Supporting Information

A Three Component 1,3-Difunctionalization of Vinyl Diazo Esters Enabled by a Cobalt Catalyzed C–H Activation/Carbene Migratory Insertion

Nandkishor Prakash Khot, Prajyot Jayadev Nagtilak, Nitish Kumar Deo, and Manmohan Kapur*

[a] Department of Chemistry, Indian Institute of Science Education and Research Bhopal, Bhopal Bypass Road, Bhauri, Bhopal 462066, MP, India.
E-mail: mk@iiserb.ac.in

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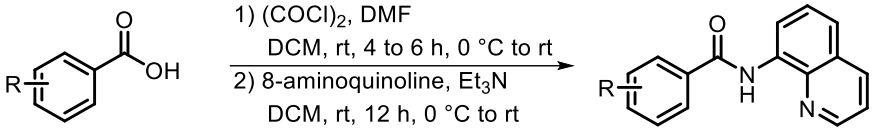
Experimental:

(1) General Methods:

All commercially available compounds were used without purification. Unless otherwise noted, all reactions were performed in oven-dried glassware. All reactions were run under an argon or nitrogen atmosphere. All solvents used in the reactions were purified before use. Dry tetrahydrofuran and toluene were distilled from sodium and benzophenone, whereas dichloroethane was distilled from CaH_2.[1] Petroleum ether with a boiling range of 40−60 °C were used. Melting points are uncorrected. ^{1}H, ^{13}C and ^{19}F NMR: Recorded on Bruker Avance III 400 MHz NMR Spectrometer, Bruker Avance III 500 MHz NMR Spectrometer and Bruker Avance III 700 MHz NMR Spectrometer; spectra were recorded at 295 K in $CDCl_3$; chemical shifts are calibrated to the residual proton and carbon resonance of the solvent: $CDCl_3$ (^{1}H δ 7.26; ^{13}C δ 77.0). HRMS: Bruker Daltonics MicroTOF Q-II with electron spray ionization (ESI) and Atmospheric Pressure Chemical Ionization (APCI). IR: Recorded on Perkin Elmer Spectrum BX FTIR, Shimadzu IRAffinity-1 FTIR, and were recorded as thin films between KBr plates. Single-crystal X-ray diffraction data were collected using a Bruker SMART APEX II CCD diffractometer with graphite monochromated Mo Kα (λ = 0.71073 Å) radiation at different low temperatures for each crystal.

(2) General procedures and analytical data of starting materials:

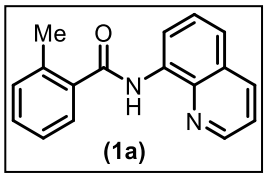
1. Synthesis of *N*-(quinolin-8-yl) benzamides:



Procedure: To an oven-dried round bottom flask, were added the benzoic acid (1.5 equiv.), DMF (3 drops) and DCM (15 mL) under a N_2 atmosphere. Oxalyl chloride (3 equiv.) was added to this dropwise under ice-cold conditions. The ice bath was removed, and the reaction mixture was stirred overnight at room temperature. The solvent was removed under reduced pressure under an atmosphere of nitrogen.

To another oven-dried round bottom flask were added 8- aminoquinoline (1 equiv.), Et_3N (1.5 equiv.) and DCM (15 mL) under a N_2 atmosphere. To this, was added dropwise, the solution of acid chloride (1.5 equiv.) in DCM (5 mL), under ice-cold condition and the mixture was stirred overnight at room temperature. Then, the reaction mixture was quenched with water and extracted with DCM (3 x 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel flash column chromatography (1:20, EtOAc: Petroleum ether) to afford the *N*-(quinolin-8-yl) benzamide.

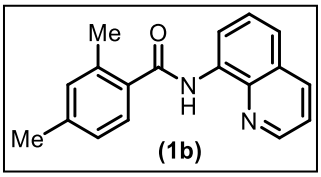
2-methyl-*N*-(quinolin-8-yl)benzamide (1a):[1a]



(1a)

Prepared by following the general procedure and the title compound was isolated in 78% yield (306 mg). Spectral data obtained were in good agreement with those reported in the literature.[1a]

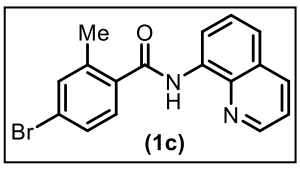
2,4-dimethyl-N-(quinolin-8-yl)benzamide (1b):[1a]



(1b)

Prepared by following the general procedure and the title compound was isolated in 78% yield (306 mg). Spectral data obtained were in good agreement with those reported in the literature.[1a]

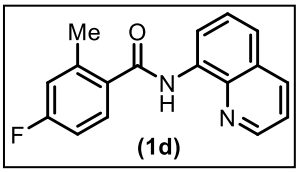
4-bromo-2-methyl-*N*-(quinolin-8-yl)benzamide (1c):[1a]



(1c)

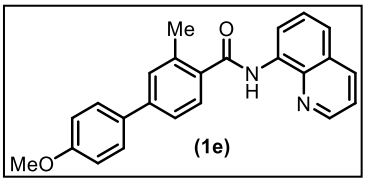
Prepared by following the general procedure and the title compound was isolated in 72% yield (368 mg). Spectral data obtained were in good agreement with those reported in the literature.[1a]

4-fluoro-2-methyl-*N*-(quinolin-8-yl)benzamide (1d):[1b]



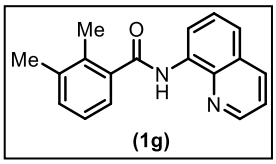
Prepared by following the general procedure and the title compound was isolated in 80% yield (336 mg). Spectral data obtained were in good agreement with those reported in the literature.[1b]

4'-methoxy-3-methyl-*N*-(quinolin-8-yl)-[1,1'-biphenyl]-4-carboxamide (1e):[1c]



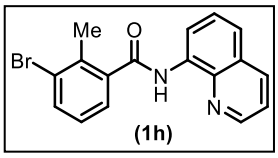
Prepared by following the general procedure and the title compound was isolated in 71% yield (390 mg). Spectral data obtained were in good agreement with those reported in the literature.[1c]

2,3-dimethyl-*N*-(quinolin-8-yl)benzamide (1g):[1b]



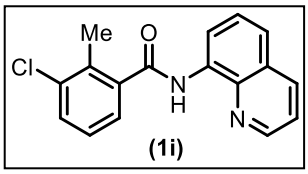
Prepared by following the general procedure and the title compound was isolated in 81% yield (336 mg). Spectral data obtained were in good agreement with those reported in the literature.[1c]

3-bromo-2-methyl-*N*-(quinolin-8-yl)benzamide (1h):[1d]



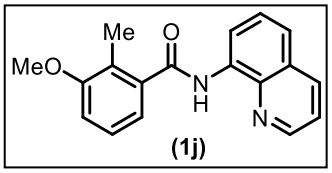
Prepared by following the general procedure and the title compound was isolated in 75% yield (383 mg). Spectral data obtained were in good agreement with those reported in the literature.[1d]

3-chloro-2-methyl-*N*-(quinolin-8-yl)benzamide (1i):[1e]



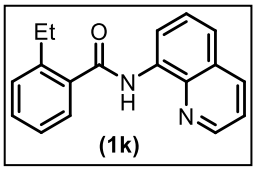
Prepared by following the general procedure and the title compound was isolated in 82% yield (365 mg). Spectral data obtained were in good agreement with those reported in the literature.[1e]

3-Methoxy-2-methyl-*N*-(quinolin-8-yl)benzamide (1j):[1e]



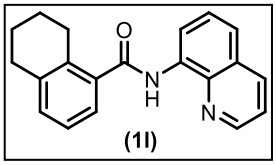
Prepared by following the general procedure and the title compound was isolated in 82% yield (365 mg). Spectral data obtained were in good agreement with those reported in the literature.[1e]

2-ethyl-*N*-(quinolin-8-yl)benzamide (1k):[1a]



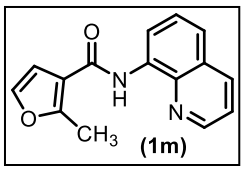
Prepared by following the general procedure and the title compound was isolated in 82% yield (340 mg). Spectral data obtained were in good agreement with those reported in the literature.[1a]

***N*-(quinolin-8-yl)-5,6,7,8-tetrahydronaphthalene-1-carboxamide (1l):**[1d]



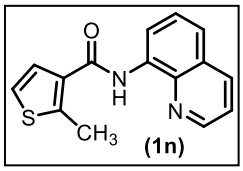
Prepared by following the general procedure and the title compound was isolated in 82% yield (381 mg). Spectral data obtained were in good agreement with those reported in the literature.[1d]

2-methyl-*N*-(quinolin-8-yl)furan-3-carboxamide (1m):



Prepared by following the general procedure, on a 0.5 mmol scale and the title compound was isolated in 45% yield (56 mg). Physical appearance: white solid; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.31 (s, 1H), 8.89 (d, *J* = 7.5 Hz, 1H), 8.86 (d, 1H), 8.21 (d, *J* = 8.2 Hz, 1H), 7.60 (t, *J* = 7.9 Hz, 1H), 7.55 (d, *J* = 8.1 Hz, 1H), 7.50 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.38 (d, *J* = 1.6 Hz, 1H), 6.87 (s, 1H), 2.77 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.21, 157.61, 148.09, 140.49, 138.39, 136.67, 134.56, 128.06, 127.58, 121.61, 121.43, 116.71, 108.97, 13.82. **HRMS** (ESI-ToF) *m/z*: $[M+Na]^+$ Calcd. for $C_{15}H_{12}N_2O_2Na$ 275.0791; Found 275.0766.

2-methyl-*N*-(quinolin-8-yl)thiophene-3-carboxamide (1n):

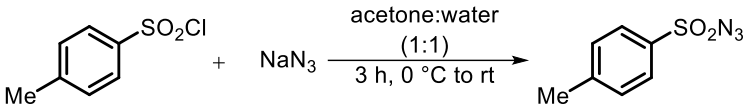


Prepared by following the general procedure on 1 mmol scale and the title compound was isolated in 65% yield (174 mg). Physical appearance: white solid; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.43 (s, 1H), 8.91 (d, *J* = 7.4 Hz, 1H), 8.85 (d, *J* = 3.1 Hz, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 7.60 (t, *J* = 16.7, 9.1 Hz, 1H), 7.57 – 7.44 (m, 3H), 7.17 (d, *J* = 5.1 Hz, 1H), 2.90 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.66, 148.22, 145.65, 138.62, 136.47, 134.74, 132.68, 128.04, 127.52, 127.02, 121.92, 121.65, 121.48, 116.46, 15.22; **HRMS** (ESI-ToF) *m/z*: $[M+H]^+$ Calcd. for $C_{15}H_{13}N_2OS$ 269.0743; Found 269.0721.

2. Preparation of vinyl diazoesters:

(A) General Procedure:

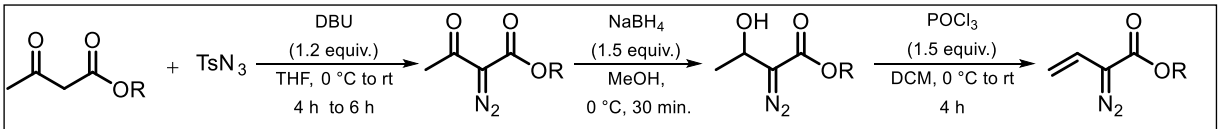
(i) Synthesis of *p*-toluenesulfonylazide:



To a solution of *p*-toluenesulfonylchloride (10 g, 52.45 mmol, 1 equiv.) in a mixture of acetone (158 mL) and H_2O (158 mL), was added sodium azide (3.41 g, 52.45 mmol, 1 equiv.) portion-wise over 15 min at 0 °C. After stirring for 3 h at room temperature, the reaction mixture was concentrated under reduced pressure until all the acetone was removed. The concentrated reaction mixture was extracted thrice with diethyl ether which is dried over Na_2SO_4 and the solvent was evaporated under reduced pressure maintaining the bath temperature at 30 °C, resulting in *p*-toluenesulfonylazide (10.25 g, 99% crude yield) as a colorless oil.

(ii) Synthesis of vinyl diazo esters (2a-g):

To a stirred solution of the alkyl acetoacetate (**A**) (1 equiv., 20 mmol) in anhydrous THF (30 mL) was added DBU (1.2 equiv., 24.0 mmol) at 0 °C. The resulting solution was stirred for 5 minutes, and to this was added a solution of tosyl azide (1.1 equiv., 22 mmol) in THF (10 mL) over 5 minutes. The resulting solution was warmed to room temperature and stirred for 4 h. The solvent was evaporated, and the resulting residue was diluted with water (100 mL) and extracted with ethyl acetate (100 mL). The organic extract was dried over anhyd. Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel flash column chromatography (hexane/ethyl acetate = 6/1) to give alkyl diazo acetoacetate (**B)** as a yellow oil.



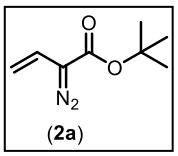
(A)	(B)	(C)	(2a - 2g)
R = ^{t}Bu	R = ^{t}Bu, 82%	R = ^{t}Bu, 88%	**2a**, R = ^{t}Bu, 80%
R = Me	R = Me, 85%	R = Me, 86%	**2b**, R = Me, 78%
R = Et	R = Et, 86%	R = Et, 89%	**2c**, R = Et, 78%
R = ^{i}Pr	R = ^{i}Pr, 88%	R = ^{i}Pr, 82%	**2d**, R = ^{i}Pr, 79%
R = Bn	R = Bn, 84%	R = Bn, 86%	**2e**, R = Bn, 82%
R = Isoamyl	R = Isoamyl, 81%	R = Isoamyl, 89%	**2f**, R = Isoamyl, 70%
R = *n*-Octane	R = *n*-Octane, 80%	R = *n*-Octane, 88%	**2g**, R = *n*-Octane, 74%

To a stirred solution of (**B**) (1 equiv., 16.1 mmol) in MeOH (20 mL) at 0 °C was added $NaBH_4$ (1.5 equiv., 24 mmol), slowly, in portions. The resulting solution was warmed to room temperature and stirred for 30 minutes following which the solvent was removed under reduced pressure and the residue was diluted with water (50 mL) and extracted with ethyl acetate (50 mL). The organic extract was dried over anhyd. Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by silica gel flash column chromatography (petroleum ether/ethyl acetate = 4/1) to give **C** as a yellow oil.

To stirred solution of **C** (1 equiv., 10 mmol) and Et_3N (4.0 equiv., 40 mmol) in DCM (100 mL) at 0 °C, was slowly added a solution of $POCl_3$ (1.5 equiv.) in DCM (10 mL) over 25 minutes. The resulting solution was warmed to room temperature and stirred for 4 h. The reaction was quenched with water (20 mL) and transferred to a separatory funnel and the layers were separated. The organic layer was dried over anhyd. Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel flash column chromatography (eluent: petroleum ether/ethyl acetate = 50/1) to give the vinyl diazo esters (**2a–2g**) as red oils.

tert-butyl 2-diazobut-3-enoate (2a): [2a]

Reaction performed by following the general procedure (II), using ethyl *tert*-butyl acetoacetate

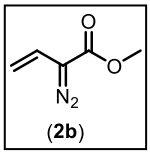


(**2a**)

(3.16 g, 20 mmol); Yield: 80%, (2.36 g); Physical appearance: red oil; TLC R_f 0.3 (50:1 Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.15 (dd, *J* = 17.4, 11.0 Hz, 1H), 5.10 (d, *J* = 11.0 Hz, 1H), 4.84 (d, *J* = 17.4 Hz, 1H), 1.52 (s, 9H). Spectral data obtained were in good agreement with those reported in the literature.[2a]

methyl 2-diazobut-3-enoate (2b): [2b]

Reaction performed by following the general procedure (II), using ethyl methyl acetoacetate

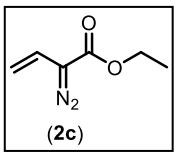


(**2b**)

(2.32 g, 20 mmol); Yield: 78% (1.69 g); Physical appearance: red oil; TLC R_f 0.3 (50:1 Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.18 (dd, *J* = 17.4, 11.0 Hz, 1H), 5.15 (d, *J* = 11.9 Hz, 1H), 4.89 (d, *J* = 17.4 Hz, 1H), 3.83 (s, 3H). Spectral data obtained were in good agreement with those reported in the literature.[2b]

ethyl 2-diazobut-3-enoate (2c): [2a]

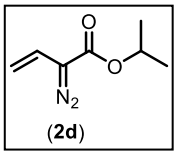
Reaction performed by following the general procedure (II), using ethyl acetoacetate (1.30 g, 10 mmol); Yield: 78% (1.09 g); Physical appearance: red oil; TLC R_f 0.3 (50:1 Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.19 (dd, *J* = 17.4, 11.0 Hz, 1H), 5.13 (d, *J* = 11.0 Hz, 1H), 4.88 (d, *J* = 17.4 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H). Spectral data obtained were in good agreement with those reported in the literature.[2a]



(**2c**)

isopropyl 2-diazobut-3-enoate (2d): [2b]

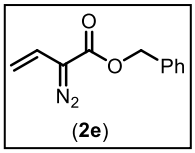
Reaction performed by following the general procedure (II), using ethyl acetoacetate (2.88 g, 20 mmol); Yield: 79% (2.00 g); Physical appearance: red oil; TLC R_f 0.3 (50:1 Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.19 (dd, *J* = 17.4, 11.0 Hz, 1H), 5.20 – 5.14 (m, 1H), 5.12 (d, *J* = 11.0 Hz, 1H), 4.86 (d, *J* = 17.4 Hz, 1H), 1.31 (s, 3H), 1.29 (s, 4H). Spectral data obtained were in good agreement with those reported in the literature.[2b]



(**2d**)

benzyl 2-diazobut-3-enoate (2e): [2a]

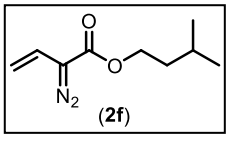
Reaction performed by following the general procedure (II), using benzyl acetoacetate (3.84 g, 20 mmol); Yield: 82%, (2.85 g); Physical appearance: red oil; TLC R_f 0.3 (50:1 Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 – 7.31 (m, 5H), 6.22 (dd, *J* = 17.4, 11.0 Hz, 1H), 5.29 (s, 2H), 5.15 (d, *J* = 11.0 Hz, 1H), 4.90 (d, *J* = 17.4 Hz, 1H). Spectral data obtained were in good agreement with those reported in the literature.[2a]



(**2e**)

isopentyl 2-diazobut-3-enoate (2f): [2a]

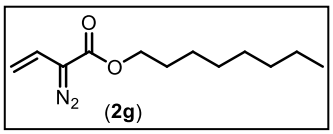
Reaction performed by following the general procedure (II), using isoamyl acetoacetate (3.44 g, 20 mmol); Yield: 90%, (2.27 g); Physical appearance: red oil; TLC R_f 0.3 (50:1 Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.19 (dd, *J* = 17.4, 11.0 Hz, 1H), 5.13 (d, *J* = 11.0 Hz, 1H), 4.88 (d, *J* = 17.4 Hz, 1H), 4.27 (t, *J* = 6.8 Hz, 2H), 1.78 – 1.67 (m, 1H), 1.63 – 1.53 (m, 3H), 0.96 (s, 3H), 0.95 (s, 3H). Spectral data obtained were in good agreement with those reported in the literature.[2a]



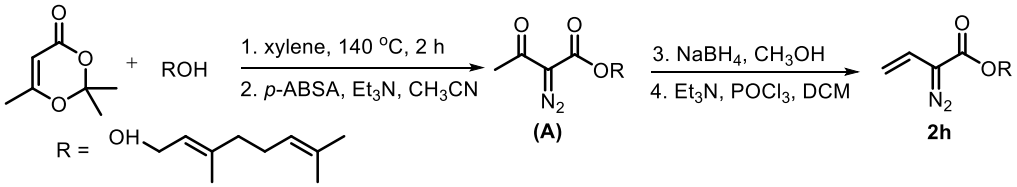
(**2f**)

octyl 2-diazobut-3-enoate (2g):

Reaction performed by following the general procedure (II), using octyl acetoacetate (4.28 g, 20 mmol); Yield: 74%, (2.92 g); Physical appearance: red oil; TLC R_f 0.3 (50:1 Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.24 – 6.03 (m, 1H), 5.11 (d, *J* = 11.0 Hz, 1H), 4.85 (d, *J* = 17.4Hz, 1H), 4.25 – 4.16 (m, 2H), 1.71 – 1.58 (m, 2H), 1.41 – 1.17 (m, 10H), 0.95 – 0.81 (m, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 164.86, 120.51, 107.24, 65.26, 31.74, 29.15, 29.13, 28.75, 25.80, 22.60, 14.02; **HRMS** (ESI-ToF) *m/z*: $[M+Na]^+$ Calcd. for $C_{12}H_{20}N_2O_2$ 247.1417; Found 247.1394.



(iii) General Procedure for the synthesis of (*E*)-3,7-dimethylocta-2,6-dien-1-yl 2-diazobut-3-enoate:



In an oven-dried round bottom flask, the (*E*)-3,7-dimethylocta-2,6-dien-1-ol (3.08 g, 20 mmol, 1 equiv.) and 2,2,6-trimethyl-1,3-dioxene-4-one (24 mmol, 1.2 equiv.) were dissolved in xylene (6 mL) and the resulting mixture was refluxed at 140 °C for 2 h under argon. The solvent was then evaporated using vacuum distillation, leaving behind a black oil. This crude mixture was purified by silica gel flash column chromatography (PE/EA = 10:1) to give the acetoacetate as a colorless oil (Yield: 2.85 g, 60%).

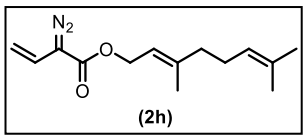
To a solution of 3,7-dimethyloct-6-en-1-yl 3-oxobutanoate (2.38 g, 10 mmol, 1 equiv.) in MeCN (25 mL), cooled to 0 °C, was added *p*-acetamidobenzenesulfonyl azide (1.1 equiv., 11 mmol,), followed by triethylamine (1.5 equiv., 15 mmol,) and the resulting reaction was warmed to rt for 2 h. The resulting pale-yellow precipitate was filtered, and the residue was concentrated under reduced pressure. This was re-dissolved in DCM and washed with brine. The organic layer was dried over anhyd. Na_2SO_4, filtered and concentrated under reduced pressure to yield a residue that was purified by silica gel flash column chromatography (PE/EA = 10:1) to give (*E*)-3,7-dimethylocta-2,6-dien-1-yl 2-diazo-3-oxobutanoate **A** as a yellow oil (Yield 2.32 g, 88%).

To a solution of (*E*)-3,7-dimethylocta-2,6-dien-1-yl 2-diazo-3-oxobutanoate (2.32 g, 8.7 mmol, 1 equiv.,) in MeOH (25 mL) cooled to 0 °C, was added $NaBH_4$ (1.5 equiv., 13.0 mmol), slowly, in portions. The resulting solution was warmed to room temperature and stirred for 1 h. Thereafter, the MeOH was evaporated under reduced pressure and the residue was diluted with water and the mixture was extracted with ethyl acetate. The resulting residue was dried over anhyd. Na_2SO_4 and filtered. After the solvent was removed under reduced pressure, the crude product was purified by silica gel flash column chromatography (PE/EA = 5:1) to give (*E*)-3,7-dimethylocta-2,6-dien-1-yl 2-diazo-3-hydroxybutanoate as a yellow viscous oil (Yield 2.10 g, 90%).

To a solution of (*E*)-3,7-dimethylocta-2,6-dien-1-yl 2-diazo-3-hydroxybutanoate (2.10 g, 8.8 mmol, 1 equiv.) and Et_3N (4.0 equiv., 35.2 mmol) in DCM (40 mL) cooled to 0 °C, was slowly added a solution of $POCl_3$ (1.5 equiv., 13.2 mmol) in DCM (10 mL) over 20 minutes. The resulting solution was warmed to room temperature and stirred for 2 h. The solution was then washed with water and the organic extract dried over anhyd. Na_2SO_4 and filtered. After the solvent was removed under reduced pressure, the crude product was purified by silica gel flash column chromatography (PE/EA = 50:1) to afford the (*E*)-3,7-dimethylocta-2,6-dien-1-yl 2-diazobut-3-enoate **2h** as a red oil (Yield 1.48 g, 76%).

(*E*)-3,7-dimethylocta-2,6-dien-1-yl 2-diazobut-3-enoate (2h):

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.19 (dd, *J* = 17.4, 11.0 Hz, 1H), 5.39 (t, *J* = 7.1 Hz, 1H), 5.16 – 5.07 (m, 2H), 4.86 (d, *J* = 17.3 Hz, 1H), 4.72 (d, *J* = 7.3 Hz, 2H), 2.21 – 2.05 (m, 4H), 1.79 (s, 3H), 1.70 (s, 3H), 1.62 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 159.69, 137.75, 127.01, 118.29, 115.36, 113.85, 102.04, 56.47, 48.21, 26.96, 21.43, 20.45, 18.30, 12.44; **ESI-HRMS**: Calcd. for $C_{14}H_{20}N_2O_2$ $[M+Na]^+$ 271.1417; Found 271.1397.



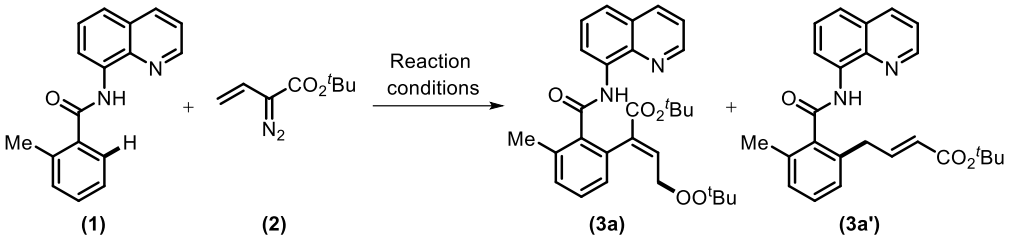
(2h)

Notes:

(a) We have never observed any explosion during the preparation and manipulation of vinyl diazo compounds at the scales indicated here.

(b) All the vinyl diazo esters were stored in the freezer at –20 °C.

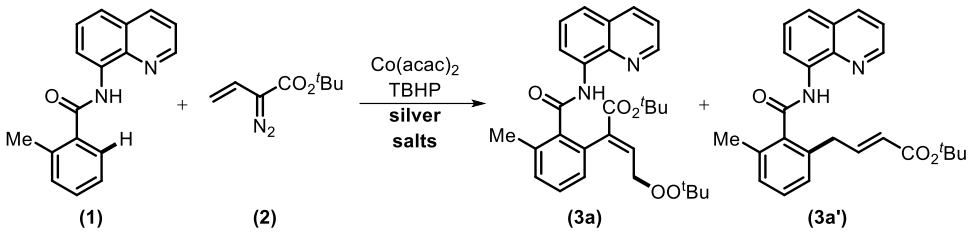
3. Table 1. Optimization of reaction conditions:



Sr. No.	Conditions	Yield[a] (3a%)	Yield[a] (3a'%)
1	$Co(OAc)_2$ (10 mol%)/ TBHP in 6M decane (2 equiv.)/ DCE/ 60 °C/ 8 h	25%	19%
2	$Co(OAc)_2.4H_2O$ (10 mol%)/ TBHP in 6M decane (2 equiv.)/ DCE/ 60 °C / 8 h	26%	24%
3	**$Co(acac)_2$** (10 mol%)/ TBHP in 6M decane (2 equiv.)/ DCE/ 60 °C/ 8 h	44%	24%
4	$Co(acac)_3$ (10 mol%)/ TBHP in 6M decane / DCE/ 60 °C / 8 h	NR	NR
5	$CoCl_2$ (10 mol%)/ TBHP in 6M decane / DCE/ 60 °C / 8 h	NR	NR
6	**$Ni(acac)_2$** (10 mol%)/ TBHP in 6M decane (2 equiv.)/ DCE/60 °C/ 8 h	NR	NR
7	$Pd(OAc)_2$ (10 mol%)/ TBHP in 6M decane (2 equiv.)/ DCE/ 60 °C/ 8 h	NR	NR
8	$Co(acac)_2$ (20 mol%)/ $(PhCO_2)_2$ (2 equiv.)/ DCE/ 60 °C/ 8 h	NR	NR
9	$Co(acac)_2$ (10 mol%)/ DTBP (2 equiv.)/ DCE/ 60 °C/ 8 h	10%	15%
10	$Co(acac)_2$ (10 mol%)/ TBPB (2 equiv.)/ DCE/ 60 °C/ 8 h	<5%	<5%
11	$Co(acac)_2$ (10 mol%)/ TBHP in 70% water (2 equiv.)/ DCE/ 60 °C/ 8 h	NR	NR
12	$Co(acac)_2$ (10 mol%)/ TBHP in 6M decane (5 equiv.)/ DCE/ 60 °C/ 8 h	51%	26%
13	**$Co(acac)_2$ (10 mol%)/ TBHP in 6M decane (3 equiv.)/ AgOAc (50 mol%)/ DCE/ 60 °C/ 8 h**	**59%**	**26%**
14	$Co(acac)_2$ (10 mol%)/ TBHP in 6M decane (3 equiv.)/ Et_3N (50 mol%)/ DCE/ 60 °C/ 8 h	22%	29%
15	$Co(acac)_2$ (10 mol%)/ TBHP in 6M decane / DBU (50 mol%)/ DCE/ 60 °C/ 8 h	NR	NR
16	$Co(acac)_2$ (10 mol%)/ TBHP in 6M decane (3 equiv.)/ AgOAc (50 mol%)/ Ph-CF_3/ 60 °C/ 8 h	40%	29%
17	$Co(acac)_2$ (10 mol%)/ TBHP in 6M decane (3 equiv.)/ AgOAc (50 mol%)/ Ph-Cl/ 60 °C/ 8 h	42%	21%
18	TBHP in 6M decane (3 equiv.)/ AgOAc (50 mol%)/ DCE/ 60 °C/ 8 h	NR	NR
19	$Co(acac)_2$ (10 mol%)/ AgOAc (50 mol%)/ DCE/ 60 °C/ 8 h	NR	NR

[a]*Isolated yield; N.R. = No reaction*

Table 2. Optimization of silver salts:

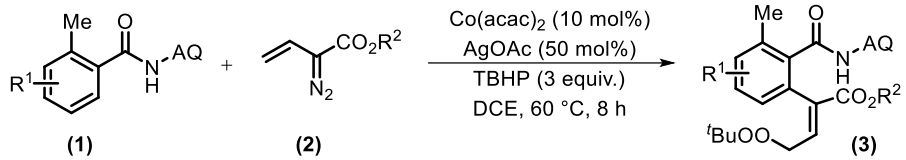


Sr. No.	Conditions	Yield[a] (3a%)	Yield[a] (3a'%)
1	$Co(acac)_2$ (10 mol%)/ TBHP in 6M decane (3 equiv.)/ **$AgBF_4$ (50 mol%)**/ DCE/ 60 °C/ 8 h	25%	19%
2	$Co(acac)_2$ (10 mol%)/ TBHP in 6M decane (3 equiv.)/ **$AgSbF_6$ (50 mol%)**/ DCE/ 60 °C/ 8 h	21%	9%
3	$Co(acac)_2$ (10 mol%)/ TBHP in 6M decane (3 equiv.)/ **$AgNTf_2$ (50 mol%)**/ DCE/ 60 °C/ 8 h	NR	NR
4	$Co(acac)_2$ (10 mol%)/ TBHP in 6M decane (3 equiv.)/ **AgOAc (25 mol%)**/ DCE/ 60 °C/ 8 h	55%	29%
5	$Co(acac)_2$ (10 mol%)/ TBHP in 6M decane (3 equiv.)/ **AgOAc (1 equiv.)/ DCE**/ 60 °C/ 8 h	51%	28%

[a]*Isolated yield; N.R. = No reaction*

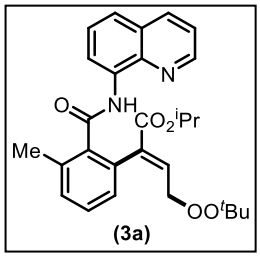
4. General procedure for 1,3-difunctionalization of vinyl diazo esters:

(I) General procedure for the cobalt-catalyzed 1,3-oxyarylation of benzamides:



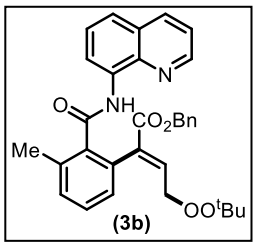
In an oven-dried pressure tube equipped with a stir bar, the *N*-(quinolin-8-yl) benzamide (1.0 equiv., 0.1 mmol) and vinyl diazo ester (3 equiv., 0.30 mmol) were dissolved in DCE (1.5 mL). The solution was degassed with nitrogen for about 10 min, following which $Co(acac)_2$ (10 mol%, 0.01 mmol), AgOAc (0.50 equiv., 0.05 mmol), and TBHP (3 equiv., 0.03 mmol, 6M soln in decane) were added, the pressure tube was sealed with a septum cap. This reaction mixture was then stirred in pre-heated oil bath for 8 hours, and the reaction progress was further monitored by TLC. Upon completion of the reaction, the reaction mixture was diluted with EtOAc and filtered through a short pad of Celite, and the filtrate was concentrated. The residue was dissolved in EtOAc and washed with saturated $NaHCO_3$ solution and brine. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure and the crude product was purified by silica gel flash column chromatography.

Isopropyl (*E*)-4-(*tert*-butylperoxy)-2-(3-methyl-2-(quinolin-8-ylcarbamoyl)phenyl)but-2-enoate (3a):



Reaction performed on 0.1 mmol scale (26 mg); Yield: 61% (29 mg); Physical appearance: colorless gel; TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.86 (s, 1H), 8.87 (dd, *J* = 7.2, 1.4 Hz, 1H), 8.76 (dd, *J* = 4.2, 3.7 Hz, 1H), 8.16 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.60 – 7.52 (m, 2H), 7.46 – 7.41 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.37 (t, *J* = 7.2 Hz, 1H), 7.30 (d, *J* = 9.9 Hz, 1H), 7.15 – 7.08 (m, 2H), 4.88 – 4.82 (sept, *J* = 6.3 Hz, 1H), 4.75 – 4.30 (m, 2H), 2.50 (s, 3H), 1.33 – 1.23 (m, 6H), 1.21 (s, 9H); **^{13}C NMR** (126 MHz, CDCl3) δ 167.51, 165.68, 148.14, 140.03, 138.54, 137.65, 136.17, 135.36, 134.48, 132.52, 130.26, 129.04, 127.92, 127.34, 121.82, 121.58, 116.70, 80.59, 72.46, 68.65, 26.26, 21.51, 19.71; **HRMS** (ESI-ToF) *m/z*: $[M+H]^+$ Calcd. for $C_{28}H_{32}N_2O_5$ 477.2384; Found 477.2402.

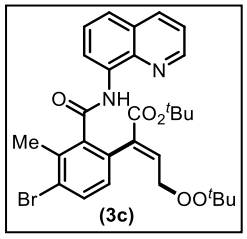
Benzyl (*E*)-4-(*tert*-butylperoxy)-2-(3-methyl-2-(quinolin-8-ylcarbamoyl)phenyl)but-2-enoate (3b):



(3b)

Reaction performed on 0.1 mmol scale (26 mg); Yield: 48% (25 mg); Physical appearance: colorless gel; TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.95 (s, 1H), 8.88 (dd, *J* = 7.0, 1.9 Hz, 1H), 8.67 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.21 – 8.14 (m, 1H), 7.62 – 7.54 (m, 2H), 7.44 – 7.41 (m, 1H), 7.41 – 7.38 (m, 1H), 7.35 – 7.31 (m, 1H), 7.23 (t, *J* = 6.2 Hz, 1H), 7.21 – 7.12 (m, 4H), 7.10 – 7.07 (m, 1H), 5.42 – 4.89 (m, 2H), 4.88 – 4.29 (m, 2H), 2.51 (s, 3H), 1.20 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.53, 165.95, 147.98, 141.42, 138.33, 137.72, 136.49, 135.94, 135.44, 134.31, 133.65, 132.23, 130.40, 129.17, 128.28, 128.21, 128.04, 127.76, 127.73, 127.49, 127.20, 121.97, 121.60, 117.07, 80.57, 77.32, 77.27, 77.07, 76.81, 72.32, 66.60, 26.32, 26.26, 19.69; **HRMS** (ESI-ToF) *m/z*: $[M+H]^+$ Calcd. for $C_{32}H_{32}N_2O_5$ 525.2384; Found 525.2408.

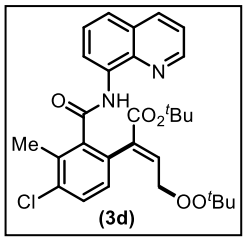
***tert*-butyl (*E*)-2-(4-bromo-3-methyl-2-(quinolin-8-ylcarbamoyl)phenyl)-4-(*tert*-butylperoxy)but-2-enoate (3c):**



(3c)

Reaction performed on 0.1 mmol scale (34 mg); Yield: 60% (34 mg); Physical appearance: colorless gel; TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.90 (s, 1H), 8.86 (d, *J* = 6.6 Hz, 1H), 8.76 (d, *J* = 7.7 Hz, 1H), 8.16 (d, *J* = 7.7 Hz, 1H), 7.65 (d, *J* = 7.76, 1H), 7.59 – 7.52 (m, 2H), 7.48 – 7.39 (m, 1H), 7.08 (t, *J* = 6.1 Hz, 1H), 6.98 (d, *J* = 7.9 Hz, 1H), 4.76 – 4.24 (m, 2H), 2.52 (s, 3H), 1.21 (s, 9H), 1.20 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.58, 164.99, 148.30, 140.19, 139.39, 138.45, 136.17, 134.93, 134.45, 134.26, 133.12, 132.14, 128.59, 127.90, 127.26, 125.67, 122.12, 121.66, 116.74, 81.43, 80.62, 72.45, 27.65, 26.27, 20.35; **HRMS** (ESI-ToF) *m/z*: $[M+H]^+$ Calcd. for $C_{29}H_{34}BrN_2O_5$ 569.1646 and 571.1627; Found 569.1634 and 571.1615.

***tert*-butyl (*E*)-4-(tert-butylperoxy)-2-(4-chloro-3-methyl-2-(quinolin-8 ylcarbamoyl)phenyl)but-2-enoate (3d):**

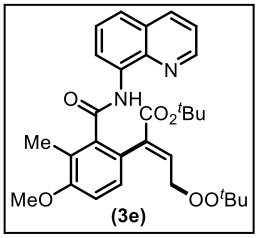


(3d)

Reaction performed on 0.1 mmol scale (30 mg); Yield: 59% (31 mg); Physical appearance: colorless gel; TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc);Physical appearance: brown gel; TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.90 (s, 1H), 8.86 (d, *J* = 6.7 Hz, 1H), 8.77 (d, *J* = 3.2 Hz, 1H), 8.18 (d, *J* = 7.5

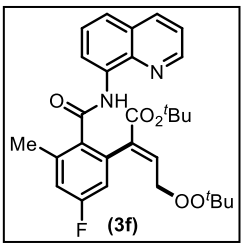
Hz, 1H), 7.64 – 7.52 (m, 2H), 7.47 (d, *J* = 6.4 Hz, 1H), 7.44 (dd, *J* = 8.1, 4.1 Hz, 1H), 7.14 – 7.01 (m, 2H), 4.76 – 4.27 (m, 2H), 2.49 (s, 3H), 1.22 (s, 9H), 1.21 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.57, 165.07, 148.29, 140.16, 139.47, 138.47, 136.16, 134.96, 134.50, 134.28, 133.31, 131.43, 129.79, 128.36, 127.90, 127.28, 122.08, 121.64, 116.75, 81.41, 80.63, 77.28, 77.03, 76.77, 72.46, 27.65, 26.27, 17.34; **HRMS** (ESI-ToF) *m/z*: $[M+H]^+$ Calcd. for $C_{29}H_{34}ClN_2O_5$ 525.2151; Found 525.2169.

***tert*-butyl *(E)*-4-(*tert*-butylperoxy)-2-(4-methoxy-3-methyl-2-(quinolin-8-ylcarbamoyl)phenyl)but-2-enoate (3e):**



Reaction performed on 0.1 mmol scale (29 mg); Yield: 58% (30 mg); Physical appearance: colorless gel; TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.90 (s, 1H), 8.88 (d, *J* = 7.4 Hz, 1H), 8.76 (dd, *J* = 4.1, 1.4 Hz, 1H), 8.17 (d, *J* = 8.1 Hz, 1H), 7.56 (dt, *J* = 8.1, 7.6 Hz, 2H), 7.43 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.11 – 7.00 (m, 2H), 6.95 (d, *J* = 8.4 Hz, 1H), 4.87 – 4.29 (m, 2H), 3.91 (s, 3H), 2.33 (s, 3H), 1.23 (s, 9H), 1.20 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.46, 165.69, 157.46, 147.91, 139.29, 138.91, 138.15, 136.55, 135.42, 134.38, 128.14, 127.97, 127.48, 124.58, 123.96, 121.81, 121.48, 117.11, 110.66, 80.96, 80.52, 77.29, 72.76, 55.67, 27.68, 26.30, 13.05; **HRMS** (ESI-ToF) *m/z*: $[M+Na]^+$ Calcd. for $C_{30}H_{36}N_2O_6$ 543.2466; Found 543.2438.

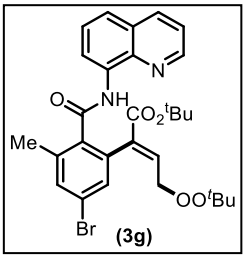
***tert-butyl* *(E)*-4-(*tert*-butylperoxy)-2-(5-fluoro-3-methyl-2-(quinolin-8-ylcarbamoyl)phenyl)but-2-enoate (3f):**



Reaction performed on 0.1 mmol scale (28 mg); Yield: 58% (29 mg); Physical appearance: brown gel; TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.91 (s, 1H), 8.86 (dd, *J* = 7.0, 2.0 Hz, 1H), 8.77 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.18 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.61 – 7.53 (m, 2H), 7.45 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.10 – 7.05 (m, 1H), 7.00 (dd, *J* = 7.4, 2.5 Hz, 1H), 6.84 (dd, *J* = 8.9, 2.6 Hz, 1H), 4.75 – 4.31 (m, 2H), 2.49 (s, 3H), 1.23 (s, 9H), 1.22 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.74, 164.83, 162.23 (d, *J* = 244.4 Hz), 148.09, 139.91, 138.37 (d, $J_{C\text{-}F}$ = 8.49 Hz), 136.42, 135.15 (d, $J_{C\text{-}F}$ = 8.1 Hz), 134.67, 134.29, 134.04 (d, $J_{C\text{-}F}$ = 2.7 Hz), 127.94, 127.37, 121.97, 121.58, 117.02, 116.92, 116.85, 114.25 (d, $J_{C\text{-}F}$ = 22.1 Hz), 81.51, 80.68, 72.33, 27.65, 26.26, 19.90; **^{19}F NMR** (376

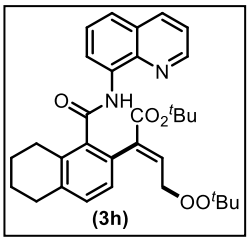
MHz, $CDCl_3$) δ –112.39; **HRMS** (ESI-ToF) *m/z*: $[M+H]^+$ Calcd. for $C_{29}H_{34}FN_2O_5$ 509.2446; Found 509.2465.

tert-butyl (_E_)-2-(5-bromo-3-methyl-2-(quinolin-8-ylcarbamoyl)phenyl)-4-(_tert_-butylperoxy)but-2-enoate (3g):



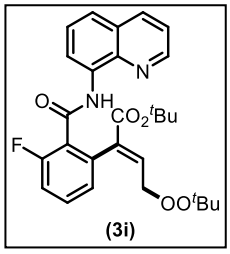
Reaction performed on 0.1 mmol scale (34 mg); Yield: 59% (33 mg); Physical appearance: brown gel; TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.91 (s, 1H), 8.85 (d, *J* = 6.9 Hz, 1H), 8.77 (d, *J* = 3.9 Hz, 1H), 8.16 (d, *J* = 8.2 Hz, 1H), 7.63 – 7.51 (m, 2H), 7.49 – 7.39 (m, 2H), 7.33 – 7.25 (m, 1H), 7.08 (t, *J* = 6.9 Hz, 1H), 4.71 – 4.36 (m, 2H), 2.47 (s, 3H), 1.24 (s, 9H), 1.21 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.53, 164.83, 148.26, 140.03, 138.46, 137.57, 136.68, 136.15, 134.67, 134.50, 134.30, 132.97, 130.14, 127.88, 127.26, 122.84, 121.98, 121.62, 116.63, 81.57, 80.75, 72.34, 27.64, 26.26, 19.56; **HRMS** (ESI-ToF) *m/z*: $[M+H]^+$ Calcd. for $C_{29}H_{34}BrN_2O_5$ 569.1646 and 571.1627; Found 569.1647 and 571.1624.

tert-butyl (_E_)-4-(_tert_-butylperoxy)-2-(1-(quinolin-8-ylcarbamoyl)-5,6,7,8 tetrahydronaphthalen-2-yl)but-2-enoate (3h):



Reaction performed on 0.1 mmol scale (30 mg); Yield: 61% (32 mg); Physical appearance: brown gel; TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.88 (s, 1H), 8.89 (dd, *J* = 7.4, 1.5 Hz, 1H), 8.76 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.59 – 7.51 (m, 2H), 7.42 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.17 (d, *J* = 7.9 Hz, 1H), 7.03 (t, *J* = 6.3 Hz, 1H), 6.99 (d, *J* = 7.8 Hz, 1H), 4.87 – 4.35 (m, 2H), 2.96 – 2.81 (m, 4H), 1.87 – 1.75 (m, 4H), 1.22 (s, 9H), 1.20 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.94, 165.59, 148.17, 139.27, 138.53, 137.60, 136.06, 135.39, 134.65, 134.04, 130.05, 129.75, 127.88, 127.31, 126.64, 126.50, 121.68, 121.50, 116.59, 81.02, 80.52, 72.71, 31.24, 29.75, 27.68, 26.29, 22.86, 22.63; **HRMS** (ESI-ToF) *m/z*: $[M+H]^+$ Calcd. for $C_{32}H_{39}N_2O_5$ 531.2853; Found 531.2859.

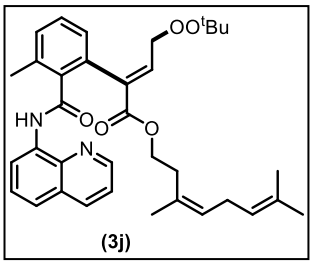
***tert*-butyl (*E*)-4-(*tert*-butylperoxy)-2-(3-fluoro-2-(quinolin-8-ylcarbamoyl)phenyl)but-2-enoate (3i):**



(3i)

Reaction performed on 0.1 mmol scale (27 mg); Yield: 24% (12 mg); Physical appearance: brown gel; TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.38 (s, 1H), 8.89 (dd, *J* = 6.1, 2.9 Hz, 1H), 8.82 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.60 – 7.52 (m, 2H), 7.51 – 7.42 (m, 2H), 7.24 (t, *J* = 7.1 Hz, 1H), 7.16 – 7.09 (m, 2H), 4.69 – 4.35 (m, 2H), 1.30 (s, 9H), 1.23 (s, 9H); **^{13}C NMR** (126 MHz, CDCl3) δ 168.14, 162.98, 159.97 (d, $J_{C\text{-}F}$ = 246.1 Hz), 148.32, 148.10, 138.45, 137.06, 136.13, 134.87, 130.33 (d, $J_{C\text{-}F}$ = 8.8 Hz), 127.90, 127.33, 127.29, 123.73 (d, $J_{C\text{-}F}$ = 2.8 Hz), 121.55, 121.52, 118.28, 116.77, 115.50 (d, $J_{C\text{-}F}$ = 22.4 Hz), 88.73, 82.16, 80.72, 73.80, 27.83, 26.49; **^{19}F NMR** (471 MHz, $CDCl_3$) δ –113.94; **HRMS** (ESI-ToF) *m/z*: $[M+H]^+$ Calcd. for $C_{28}H_{32}FN_2O_5$ 495.2290; Found 495.2295.

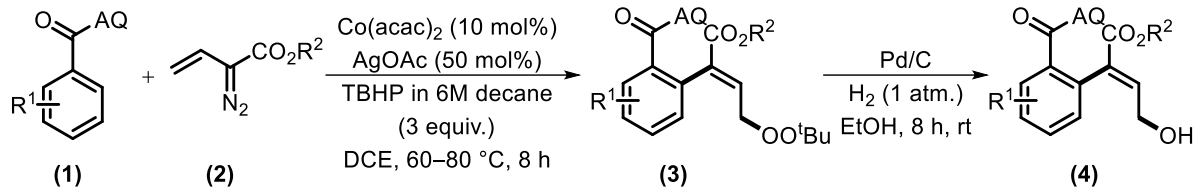
(*E*)-3,7-dimethylocta-3,6-dien-1-yl (*Z*)-4-(*tert*-butylperoxy)-2-(3-methyl-2-(quinolin-8-ylcarbamoyl)phenyl)but-2-enoate (3j):



(3j)

Reaction performed on 0.1 mmol scale (26 mg); Yield: 45% (25 mg); Physical appearance: brown gel; TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.89 (s, 1H), 8.88 (d, *J* = 7.1 Hz, 1H), 8.76 (dd, *J* = 3.8, 1.9 Hz, 1H), 8.17 (d, *J* = 7.7 Hz, 1H), 7.61 – 7.51 (m, 2H), 7.43 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.38 (t, *J* = 7.7 Hz, 1H), 7.31 (s, 1H), 7.17 (t, *J* = 6.2 Hz, 1H), 7.11 (d, *J* = 7.6 Hz, 1H), 5.12 (t, *J* = 7.0 Hz, 1H), 4.99 (s, 1H), 4.70 – 4.41 (m, 4H), 2.50 (s, 3H), 1.94 (d, *J* = 3.5 Hz, 3H), 1.69 – 1.62 (m, 4H), 1.60 – 1.47 (m, 6H), 1.20 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.47, 166.09, 148.09, 141.60, 140.74, 138.58, 137.70, 136.18, 135.36, 134.48, 133.96, 132.40, 131.94, 130.27, 129.07, 127.97, 127.37, 127.22, 123.63, 121.83, 121.56, 119.33, 116.78, 80.52, 72.34, 61.91, 32.07, 26.54, 26.25, 25.68, 23.26, 19.70, 17.63; **HRMS** (ESI-ToF) *m/z*: $[M+H]^+$ Calcd. for $C_{35}H_{43}N_2O_5$ 571.3166; Found 571.3175.

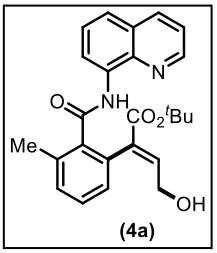
(II) General procedure for the cobalt-catalyzed 1,3-oxyarylation of benzamides followed by hydrogenation:



In an oven-dried pressure tube equipped with a stir bar, the *N*-(quinolin-8-yl) benzamide (1.0 equiv., 0.1 mmol) and the vinyl diazo ester (3 equiv., 0.30 mmol) were dissolved in DCE (1.5 mL mL). The solution was degassed with nitrogen for about 10 min, following which $Co(acac)_2$ (10 mol%, 0.01 mmol), AgOAc (0.50 equiv., 0.05 mmol), and TBHP (5 equiv., 0.05 mmol, 6M soln in decane) were added, the pressure tube was sealed with a septum cap. This reaction mixture was then stirred in an oil bath pre-heated to 60 ^oC for 8 hours, and the reaction progress was monitored by TLC. Upon completion of the reaction, the reaction mixture was diluted with EtOAc and filtered through a short pad of Celite, and the filtrate was concentrated. The residue was dissolved in EtOAc and washed with saturated $NaHCO_3$ solution and brine. The organic layer was dried over anhyd. Na_2SO_4, filtered, and concentrated under reduced pressure and the crude product was purified by silica gel flash column chromatography.

After this, the isolated 1,3-oxyarylated product was dissolved in EtOH (2 mL). The solution was degassed with nitrogen for 10 min, following which Pd/C (15 mol%,) was added and the reaction flask was evacuated and back filled with H_2 and this mixture was stirred under a hydrogen balloon for 8 hours. The progress of the reaction was monitored by TLC. Upon completion of the reaction, the flask was purged with nitrogen and the reaction mixture was diluted with EtOAc. Upon passing through a pad of Celite, and eluting with EtOAc, the filtrate was concentrated under reduced pressure and the crude product was purified by silica gel flash column chromatography.

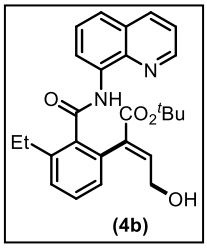
***tert*-butyl (*E*)-4-hydroxy-2-(3-methyl-2-(quinolin-8-ylcarbamoyl)phenyl)but-2-enoate (4a):**



Reaction performed on 0.1 mmol scale (26 mg); Yield: 59% (29 mg); TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); Hydrogenation reaction performed on 0.06 mmol scale (29 mg): Yield: 70% (20 mg); TLC R_f 0.2 (8:2, Petroleum ether: EtOAc); Physical appearance: Colourless gel; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.98 (s, 1H), 8.90 (dd, *J* = 6.3, 2.7 Hz, 1H), 8.76 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.64 – 7.55 (m, 2H), 7.45 (dd, *J* = 8.2,

4.2 Hz, 1H), 7.38 (t, *J* = 7.7 Hz, 1H), 7.30 (d, *J* = 7.9 Hz, 1H), 7.08 (t, *J* = 6.9 Hz, 1H), 7.03 (d, *J* = 7.6 Hz, 1H), 4.10 – 3.95 (m, 2H), 3.46 (bs, 1H), 2.49 (s, 3H), 1.20 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.07, 165.64, 148.36, 141.95, 138.44, 137.23, 136.31, 134.74, 134.70, 134.06, 132.91, 129.85, 129.05, 127.94, 127.35, 127.31, 122.36, 121.65, 117.04, 81.22, 59.47, 27.62, 19.47; **HRMS** (ESI-ToF) *m/z*: $[M+H]^+$ Calcd. for $C_{25}H_{27}N_2O_4$ 419.1965; Found 419.1989.

