolved in dichloromethane (20 mL) and stirred at 20 °C. To this was added neat acetyl chloride (715 μL, 10.03 mmol) followed by NaOH (2.8 mL of 30% aq. solution) and the resulting mixture was stirred for 4h. The reaction was quenched with water (70 mL) and extracted with dichloromethane (3 x 50 mL). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure to yield the title compound as a colourless oil (740mg, 100%). $[a]_D^{20} =$ +174 (c = 0.1, $CHCl_3$) IR (neat, cm^{-1}) 2930.4, 1746.1, 1470.4, 1249.0, 1218.0, 1023.82. ^1H NMR ($CDCl_3$, 400MHz) δ 8.72 (d, 1H, H-c), 8.01 (d, 1H, H-e), 7.53 (s, 1H, H-b), 7.39 (d, 1H, H-f), 7.29 (d, 1H, H-h), 6.90 (bs, 1H, H-1), 4.04 (s, 3H, H-13), 3.32 (sextet, 1H, H-2), 3.14-2.83 (m, 4H, H-6 + H-7), 2.19 (s, 3H, H-12), 2.02 (t, 1H, H-3), 1.86 (s, 1H, H-8), 1.63-1.55 (m, 5H, H-9 + H-5 + H-4), 1.40 (septet, 1H, H-3), 0.92 (t, 3H, H-10). ^{13}C NMR ($CDCl_3$, 100MHz) δ 168.98 (C-12), 158.60 (C-g) 146.96 (C-c), 144.52 (C-a), 142.31 (C-d), 131.58 (C-e), 126.34 (C-i), 122.70 (C-f), 117.58 (C-h), 101.04 (C-b), 66.19 (C-1), 58.25 (C-2), 56.38 (C-13), 49.95 (C-6), 49.38 (C-7), 36.17 (C-5), 25.65 (C-4), 25.11 (C-9), 22.39 (C-8), 21.14 (C-11), 21.01 (C-3), 11.73 (C-10). HRMS required for $C_{22}H_{29}O_3N_2$ $[M+H]^+$ is 369.2173, found 369.2171.



(*S*)-((1*S*,2*R*,4*S*,5*R*)-5-ethylquinuclidin-2-yl)(6-hydroxyquinolin-4-yl)methyl acetate XV. (*S*)-[(1*S*,2*R*,4*S*,5*R*)-5-ethylquinuclidin-2-yl)(6-methoxyquinolin-4-yl)methyl acetate **12** (740 mg, 2 mmol) was dissolved in dichloromethane (40 mL) and stirred under nitrogen at -78°C. To this was added 1M BBr_3 solution in heptane (8 mL, 8 mmol) and the reaction allowed to warm to room temperature. It was then heated to 40°C for 1h, before being cooled and quenched with 30% NH_4OH solution (25 mL) and stirred for 30 min. The reaction was then diluted with water (50 mL) and the extracted with dichloromethane (2 x 50 mL). The combined organic extracts were dried over $MgSO_4$, filtered and removed under reduced pressure to give a crude residue that was purified using column chromatography (100% EtOAc), giving the title compound as a light yellow solid, (316 mg, 55%). MPt = 198-201°C. $[a]_D^{20} =$ +245 (c = 0.1, $CHCl_3$). IR (neat, cm^{-1}) 2934.2, 1749.9, 1621.8, 1507.2, 1229.6, 1027.7. ^1H NMR ($CDCl_3$, 400MHz) δ 8.66 (d, 1H, H-c), 7.90 (d, 1H, H-e), 7.53 (s, 1H, H-b), 7.29 (d, 1H, H-f), 7.19 (d, 1H, H-h), 6.59 (d, 1H, H-1), 3.27 (q, 1H, H-2), 3.02 (q, 1H, H-6), 2.79 (m, 2H, H-6 + H-7), 2.70 (t, 1H, H-7), 2.11 (s, 3H, H-12), 1.89 (t, 1H, H-3), 1.76 (s, 1H, H-8), 1.57-1.49 (m, 5H, H-9 + H-5 + H-4), 1.37-1.21 (t, 1H, H-3), 0.92 (t, 3H, H-10). ^{13}C NMR ($CDCl_3$, 100MHz) δ 169.61 (C-11), 158.69 (C-g) 146.24 (C-c), 143.69 (C-d), 142.92 (C-a), 131.60 (C-e), 127.04 (C-i), 122.88 (C-h), 118.31 (C-f), 105.69 (C-b), 73.19 (C-1), 58.28 (C-2), 50.76 (C-6), 49.82 (C-7), 37.00(C-5), 26.72 (C-8), 25.70 (C-9), 25.24 (C-4), 22.02 (C-3), 21.16 (C-12), 11.95 (C-10). HRMS required for $C_{21}H_{27}O_3N_2$ $[M+H]^+$ is 355.2016, found 355.2013.

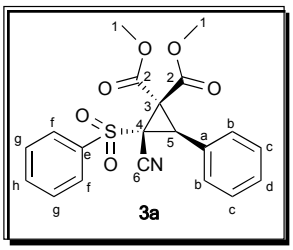
3. Asymmetric Cyclopropanation



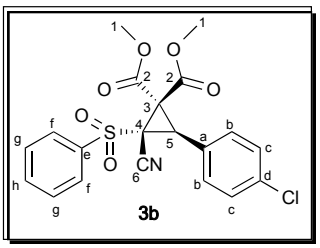
Scheme 2 : General scheme for asymmetric cyclopropanation

3.1 General Procedure for the Asymmetric Cyclopropanation

To an oven-dried flask was added conjugate cyanosulfone **1** (1 eq), organocatalyst **VII** (10 mol%) and oven-dried K_2CO_3 (1 eq), which were dissolved in dry dichloromethane. The reaction was cooled to -10 °C and stirred for 1h. After this time, dimethyl bromomalonate **2** (1.5 eq) was added, and the reaction stirred for 96 h at -10 °C. The reaction was then diluted with saturated aqueous NH_4Cl solution (30 mL) and extracted with DCM (2 x 30 mL). The organic extracts were combined, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography, and then recrystallized to give the title compound.

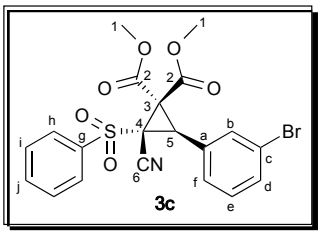


Dimethyl (2*S*,3*R*)-2-cyano-3-phenyl-2-(phenylsulfonyl)cyclopropane-1,1-dicarboxylate 3a. Prepared according to the general procedure using (*E*)-3-phenyl-2-(phenylsulfonyl)acrylonitrile (20 mg, 0.074 mmol) **1a**, organocatalyst **VII** (3 mg, 0.007 mmol), oven-dried K_2CO_3 (10 mg, 0.074mmol) and dimethyl bromomalonate **2** (15 μL, 0.11 mmol). The resulting residue was purified by column chromatography (1:4 EtOAc:Hexane) to give a white crystalline compound (37mg, 92%). The compound was enantiomerically enriched by recrystallisation in isopropanol to yield white prisms. Mpt = 147–150°C. The enantiomeric excess was determined by HPLC analysis [Chiralpak AD-H column (0.46 cm ø X 25 cm); 1:9 isopropanol:hexane; flow rate = 1 mL/min; detection wavelength = 210 nm] tR 25.70 min, tR 34.34 min. $[\alpha]_D^{20} =$ +42.47 (c = 0.1, $CHCl_3$) IR (neat, cm^{-1}) 1747.2, 1234.7, 1165.8, 1143.5. ^1H NMR ($CDCl_3$, 400MHz) δ 8.12 (d, 2H, H-f), 7.81 (t, 1H, H-h), 7.68 (t, 2H, H-g), 7.32 (m, 3H, H-c + H-d) 7.12 (s, 2H, H-b), 4.17 (s, 1H, H-4), 3.97 (s, 3H, H-1), 3.69 (s, 3H, H-1). ^{13}C NMR ($CDCl_3$, 100MHz) δ 163.50 (C-2), 162.46 (C-2), 135.88 (C-e), 135.68 (C-h), 130.14 (C-f), 129.61 (C-g), 129.06 (C-d), 129.02 (C-c), 128.37 (C-a), 128.16 (C-b), 54.25 (C-1), 53.87 (C-1), 48.42 (C-4), 47.43 (C-3), 37.00 (C-5). HRMS required for $C_{25}H_{33}O_3N_2$ $[M+NH_4]^+$ is 417.1115, found 417.1106.

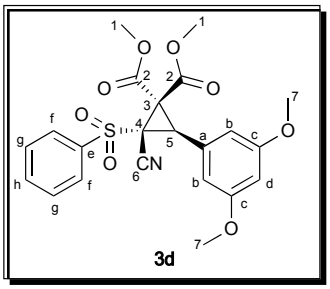


Dimethyl (2*S*,3*R*)-3-(4-chlorophenyl)-2-cyano-2-(phenylsulfonyl)cyclopropane-1,1-dicarboxylate 3b. Prepared according to the general procedure using (*E*)-3-(4-chlorophenyl)-2-(phenylsulfonyl)acrylonitrile **1b** (23mg, 0.075 mmol), organocatalyst **VII** (3 mg, 0.007 mmol), oven-dried K_2CO_3 (10 mg, 0.074 mmol), and dimethyl bromomalonate **2** (15 μL, 0.11 mmol). The resulting residue was purified by column chromatography (1:3 EtOAc:Hexane) to give a white crystalline compound (35 mg, 100%). The compound was enantiomerically enriched by recrystallisation in isopropanol to yield white needles. MPt = 160-162°C The enantiomeric excess was determined by HPLC analysis [Chiralpak AD-H column (0.46 cm ø X 25 cm); 1:9

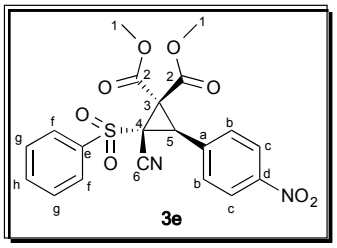
isopropanol:hexane; flow rate = 1 mL/min; detection wavelength = 210 nm] tR 37.44 min, tR 58.55 min. $[a]_D^{20} =$ +89.63 (c = 0.1, $CHCl_3$) IR (neat, cm^{-1}) 1746.2, 1252.7, 1229.8, 1162.5. ^1H NMR ($CDCl_3$, 400MHz) δ 8.11(d, 2H, H-f), 7.82 (t, 1H, H-h), 7.69 (t, 2H, H-g), 7.31 (d, 2H, H-b) 7.08 (d, 2H, H-c), 4.11 (s, 1H, H-5), 3.97 (s, 3H, H-1), 3.70 (s, 3H, H-1). ^{13}C NMR ($CDCl_3$, 100MHz) δ 163.23 (C-2), 162.23 (C-2), 135.78 (C-h), 135.69 (C-a), 135.26 (C-e), 130.15 (C-f), 129.64 (C-g), 129.60 (C-c), 129.38 (C-b), 126.90 (C-d), 111.17 (C-6), 54.30 (C-1), 54.04 (C-1), 48.30 (C-4), 47.26 (C-3), 36.11 (C-5). HRMS required for $C_{20}H_{16}O_6NSClNa$ $[M+Na]^+$ is 456.0281, found 456.0279.



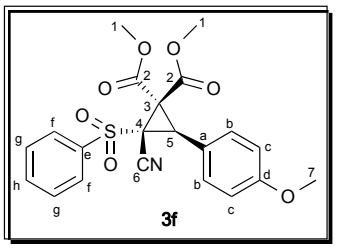
Dimethyl (2*S*,3*R*)-3-(3-bromophenyl)-2-cyano-2-(phenylsulfonyl)cyclopropane-1,1-dicarboxylate 3c. Prepared according to the general procedure using (*E*)-3-(3-bromophenyl)-2-(phenylsulfonyl)acrylonitrile **1c** (26 mg, 0.074 mmol), organocatalyst **VII** (3 mg, 0.007 mmol), oven-dried K_2CO_3 (10 mg, 0.074 mmol), and dimethyl bromomalonate **2** (15 μL, 0.11 mmol). The resulting residue was purified by column chromatography (1:3 EtOAc:Hexane) to give a white crystalline compound (37 mg, 100%). The compound was enantiomerically enriched by recrystallisation in isopropanol to yield white prisms. MPt = 116-120°C. The enantiomeric excess was determined by HPLC analysis [Chiralpak AD-H column (0.46 cm ø X 25 cm); 1:4 isopropanol:hexane; flow rate = 1 mL/min; detection wavelength = 210 nm] tR 13.32 min, tR 20.79 min. $[a]_D^{20} =$ +87 (c = 1, $CHCl_3$) IR (neat, cm^{-1}) 1746.4, 1240.71, 1160.0. ^1H NMR ($CDCl_3$, 400MHz) δ 8.11 (d, 2H, H-h), 7.83 (t, 1H, H-j), 7.69 (t, 2H, H-i), 7.47 (d, 1H, H-d) 7.26 (s, 1H, H-b), 7.19 (t, 1H, H-e), 7.08 (d, 1H, H-f), 4.12 (s, 1H, H-5), 3.98 (s, 3H, H-1), 3.72 (s, 3H, H-1). ^{13}C NMR ($CDCl_3$, 100MHz) δ 163.09 (C-2), 162.17 (C-2), 135.82 (C-j) , 135.61 (C-a), 132.27 (C-d), 131.34 (C-b), 130.63 (C-e), 130.57 (C-g), 130.14 (C-h), 129.66 (C-i), 126.90 (C-f), 122.88 (C-c), 111.02 (C-6), 54.32 (C-1), 54.05 (C-1), 48.20 (C-4), 47.19 (C-3), 35.89 (C-5). HRMS required for $C_{20}H_{16}O_6NSBrNa$ $[M+Na]^+$ is 499.9774, found 499.9772.



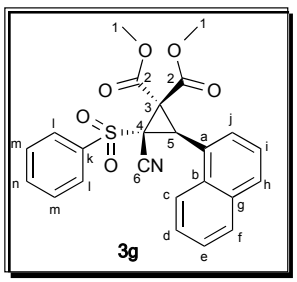
Dimethyl-(2*S*,3*R*)-2-cyano-3-(3,5-dimethoxyphenyl)-2-(phenylsulfonyl)-cyclopropane-1,1-dicarboxylate 3d. Prepared according to the general procedure using (*E*)-3-(3,5-dimethoxyphenyl)-2-(phenylsulfonyl)acrylonitrile **1d** (25 mg, 0.076 mmol), organocatalyst **VII** (3 mg, 0.007 mmol), oven-dried K_2CO_3 (10 mg, 0.074 mmol) and dimethyl bromomalonate **2** (15 μL, 0.11 mmol). The resulting residue was purified by column chromatography (1:4 EtOAc:Hexane) to give a light brown crystalline compound (30 mg, 86%). The compound was enantiomerically enriched by recrystallisation in isopropanol to yield white prisms. MPt = 145-148°C. The enantiomeric excess was determined by HPLC analysis [Chiralpak AD-H column (0.46 cm ø X 25 cm); 1:4 isopropanol:hexane; flow rate = 1 mL/min; detection wavelength = 210 nm] tR 17.05 min, tR 24.42 min. $[a]_D^{20} =$ +47.54 (c = 0.1, $CHCl_3$). IR (neat, cm^{-1}) 1743.6, 1595.8, 1252.5, 1209.1, 1151.1, 1068.3. ^1H NMR ($CDCl_3$, 400MHz) δ 8.12 (d, 2H, H-f), 7.81 (t, 1H, H-h), 7.68 (t, 2H, H-g), 6.38 (s, 1H, H-d) 6.22 (s, 2H, H-b), 4.10 (s, 1H, H-5), 3.97 (s, 3H, H-1), 3.72 (s, 3H, H-1), 3.69 (s, 6H, H-7). ^{13}C NMR (CDCl3, 100MHz) δ 163.42 (C-2), 162.43 (C-2), 161.09 (C-c), 135.70 (C-e), 135.60 (C-h), 130.16 (C-g), 129.58 (C-f), 111.40 (C-6), 106.07 (C-b), 101.27 (c-d), QUATERNARY 55.34 (C-7), 54.23 (C-1), 53.95 (C-1), 48.15 (C-4), 47.46 (C-3), 37.13 (C-5). HRMS required for $C_{22}H_{21}O_8NSNa$ $[M+Na]^+$ is 482.0880, found 482.0880.



Dimethyl (2*S*,3*R*)-2-cyano-3-(4-nitrophenyl)-2-(phenylsulfonyl)cyclopropane-1,1-dicarboxylate 3e. Prepared according to the general procedure using (*E*)-3-(4-nitrophenyl)-2-(phenylsulfonyl)acrylonitrile **1e** (25mg, 0.079mmol), organocatalyst **VII** (3 mg, 0.007mmol), oven-dried K_2CO_3 (10 mg, 0.074mmol), and dimethyl bromomalonate (15 μL, 0.11 mmol). The resulting residue was purified by column chromatography (1:4 EtOAc:Hexane) to give a light brown crystalline compound (34 mg, 96%). The compound was enantiomerically enriched by recrystallisation in isopropanol to yield white prisms. MPt = 152-153°C. The enantiomeric excess was determined by HPLC analysis [Chiralpak AD-H column (0.46 cm ø X 25 cm); 1:4 isopropanol:hexane; flow rate = 1 mL/min; detection wavelength = 210 nm] tR 42.67 min, tR 56.55 min. $[a]_D^{20} =$ +97 (c = 0.1, $CHCl_3$) IR (neat, cm^{-1}) 1747.4, 1731.3, 1352.5, 1235.6, 1159.1, 1143.0. ^{1}H NMR ($CDCl_3$, 400MHz) δ 8.21 (d, 2H, H-c), 8.12 (d, 2H, H-f), 7.85 (t, 1H, H-h), 7.71 (t, 2H, H-g) 7.35 (d, 2H, H-b), 4.20 (s, 1H, H-5), 3.97 (s, 3H, H-1), 3.73 (s, 3H, H-1). ^{13}C NMR ($CDCl_3$, 100MHz) δ 162.83 (C-2), 162.03 (C-2), 136.02 (C-h), 148.33 (C-a), 135.62 (C-d), 135.40 (C-e), 130.23 (C-f), 129.73 (C-g), 129.51 (C-b), 124.25 (C-c), 111.00 (C-6), 54.43 (C-1), 54.26 (C-1), 48.25 (C-4), 47.26 (C-3), 35.87 (C-5). HRMS required for $C_{20}H_{16}O_8N_2SNa$ $[M+Na]^+$ is 467.0520, found 467.0517.

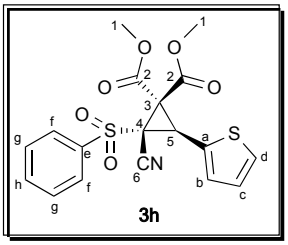


dimethyl (2*S*,3*R*)-2-cyano-3-(4-methoxyphenyl)-2-(phenylsulfonyl)cyclopropane-1,1-dicarboxylate 3f. Prepared according to the general procedure using (*E*)-3-(4-methoxyphenyl)-2-(phenylsulfonyl)acrylonitrile **1f** (22 mg, 0.074mmol), organocatalyst **VII** (3 mg, 0.007 mmol), oven-dried K_2CO_3 (10 mg, 0.074mmol), and dimethyl bromomalonate **2** (15 μL, 0.11 mmol). The resulting residue was purified by column chromatography (1:4 EtOAc:Hexane) to give a white crystalline compound (24 mg, 73%). The compound was enantiomerically enriched by recrystallisation in isopropanol to yield white prisms. MPt = 164-166°C. The enantiomeric excess was determined by HPLC analysis [Chiralpak AD-H column (0.46 cm ø X 25 cm); 1:9 isopropanol:hexane; flow rate = 1 mL/min; detection wavelength = 210 nm] tR 53.15 min, tR 75.09 min. $[a]_D^{20} =$ +54.74 (c = 0.1, $CHCl_3$) IR (neat, cm^{-1}) 1726.2, 1246.9, 1231.4, 1021.5. ^{1}H NMR ($CDCl_3$, 400MHz) δ 8.11(d, 2H, H-f), 7.81 (t, 1H, H-h), 7.67 (t, 2H, H-g), 7.04 (d, 2H, H-b) 6.83 (d, 2H, H-c), 4.11 (s, 1H, H-5), 3.97 (s, 3H, H-1), 3.77 (s, 3H, H-7), 3.70 (s, 3H, H-1). ^{13}C NMR ($CDCl_3$, 400MHz) δ 163.62 (C-2), 162.44 (C-2), 160.09 (C-d), 135.96 (C-e), 135.63 (C-h), 130.10 (C-g), 129.58 (C-f), 129.44 (C-b), 120.28 (C-a), 114.51 (C-c), 111.54 (C-6), 55.29 (C-7), 54.23 (C-1), 53.91 (C-1), 48.48 (C-4), 47.52 (C-3), 36.58 (C-5). HRMS required for $C_{21}H_{19}O_7NSNa$ $[M+Na]^+$ is 452.0774, found 452.0781.

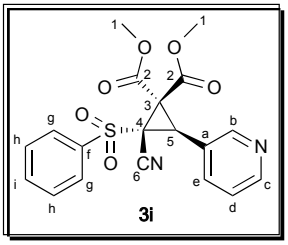


Dimethyl (2*S*,3*R*)-2-cyano-3-(naphthalen-1-yl)-2-(phenylsulfonyl)cyclopropane-1,1-dicarboxylate 3g. Prepared according to the general procedure using (*E*)-3-(naphthalen-1-yl)-2-(phenylsulfonyl)acrylonitrile **1g** (24 mg, 0.075mmol), organocatalyst **VII** (3 mg, 0.007 mmol), oven-dried K_2CO_3 (10 mg, 0.074 mmol), and dimethyl bromomalonate **2** (15 μL, 0.11 mmol). The resulting residue was purified by column chromatography (1:4 EtOAc:Hexane) to give a light brown crystalline compound (32mg, 91%). The compound

was enantiomerically enriched by recrystalisation in isopropanol to yield white prisms. MPt = 203-206°C. The enantiomeric excess was determined by HPLC analysis [Chiralpak AD-H column (0.46 cm ø X 25 cm); 1:9 isopropanol:hexane; flow rate = 1 mL/min; detection wavelength = 210 nm] tR 12.59 min, tR 24.85 min. $[a]_D^{20} =$ +50.24 (c = 0.1, $CHCl_3$) IR (neat, cm^{-1}) 1737.5, 1336.4, 1280.1, 1244.8, 1157.7. ^1H NMR ($CDCl_3$, 400MHz) δ 8.39 (d, 1H, H-c), 8.17 (d, 2H, H-l), 7.86-7.81 (m, 3H, H-n + H-f + H-h), 7.69 (t, 2H, H-m), 7.58-7.49 (m, 2H, H-e + H-i), 7.36 (t, 1H, H-d), 7.26 (d, 1H, H-j), 4.44 (s, 1H, H-5), 4.07 (s, 3H, H-1), 3.34 (s, 3H, H-1). ^{13}C NMR (CDCl3, 100MHz) δ 163.89 (C-2), 162.15 (C-2), 135.99 (C-a), 135.75 (C-n), 133.59 (C-k), 131.78 (C-g), 130.23 (C-l), 129.67 (C-m + C-f), 128.94 (C-h), 127.01 (C-i), 126.82 (C-j), 126.33 (C-e), 125.18 (C-d), 124.39 (C-b), 122.94 (C-c), 111.91 (C-6), 54.28 (C-1), 53.64 (C-1), 48.30 (C-4), 47.03 (C-3), 36.37 (C-5). HRMS required for $C_{24}H_{19}O_6NSNa$ $[M+Na]^+$ is 472.0835, found 472.0832.

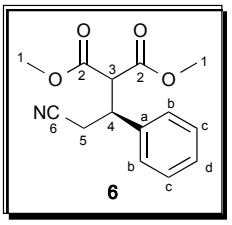


Dimethyl (2*S*,3*S*)-2-cyano-2-(phenylsulfonyl)-3-(thiophen-2-yl)cyclopropane-1,1-dicarboxylate 3h. Prepared according to the general procedure using (*E*)-2-(phenylsulfonyl)-3-(thiophen-2-yl)acrylonitrile **1h** (21 mg, 0.075 mmol), organocatalyst **VII** (3 mg, 0.07 mmol), oven-dried K_2CO_3 (10 mg, 0.074mmol), and dimethyl bromomalonate **2** (15 μL, 0.11 mmol). The resulting residue was purified by column chromatography (1:4 EtOAc:Hexane) to give a light brown crystalline compound (28 mg, 91%). The compound was enantiomerically enriched by recrystalisation in isopropanol to yield white prisms. MPt = 114-117°C. The enantiomeric excess was determined by HPLC analysis [Chiralpak AD-H column (0.46 cm ø X 25 cm); 1:4 isopropanol:hexane; flow rate = 1 mL/min; detection wavelength = 210 nm] tR 15.63 min, tR 23.92 min. $[a]_D^{20} =$ -15 (c = 0.1, $CHCl_3$) IR (neat, cm^{-1}) 1738.5, 1345.1, 1270.3, 1247.6, 1150.2. ^1H NMR ($CDCl_3$, 400MHz) δ 8.09 (d, 2H, H-f), 7.81 (t, 1H, H-h), 7.67 (t, 2H, H-g), 7.28 (dd, 1H, H-d) 6.98-6.94 (m, 2H, H-c + H-b), 4.19 (s, 1H), 3.96 (s, 3H), 3.76 (s, 3H). ^{13}C NMR (CDCl3, 100MHz) δ 162.83 (C-2), 161.89 (C-2), 135.86 (C-e), 135.73 (C-h), 129.97 (C-g), 129.65 (C-f), 129.34 (C-a), 128.33 (C-c), 127.46 (C-b), 127.20 (C-d), 111.14 (C-6), 54.36 (C-1), 54.14 (C-1), 48.88 (C-4), 48.06 (C-3), 32.97 (C-5). HRMS required for $C_{18}H_{15}O_6NS_2Na$ $[M+Na]^+$ is 428.0233, found 428.0236.

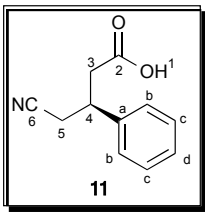


Dimethyl (2*S*,3*R*)-2-cyano-2-(phenylsulfonyl)-3-(pyridin-3-yl)cyclopropane-1,1-dicarboxylate 3i. Prepared according to the general procedure using (*E*)-2-(phenylsulfonyl)-3-(pyridin-3-yl)acrylonitrile **1i** (20 mg, 0.074 mmol), organocatalyst **VII** (3 mg, 0.007 mmol), oven-dried K_2CO_3 (10 mg, 0.074 mmol) and dimethyl bromomalonate **2** (15 μL, 0.11mmol). The resulting residue was purified by column chromatography (1:4 EtOAc:Hexane) to give a light brown crystalline compound (28 mg, 95%). The compound was enantiomerically enriched by recrystalisation in isopropanol to yield white prisms. MPt : 151 °C (evidently decomposes at this temperature). The enantiomeric excess was determined by HPLC analysis [Chiralcel OD column (0.46 cm ø X 25 cm); 1:4 isopropanol:hexane; flow rate = 1 mL/min; detection wavelength = 210 nm] tR 15.29 min, tR 16.66 min. $[a]_D^{20} =$ +66.92 (c = 0.1, $CHCl_3$) IR (neat, cm^{-1}) 1755.5, 1739.4, 1336.4, 1308.2, 1292.1, 1251.76, 1151.0. ^1H NMR ($CDCl_3$, 400MHz) δ 8.59 (s, 1H, H-b), 8.38 (s, 1H, H-c), 8.11 (d, 2H, H-g), 7.84 (t, 1H, H-i), 7.70 (d, 2H, H-h), 7.52 (d, 1H, H-e), 7.29 (t, 1H, H-d), 4.12 (s, 1H, H-5), 3.99 (s, 3H, H-1), 3.73 (s, 3H, H-1). ^{13}C NMR (CDCl3, 100MHz) δ 163.06 (C-2), 162.26 (C-2), 150.22 (C-b), 149.50 (C-c), 135.90 (C-e), 135.57 (C-a), 130.16 (C-h), 129.71 (C-g),

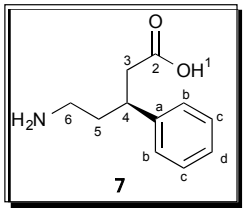
125.07 (C-f), 123.67 (C-d), 111.17 (C-6), 54.38 (C-1), 54.21 (C-1), 48.23 (C-4), 47.21 (C-3), 34.40 (C-5). HRMS required for $C_{19}H_{17}O_6N_2S$ $[M+H]^+$ is 401.0802, found 401.0803.



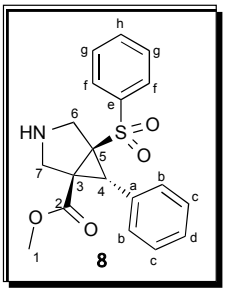
Dimethyl (*S*)-2-(2-cyano-1-phenylethyl)malonate 6. To an oven-dried flask was added dimethyl (2*S*,3*R*)-2-cyano-3-phenyl-2-(phenylsulfonyl)cyclopropane-1,1-dicarboxylate **3a** of 74% enantiomeric excess (320 mg, 0.81mmol) and magnesium turnings (250 mg, 10 mmol). The system was placed under nitrogen and dry methanol (30 mL) was added. The reaction was then stirred at 60°C for 20 h until TLC showed complete consumption of the starting material. The reaction was cooled, filtered through Celite® which was subsequently washed with MeOH. The collected solvent was removed under reduced pressure, yielding a crude yellow solid which was purified by column chromatography (3:7, EtOAc:Hexane) to yield the title compound as an off-white solid (160 mg, 77%). The enantiomeric excess remained at 74% and was determined by HPLC analysis [Chiralpak AD-H column (0.46 cm ø X 25 cm); 1:9 isopropanol:hexane; flow rate = 1 mL/min; detection wavelength = 210 nm] tR 12.59 min, tR 24.85 min. $[\alpha]_D^{20} =$ +61.72 (c = 0.1, $CHCl_3$) IR (neat, cm^{-1}) 2924.1, 2248.8, 1725.4, 1435.5, 1246.7, 1163.0. ^{1}H NMR ($CDCl_3$, 400MHz) δ 7.37-7.26 (m, 5H, H-b + H-c + H-d), 3.89 (d, 1H, H-3), 3.79-3.73 (m, 3H, H-1 + H-4), 3.51 (s, 3H, H-1), 2.91-2.87 (m, 2H, H-5). ^{13}C NMR (CDCl3, 100MHz) δ 167.78 (C-2), 166.96 (C-2), 137.83 (C-a), 129.04 (C-c), 128.34 (C-d), 127.61 (c-b), 117.62 (C-6), 55.67 (C-4), 53.06 (C-1), 52.73 (C-1), 41.28 (C-3), 22.59 (C-5). HRMS required for $C_{14}H_{19}O_4N_2$ $[M+NH_4]^+$ is 279.1345, found 279.1338.



(*S*)-4-cyano-3-phenylbutanoic acid 11. Dimethyl (*S*)-2-(2-cyano-1-phenylethyl)malonate **6** (70mg, 0.27mmol) was dissolved in ethanol (6 mL). 30% aqueous KOH (2.5 mL) was then added to the reaction mixture, and stirring continued at 20 °C for 16h. After this time, the solvent was removed under reduced pressure, and the aqueous residue acidified to pH 2 with 5M HCl (aq), which was then extracted with ethyl acetate (3 x 50 mL). The combined organic extracts were dried over $MgSO_4$, filtered and removed under reduced pressure, yielding the dicarboxylic acid as a yellow oil. This was dissolved in *m*-xylene (5 mL) and refluxed under an atmosphere of nitrogen for 5h. After this time, the reaction was cooled and the solvent removed under reduced pressure to yield the crude product as a brown oil. This was purified by column chromatography (3:7:0.1 EtOAc:Hexane:AcOH) to give the product as a light brown solid (35mg, 70%) IR (neat, cm^{-1}) 3142.0, 3035.2, 2252. 8, 1709.2, 1408.2, 1274.3, 1159.7. ^{1}H NMR ($CDCl_3$, 400MHz) δ 8.41 (bs, H-1), 7.39-7.17 (m, 5H, H-b + H-c + H-d), 3.43 (t, 1H, H-4), 2.94-2.75 (m, 2H, H-5), 2.72 (d, 2H, H-3). ^{13}C NMR (CDCl3, 100MHz) δ 140.14 (C-a), 129.21 (C-c), 127.99 (C-d), 126.37 (C-b), 117.80 (C-6), 38.80 (C-5), 37.80 (C-4), 24.44 (C-3). HRMS required for $C_{11}H_{11}O_2NNa$ $[M+Na]^+$ is 212.0682, found 212.0681.



(*S*)-5-amino-3-phenylpentanoic acid 7. (*S*)-4-cyano-3-phenylbutanoic acid **11** (30mg, 0.16mmol) and 10% palladium on activated carbon (300 mg) were added to acetic acid (15 mL). The system was placed under 3 atm of hydrogen and shaken for four days. The reaction was vacuum-filtered through a glass fibre pad, and the resulting filtrate syringe-filtered through a 20 μm PVDF filter. The solvent was then removed under reduced pressure to give a pink oil. HRMS required for $C_{11}H_{16}NO_2$ $[M+H]^+$ is 194.1181, found 194.1176.



Methyl (1*R*,5*S*,6*R*)-6-phenyl-5-(phenylsulfonyl)-3-azabicyclo[3.1.0]hexane-1-carboxylate 8. Dimethyl (2*S*,3*R*)-2-cyano-3-phenyl-2-(phenylsulfonyl)cyclopropane-1,1-dicarboxylate **3a** (300 mg, 0.78 mmol) was dissolved in dry THF (2 mL) and the resulting solution stirred at 0°C. To this was added borane-dimethylsulfide complex (450 μL, 3.62 mmol), and the reaction stirred for 2h at 0°C, then at 48 h at 20 °C. The reaction was quenched by drop-wise addition of methanol, and the solvents removed by under reduced pressure. The crude product was purified by column chromatography (1:1:0.1 EtOAc:Hexane:Et_3N), to yield the product as a light yellow oil (86 mg, 31%). IR (neat, cm^{-1}) 2924.5, 2858.7, 1730.5, 1445.1, 1309.2, 1152.0 1084.0, 1027.7. ^1H NMR ($CDCl_3$, 400MHz) δ 7.90 (d, 2H, H-f), 7.66 (t, 1H, H-h), 7.56 (t, 2H, H-g), 7.22-7.19 (m, 3H, H-b + H-d), 6.94 (t, 2H, H-c), 4.01 (s, 1H, H-4), 3.81 (s, 3H, H-1), 3.54 (d, 1H, H-6), 3.42 (d, 1H, H-7), 3.17 (d, 1H, H-6), 2.97 (d, 1H, H-7). ^{13}C NMR (CDCl3, 100MHz) δ 166.95 (C-2), 137.81 (C-e), 133.09 (C-h), 130.43 (C-a), 128.42 (C-g), 128.32 (C-c), 127.45 (C-f), 127.01 (C-d), 125.89 (C-b), 60.59 (C-5), 52.03 (C-1), 49.31 (C-7), 47.82 (C-6), 45.95 (C-3), 30.85 (C-4). HRMS required for $C_{19}H_{20}O_4NSNa$ $[M+H]^+$ is 358.1113, found 358.1.

4. References

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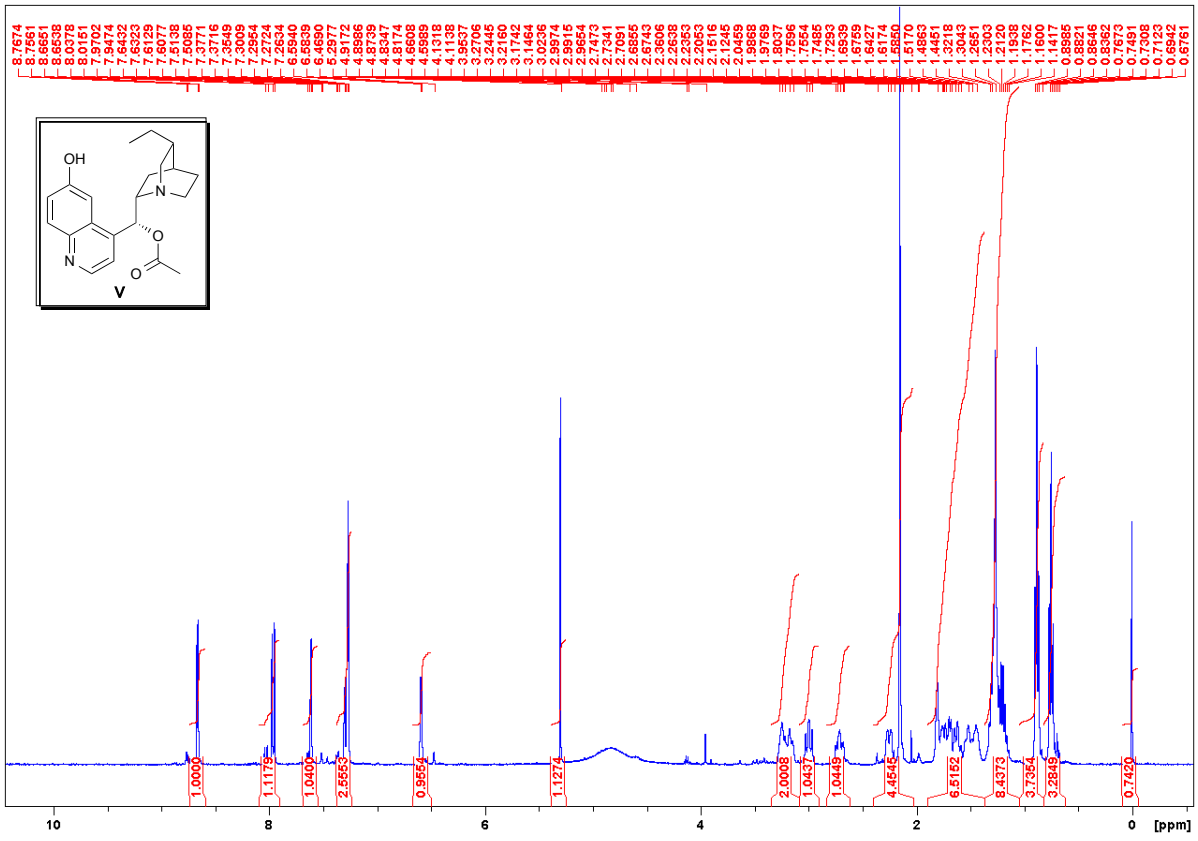
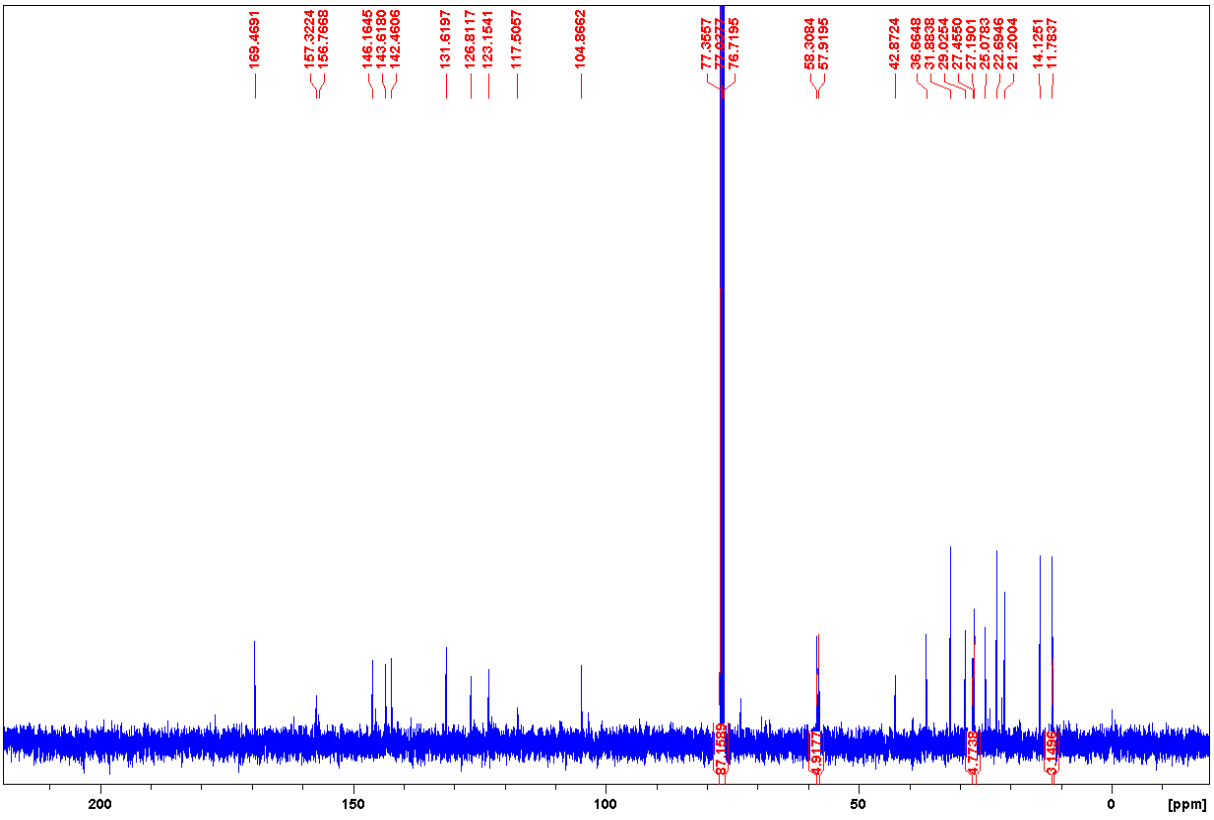
5. Spectra of New Catalysts and their Intermediates

5.1 (*R*)-((1*S*,2*S*,4*S*,5*R*)-5-ethylquinuclidin-2-yl)(6-hydroxyquinolin-4-yl)methyl acetate **V**

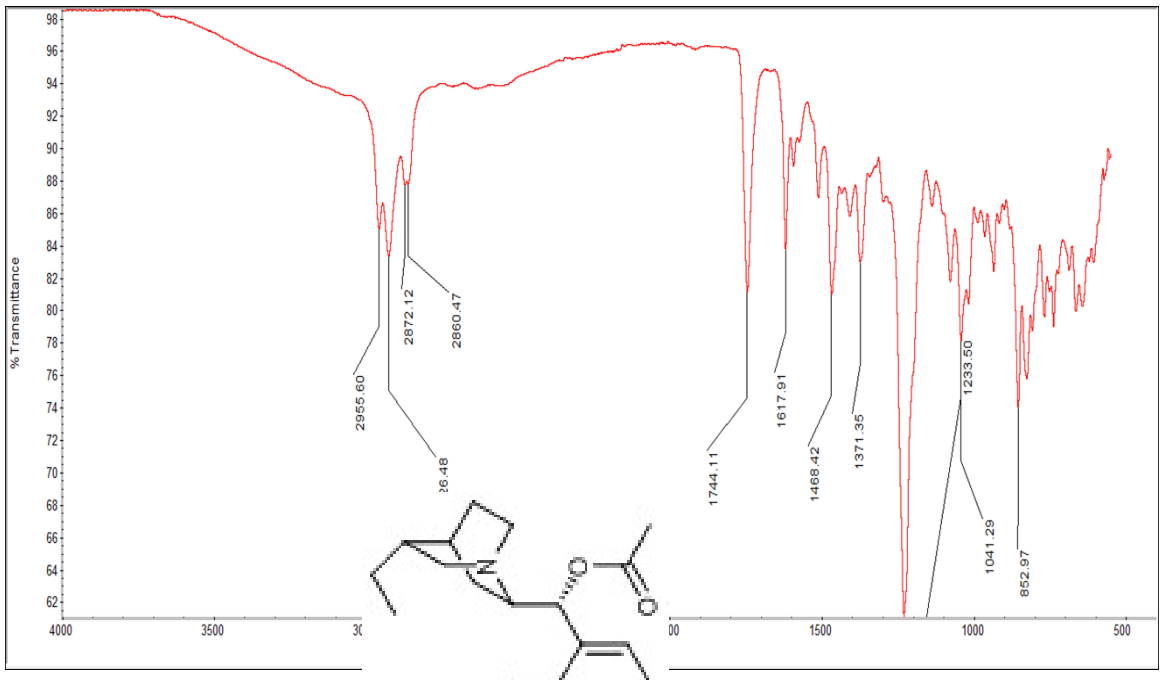
^{1}H NMR (400 MHz, $CDCl_3$)



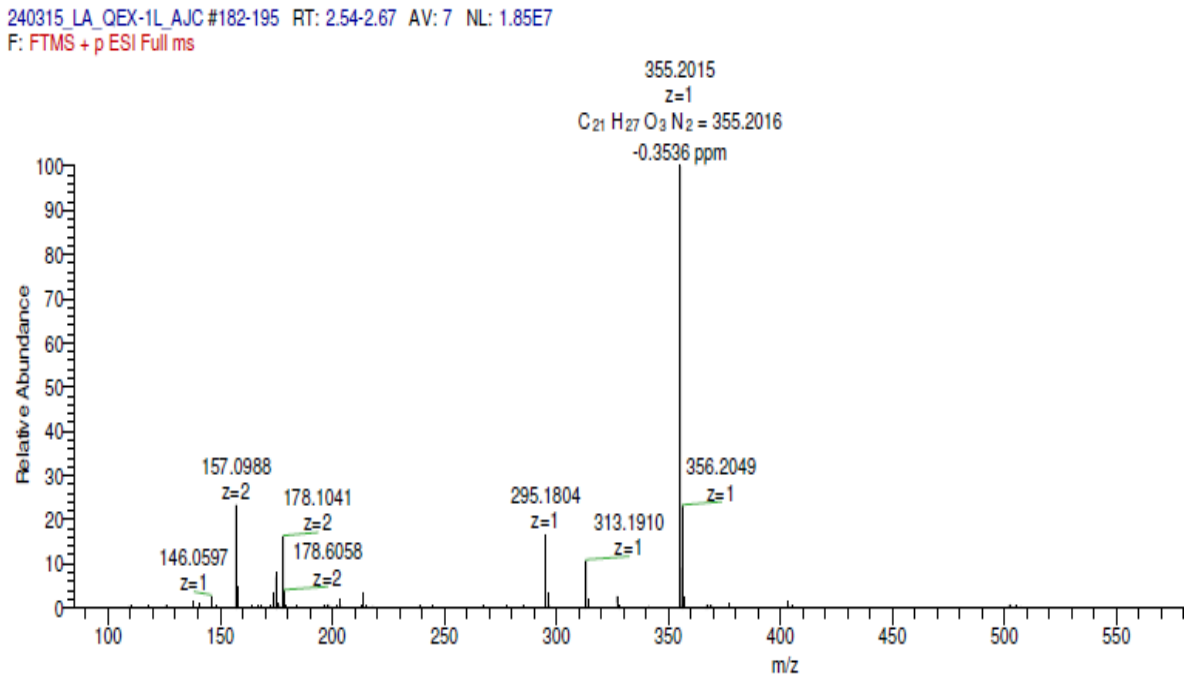
^{13}C NMR (100 MHz, $CDCl_3$)



IR Spectrum of **V**

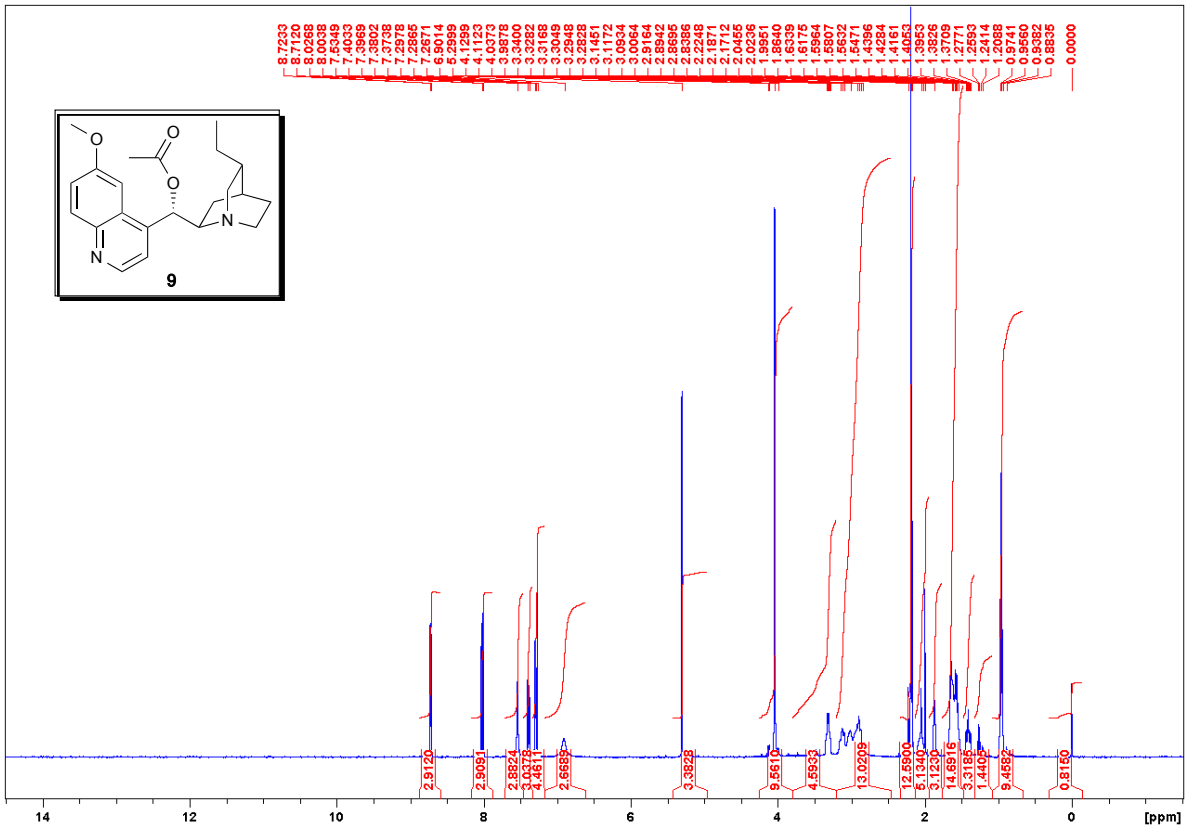


MS profile of **V**

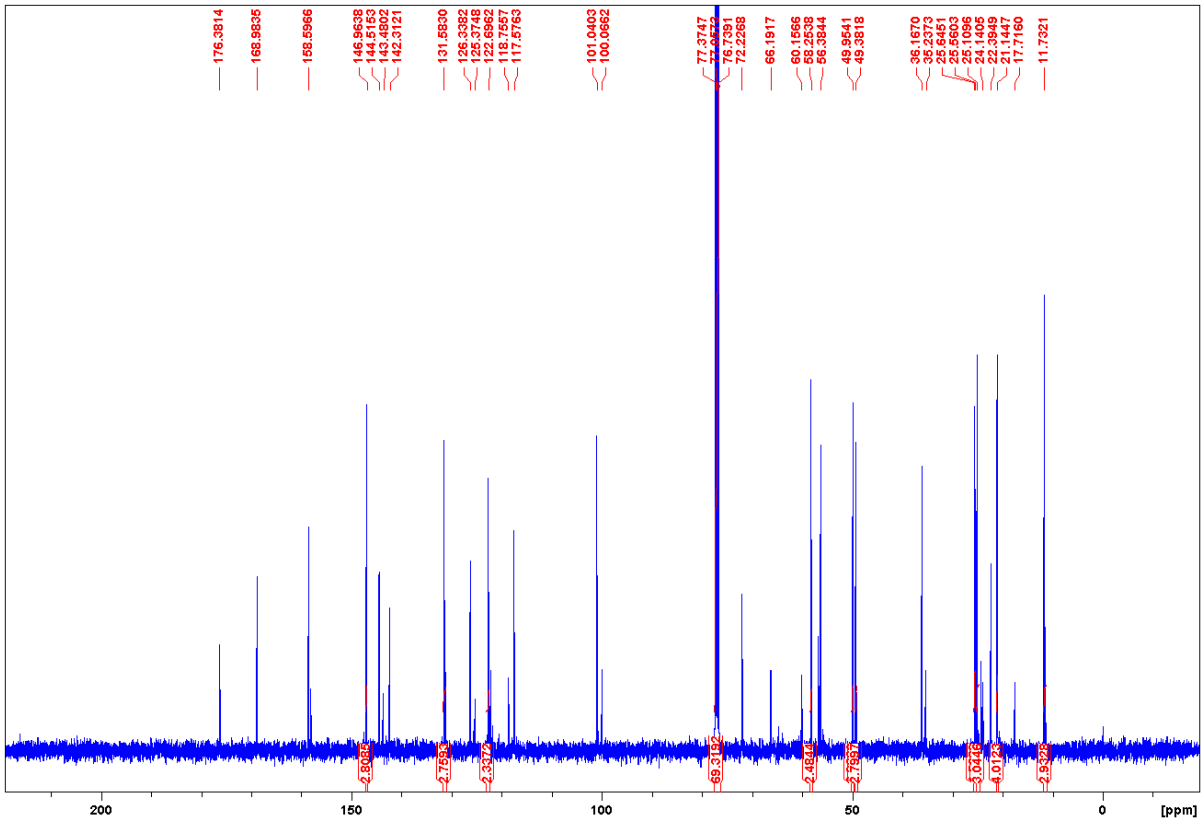


5.2 (*S*)-((1*S*,2*R*,4*S*,5*R*)-5-ethylquinuclidin-2-yl)(6-methoxyquinolin-4-yl)methyl acetate **12**

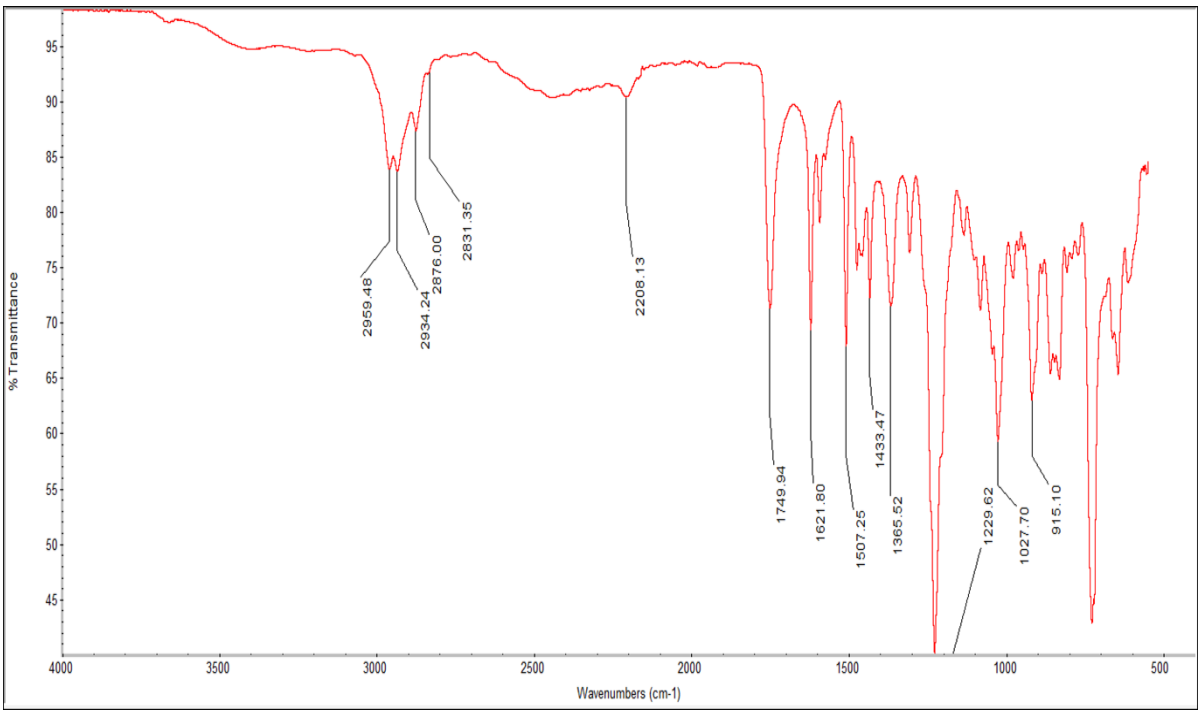
^{1}H NMR (400 MHz, $CDCl_3$)



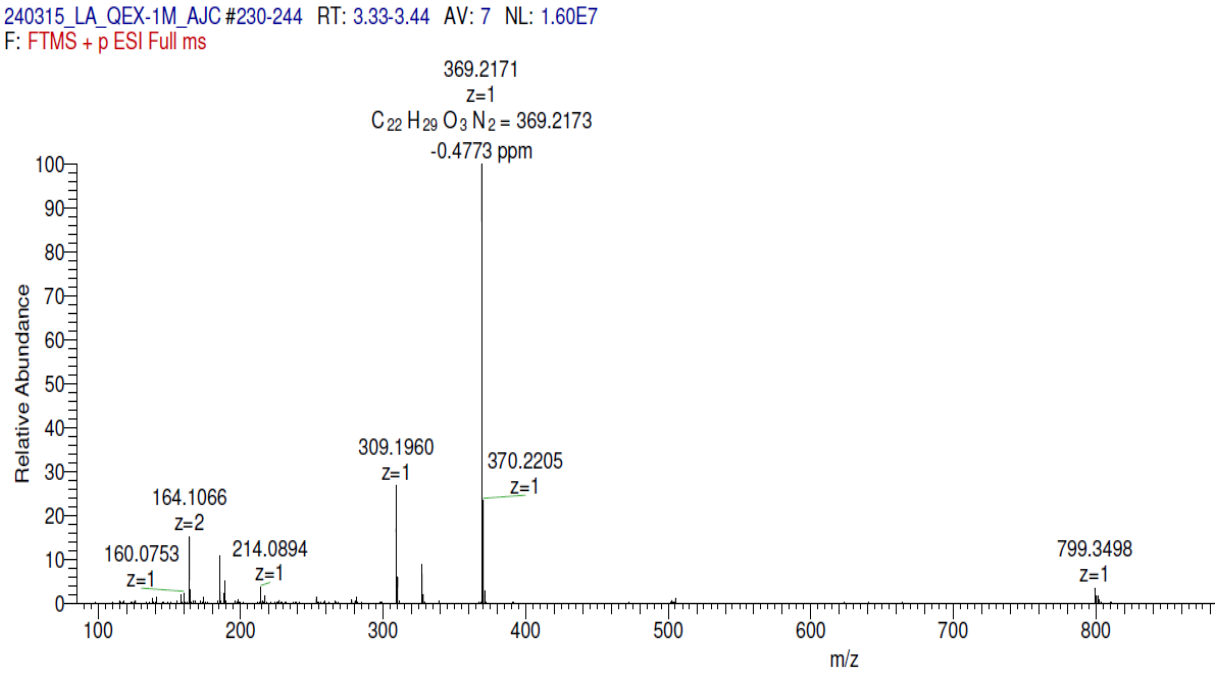
^{13}C NMR (100 MHz, $CDCl_3$)



IR Spectrum of **12**

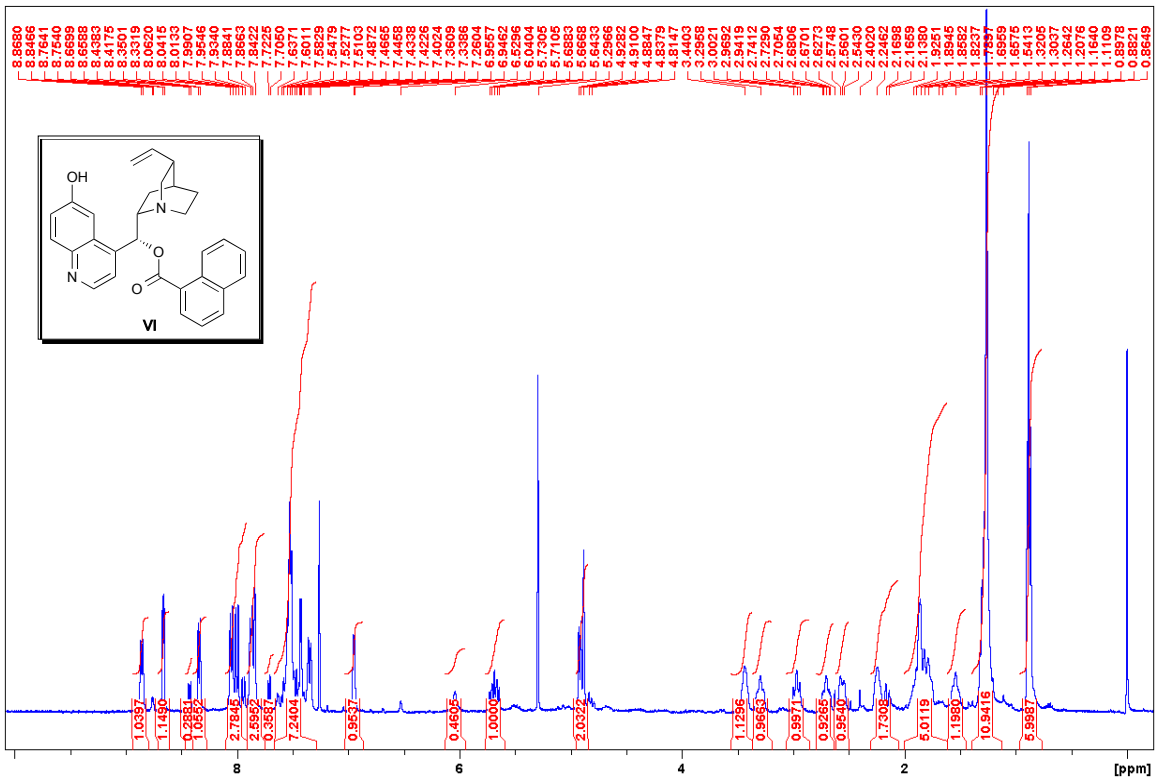


MS Profile of **12**

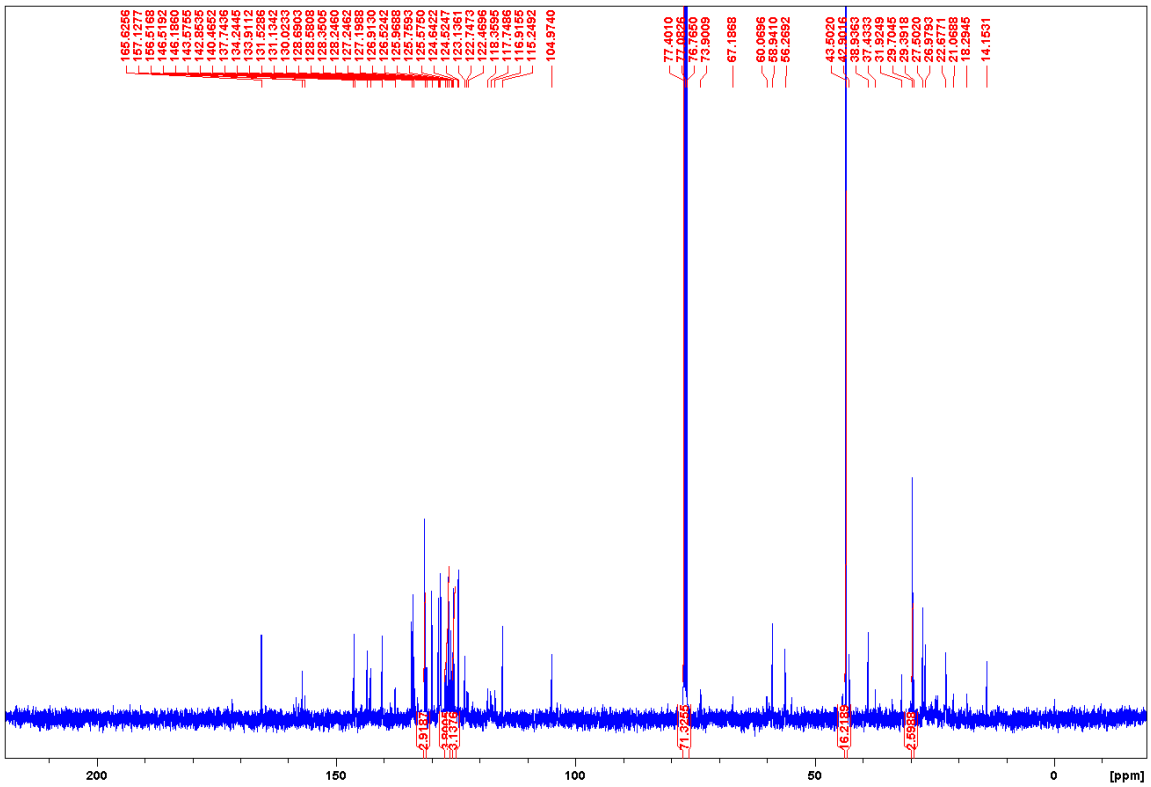


5.3 (*R*)-(6-hydroxyquinolin-4-yl)((1*S*,2*S*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl 1-naphthoate **VI**

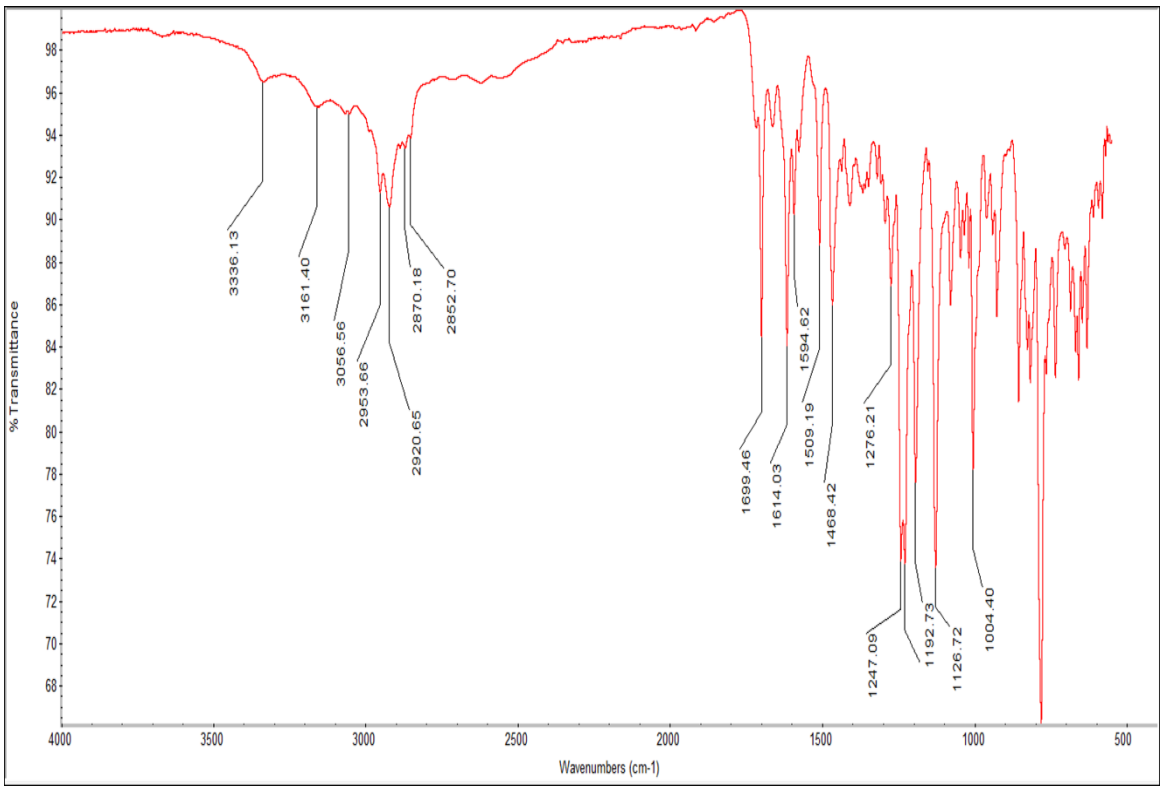
^{1}H NMR (400 MHz, $CDCl_3$)



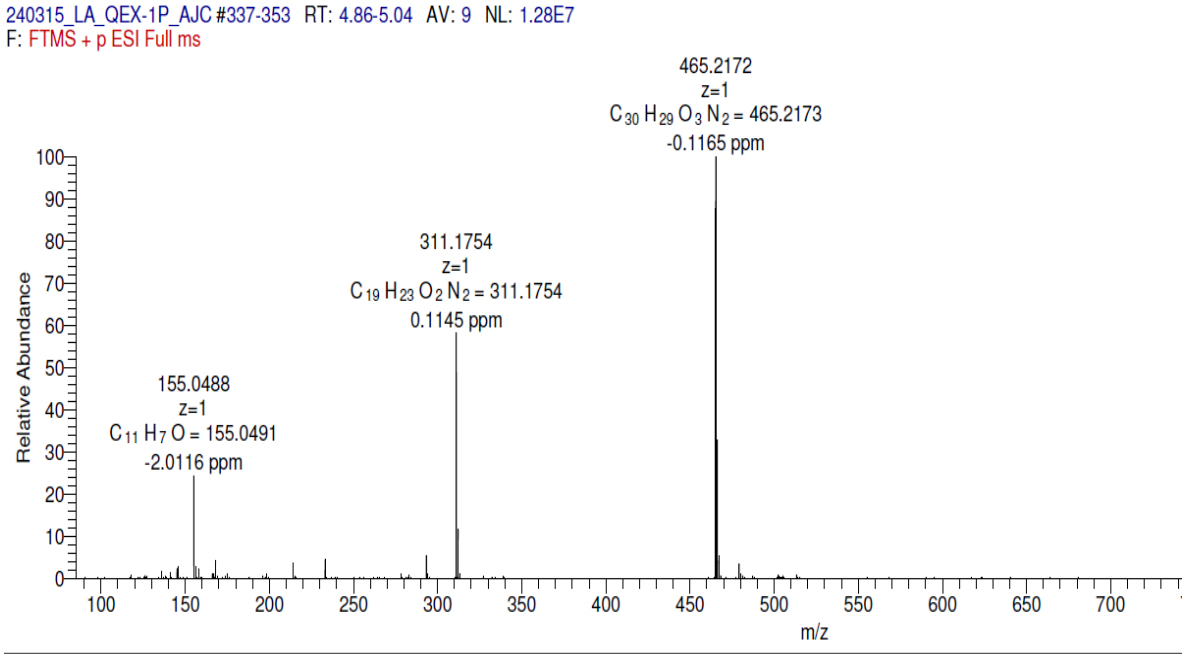
^{13}C NMR (100 MHz, $CDCl_3$)



IR Spectrum of **VI**

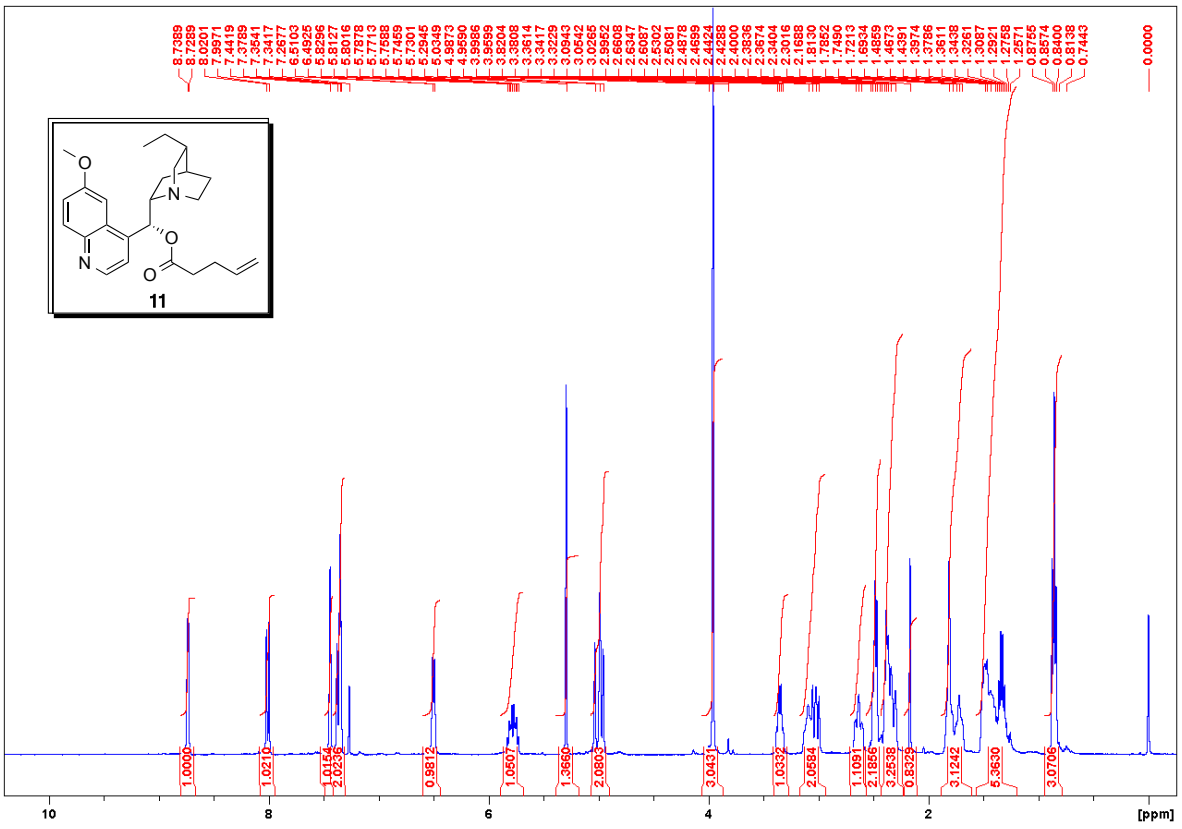


MS Profile of **VI**

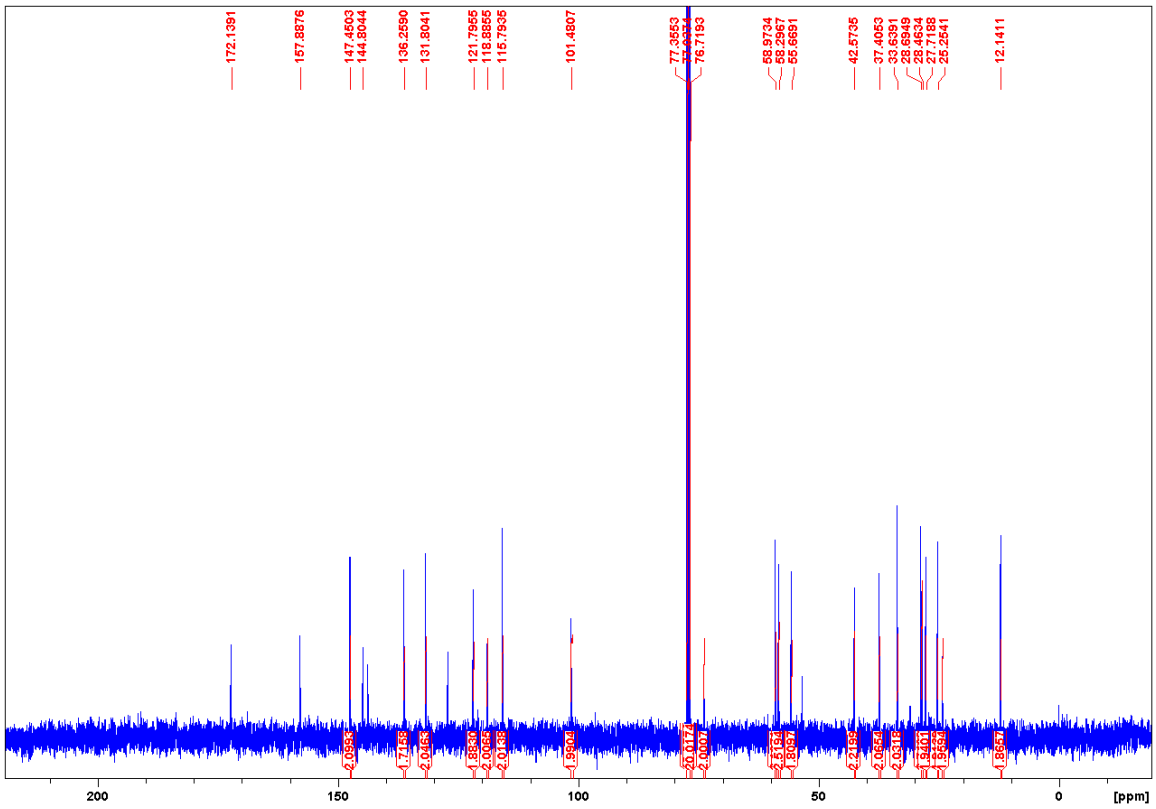


5.4 (*R*)-(6-methoxyquinolin-4-yl)((1*S*,2*S*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl pent-4-enoate **11**