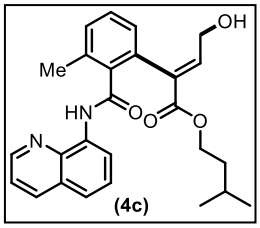
***tert*-butyl (*E*)-2-(3-ethyl-2-(quinolin-8-ylcarbamoyl)phenyl)-4-hydroxybut-2-enoate (4b):**



(4b)

Reaction performed on 0.1 mmol scale (27 mg); Yield: 56% (28 mg); TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); Hydrogenation reaction performed on 0.057 mmol scale (28 mg): Yield: 71% (17 mg); TLC R_f 0.2 (8:2, Petroleum ether: EtOAc); Physical appearance: colorless gel; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.00 (s, 1H), 8.89 (dd, *J* = 6.3, 2.6 Hz, 1H), 8.75 (dd, *J* = 4.3, 1.6 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.63 – 7.55 (m, 2H), 7.48 – 7.40 (m, 2H), 7.34 (d, *J* = 7.7 Hz, 1H), 7.08 (dd, *J* = 8.5, 6.4 Hz, 1H), 7.04 (dd, *J* = 7.5, 1.2 Hz, 1H), 4.09 – 3.93 (m, 2H), 3.50 (bs, 1H), 2.80 (q, *J* = 7.4 Hz, 2H), 1.30 (t, *J* = 7.5 Hz, 3H), 1.18 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.15, 165.68, 148.37, 141.94, 140.82, 138.42, 136.77, 136.26, 134.77, 134.05, 132.88, 129.23, 128.17, 127.92, 127.35, 127.29, 122.35, 121.65, 117.00, 81.18, 59.48, 27.59, 26.53, 15.79; **HRMS** (ESI-ToF) *m/z*: $[M+H]^+$ Calcd. for $C_{26}H_{29}N_2O_4$ 433.2122; Found 433.2110.

Isopentyl (*E*)-4-hydroxy-2-(3-methyl-2-(quinolin-8-ylcarbamoyl)phenyl)but-2-enoate (4c):

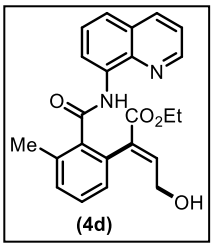


(4c)

Reaction performed on 0.1 mmol scale (26 mg); Yield: 56% (28 mg); TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); Hydrogenation reaction performed on 0.055 mmol scale (28 mg): Yield: 71% (17 mg); TLC R_f 0.2 (8:2, Petroleum ether: EtOAc); Physical appearance: Colourless gel; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.98 (s, 1H), 8.97 – 8.82 (m, 1H), 8.80 – 8.67 (m, 1H), 8.19 (d, *J* = 8.3 Hz, 1H), 7.65 – 7.55 (m, 2H), 7.50 – 7.43 (m, 1H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.31 (d, *J* = 7.8 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.05 (d, *J* = 7.6 Hz, 1H), 4.20 – 3.84 (m, 4H), 3.42 (bs, 1H), 2.49 (s, 3H), 1.46 – 1.37 (m, 1H), 1.37 – 1.20 (m, 2H), 0.81 – 0.51 (m, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 168.97, 166.44, 148.28, 143.05, 138.51, 137.24, 136.39, 134.85, 133.97, 133.25, 132.54, 130.03, 129.12, 128.02, 127.38,

127.31, 122.45, 121.70, 117.16, 63.92, 59.37, 36.96, 25.02, 22.30, 19.51; **HRMS** (ESI-ToF) *m/z*: $[M+Na]^+$ Calcd. for $C_{26}H_{28}N_2O_4Na$ 455.1941; Found 455.1976.

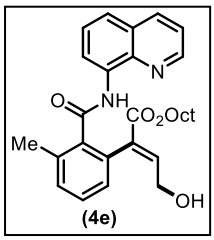
Ethyl (*E*)-4-hydroxy-2-(3-methyl-2-(quinolin-8-ylcarbamoyl)phenyl)but-2-enoate (4d):



(4d)

Reaction performed on 0.1 mmol scale (26 mg); Yield: 56% (26 mg); TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); Hydrogenation reaction performed on 0.056 mmol scale (26 mg): Yield: 71% (16 mg); TLC R_f 0.2 (8:2, Petroleum ether: EtOAc); Physical appearance: Brown semi-solid; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.98 (s, 1H), 8.94 – 8.80 (m, 1H), 8.75 (dd, *J* = 4.3, 1.6 Hz, 1H), 8.20 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.65 – 7.53 (m, 2H), 7.46 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.40 (t, *J* = 7.7 Hz, 1H), 7.32 (d, *J* = 7.7 Hz, 1H), 7.17 (t, *J* = 7.3 Hz, 1H), 7.05 (d, *J* = 7.5 Hz, 1H), 4.13 – 3.93 (m, 4H), 3.39 (bs, 1H), 2.50 (s, 3H), 1.08 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 168.95, 166.39, 148.24, 143.22, 138.49, 137.26, 136.41, 134.91, 133.99, 133.20, 132.49, 130.05, 129.13, 128.00, 127.38, 127.32, 122.46, 121.71, 117.14, 61.21, 59.35, 19.51, 13.91; **HRMS** (ESI-ToF) *m/z*: $[M+Na]^+$ Calcd. for $C_{23}H_{22}N_2O_4Na$ 413.1472; Found 413.1461.

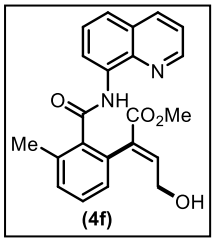
Octyl (*E*)-4-hydroxy-2-(3-methyl-2-(quinolin-8-ylcarbamoyl)phenyl)but-2-enoate (4e):



(4e)

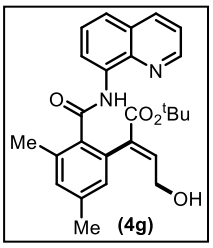
Reaction performed on 0.1 mmol scale (26 mg); Yield: 64% (36 mg); TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); Hydrogenation reaction performed on 0.057 mmol scale (31 mg): Yield: 74% (20 mg); TLC R_f 0.2 (8:2, Petroleum ether: EtOAc); Physical appearance: Off-white solid; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.97 (s, 1H), 8.93 – 8.84 (m, 1H), 8.74 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.19 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.63 – 7.55 (m, 2H), 7.46 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.39 (t, *J* = 7.7 Hz, 1H), 7.31 (d, *J* = 7.7 Hz, 1H), 7.15 (t, *J* = 7.1 Hz, 1H), 7.05 (d, *J* = 7.5 Hz, 1H), 4.09 – 3.89 (m, 4H), 3.37 (bs, 1H), 2.49 (s, 3H), 1.50 – 1.37 (m, 2H), 1.31 – 1.22 (m, 2H), 1.21 – 1.01 (m, 8H), 0.89 (t, *J* = 7.3 Hz, 3H).; **^{13}C NMR** (126 MHz, $CDCl_3$) δ 168.99, 166.44, 148.24, 143.04, 138.51, 137.24, 136.39, 134.85, 133.99, 133.25, 132.56, 130.01, 129.11, 128.01, 127.38, 127.28, 122.45, 121.69, 117.16, 65.32, 59.36, 31.71, 29.06, 29.00, 28.31, 25.64, 22.62, 19.50, 14.11; **HRMS** (ESI-ToF) *m/z*: $[M+Na]^+$ Calcd. for $C_{29}H_{34}N_2O_4Na$ 497.2411; Found 497.2434.

Methyl (*E*)-4-hydroxy-2-(3-methyl-2-(quinolin-8-ylcarbamoyl)phenyl)but-2-enoate (4f):



Reaction performed on 0.1 mmol scale (26 mg); Yield: 62% (28 mg); TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); Hydrogenation reaction performed on 0.062 mmol scale (28 mg): Yield: 70% (16 mg); TLC R_f 0.2 (8:2, Petroleum ether: EtOAc); Physical appearance: Off-white solid; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.00 (s, 1H), 8.93 – 8.82 (m, 1H), 8.75 (d, *J* = 3.9 Hz, 1H), 8.20 (d, *J* = 8.2 Hz, 1H), 7.59 (t, *J* = 6.5 Hz, 2H), 7.47 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.35 – 7.29 (m, 1H), 7.18 (t, *J* = 7.3 Hz, 1H), 7.05 (d, *J* = 7.6 Hz, 1H), 4.11 – 30.94 (m, 2H), 3.63 (s, 3H), 3.29 (s, 1H), 2.50 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 168.93, 166.84, 148.29, 143.79, 138.50, 137.36, 136.47, 135.04, 133.98, 132.81, 132.33, 130.12, 129.17, 128.04, 127.42, 127.21, 122.51, 121.73, 117.17, 59.29, 52.40, 19.46; **HRMS** (ESI-ToF) *m/z*: $[M+H]^+$ Calcd. for $C_{22}H_{21}N_2O_4$ 377.1496; Found 377.1474.

***tert*-butyl (*E*)-2-(3,5-dimethyl-2-(quinolin-8-ylcarbamoyl)phenyl)-4-hydroxybut-2-enoate (4g):**

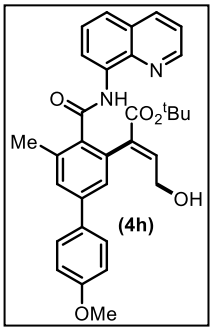


Reaction performed on 0.1 mmol scale (27 mg); Yield: 59% (30 mg); TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); Hydrogenation reaction performed on 0.061 mmol scale (30 mg): Yield: 66% (16 mg); TLC R_f 0.2 (8:2, Petroleum ether: EtOAc); Physical appearance: colorless gel; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.97 (s, 1H), 8.89 (dd, *J* = 6.4, 2.8 Hz, 1H), 8.75 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.18 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.66 – 7.53 (m, 2H), 7.44 (dd, *J* = 7.9, 4.0 Hz, 1H), 7.11 (s, 1H), 7.05 (t, *J* = 7.2 Hz, 1H), 6.84 (s, 1H), 4.13 – 3.94 (m, 2H), 3.51 (bs, 1H), 2.44 (s, 3H), 2.40 (s, 3H), 1.19 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.35, 165.76, 148.33, 141.61, 138.94, 138.43, 136.26, 134.92, 134.65, 134.61, 134.16, 132.80, 130.70, 127.92, 127.82, 127.35, 122.23, 121.62, 116.93, 81.15, 59.49, 27.63, 21.28, 19.44; **HRMS** (APCI-ToF) *m/z*: $[M+Na]^+$ Calcd. for $C_{26}H_{28}N_2O_4Na$ 455.1941; Found 455.1942.

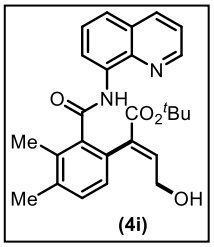
***tert*-butyl (*E*)-4-hydroxy-2-(4'-methoxy-5-methyl-4-(quinolin-8-ylcarbamoyl)-[1,1'-biphenyl]-3-yl)but-2-enoate (4h):**

Reaction performed on 0.1 mmol scale (37 mg); Yield: 57% (35 mg); TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); Hydrogenation reaction performed on 0.058 mmol scale (35 mg): Yield: 61% (19 mg); TLC R_f 0.2 (8:2, Petroleum ether: EtOAc); Physical appearance: colorless gel; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.03 (s, 1H), 8.92 (dd, *J* = 6.6, 2.4 Hz, 1H), 8.77

(dd, *J* = 4.2, 1.6 Hz, 1H), 8.19 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.65 – 7.53 (m, 4H), 7.48 (d, *J* = 1.7 Hz, 1H), 7.46 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.21 (d, *J* = 1.7 Hz, 1H), 7.14 – 7.07 (m, 1H), 7.02 (d, *J* = 8.1 Hz, 2H), 4.19 – 3.99 (m, 2H), 3.89 (s, 3H), 3.49 (bs, 1H), 2.54 (s, 3H), 1.21 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.07, 165.65, 159.53, 148.37, 141.90, 141.54, 138.44, 136.32, 135.58, 135.26, 134.96, 134.12, 133.41, 132.63, 128.31, 128.21, 127.95, 127.37, 125.57, 122.33, 121.66, 117.02, 114.28, 81.28, 59.51, 55.39, 27.66, 19.74; **HRMS** (ESI-ToF) *m/z*: $[M+H]^+$ Calcd. for $C_{32}H_{33}N_2O_5$ 525.2384; Found 525.2406.



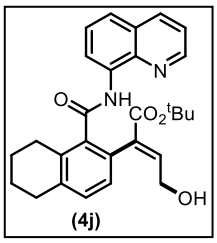
tert-butyl (_E_)-2-(3,4-dimethyl-2-(quinolin-8-ylcarbamoyl)phenyl)-4-hydroxybut-2-enoate (4i):



Reaction performed on 0.1 mmol scale (27 mg); Yield: 61% (30 mg); TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); Hydrogenation reaction performed on 0.059 mmol scale (30 mg): Yield: 69% (17 mg); TLC R_f 0.2 (8:2, Petroleum ether: EtOAc); Physical appearance: colorless gel; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.99 (s, 1H), 8.90 (dd, *J* = 6.5, 2.5 Hz, 1H), 8.75 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.63 – 7.54 (m, 2H), 7.44 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.27 (d, *J* = 7.8 Hz, 1H), 7.10 – 7.02 (m, 1H), 6.94 (d, *J* = 7.7 Hz, 1H), 4.08 – 3.89 (m, 2H), 3.47 (bs, 1H), 2.37 (s, 3H), 2.36 (s, 3H), 1.18 (s, 9H).; **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.79, 165.85, 148.33, 141.83, 138.45, 137.51, 137.00, 136.24, 134.83, 134.11, 132.88, 130.51, 130.37, 127.91, 127.34, 127.09, 122.32, 121.63, 116.99, 81.06, 59.48, 27.61, 20.09, 16.65; **HRMS** (ESI-ToF) *m/z*: $[M+H]^+$ Calcd. for $C_{26}H_{29}N_2O_4$ 433.2122; Found 433.2098.

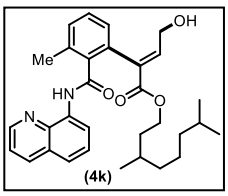
tert-butyl (_E_)-4-hydroxy-2-(1-(quinolin-8-ylcarbamoyl)-5,6,7,8-tetrahydronaphthalen-2-yl)but-2-enoate (4j):

Reaction performed on 0.1 mmol scale (30 mg); Yield: 59% (29 mg); TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); Hydrogenation reaction performed on 0.059 mmol scale (29 mg): Yield: 64% (18 mg); TLC R_f 0.2 (8:2, Petroleum ether: EtOAc); Physical appearance: colorless gel; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.99 (s, 1H), 8.92 – 8.88 (m, 1H), 8.75 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.20 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.59 (d, *J* = 4.5 Hz, 2H), 7.46 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.21 (d, *J* = 7.9 Hz, 1H), 7.16 (t, *J* = 7.1 Hz, 1H), 6.95 (d, *J* = 7.8 Hz, 1H), 4.12 – 3.92 (m, 2H), 3.63 (s, 3H), 3.31 (bs, 1H), 2.98 – 2.82 (m, 4H), 1.89 – 1.80 (m, 4H); **^{13}C NMR** (126



MHz, CDCl3) δ 169.28, 167.04, 148.23, 143.72, 138.48, 137.78, 136.42, 134.03, 133.95, 132.85, 130.17, 129.37, 128.02, 127.42, 126.65, 122.42, 121.68, 117.11, 59.28, 52.38, 29.69, 26.59, 22.73, 22.58; **HRMS** (ESI-ToF) *m/z*: $[M+H]^+$ Calcd. for $C_{25}H_{25}N_2O_4$ 417.1809; Found 417.1829.

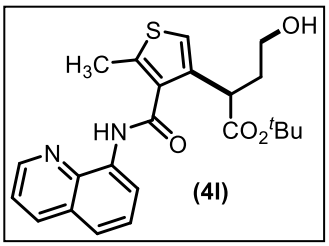
***tert*-butyl (*Z*)-4-hydroxy-2-(1-(quinolin-8-ylcarbamoyl)-5,6,7,8-tetrahydronaphthalen-2-yl)but-2-enoate (4k):**



Reaction performed on 0.1 mmol scale (26 mg); Yield: 48% (27 mg); TLC R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); Hydrogenation reaction performed on 0.047 mmol scale (27 mg): Yield: 57% (14 mg); TLC R_f 0.2 (8:2, Petroleum ether: EtOAc); Physical appearance: colorless gel; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.97 (s, 1H), 8.88 (dd, *J* = 5.1, 3.9 Hz, 1H), 8.75 (dd, *J* = 4.3, 1.6 Hz, 1H), 8.20 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.59 (s, 2H), 7.46 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.38 (d, *J* = 7.7 Hz, 1H), 7.31 (d, *J* = 7.7 Hz, 1H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.04 (d, *J* = 7.6 Hz, 1H), 4.16 – 3.92 (m, 4H), 3.36 (s, 1H), 2.49 (s, 3H), 1.59 (d, *J* = 9.2 Hz, 6H), 1.33 – 1.19 (m, 4H), 0.89 – 0.79 (m, 6H), 0.77 – 0.55 (m, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 168.97, 166.44, 148.26, 143.02, 138.52, 137.25, 136.39, 134.84, 133.98, 133.28, 130.01, 129.11, 128.01, 127.39, 127.28, 122.44, 121.69, 117.17, 59.36, 39.14, 35.23, 27.92, 24.53, 22.70, 22.60, 19.51; **HRMS** (ESI-ToF) *m/z*: $[M+Na]^+$ Calcd. for $C_{31}H_{38}N_2O_4$ 525.2724; Found 525.2706.

***tert*-butyl 4-hydroxy-2-(5-methyl-4-(quinolin-8-ylcarbamoyl)thiophen-3-yl)butanoate (4l):**

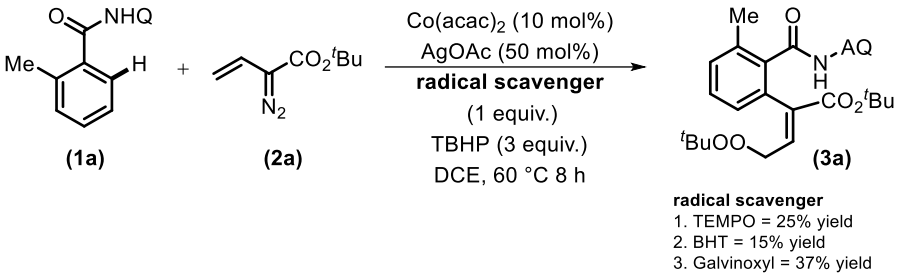
Reaction performed on 0.1 mmol scale (27 mg); Yield: 21% (10 mg) (qualitative yield); TLC



R_f 0.2 (6:2:2, Petroleum ether: DCM: EtOAc); Hydrogenation reaction performed on 0.042 mmol scale (20 mg): Yield: 17% (3 mg); TLC R_f 0.2 (8:2, Petroleum ether: EtOAc); Physical appearance: colorless gel; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.22 (s, 1H), 8.96 (d, *J* = 7.3 Hz, 1H), 8.85 (d, *J* = 3.2 Hz, 1H), 8.29 (d, *J* = 8.1 Hz, 1H), 7.72 – 7.58 (m, 2H), 7.54 (dd, *J* = 8.0, 3.9 Hz, 1H), 6.86 (s, 1H), 4.07 (dd, *J* = 7.7, 3.8 Hz, 1H), 3.05 – 2.85 (m, 2H), 2.72 (s, 3H), 2.19 – 2.10 (m, 1H), 2.02 – 1.92 (m, 1H), 1.40 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.31, 164.58, 140.93, 124.73, 122.12, 121.57, 118.81, 82.30, 69.92, 35.09, 27.91, 25.03, 15.00; **HRMS** (ESI-ToF) *m/z*: $[M+Na]^+$ Calcd. for $C_{23}H_{26}N_2O_4SNa$ 449.1505; Found 449.1494.

5. Mechanistic Studies

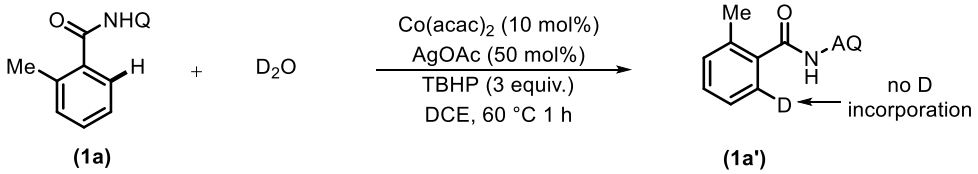
(I) Radical quenching experiment:



In an oven-dried pressure tube equipped with a stir bar, the *N*-(quinolin-8-yl) benzamide (1.0 equiv., 0.1 mmol) and vinyl diazo ester (3 equiv., 0.30 mmol) were dissolved in DCE (1.5 mL). The solution was degassed with nitrogen for about 10 min, following which $Co(acac)_2$ (10 mol%, 0.01 mmol), AgOAc (0.50 equiv., 0.05 mmol), TBHP (5 equiv., 0.05 mmol, 6M soln in decane) and 1 equiv. of radical scavenger (TEMPO or BHT or Galvinoxyl) were added, and the pressure tube was sealed. This reaction mixture was then stirred in an oil bath pre-heated at 60 ^oC, for 8 hours, and the reaction progress was monitored by TLC. Upon completion of the reaction, the reaction mixture was diluted with EtOAc and filtered through a short pad of Celite, and the filtrate was concentrated. The residue was dissolved in EtOAc and washed with saturated $NaHCO_3$ solution and brine. The organic extract was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure and the crude product was purified by silica gel flash column chromatography. The presence of TEMPO, BHT, and Galvinoxyl reduced the yield of the reaction to 25%, 15%, and 37% respectively, indicating that the reaction may proceed *via* a single electron transfer pathway.

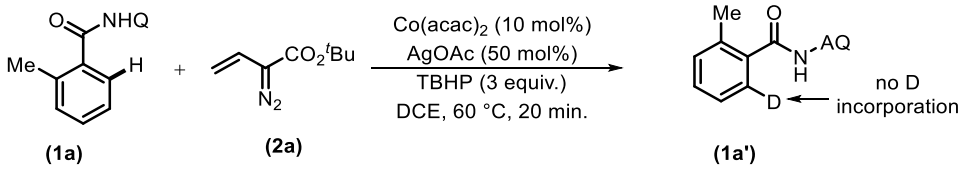
(III) Reversibility experiment: To investigate the reversibility of the formation of the cobaltacycle, we performed D-quenching studies, both in the presence and absence of the coupling partner

(A) Reversibility experiment in absence of vinyl diazo ester:



In an oven-dried pressure tube equipped with a stir bar, the *N*-(quinolin-8-yl) benzamide (1.0 equiv., 0.1 mmol) and vinyl diazo ester (3 equiv., 0.30 mmol) were dissolved in DCE (1.5 mL). The solution was degassed with nitrogen for about 10 min, following which $Co(acac)_2$ (10 mol%, 0.01 mmol), AgOAc (0.50 equiv., 0.05 mmol), and TBHP (5 equiv., 0.05 mmol, 6M in decane) were added, and the pressure tube was sealed with a septum cap. This reaction mixture was then stirred in an oil bath pre-heated at 60 °C, for 1 hour, after which, the reaction mixture was diluted with EtOAc and filtered through a short pad of Celite, and the filtrate was concentrated. The residue was dissolved in EtOAc and washed with saturated $NaHCO_3$ solution and brine. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure and the crude starting material was purified by silica gel flash column chromatography and analyzed by NMR.

(B) Reversibility experiment in the presence of vinyl diazo ester:



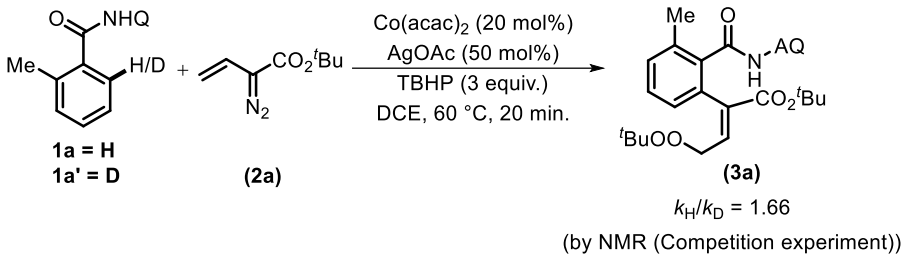
(1a) (2a) (1a')

In an oven-dried pressure tube equipped with a stir bar, the *N*-(quinolin-8-yl) benzamide (1.0 equiv., 0.1 mmol) and vinyl diazo ester (3 equiv., 0.30 mmol) were dissolved in DCE (1.5 mL mL). The solution was degassed with nitrogen for about 10 min, following which $Co(acac)_2$ (10 mol%, 0.01 mmol), AgOAc (0.50 equiv., 0.05 mmol), and TBHP (5 equiv., 0.05 mmol, 6M soln in decane) were added, and the pressure tube was sealed. This reaction mixture was then stirred in an oil bath pre-heated at 60 °C, for 20 minutes, following which, the reaction mixture was diluted with EtOAc and filtered through a short pad of Celite, and the filtrate was concentrated under reduced pressure. The residue was dissolved in EtOAc and washed with saturated $NaHCO_3$ solution and brine. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure and the crude starting material and product were purified by silica gel flash column chromatography and analyzed by NMR.

No D-incorporation was observed in the starting material at the *ortho* position of the benzamide, both, in the absence of the coupling partner as well as in the presence of the coupling partner, which suggests that the C–H activation is irreversible in nature.

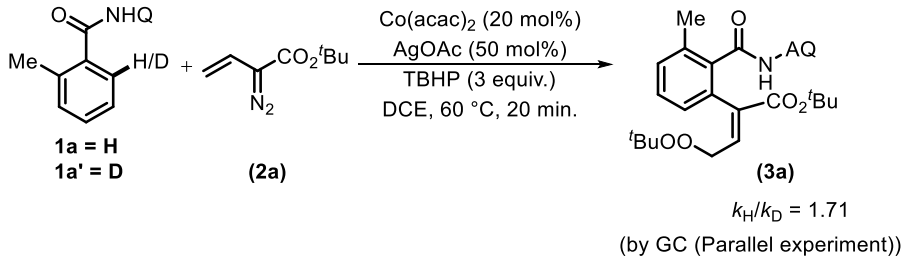
(IV) Studies to check for a Kinetic Isotopic Effect: To further investigate whether the C−H metalation step is rate-limiting, we carried out studies to check for a kinetic isotope effect.

(A) Competition Experiment (by NMR):



In an oven-dried pressure tube equipped with a stir bar, 2-methyl-*N*-(quinolin-8-yl)benzamide (1.0 equiv., 0.05 mmol) and 2-methyl-*N*-(quinolin-8-yl)benzamide-6-*d* (1 equiv., 0.05 mmol) and *tert*-butyl 2-diazobut-3-enoate (3 equiv., 0.30 mmol) were dissolved in DCE (1.5 mL). The solution was degassed with nitrogen for about 10 min, following which $Co(acac)_2$ (10 mol%, 0.01 mmol), AgOAc (0.50 equiv., 0.05 mmol), and TBHP (5 equiv., 0.05 mmol, 6M soln in decane) were added, the pressure tube was sealed. This reaction mixture was then stirred in an oil bath pre-heated to 60 ^oC, for 20 minutes, after which, the reaction mixture was diluted with EtOAc and filtered through a short pad of Celite, and the filtrate was concentrated. The residue was re-dissolved in EtOAc and washed with saturated $NaHCO_3$ solution and brine. The organic extract was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure and the crude starting material was purified by silica gel flash column chromatography and analyzed by NMR.

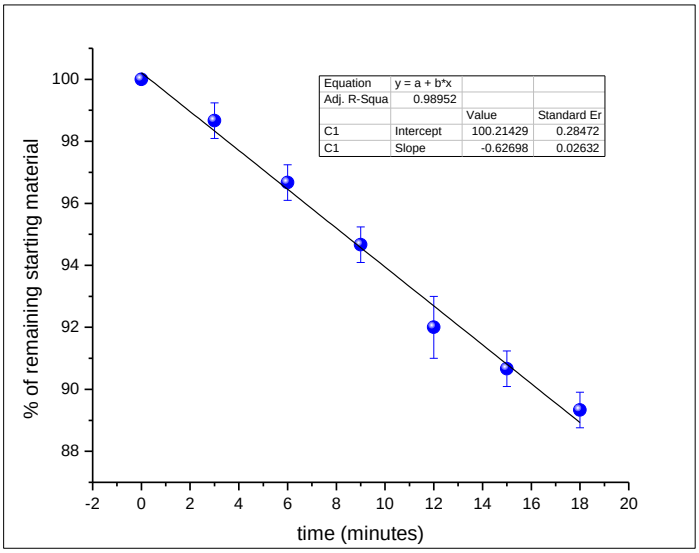
(B) Parallel Experiment (by GC):



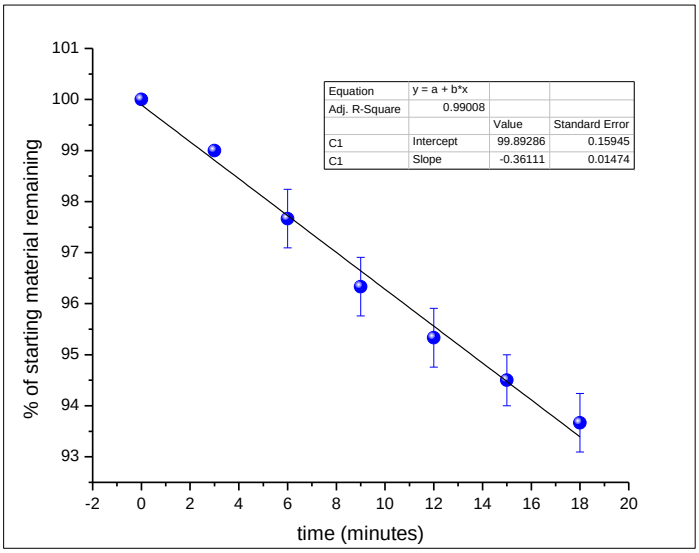
Two parallel reactions for 2-methyl-*N*-(quinolin-8-yl)benzamide (1 equiv., 0.1 mmol) and 2-methyl-*N*-(quinolin-8-yl)benzamide-6-*d* (1 equiv., 0.1 mmol) with *tert*-butyl 2-diazobut-3-enoate (2 equiv., 0.4 mmol) were performed according to the general procedure I, using dodecane (0.5 equiv., 0.05 mmol) as the internal standard. Aliquots were drawn at intervals of

18 minutes and conversions were checked by GC. The consumption of the starting material was plotted with time and k_H/k_D was found to be 1.71 (average of 3 runs).

Plot A (Rate of reaction of 2-methyl-*N*-(quinolin-8-yl)benzamide):



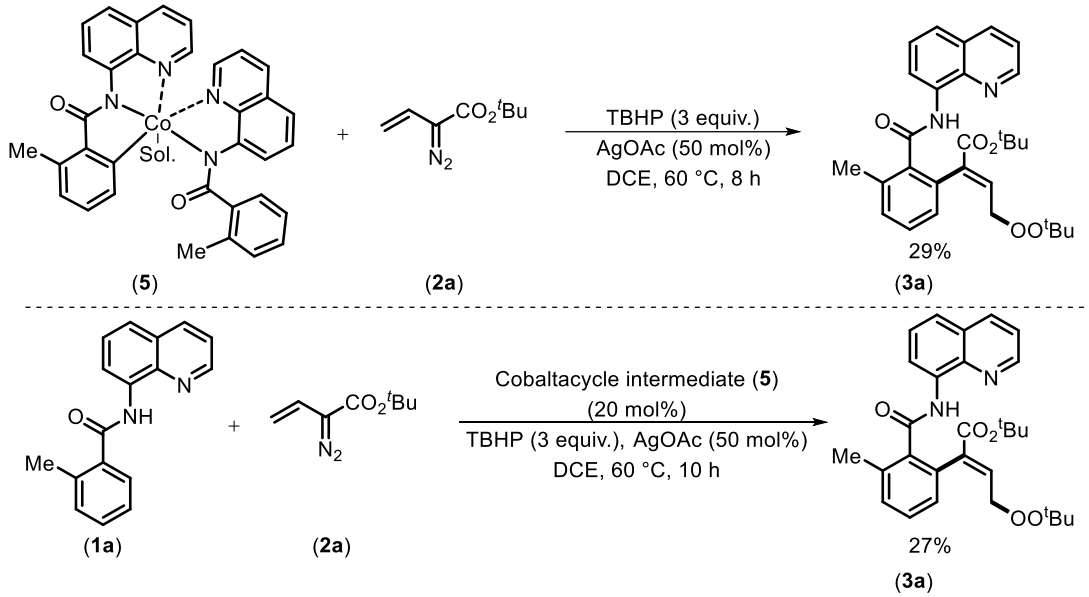
Plot B (Rate of reaction of 2-methyl-*N*-(quinolin-8-yl)benzamide-6-*d*):



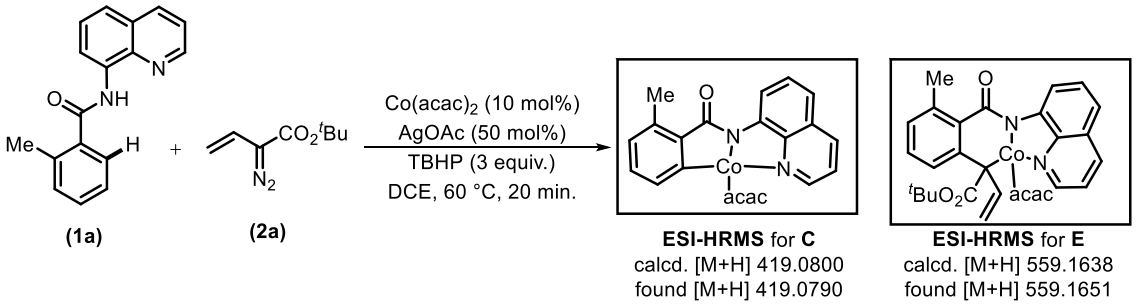
These experiments indicated that the C-H metalation step is the rate-limiting step in the catalytic cycle.

(V) Reactions with pre-formed cobaltacycle intermediate

Additionally, we performed a reaction with a stoichiometric amount of the isolated cobaltacyle **5** under the optimized condition. This afforded the corresponding 1,3-difunctionalized product (**3a**) in 29% yield. This was followed using cobaltacycle **5** in a catalytic amount and this also yielded the 1,3-difunctionalized product (**3a**) in 27% yield. These results suggest that this type of cobaltacycle intermediate may be present in the catalytic cycle.



(VI) Mass Spectrometry Experiment:

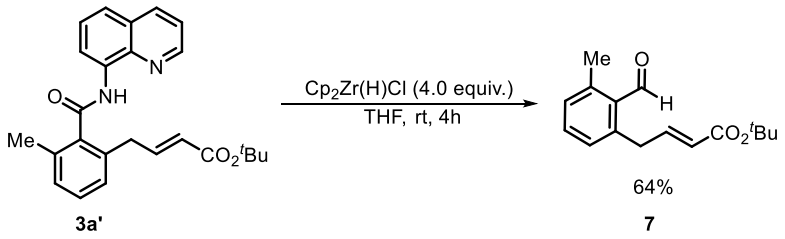


Procedure: In an oven-dried pressure tube equipped with a stir bar, the 2-methyl-*N*-(quinolin-8-yl)benzamide (1.0 equiv., 0.1 mmol) and *tert*-butyl 2-diazobut-3-enoate (1.5 equiv., 0.15 mmol) were dissolved in DCE (1 mL). The solution was degassed with nitrogen for about 10 min, following which $Co(acac)_2$ (20 mol%, 0.02 mmol), AgOAc (0.50 equiv., 0.05 mmol), and TBHP (5 equiv., 0.05 mmol, 6M solution in decane) were added, the pressure tube was sealed with a septum cap at 60 ^{o}C. An aliquot was drawn, passed through a frit, and immediately subjected to mass analysis.

Efforts towards the removal of the 8-AQ directing group:[4]

While we were able to remove the 8-AQ directing group quite easily in substrate **3a'**, we faced considerable difficulty in removal of the DG in substrates **4a** and **3a**.

A) Cleavage of the 8-AQ directing group in product **3a':**

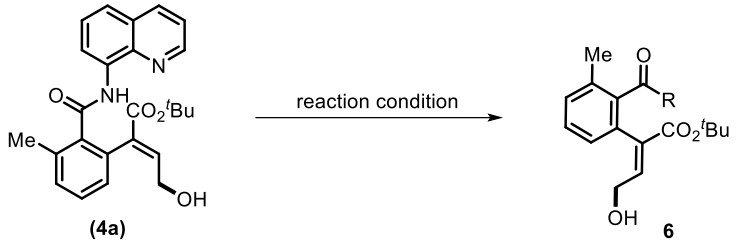


3a' **7**

To a solution of compound **3a'** (20 mg, 0.05 mmol) in THF (1 mL) was added $Cp_2Zr(H)Cl$ (51 mg, 0.2 mmol) under N_2. The reaction was stirred at room temperature and the progress was further monitored by TLC. Upon completion of the reaction, the reaction mixture was diluted with EtOAc and concentrated under reduced pressure. The resulting residue was purified by the silica gel flash column chromatography to give the desired product **7** in 64% yield (8 mg).

TLC *Rf* 0.6 (20:1, Petroleum ether: EtOAc); Physical appearance: yellow gel; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.56 (s, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.19 (d, *J* = 7.6 Hz, 1H), 7.12 (d, *J* = 7.6 Hz, 1H), 7.05 (dt, *J* = 15.6, 6.3 Hz, 1H), 5.63 (d, *J* = 15.7, 1.8 Hz, 1H), 3.88 (d, *J* = 6.3, 1.8 Hz, 2H), 2.66 (s, 3H), 1.48 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 193.02, 165.75, 145.82, 141.82, 140.45, 133.37, 132.14, 130.75, 129.52, 124.25, 99.98, 80.32, 35.81, 28.12, 20.38; **HRMS** (ESI-ToF) m/z: $[M+H]^+$ Calcd. for $C_{16}H_{20}O_3$ 261.1485; Found 261.1480

B) Efforts towards the removal of the 8-AQ in substrate **4a**:

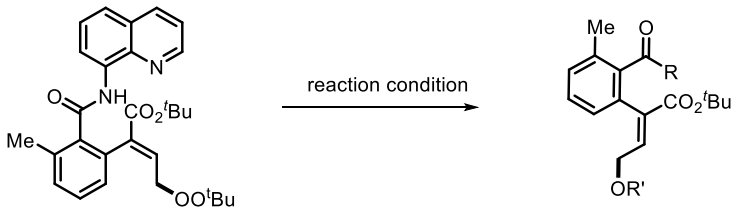


(4a) **6**

Sr. No.	Reaction Conditions	Result
1.	TfOH (3.0 equiv.), PhMe/H_2O, 100 °C, 12 h	SM recovered
2	TsOH (3.0 equiv.), MeOH, 100 °C, 12 h	**4f**, (transesterification product)

3	HCl, MeOH, 100 °C, 12h	Complex reaction mixture
4	HBr in AcOH, 100 °C, 12 h	Complex reaction mixture
5	HBr in H_2O, 100 °C, 12 h	Complex reaction mixture
6	K_2CO_3 (4.0 equiv.), H_2O (5.0 equiv.), MeOH, 75 °C, 12 h	Complex reaction mixture
7	LiOH (10.0 equiv.), MeOH, 75 °C, 12 h	Complex reaction mixture
8	NaOH (10.0 equiv.), MeOH, 100 °C, 12 h	Complex reaction mixture
9	KOH (10.0 equiv.), MeOH, 100 °C, 12 h	Complex reaction mixture
10	$BF_3.OEt_2$ (10.0 equiv.), MeOH, 100 °C, 12 h	Complex reaction mixture
11	IBX (2.0 equiv.), HFIP:H_2O, 60 °C, 12 h	SM recovered
12	DIBAL-H (5.0 equiv.), −78 °C, DCM, 0.5 h	SM recovered
13	$Cp_2Zr(H)Cl$ (3.0 equiv.), THF, rt, 4 h	Complex reaction mixture
14	$Cp_2Zr(H)Cl$ (3.0 equiv.), 1,4-dioxane, rt to 60 °C, 4 h	Complex reaction mixture
15	$Cp_2Zr(H)Cl$ (3.0 equiv.), DCM, rt, 2 h	Complex reaction mixture
16	$Cp_2Zr(H)Cl$ (3.0 equiv.), DCE, rt, 2 h	SM recovered
17	$Ni(tmhd)_2$ (5 mol%), MeOH, 100 °C, 12 h	Complex reaction mixture

C) Efforts towards the removal of the 8-AQ in substrate **3a:**



3a **6'**

Sr. No.	Reaction Conditions	Result
1	$Cp_2Zr(H)Cl$ (5.0 equiv.), THF, rt, 4 h	Complex reaction mixture
2	IBX (2.0 equiv.), HFIP:H_2O, 60 °C, 12 h	SM recovered
3	K_2CO_3 (4.0 equiv.), H_2O (5.0 equiv.), MeOH, 75 °C, 12 h	Complex reaction mixture
4	LiOH (10.0 equiv.), MeOH, 75 °C, 12 h	Complex reaction mixture

6. References

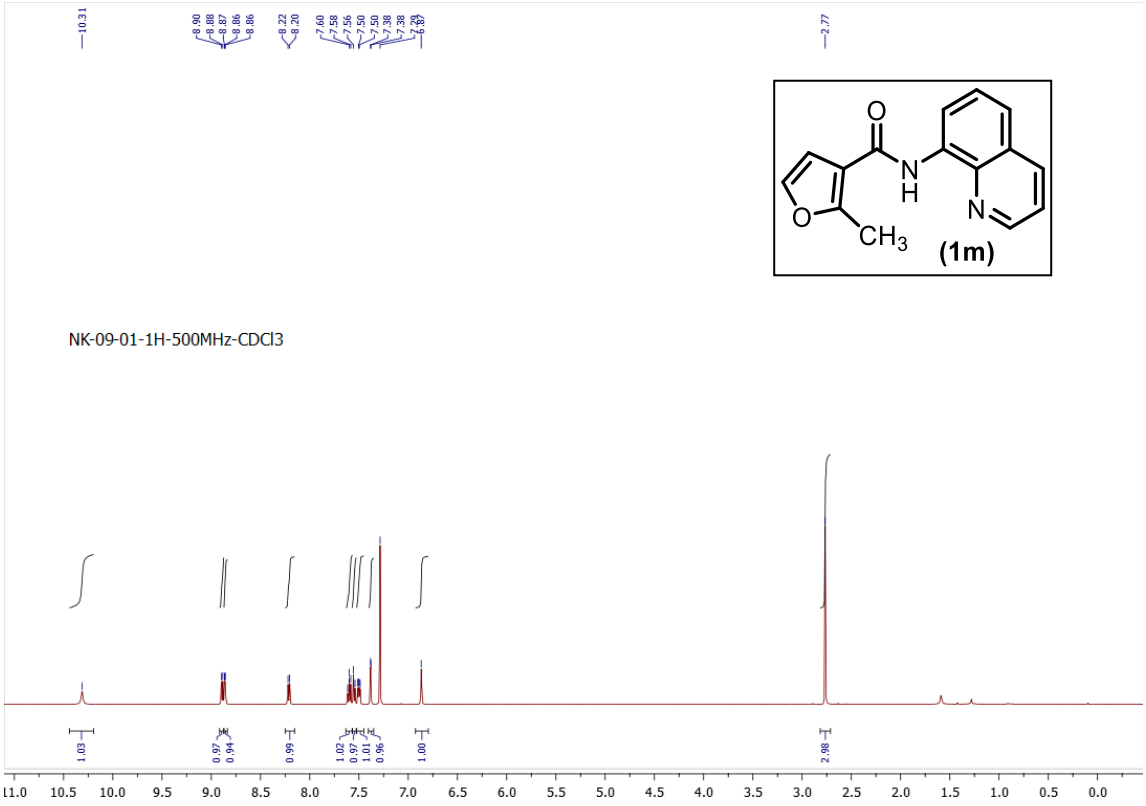
1. (a) B. He, X. Liu, H. Li, X. Zhang, Y. Ren and W. Su, *Org. Lett.* 2021, **23**, 4191. (b) J. Tang, P. Liu and X. Zeng, *Chem. Commun.* 2018, **54**, 9325. (c) W. Sarkar, A. Mishra, A. Bhowmik, and I. Deb, *Org. Lett.* 2021, **23**, 4521. (d) S. Liu, B. He, H. Li, X. Zhang, Y. Shang and W. Su, *Chem. –Eur. J.* 2021, **27**, 15628. (e) A. P. Honeycutt and J. M. Hoover, *Org. Lett.* 2018, **20**, 7216. (f) G. Rouquet and N. Chatani, *Chem. Sci.* 2013, **4**, 2201.

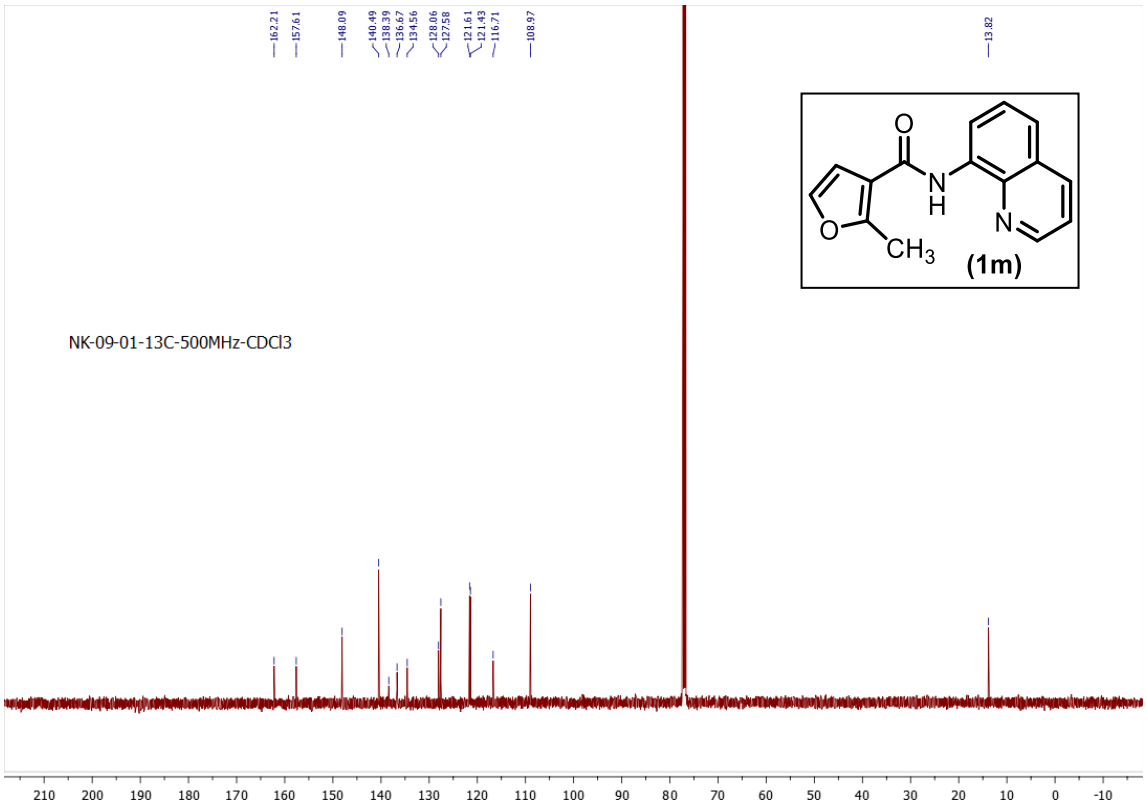
2. (a) J.-Q. Wu, Z. Yang, S.-S. Zhang, C.-Y. Jiang, Q. Li, Z.-S. Huang and H. Wang, *ACS Catal.* 2015, **5**, 6453. (b) L. De Angelis, H. Zheng, M. T. Perz, H. Arman and M. P. Doyle, *Org. Lett.* 2021, **23**, 6542. (c) W. Li, X. Zhou, X. Xiao, Z. Ke and L. Zhou *CCS Chem.* 2022, **4**, 638.

3. S. Maity, R. Kancherla, U. Dhawa, E. Hoque, S. Pimparkar and D. Maiti, *ACS Catal.* 2016, **6**, 5493.

4. L. S. Fitzgerald and M. L. O'Duill, *Chem. -Eur J.* 2021, **27**, 8411.

7. Copies of ^{1}H, ^{13}C, ^{19}F and ESI-HRMS data:





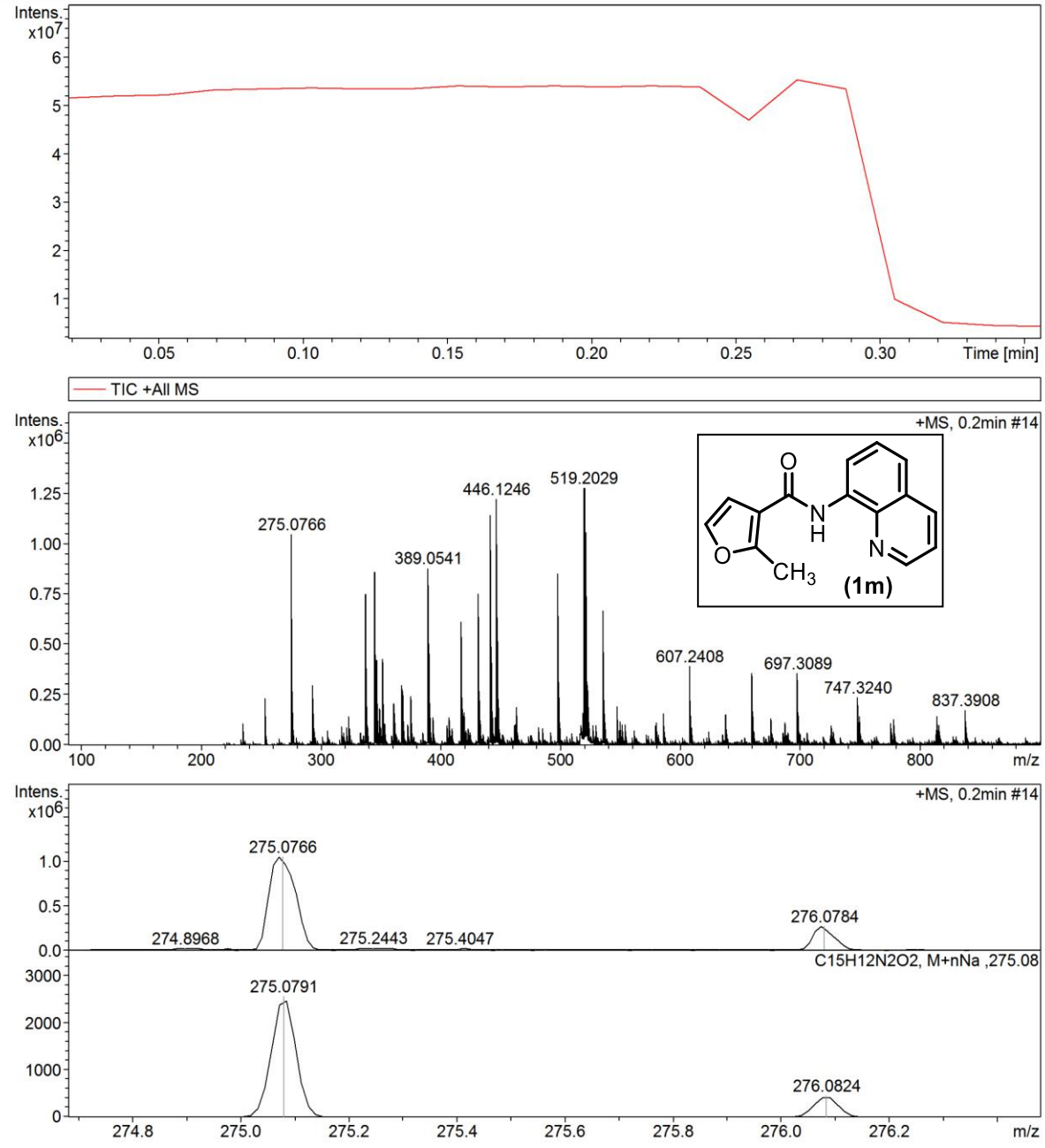
Display Report

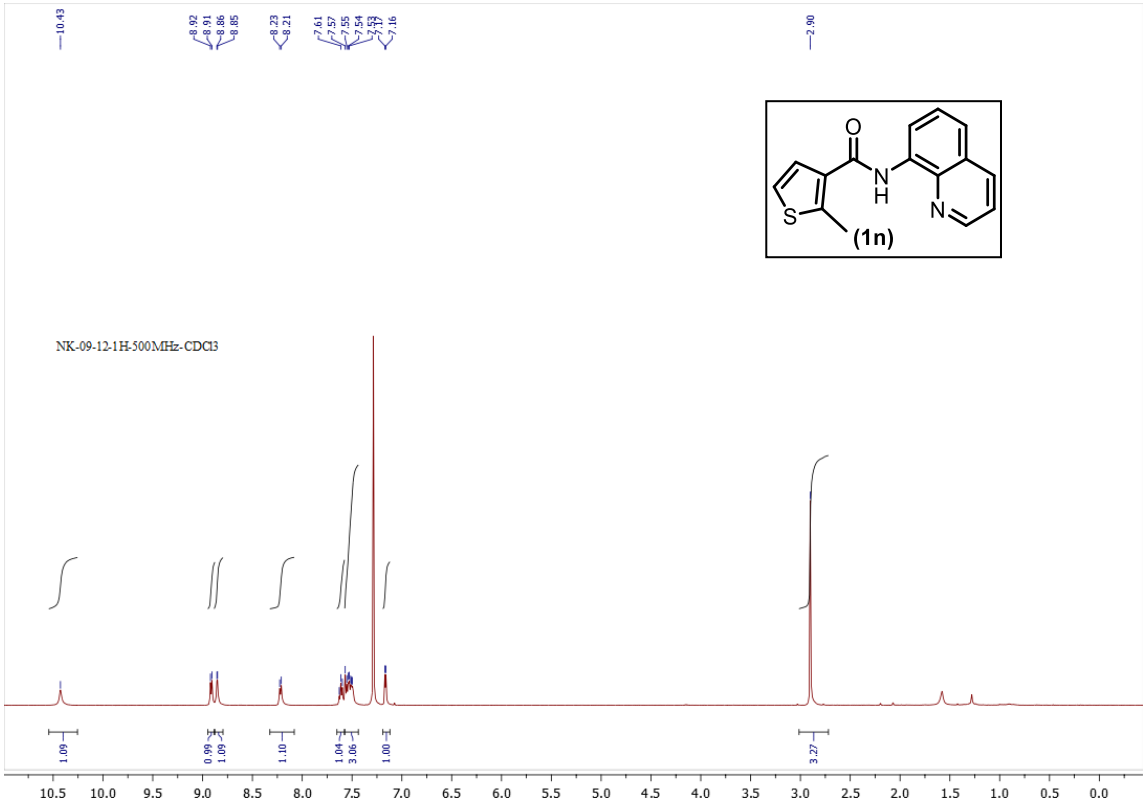
Analysis Info

Analysis Name	D:\Data\USER DATA 2023\Feb\24-02-2023\Prof M Kapur-NK-09-14-LS.d	Acquisition Date	24-02-2023 10:04:29
Method	tune_low_Jan23.m	Operator	Bruker
Sample Name	NK-09-14-LS	Instrument	micrOTOF-Q 10330
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.8 Bar
Focus	Not active	Set Capillary	4600 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	7.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	400.0 Vpp	Set Divert Valve	Waste

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8.91
8.86
8.85
8.23
8.21
7.61
7.57
7.55
7.54
7.53
7.17
7.16
2.90
O
N
H
S
N
(1n)
NK-09-12-1H-500MHz-CDCl3
1.09
0.99
1.09
1.10
1.04
3.06
1.00
3.27
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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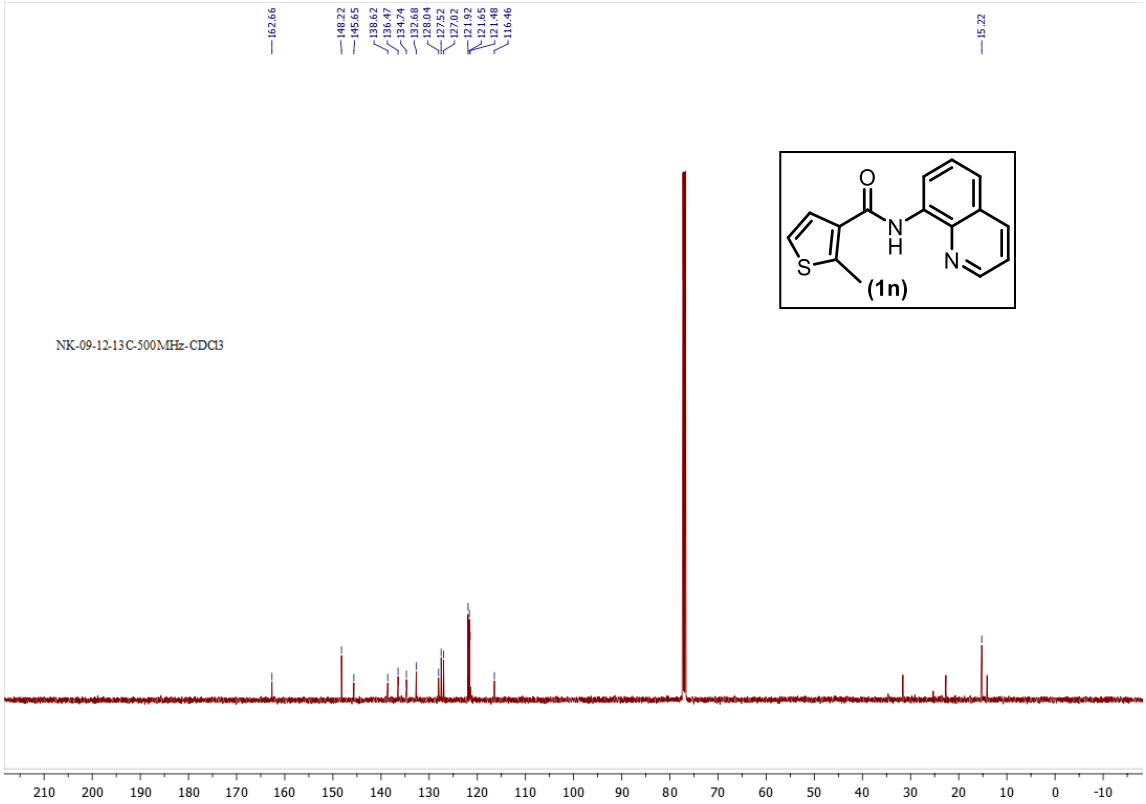
2.0
1.5
1.0
0.5
0.0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136.47
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128.04
127.52
127.02
121.92
121.65
121.48
116.46
15.22
O
N
H
S
N
(1n)
NK-09-12-13C-500MHz-CDCl3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

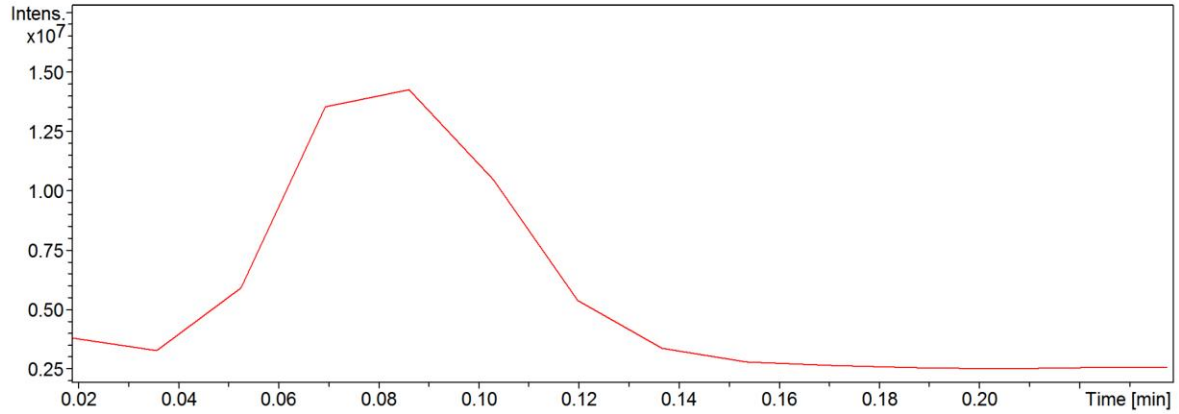
Display Report

Analysis Info

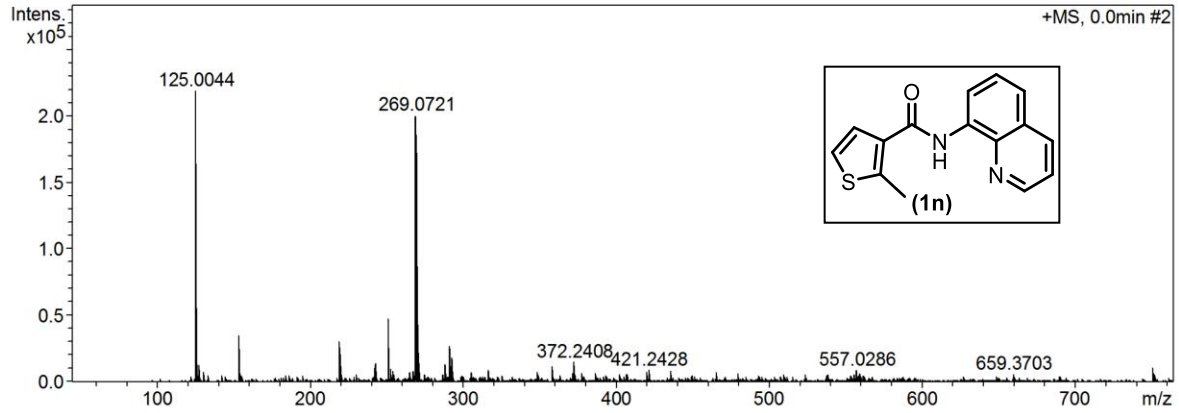
Analysis Name	D:\Data\USER DATA 2023\Feb\24-02-2023\Prof M Kapur-NK-09-12.d	Acquisition Date	24-02-2023 09:32:04
Method	tune_low_Jan23.m	Operator	Bruker
Sample Name	NK-09-12	Instrument	micrOTOF-Q 10330
Comment			

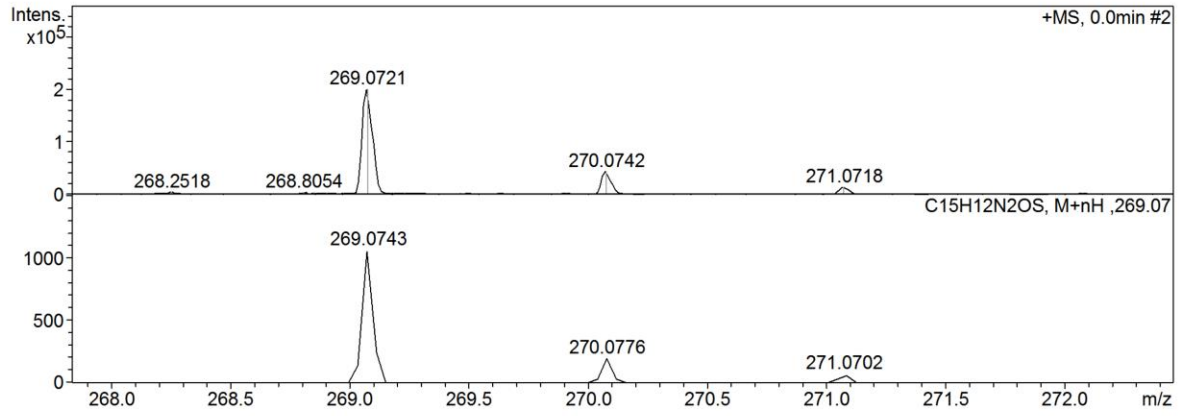
Acquisition Parameter

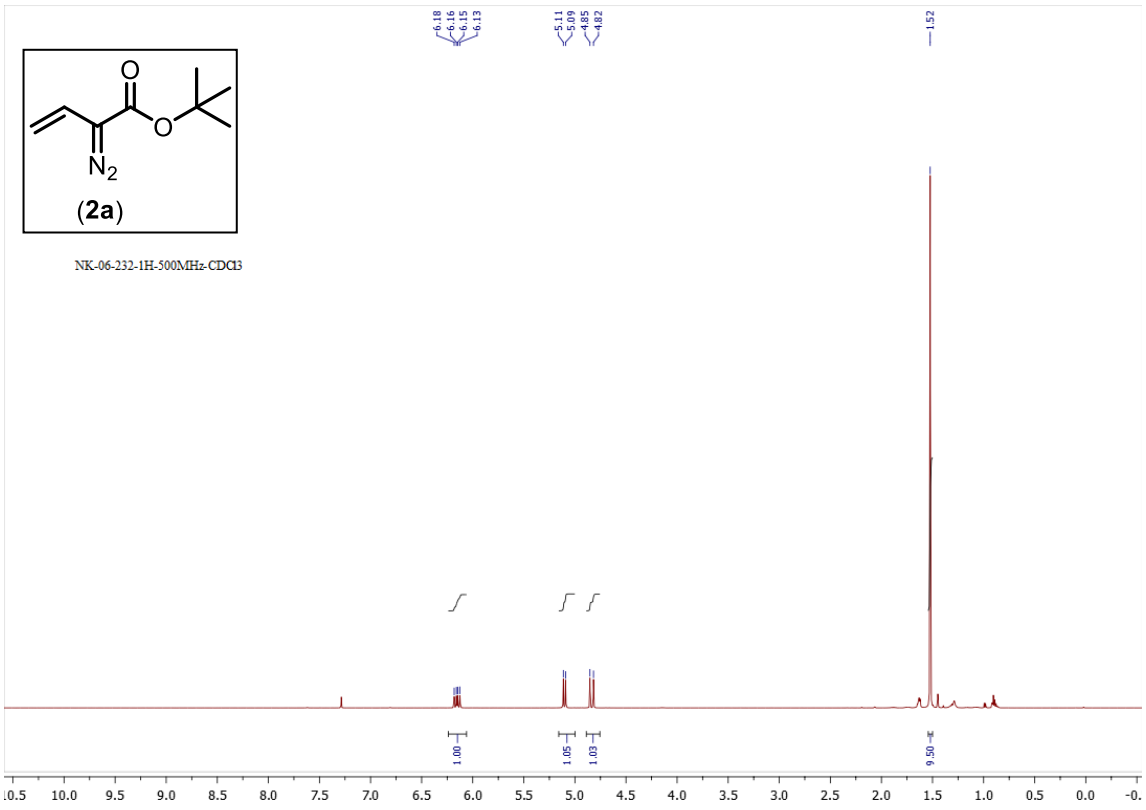
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.8 Bar
Focus	Not active	Set Capillary	4600 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	7.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	150.0 Vpp	Set Divert Valve	Waste



TIC +All MS



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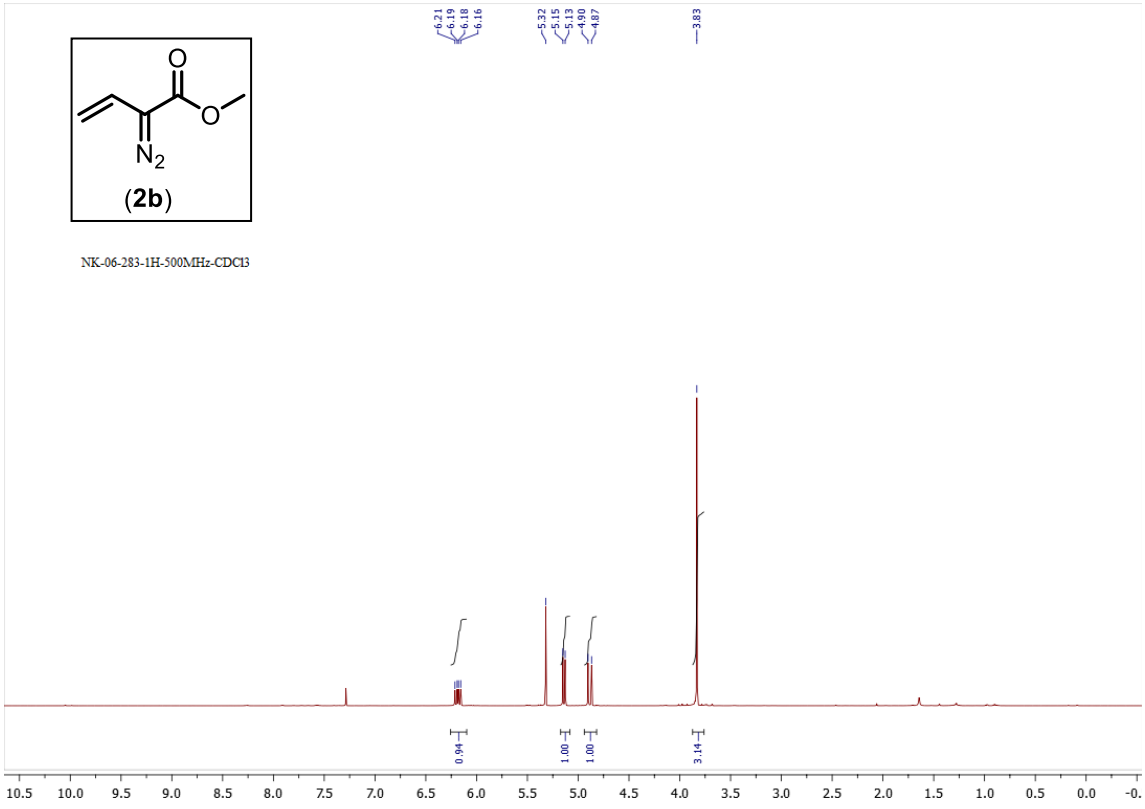
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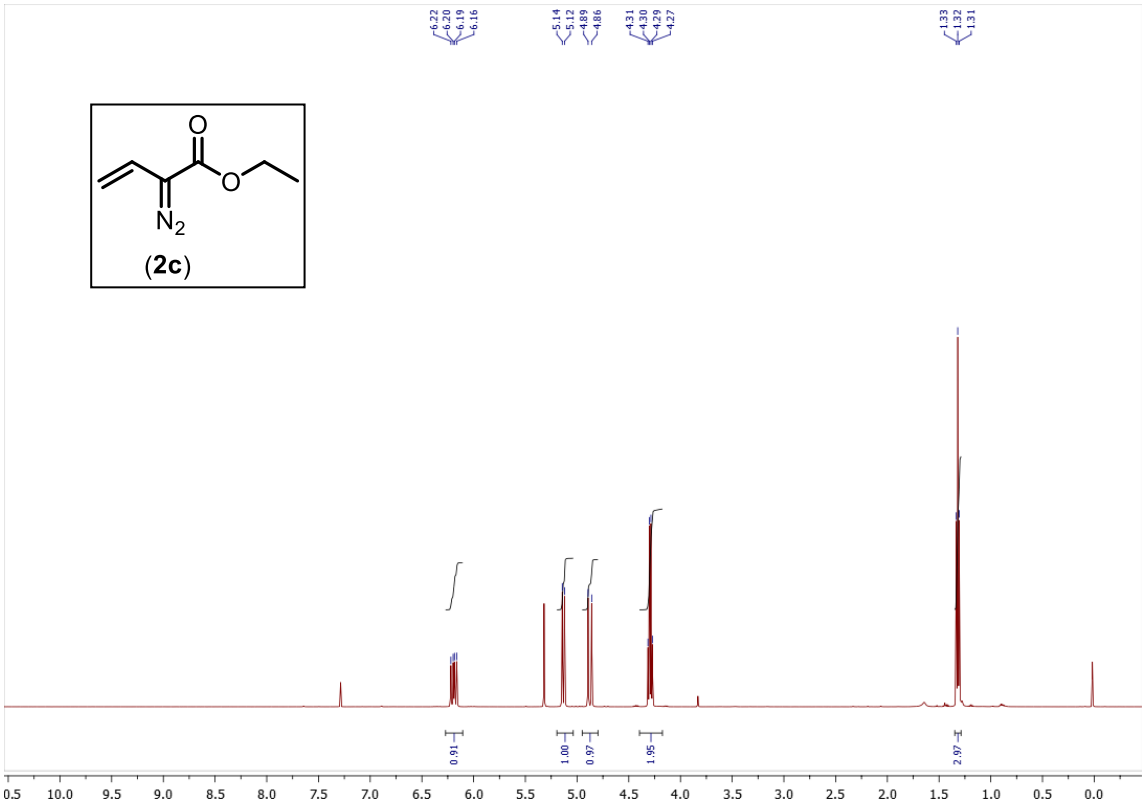
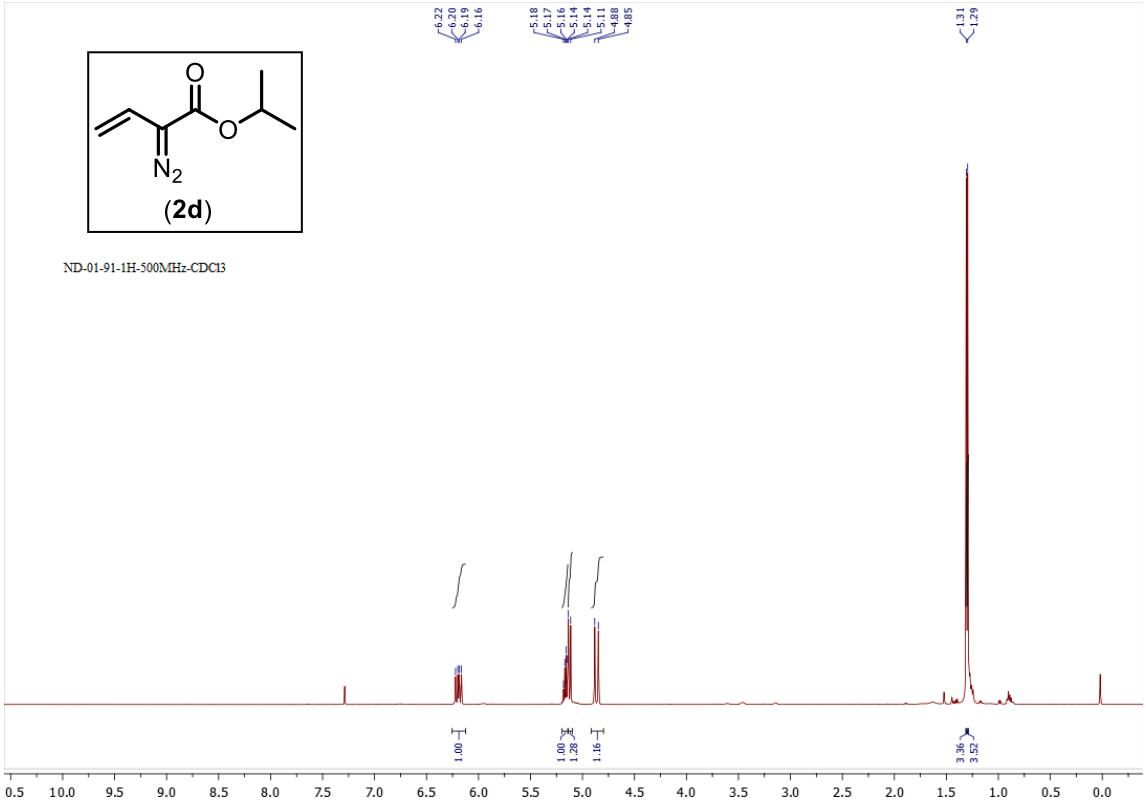

(2c)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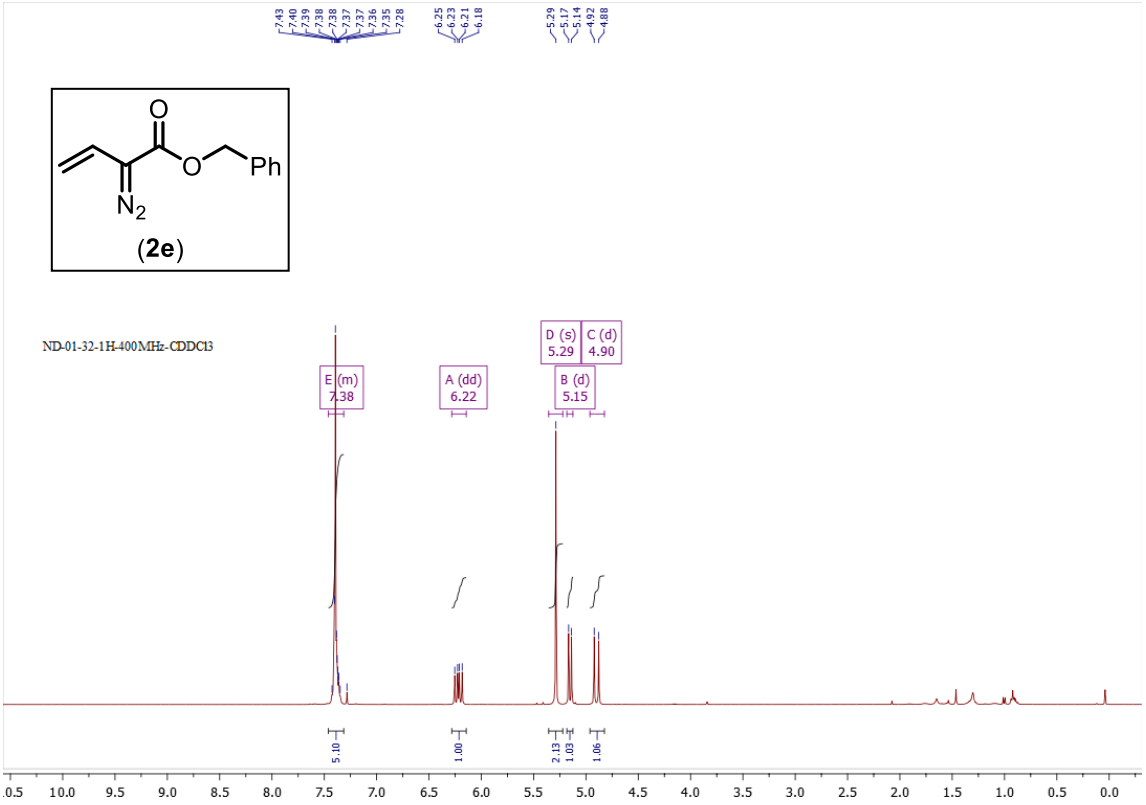
(2e)
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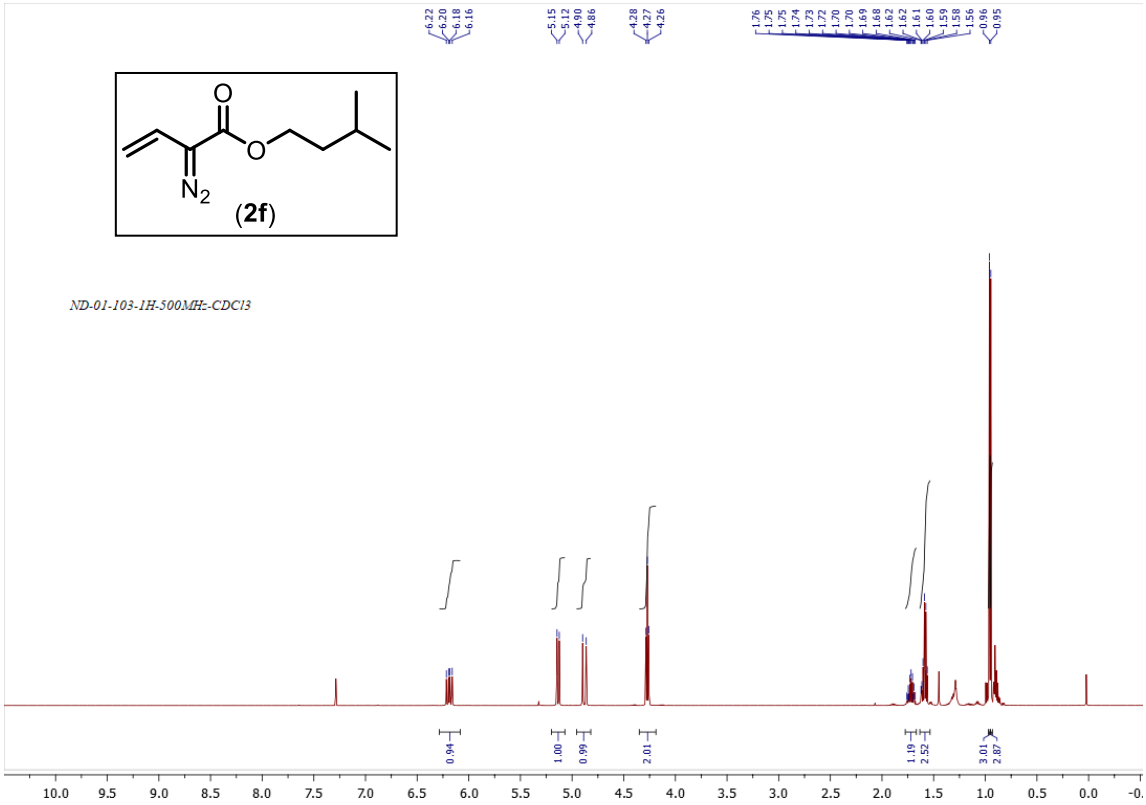
A (dd) 6.22
D (s) 5.29
C (d) 4.90
B (d) 5.15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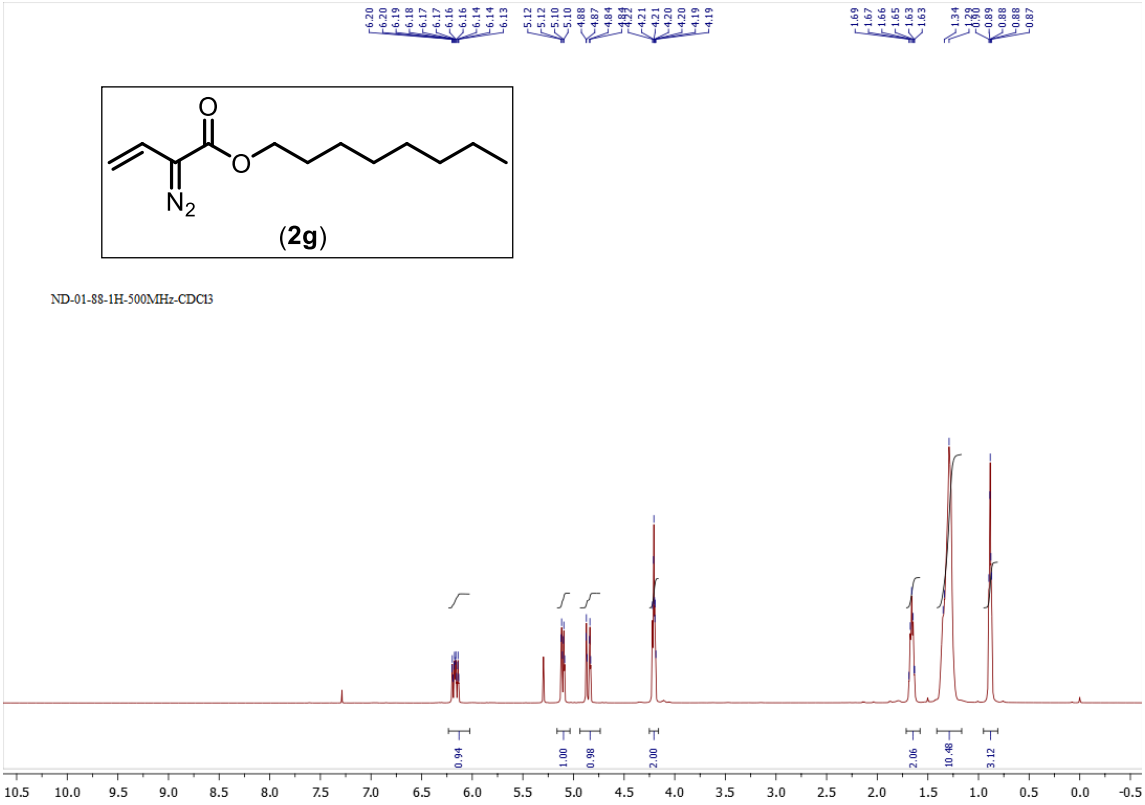
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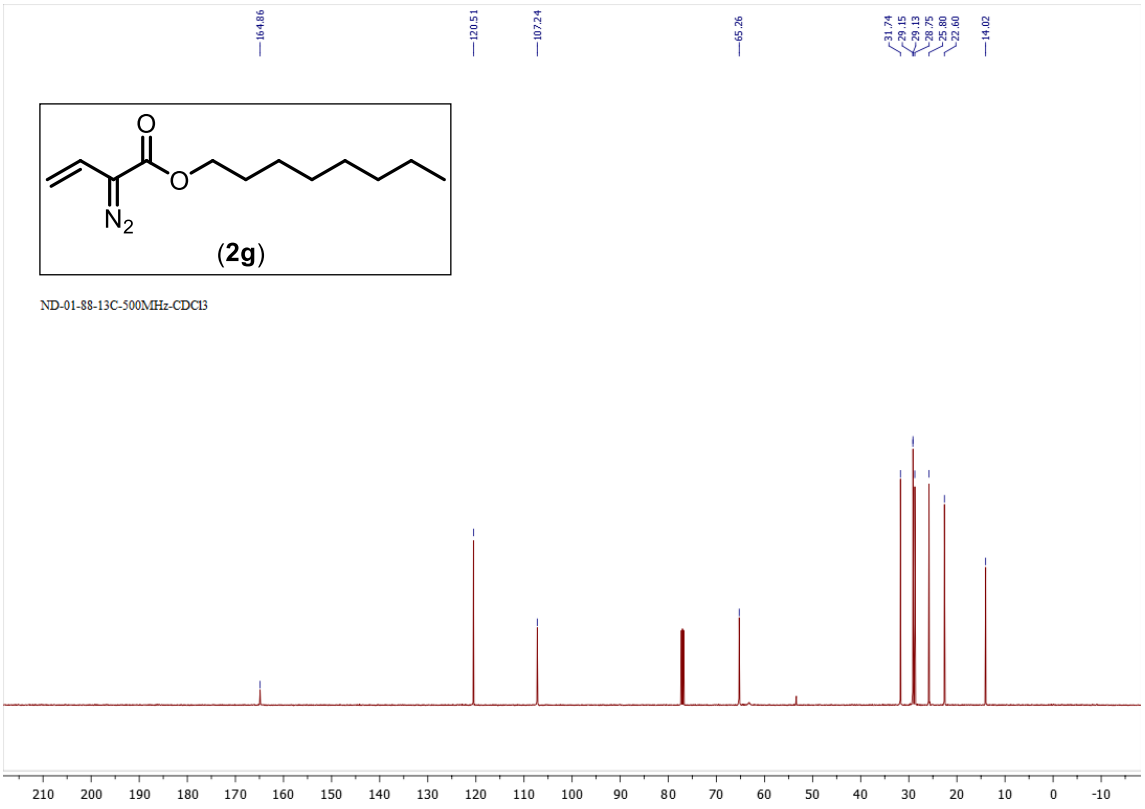
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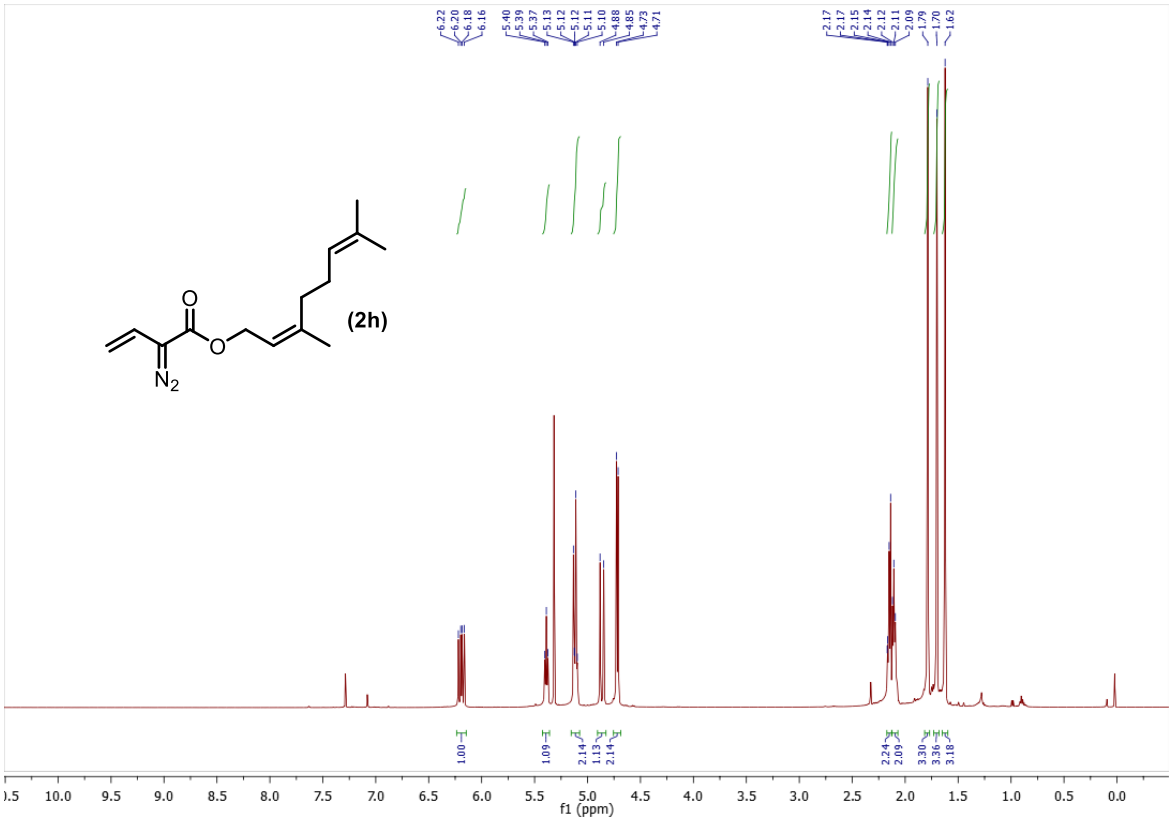
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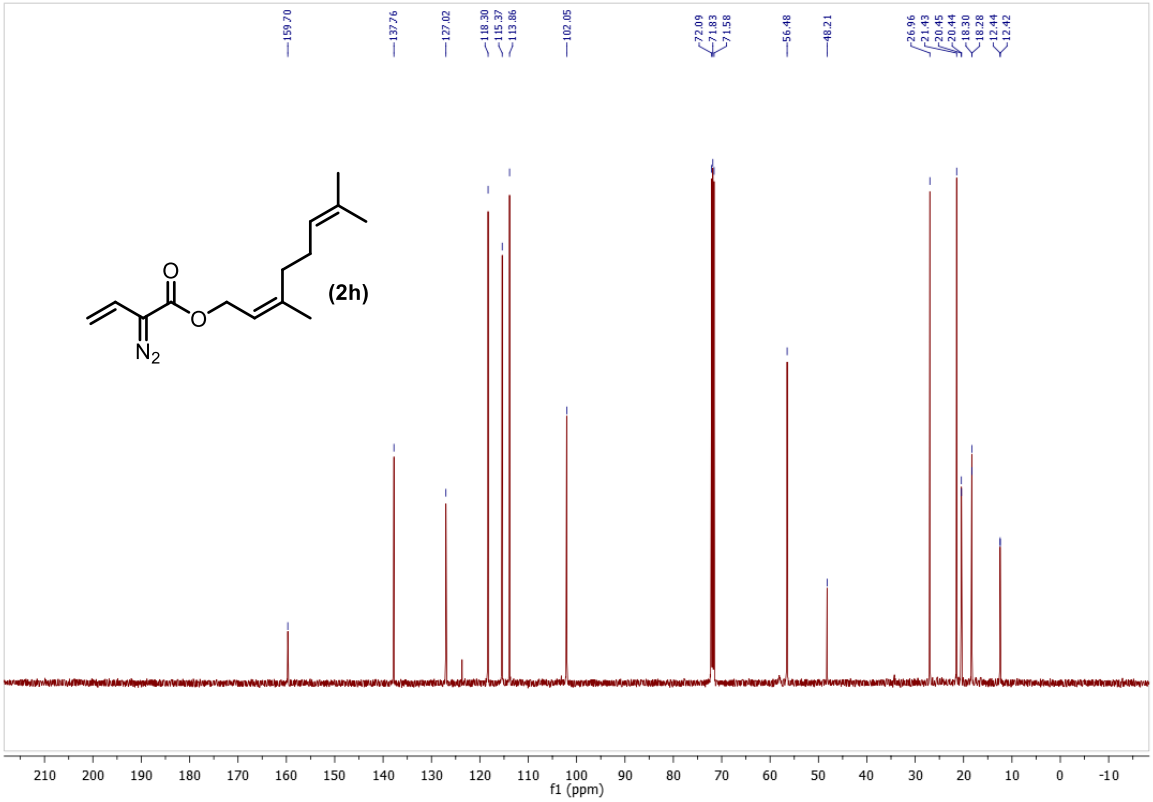
f1 (ppm)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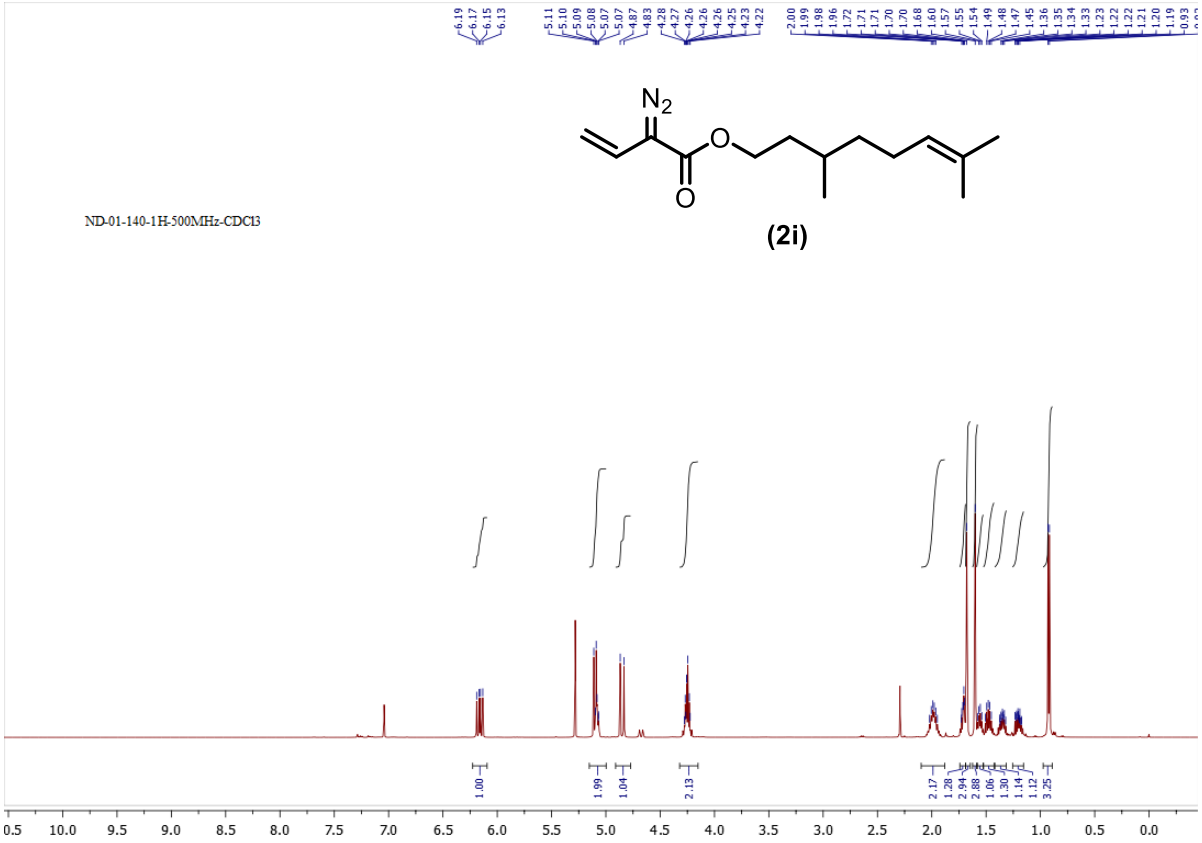
f1 (ppm)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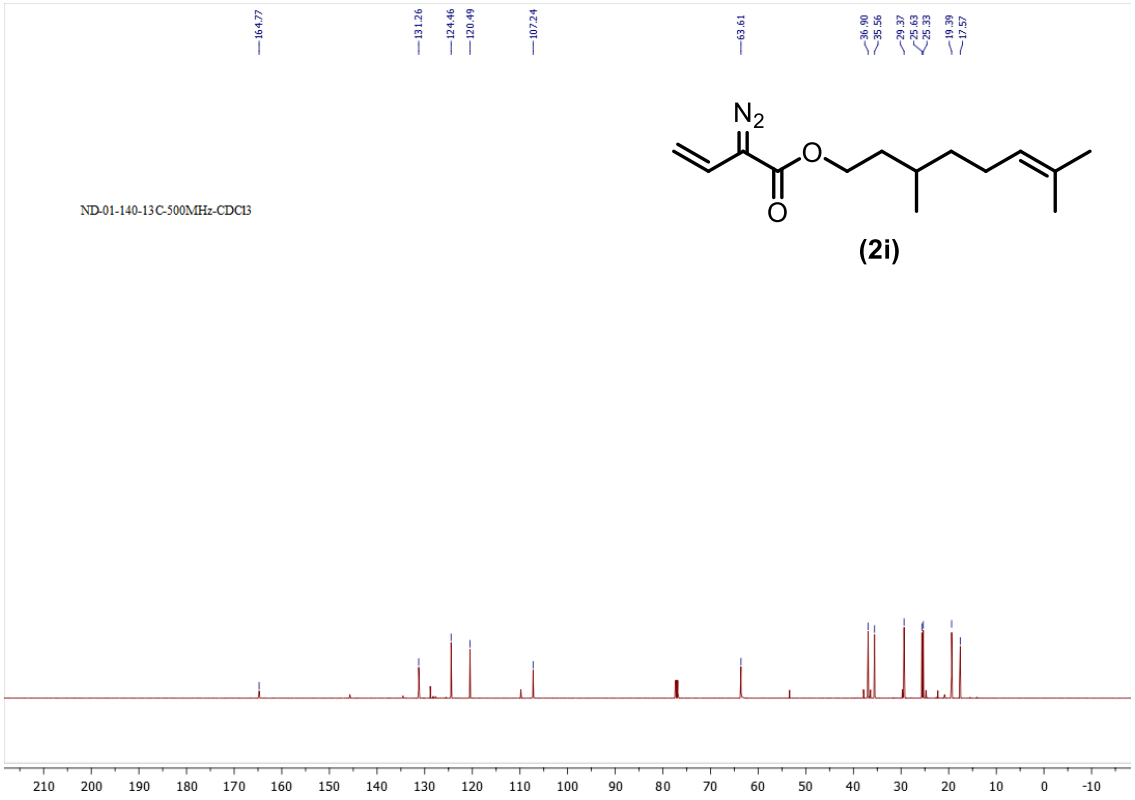
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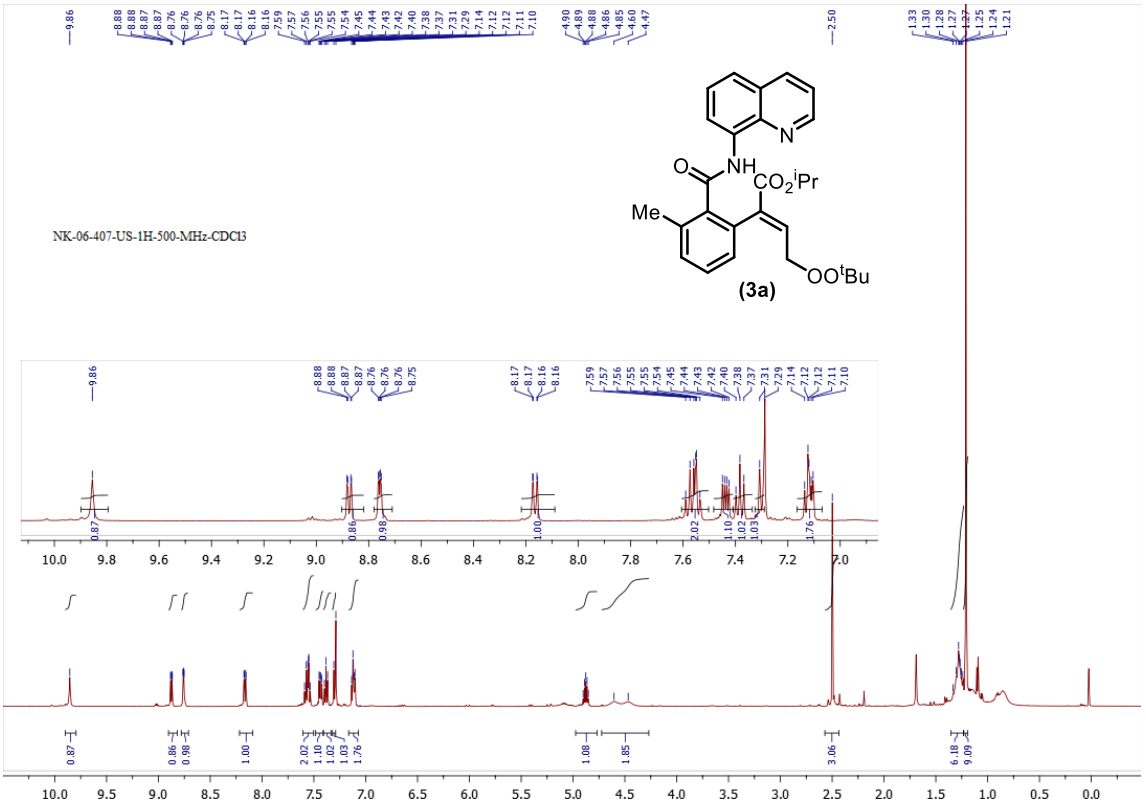
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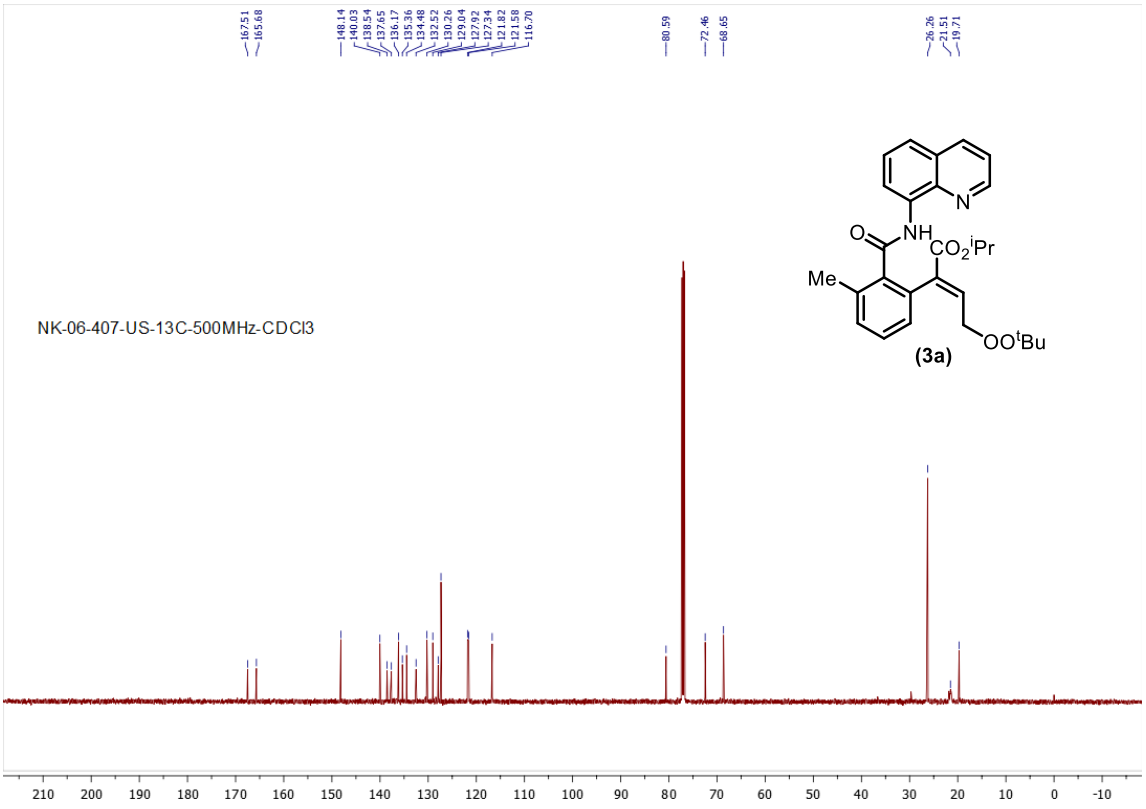
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Display Report

Analysis Info

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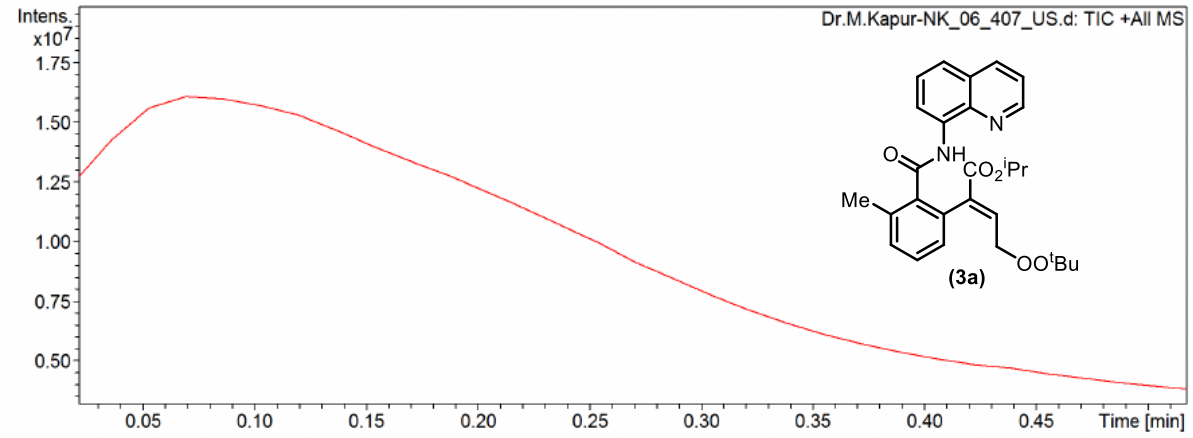
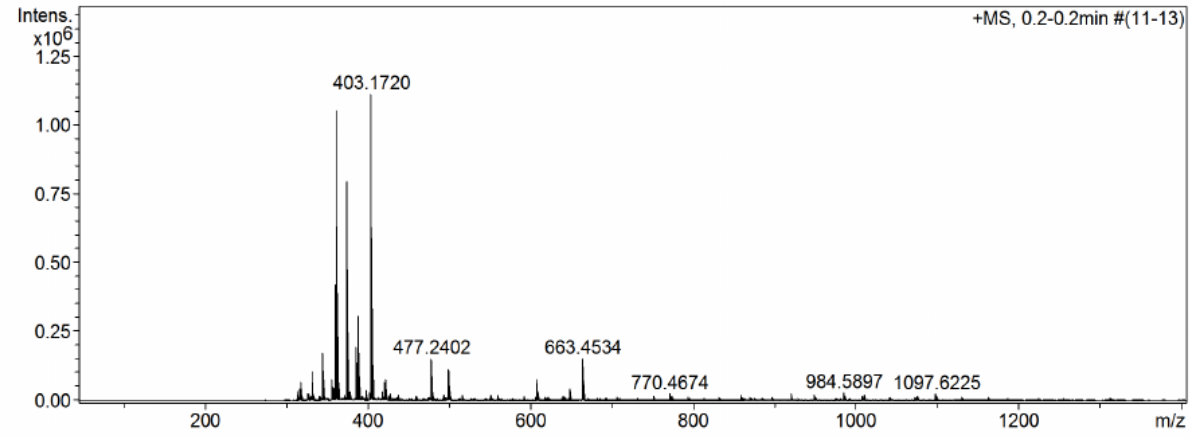
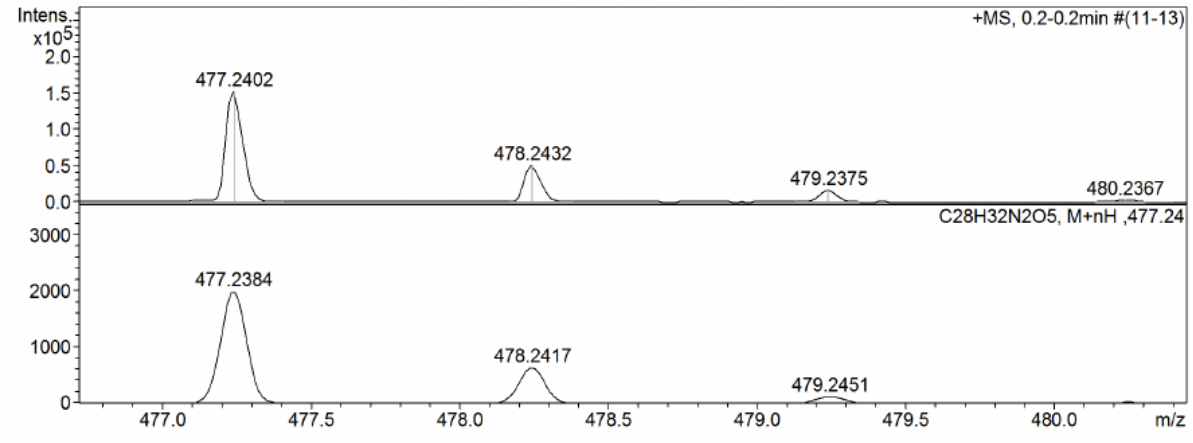
Method	tune_wide _APCI_23.06.m	Operator	Bruker
Sample Name	NK_06_407_US	Instrument	micrOTOF-Q 10330
Comment			