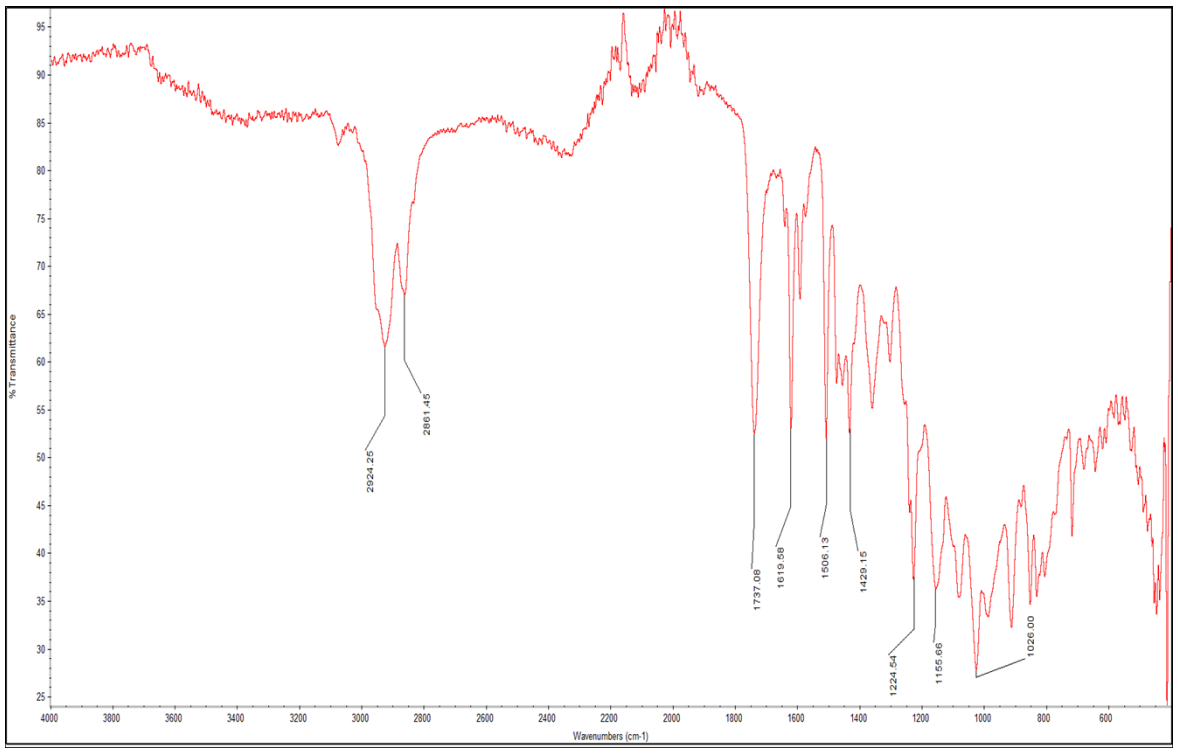
^{1}H NMR (400 MHz, $CDCl_3$)



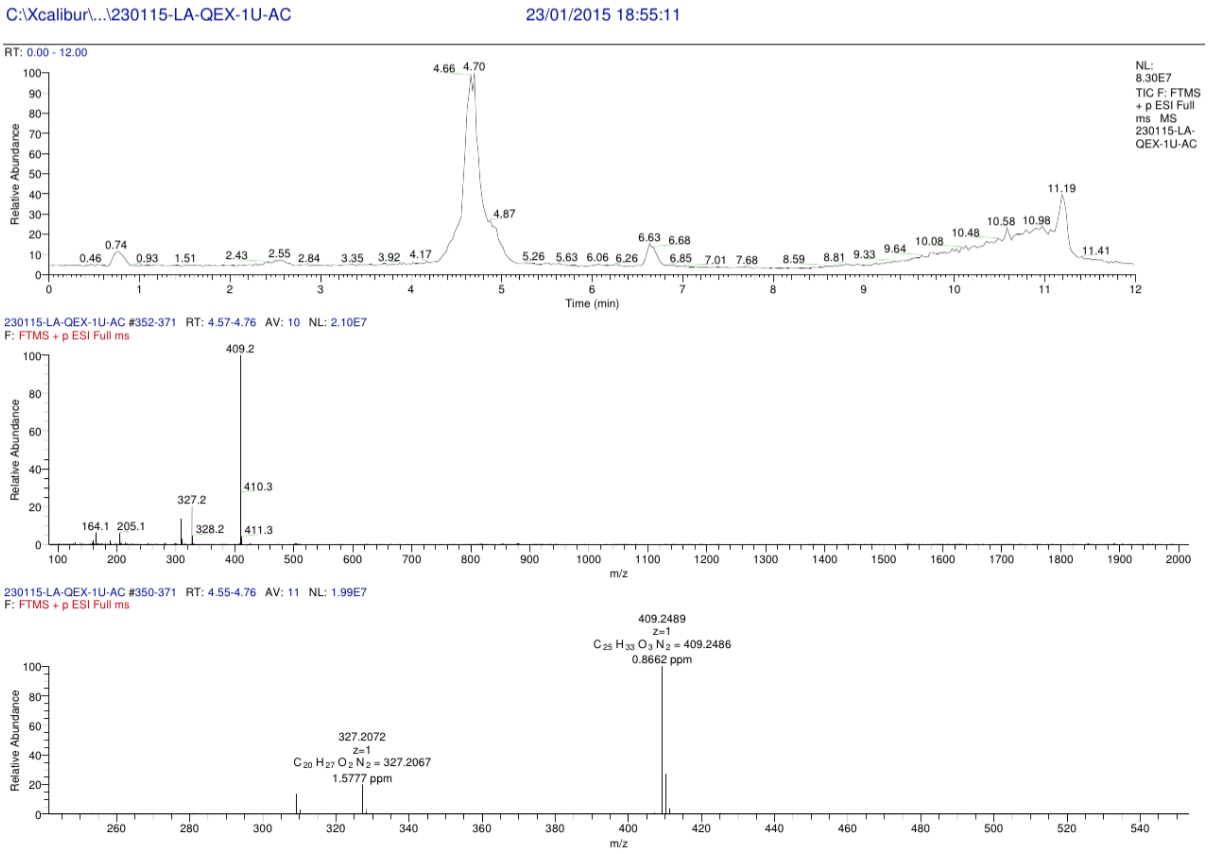
^{13}C NMR (100 MHz, $CDCl_3$)



IR Spectrum of **11**

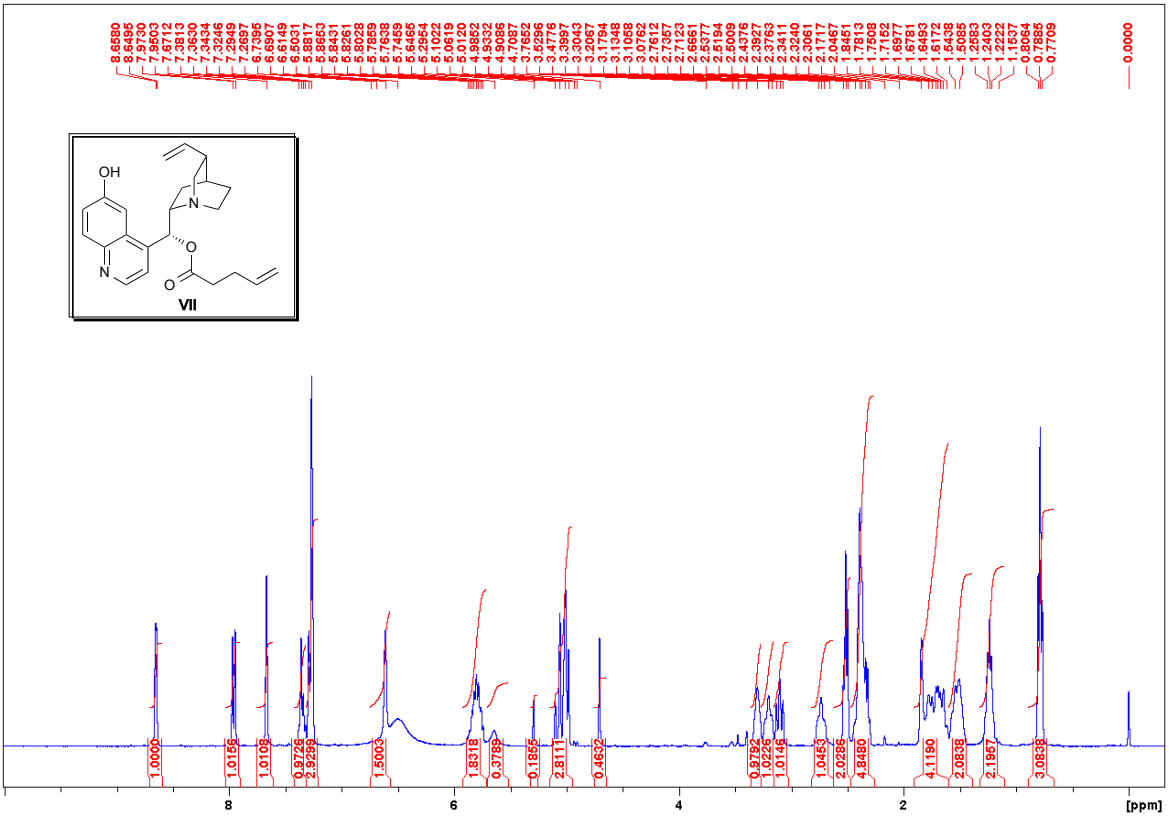


MS Profile of **11**

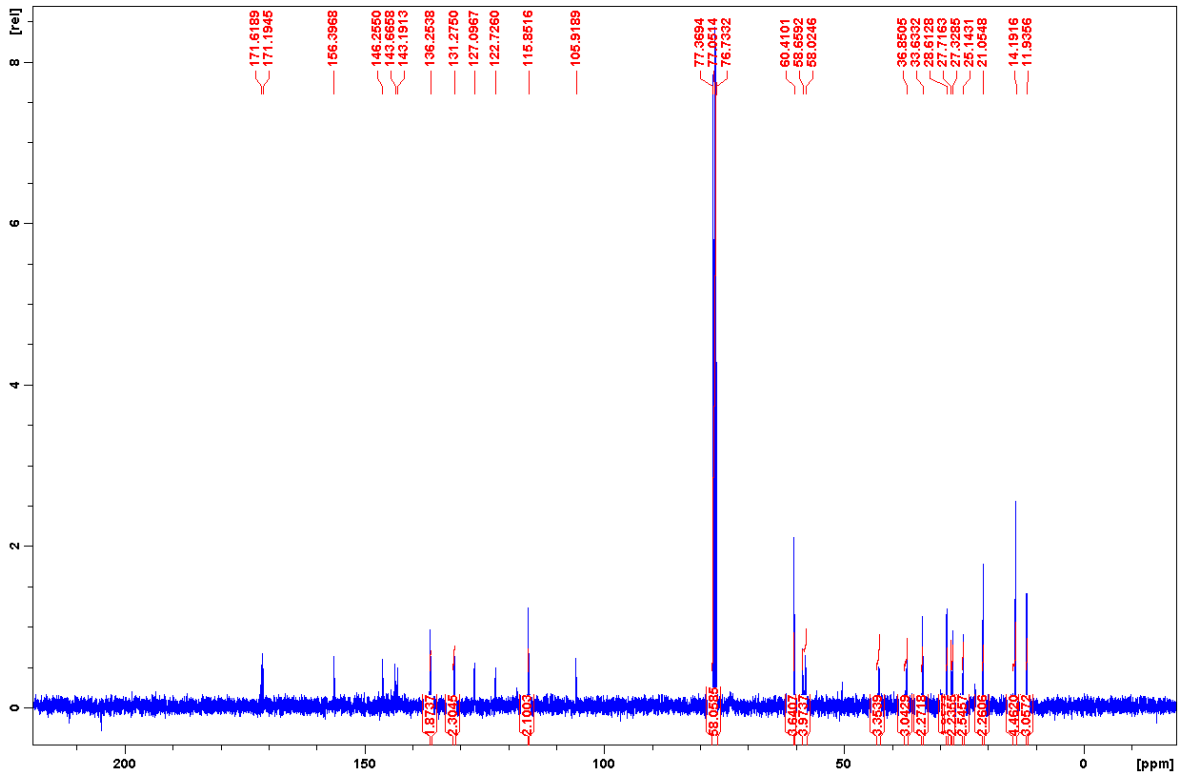


5.5 (*R*)-(6-hydroxyquinolin-4-yl)((1*S*,2*S*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl pent-4-enoate **VII.**

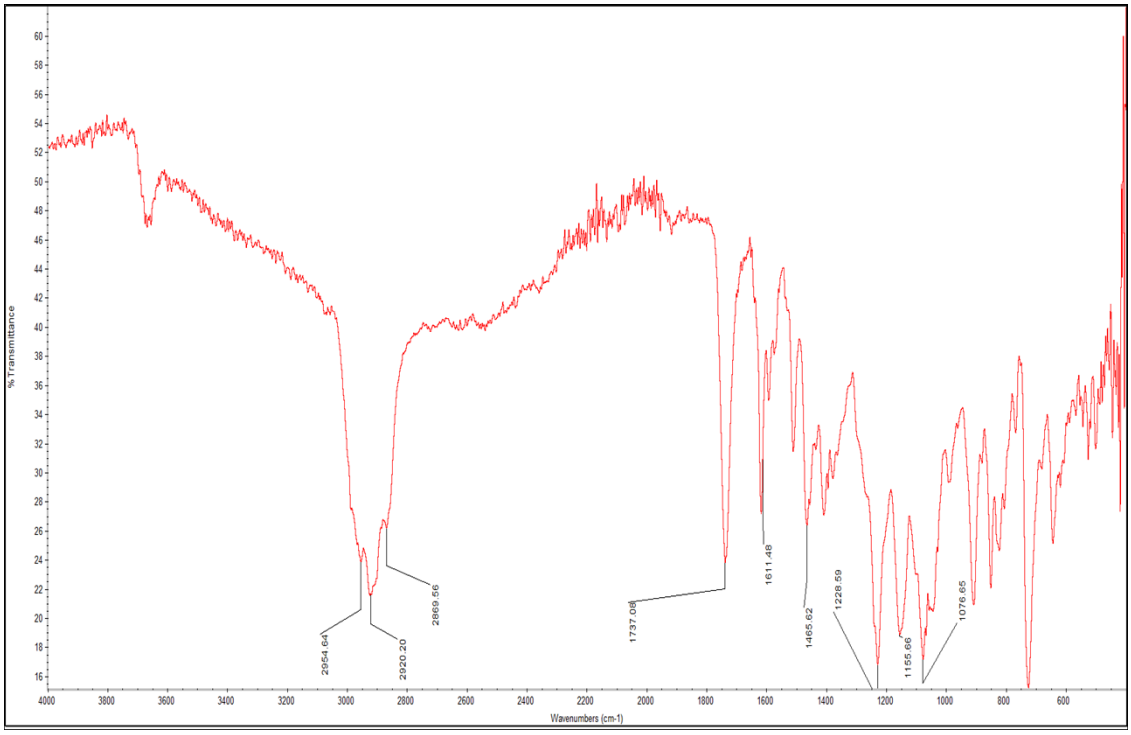
^{1}H NMR (400 MHz, $CDCl_3$)



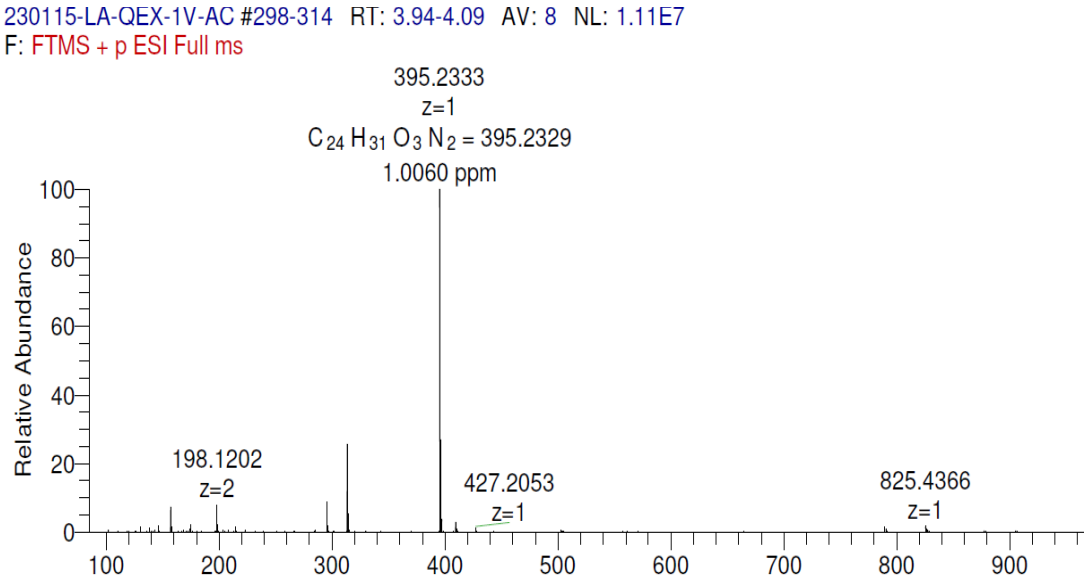
^{13}C NMR (100 MHz, $CDCl_3$)



IR Spectra of **VII**

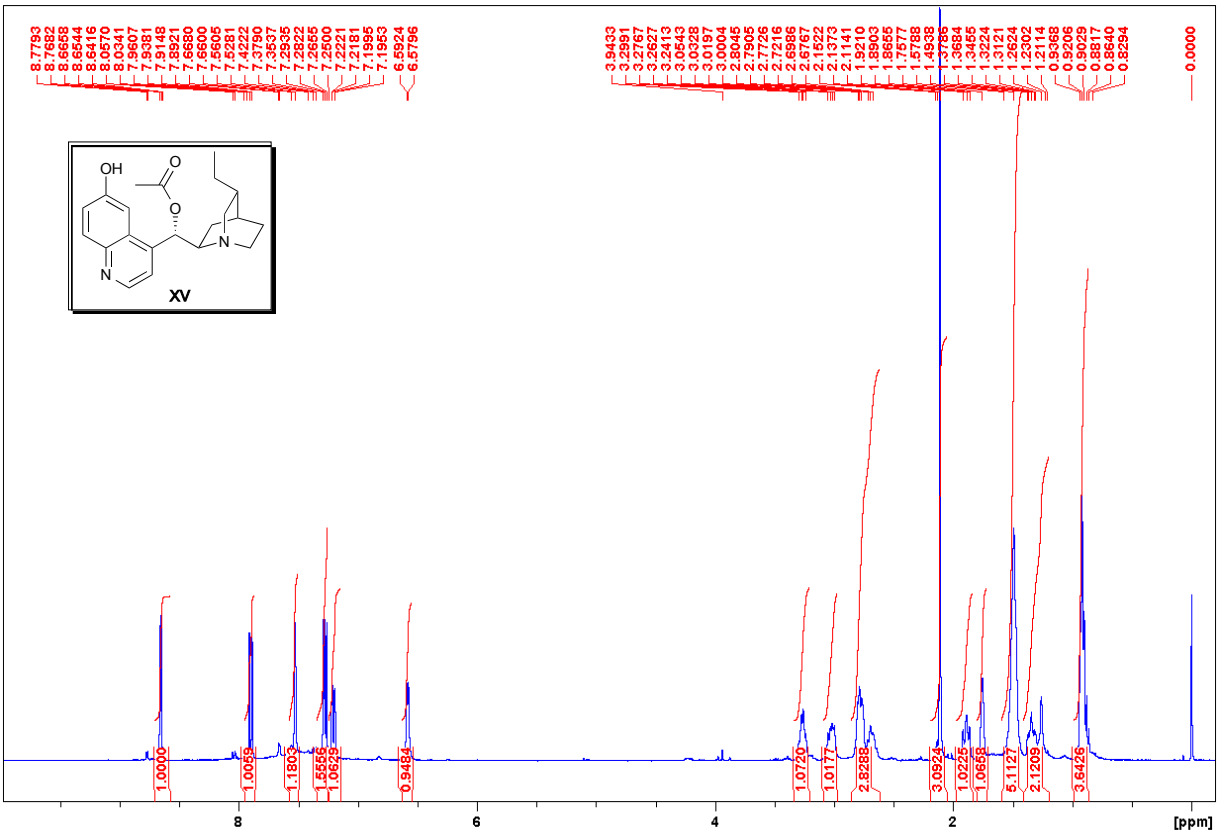


MS Profile of **VII**

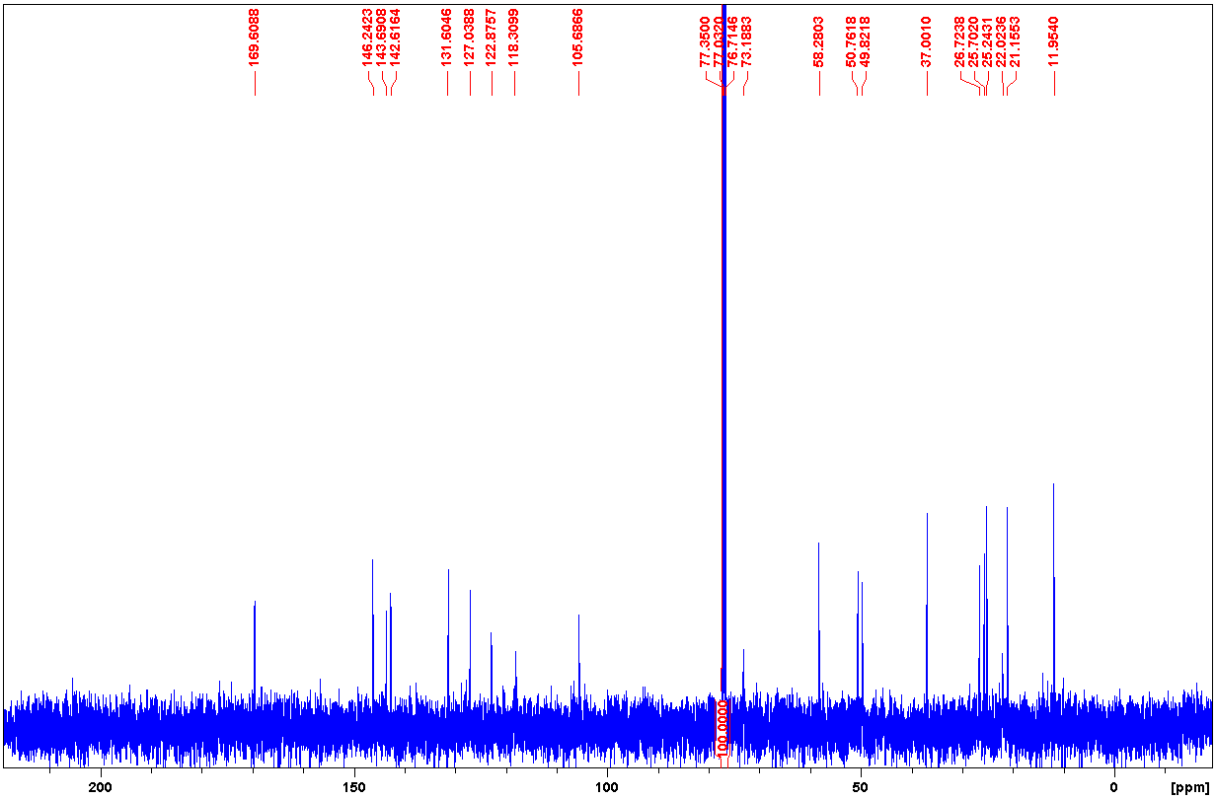


5.6 (*S*)-((1*S*,2*R*,4*S*,5*R*)-5-ethylquinuclidin-2-yl)(6-hydroxyquinolin-4-yl)methyl acetate **XV**

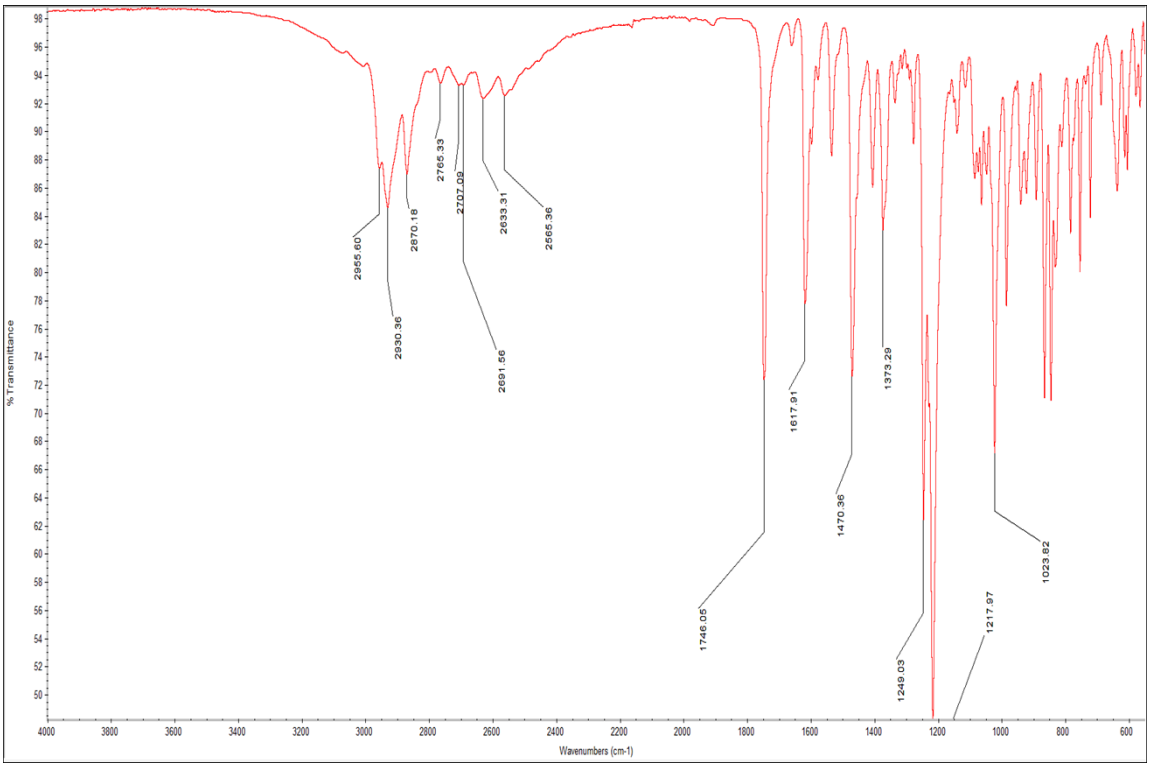
^{1}H NMR (400 MHz, $CDCl_3$)



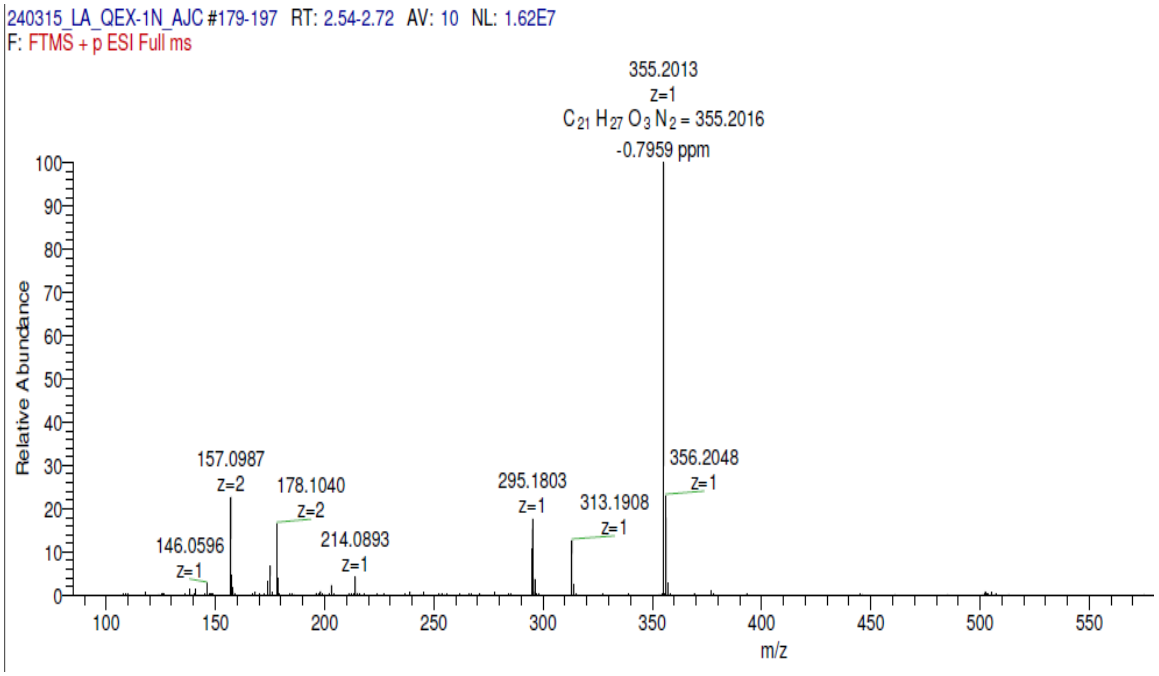
^{13}C NMR (100 MHz, $CDCl_3$)



IR Spectrum of **XV**



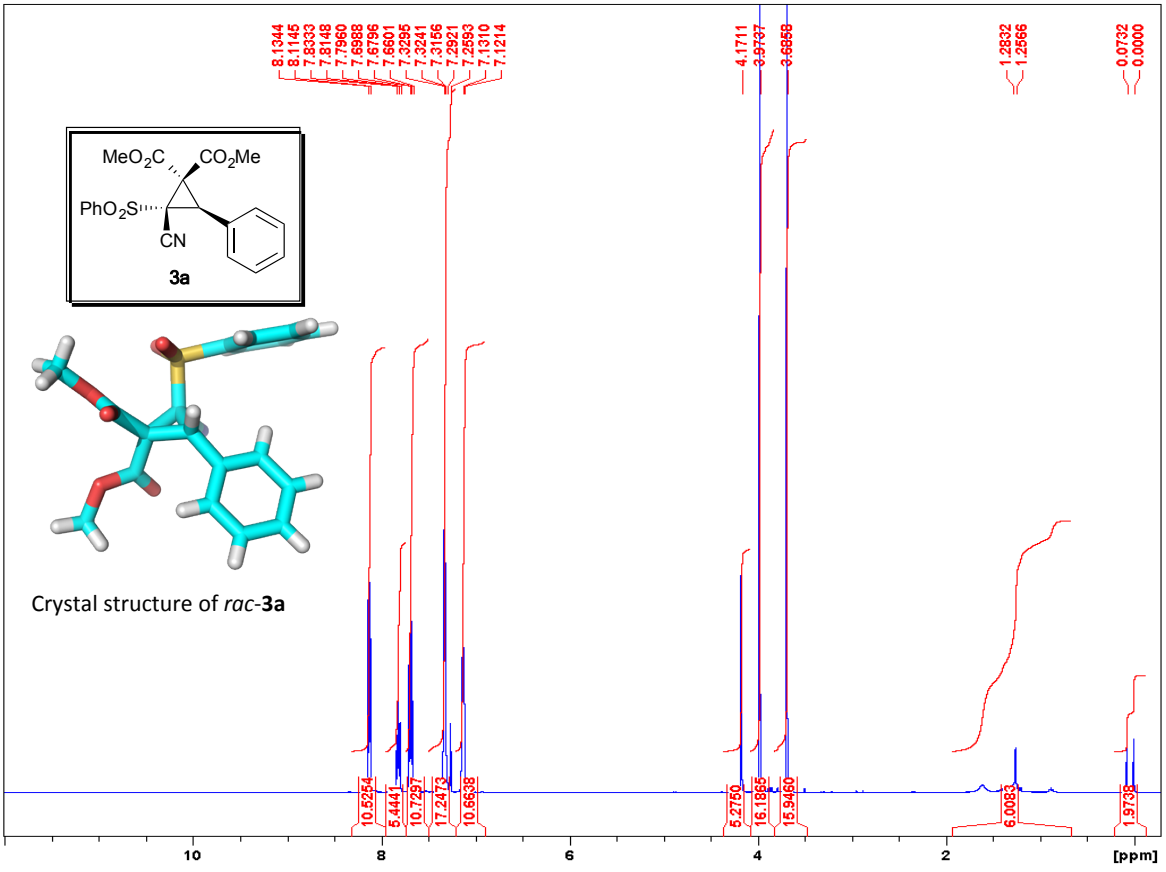
MS Profile of **XV**



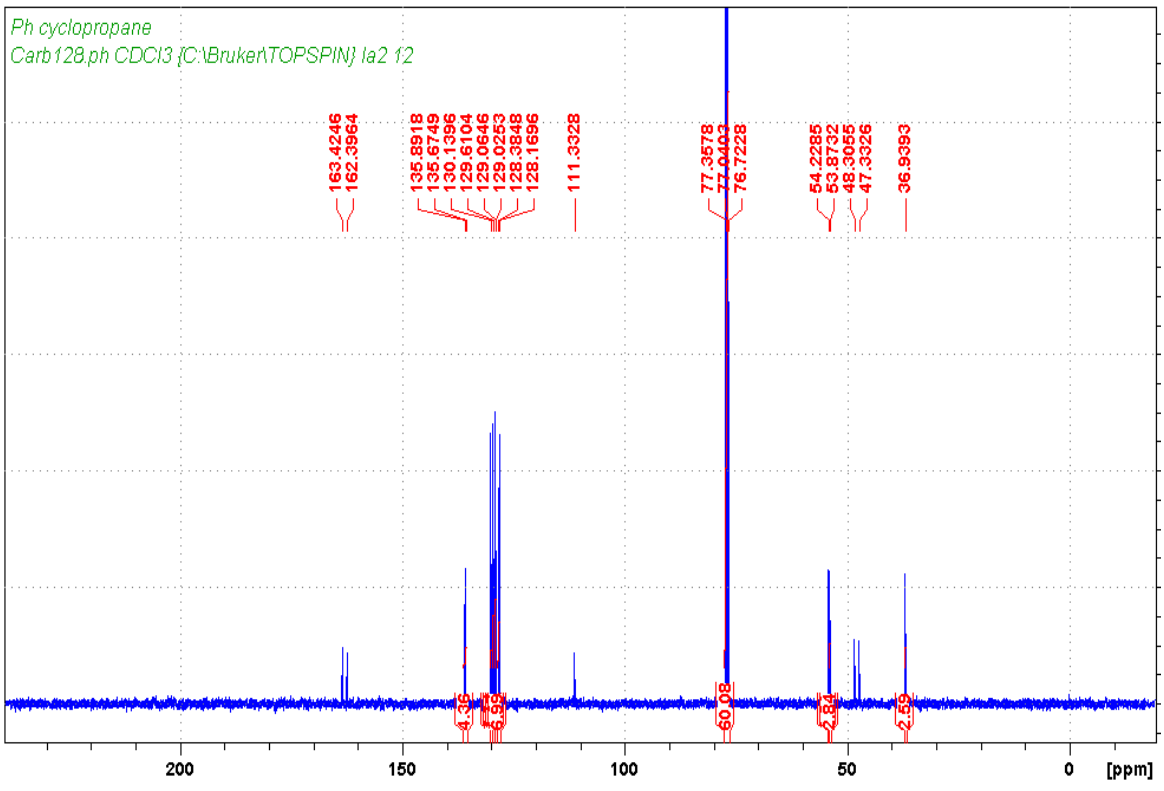
6. Spectra and HPLC Traces for Products of the Substrate Scope and their Derivatives

6.1 Dimethyl-(2*S*,3*R*)-2-cyano-3-phenyl-2-(phenylsulfonyl)cyclopropane-1,1-dicarboxylate **3a**

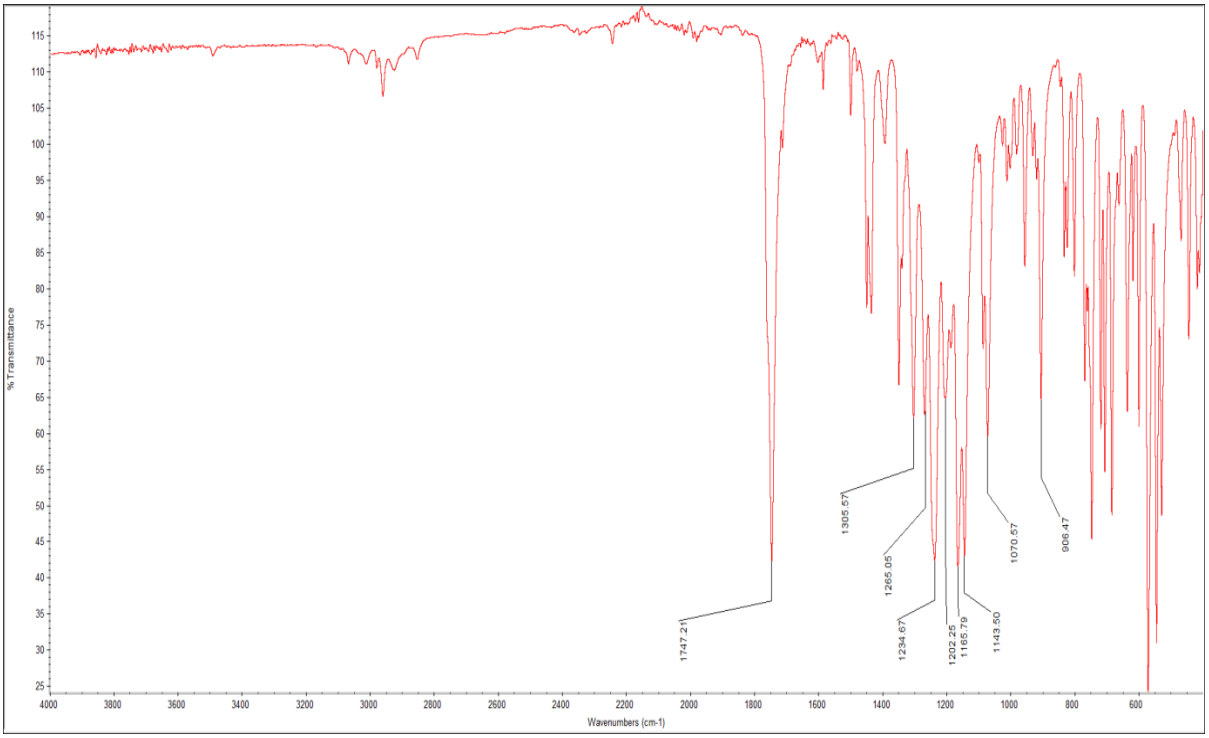
^{1}H NMR (400 MHz, $CDCl_3$)



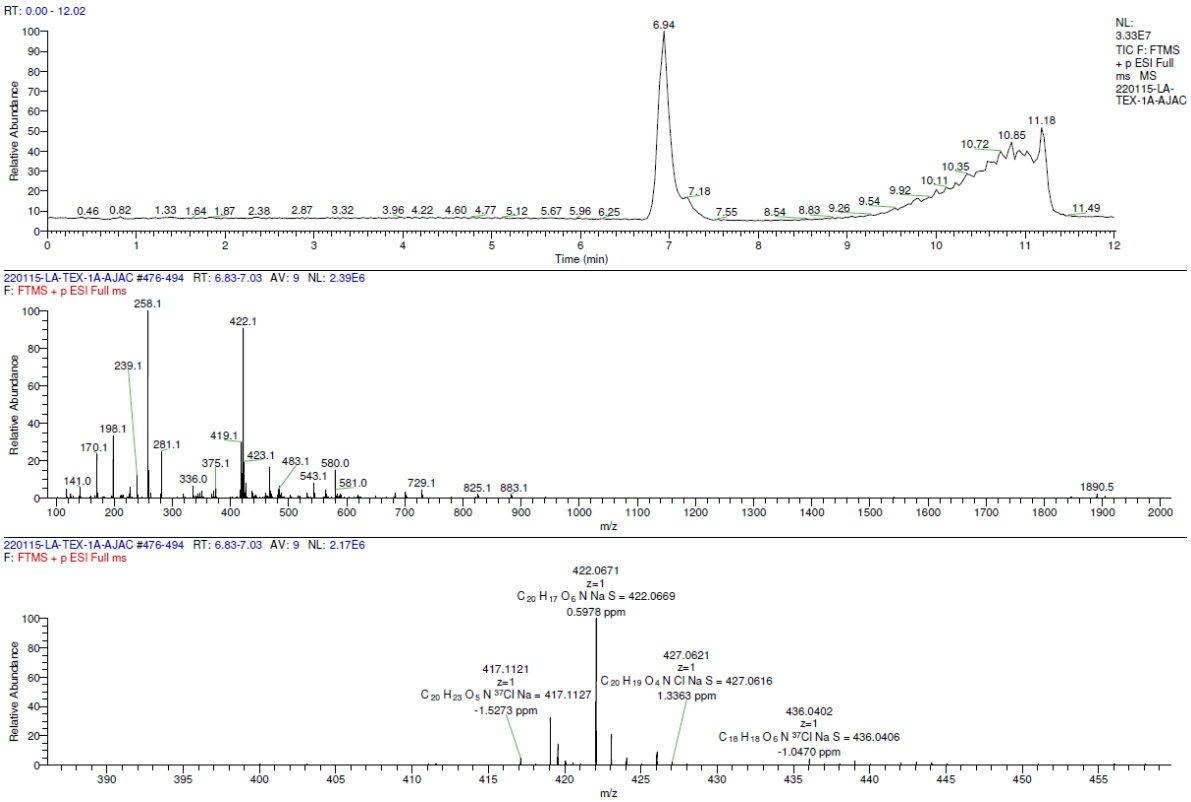
^{13}C NMR (100 MHz, $CDCl_3$)



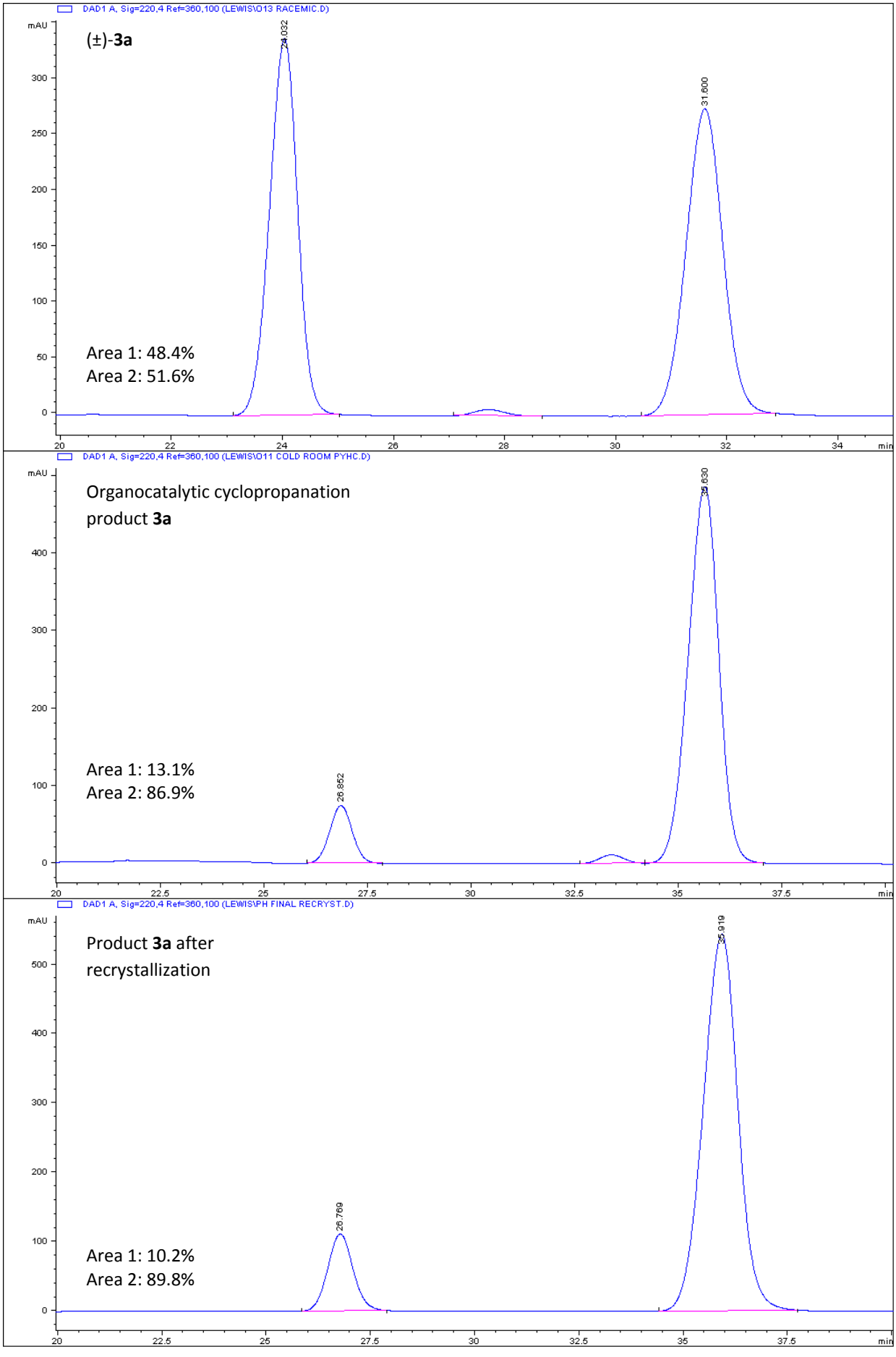
IR Spectrum for **3a**



MS Profile for **3a**

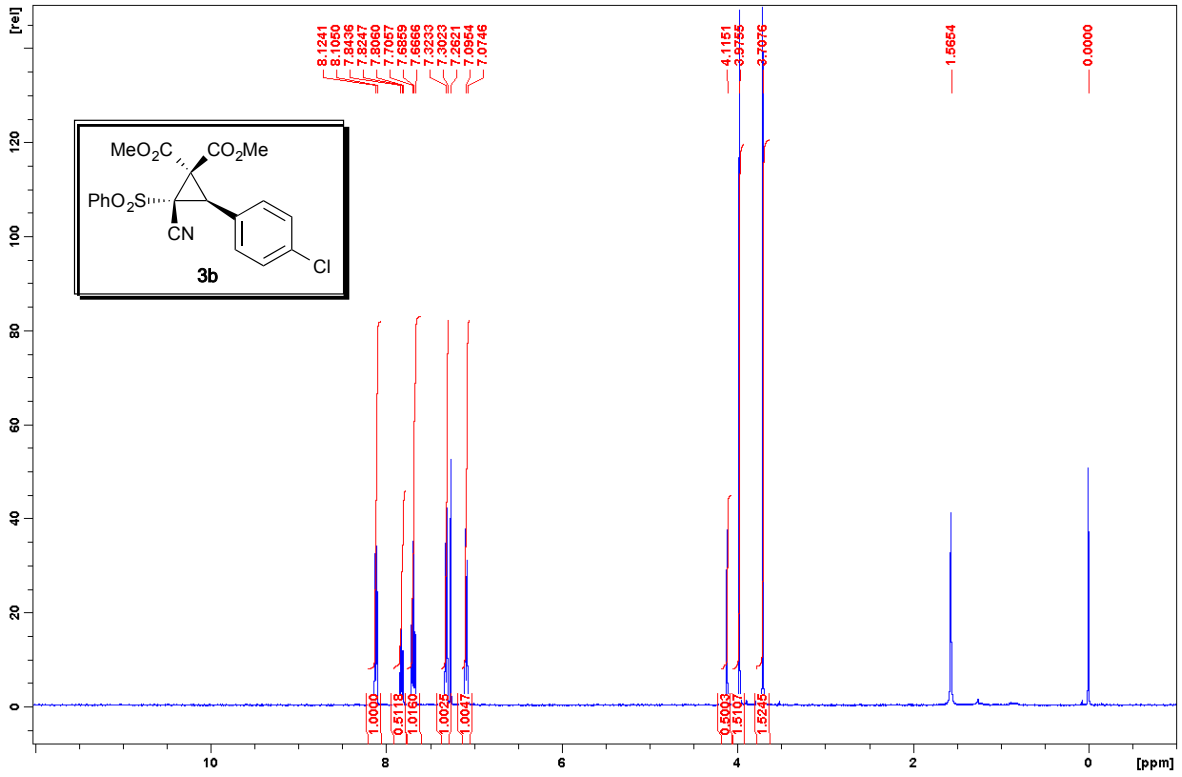


HPLC Traces for **3a** : racemic (top), obtained (middle), recrystallized (bottom)

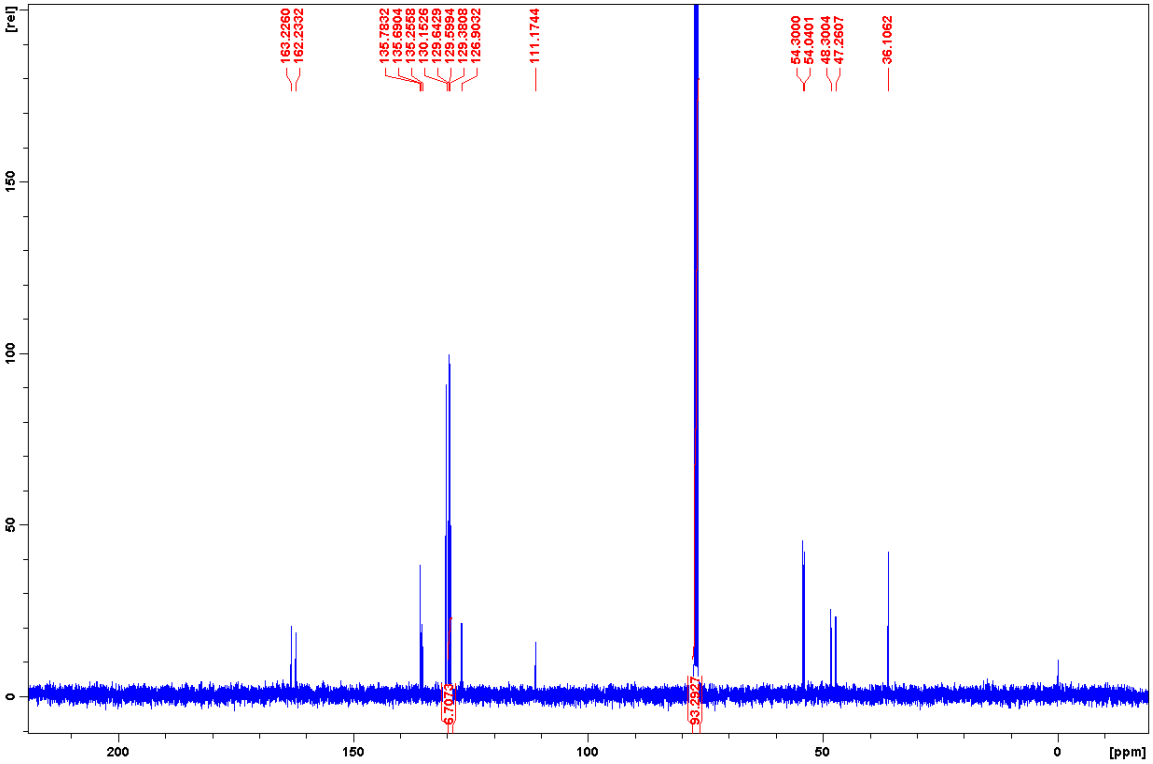


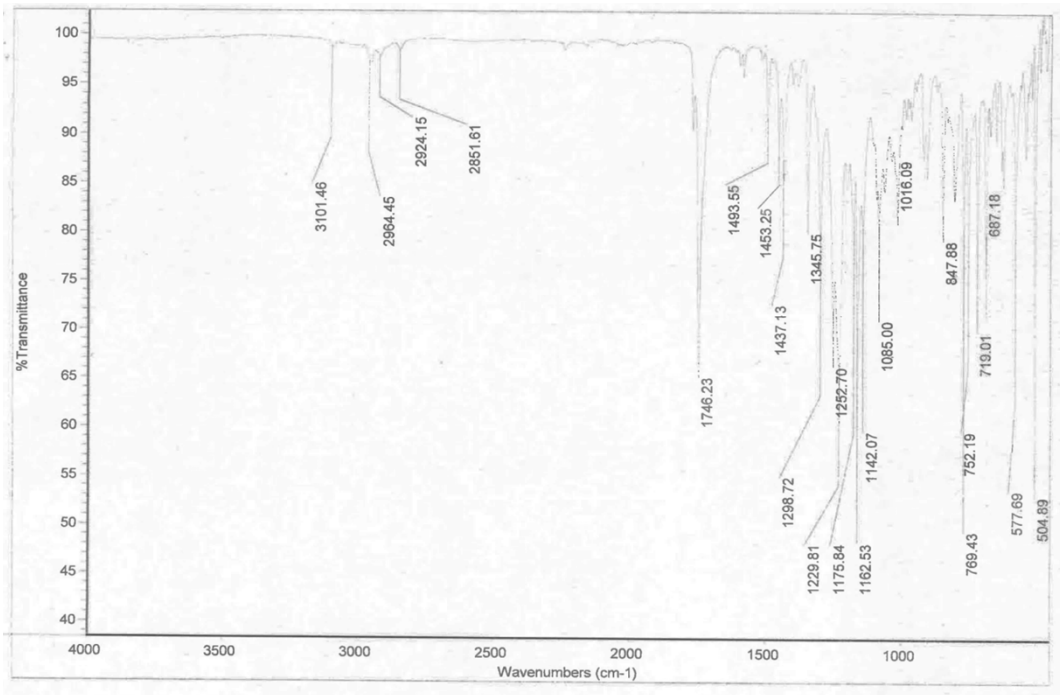
6.2 Dimethyl (2*S*,3*R*)-3-(4-chlorophenyl)-2-cyano-2-(phenylsulfonyl)cyclopropane-1,1-dicarboxylate **3b**

^{1}H NMR (400 MHz, $CDCl_3$)



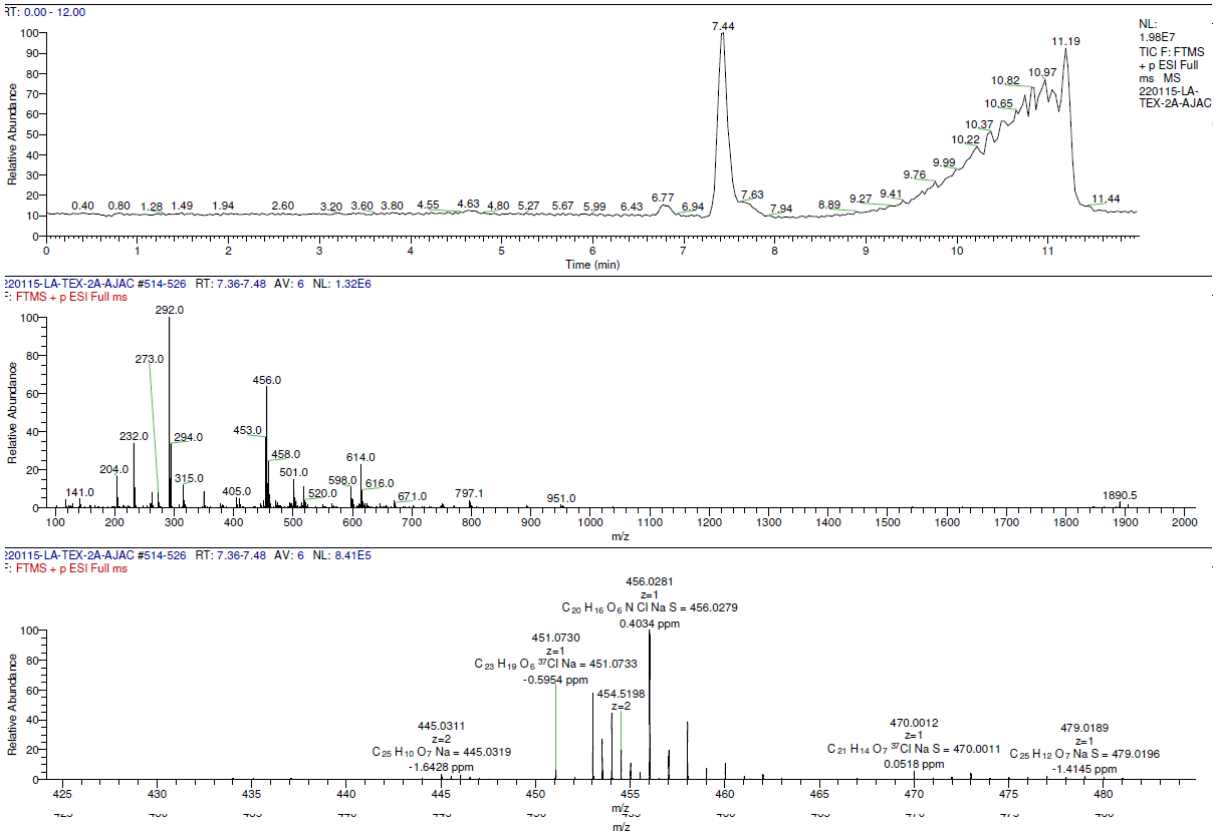
^{13}C NMR (100 MHz, $CDCl_3$)



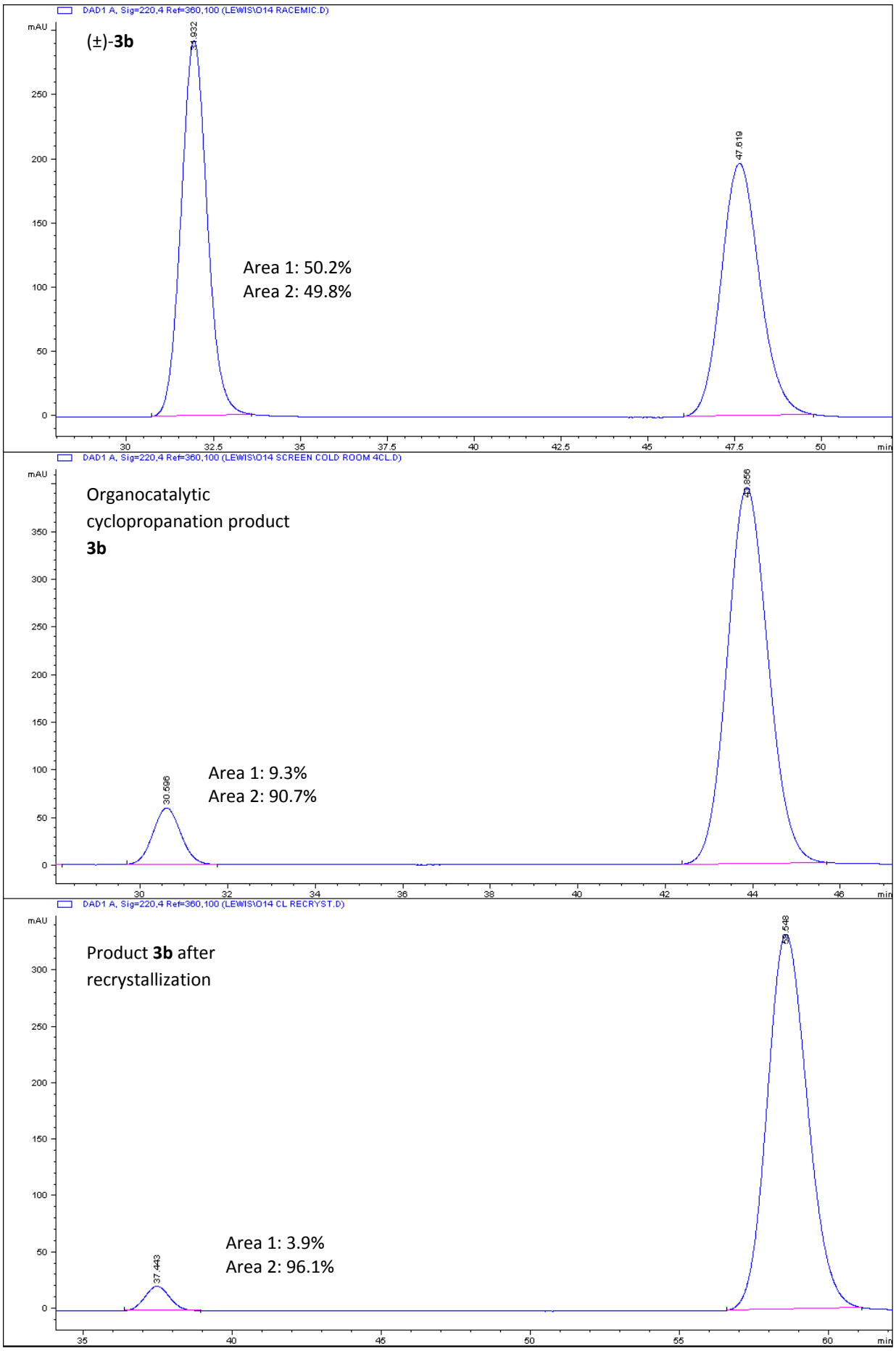


IR Spectrum of **3b**

MS Profile of **3b**

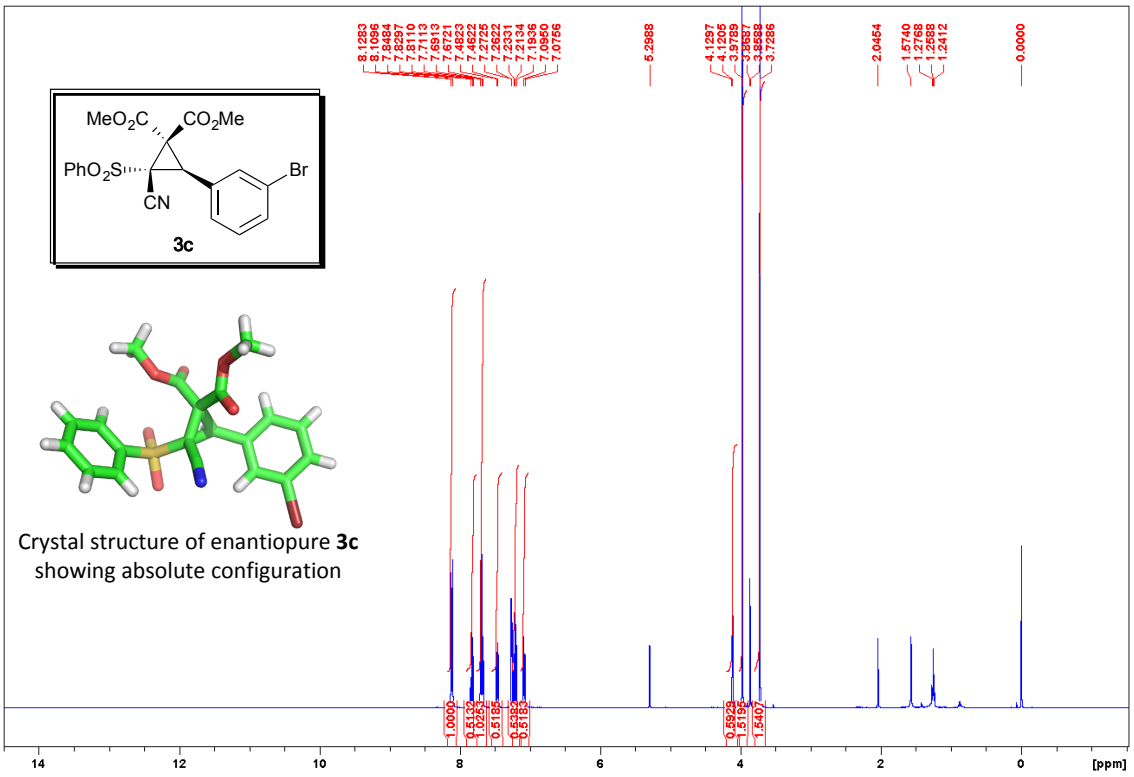


HPLC Traces for **3b** : racemic (top), obtained (middle), recrystallized (bottom)

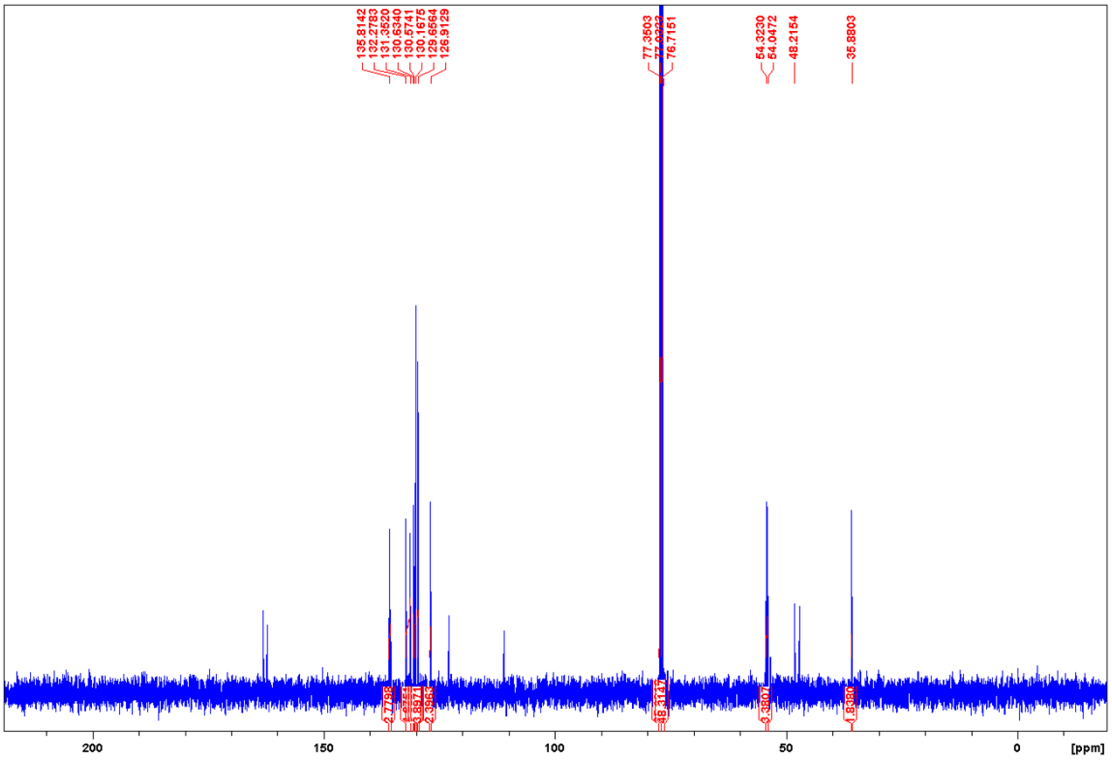


6.3 Dimethyl (2*S*,3*R*)-3-(3-bromophenyl)-2-cyano-2-(phenylsulfonyl)cyclopropane-1,1-dicarboxylate **3c**

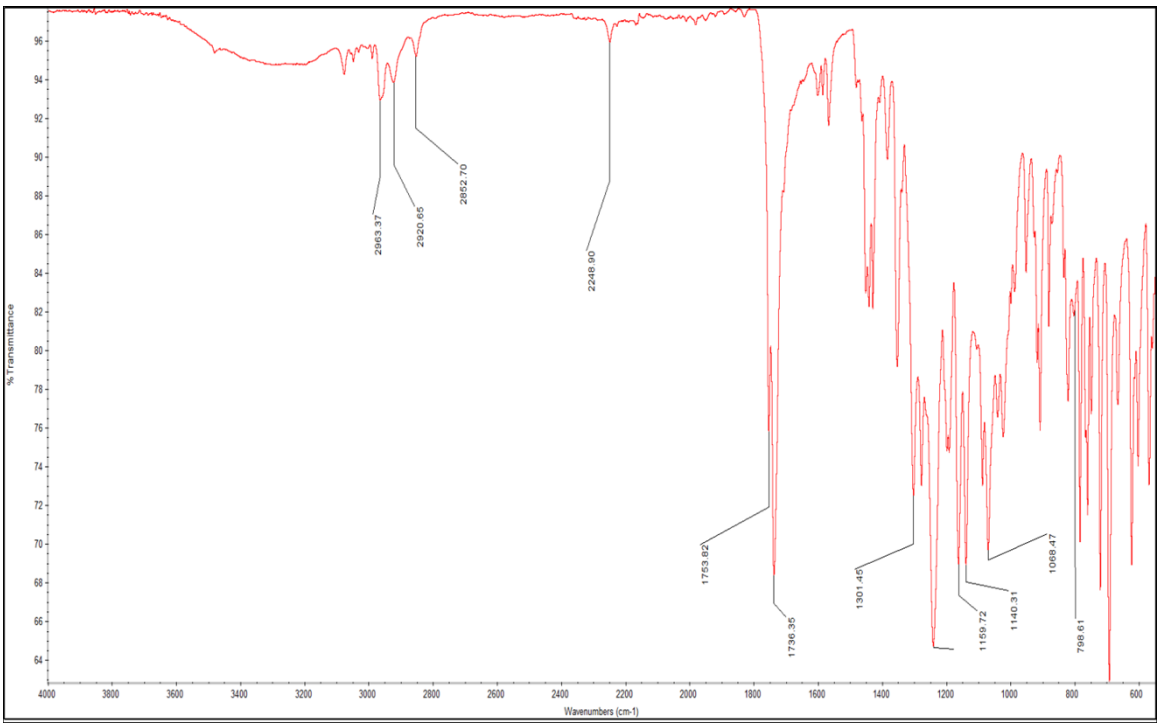
^{1}H NMR (400 MHz, $CDCl_3$)