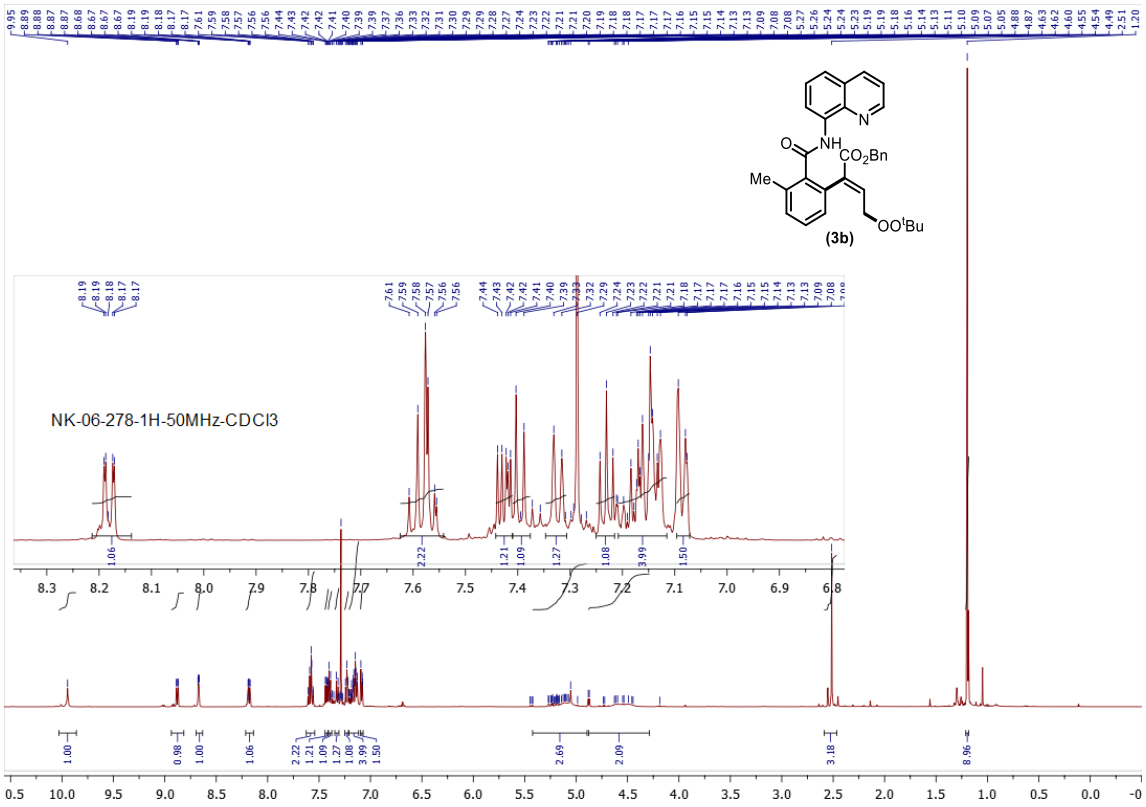
Acquisition Parameter

Source Type	Multi Mode	Ion Polarity	Positive	Set Nebulizer	2.0 Bar
Focus	Not active	Set Capillary	2500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	5.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	600.0 Vpp	Set Divert Valve	Source








NK-06-278-1H-50MHz-CDCl3
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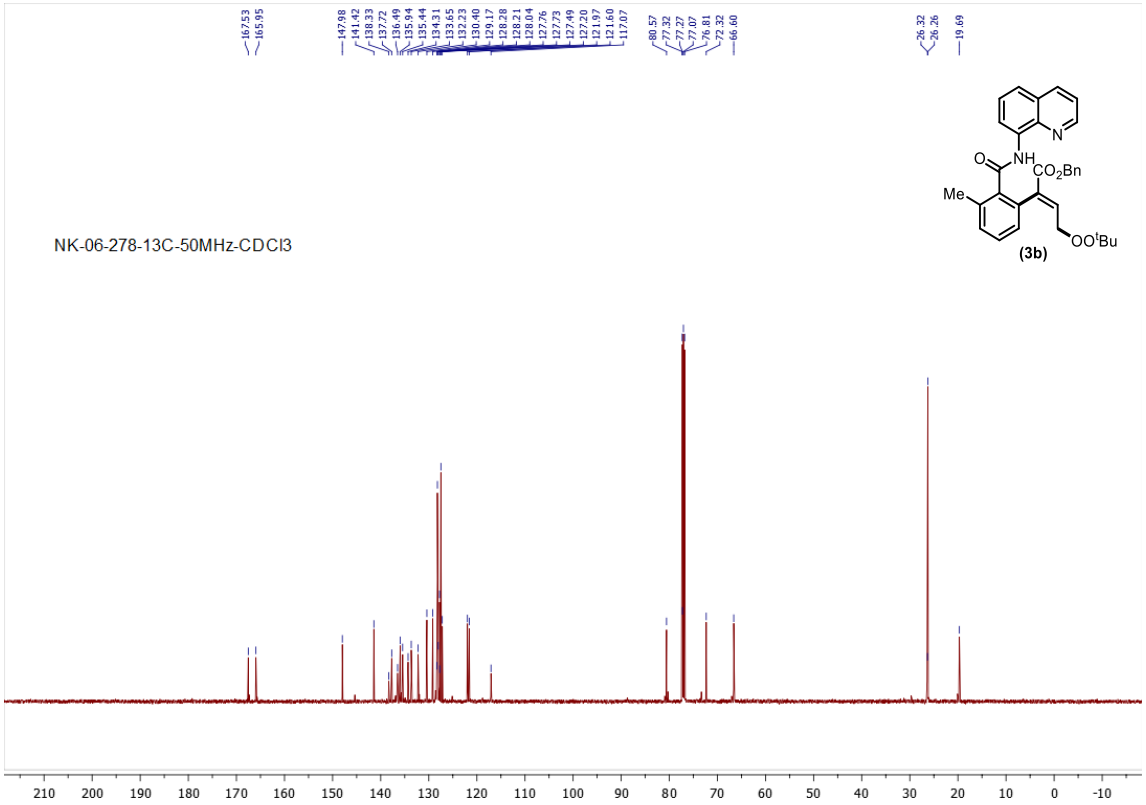
NK-06-278-13C-50MHz-CDCl3
(3b)

Display Report

Analysis Info

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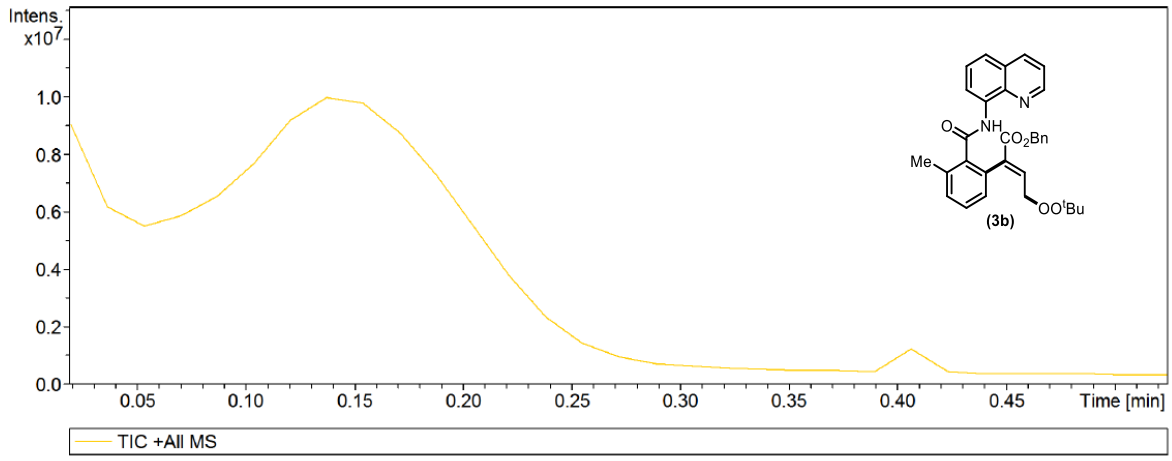
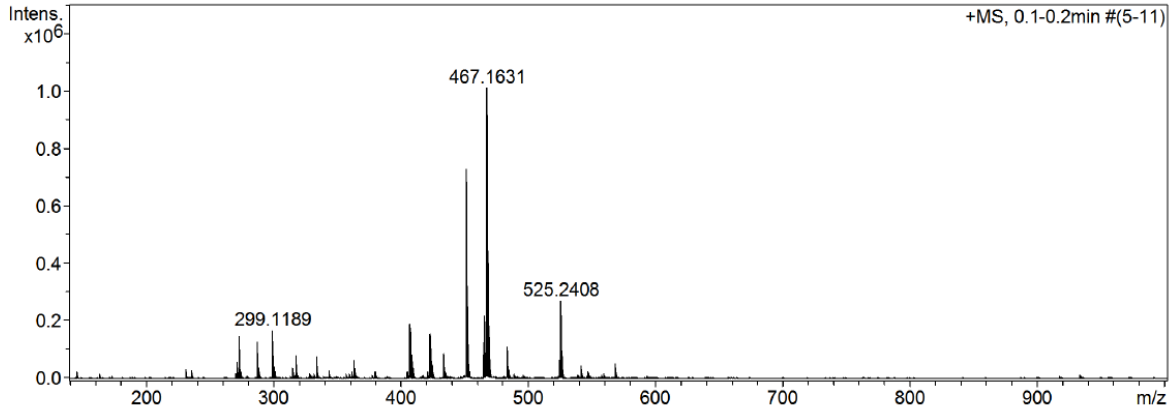
Analysis Name	D:\Data\USER DATA 2022\AUG2022\08-08-2022\Prof.M.Kapur-NK_06_287_US.d		
Method	tune mix_low.New.021117.m	Operator	Bruker
Sample Name	NK_06_287_US	Instrument	micrOTOF-Q 10330
Comment			

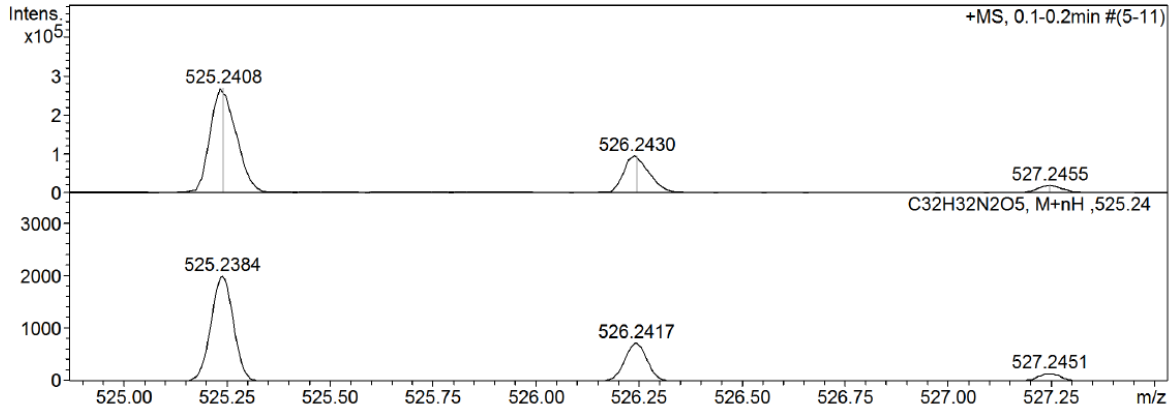
Acquisition Parameter

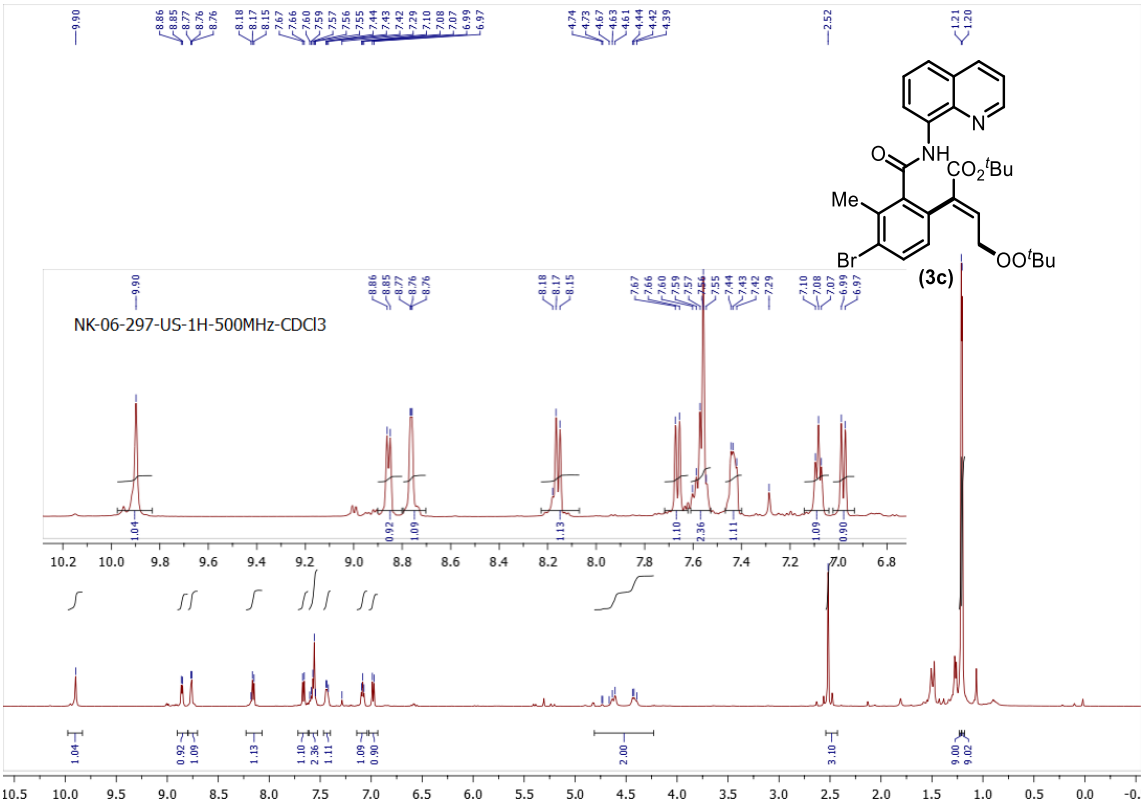
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4600 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	100.0 Vpp	Set Divert Valve	Source



TIC +All MS



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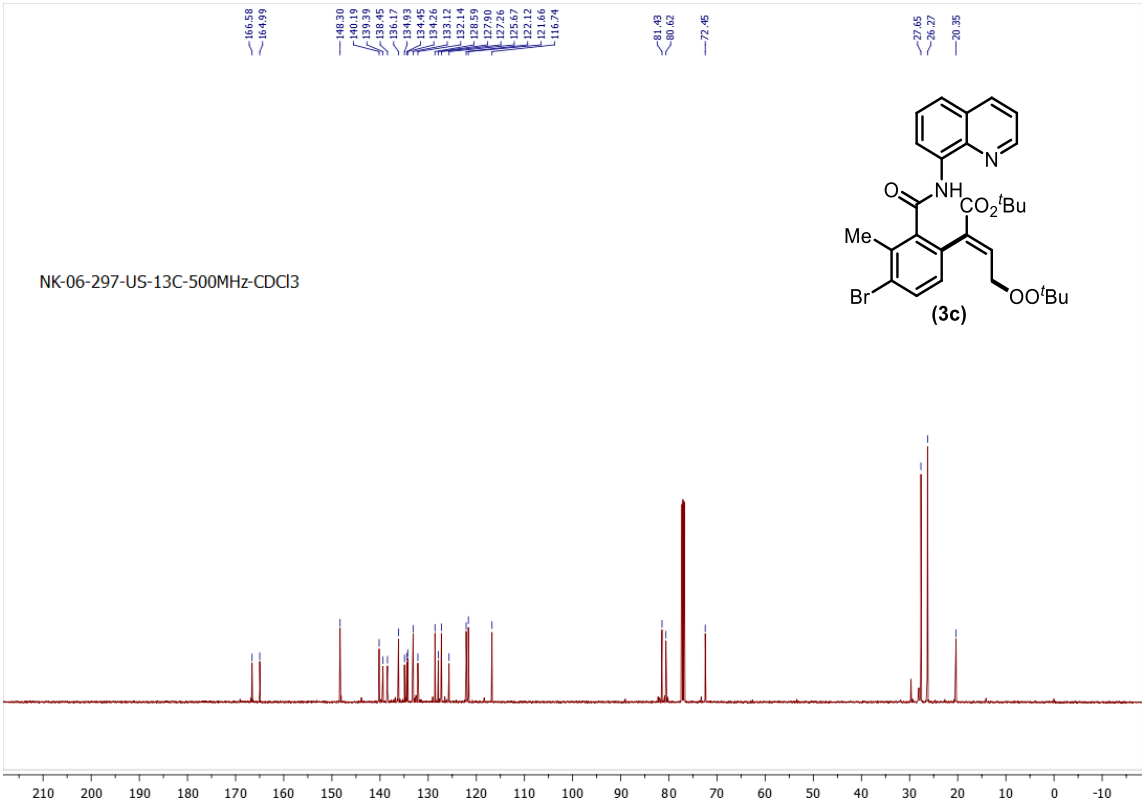
NK-06-297-US-13C-500MHz-CDCl3
(3c)

Display Report

Analysis Info

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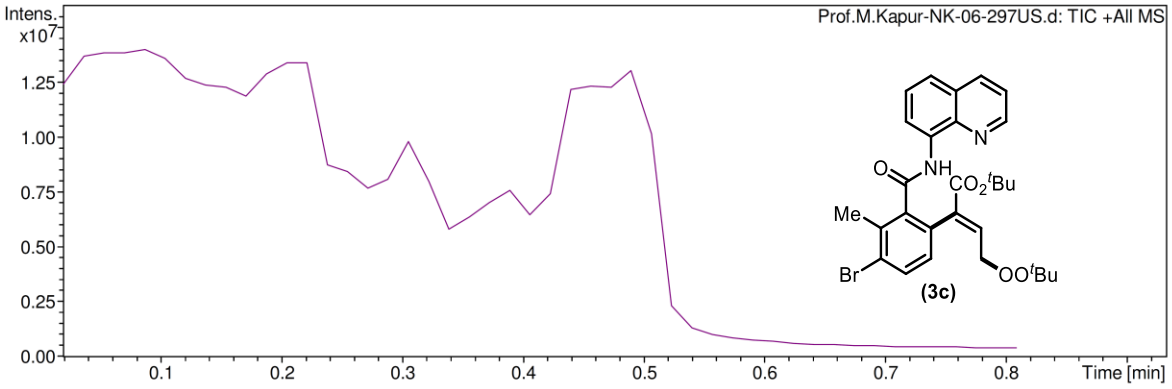
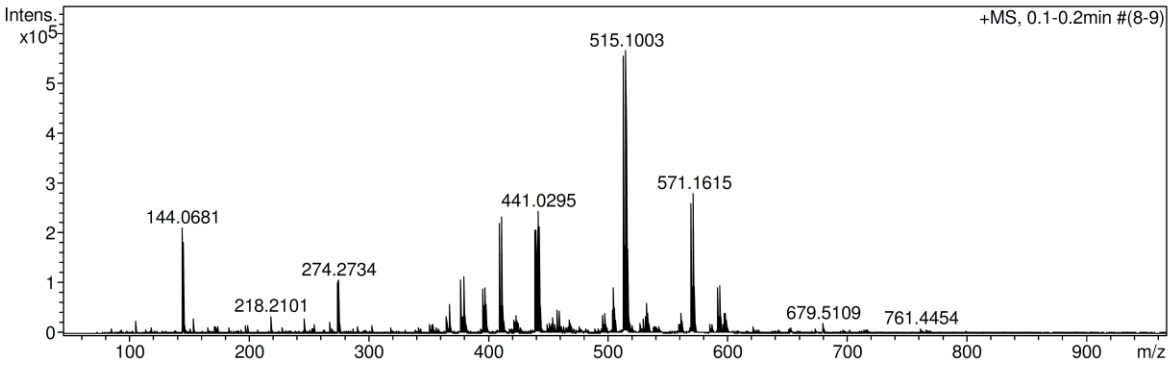
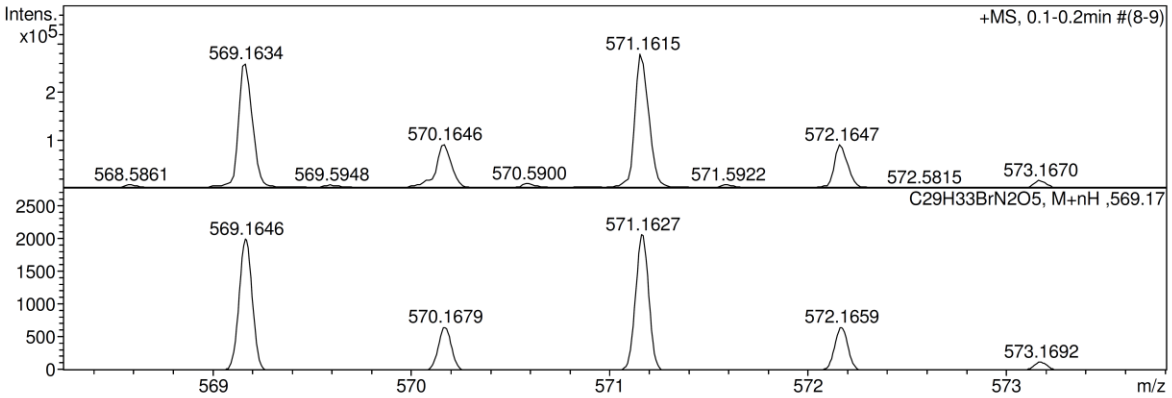
Method	tune mix_low.New.021117.m	Operator	RUCHI
Sample Name	NK-06-297US	Instrument	micrOTOF-Q II 10330
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4600 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	100.0 Vpp	Set Divert Valve	Waste







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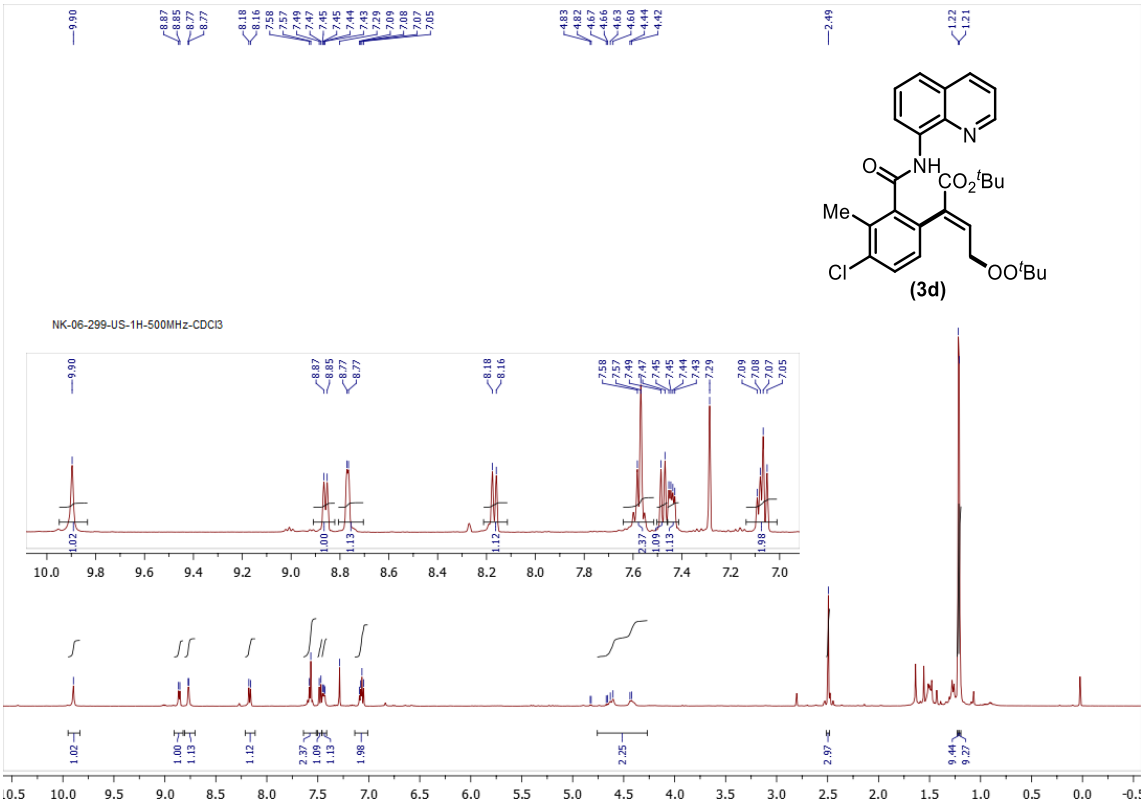
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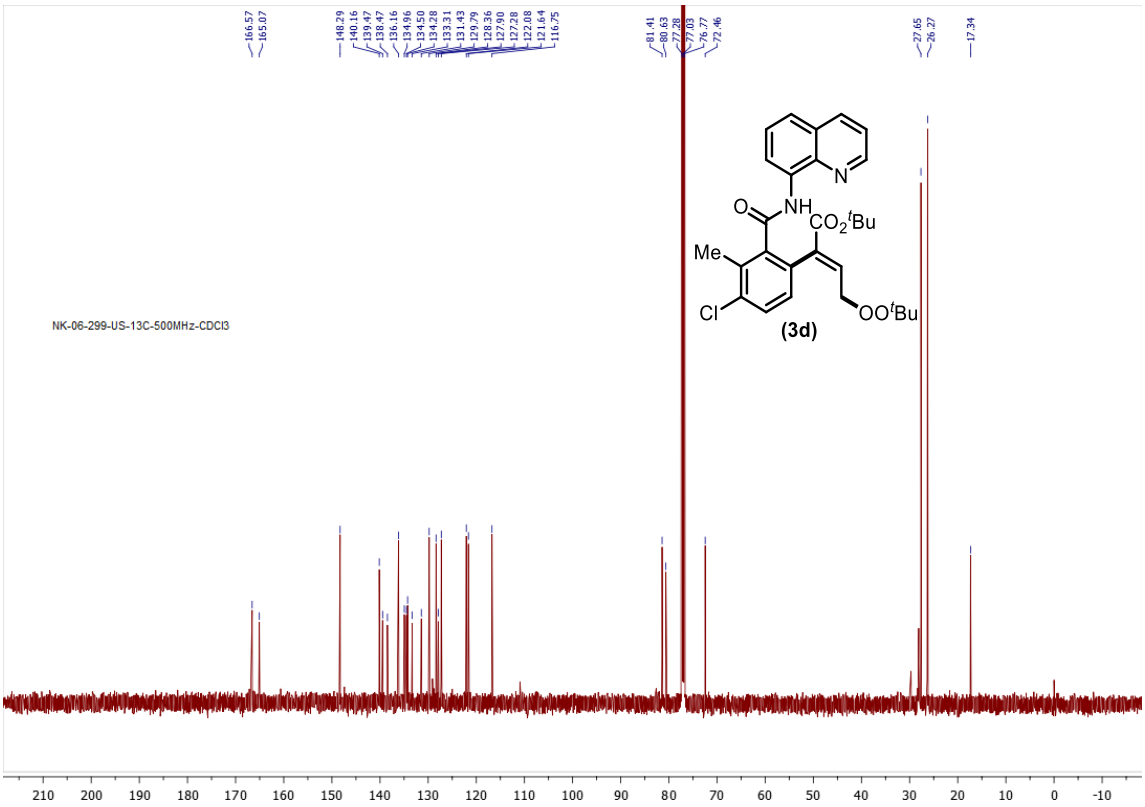
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(3d)

Display Report

Analysis Info

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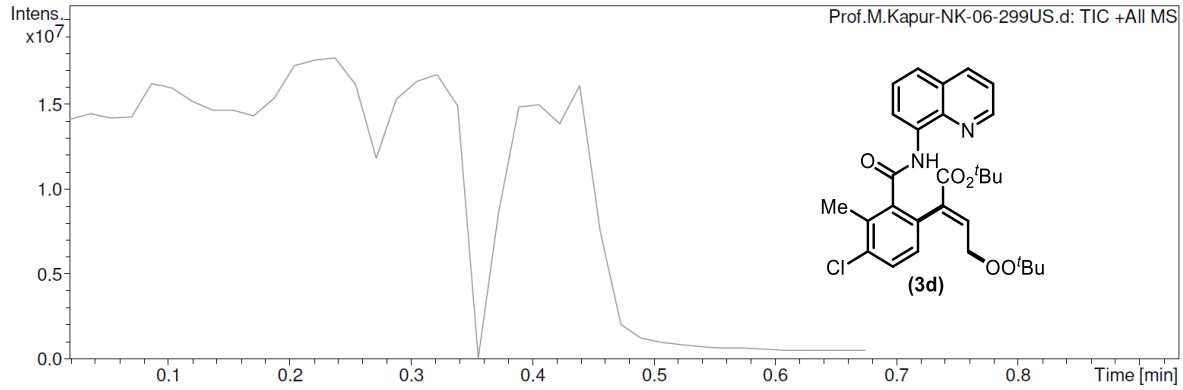
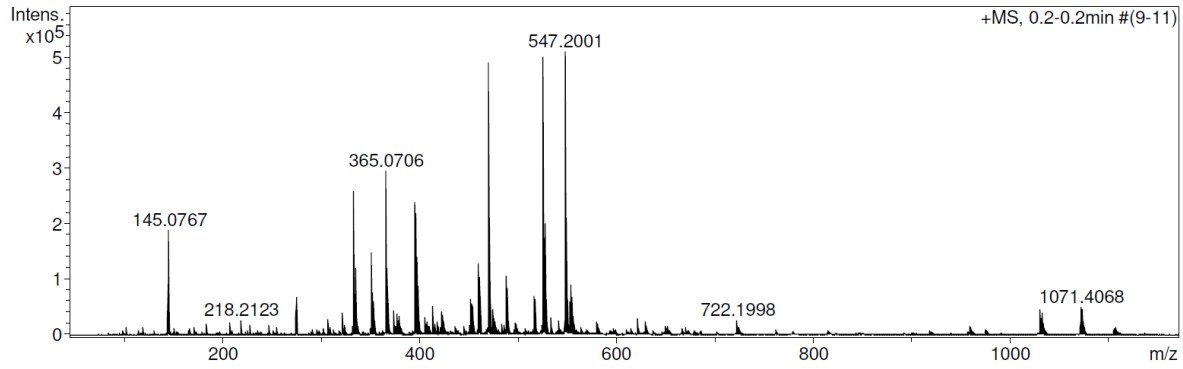
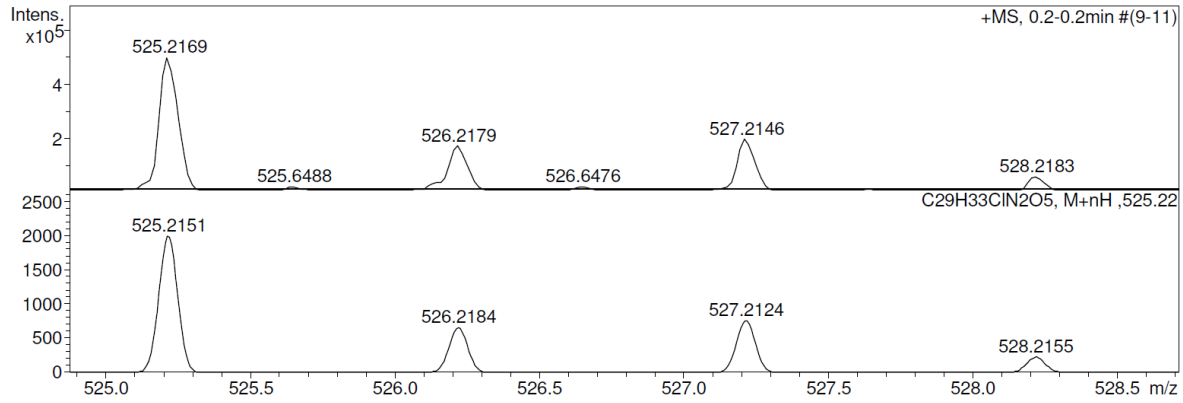
Method	tune mix_low.New.021117.m	Operator	RUCHI
Sample Name	NK-06-299US	Instrument	micrOTOF-Q II 10330
Comment			

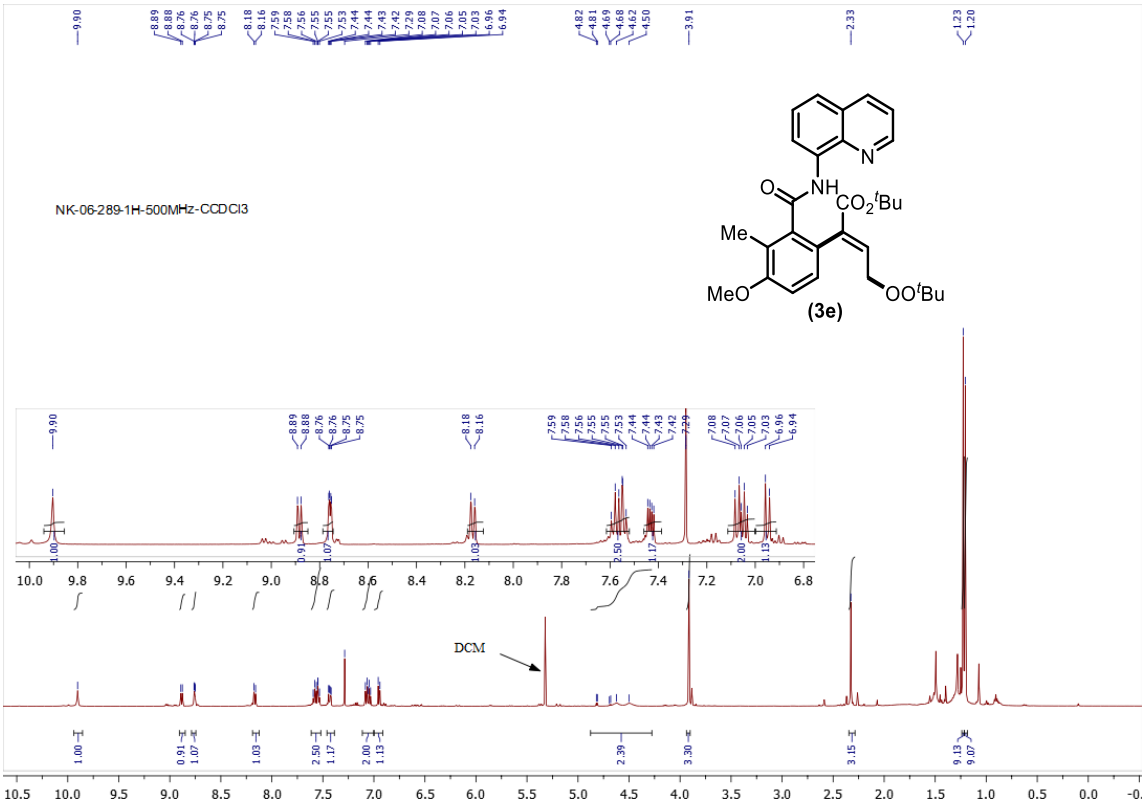
Acquisition Parameter

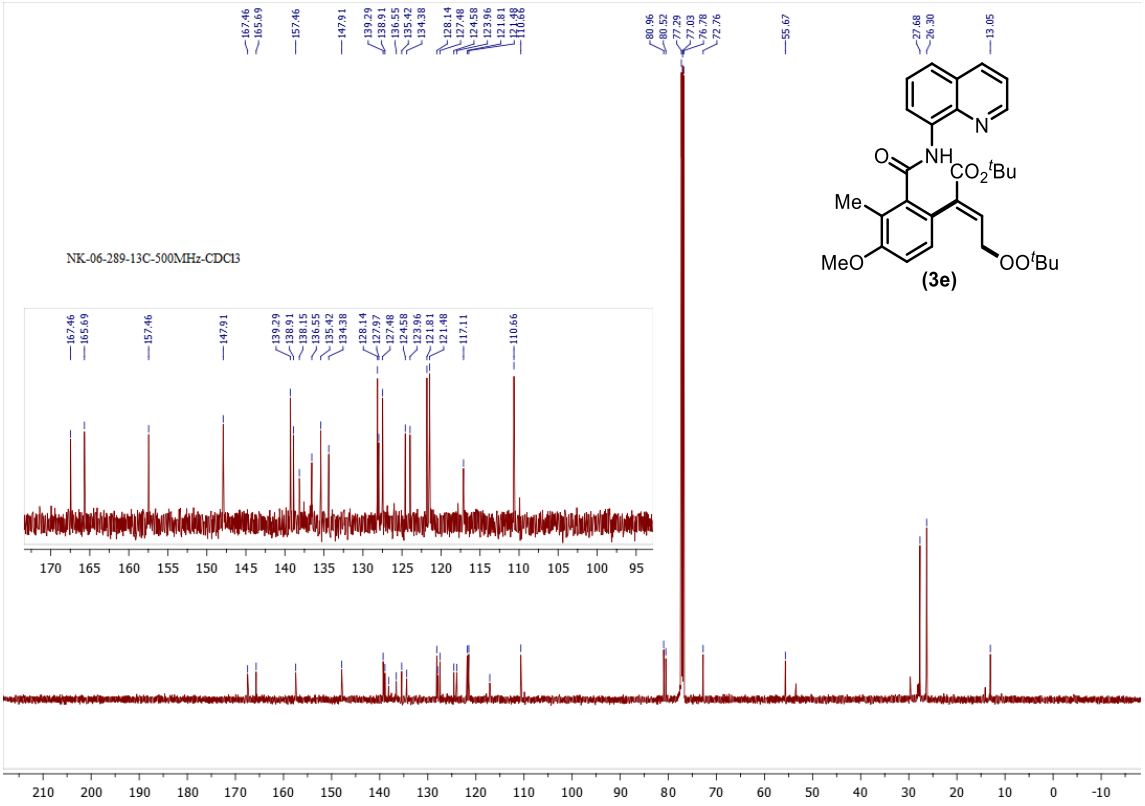
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4600 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	100.0 Vpp	Set Divert Valve	Waste








NK-06-289-1H-500MHz-CCDCl3
DCM
(3e)


NK-06-289-13C-500MHz-CDCl3
(3e)

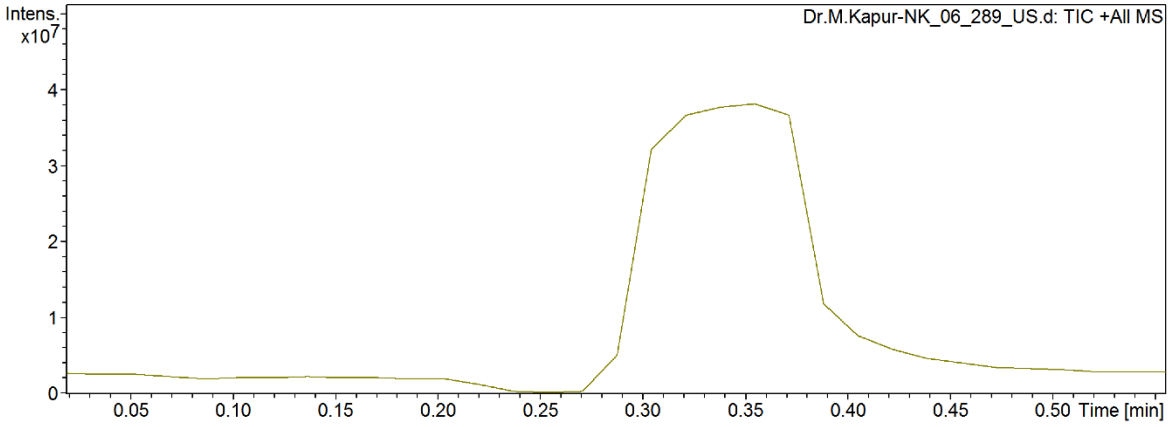
Display Report

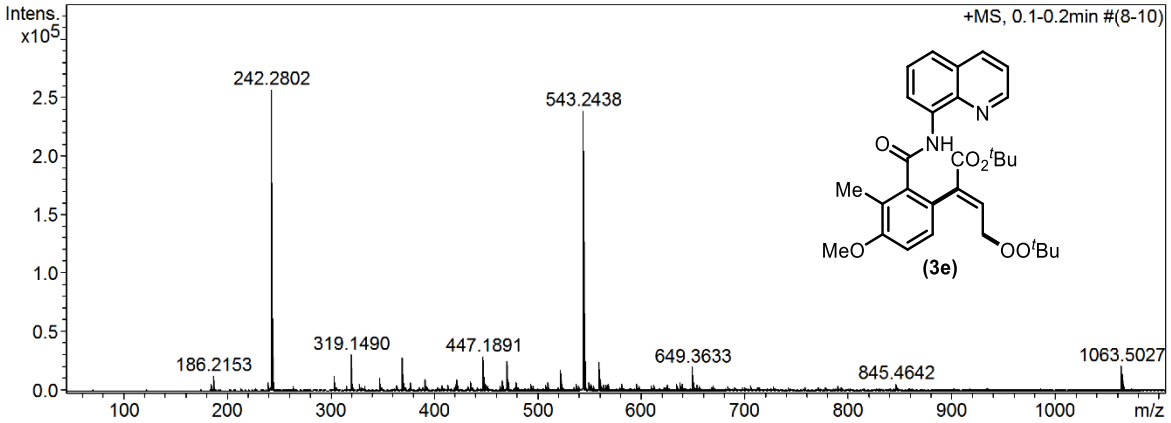
Analysis Info

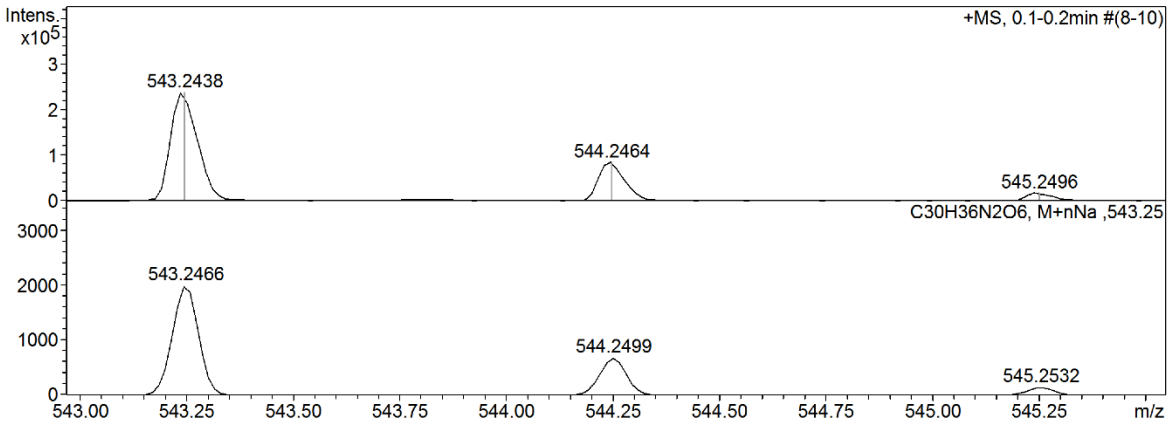
Analysis Name	D:\Data\USER DATA 2022\DEC\02-12-2022\Dr.M.Kapur-NK_06_289_US.d	Acquisition Date	02-12-2022 15:09:26
Method	tune mix_low.New.021117.m	Operator	Bruker
Sample Name	NK_06_289_US	Instrument	micrOTOF-Q 10330
Comment			

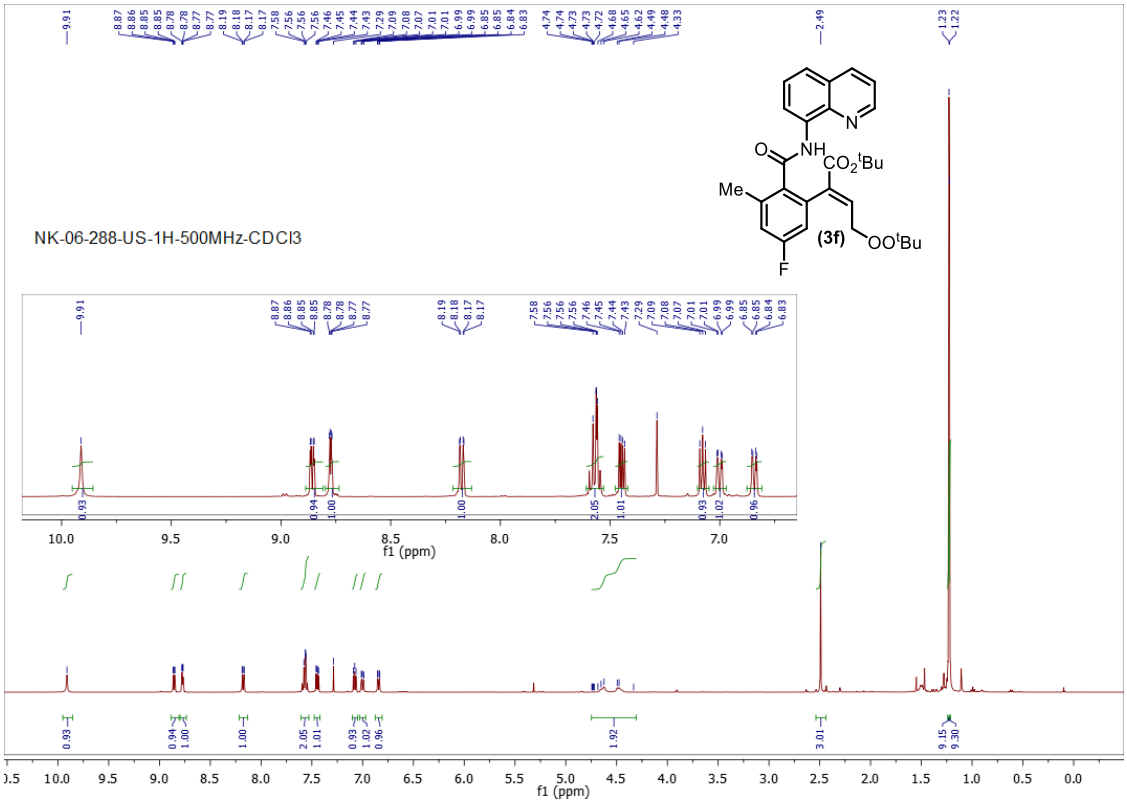
Acquisition Parameter

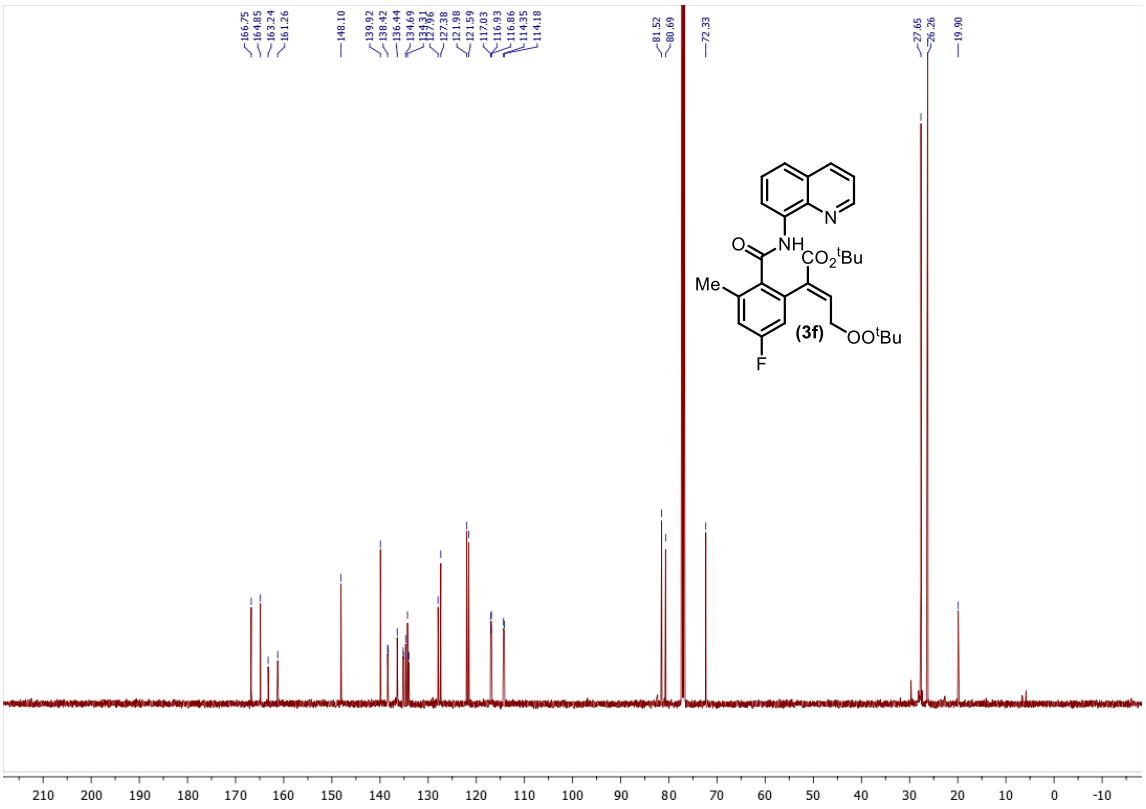
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4600 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	300.0 Vpp	Set Divert Valve	Waste

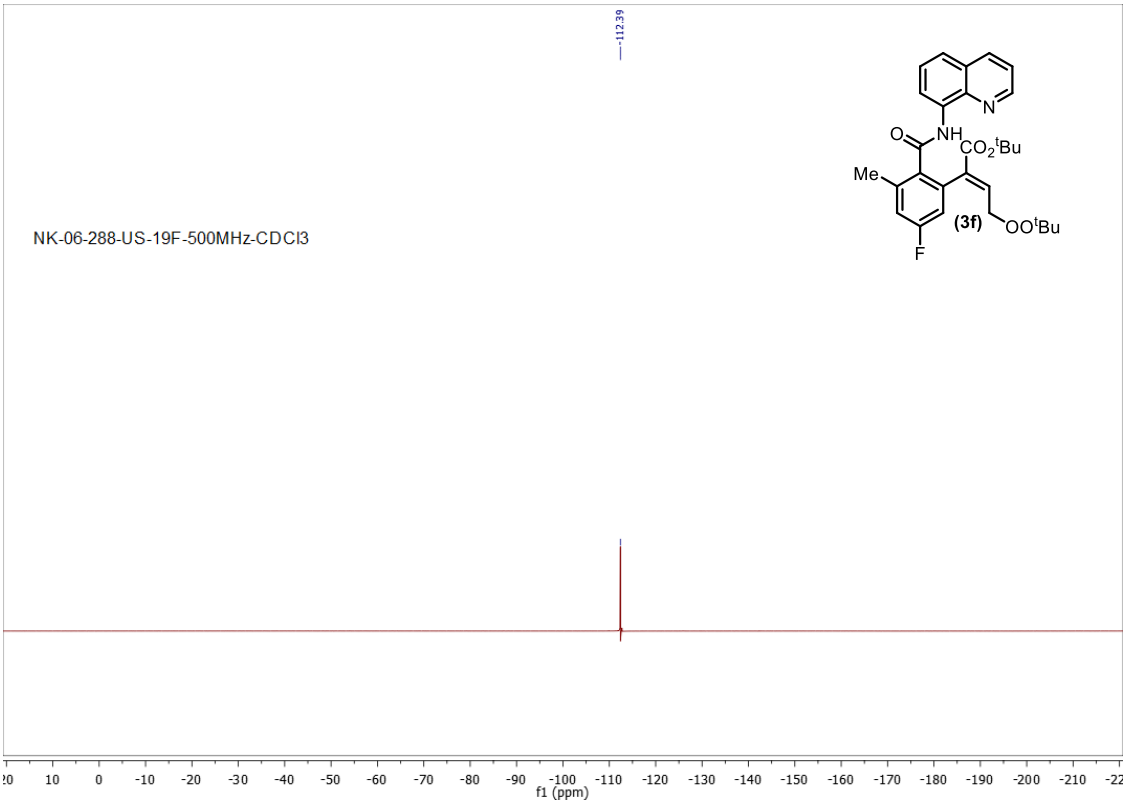







NK-06-288-US-1H-500MHz-CDCl3
(3f)
f1 (ppm)


(3f)


-112.39
NK-06-288-US-19F-500MHz-CDCl3
O
NH
N
CO2tBu
Me
(3f)
OOtBu
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

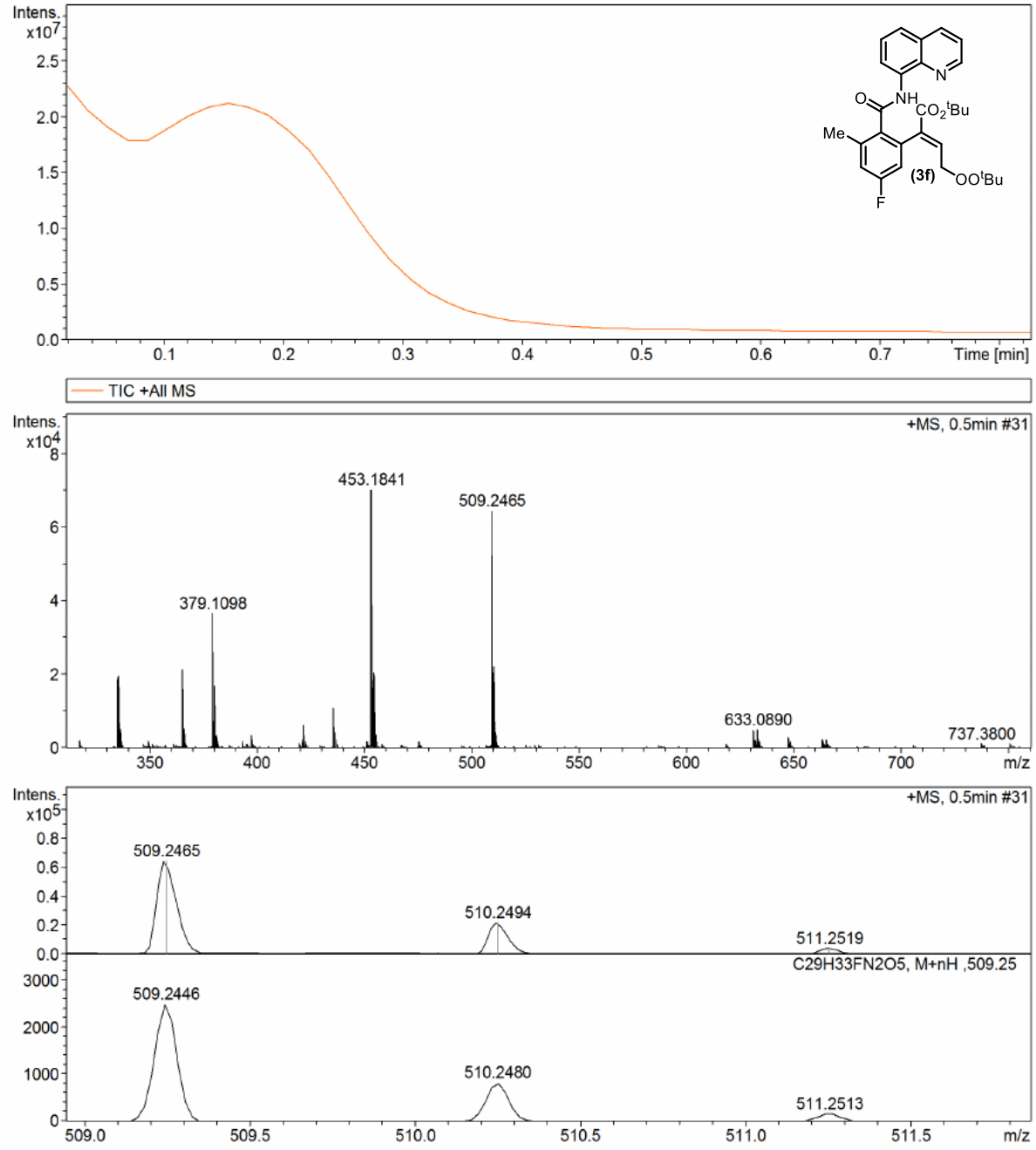
Display Report

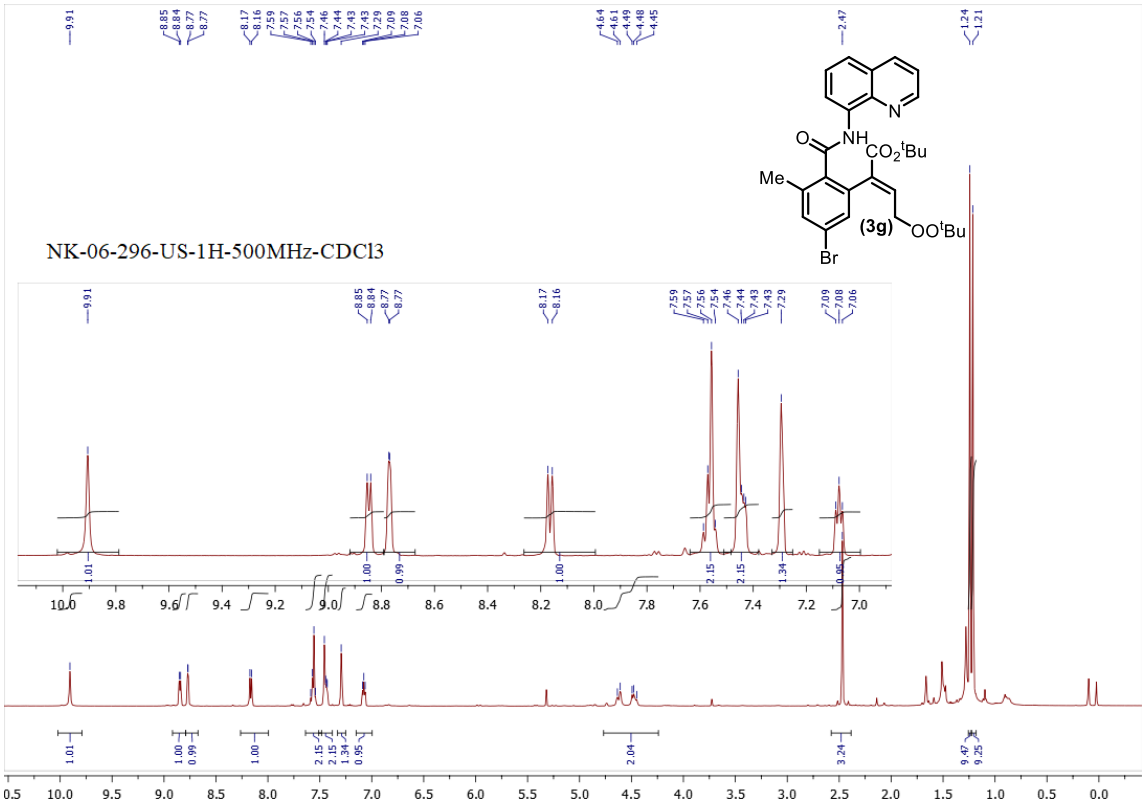
Analysis Info

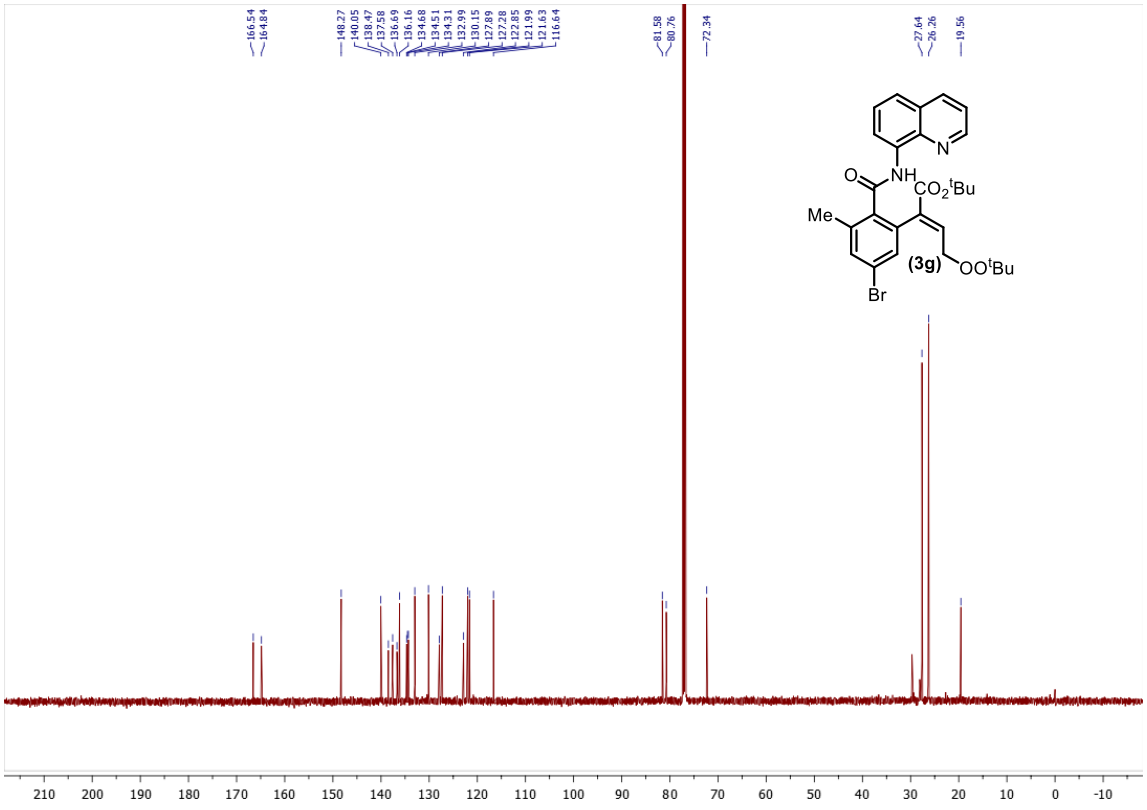
Analysis Name	D:\Data\USER DATA 2022\AUG2022\10-08-2022\Prof.M.Kapur-NK_06_288_US_R.d	Acquisition Date	10-08-2022 12:01:30
Method	tune_wide.m	Operator	Bruker
Sample Name	NK_06_288_US_R	Instrument	micrOTOF-Q 10330
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	600.0 Vpp	Set Divert Valve	Source




NK-06-296-US-1H-500MHz-CDCl3
(3g)


(3g)

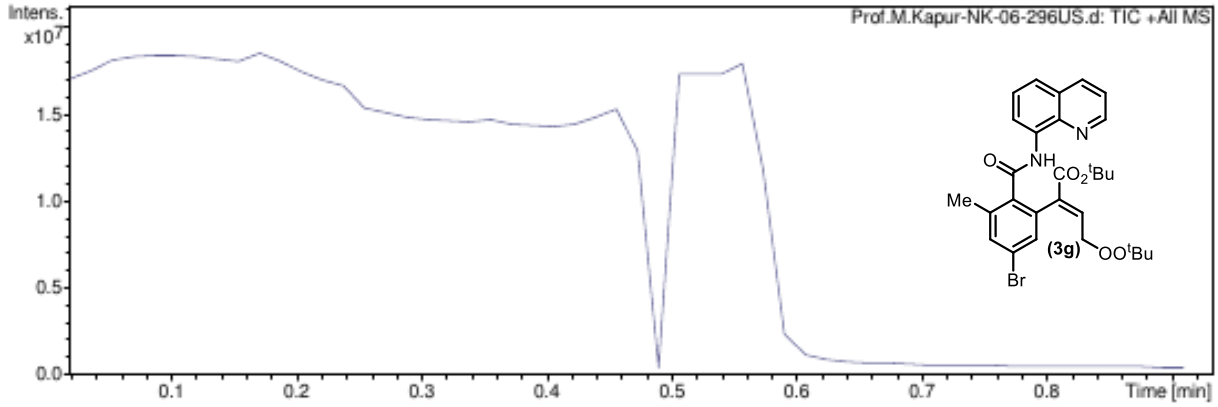
Display Report

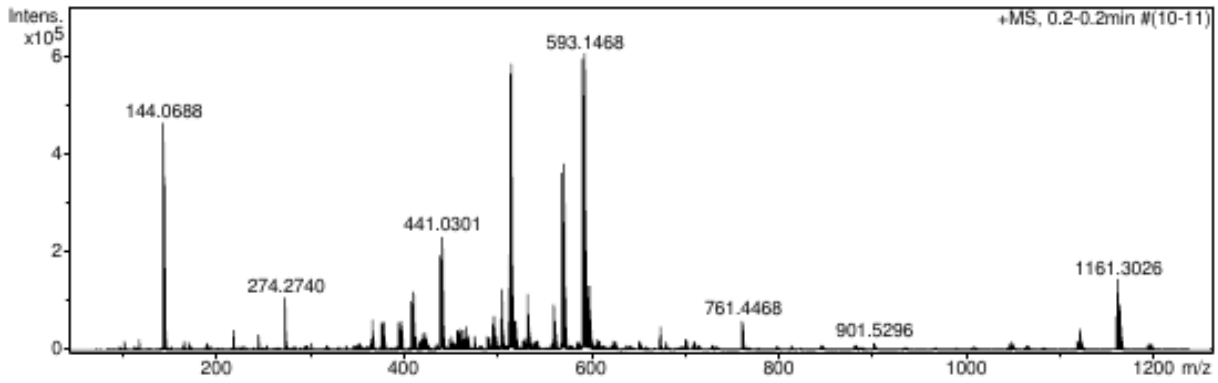
Analysis Info

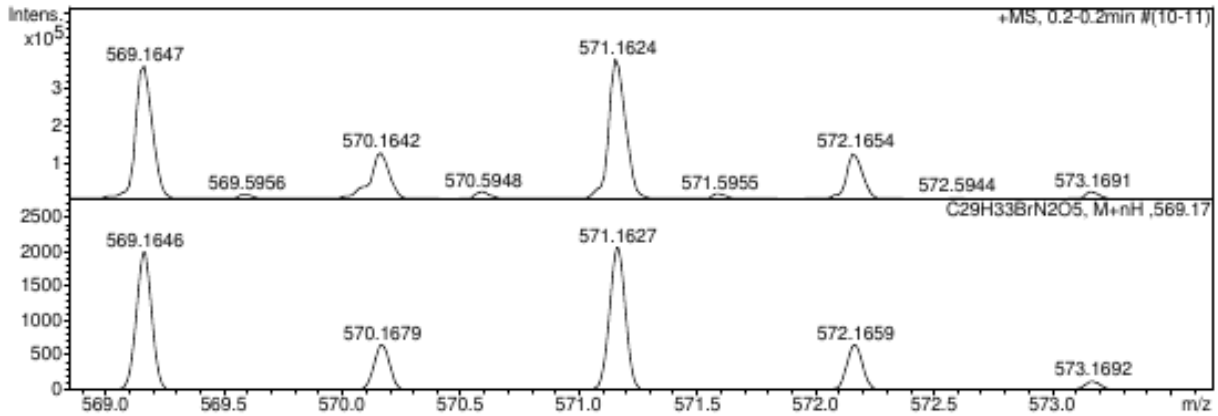
Acquisition Date	10/22/2021 10:47:56 AM		
Analysis Name	D:\Data\new user data 2021\Oct-2021\22-oct\Prof.M.Kapur-NK-06-296US.d		
Method	tune mix_low.New.021117.m	Operator	RUCHI
Sample Name	NK-06-296US	Instrument	micrOTOF-Q II 10330
Comment			

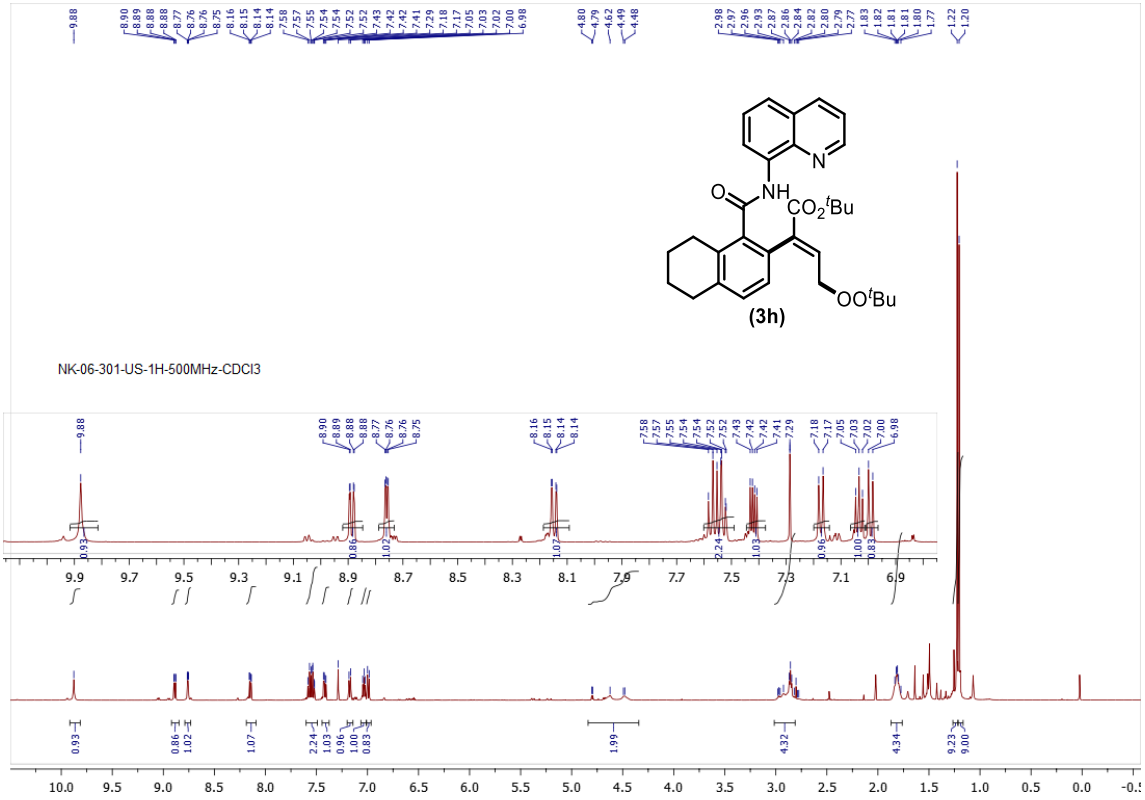
Acquisition Parameter

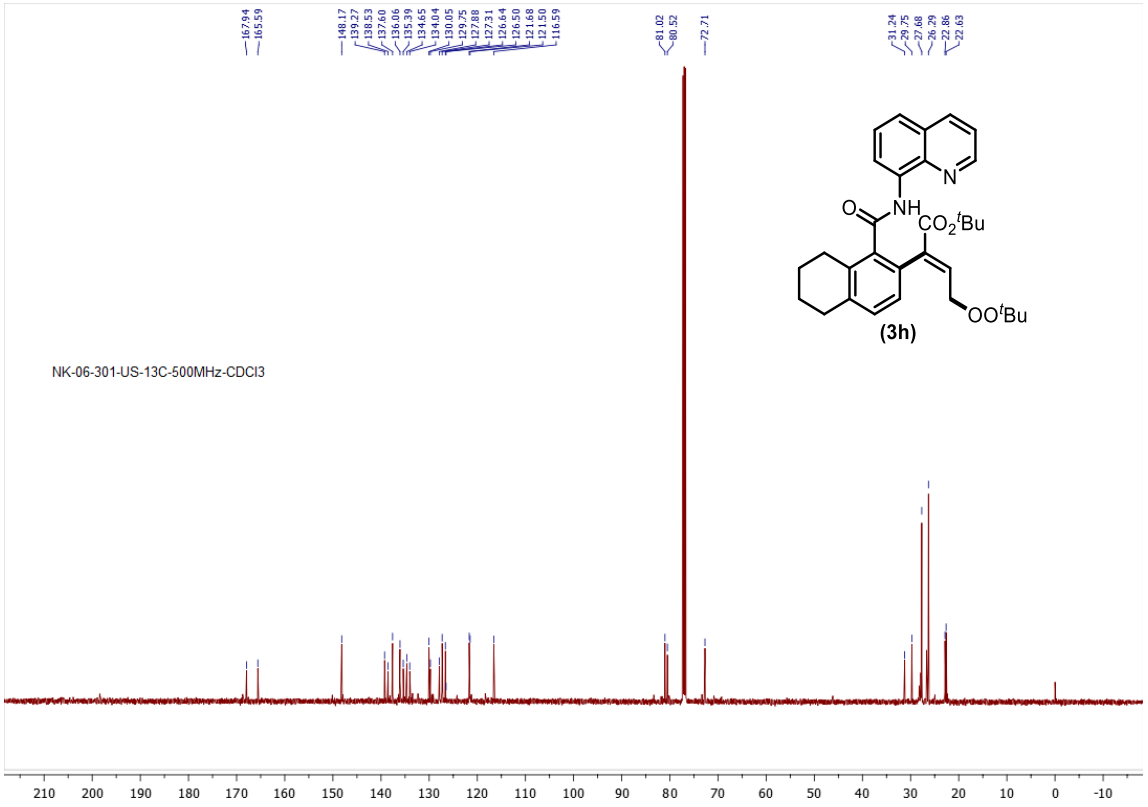
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4600 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	100.0 Vpp	Set Divert Valve	Waste








NK-06-301-US-1H-500MHz-CDCl3
(3h)


NK-06-301-US-13C-500MHz-CDCl3
(3h)

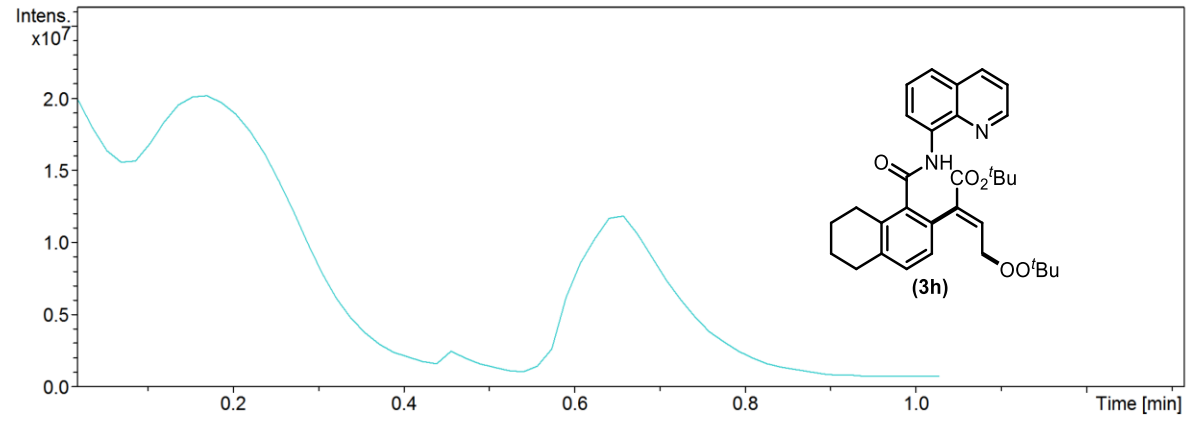
Display Report

Analysis Info

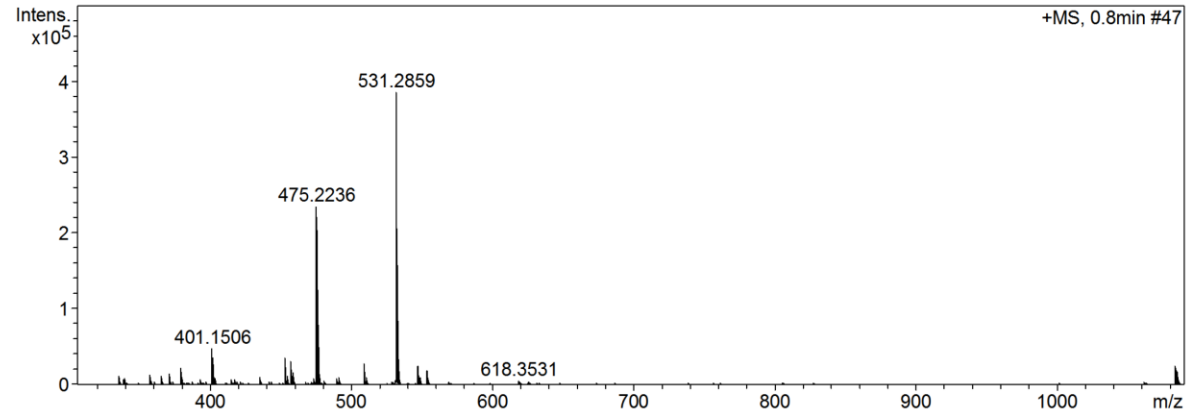
Acquisition Date	10-08-2022 12:04:10		
Analysis Name	D:\Data\USER DATA 2022\AUG2022\10-08-2022\Prof.M.Kapur-NK_06_301_US.d		
Method	tune_wide.m	Operator	Bruker
Sample Name	NK_06_301_US	Instrument	micrOTOF-Q 10330
Comment			

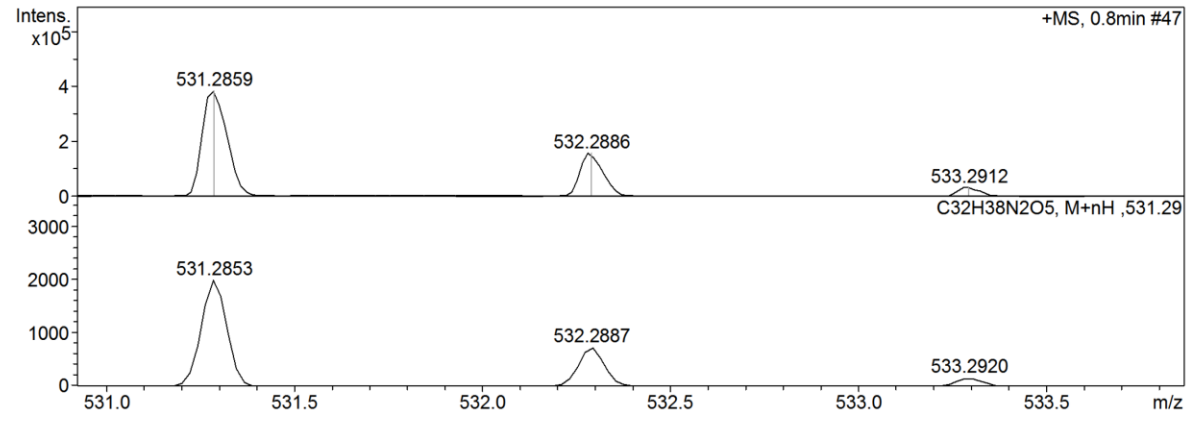
Acquisition Parameter

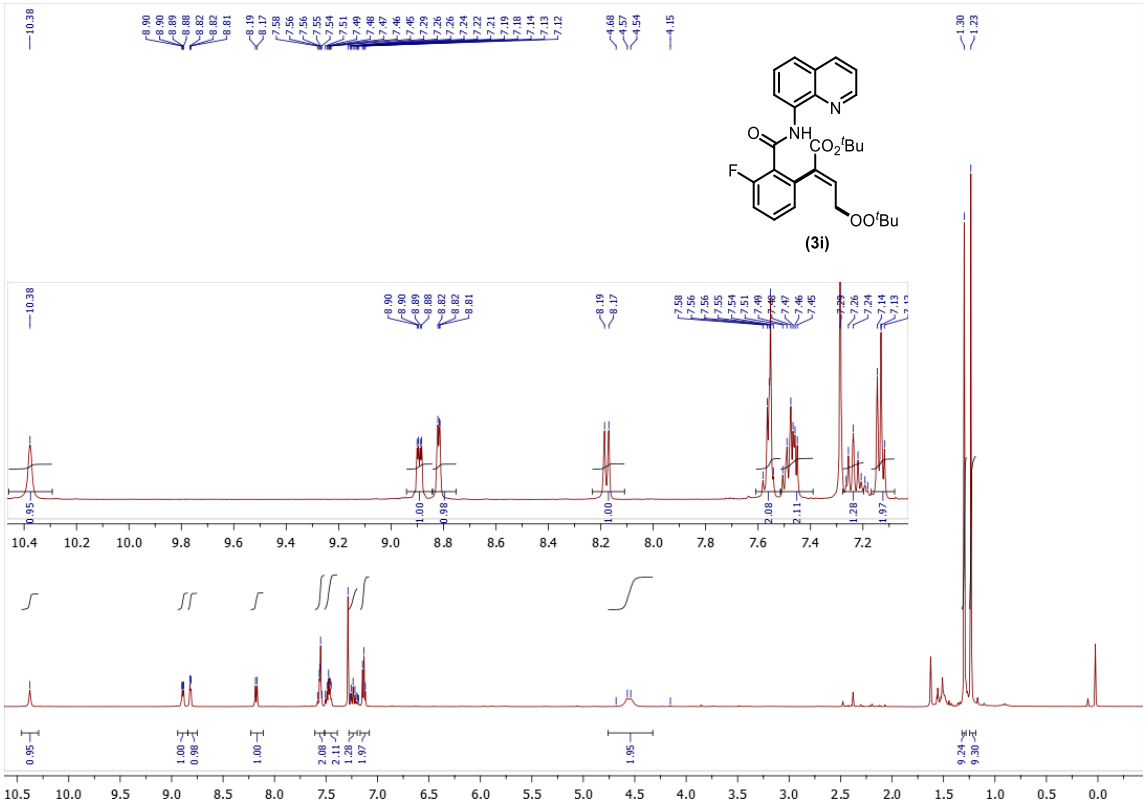
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	600.0 Vpp	Set Divert Valve	Source

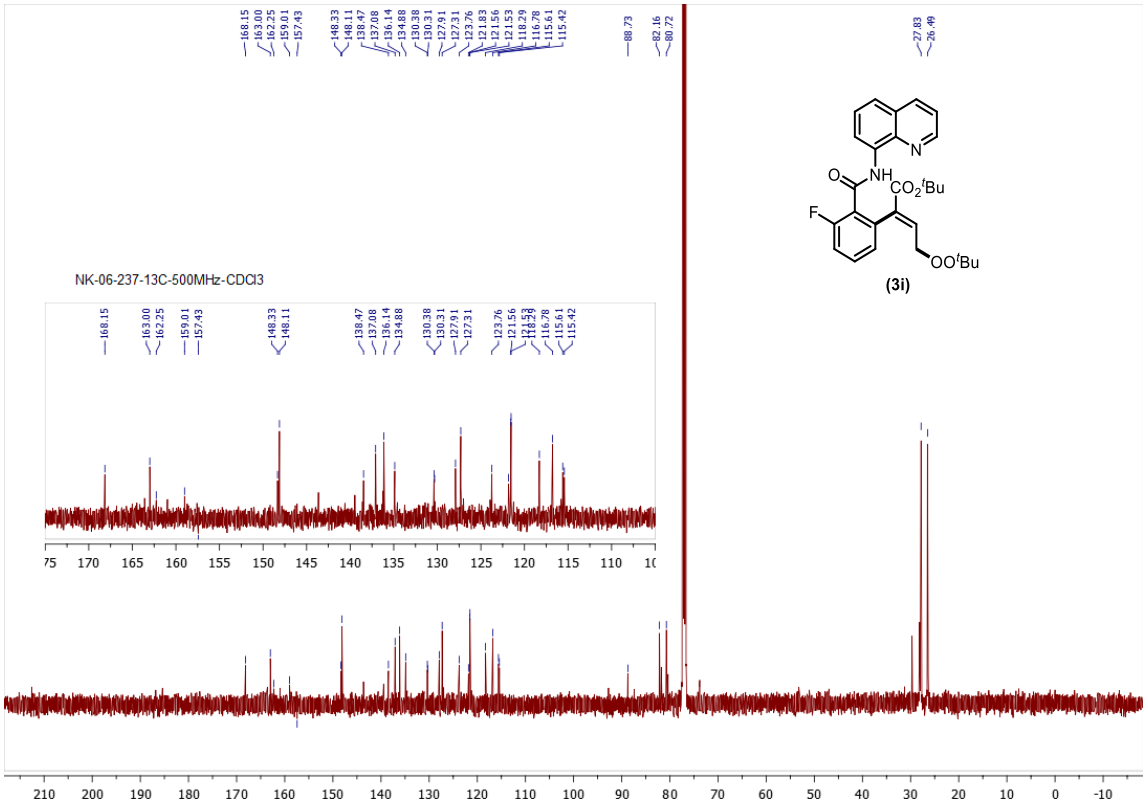


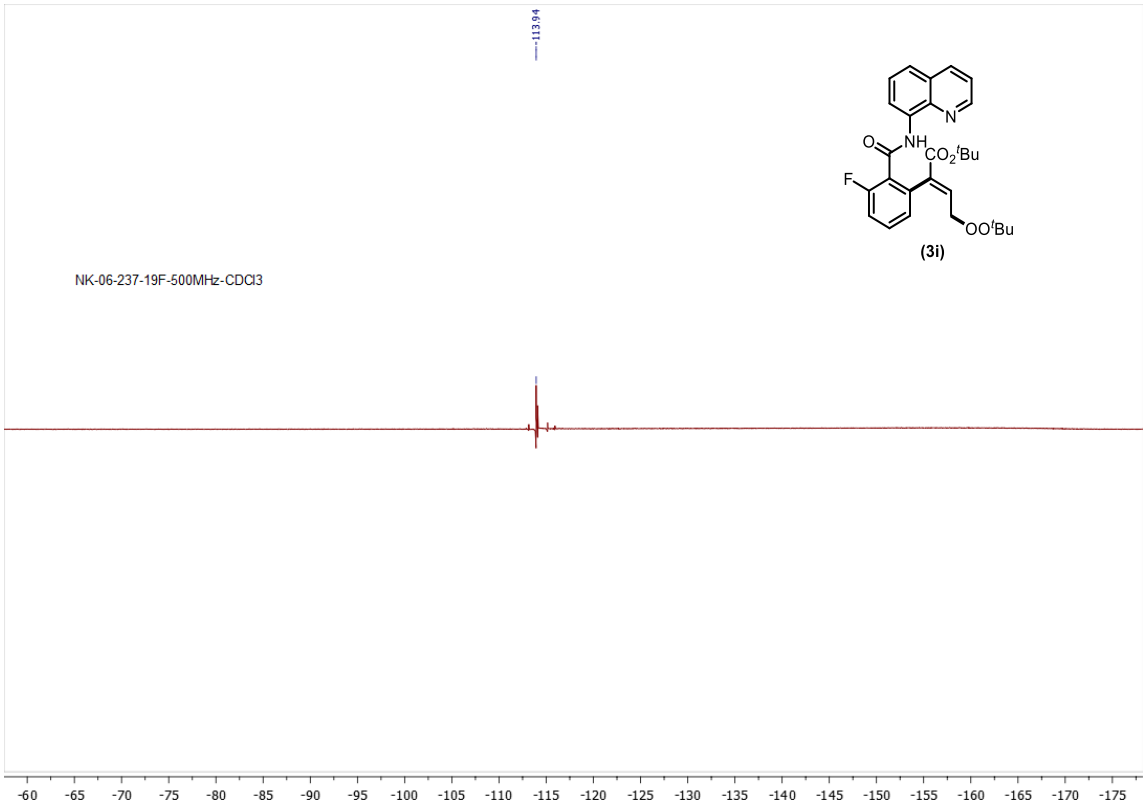
TIC +All MS






(3i)


NK-06-237-13C-500MHz-CDCl3
(3i)


-113.94
NK-06-237-19F-500MHz-CDCl3
-60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175

(3i)

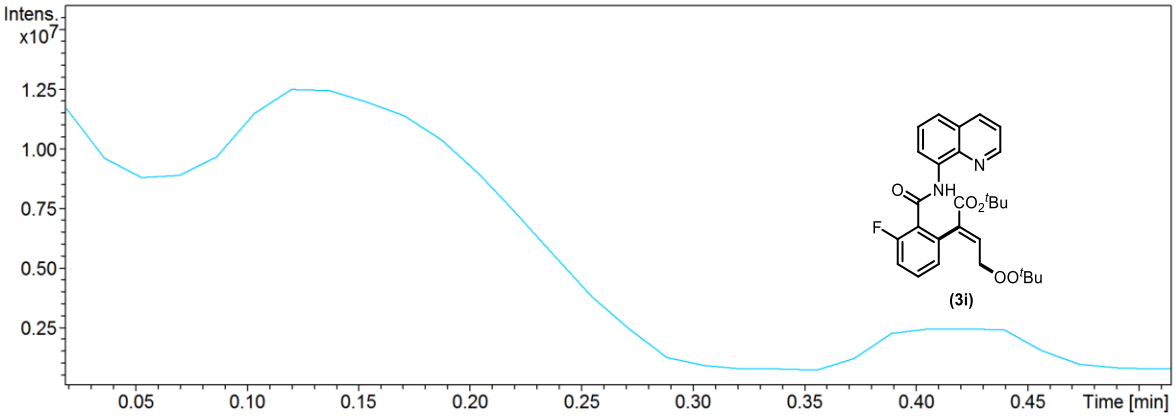
Display Report

Analysis Info

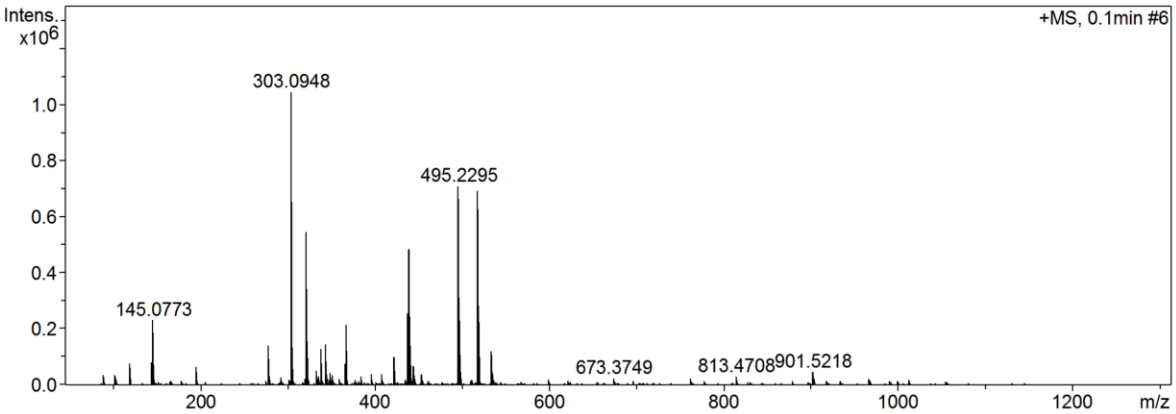
Analysis Name	D:\Data\USER DATA 2022\JULY2022\15-07-22\Dr.M.Kapur-NK_06_237.d	Acquisition Date	15-07-2022 12:38:40
Method	tune mix_low.New.021117.m	Operator	Bruker
Sample Name	NK_06_237	Instrument	micrOTOF-Q 10330
Comment			

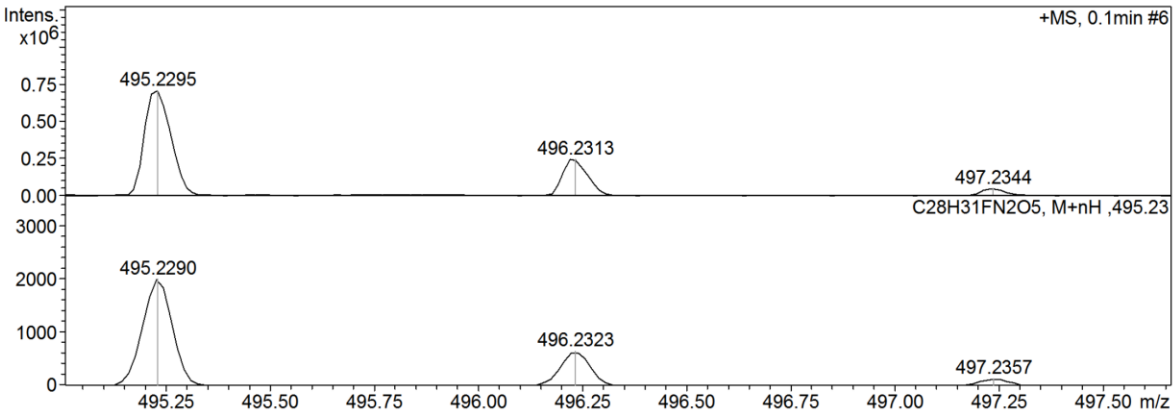
Acquisition Parameter

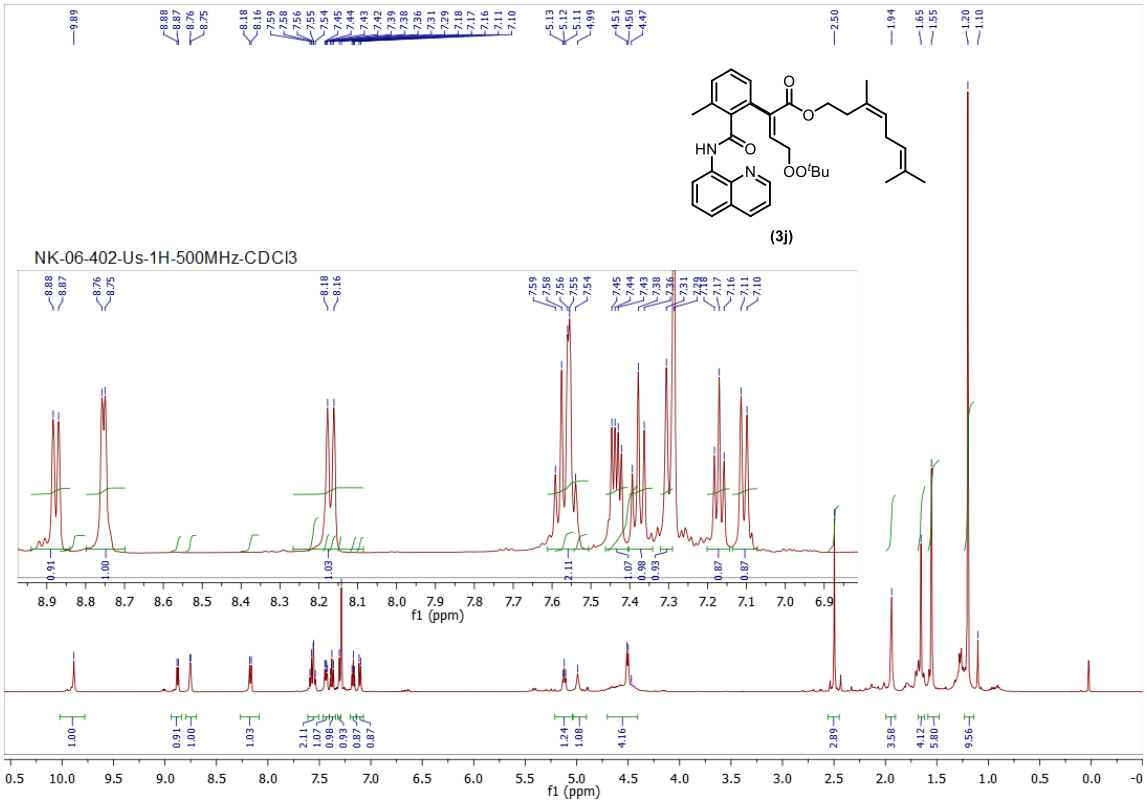
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4600 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	100.0 Vpp	Set Divert Valve	Source

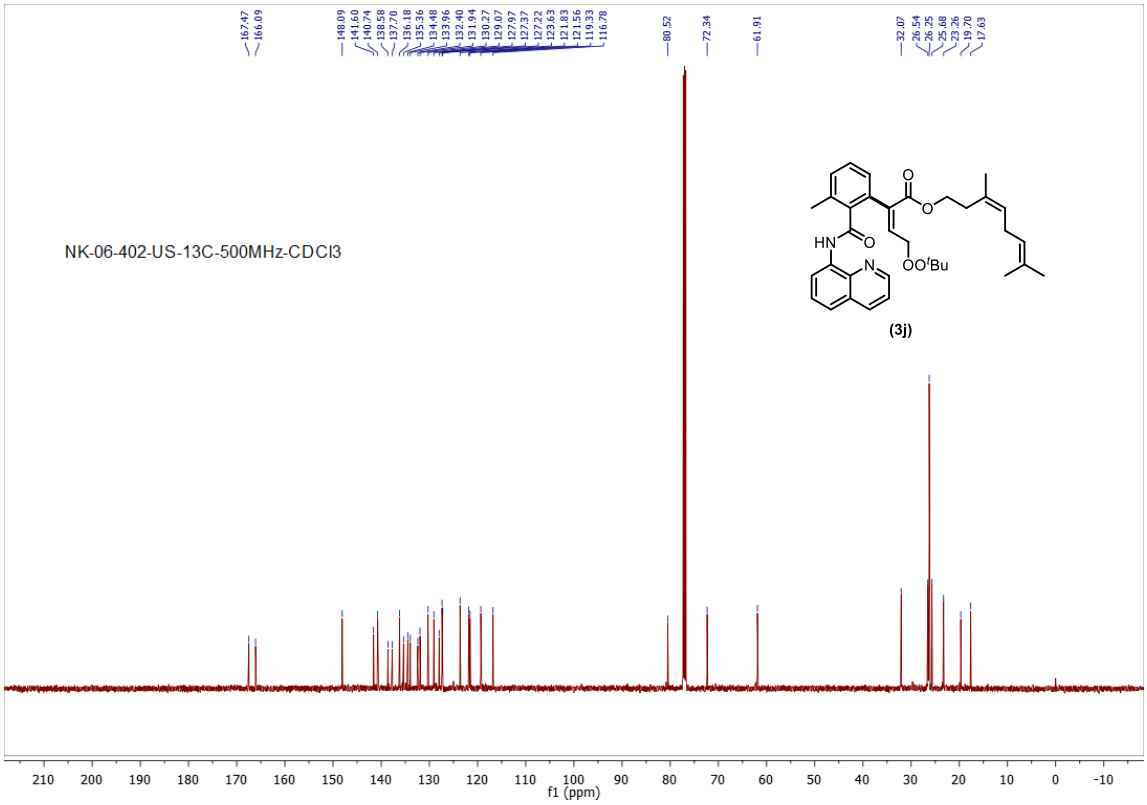


TIC +All MS






NK-06-402-Us-1H-500MHz-CDCl3
(3j)
f1 (ppm)


NK-06-402-US-13C-500MHz-CDCl3
(3j)
f1 (ppm)

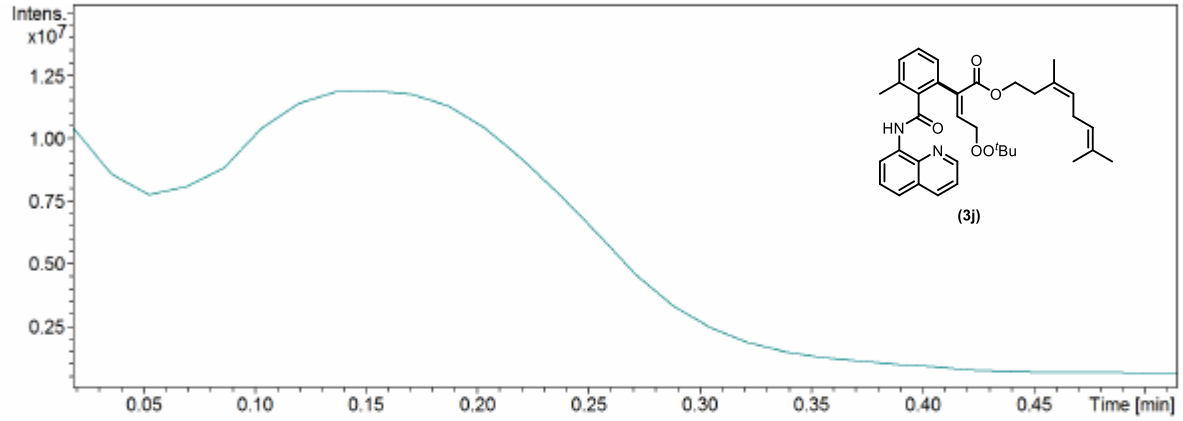
Display Report

Analysis Info

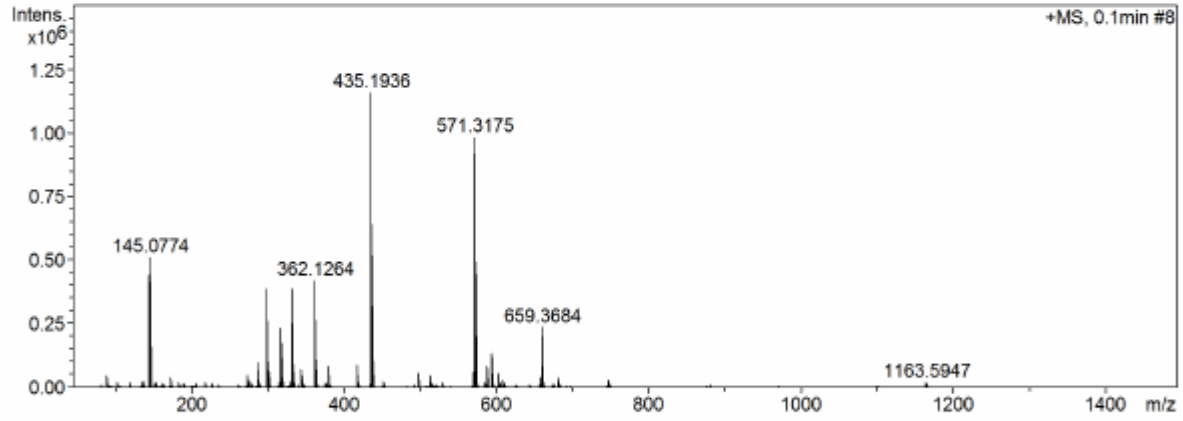
Analysis Name	D:\Data\USER DATA 2022\JULY2022\15-07-22\Dr.M.Kapur-NK_06_402_US.d	Acquisition Date	15-07-2022 12:33:44
Method	tune mix_low.New.021117.m	Operator	Bruker
Sample Name	NK_06_402_US	Instrument	micrOTOF-Q 10330
Comment			

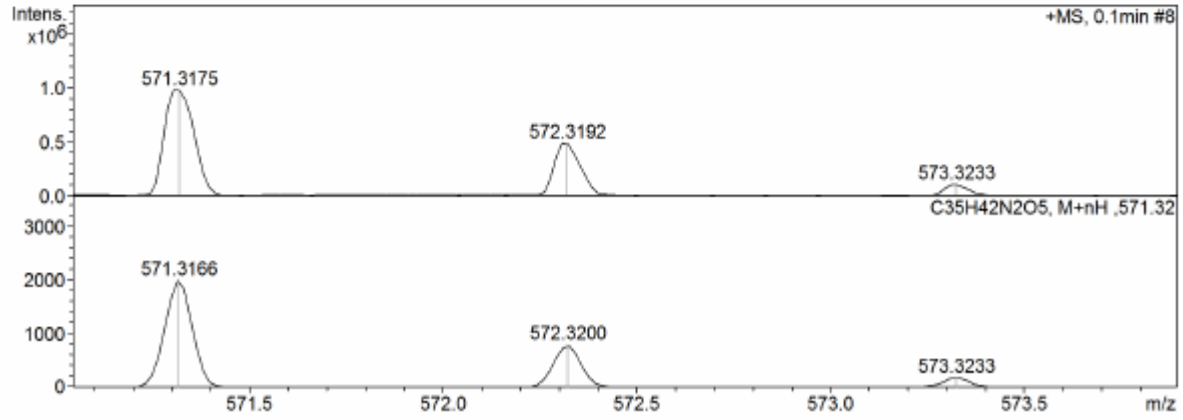
Acquisition Parameter

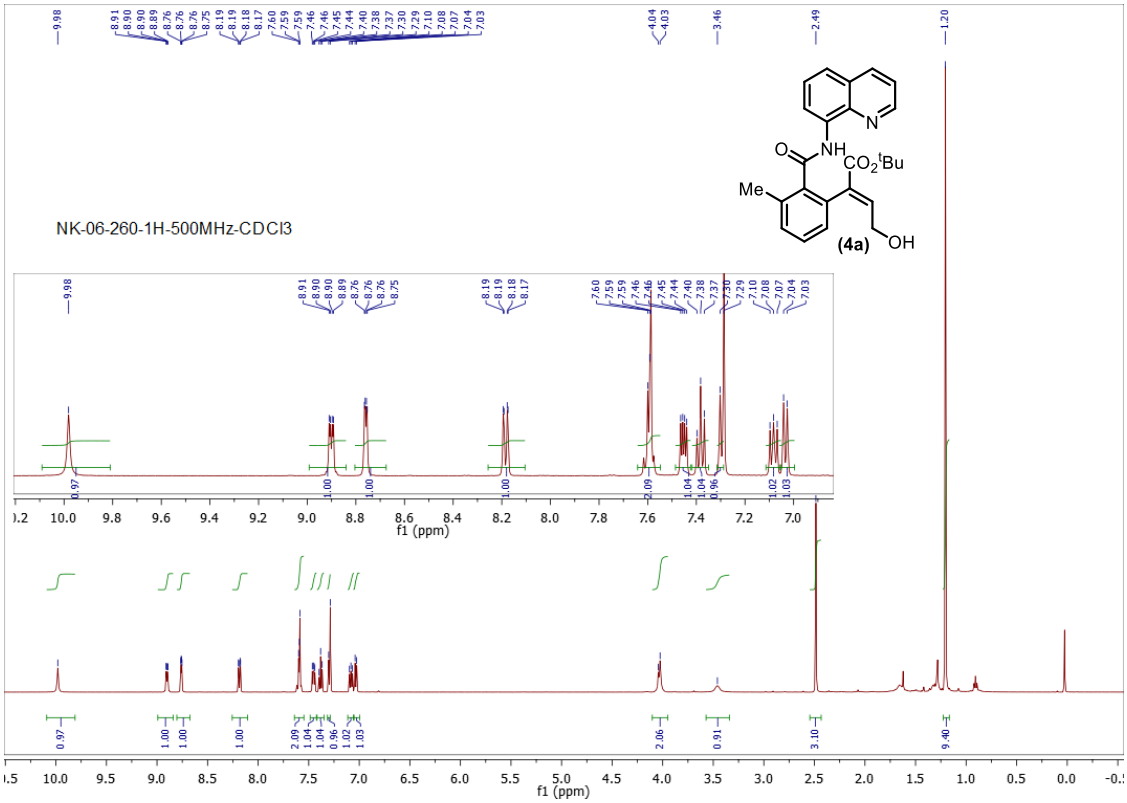
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4600 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	100.0 Vpp	Set Divert Valve	Source