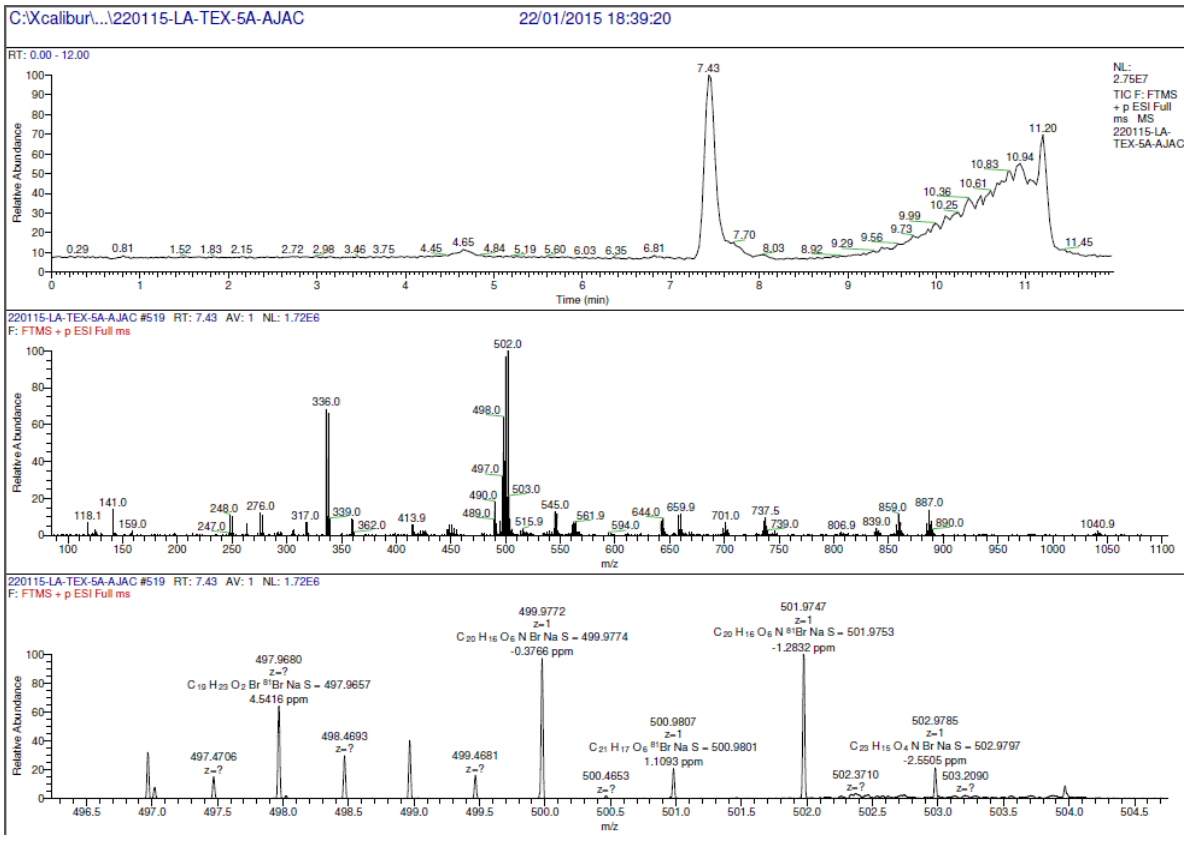
^{13}C NMR (100 MHz, $CDCl_3$)



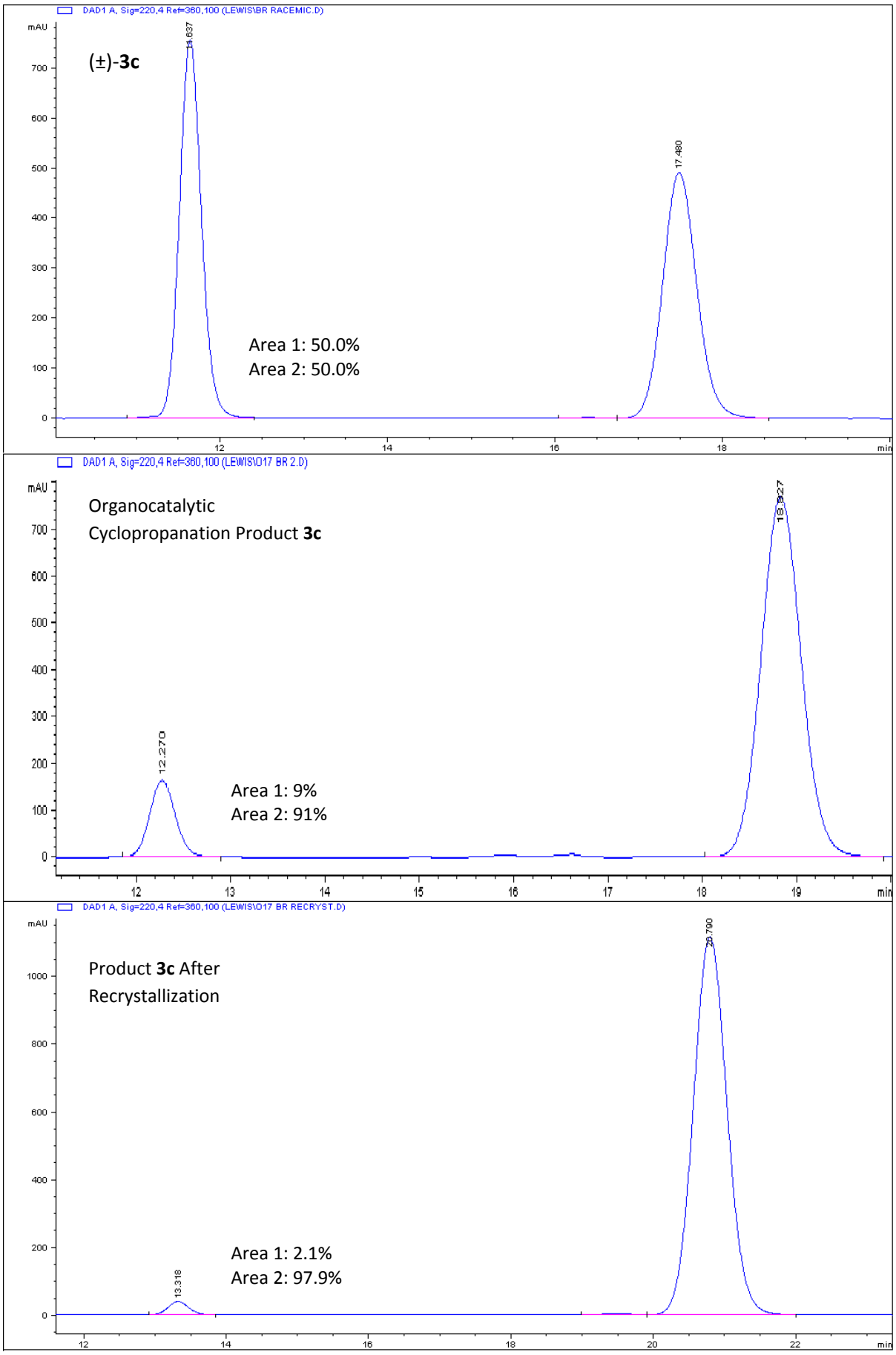
IR Spectrum of **3c**



MS Profile of **3c**

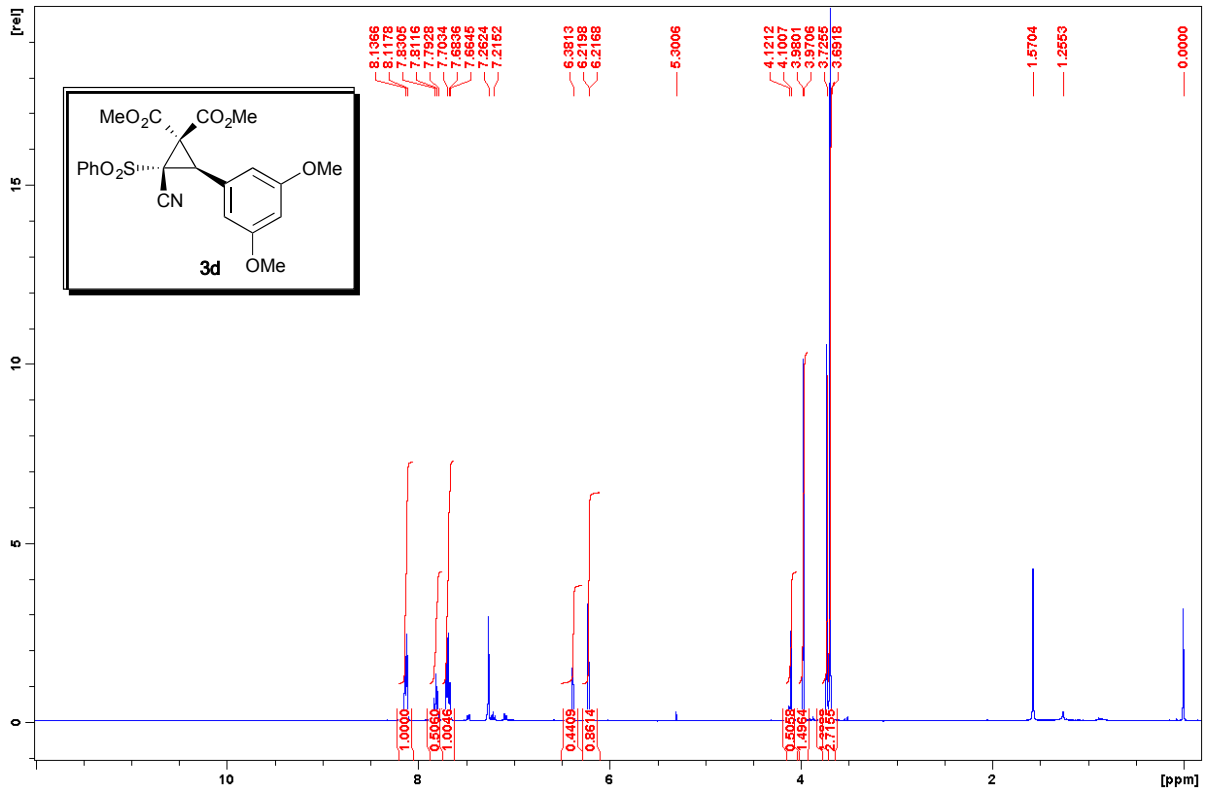


HPLC Traces for **3c** : racemic (top), obtained (middle), recrystallized (bottom)

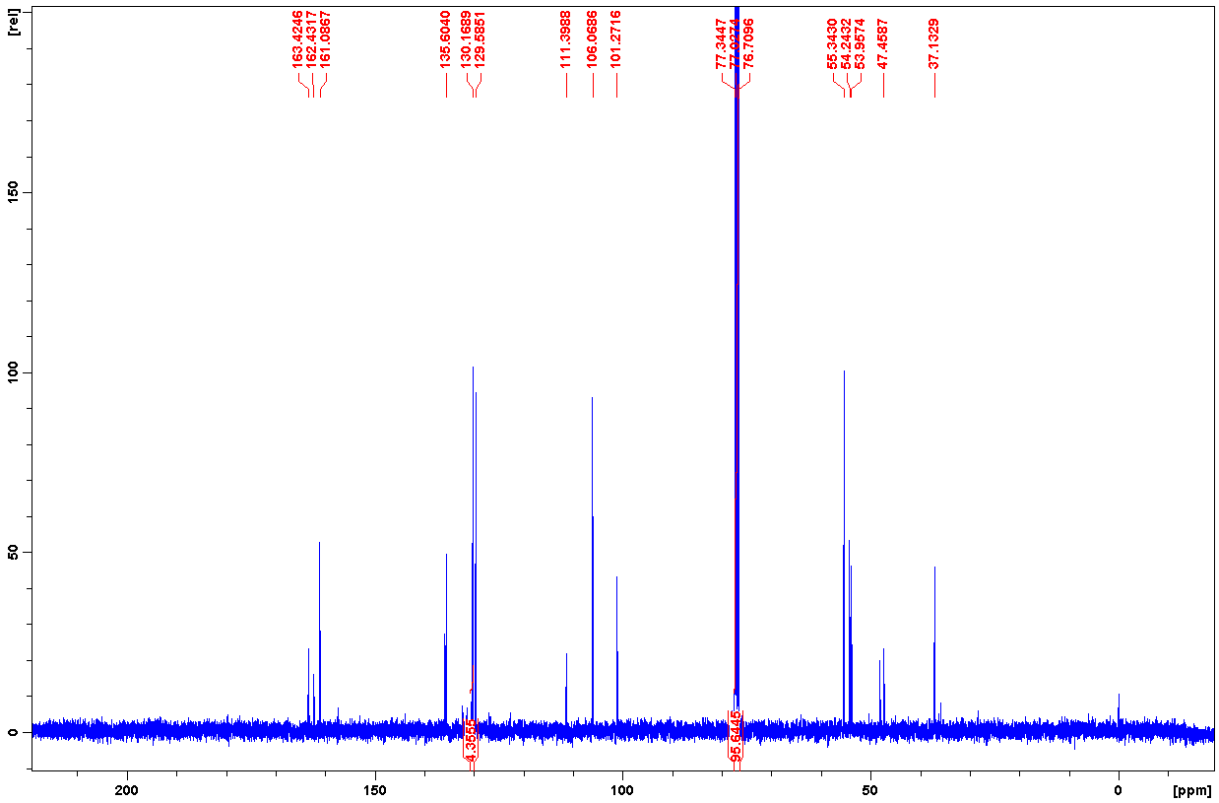


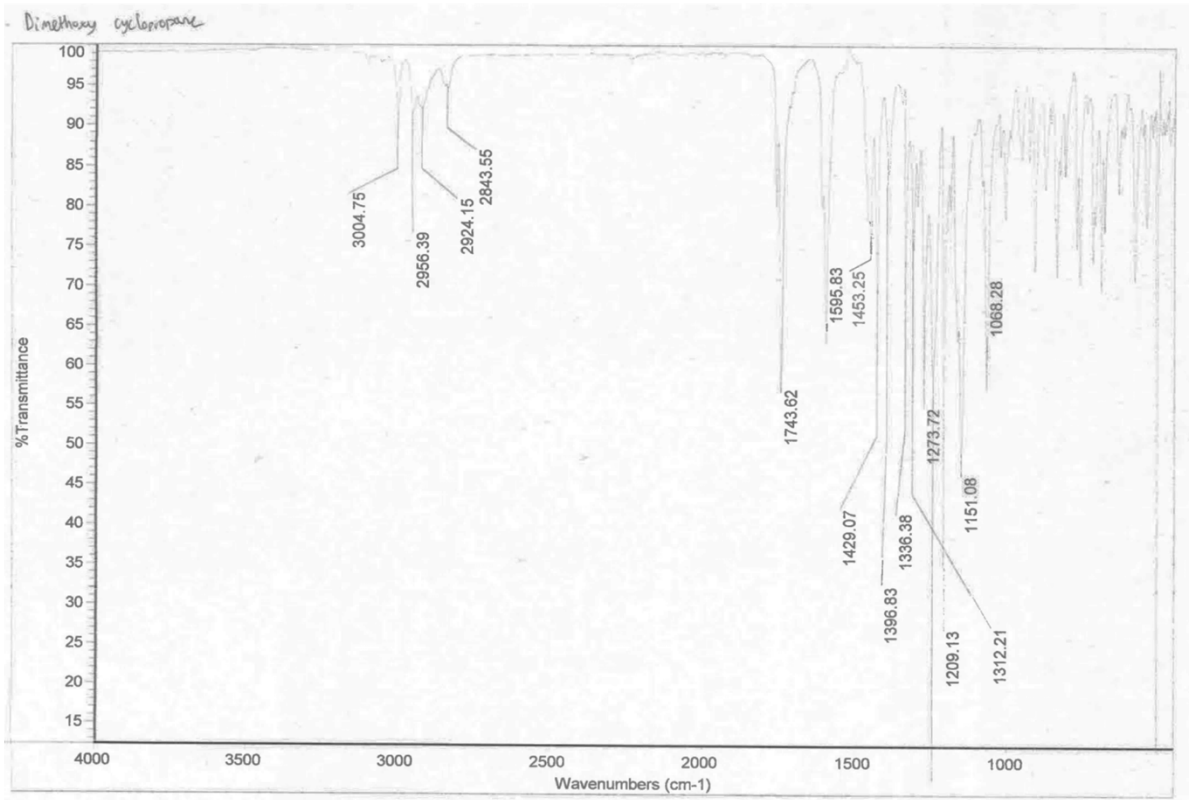
6.4 Dimethyl (2S,3R)-2-cyano-3-(3,5-dimethoxyphenyl)-2-(phenylsulfonyl)cyclopropane-1,1-dicarboxylate **3d**

^{1}H NMR (400 MHz, $CDCl_3$)



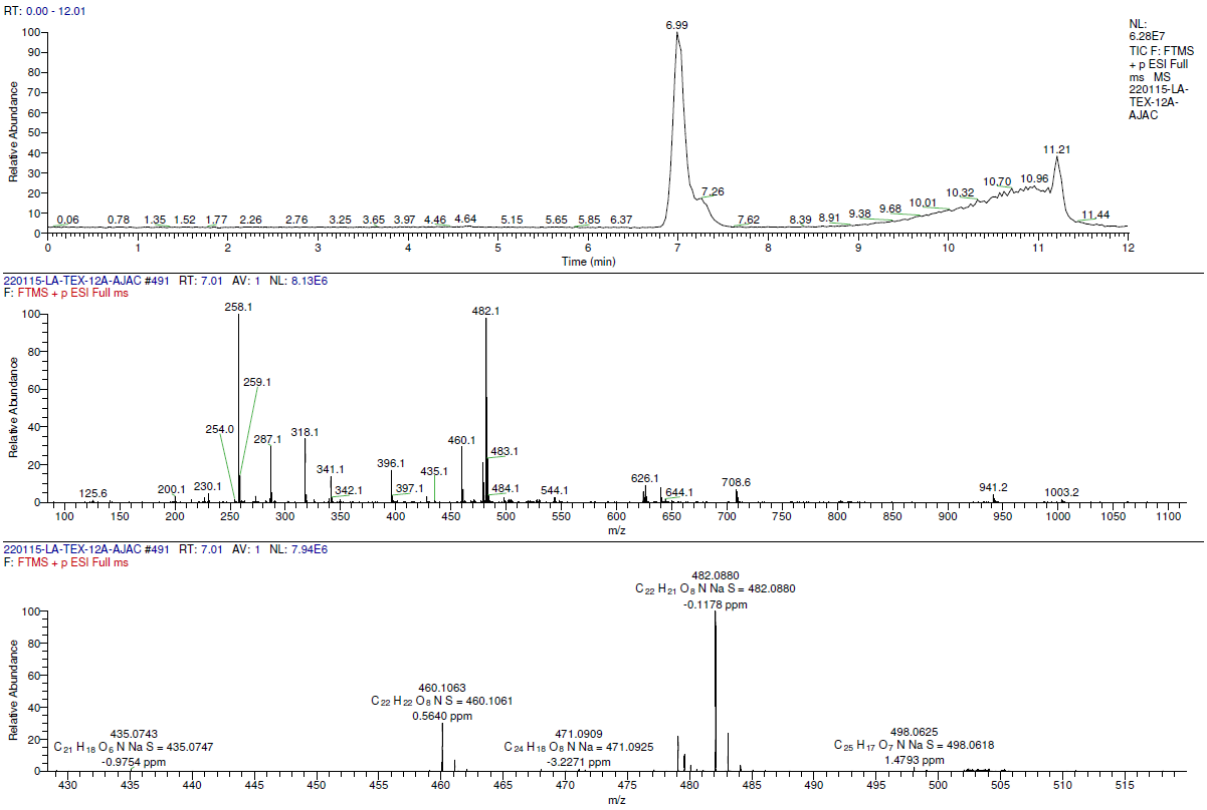
^{13}C NMR (100 MHz, $CDCl_3$)





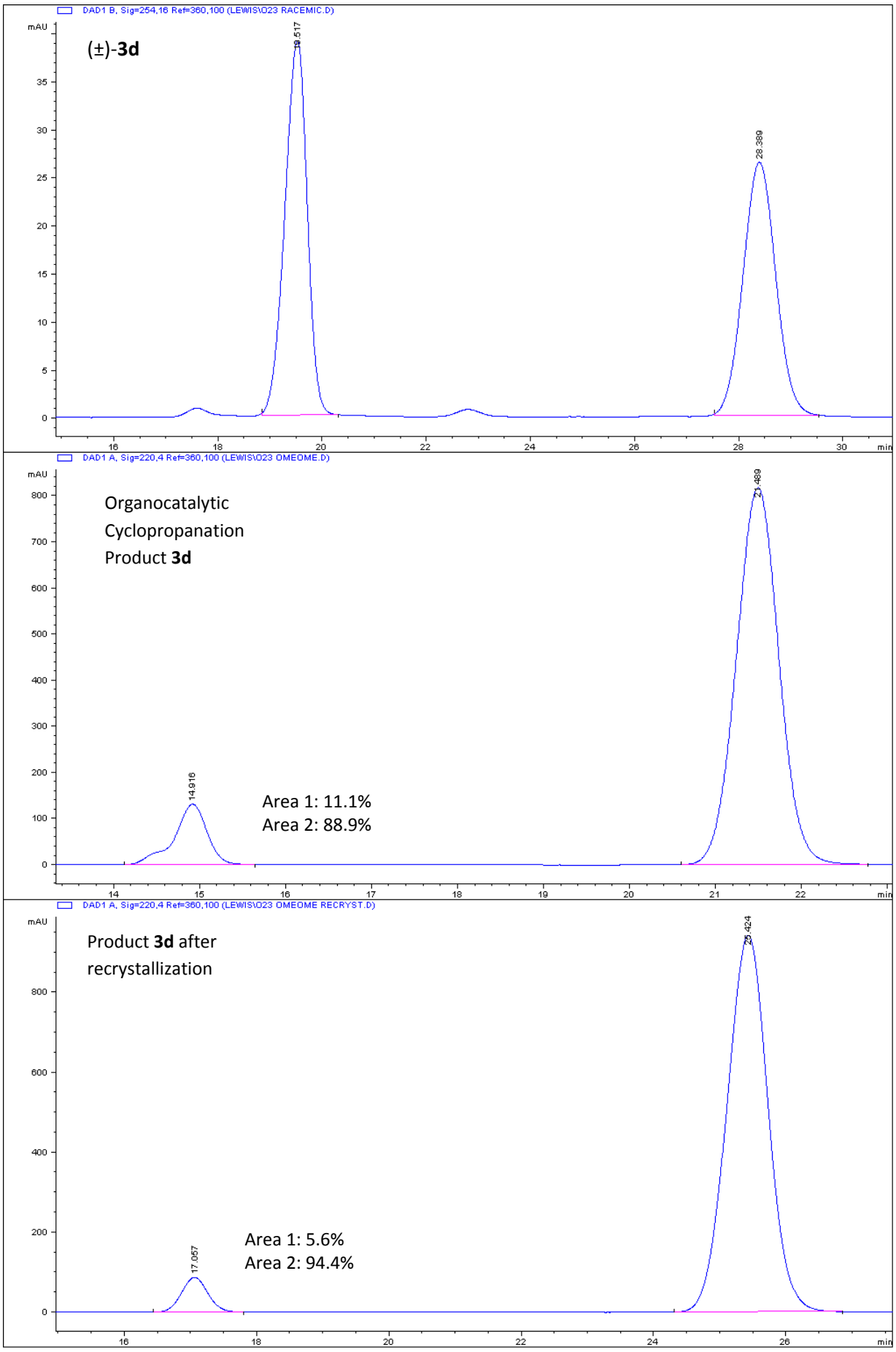
IR Spectrum of **3d**

MS Profile of **3d**



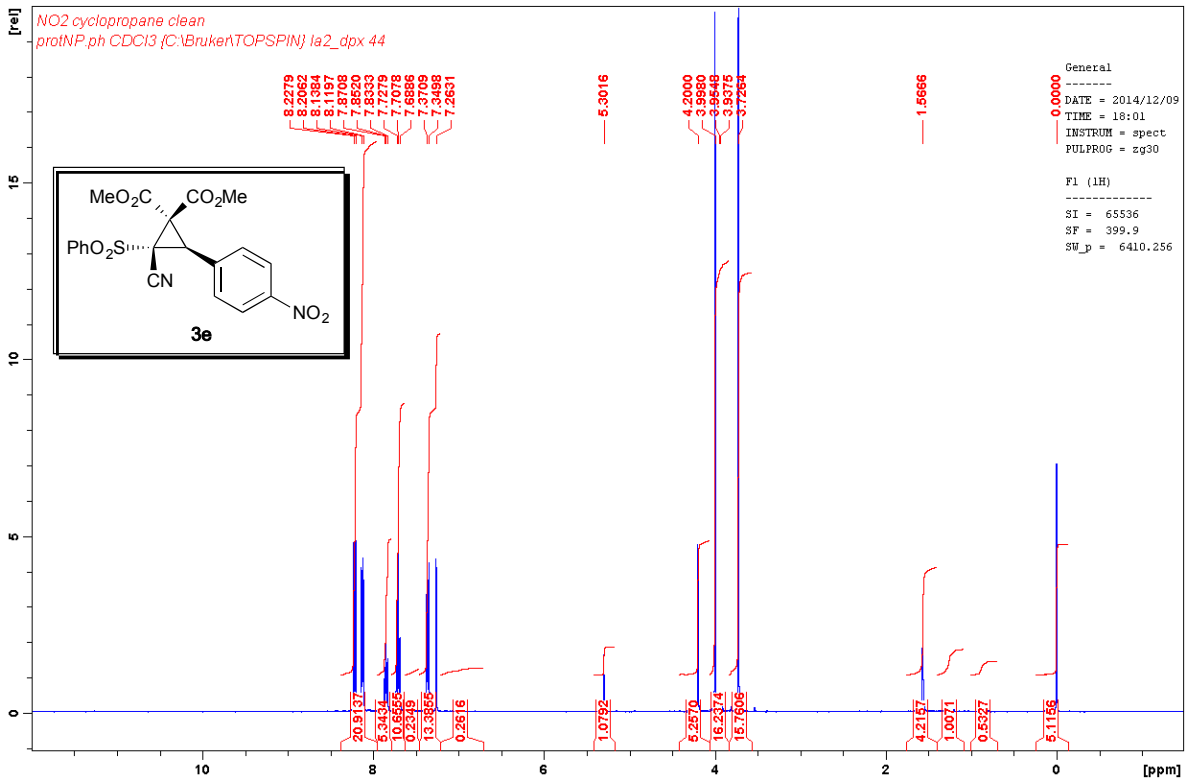
HPLC Traces for **3d** : racemic (top), obtained (middle), recrystallized (bottom)

Area 1: 50.0%
Area 2: 50.0%

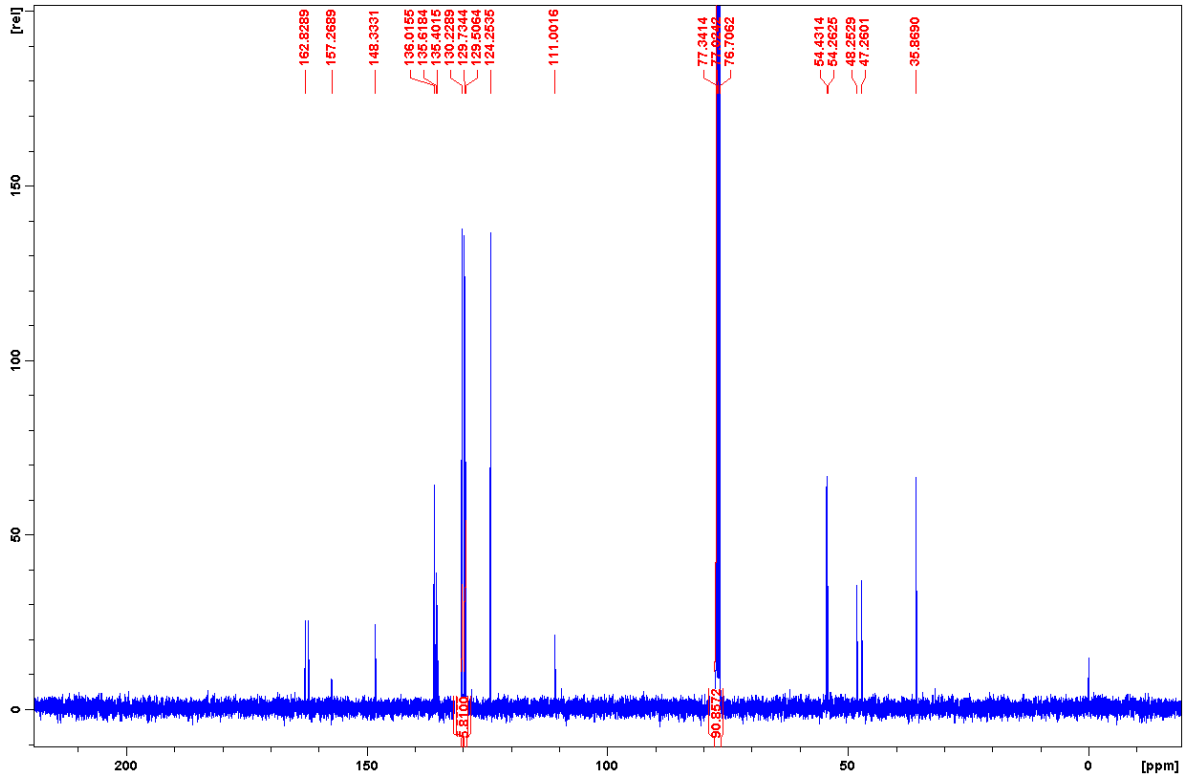


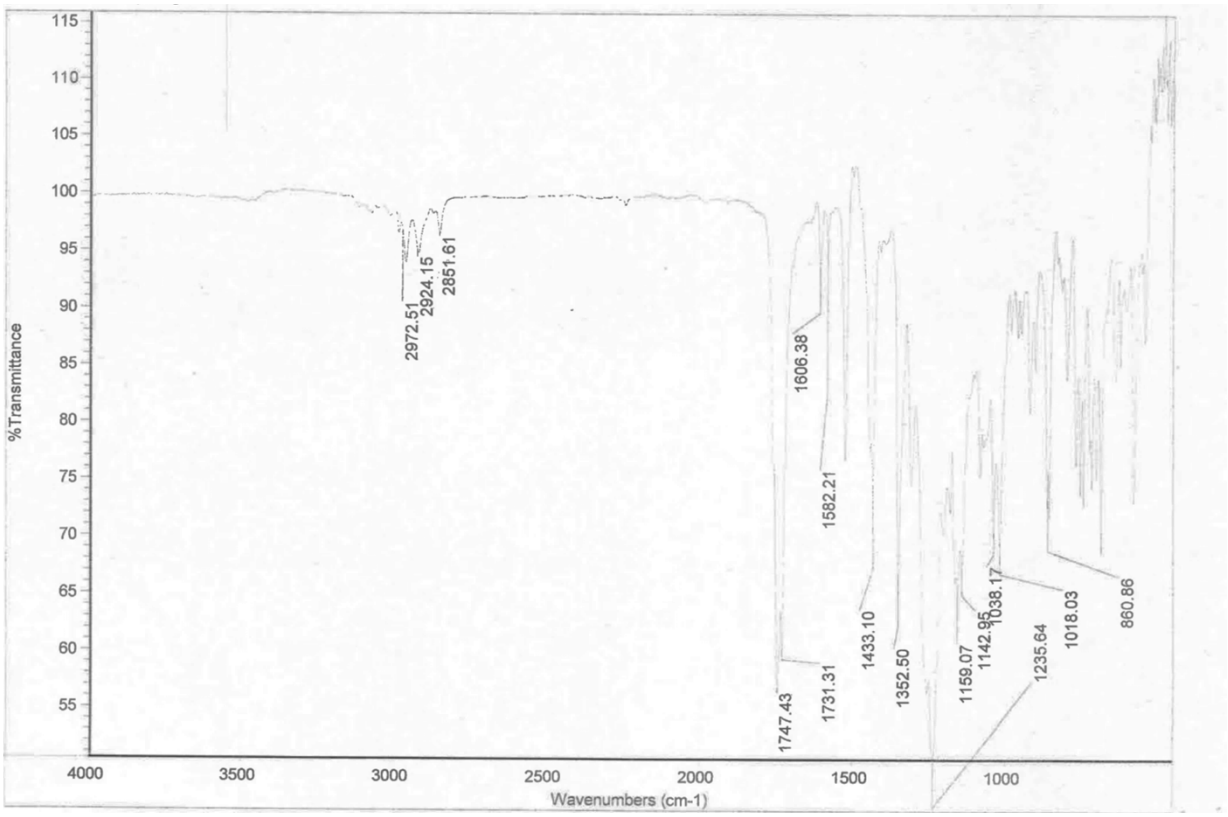
6.5 Dimethyl (2S,3R)-2-cyano-3-(4-nitrophenyl)-2-(phenylsulfonyl)cyclopropane-1,1-dicarboxylate **3e**

^{1}H NMR (400 MHz, $CDCl_3$)



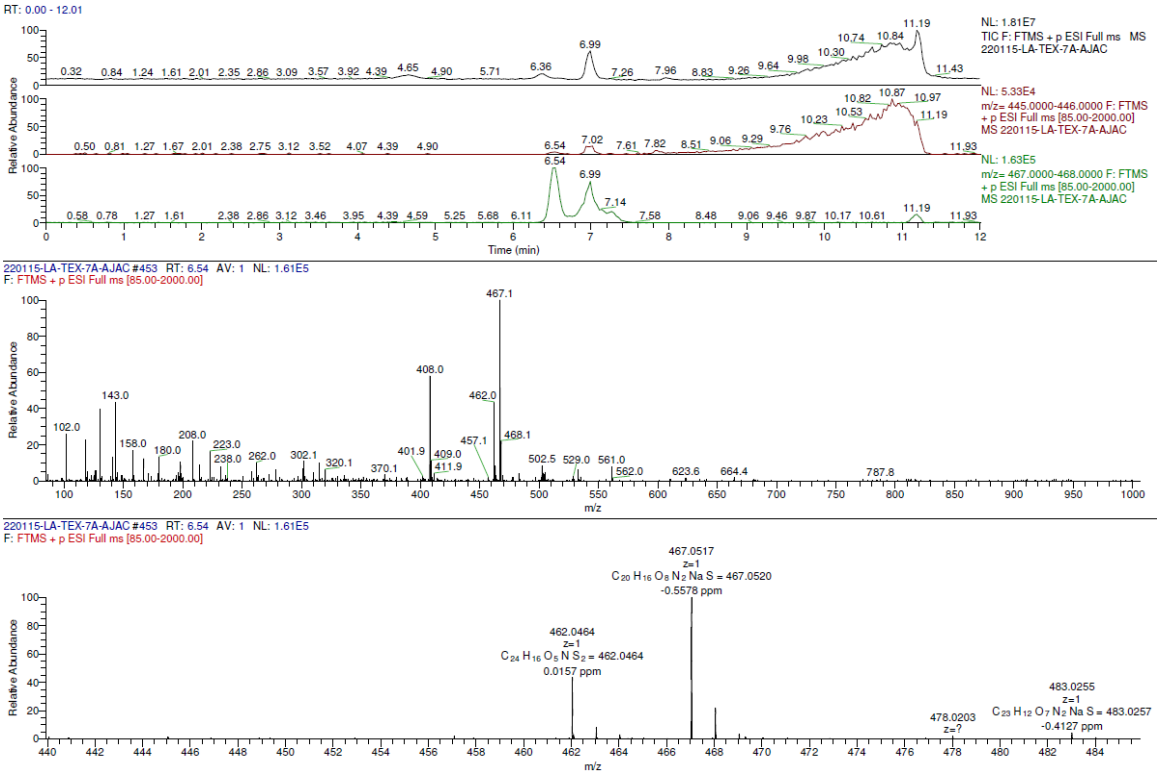
^{13}C NMR (100 MHz, $CDCl_3$)