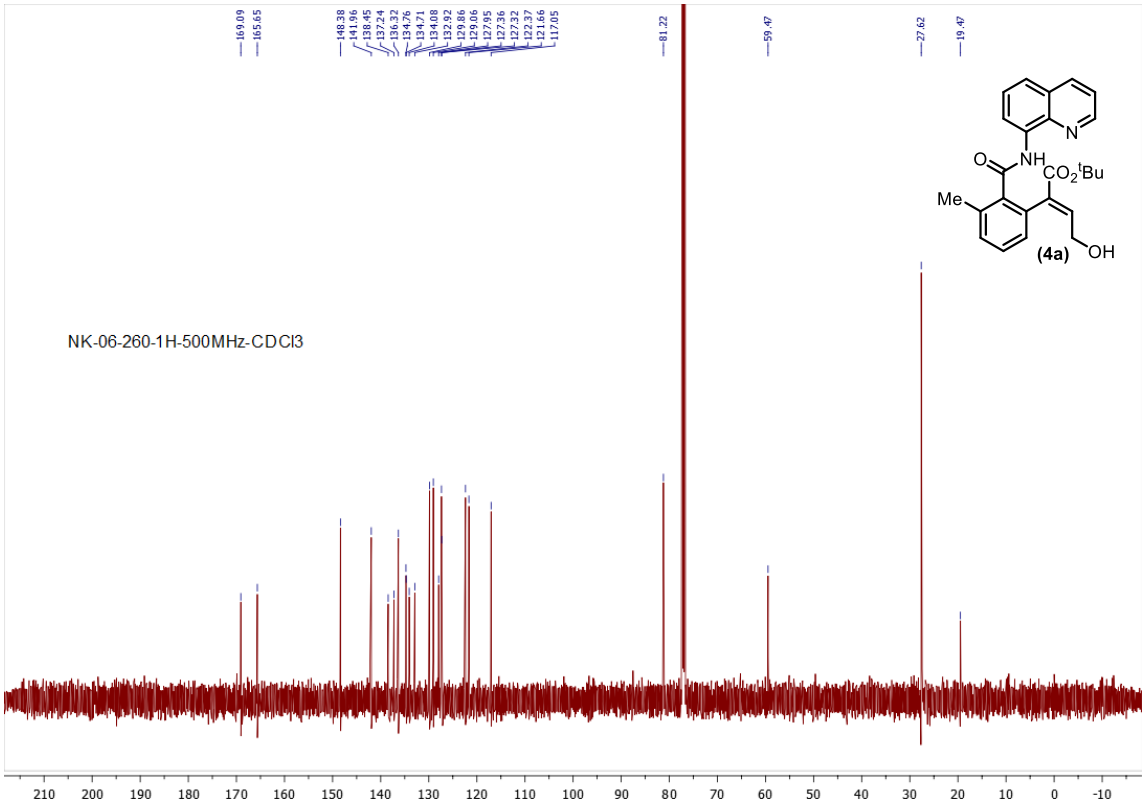


TIC +All MS






NK-06-260-1H-500MHz-CDCl3
(4a)
f1 (ppm)


NK-06-260-1H-500MHz-CDCl3
(4a)

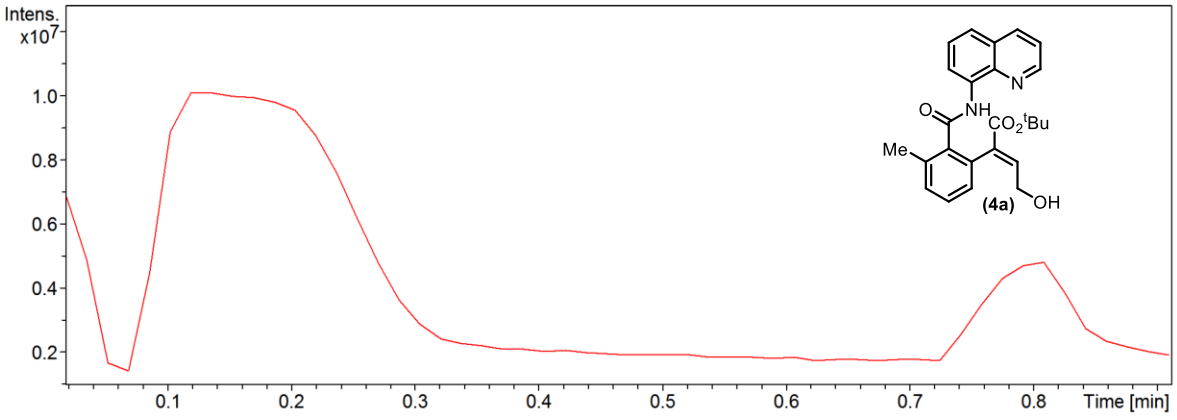
Display Report

Analysis Info

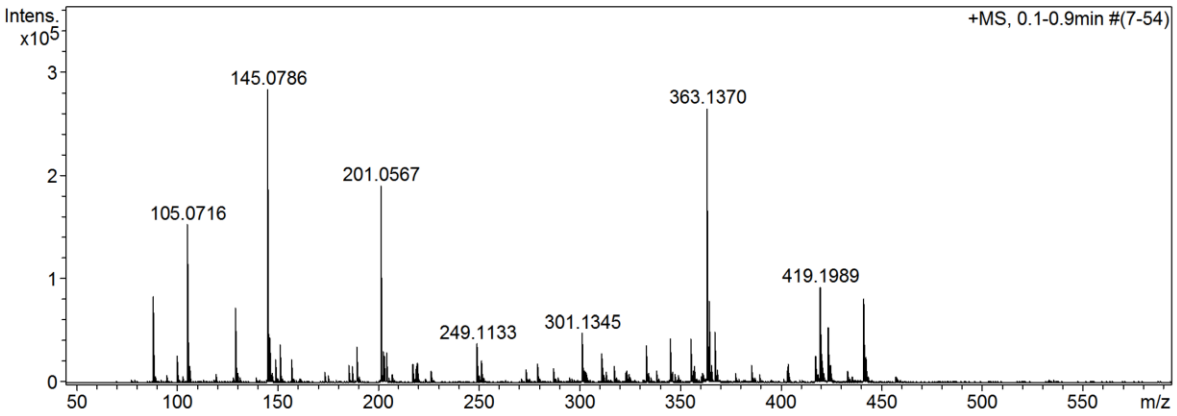
Analysis Name	D:\Data\USER DATA 2022\AUG2022\10-08-2022\Dr.M.Kapur-NK_06_260.d	Acquisition Date	10-08-2022 16:09:29
Method	tune mix_low.New.021117.m	Operator	Bruker
Sample Name	NK_06_260	Instrument	micrOTOF-Q 10330
Comment			

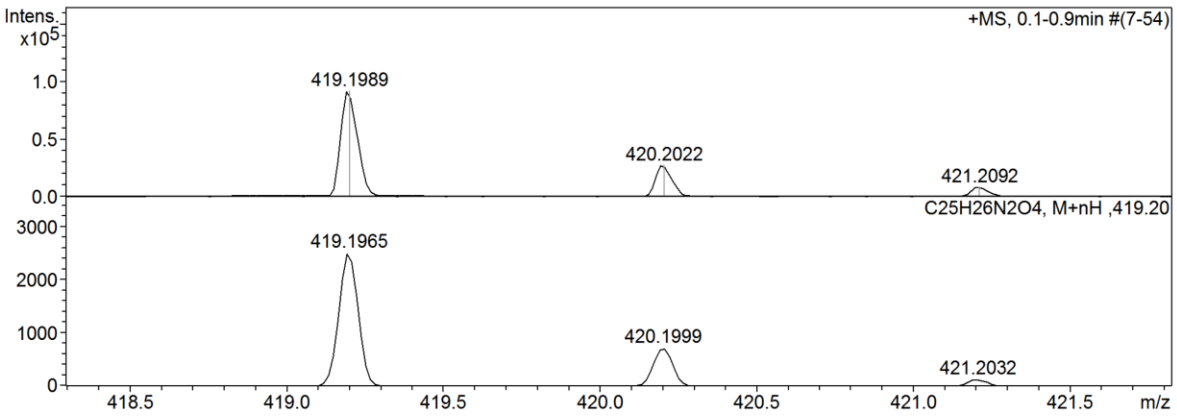
Acquisition Parameter

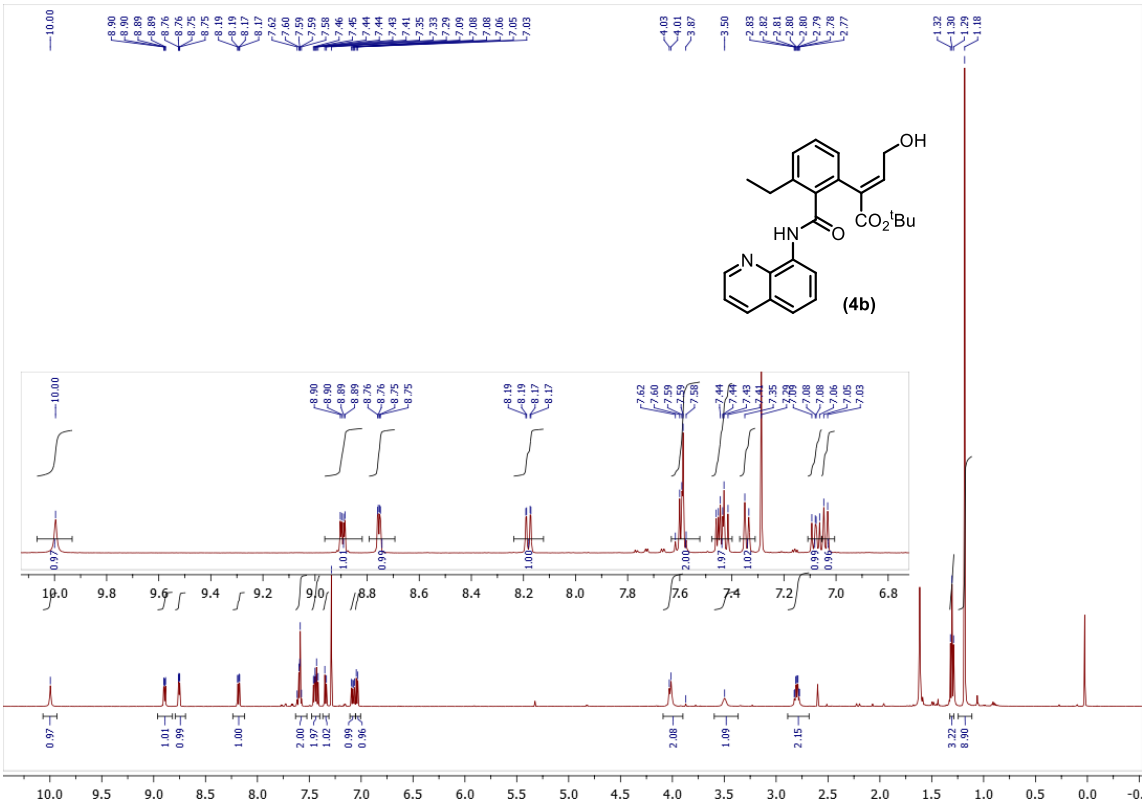
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4600 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	100.0 Vpp	Set Divert Valve	Source

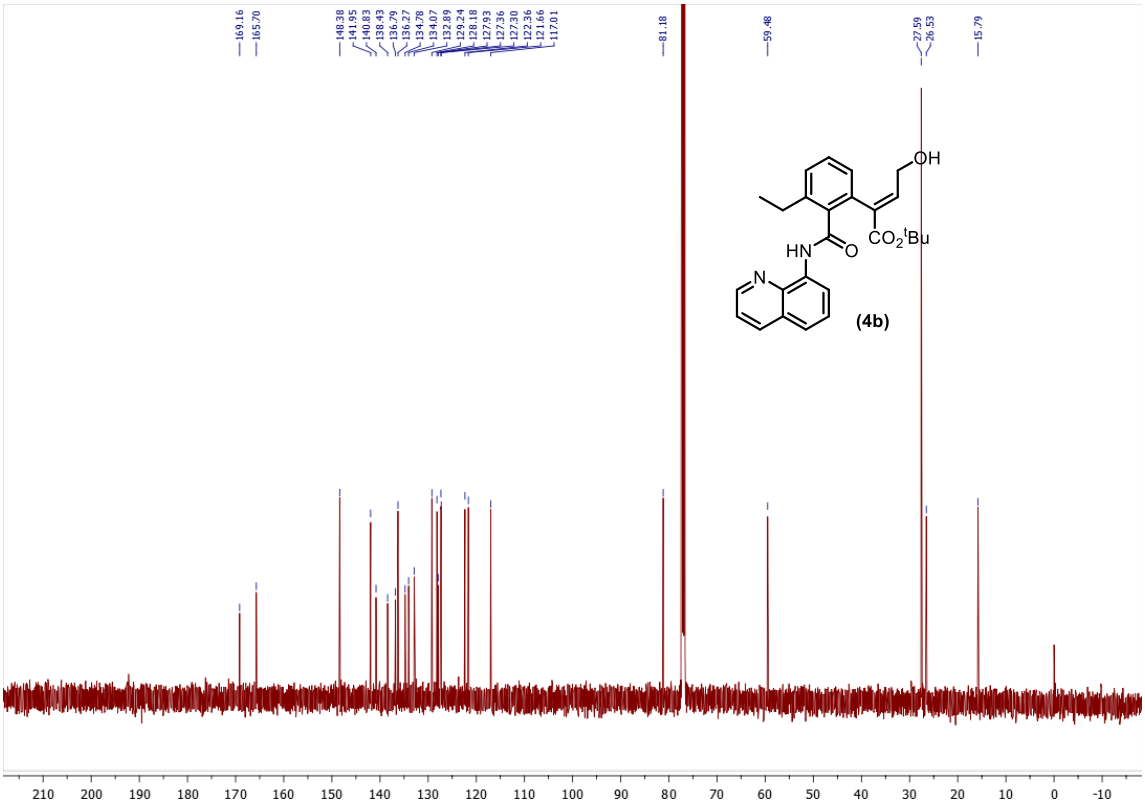


TIC +All MS






OH
CO2tBu
HN
O
N
(4b)


OH
CO2tBu
HN
O
N
(4b)

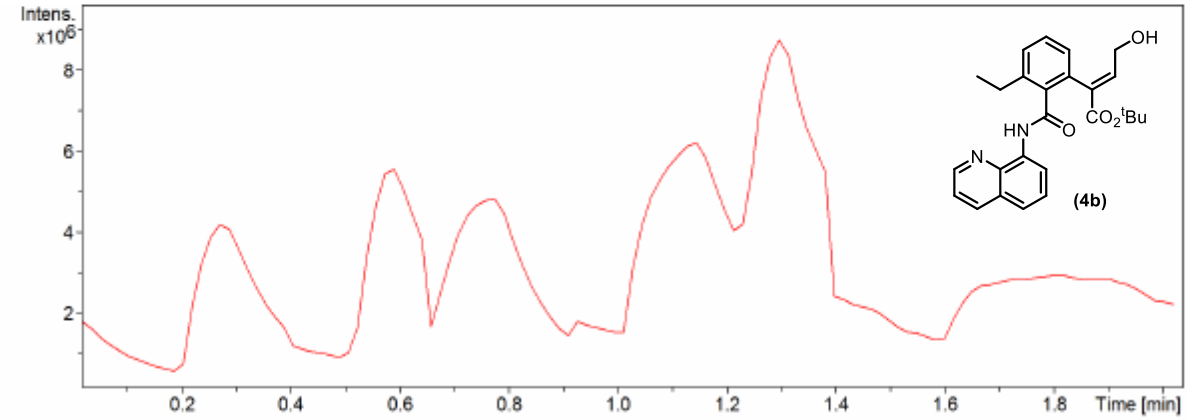
Display Report

Analysis Info

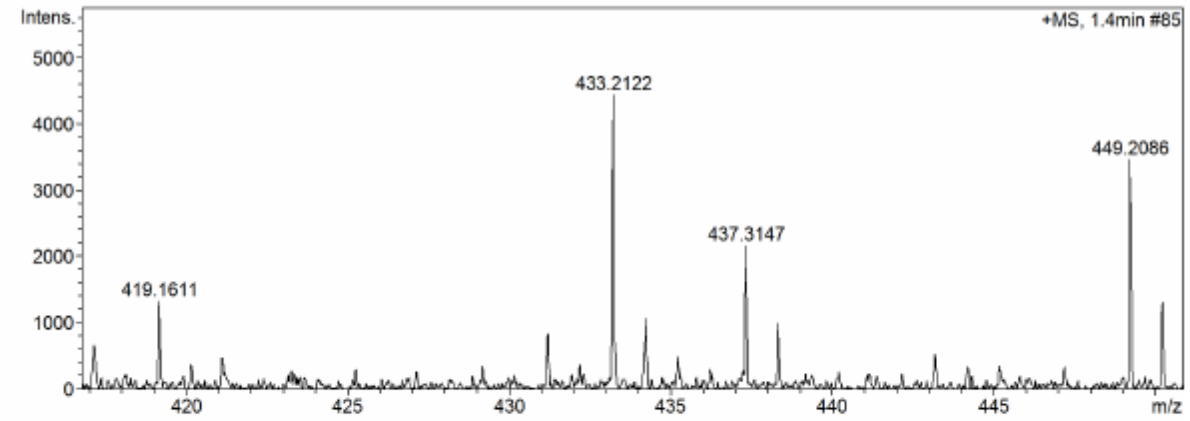
Analysis Name	D:\Data\USER DATA 2022\AUG2022\11-08-2022\Prof M Kapur_NK_07_12.d	Acquisition Date	11-08-2022 11:51:17
Method	tune_wide _APCI_23.06.m	Operator	Bruker
Sample Name	NK_07_12	Instrument	micrOTOF-Q 10330
Comment			

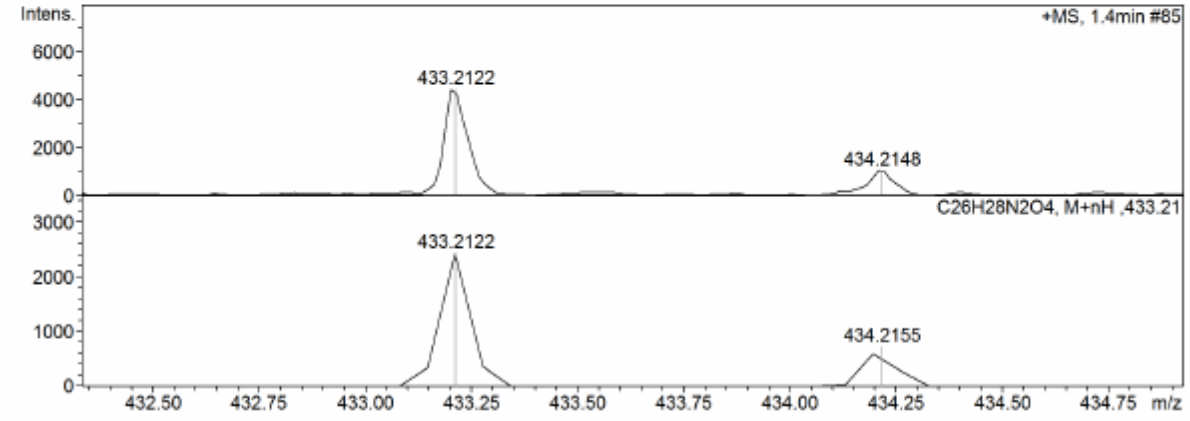
Acquisition Parameter

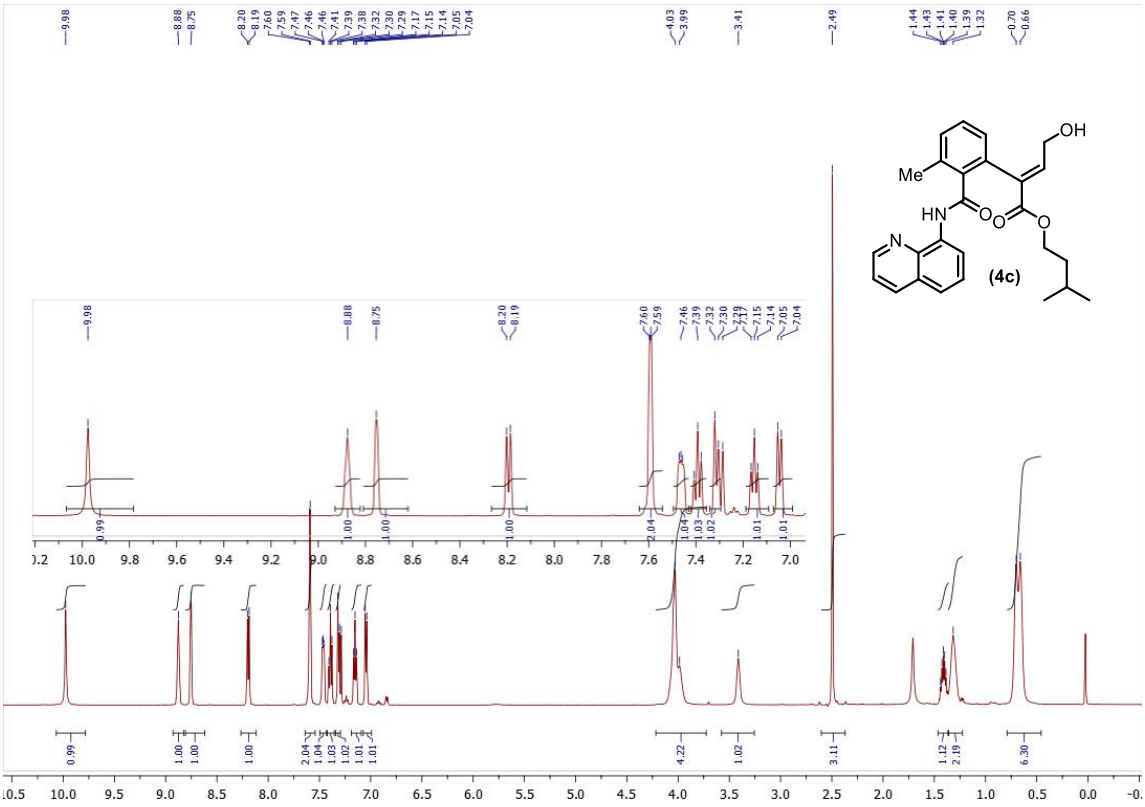
Source Type	Multi Mode	Ion Polarity	Positive	Set Nebulizer	2.0 Bar
Focus	Not active	Set Capillary	2500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	5.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	300.0 Vpp	Set Divert Valve	Waste

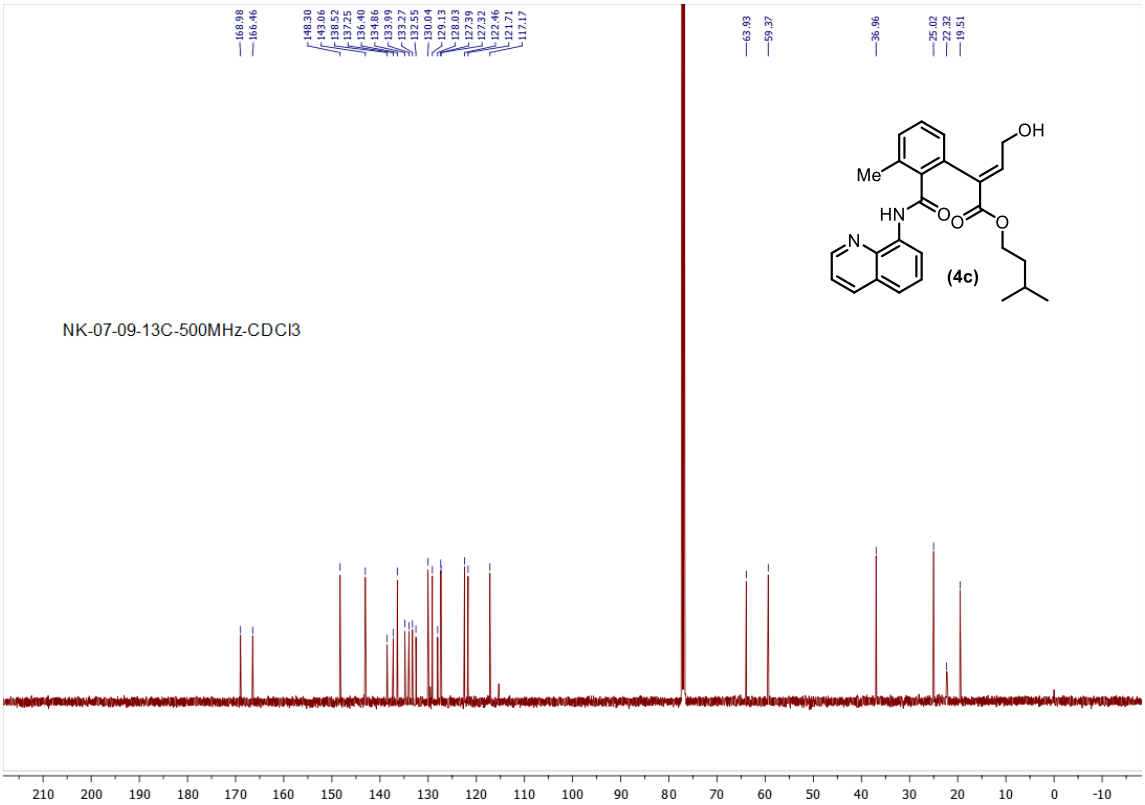


TIC +All MS






OH
Me
HN
O
O
O
N
(4c)


OH
Me
HN
O
O
O
N
(4c)
NK-07-09-13C-500MHz-CDCl3

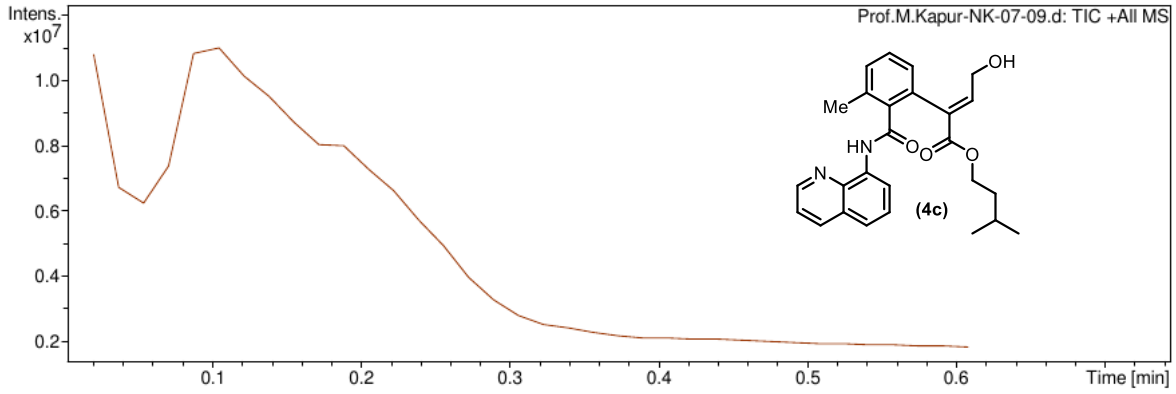
Display Report

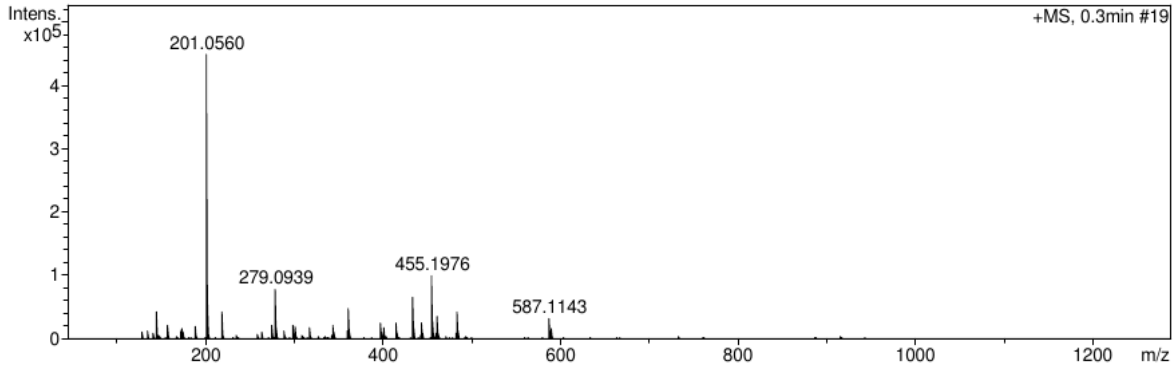
Analysis Info

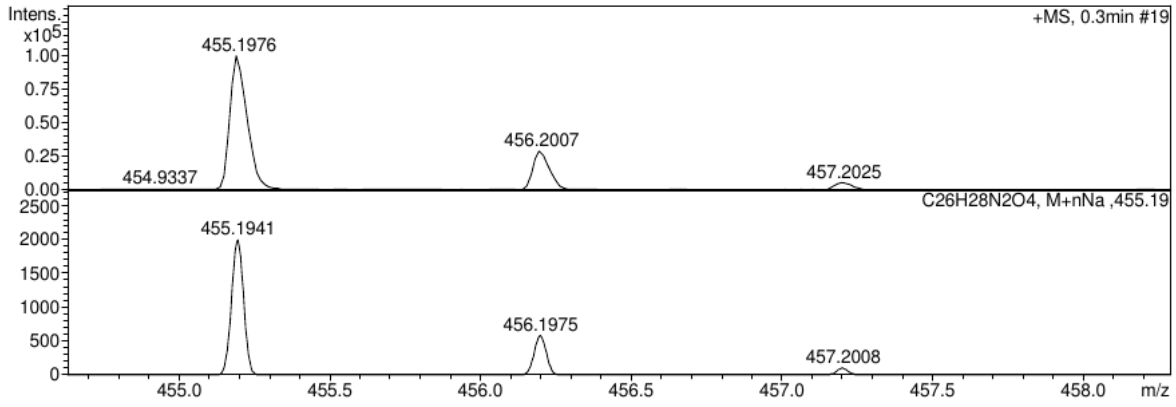
Analysis Name	D:\Data\NEW USER DATA 2022\Jan-2022\07-jan-2022\Prof.M.Kapur-NK-07-09.d	Acquisition Date	1/7/2022 4:34:23 PM
Method	tune mix_low.New.021117.m	Operator	RUCHI
Sample Name	NK-07-09	Instrument	micrOTOF-Q II 10330
Comment			

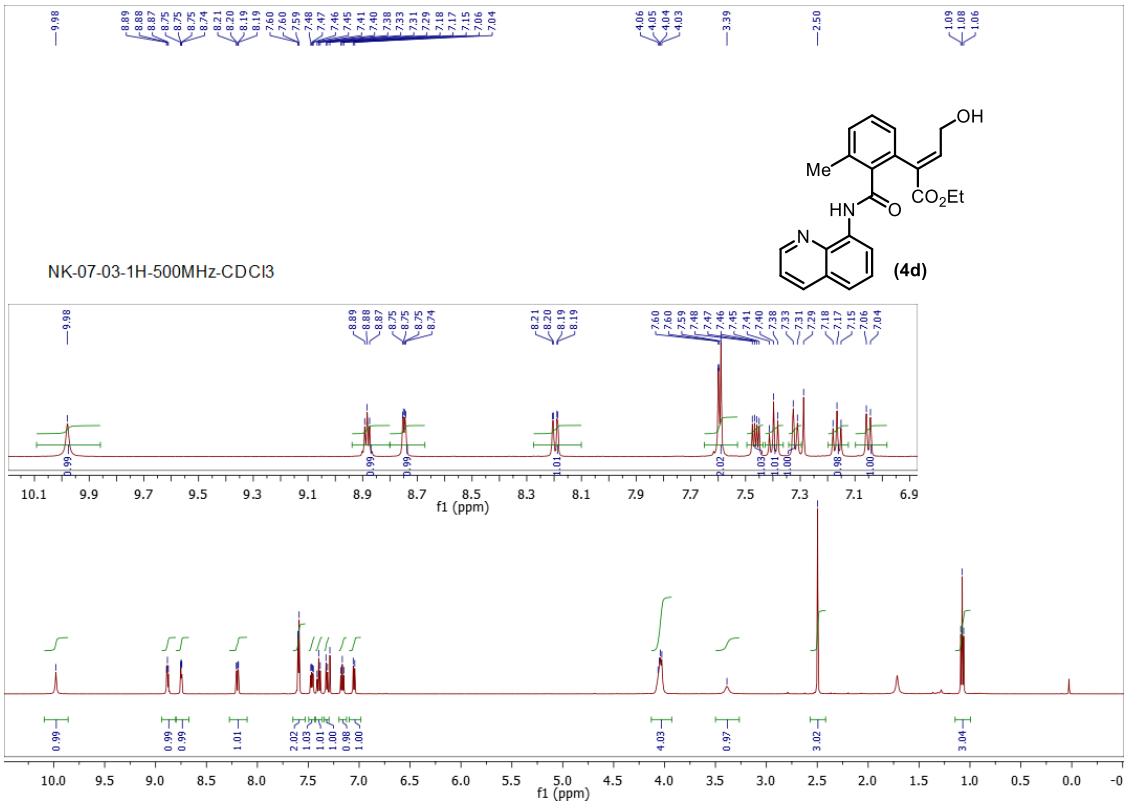
Acquisition Parameter

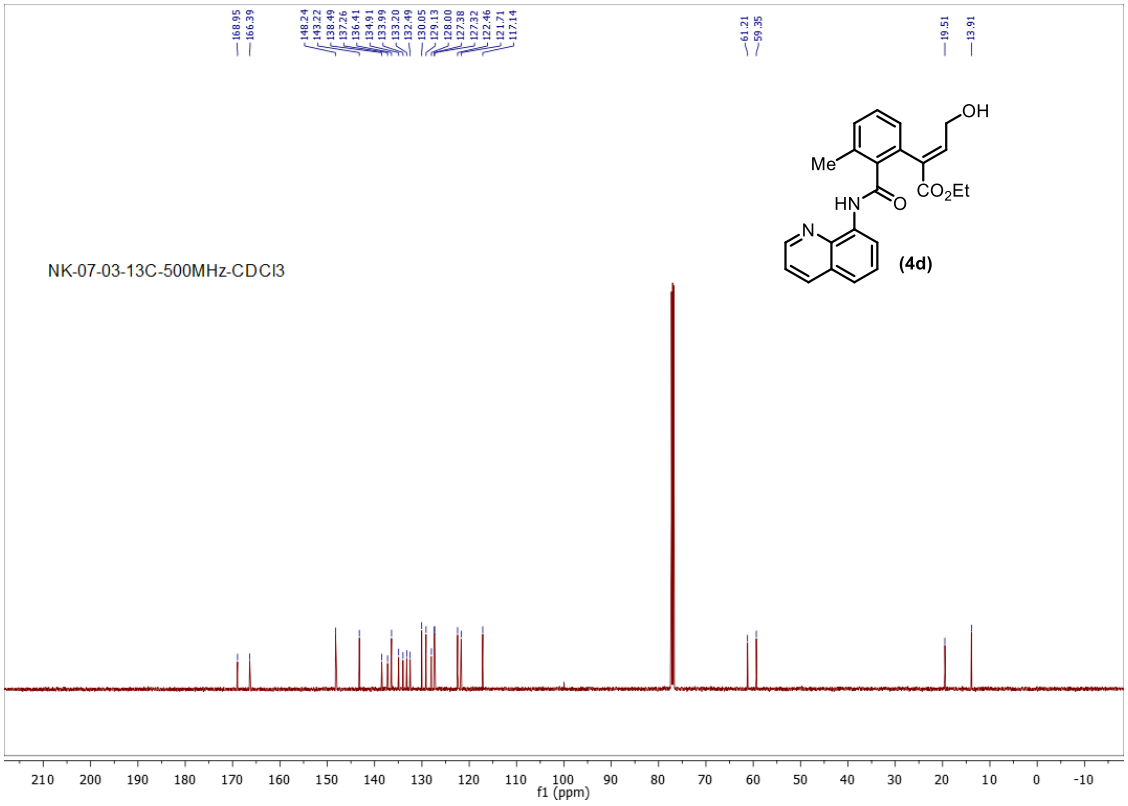
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4600 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	100.0 Vpp	Set Divert Valve	Source








NK-07-03-1H-500MHz-CDCl3
(4d)
f1 (ppm)


NK-07-03-13C-500MHz-CDCl3
(4d)
f1 (ppm)

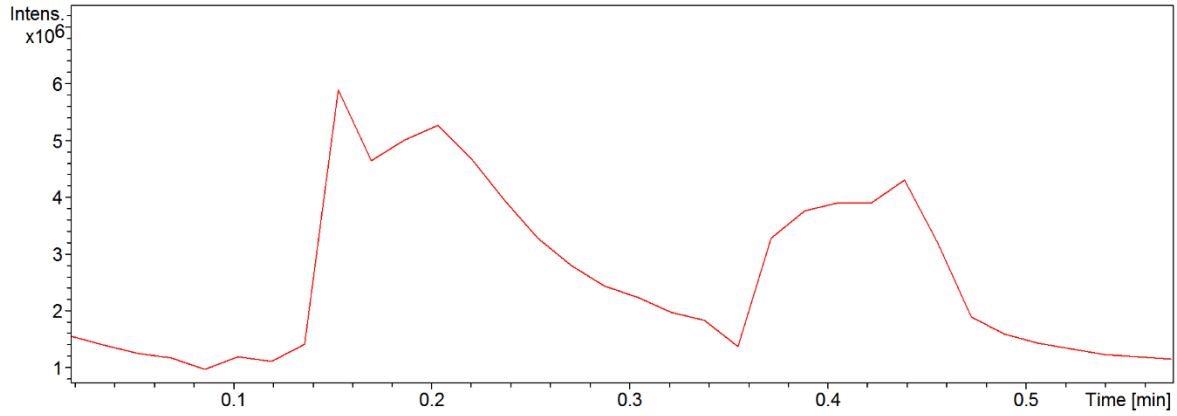
Display Report

Analysis Info

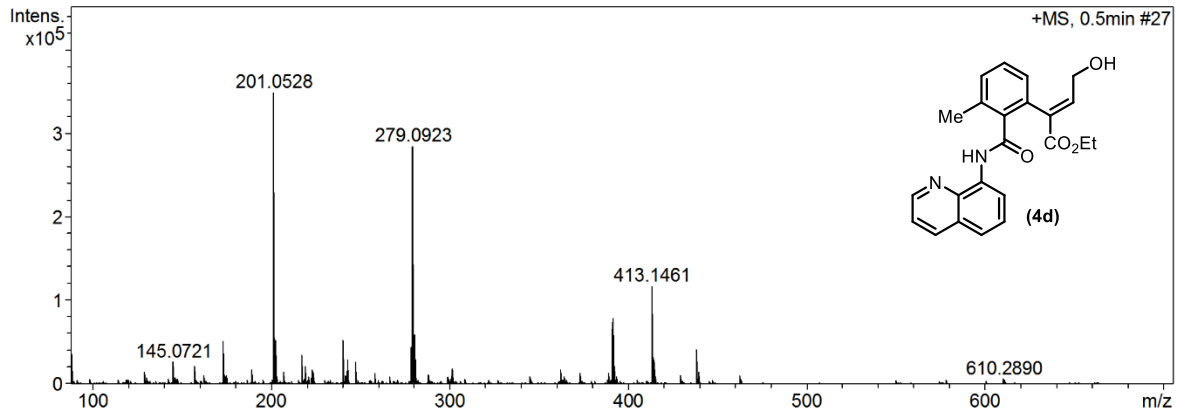
Analysis Name	D:\Data\USER DATA 2022\DEC\05-12-2022\Prof M K apur-NK-07-03-R.d	Acquisition Date	05-12-2022 15:54:39
Method	tune mix_low.New.021117.m	Operator	Bruker
Sample Name	NK-07-03-R	Instrument	micrOTOF-Q 10330
Comment			

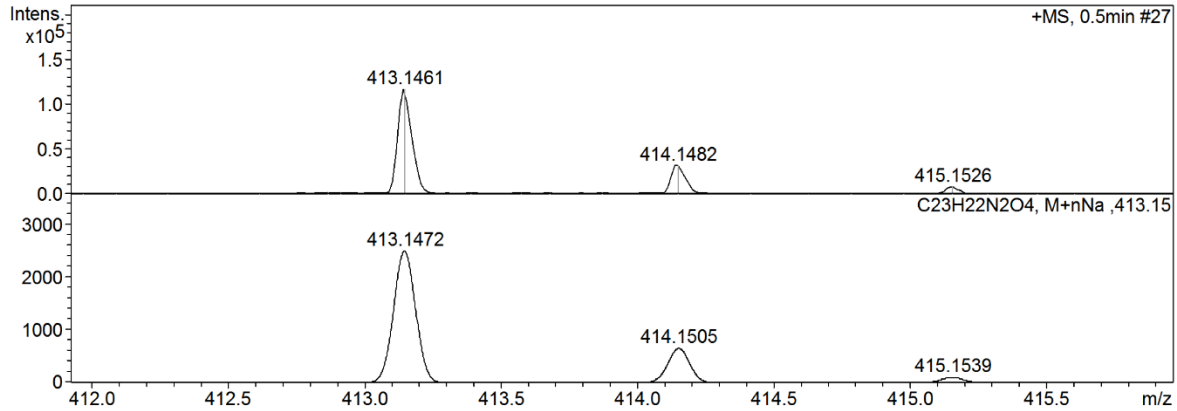
Acquisition Parameter

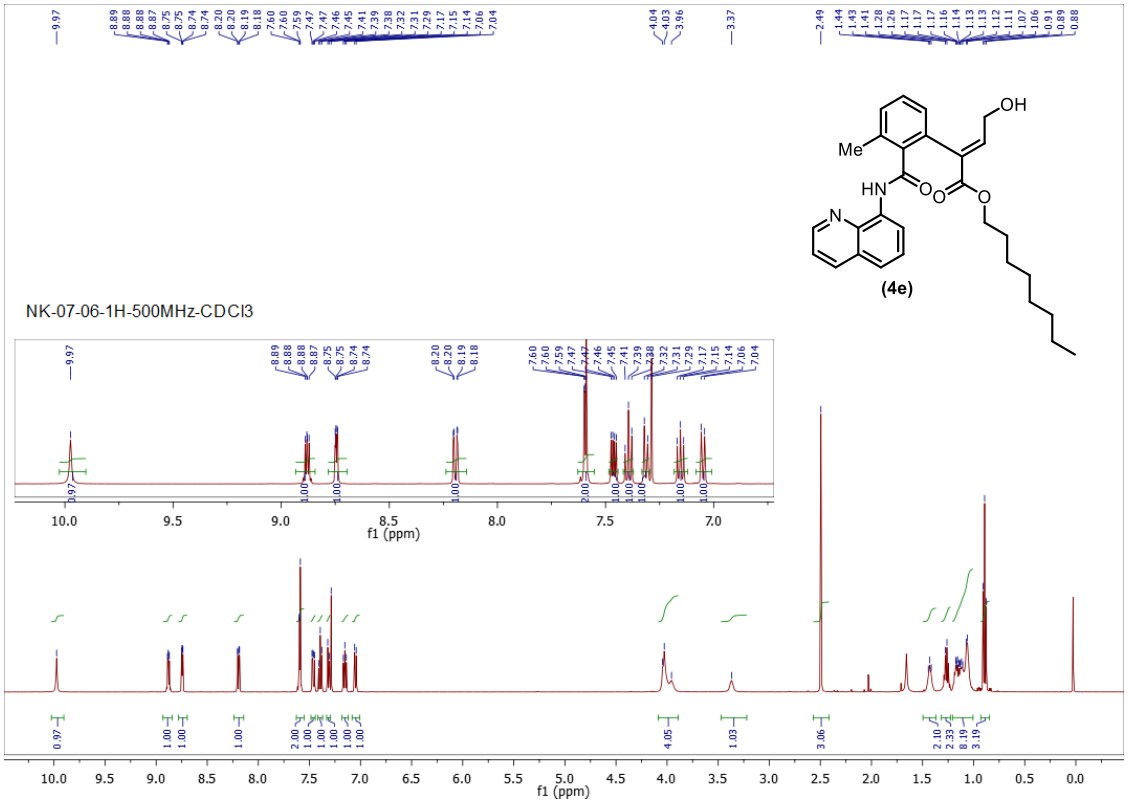
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4600 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	100.0 Vpp	Set Divert Valve	Source

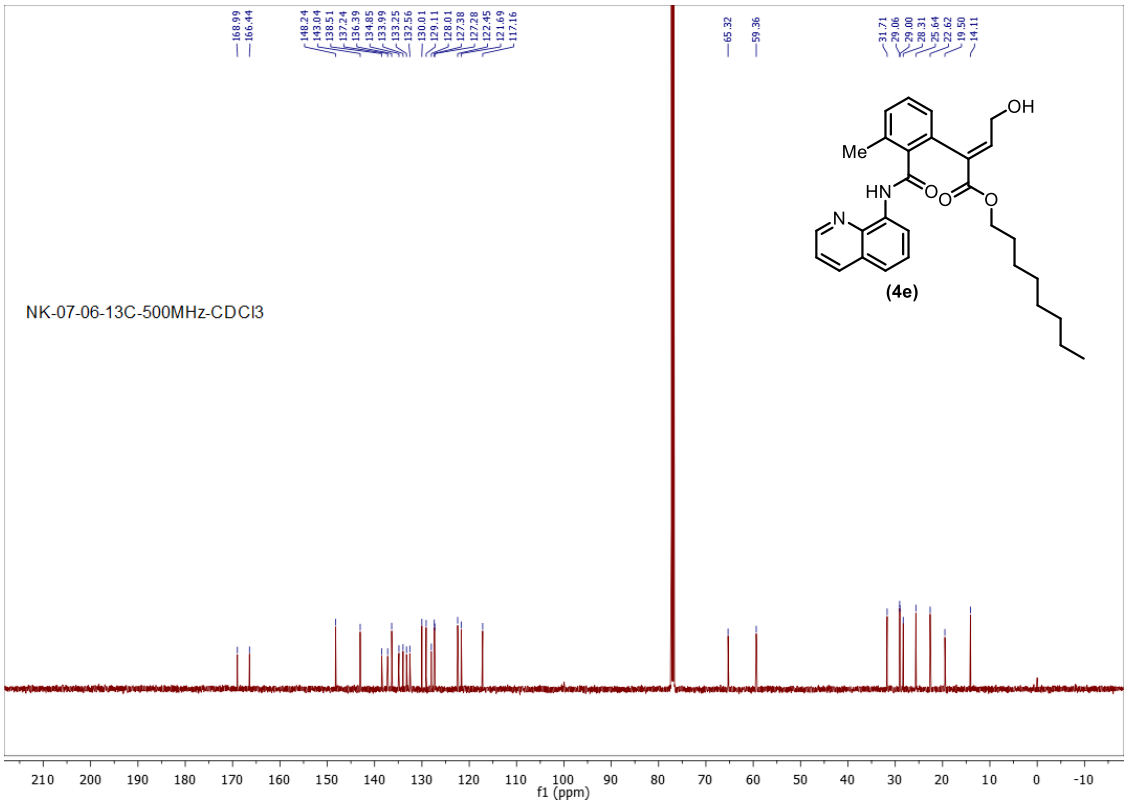


TIC +All MS






NK-07-06-1H-500MHz-CDCl3
(4e)
f1 (ppm)


NK-07-06-13C-500MHz-CDCl3
(4e)
f1 (ppm)

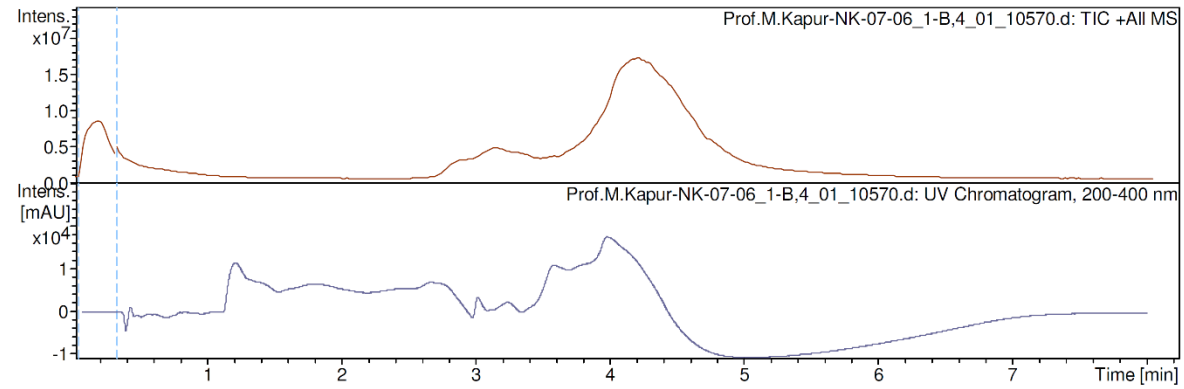
Display Report

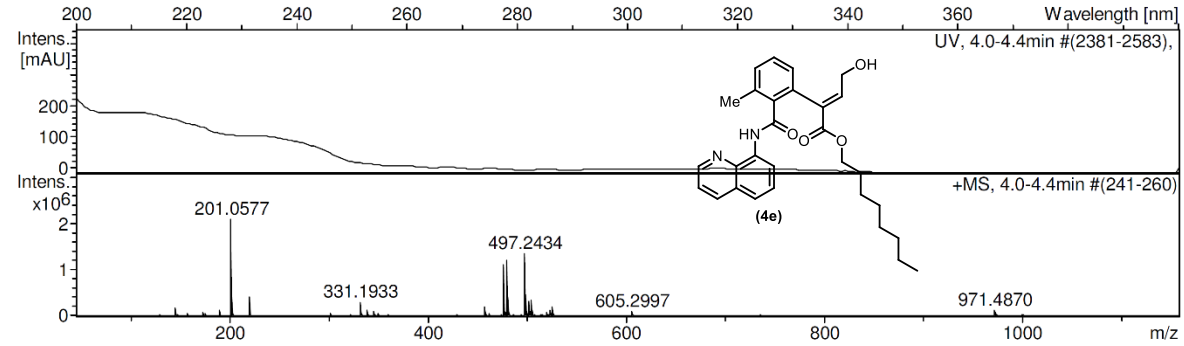
Analysis Info

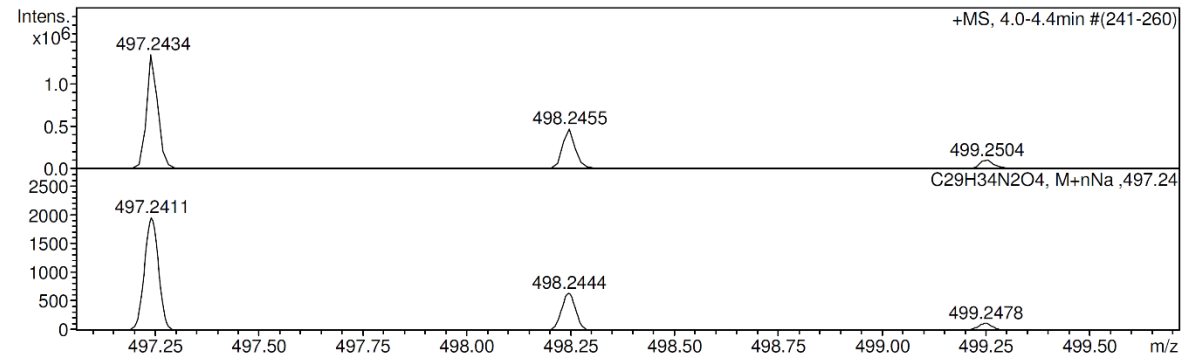
Analysis Name	D:\Data\new user data 2021\Dec-2021\20-dec\Prof.M.Kapur-NK-07-06_1-B,4_01_10570.d	Acquisition Date	12/20/2021 1:23:03 PM
Method	hrlcms-20 sept.m	Operator	RUCHI
Sample Name	Prof.M.Kapur-NK-07-06	Instrument	micrOTOF-Q II 10330
Comment			