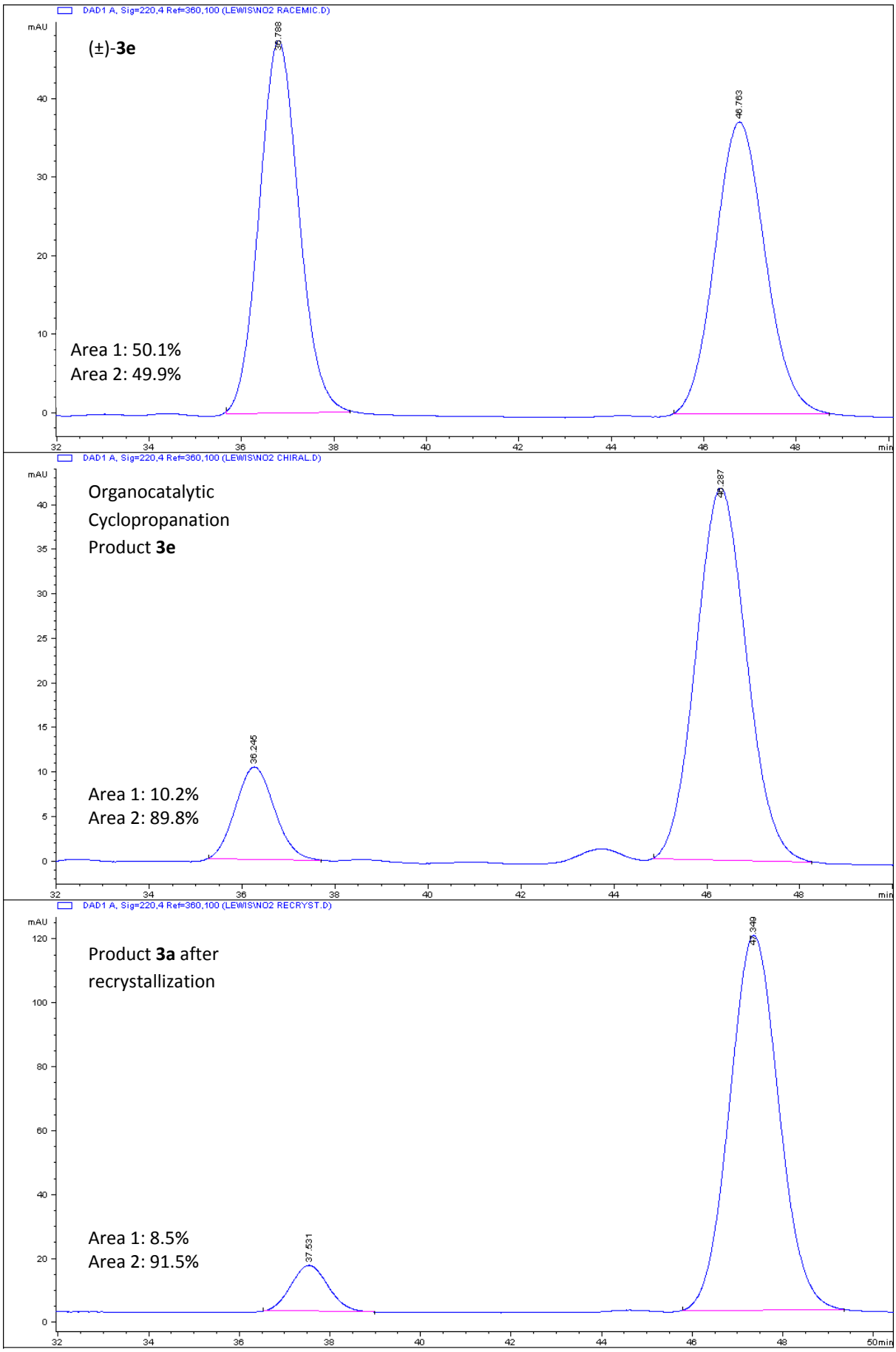


IR Spectrum of **3e**

MS Profile of **3e**

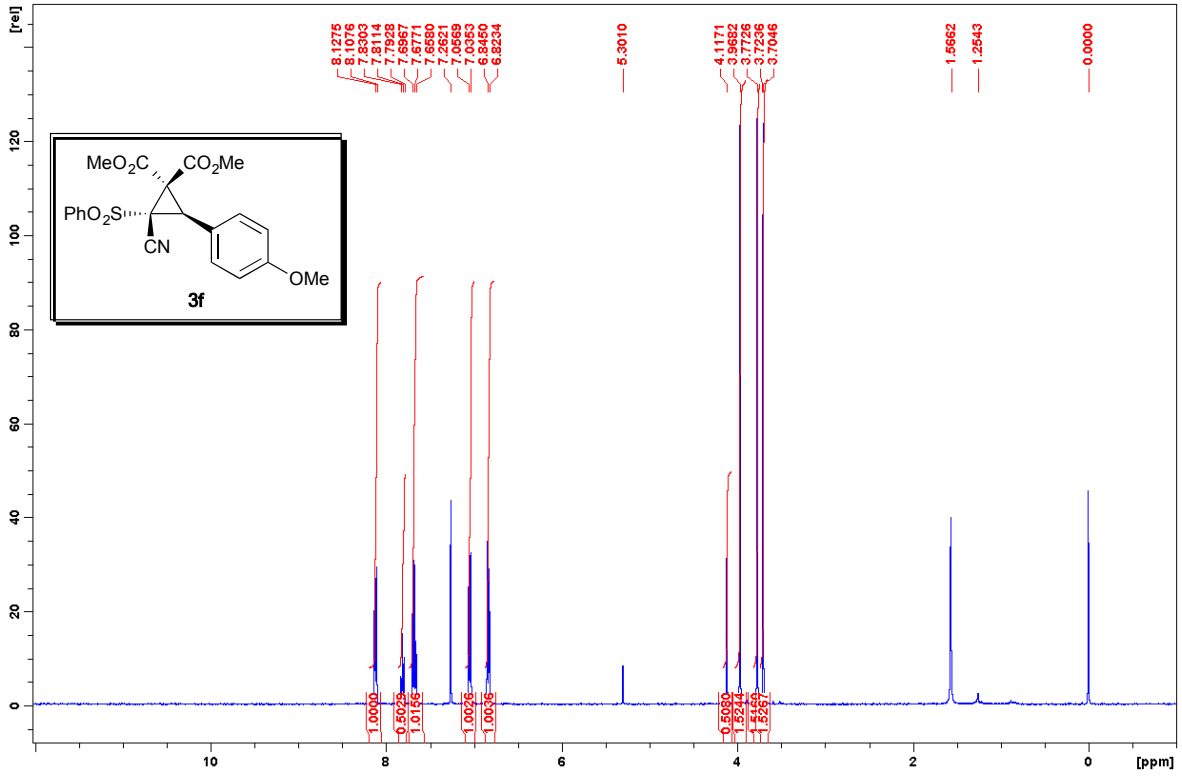


HPLC Traces for **3e** : racemic (top), obtained (middle), recrystallized (bottom)

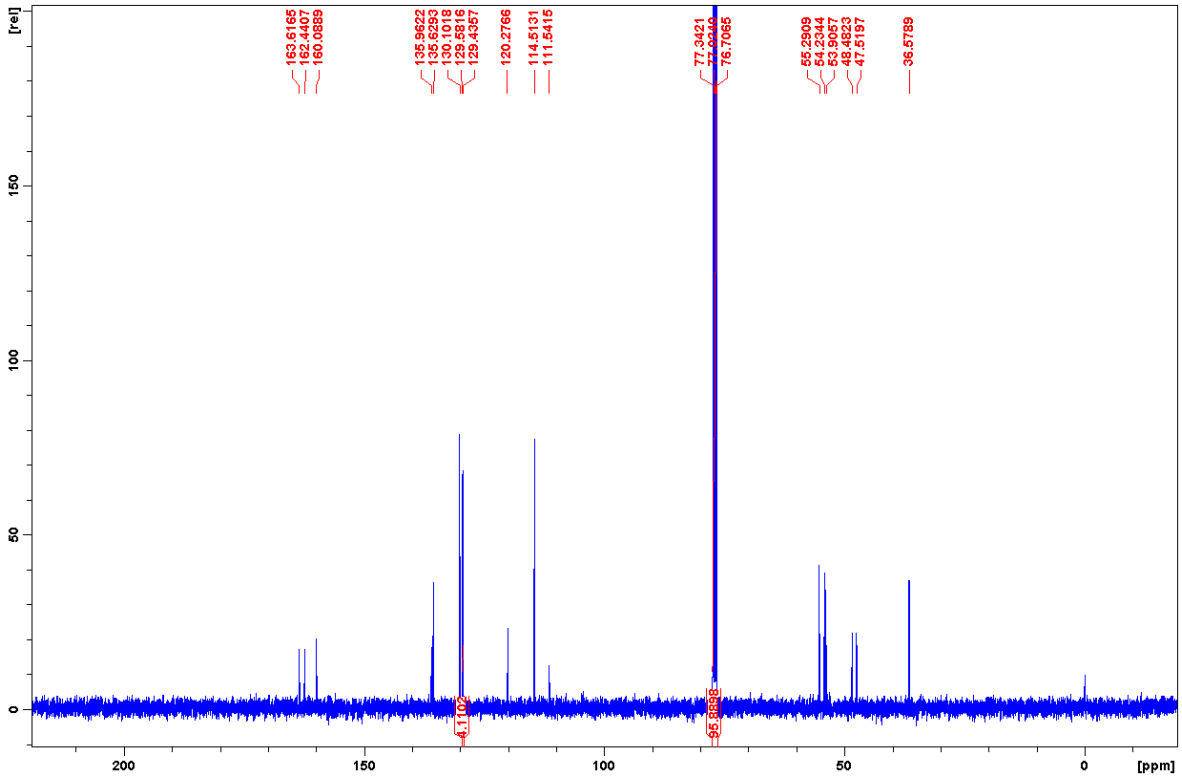


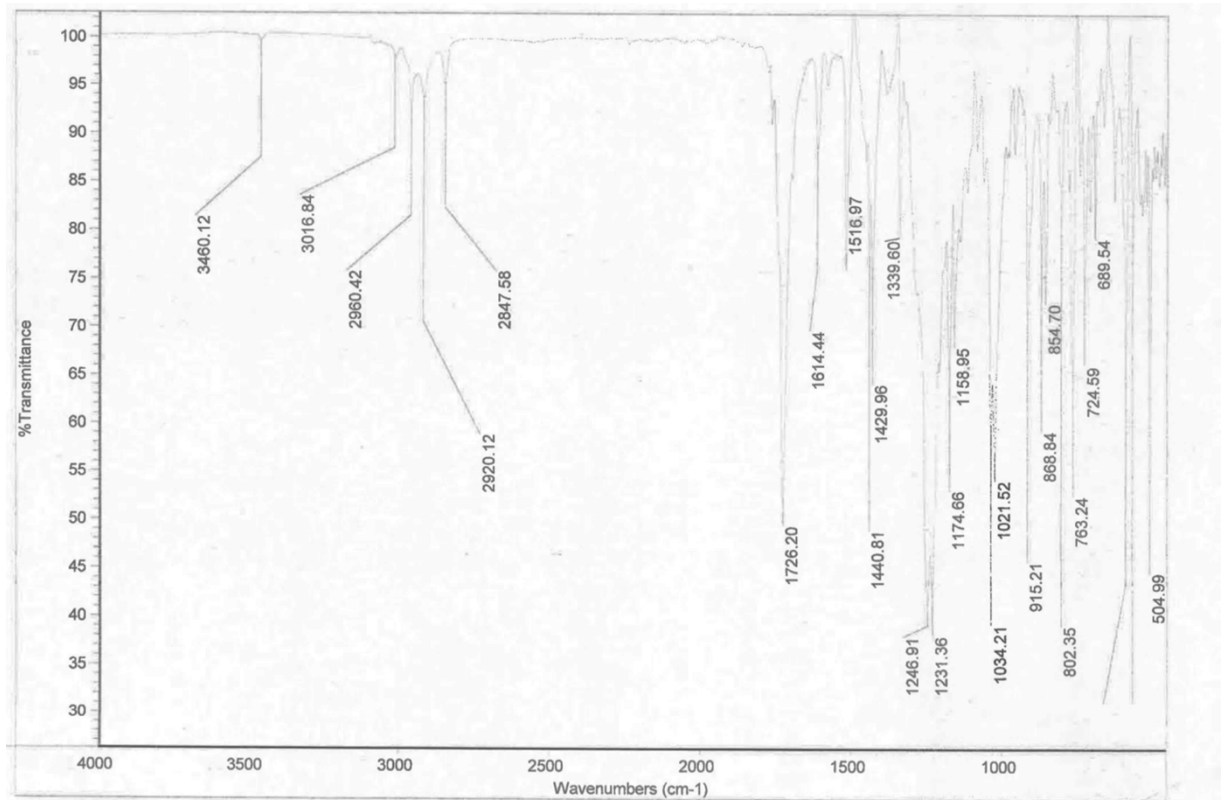
6.6 Dimethyl (2*S*,3*R*)-2-cyano-3-(4-methoxyphenyl)-2-(phenylsulfonyl)cyclopropane-1,1-dicarboxylate **3f**

^{1}H NMR (400 MHz, $CDCl_3$)



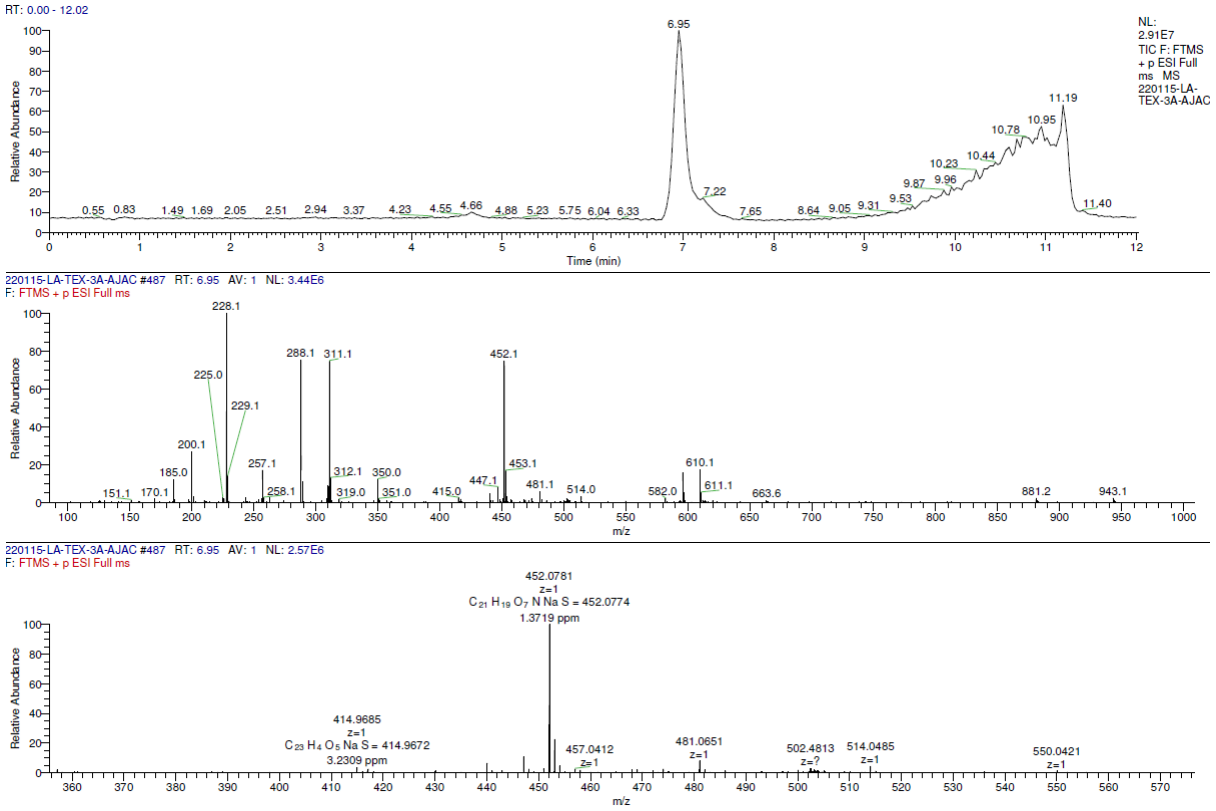
^{13}C NMR (100 MHz, $CDCl_3$)



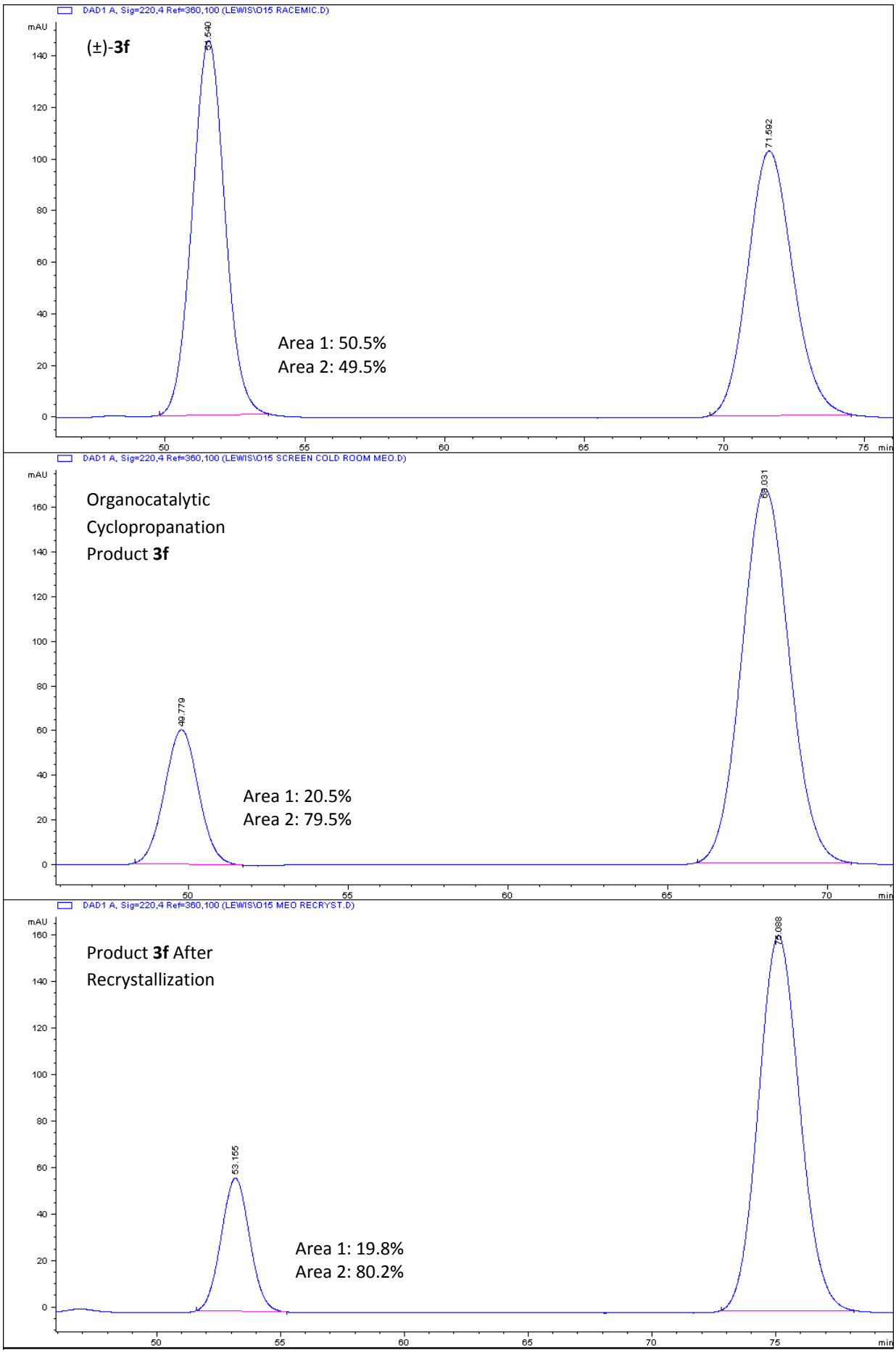


IR Spectrum of **3f**

MS Profile of **3f**

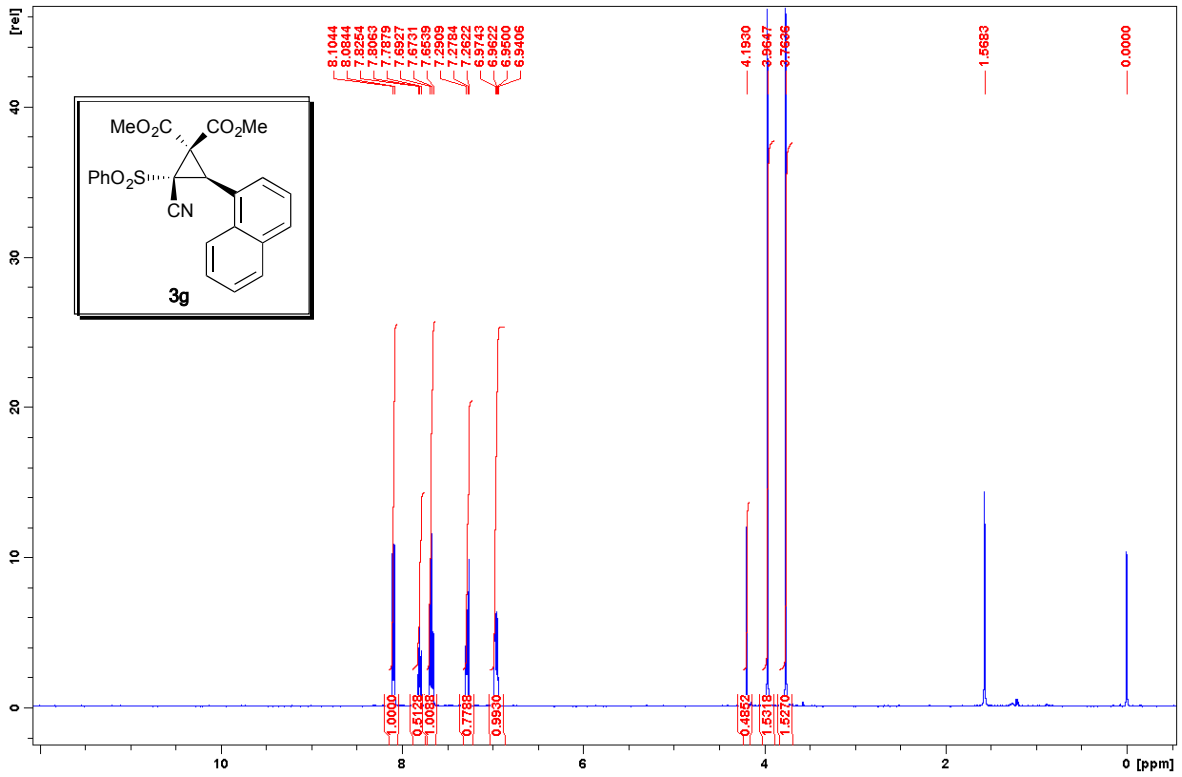


HPLC Traces for **3f** : racemic (top), obtained (middle), recrystallized (bottom)

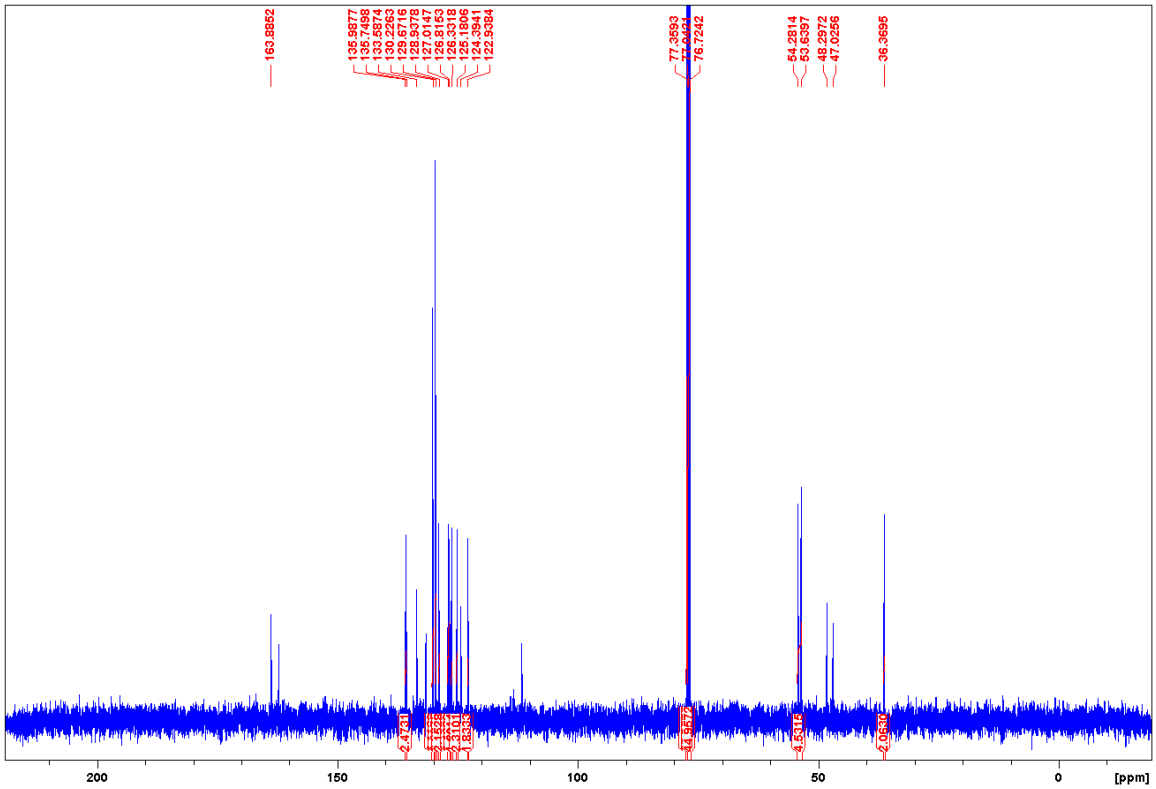


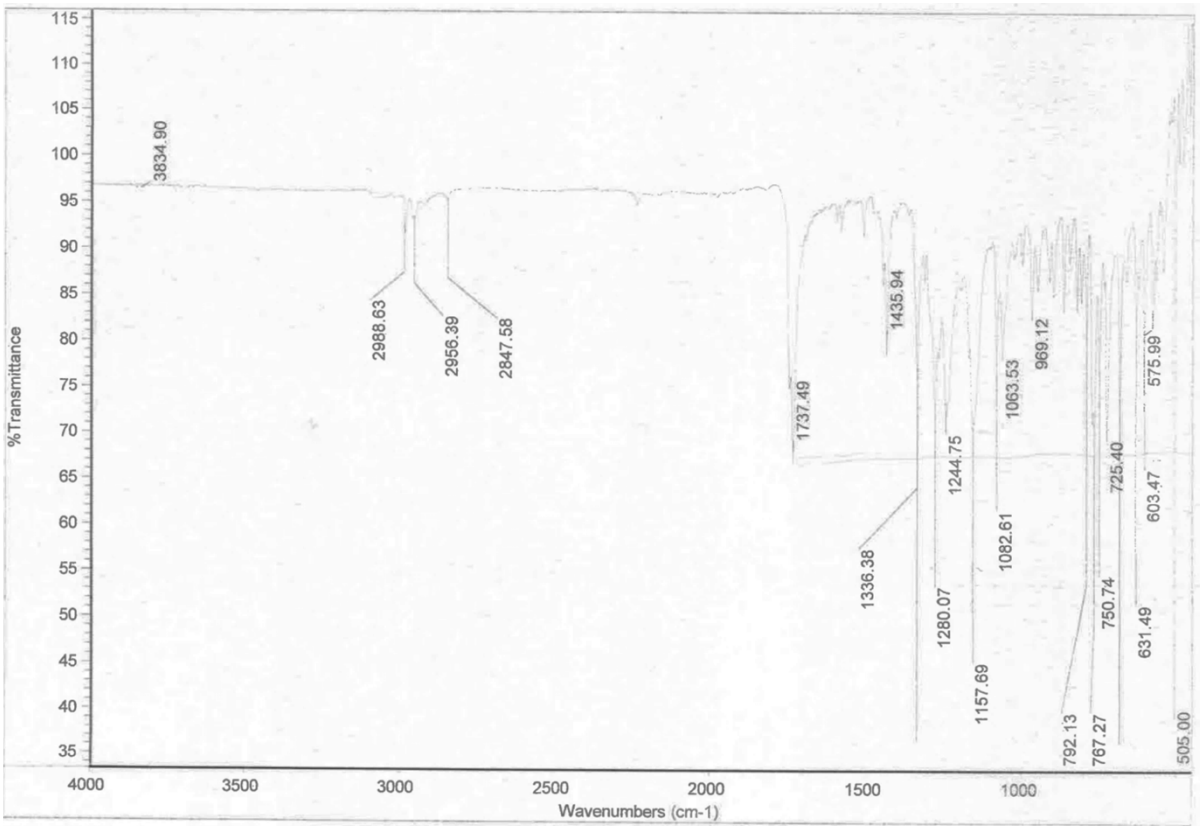
6.7 Dimethyl (2S,3R)-2-cyano-3-(naphthalen-1-yl)-2-(phenylsulfonyl)cyclopropane-1,1-dicarboxylate **3g**

^{1}H NMR (400 MHz, $CDCl_3$)



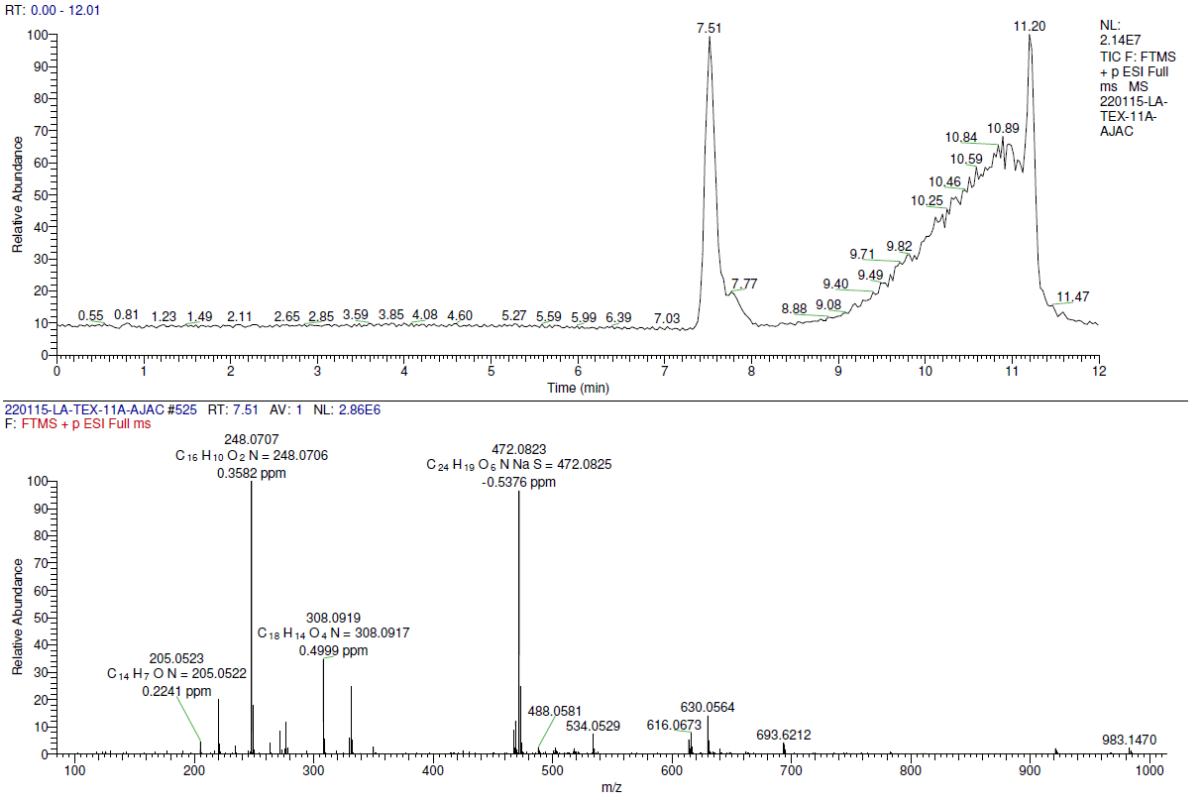
^{13}C NMR (100 MHz, $CDCl_3$)





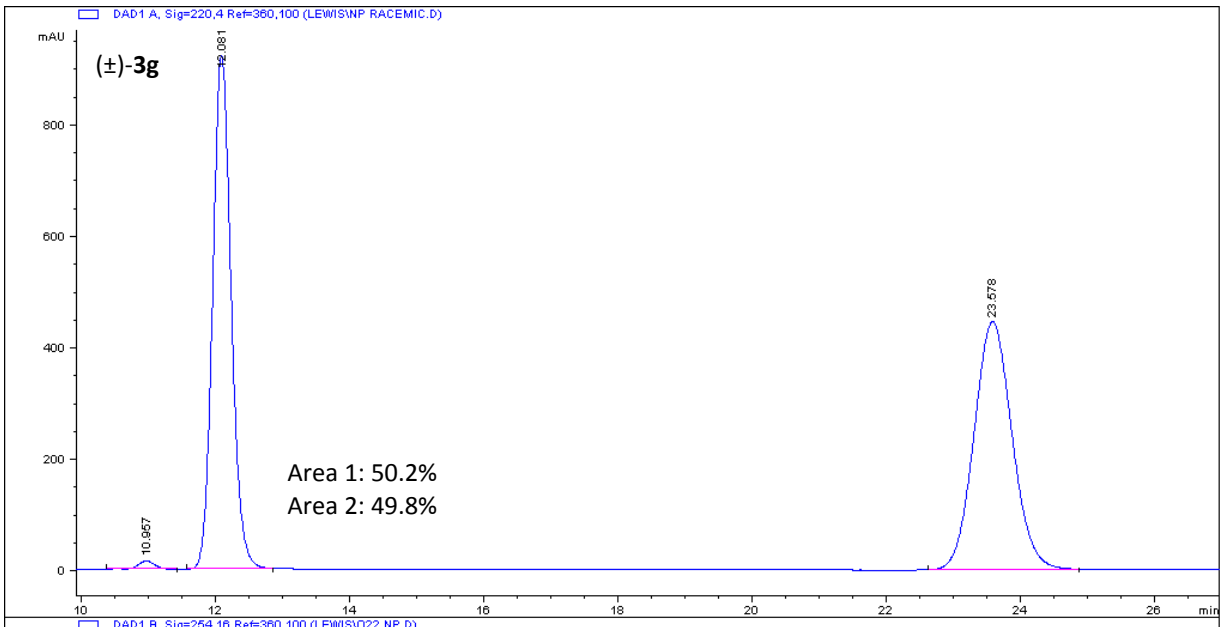
IR Spectrum for **3g**

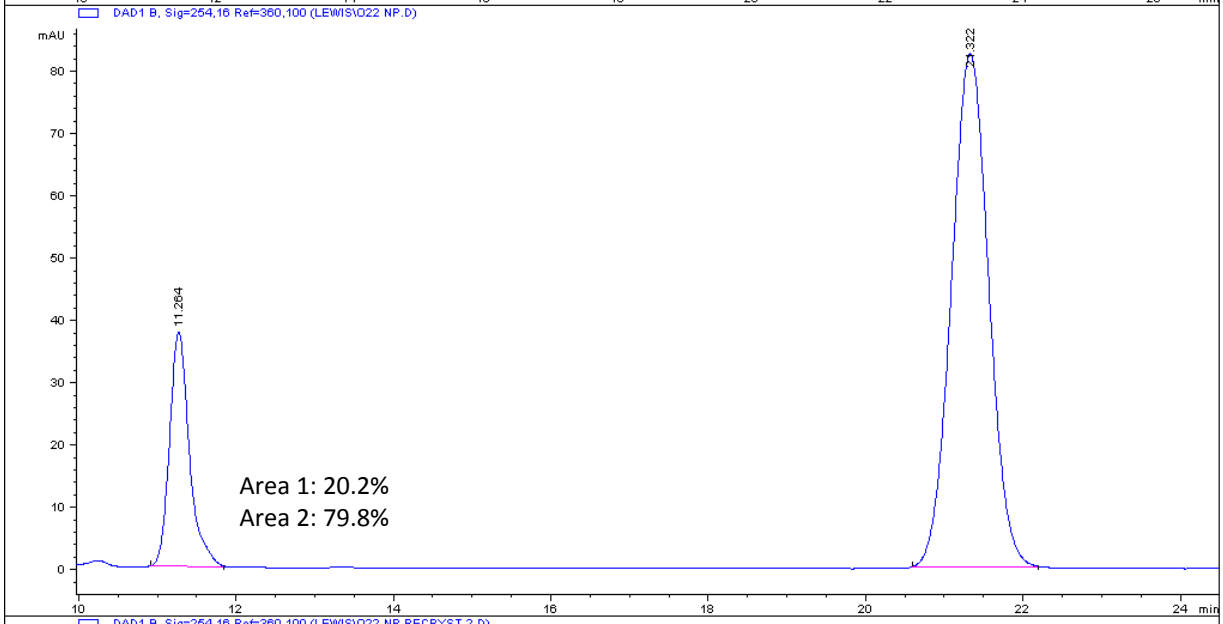
MS Profile for **3g**

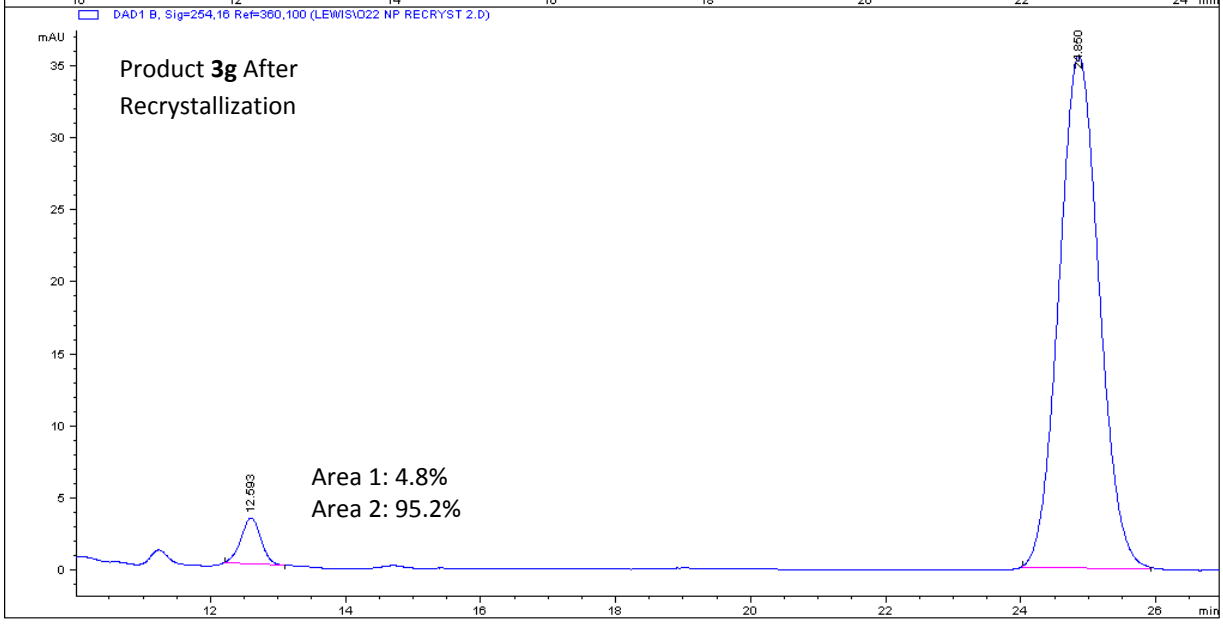


HPLC Traces for **3g** : racemic (top), obtained (middle), recrystallized (bottom)

Organocatalytic
Cyclopropanation
Product **3g**

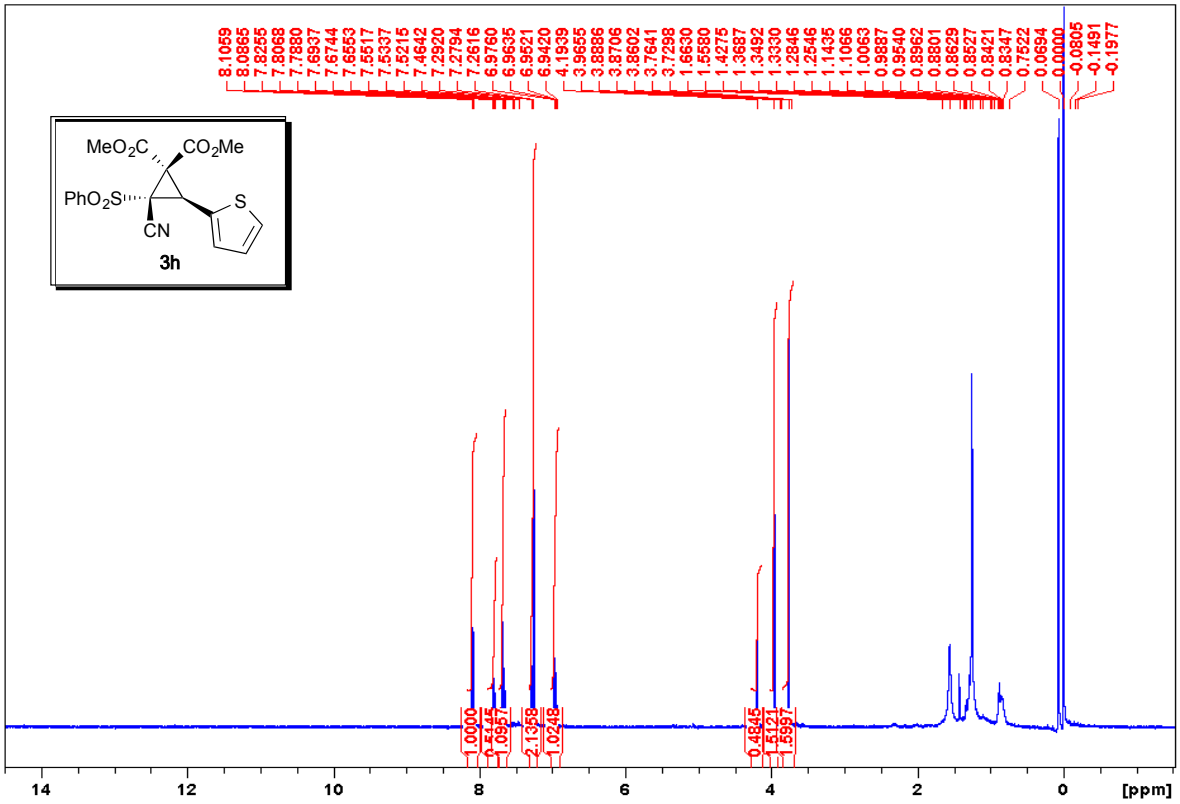




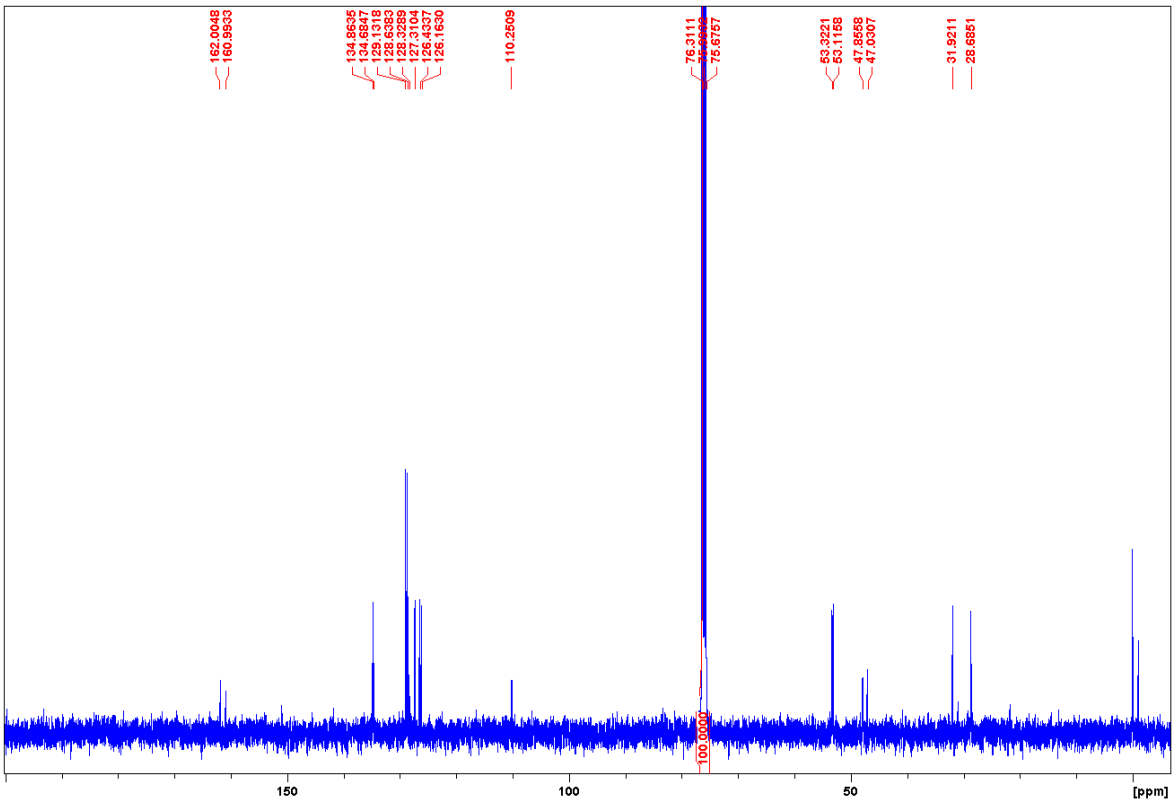


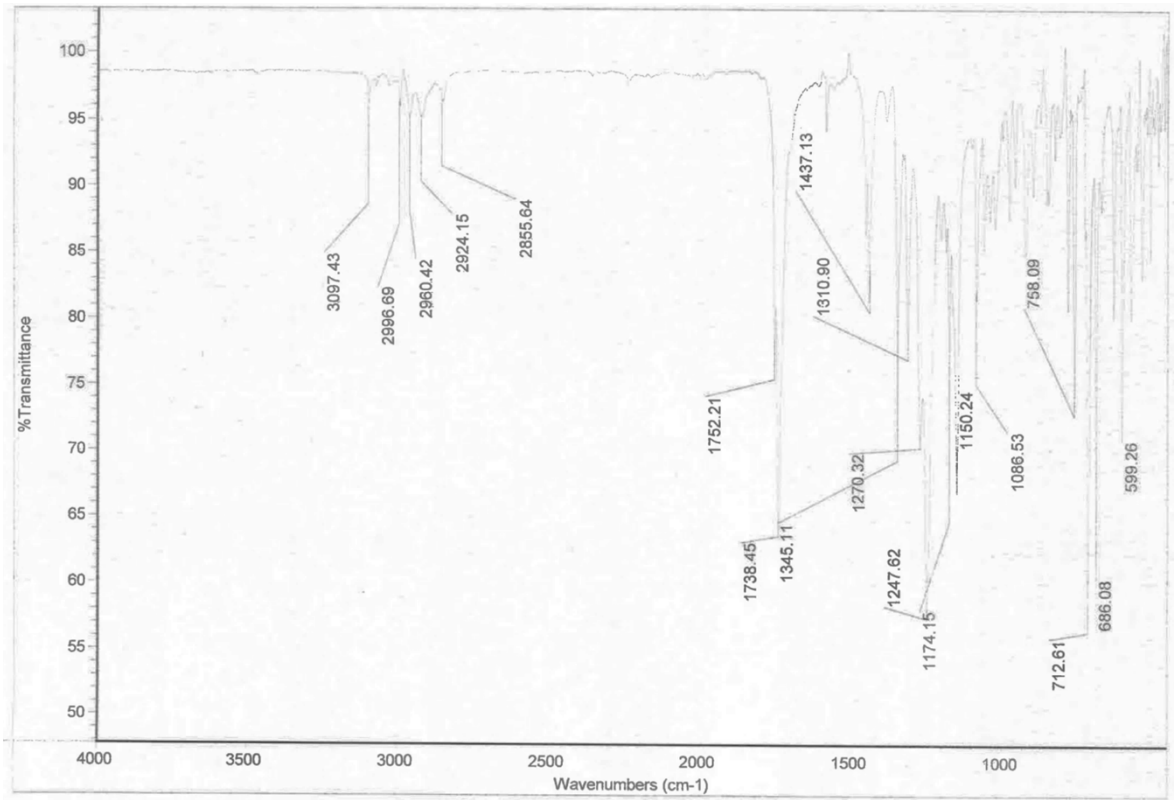
6.8 Dimethyl (2S,3S)-2-cyano-2-(phenylsulfonyl)-3-(thiophen-2-yl)cyclopropane-1,1-dicarboxylate **3h**

^{1}H NMR (400 MHz, $CDCl_3$)



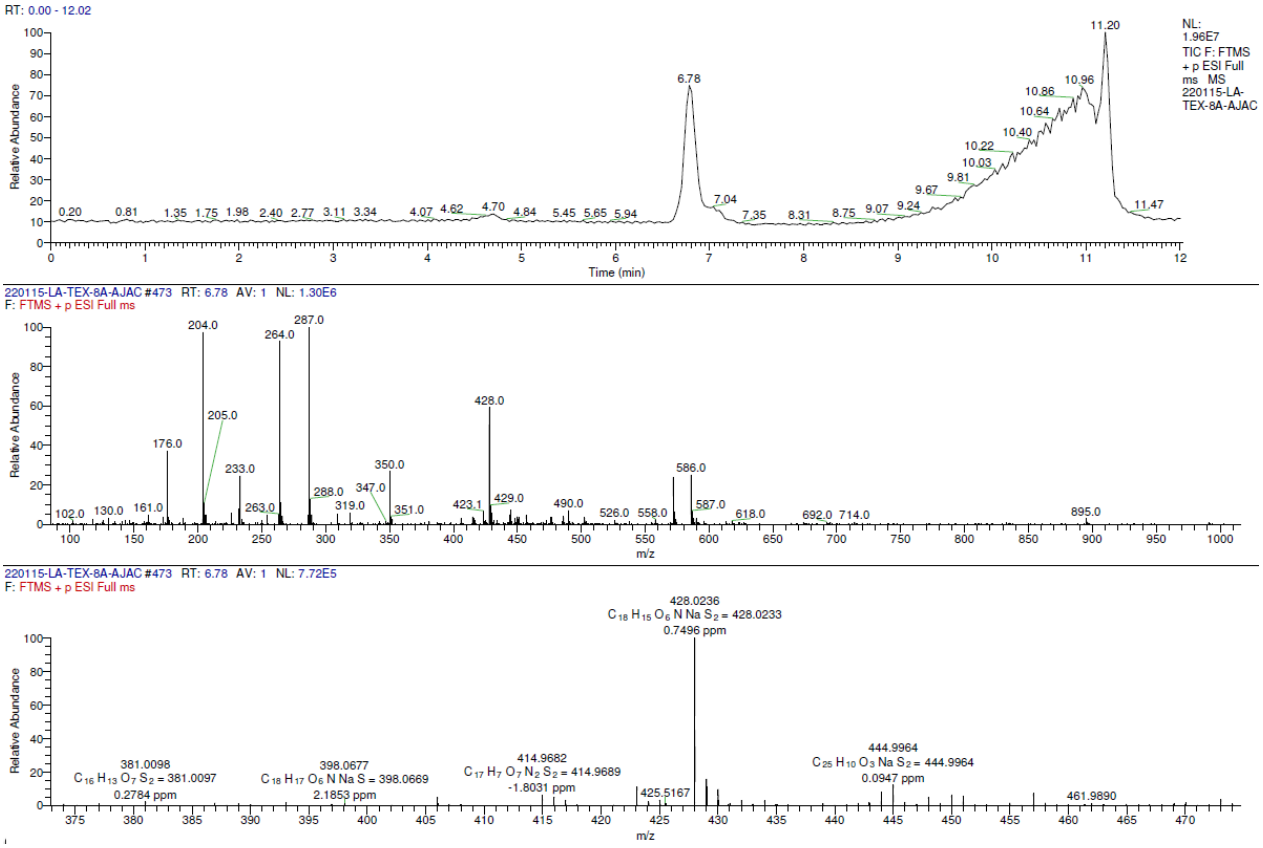
^{13}C NMR (100 MHz, $CDCl_3$)



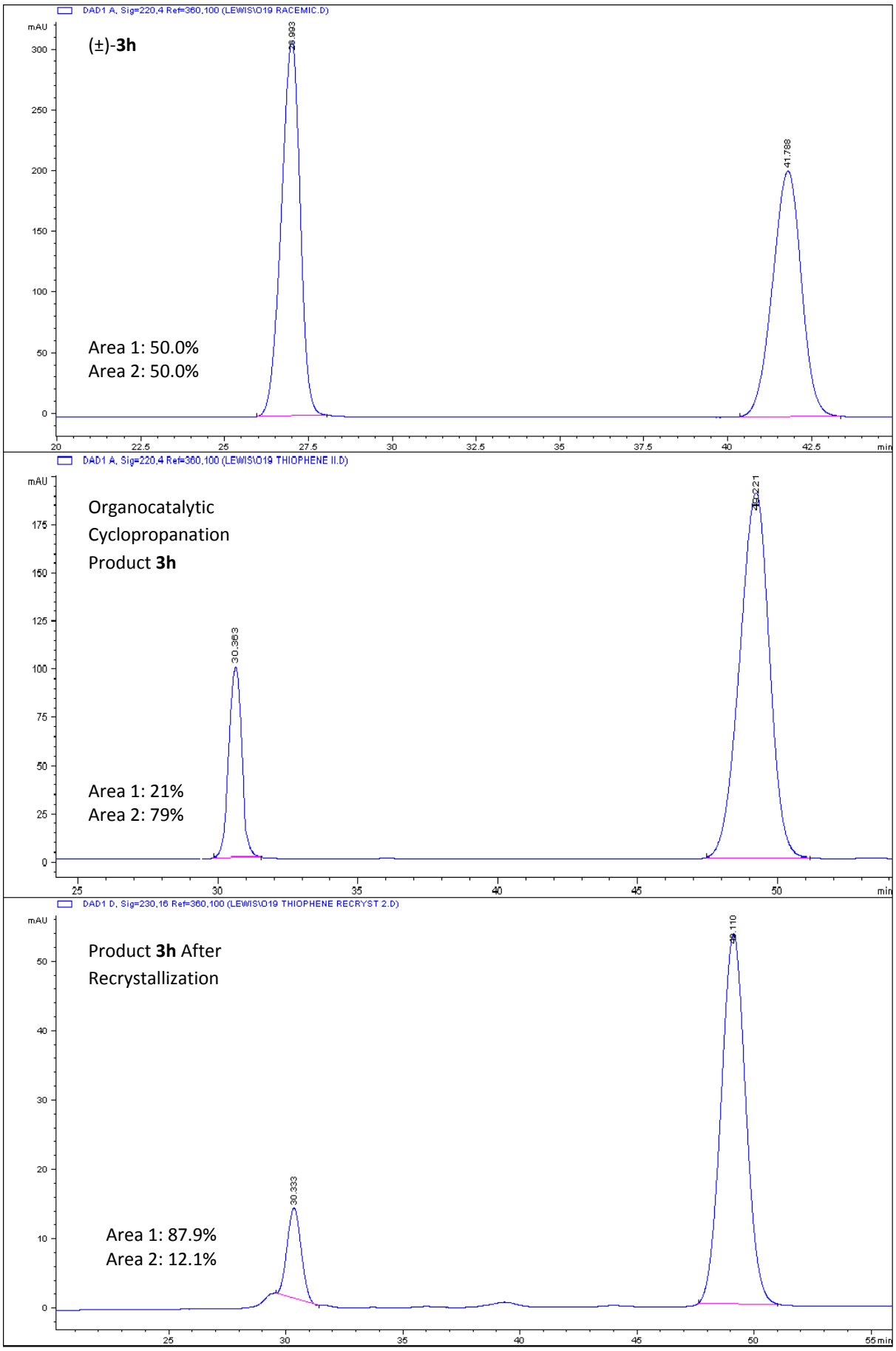


IR Spectrum of **3h**

MS Profile for **3h**

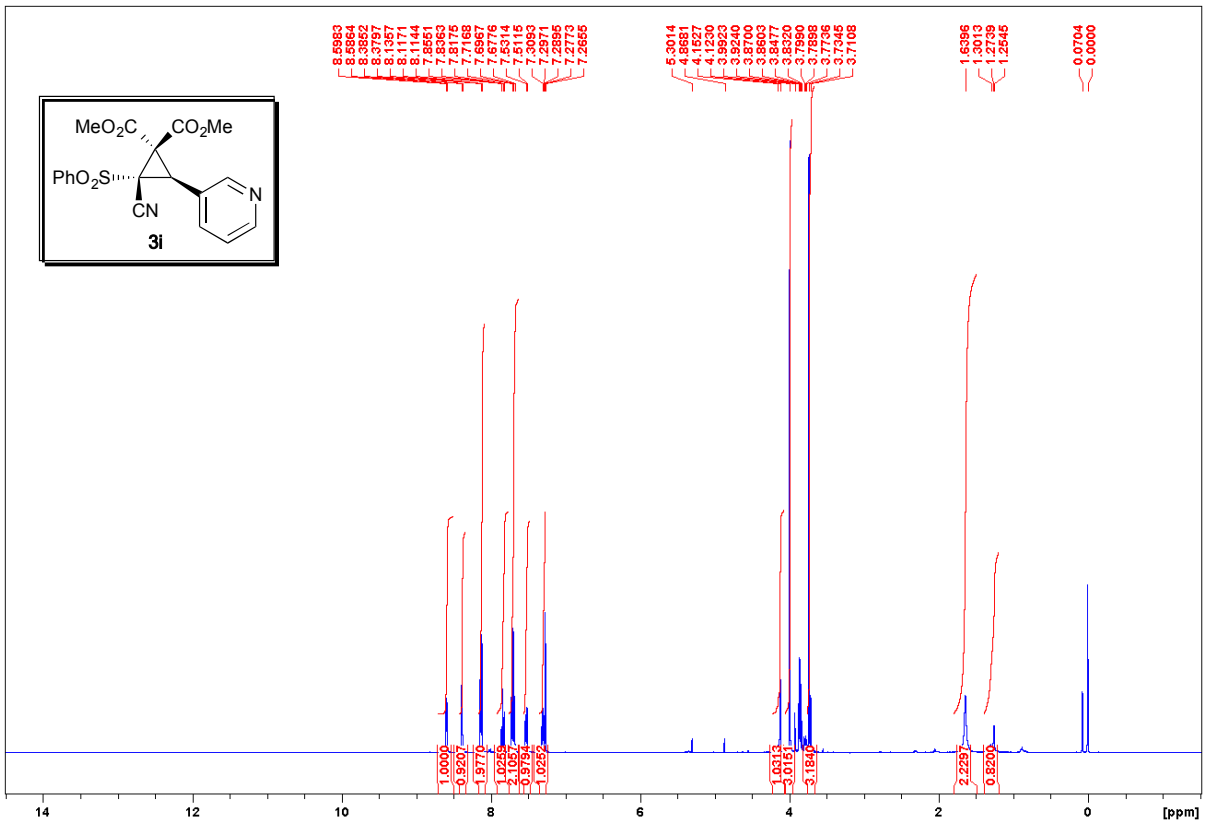


HPLC Traces for **3h** : racemic (top), obtained (middle), recrystallized (bottom)

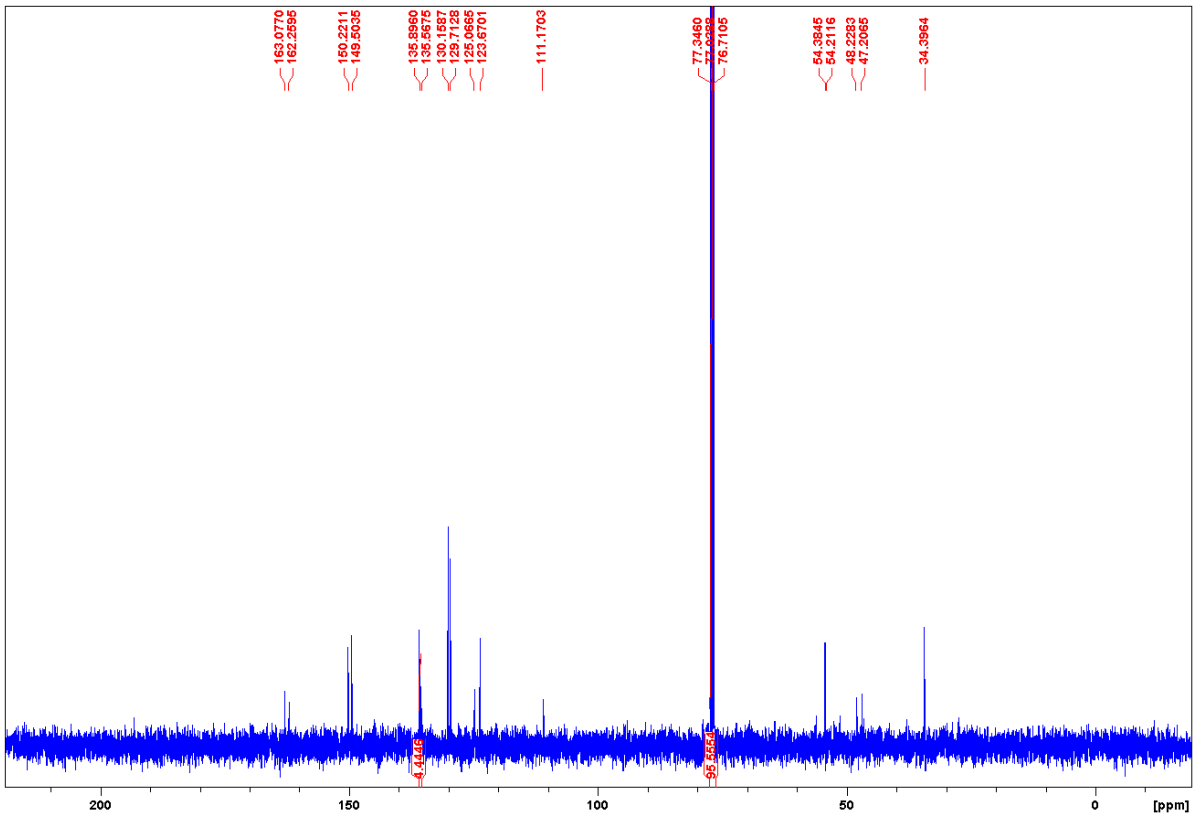


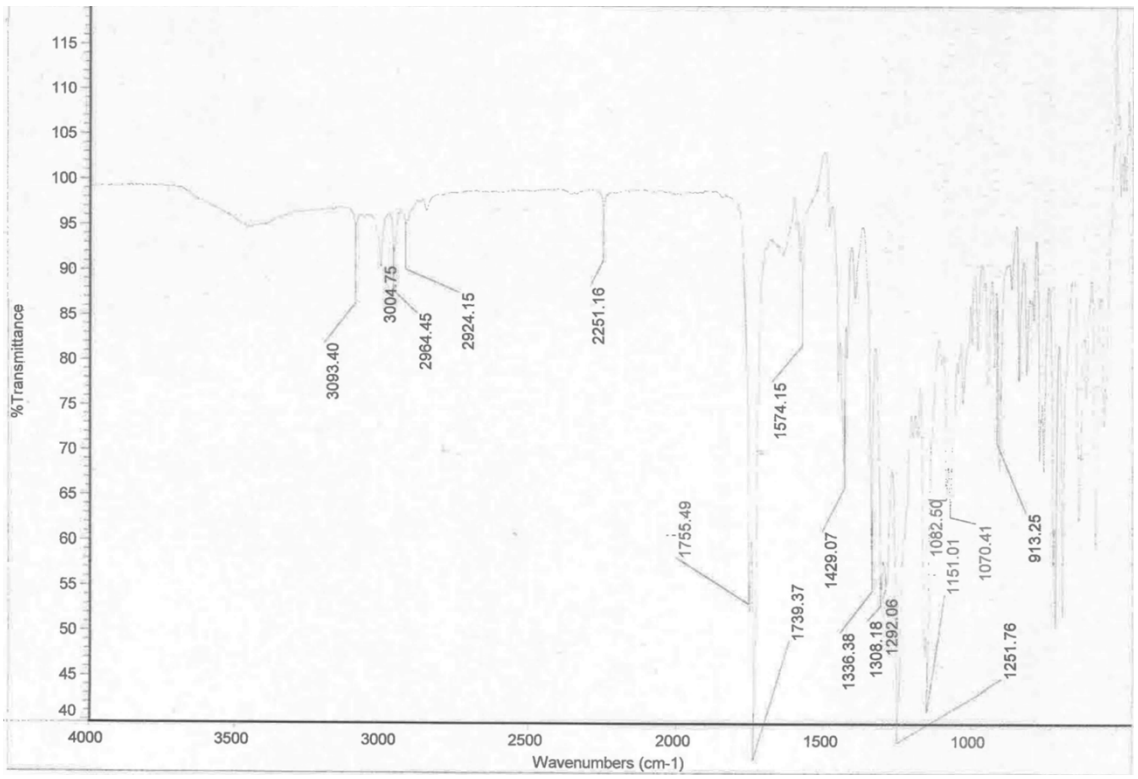
6.9 Dimethyl (2*S*,3*R*)-2-cyano-2-(phenylsulfonyl)-3-(pyridin-3-yl)cyclopropane-1,1-dicarboxylate **3i**

^{1}H NMR (400 MHz, $CDCl_3$)



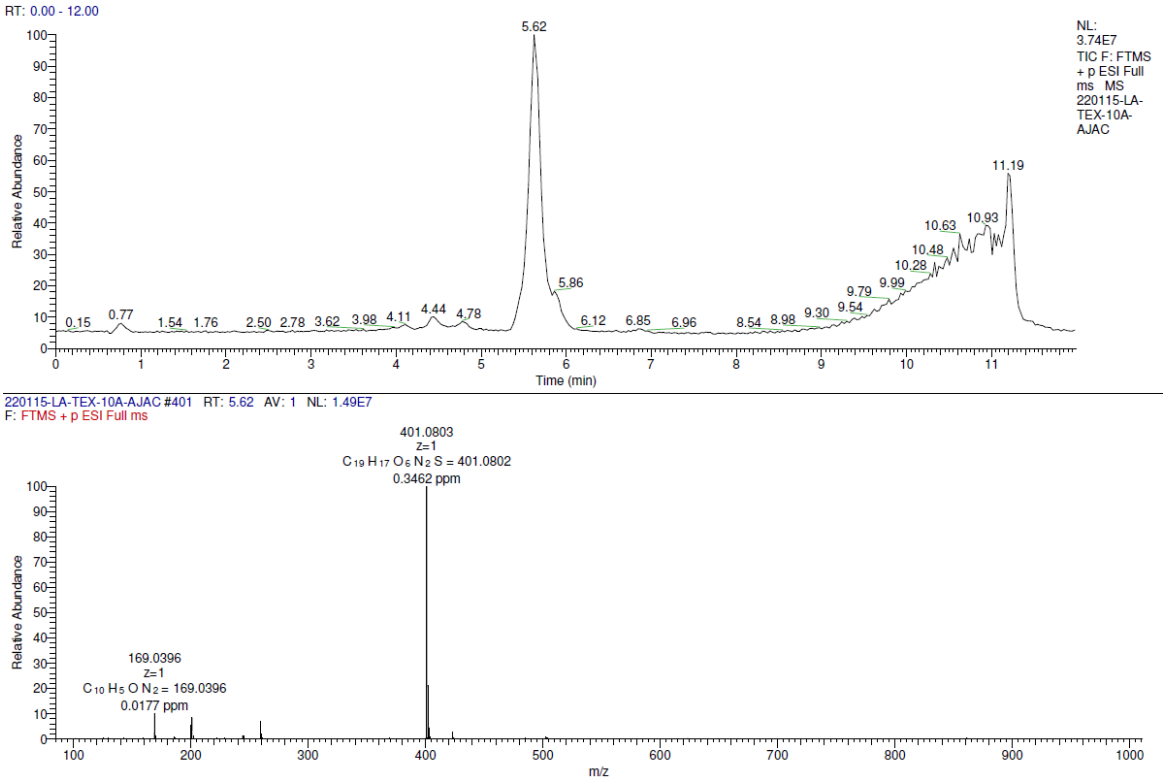
^{13}C NMR (100 MHz, $CDCl_3$)



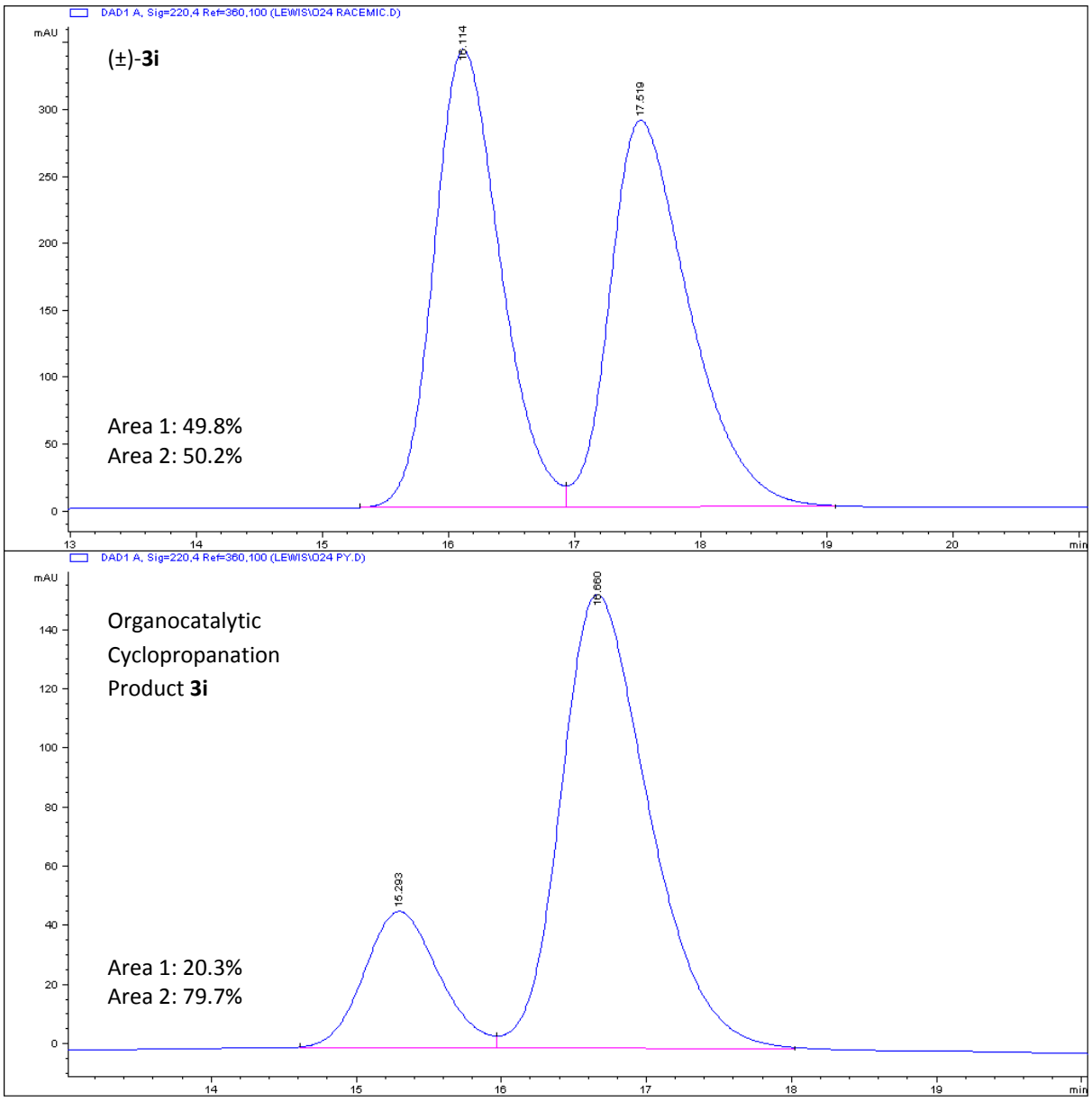


IR Spectrum of **3i**

MS Profile for **3i**

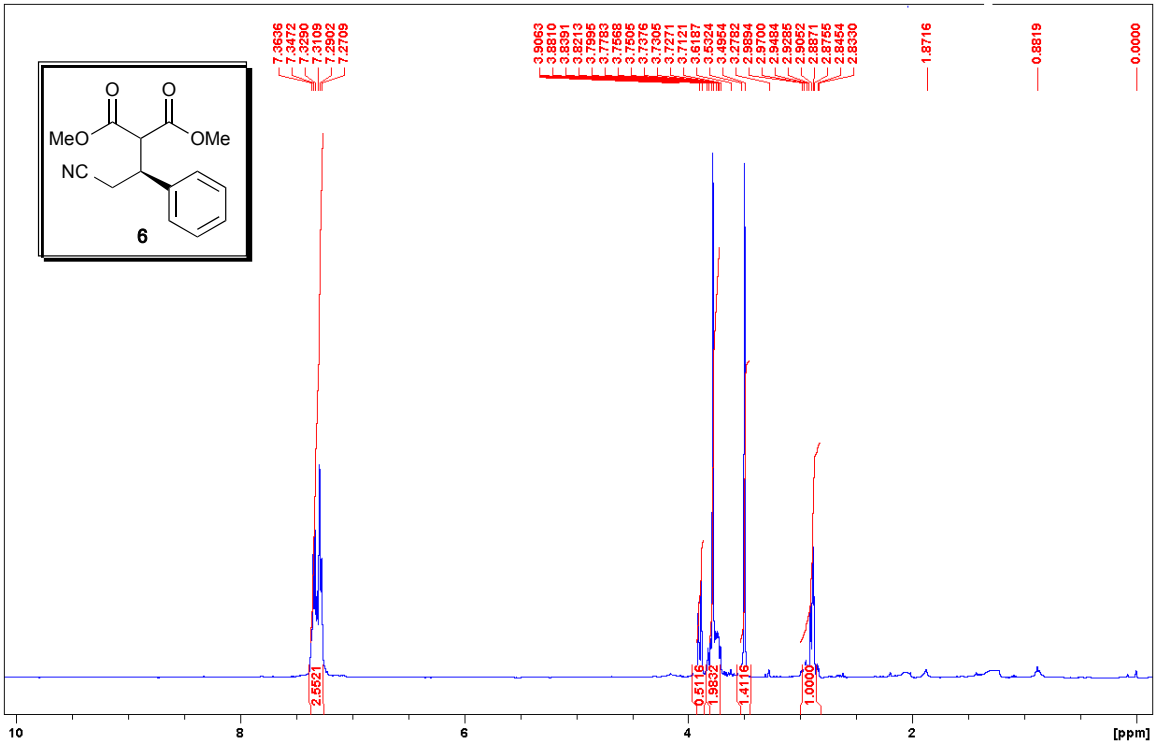


HPLC Traces for **3i** : racemic (top), obtained (bottom)