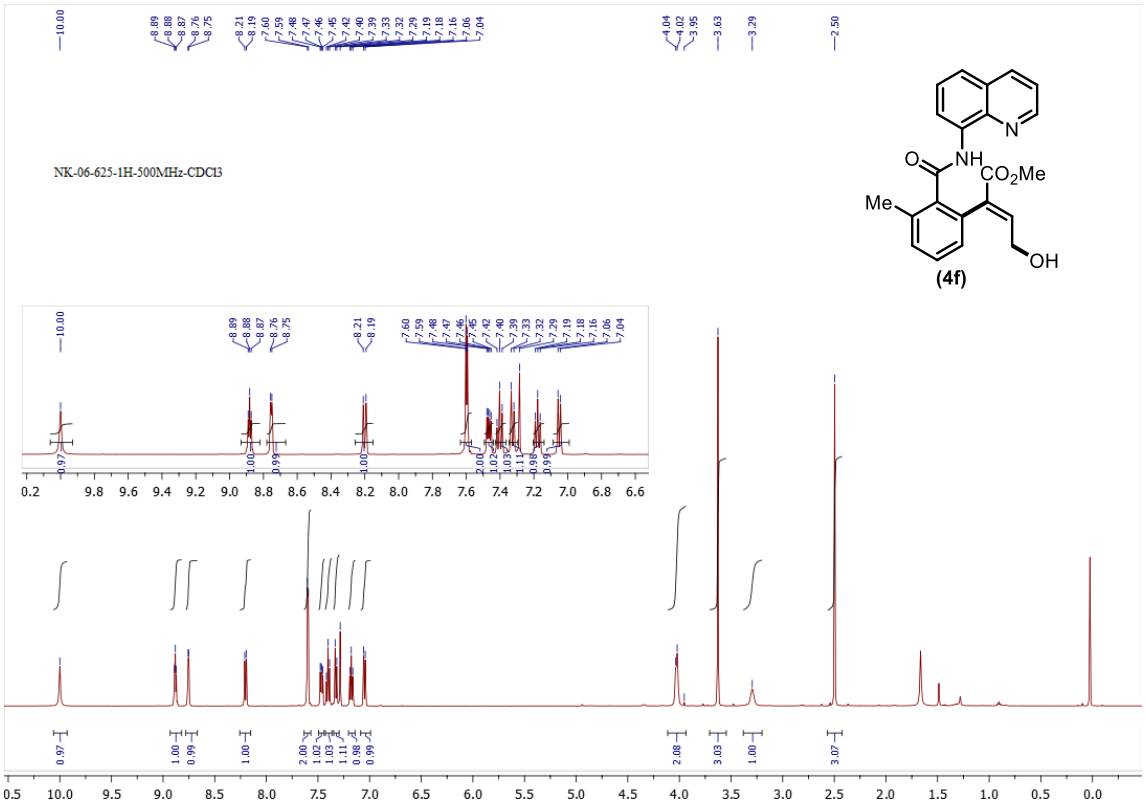
Acquisition Parameter

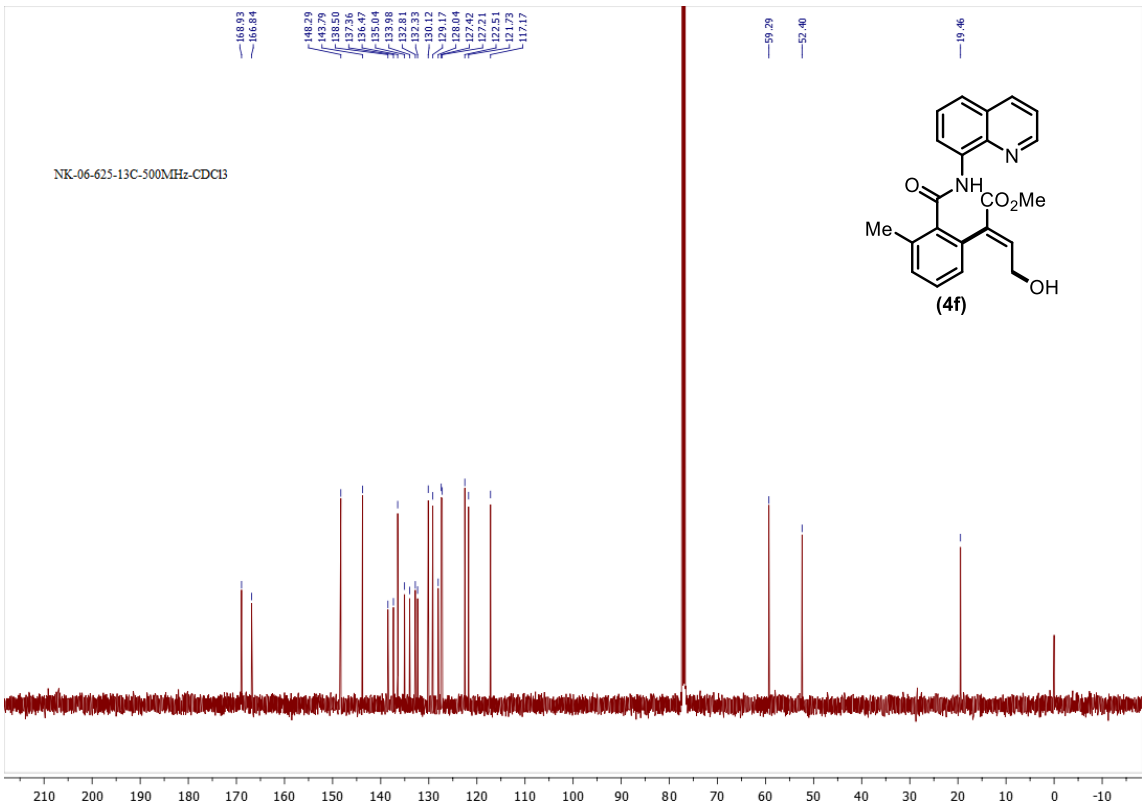
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.2 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	130.0 Vpp	Set Divert Valve	Waste

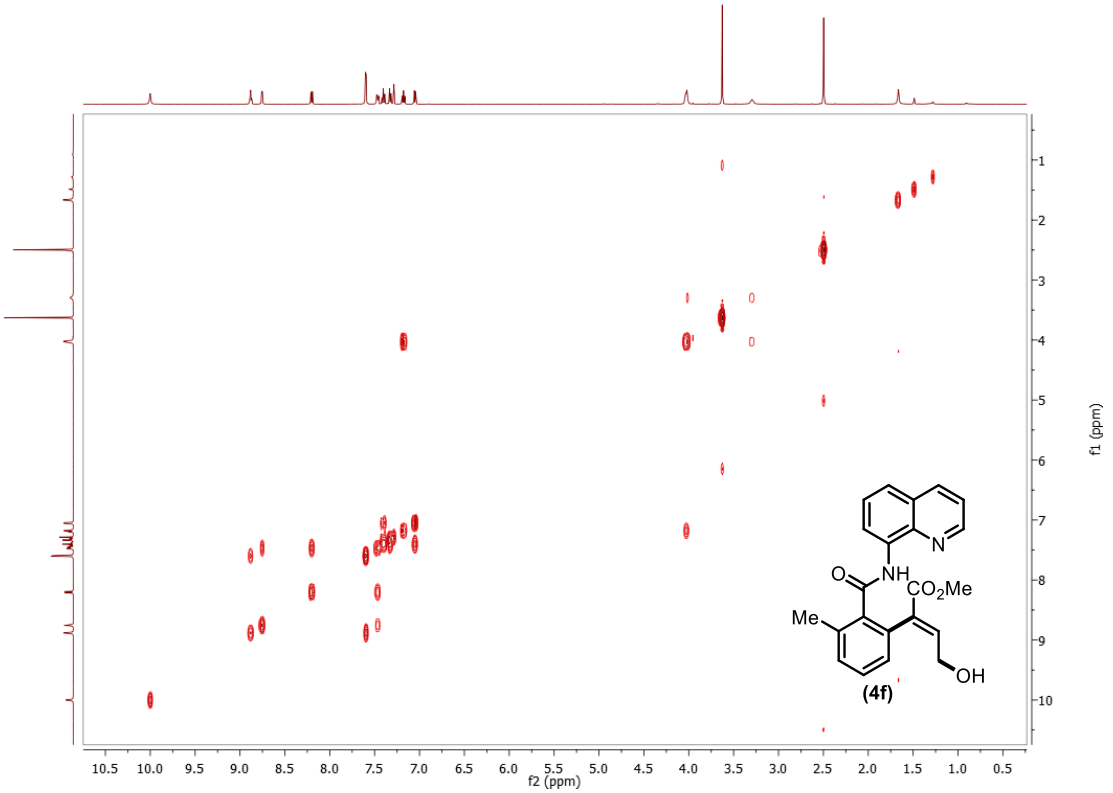


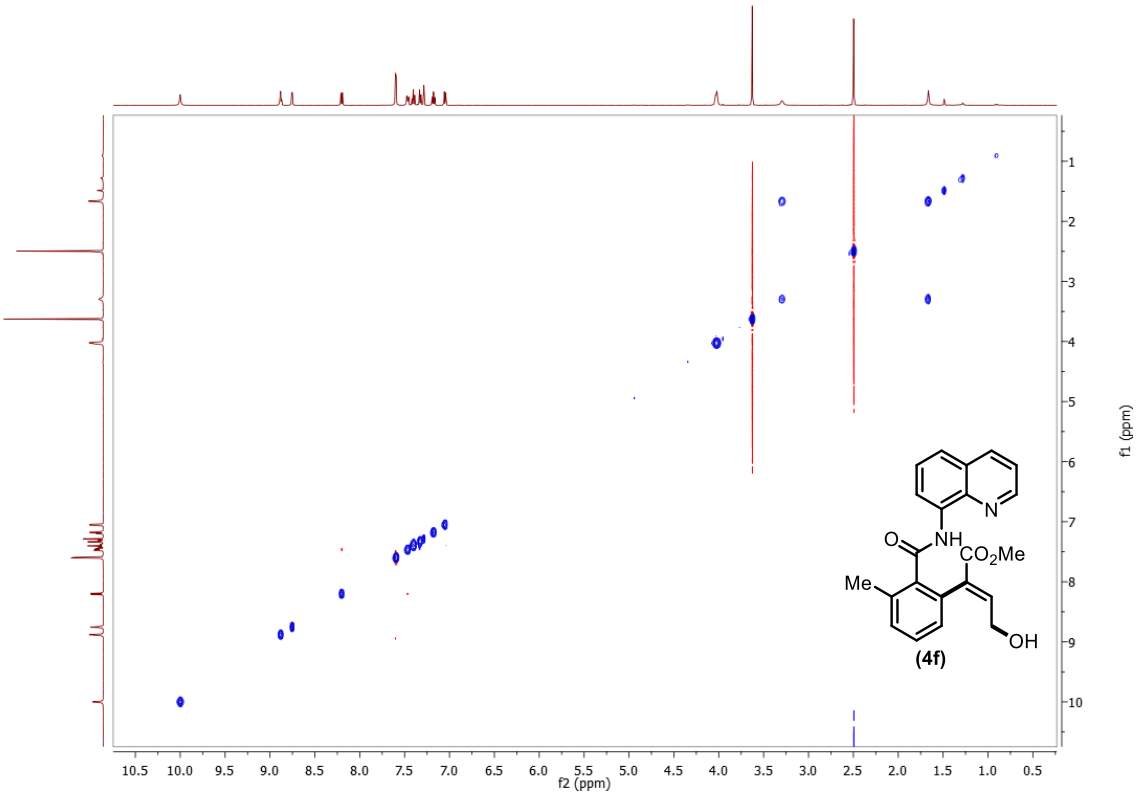





NK-06-625-1H-500MHz-CDCl3
(4f)


NK-06-625-13C-500MHz-CDCl3
(4f)


f2 (ppm)
f1 (ppm)
N
NH
O
CO2Me
Me
OH
(4f)


f2 (ppm)
f1 (ppm)
N
NH
O
CO2Me
Me
OH
(4f)

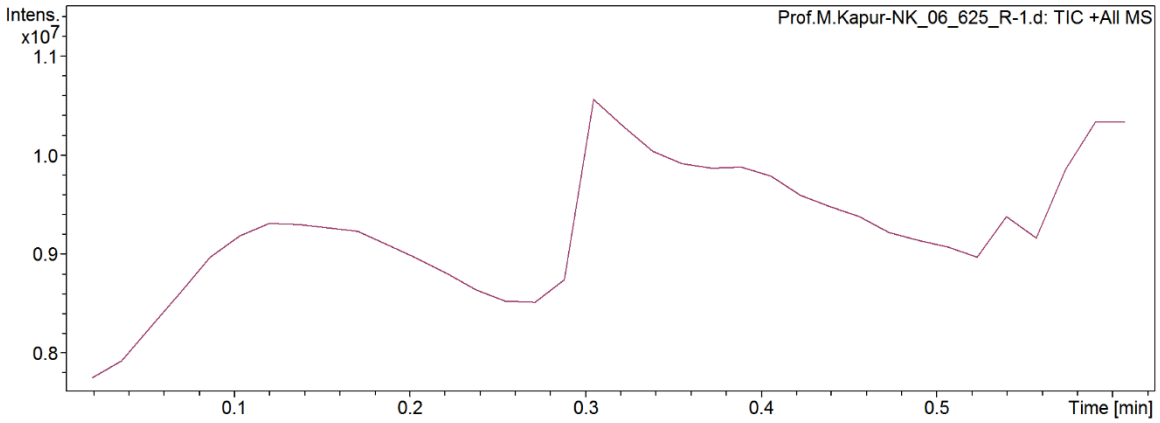
Display Report

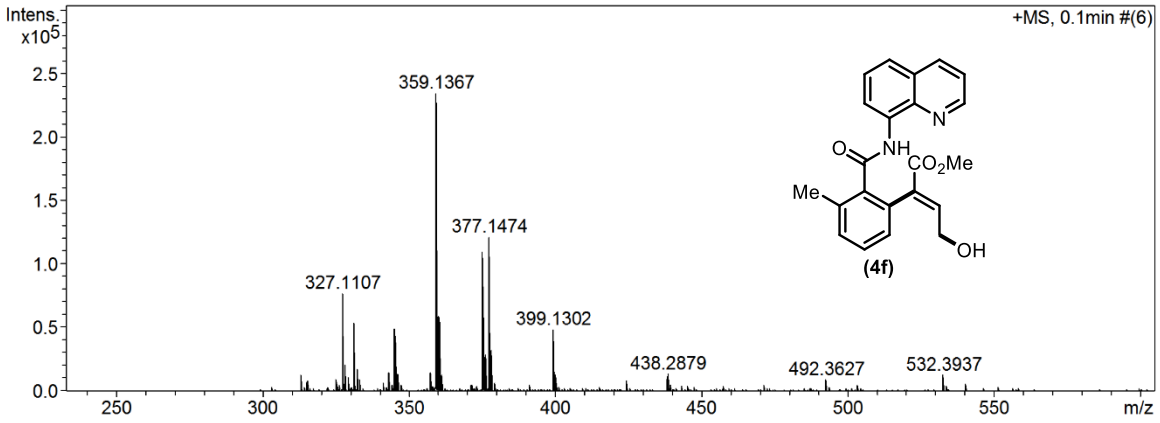
Analysis Info

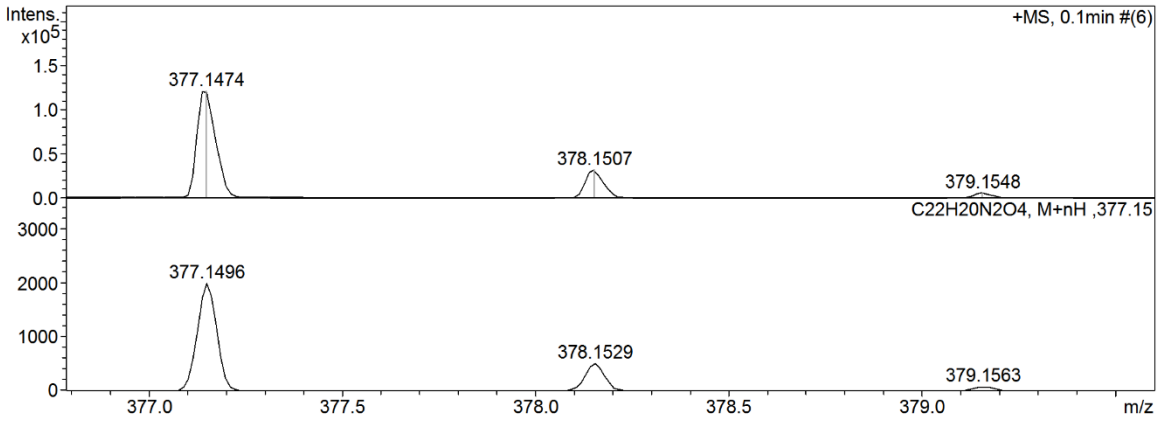
Analysis Name	D:\Data\USER DATA 2022\Nov-2022\03-11-2022\Prof.M.Kapur-NK_06_625_R-1.d	Acquisition Date	03-11-2022 12:34:14
Method	tune_wide _APCI_23.06.m	Operator	Bruker
Sample Name	NK_06_625_R-1	Instrument	micrOTOF-Q 10330
Comment			

Acquisition Parameter

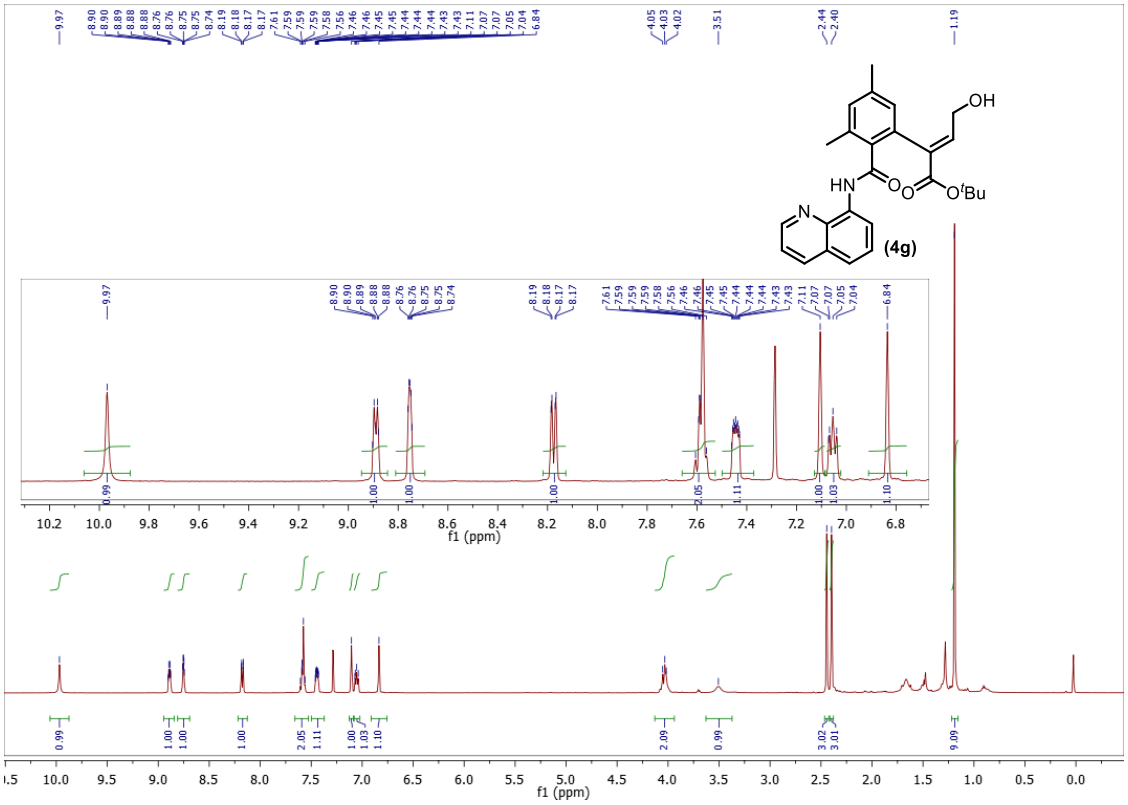
Source Type	Multi Mode	Ion Polarity	Positive	Set Nebulizer	2.0 Bar
Focus	Not active	Set Capillary	2500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	5.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	600.0 Vpp	Set Divert Valve	Source

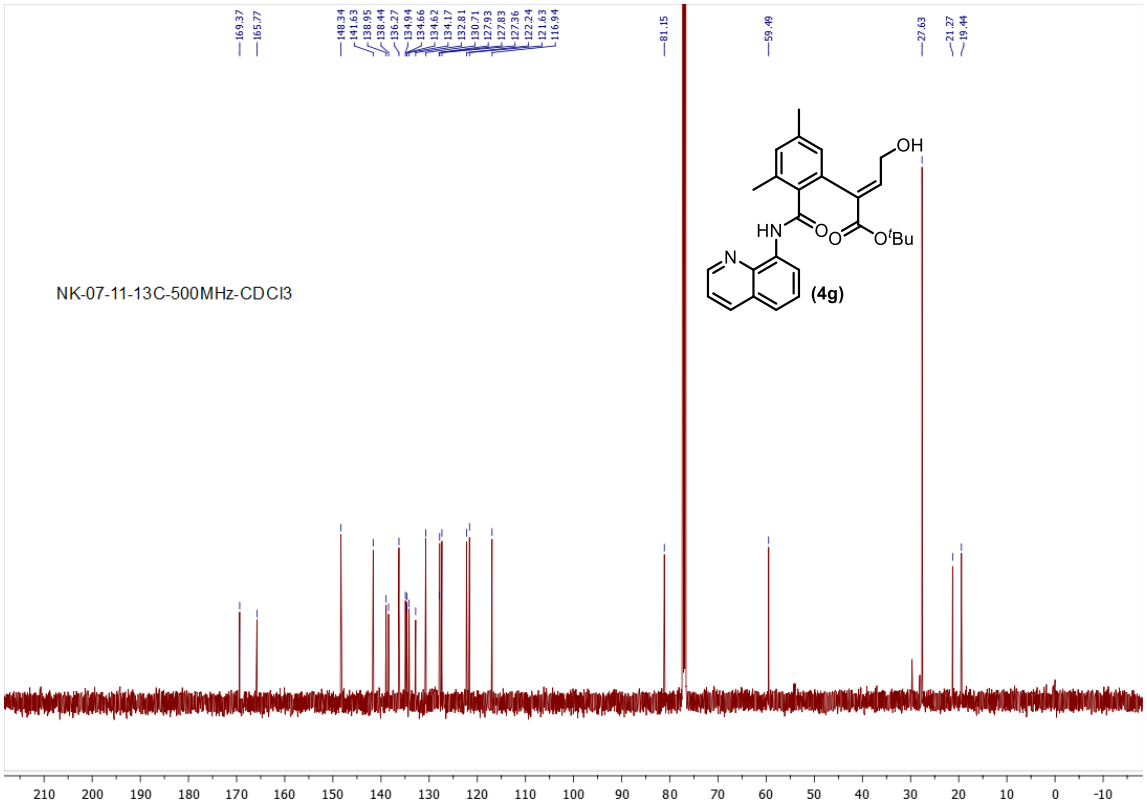






Bruker Compass DataAnalysis 4.0 printed: 03-11-2022 12:35:38 Page 1 of 1


OH
HN
O
O
O'Bu
N
(4g)
f1 (ppm)


NK-07-11-13C-500MHz-CDCl3
OH
HN
O
O
O'Bu
N
(4g)

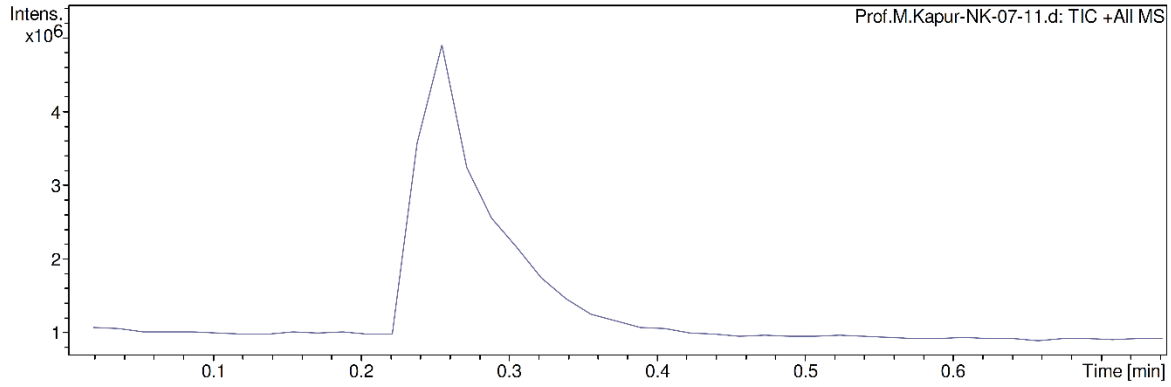
Display Report

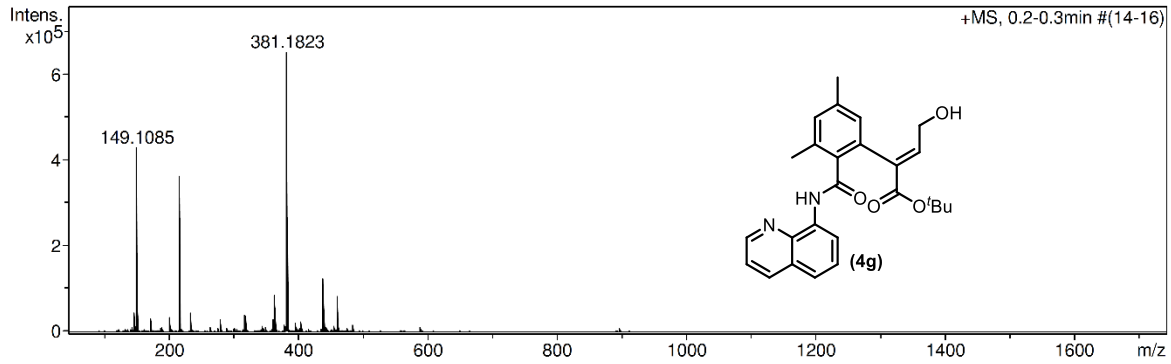
Analysis Info

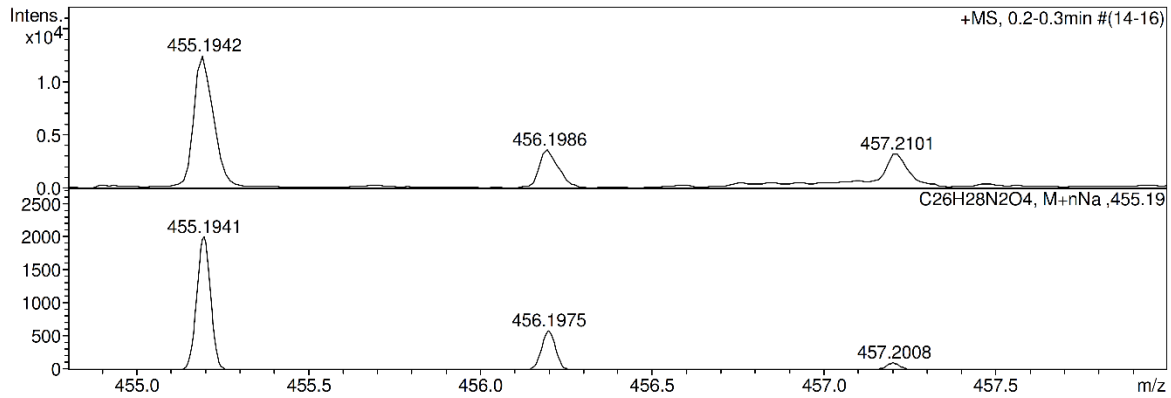
Analysis Name	D:\Data\NEW USER DATA 2022\Jan-2022\07-jan-2022\Prof.M.Kapur-NK-07-11.d	Acquisition Date	1/7/2022 4:36:40 PM
Method	tune mix_low.New.021117.m	Operator	RUCHI
Sample Name	NK-07-11	Instrument	micrOTOF-Q II 10330
Comment			

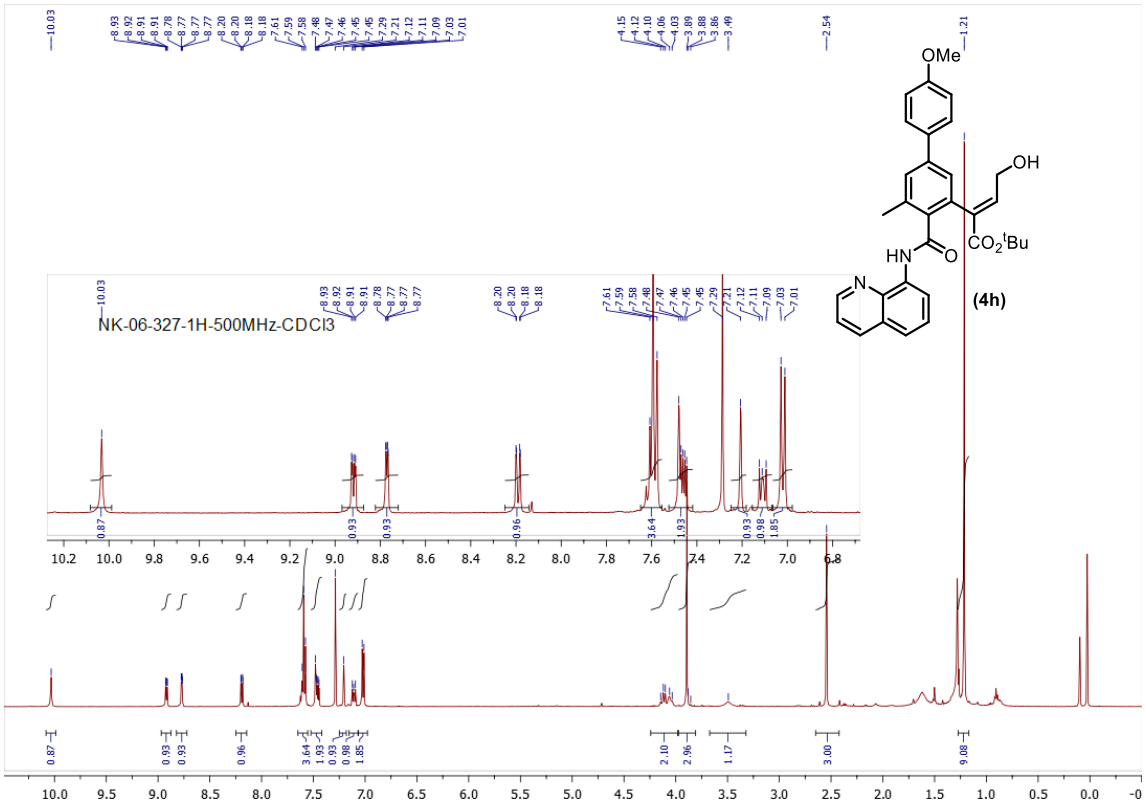
Acquisition Parameter

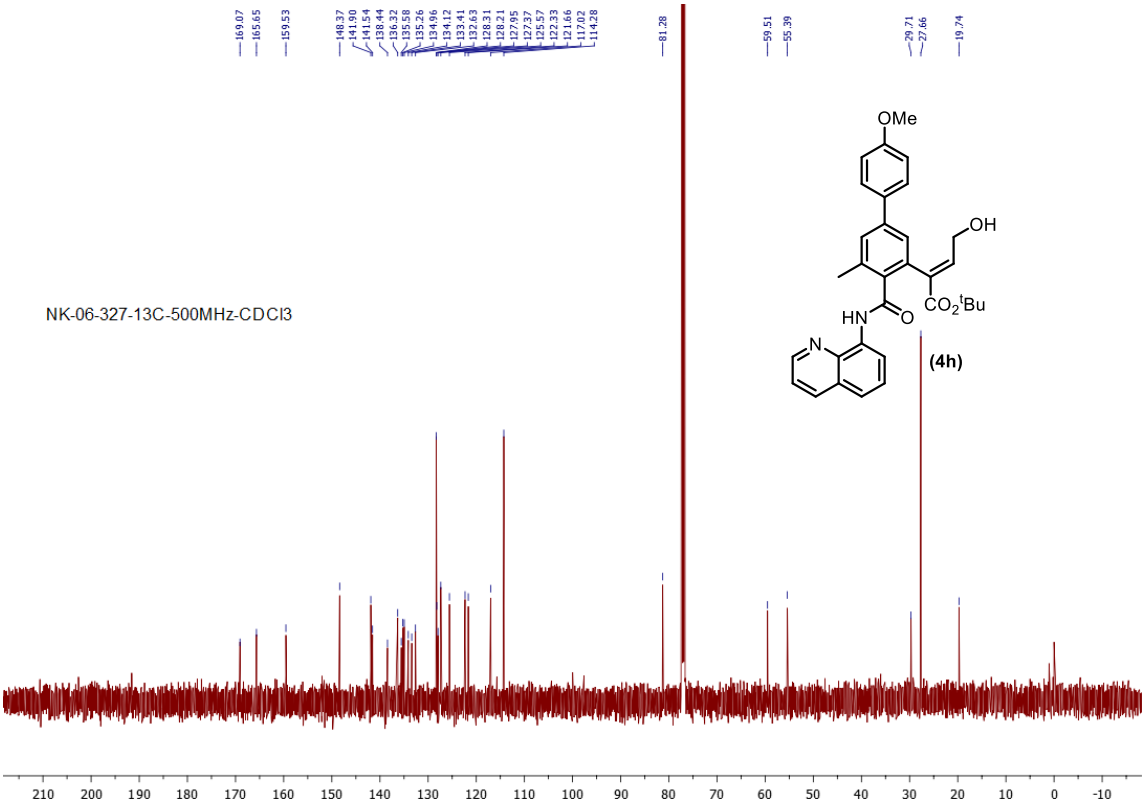
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4600 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	100.0 Vpp	Set Divert Valve	Waste








NK-06-327-1H-500MHz-CDCl3
OMe
OH
HN
O
$CO_2{}^tBu$
N
(4h)


NK-06-327-13C-500MHz-CDCl3
OMe
OH
HN
O
$CO_2{}^tBu$
N
(4h)

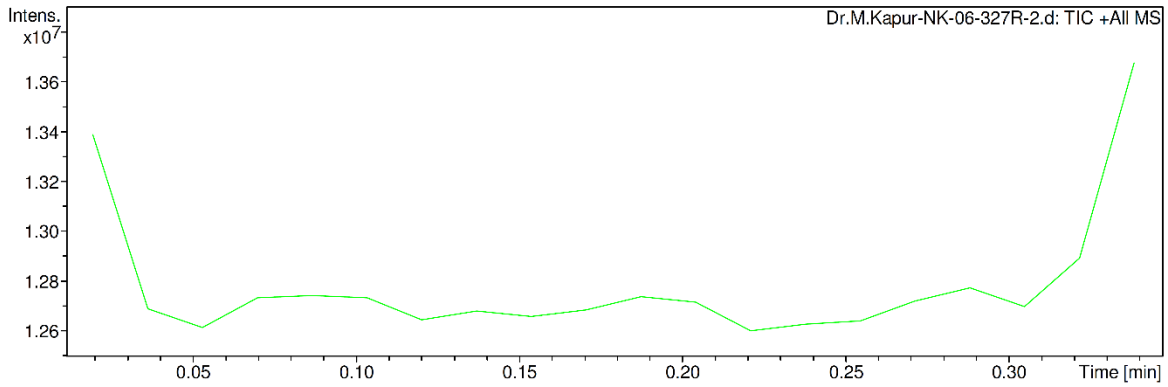
Display Report

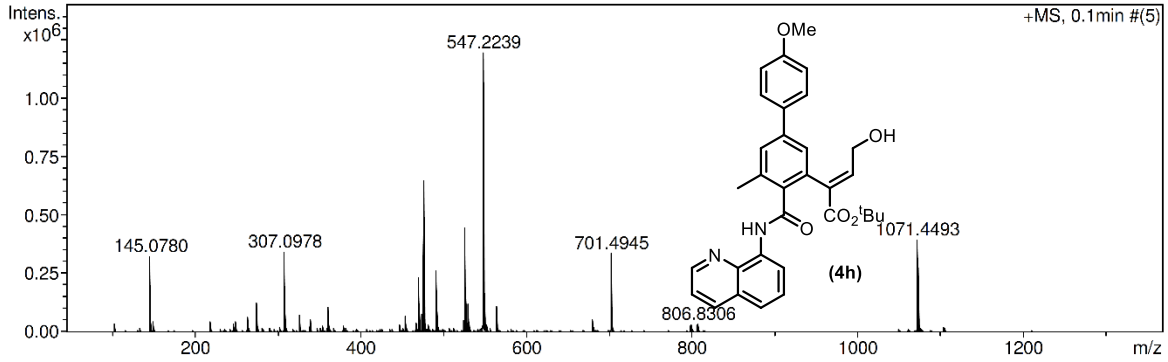
Analysis Info

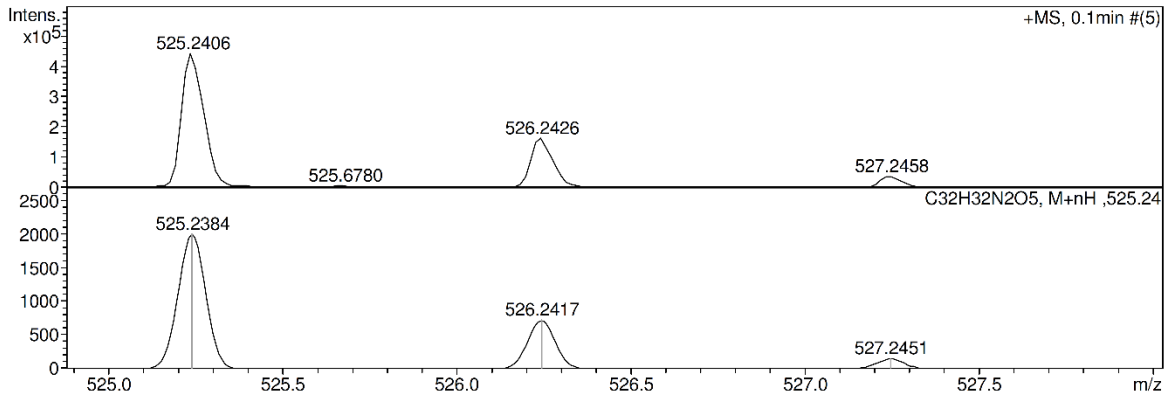
Acquisition Date	11/17/2021 3:59:18 PM		
Analysis Name	D:\Data\new user data 2021\Nov-2021\17-Nov\Dr.M.Kapur-NK-06-327R-2.d		
Method	tune mix_low.New.021117.m	Operator	RUCHI
Sample Name	NK-06-327R-2	Instrument	micrOTOF-Q II 10330
Comment			

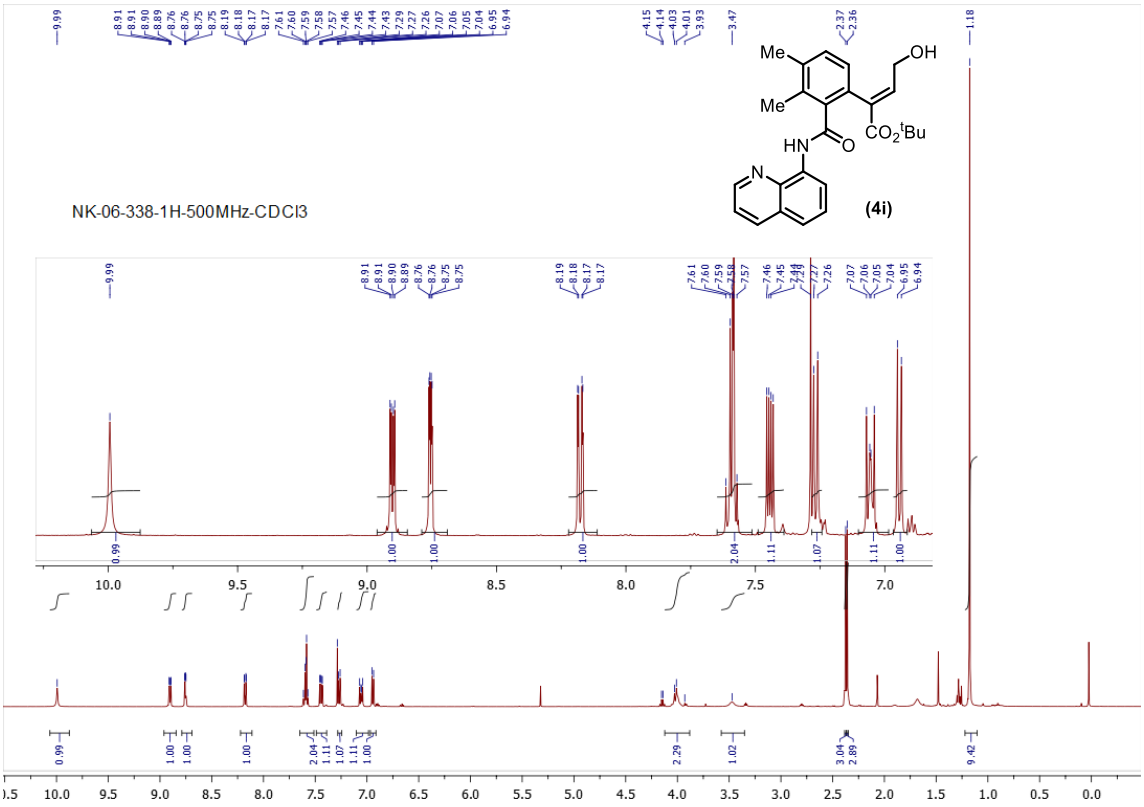
Acquisition Parameter

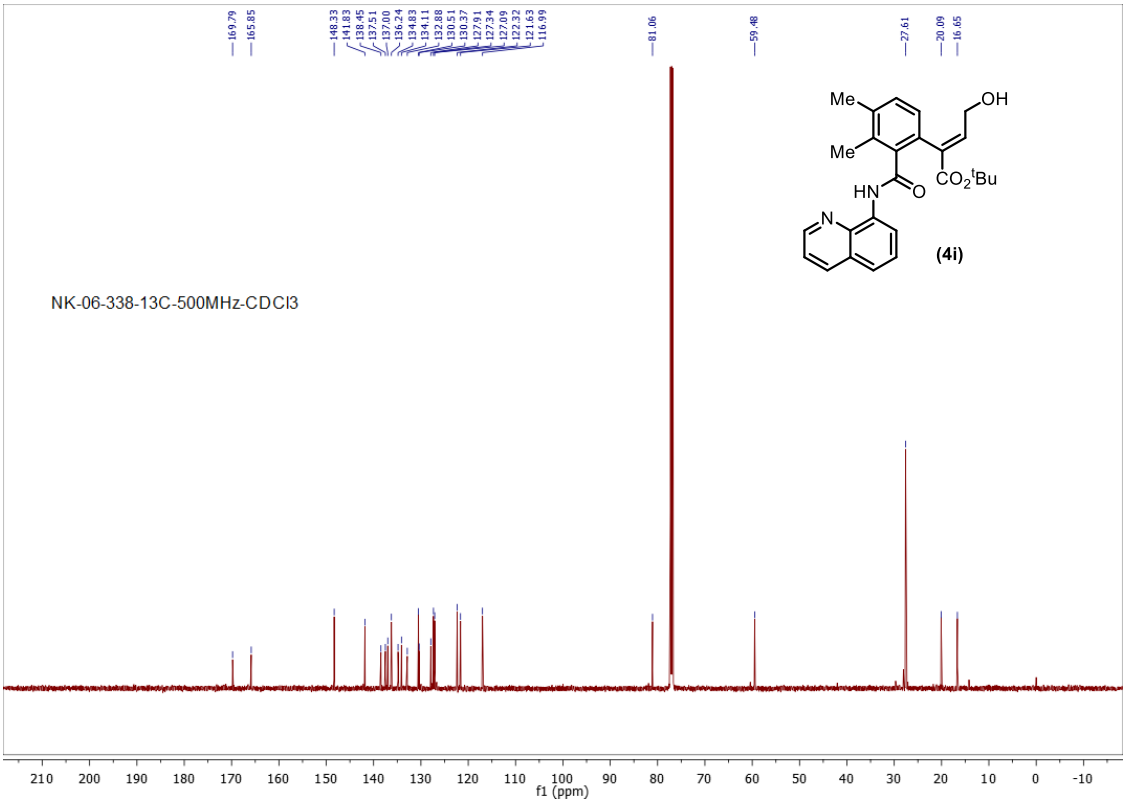
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4600 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	100.0 Vpp	Set Divert Valve	Waste








NK-06-338-1H-500MHz-CDCl3
Me
Me
OH
HN
O
N
CO2tBu
(4i)


NK-06-338-13C-500MHz-CDCl3
Me
Me
OH
HN
O
N
CO2tBu
(4i)
f1 (ppm)

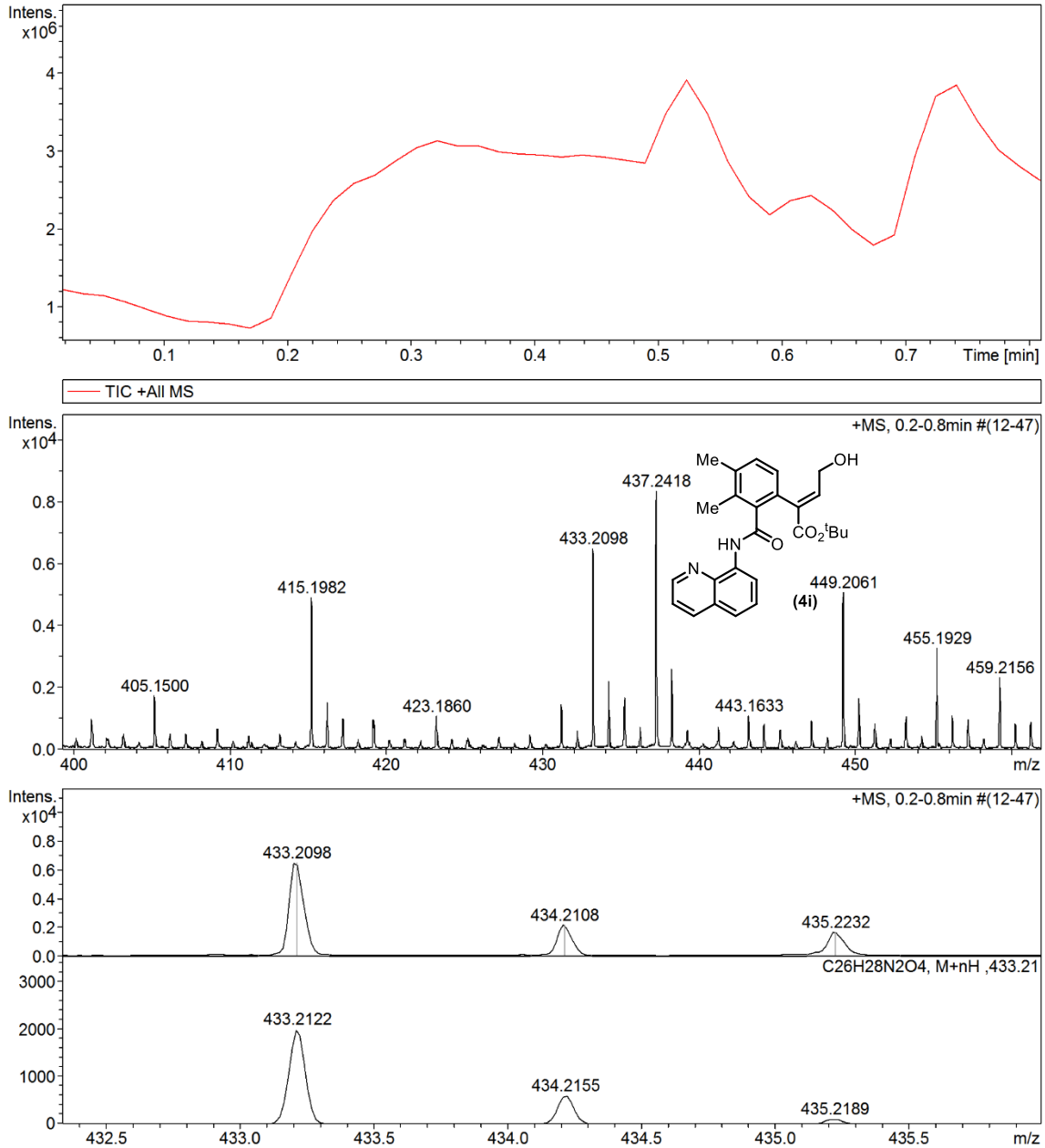
Display Report

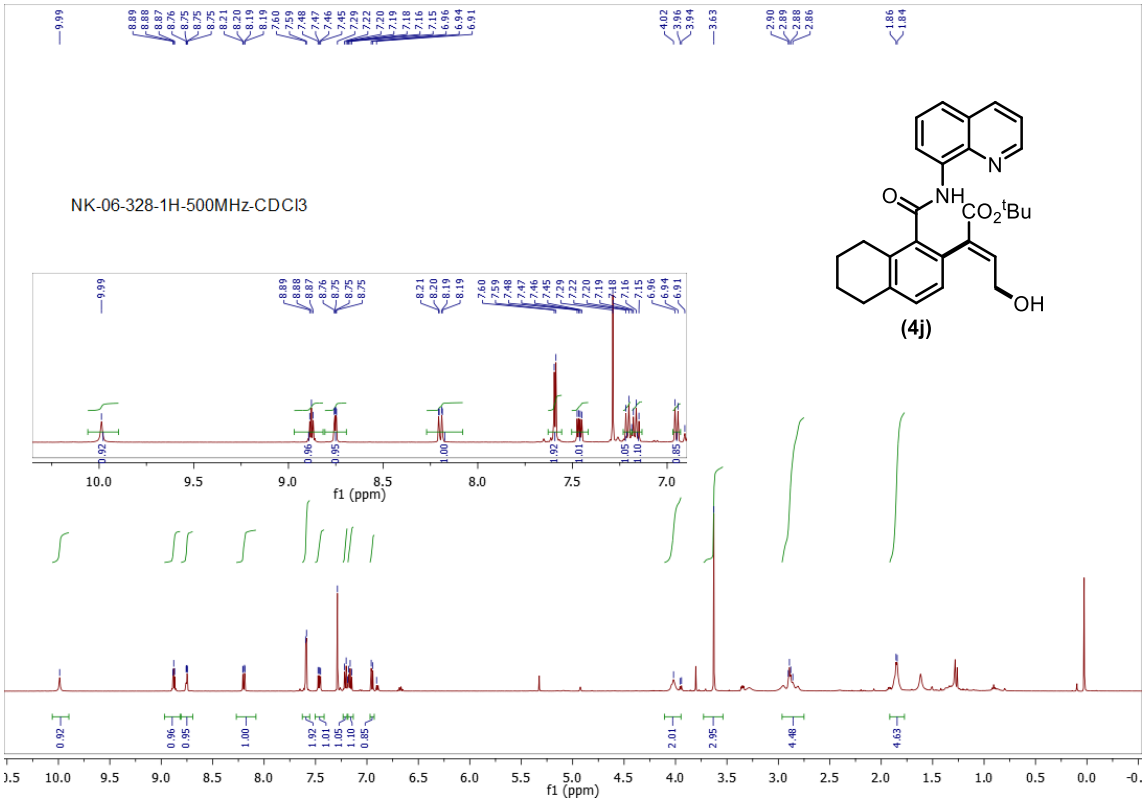
Analysis Info

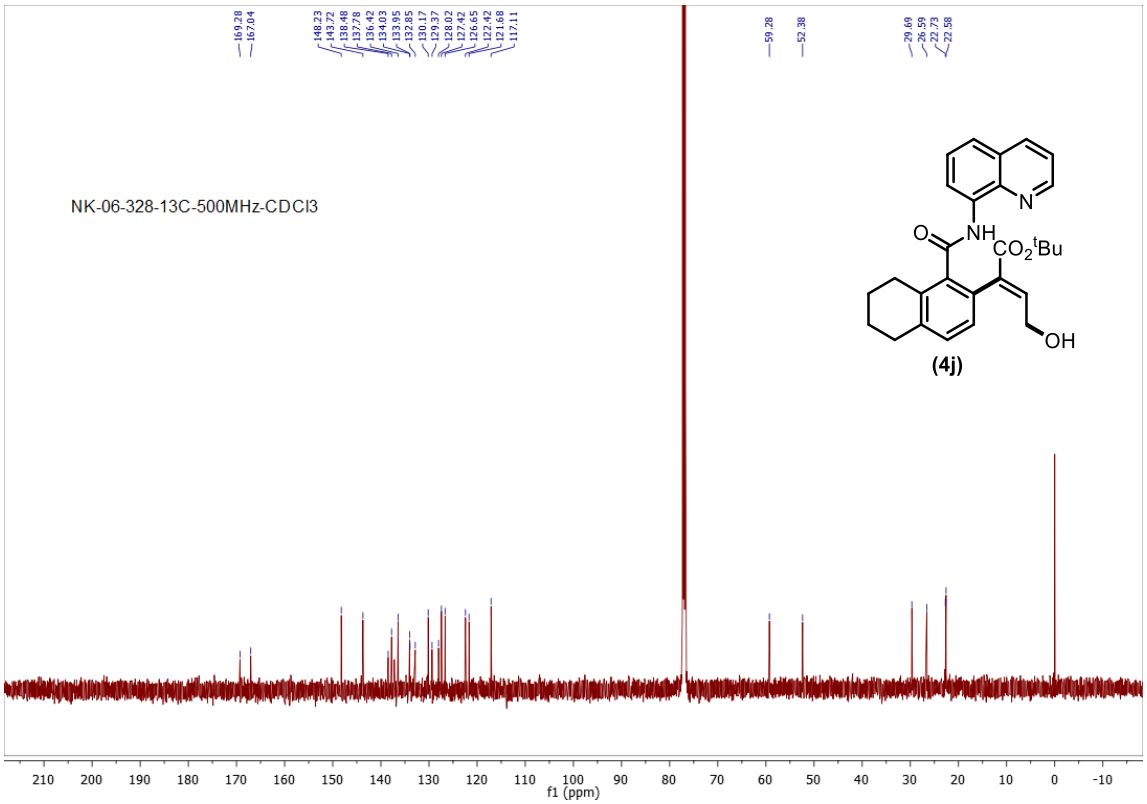
Acquisition Date	11-08-2022 11:59:33		
Analysis Name	D:\Data\USER DATA 2022\AUG2022\11-08-2022\Prof M KAPUR-NK-06-338-R.d		
Method	tune_wide _APCI_23.06.m	Operator	Bruker
Sample Name	NK-06-338-R	Instrument	micrOTOF-Q 10330
Comment			

Acquisition Parameter

Source Type	Multi Mode	Ion Polarity	Positive	Set Nebulizer	2.0 Bar
Focus	Not active	Set Capillary	2500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	5.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	100.0 Vpp	Set Divert Valve	Waste




NK-06-328-1H-500MHz-CDCl3
(4j)
f1 (ppm)


NK-06-328-13C-500MHz-CDCl3
(4j)
f1 (ppm)