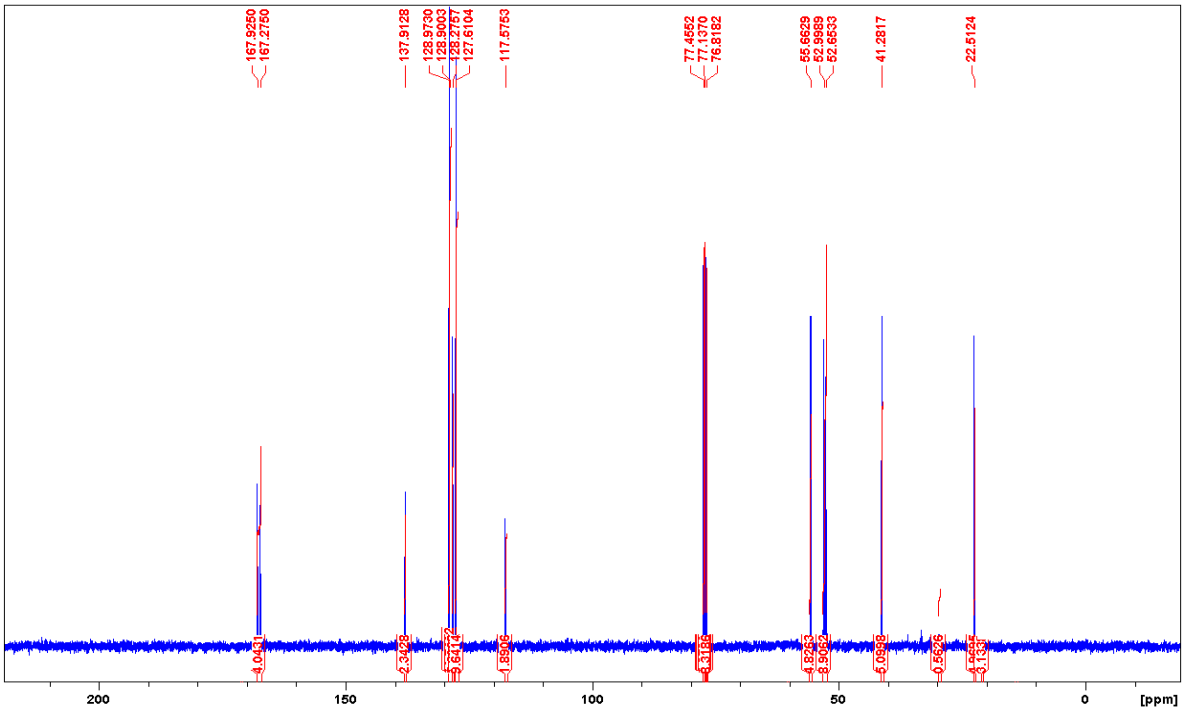


6.10 Dimethyl (*S*)-2-(2-cyano-1-phenylethyl)malonate **6**

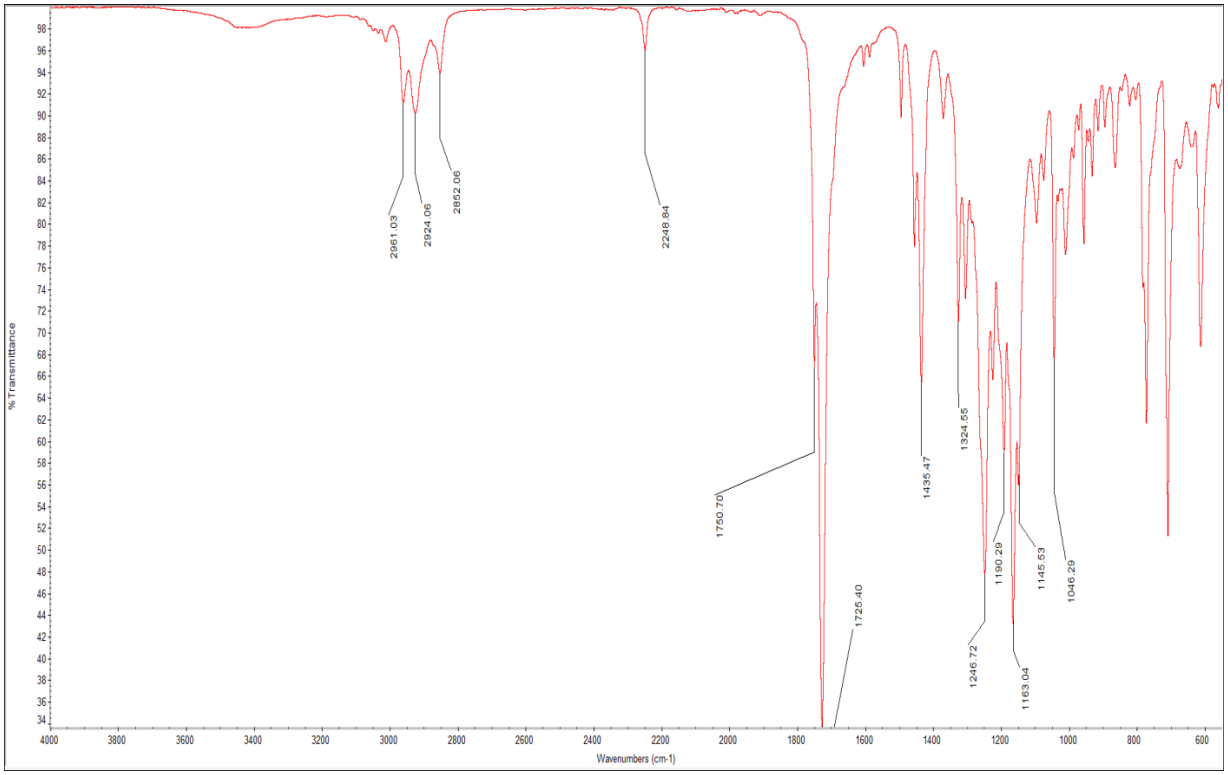
^{1}H NMR (400 MHz, $CDCl_3$)



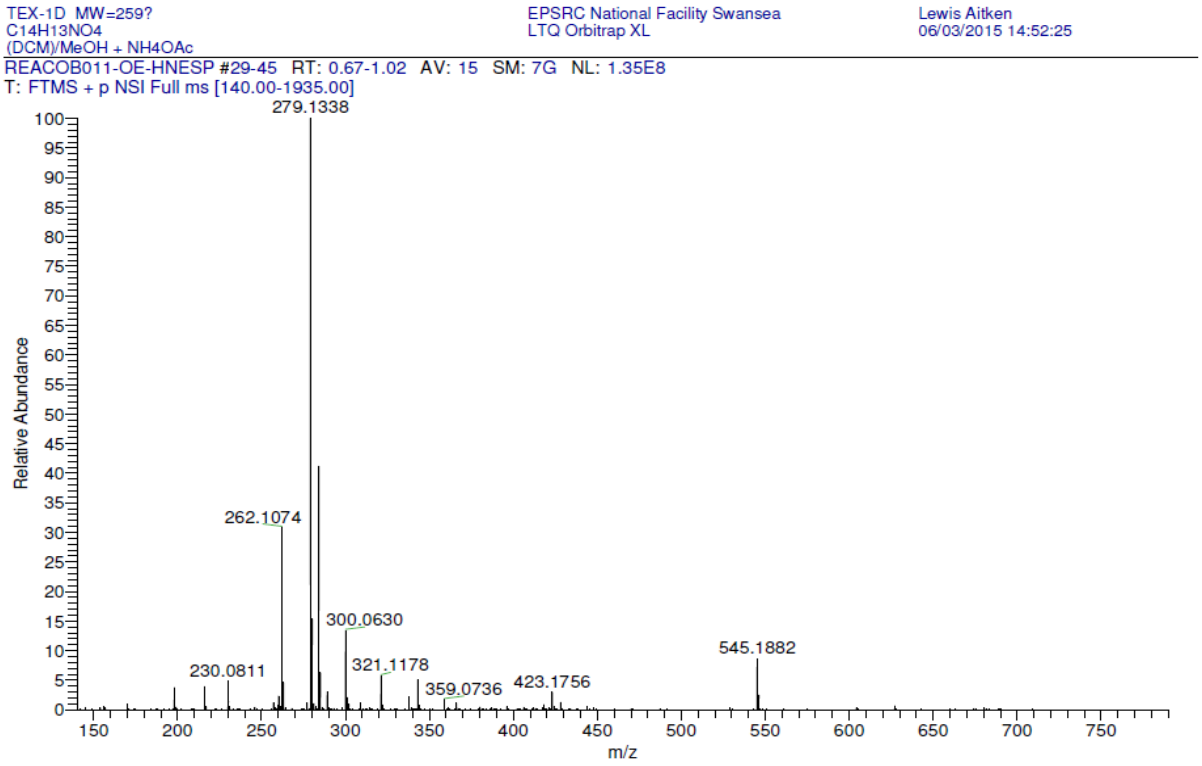
^{13}C NMR (100 MHz, $CDCl_3$)



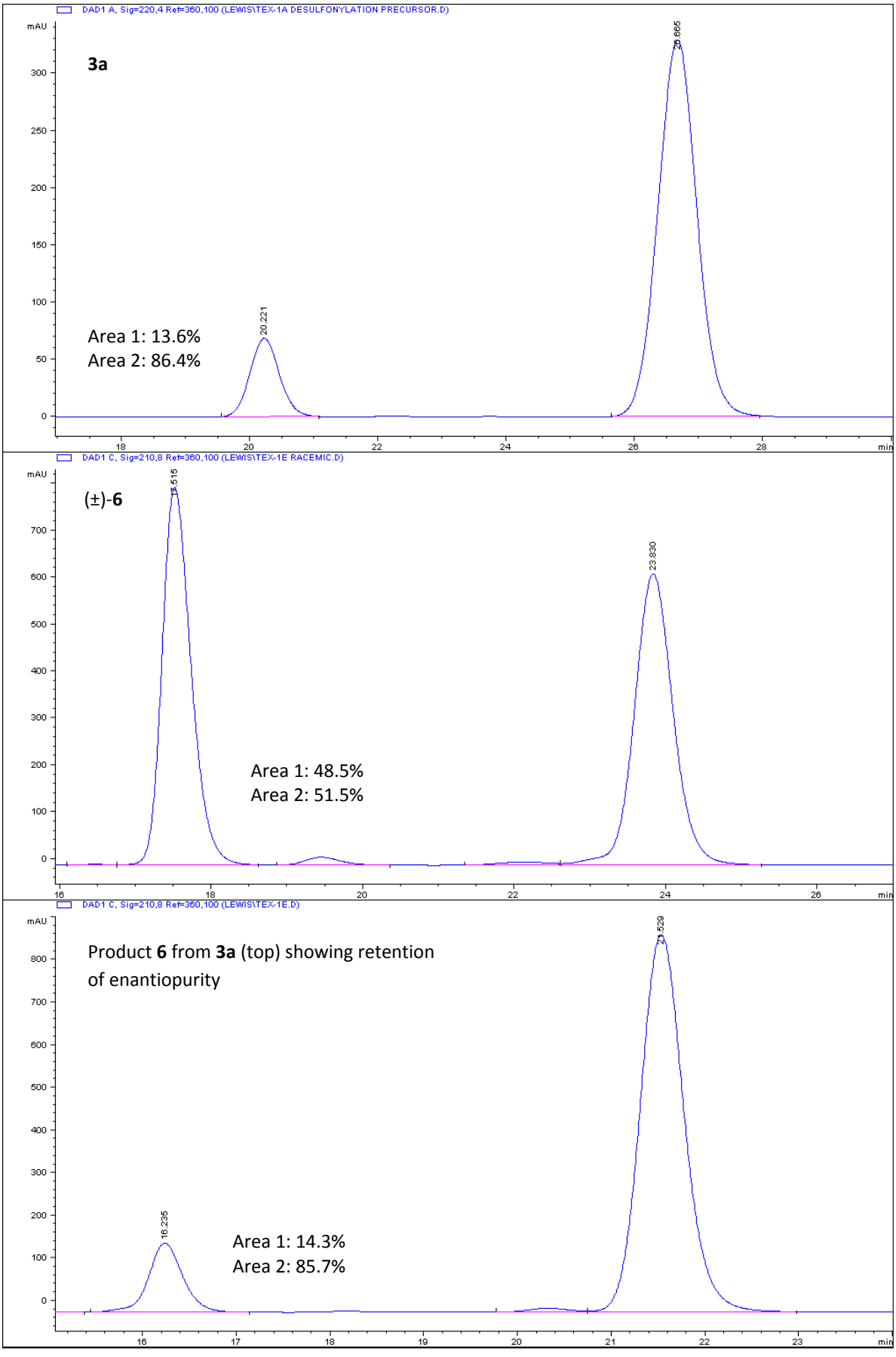
IR Spectrum of **6**



MS Profile of **6**

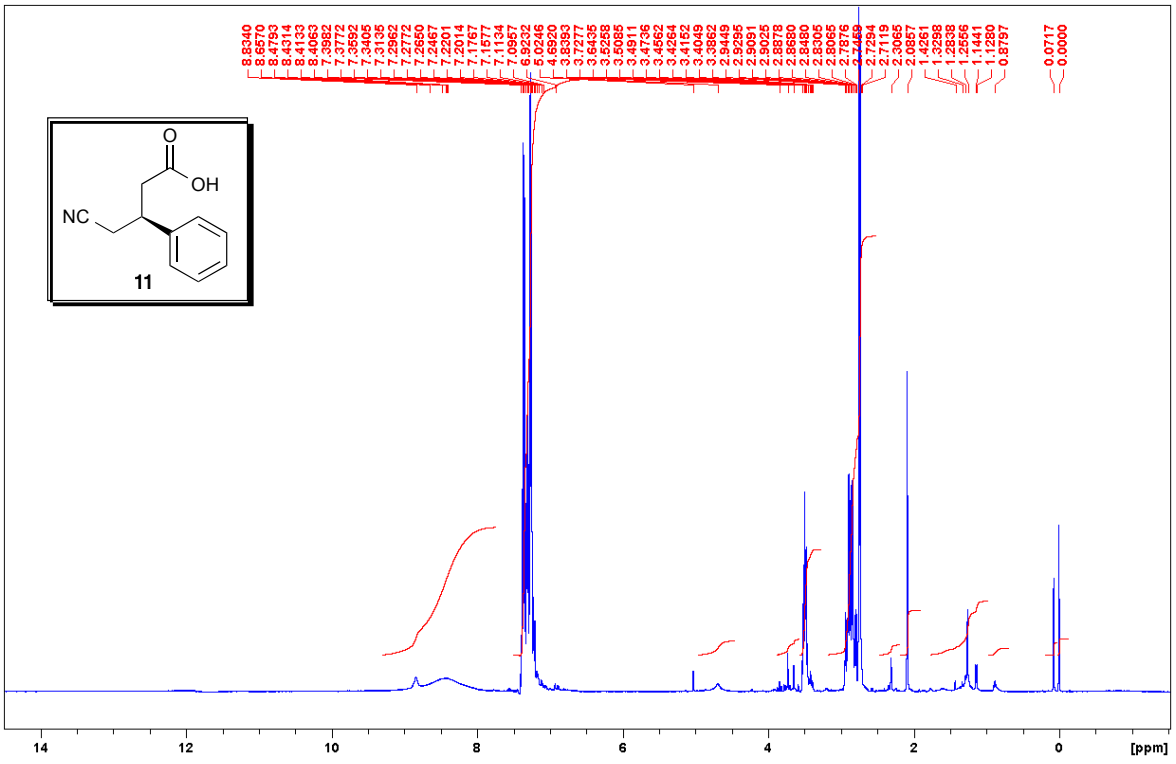


HPLC Traces for **3h** : HPLC trace of starting material **3a** (top - less pure enantiomeric excess from catalyst screen deliberately used in order to assess the integrity of the stereogenic center), racemic trace of **6** (middle), trace for **6** showing retention of enantiomeric excess (bottom).

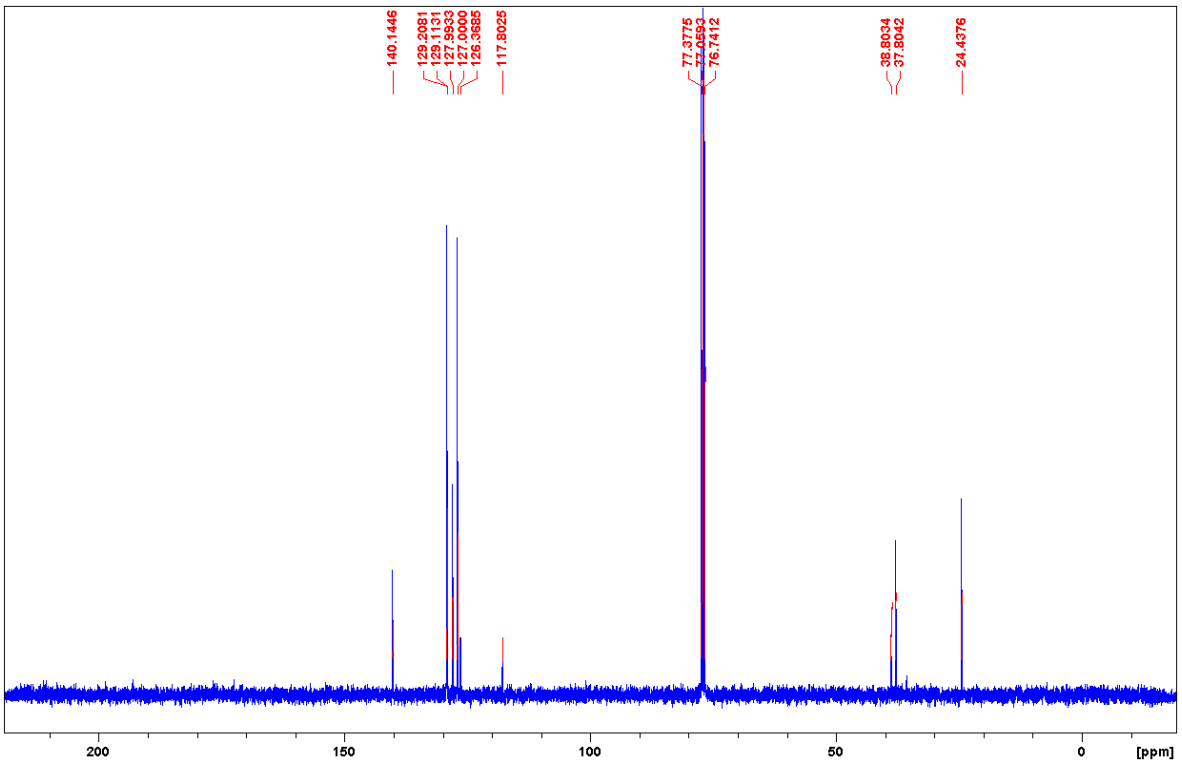


6.11 (*S*)-4-cyano-3-phenylbutanoic acid **11**

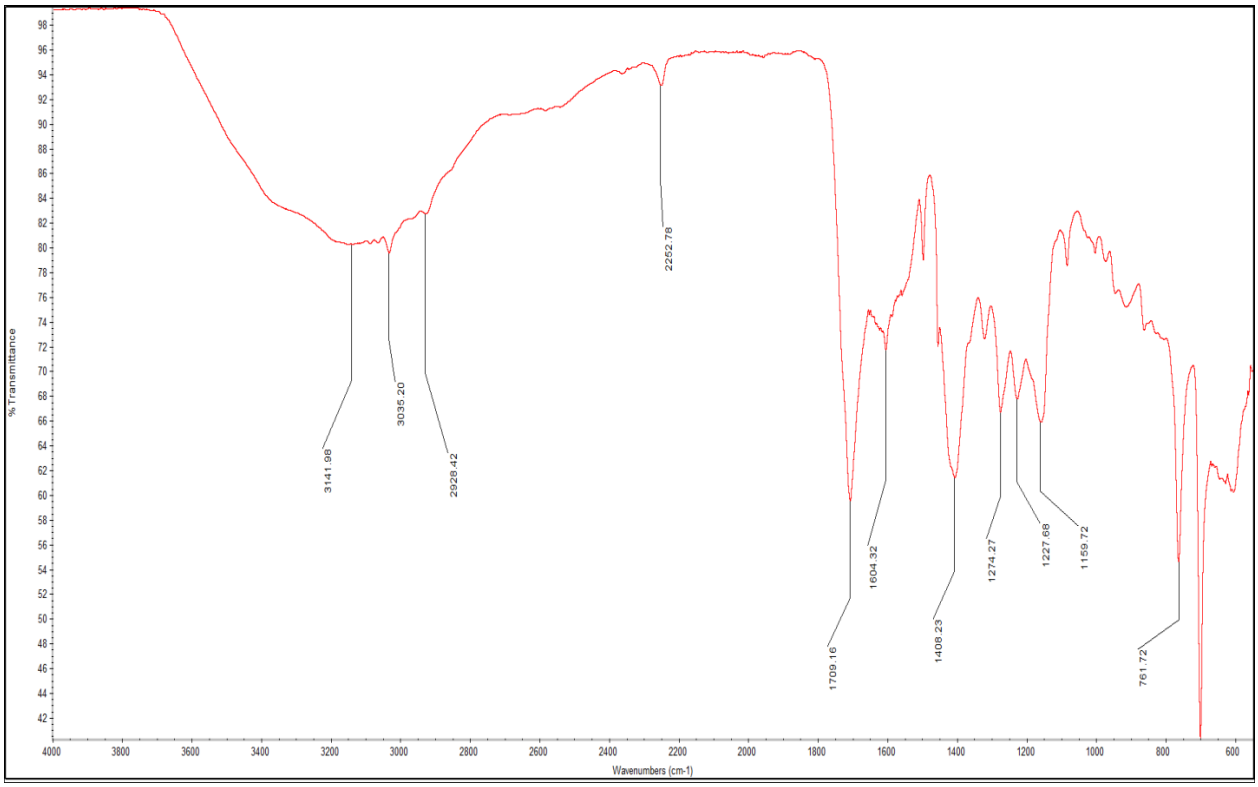
^{1}H NMR (400 MHz, $CDCl_3$)



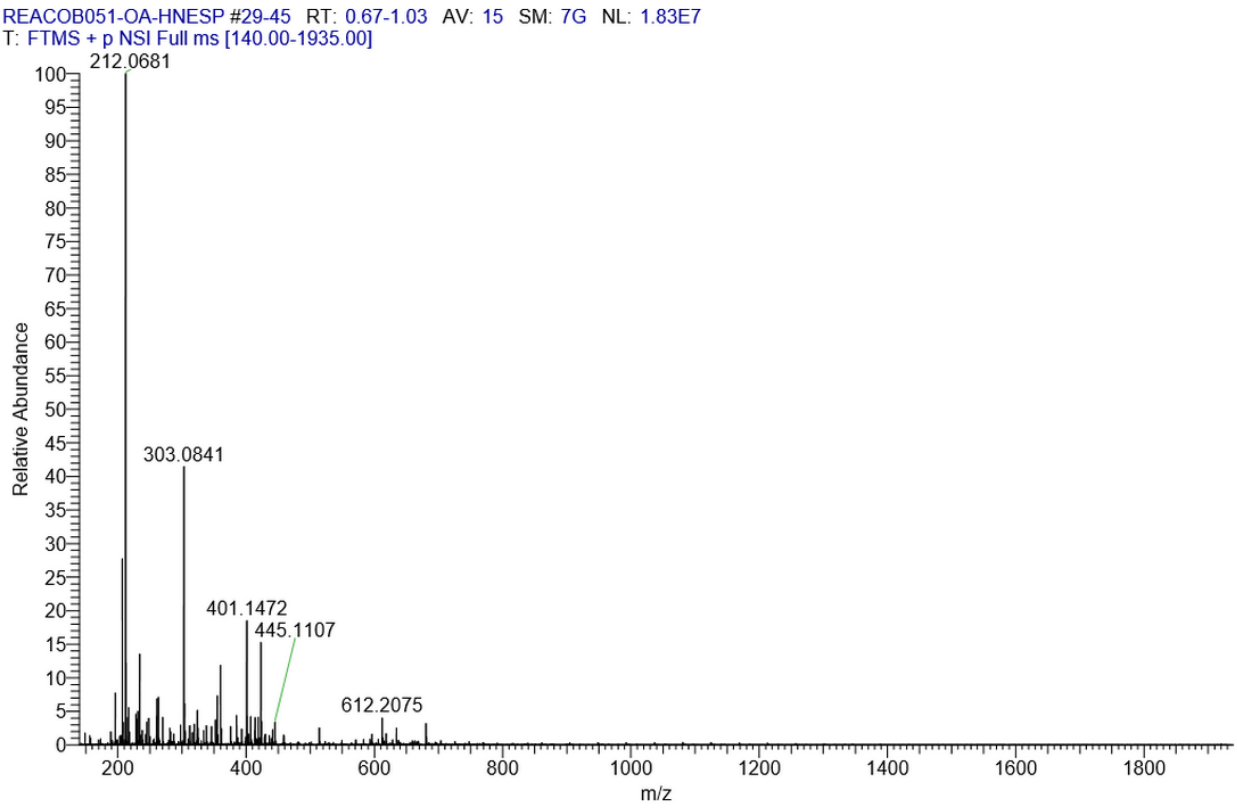
^{13}C NMR (100 MHz, $CDCl_3$)



IR Spectrum of **11**

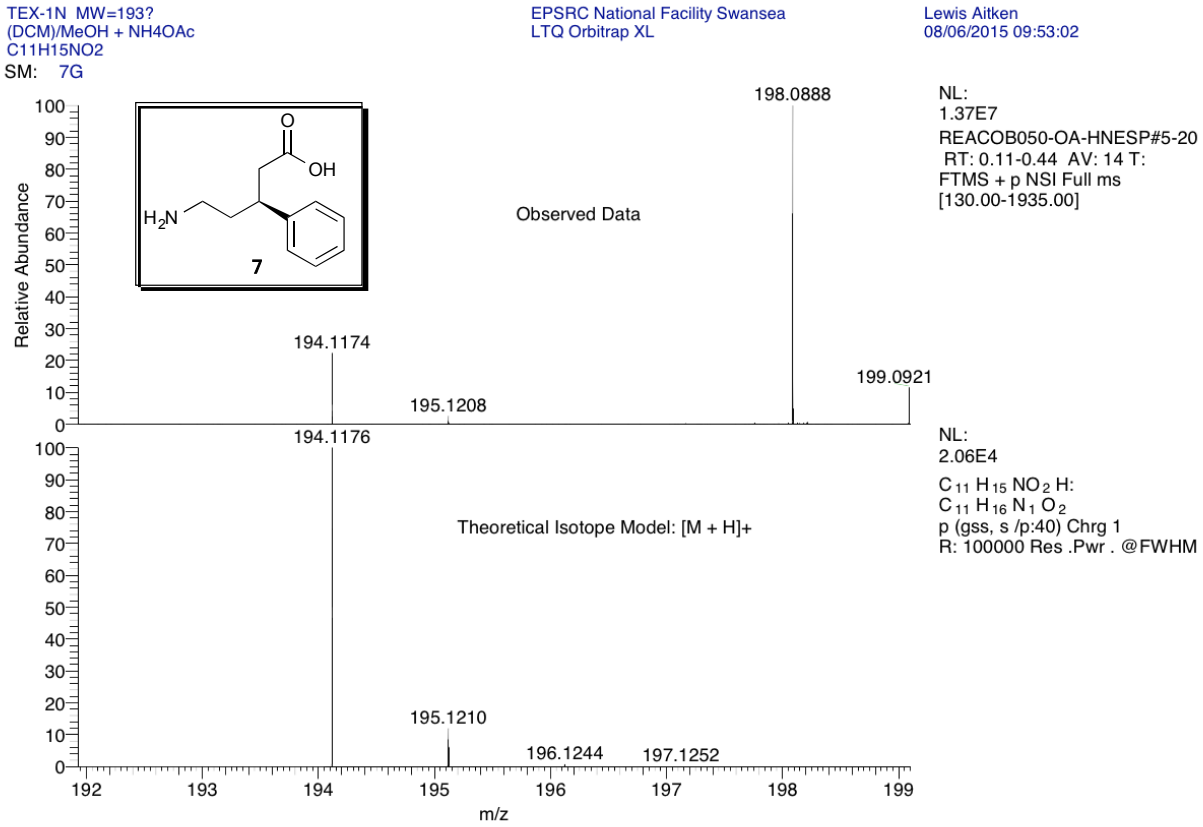


MS Profile for **11**



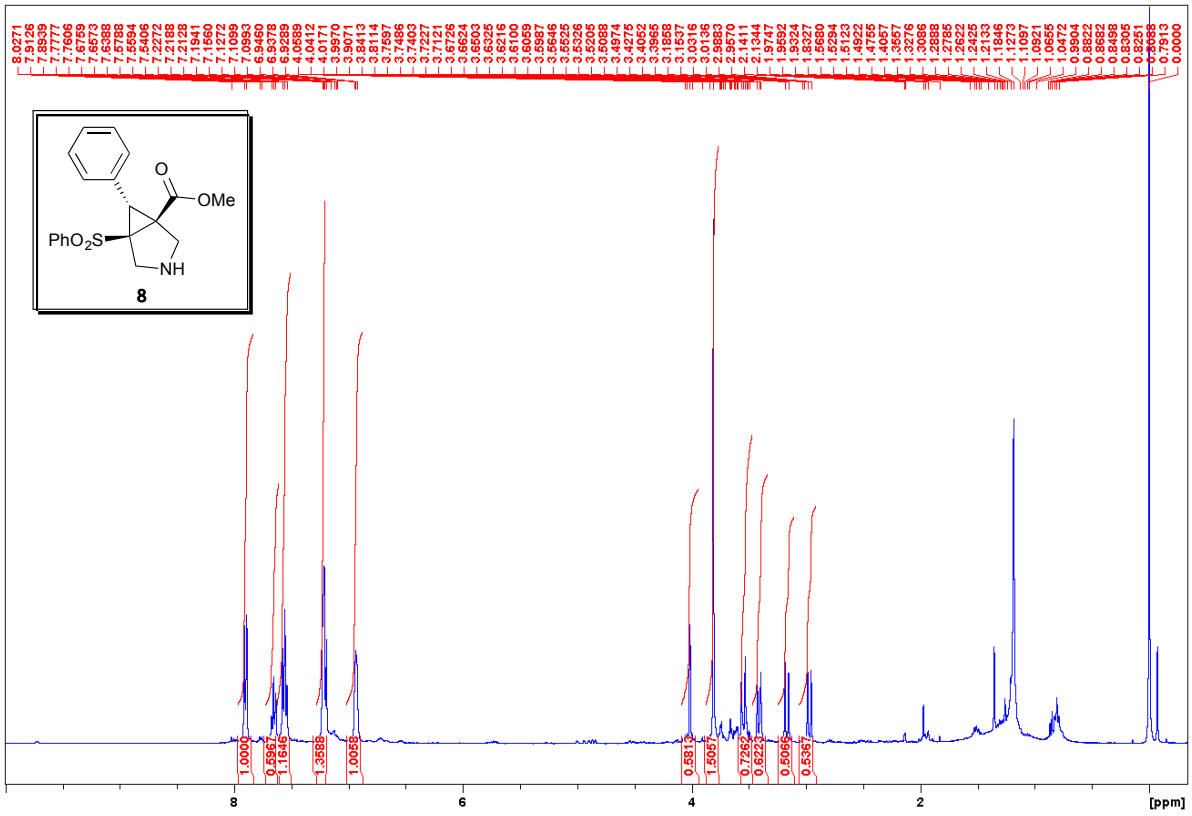
6.12 (*S*)-5-amino-3-phenylpentanoic acid **7**

MS Profile for **7**

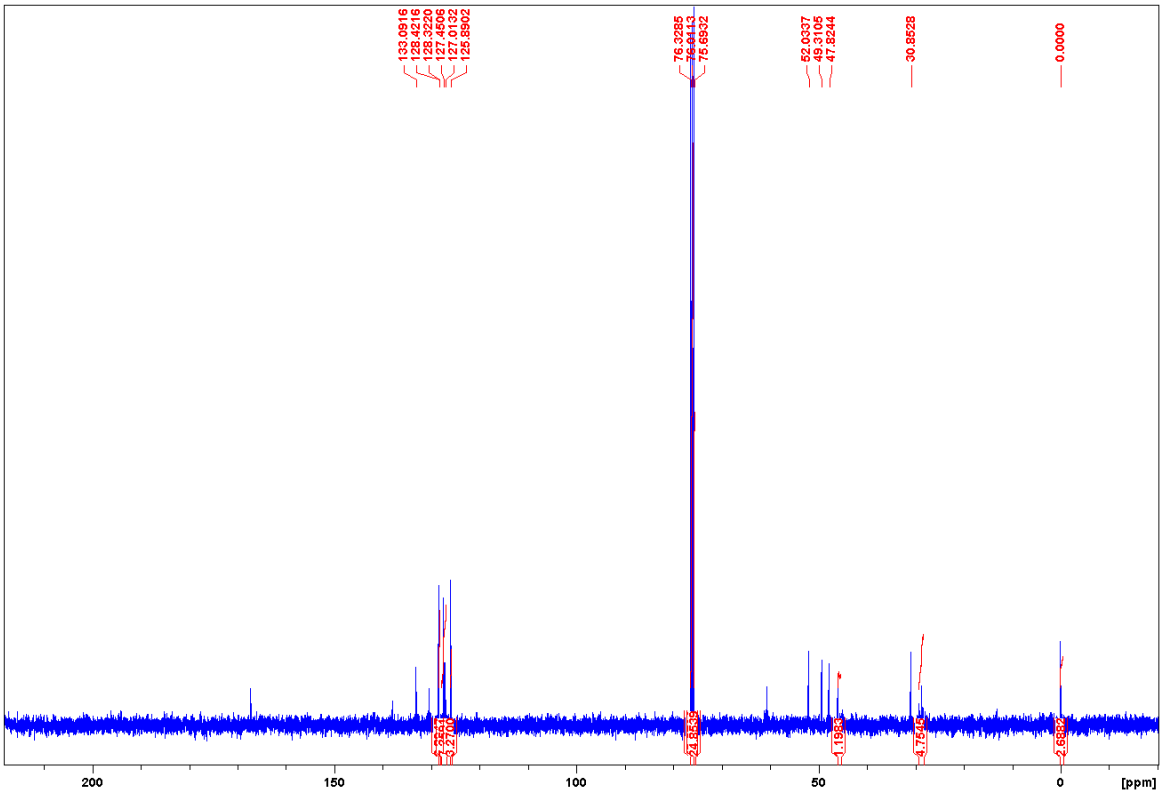


6.13 Methyl-(1*R*,5*S*,6*R*)-6-phenyl-5-(phenylsulfonyl)-3-azabicyclo[3.1.0]hexane-1-carboxylate **8**

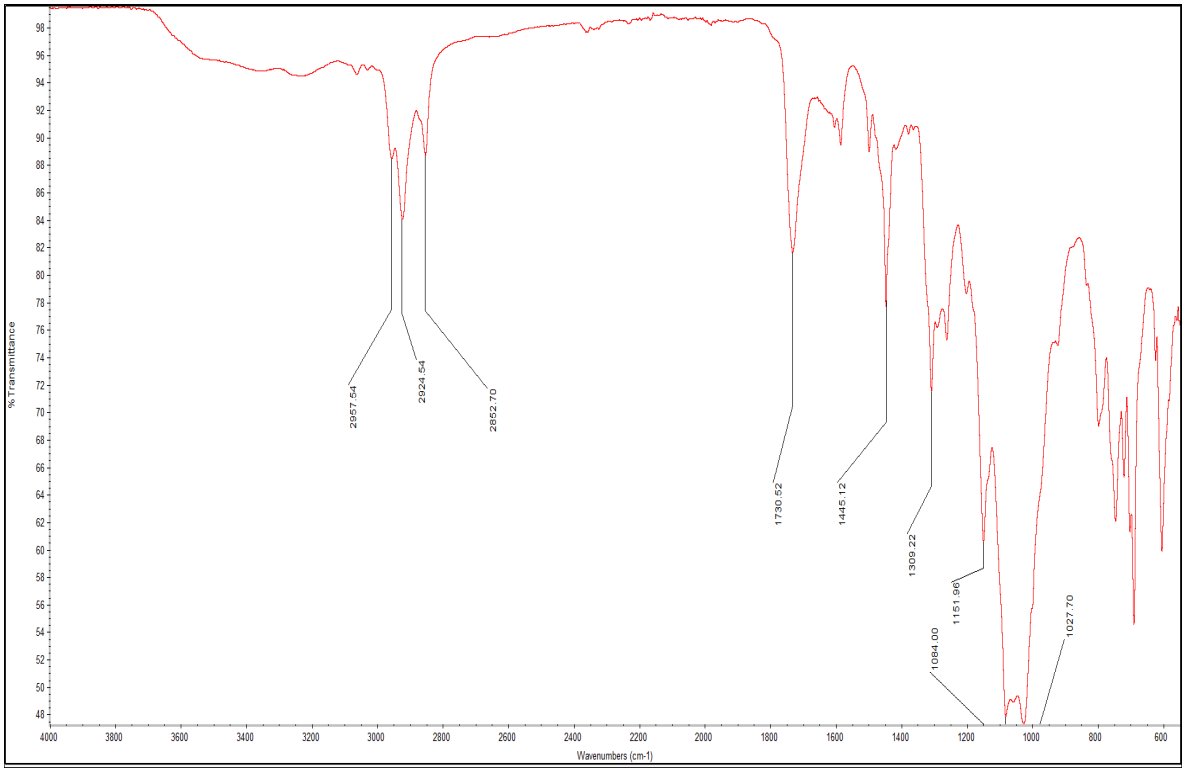
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)



IR Spectrum of **8**



MS Profile of **8**