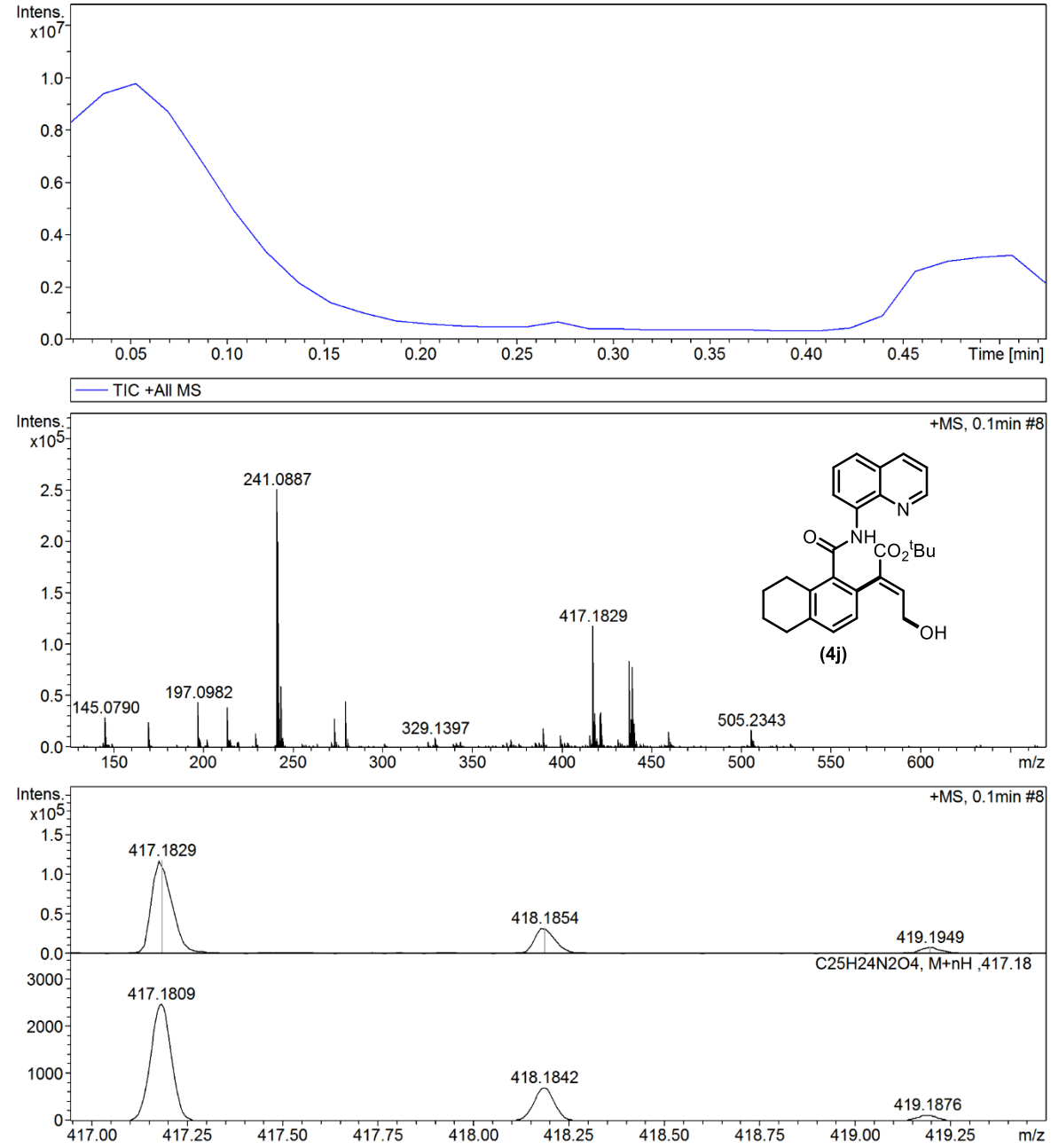
Display Report

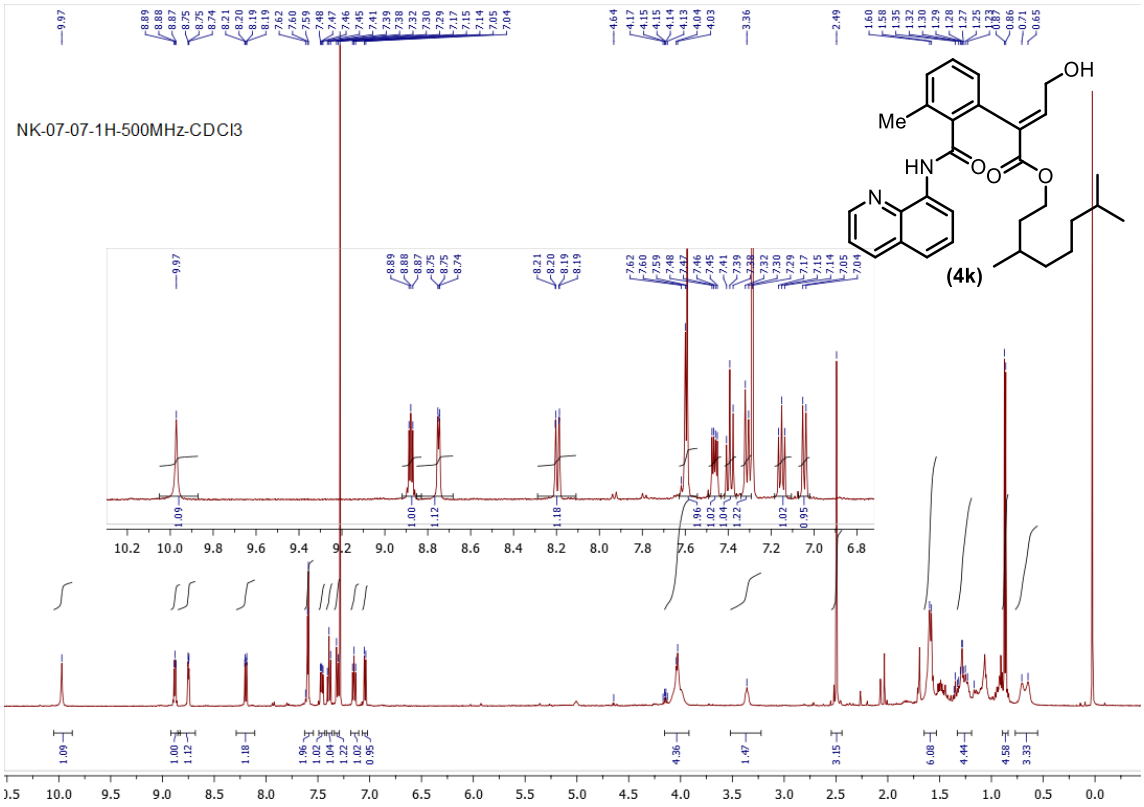
Analysis Info

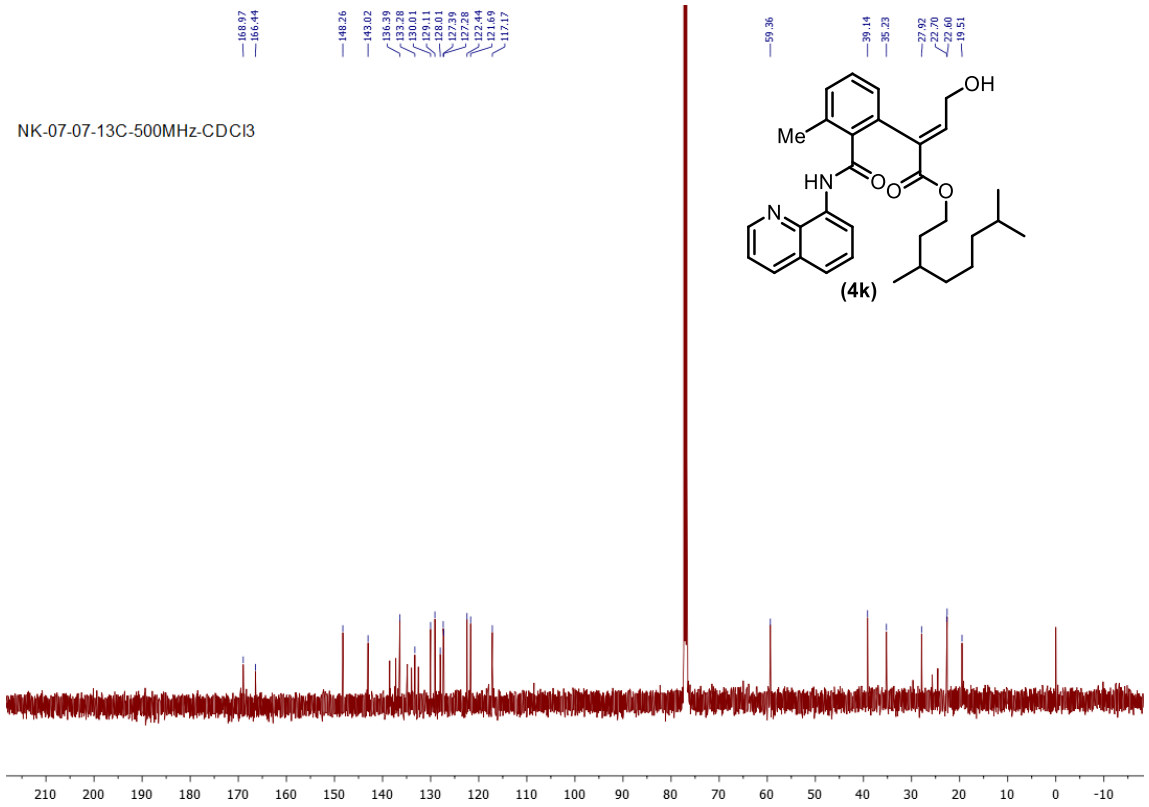
Analysis Name	D:\Data\USER DATA 2022\AUG2022\08-08-2022\Prof.M.Kapur-NK_06_328_R2.d	Acquisition Date	08-08-2022 11:52:40
Method	tune mix_low.New.021117.m	Operator	Bruker
Sample Name	NK_06_328_R2	Instrument	micrOTOF-Q 10330
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4600 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	100.0 Vpp	Set Divert Valve	Source




NK-07-07-1H-500MHz-CDCl3
OH
Me
HN
O
O
O
N
(4k)


NK-07-07-13C-500MHz-CDCl3
OH
Me
HN
O
O
O
N
(4k)

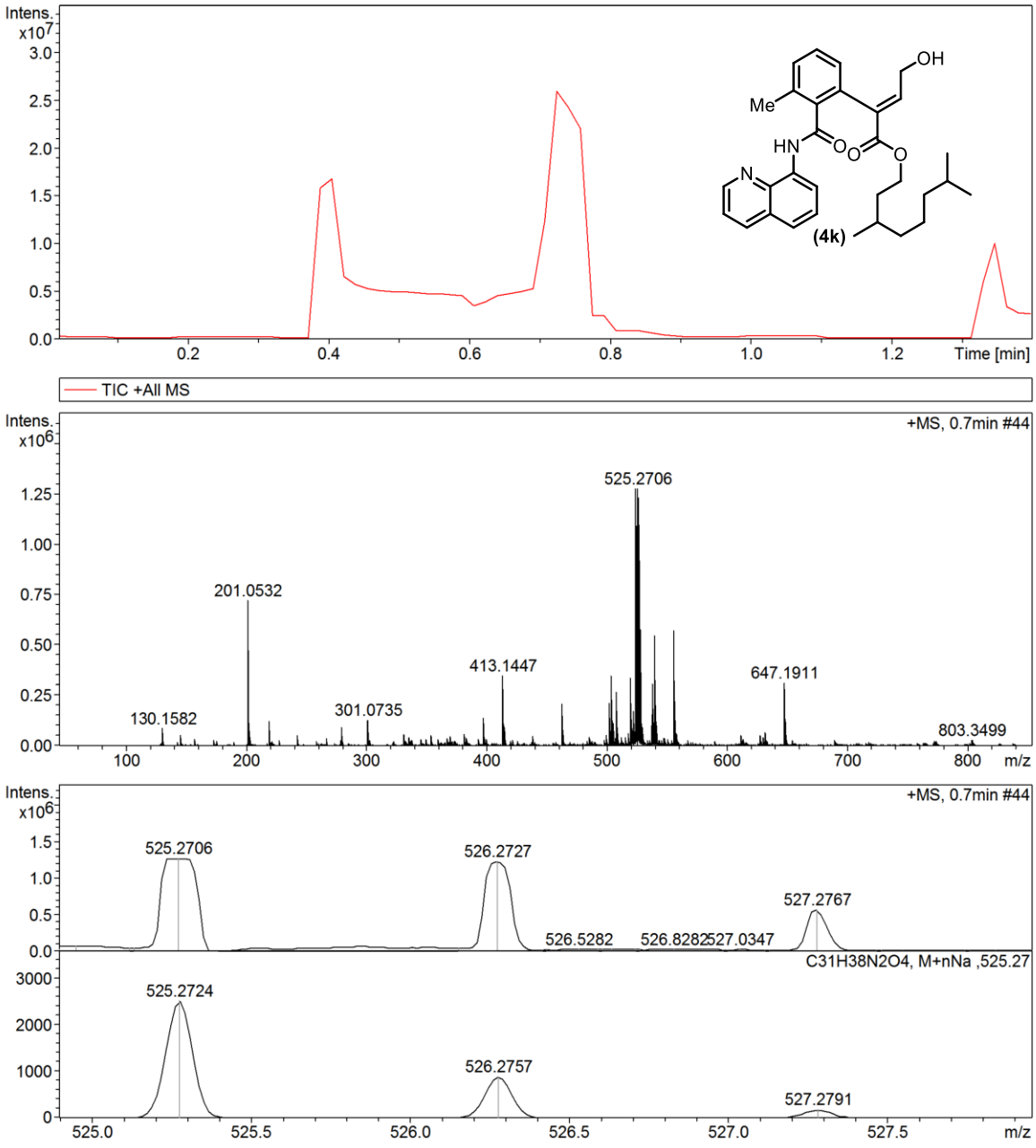
Display Report

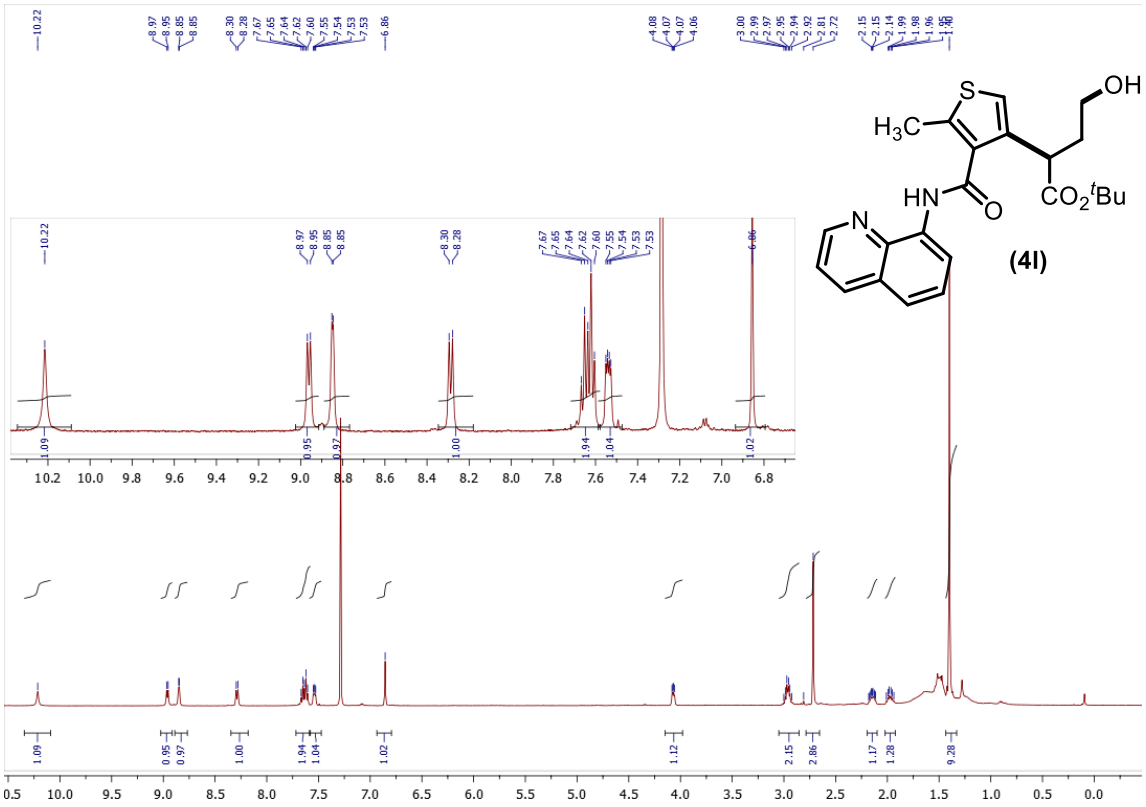
Analysis Info

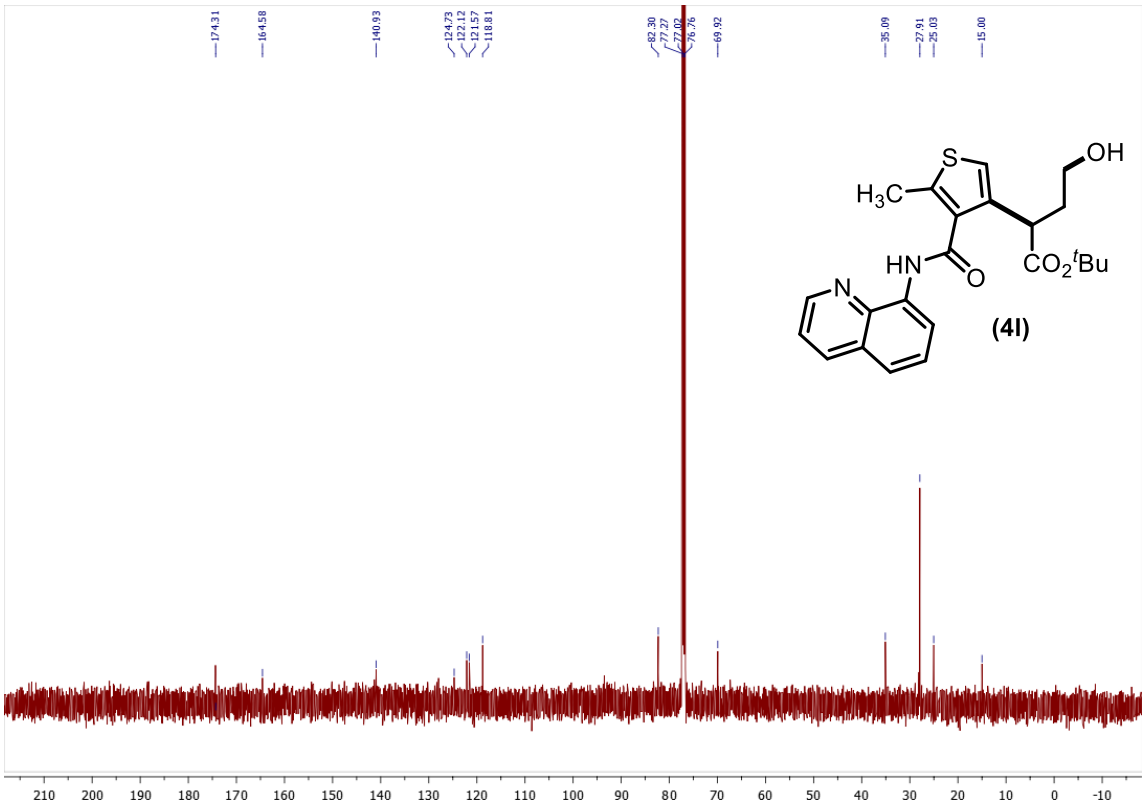
Analysis Name	D:\Data\USER DATA 2022\DEC\06-12-2022\Prof M Kapur-NK-07-07.d	Acquisition Date	06-12-2022 11:50:08
Method	tune mix_low.New.021117.m	Operator	Bruker
Sample Name	NK-07-07	Instrument	micrOTOF-Q 10330
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4600 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	300.0 Vpp	Set Divert Valve	Waste




OH
S
H3C
HN
O
CO2tBu
N
(4l)


OH
S
H3C
HN
O
CO2tBu
N
(4l)

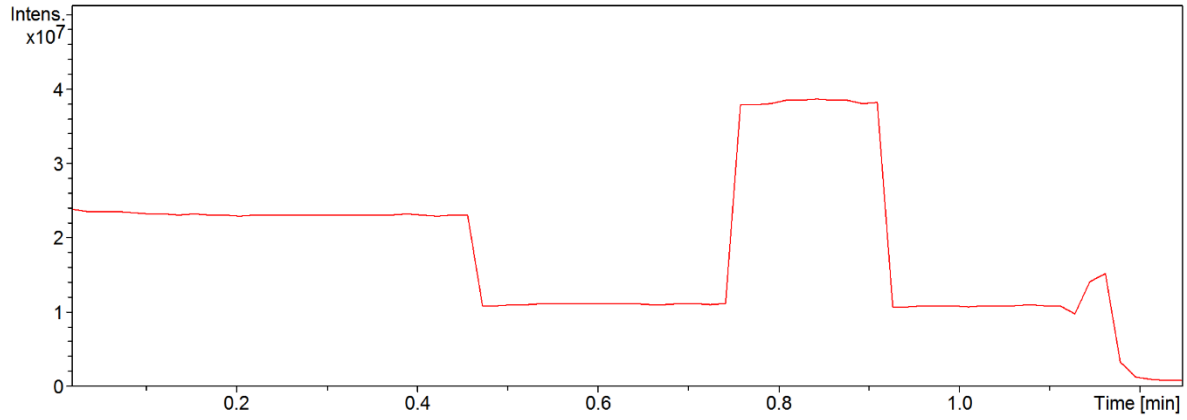
Display Report

Analysis Info

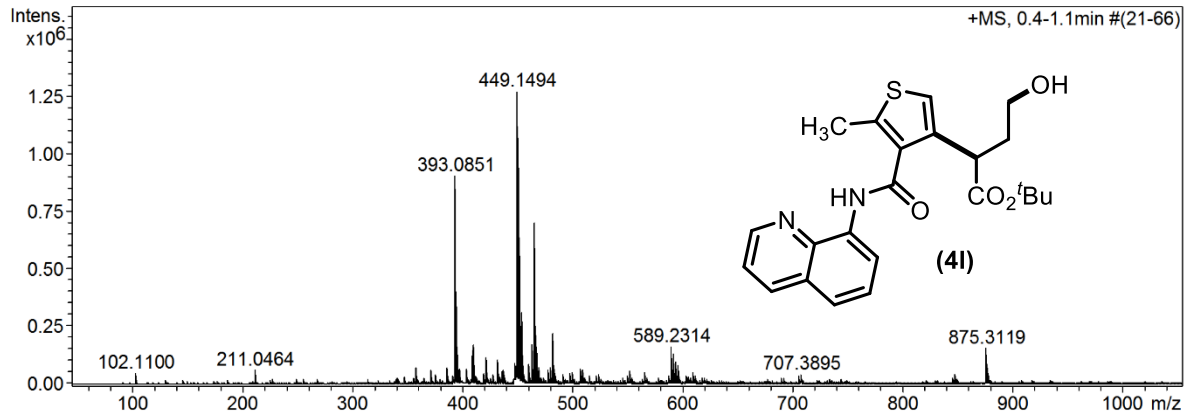
Analysis Name	D:\Data\USER DATA 2023\Feb\01-03-2023\Prof M Kapur-NK-09-18A.d	Acquisition Date	01-03-2023 11:51:29
Method	tune_low_Jan23.m	Operator	Bruker
Sample Name	NK-09-18A	Instrument	micrOTOF-Q 10330
Comment			

Acquisition Parameter

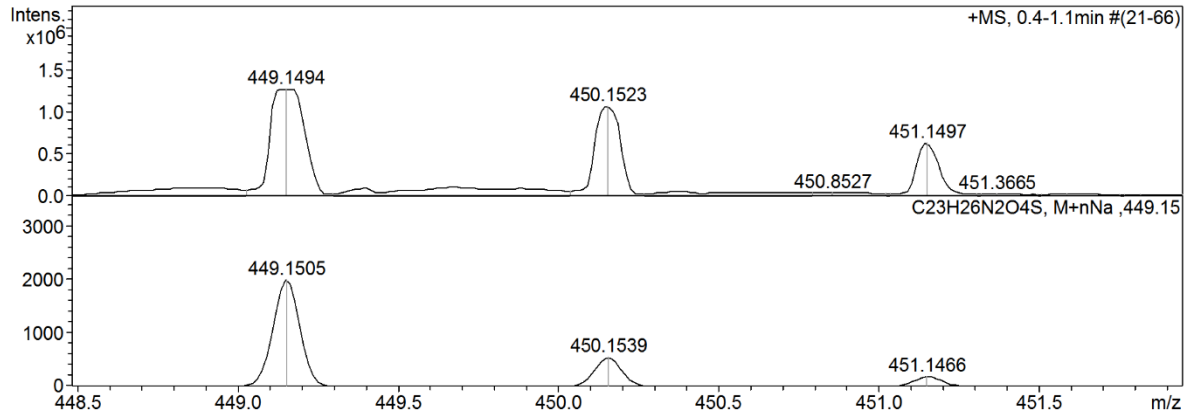
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.8 Bar
Focus	Not active	Set Capillary	4600 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	7.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	150.0 Vpp	Set Divert Valve	Waste

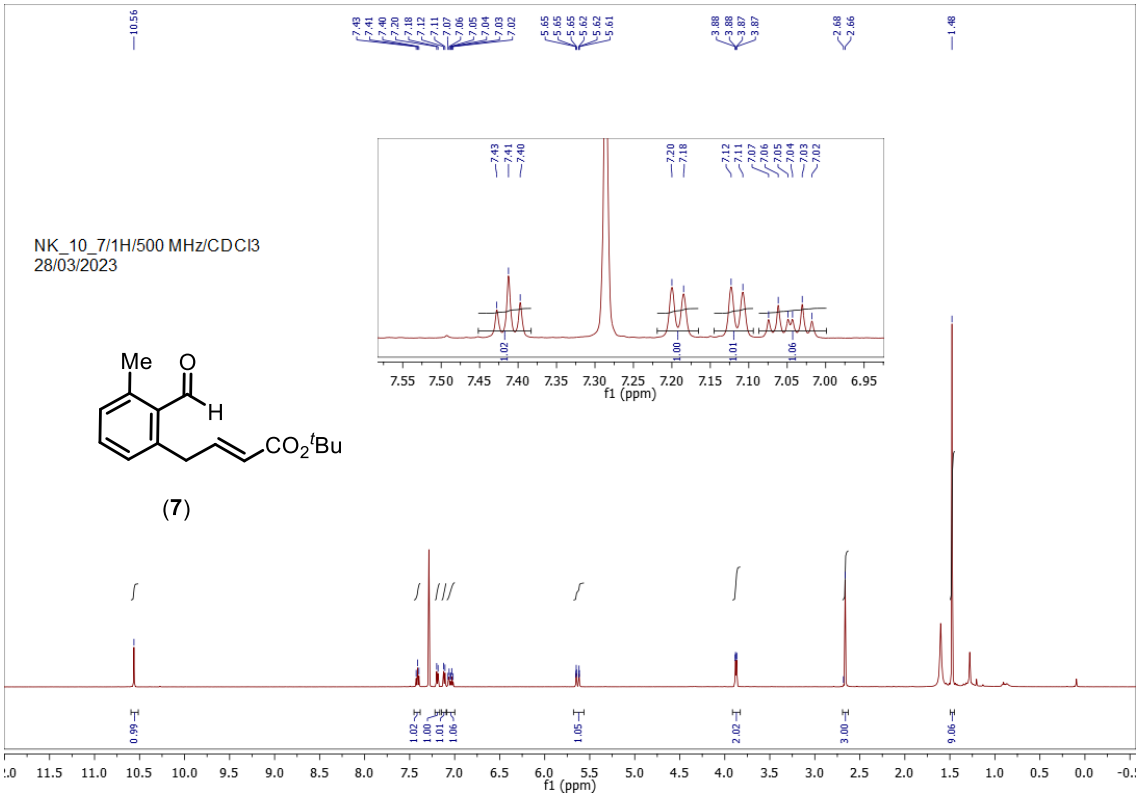


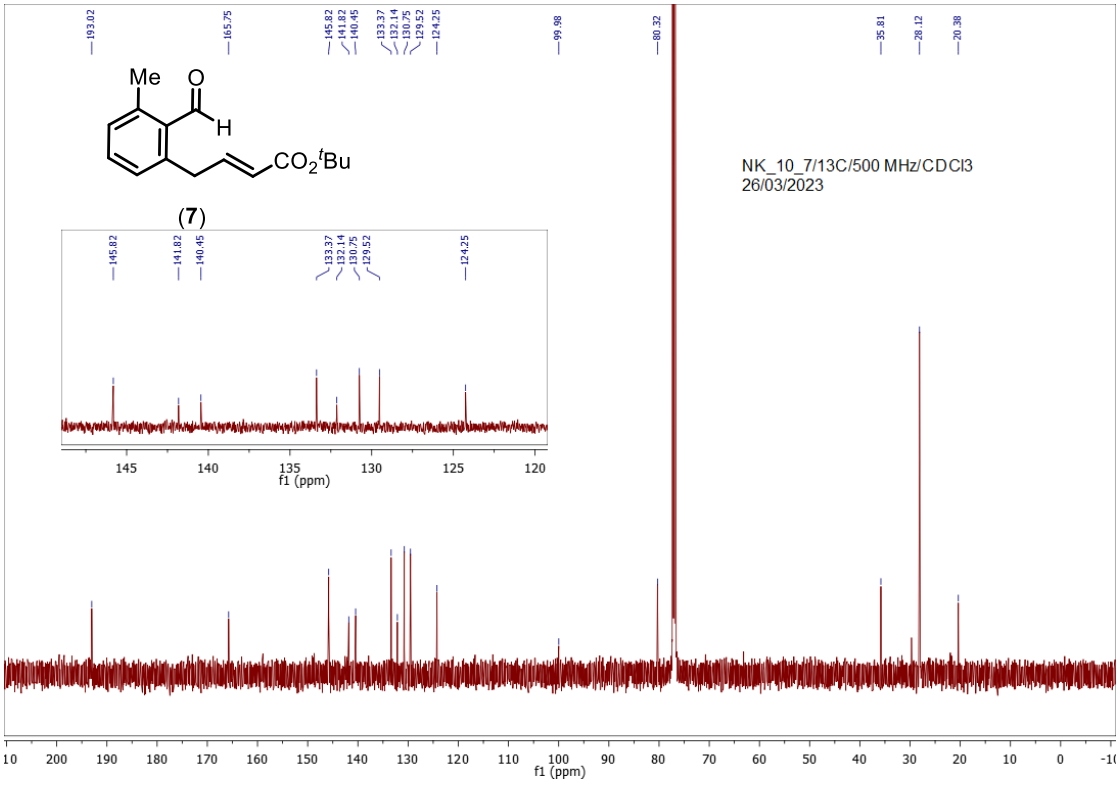
TIC +All MS



(4l)




NK_10_7/1H/500 MHz/CDCl3
28/03/2023
Me
O
H
CO2tBu
(7)
f1 (ppm)


NK_10_7/13C/500 MHz/CDCl3
26/03/2023
Me
O
H
CO2tBu
(7)
f1 (ppm)

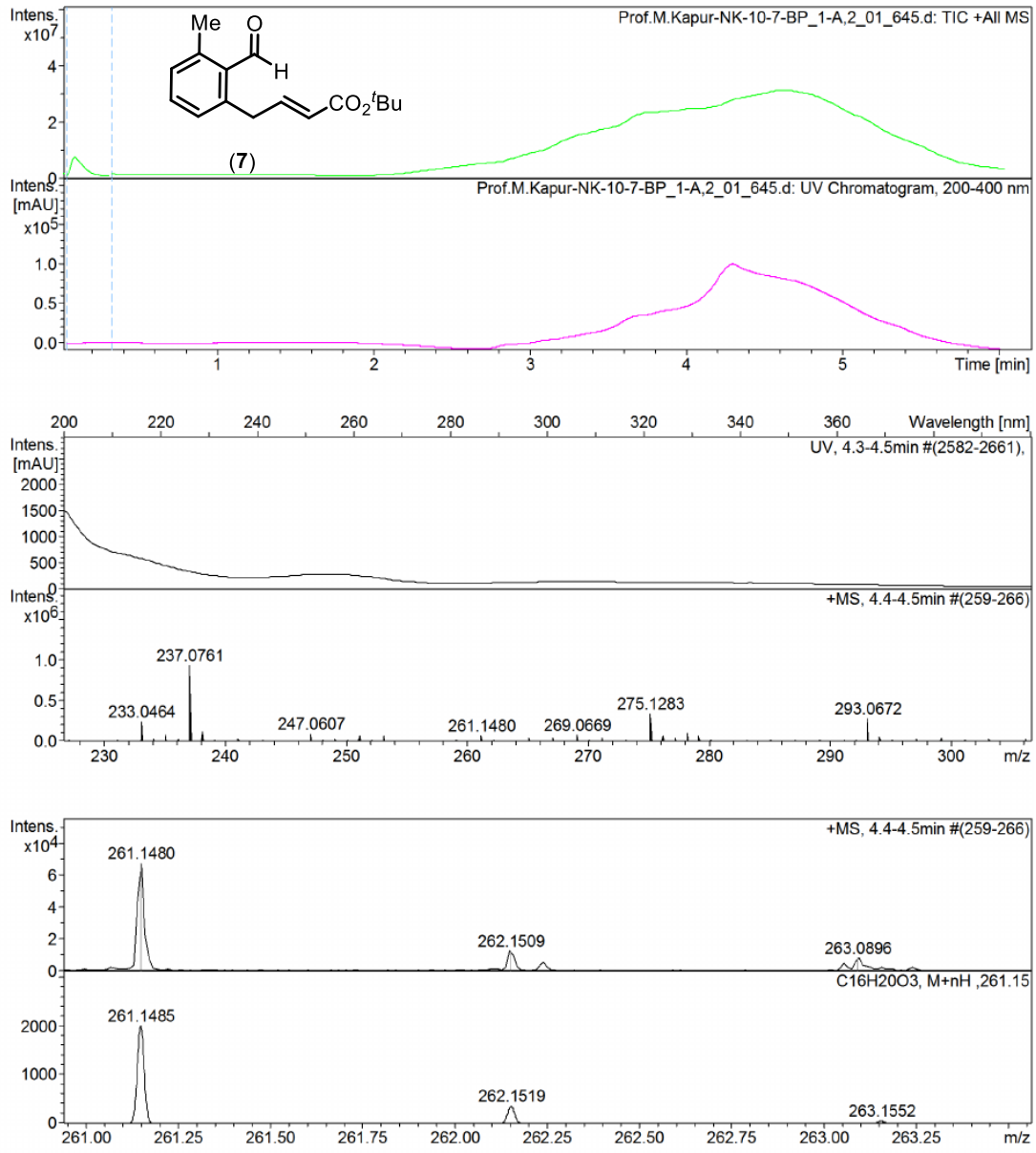
Display Report

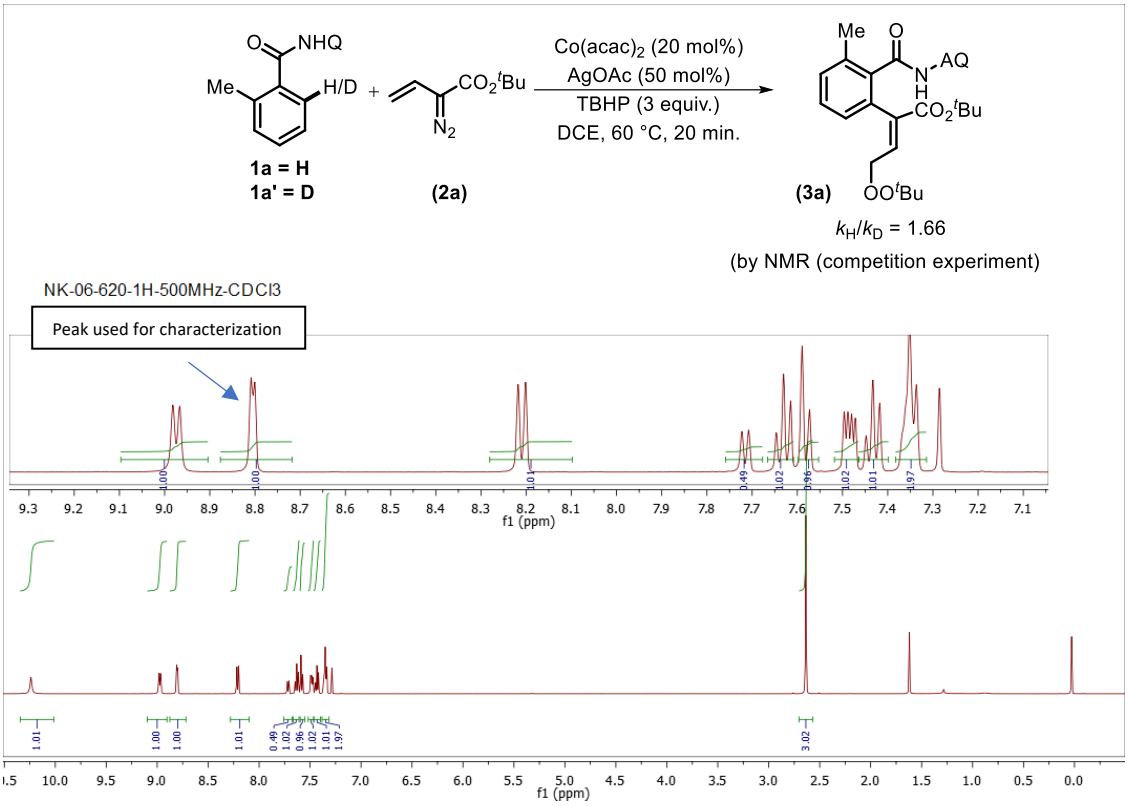
Analysis Info

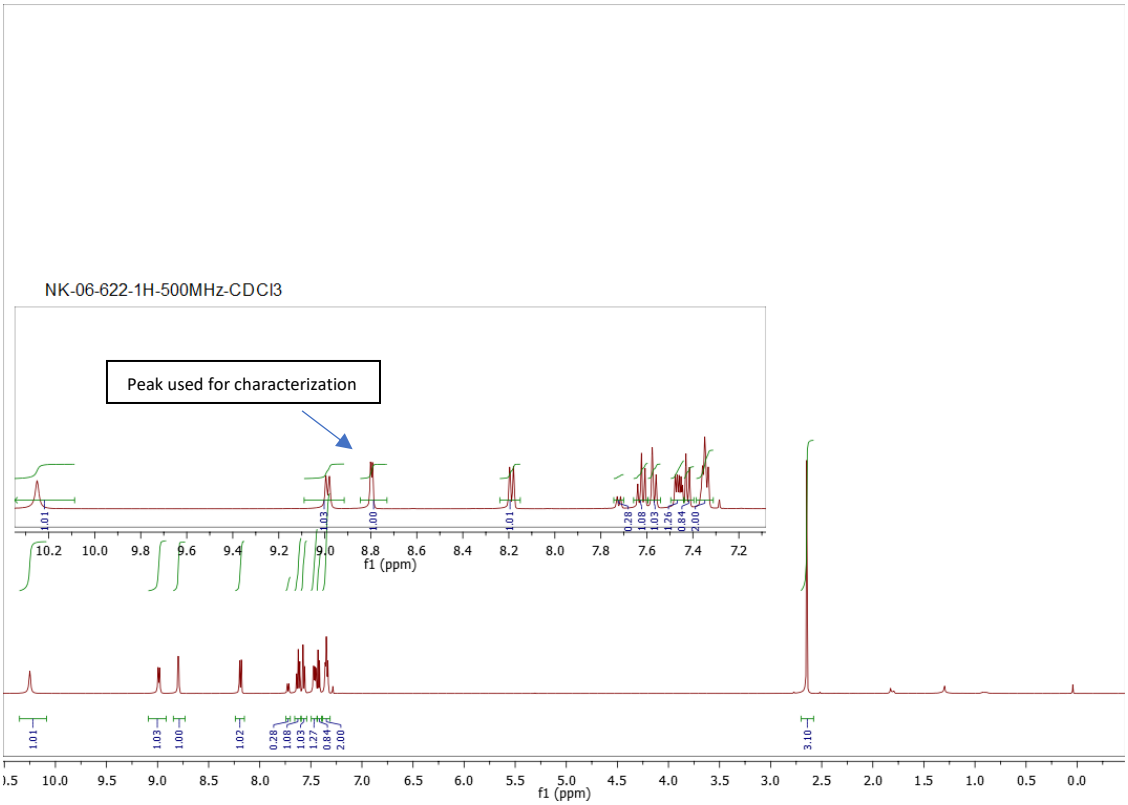
Acquisition Date	11-04-2023 11:39:15		
Analysis Name	D:\Data\USER DATA 2023\April\11-april\Prof.M.Kapur-NK-10-7-BP_1-A,2_01_645.d		
Method	HRLCMS-20 Sept.m	Operator	Bruker
Sample Name	Prof.M.Kapur-NK-10-7-BP	Instrument	micrOTOF-Q 10330
Comment			

Acquisition Parameter

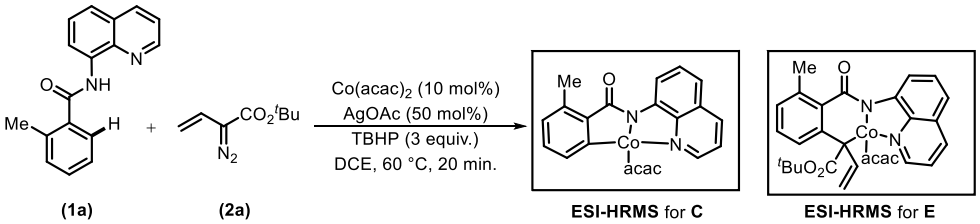
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.2 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	130.0 Vpp	Set Divert Valve	Waste




Co(acac)2 (20 mol%)
AgOAc (50 mol%)
TBHP (3 equiv.)
DCE, 60 °C, 20 min.
1a = H
1a' = D
(2a)
(3a)
kH/kD = 1.66
(by NMR (competition experiment)
NK-06-620-1H-500MHz-CDCl3
Peak used for characterization
f1 (ppm)


NK-06-622-1H-500MHz-CDCl3
Peak used for characterization
f1 (ppm)

8. Detection of intermediates by mass spectrometry



(1a) **(2a)**

ESI-HRMS for **C**
calcd. $[M+H]^+$ 419.0800
found $[M+H]^+$ 419.0790

ESI-HRMS for **E**
calcd. $[[M+H]^+$ 559.1638
found $[[M+H]^+$ 559.1651

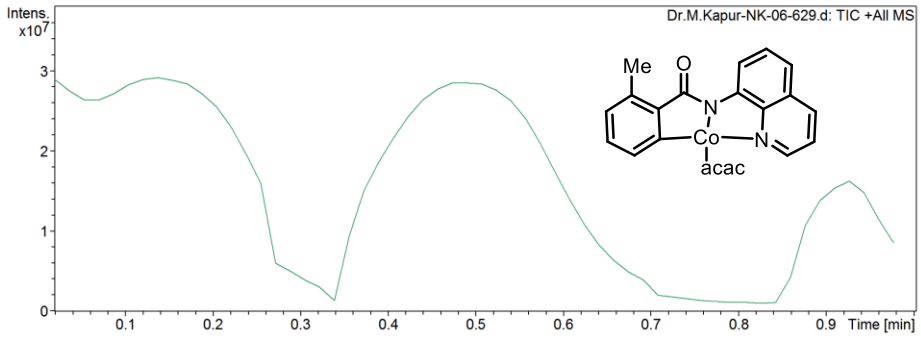
Display Report

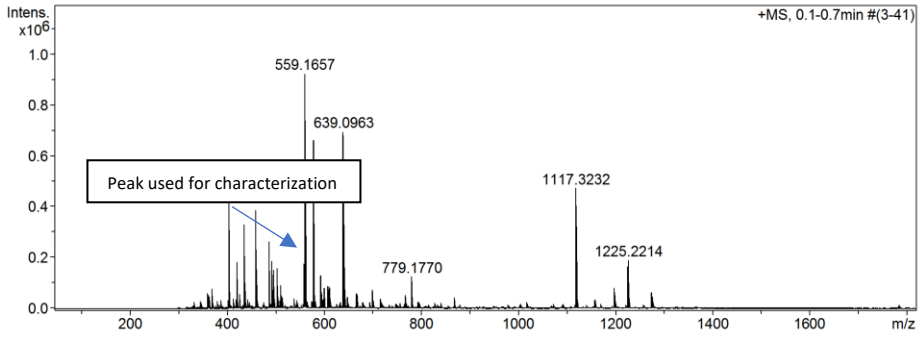
Analysis Info

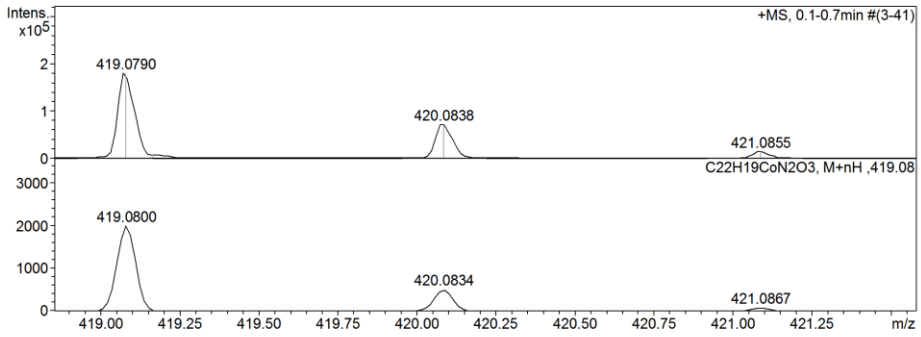
Analysis Name	D:\Data\USER DATA 2022\AUG2022\18-08-2022\Dr.M.Kapur-NK-06-629.d	Acquisition Date	18-08-2022 10:30:04
Method	tune_wide.m	Operator	Bruker
Sample Name	NK-06-629	Instrument	micrOTOF-Q 10330
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	600.0 Vpp	Set Divert Valve	Source







Bruker Compass DataAnalysis 4.0 printed: 18-08-2022 14:29:35 Page 1 of 1

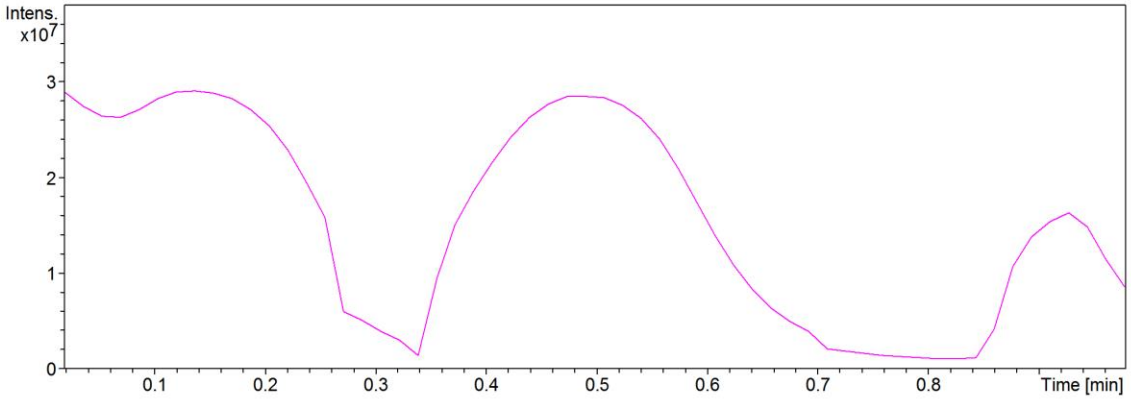
Display Report

Analysis Info

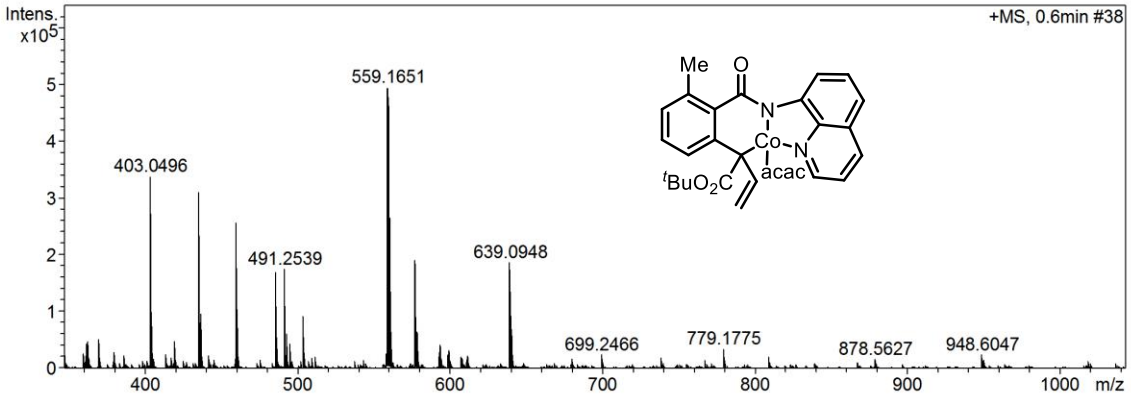
Analysis Name	D:\Data\USER DATA 2022\AUG2022\18-08-2022\Dr.M.Kapur-NK-06-629.d	Acquisition Date	18-08-2022 10:30:04
Method	tune_wide.m	Operator	Bruker
Sample Name	NK-06-629	Instrument	micrOTOF-Q 10330
Comment			

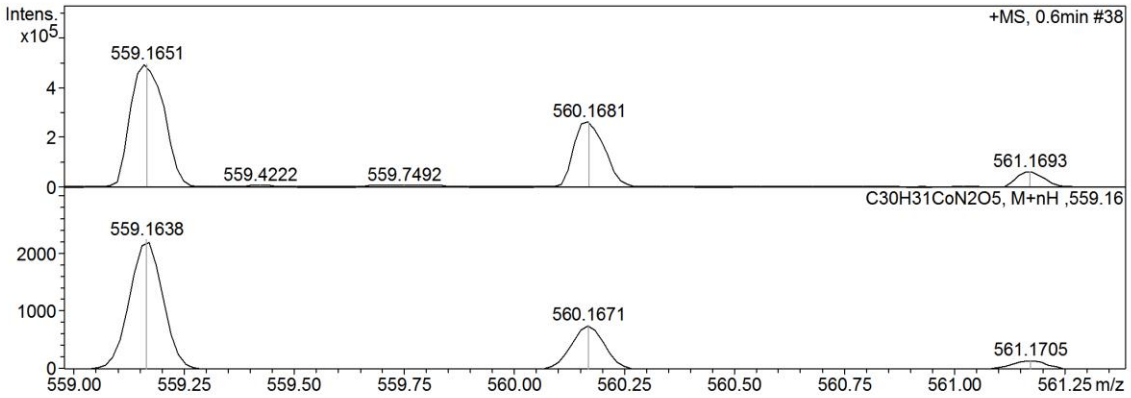
Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	600.0 Vpp	Set Divert Valve	Source



TIC +All MS





9. X-ray diffraction structural analysis data of 4j

Sample preparation: 5 mg of **4j** (colorless solid) was taken in a 10 mL beaker and dissolved in minimal amount of chloroform. Hexane (3 mL) was added to the beaker along the wall. The beaker was capped loosely and kept at room temperature for slow evaporation. After 5 days, single crystal was obtained which was subjected to X-ray diffraction.

Table E1: Crystal data and structure refinement for 4j

Identification code	4j
Empirical formula	C25H24N2O4
Formula weight	416.46
Temperature/K	140.00
Crystal system	triclinic
Space group	P-1
a/Å	8.8175(6)
b/Å	10.9007(8)
c/Å	11.0914(9)
α/°	91.044(3)
β/°	101.160(2)
γ/°	98.536(2)
Volume/Å3	1033.11(13)
Z	2
ρcalcg/cm3	1.339
μ/mm-1	0.091
F(000)	462.5
Crystal size/mm3	1 × 0.8 × 0.6
Radiation	Mo Kα (λ = 0.71073) 2Θ range for data collection/° 3.74 to 59.2

Index ranges	-12 ≤ h ≤ 12, -15 ≤ k ≤ 15, -15 ≤ l ≤ 15
Reflections collected	35615
Independent reflections	5759 [Rint = 0.0884, Rsigma = 0.0573]
	Data/restraints/parameters
Goodness-of-fit on F2	1.042
Final R indexes [I>=2σ (I)]	R1 = 0.0548, wR2 = 0.1300
Final R indexes [all data]	R1 = 0.0768, wR2 = 0.1475
Largest diff. peak/hole	e Å-3 0.48/-0.31
Identification code	4j
Empirical formula	$C_{25}H_{24}N_2O_4$
Formula weight	416.46
Temperature/K	140.00

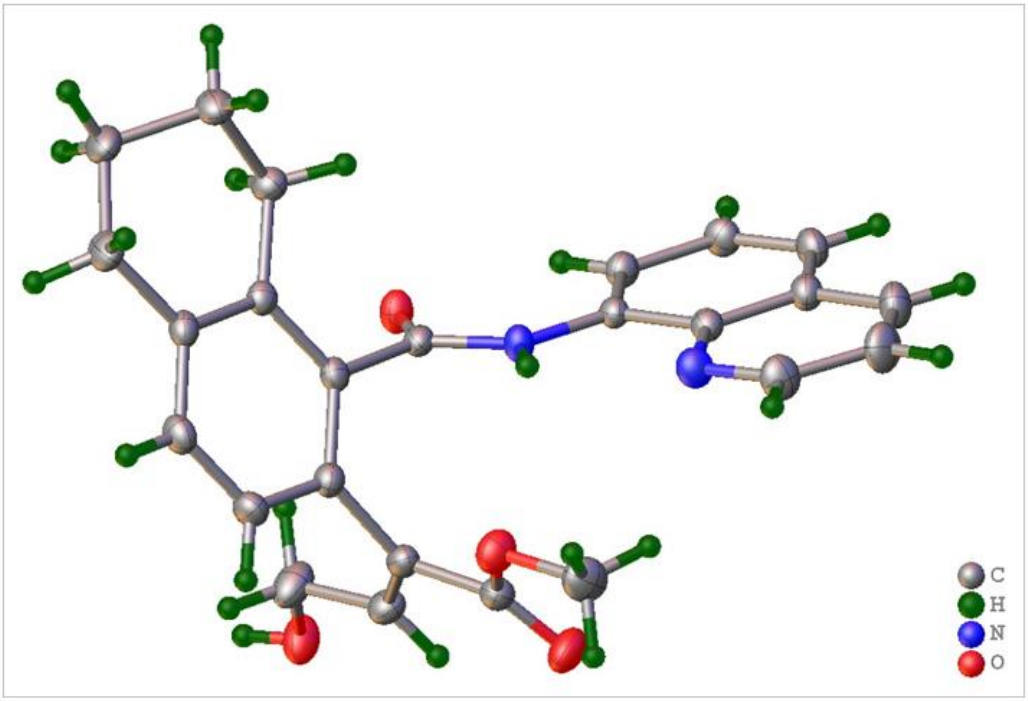


Fig. E1. X-ray structure of *tert*-butyl (*E*)-4-hydroxy-2-(1-(quinolin-8-ylcarbamoyl)-5,6,7,8-tetrahydronaphthalen-2-yl)but-2-enoate (**4j**) (*ORTEP* view at 50% ellipsoidal probability).