Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Supporting Information - A

Ugi and Passerini reactions enable the incorporation of ΔAA into *N*-alkylated peptides and depsipeptides

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Experimental Section

General

All solvents were dried and distilled before use by standard procedures and reagents were of the highest commercially available grade purchased from Sigma-Aldrich, Oakwood Chemicals, and Strem Chemicals and used as received or purified according to the procedures outlined in Purification of Common Laboratory Chemicals.[1] Glassware used was dried in oven or flame dried under vacuum and cooled under an inert atmosphere. Flash Column chromatography was performed using silica gel 60 (230−400 mesh), and analytical thin-layer chromatography (TLC) was performed using silica gel aluminum sheets. Compounds were visualized on TLC by UV-light, $KMnO_4$, I_2, $H_3[P(Mo_3O_{10})_4]$ x H_2O (PMA) and Vanillin. Yields refer to chromatographically and spectroscopically pure compounds unless otherwise noted. ^1H NMR and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively. Chemical shifts (δ) are reported in parts per million relative to the residual solvent signals,[2] and coupling constants (J) are reported in hertz. the following abbreviations indicate the multiplicity of each signal: (s), singlet; (bs), broad singlet; (d), doublet; (t), triplet; (q), quartet; (p), pentet; (m), multiplet; (dd), doublet of doublets; (dt), doublet of triplets; (dq), doublet of quartet; (dp), doublet of pentet; (td), triplet of doublets; (ddt), doublet of doublet of triplets; (dtd), doublet of triplet of doublets; (ddd), doublet of doublet of doublets; (dddd), doublet of doublet of doublet of doublets; (heptd), heptet of doublets. High-resolution ESI mass spectra were obtained from a quadrupole-time-of-flight mass spectrometer equipped with an atmospheric pressure electrospray ion source (Compact ESI-QTOF, Bruker Daltonik GmbH, Bremen, Germany).

General organocatalytic procedure to the synthesis of 2-(phenylselanyl)aldehyde [3] :

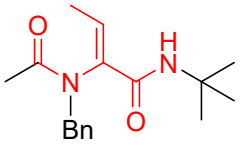
In a standard vial equipped with a Teflon-coated magnetic stir bar, piperidine (2 mmol, 20 mol%) and acetic acid (2 mmol, 20 mol%) were dissolved in 20 mL of $CHCl_3$ (0.5 M). After adding aldehyde (10 mmol, 1 equiv.), the solution was stirred for 10 minutes at 25°C. Then *N*-(Phenylseleno)-phthalimide (10 mmol, 1 equiv.) was added in one portion, the vial was capped with a rubber stopper and stirring was continued for the specific time (generally 3h). After completion (monitored by TLC) the mixture was filtered, and the volatiles were concentrated under reduced pressure, and the resulting crude product was purified by flash column chromatography.

General Ugi-4CR/oxidative-elimination procedure (A):

The 2-(phenylselanyl)aldehyde (0.2 mmol, 1.0 equiv.), the amine (0.2 mmol, 1.0 equiv.), the carboxylic acid (0.2 mmol, 1.0 equiv.) and the isocyanide (0.2 mmol, 1.0 equiv.) were dissolved in 2-MeTHF (5 mL) and stirred at 25 °C for 24 h. TLC monitored the reaction progress until the consumption of the starting material. After completion, aqueous $NaIO_4$ (171 mg, 4 equiv., 0.2 M) was added dropwise to the reaction, and the mixture was stirred at rt until the reaction was finished as determined by the disappearance of starting material on TLC (45 min to 12 h). The reaction mixture was then diluted with CH_2Cl_2 and washed with water, saturated $NaHCO_3$, water and brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The volatiles were concentrated under reduced pressure, and the resulting crude product was purified by flash column chromatography.

General P-3CR/oxidative elimination procedure (B):

The 2-(phenylselanyl)aldehyde (0.2 mmol, 1.0 equiv.), the carboxylic acid (0.2 mmol, 1.0 equiv.) and the isocyanide (0.2 mmol, 1.0 equiv.) were dissolved in 2-MeTHF (5 mL) and stirred at 25 °C for 24 h. TLC monitored the reaction progress until the consumption of the starting material. After completion, aqueous $NaIO_4$ (171 mg, 4 equiv., 0.2 M) was added dropwise to the reaction, and the mixture was stirred at rt until the reaction was finished as determined by the disappearance of starting material on TLC (45 min to 12 h). The reaction mixture was then diluted with CH_2Cl_2 and washed with water, saturated $NaHCO_3$, water and brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The volatiles were concentrated under reduced pressure, and the resulting crude product was purified by flash column chromatography.



(Z)-2-(N-benzylacetamido)-N-(tert-butyl)but-2-enamide (1a)

2-(phenylselanyl)propanal (43 mg, 0.2 mmol, 1 equiv.), benzylamine (22 µL, 0.2 mmol), acetic acid (11 µL, 0.2 mmol), and terbutyl isocyanide (23 µL, 0.2 mmol) were dissolved in 1mL of THF and reacted according to the general Ugi-4CR/oxidative-elimination procedure (A). Flash column chromatography purification (Hex/EtOAc from 4:1 to 1:1 v/v) afforded compound ***1a*** (42 mg, 73%) as a yellow sticky oil. R_f = 0.55 (Hex/EtOAc 1:1 v/v). A mixture of rotamers in a 3:2 ratio was observed by NMR analysis.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.28 (m, 5H), 7.00, 5.93 (2xq, J = 7.4 Hz, 1H), 5.26, 4.02 (2xd, J = 13.7 Hz, 2H), 4.71 (s, 1H, NH), 2.13,1.64 (2xd, J = 7.5 Hz, 3H), 2.04,1.94 (2xs, 3H), 1.13,1.06 (2xs, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 171.2, 163.6, 162.6, 137.8, 137.3, 137.2, 136.0, 134.5, 130.0, 129.6, 129.1, 129.0, 128.4, 128.1, 52.5, 51.5, 51.1, 51.0, 28.4, 28.2, 22.3, 21.9, 14.6, 13.4.

HRMS (ESI-FT-ICR) *m/z*: 311.1735 $[M+Na]^+$; calcd. for $C_{17}H_{24}N_2NaO_2$: 311.1735.

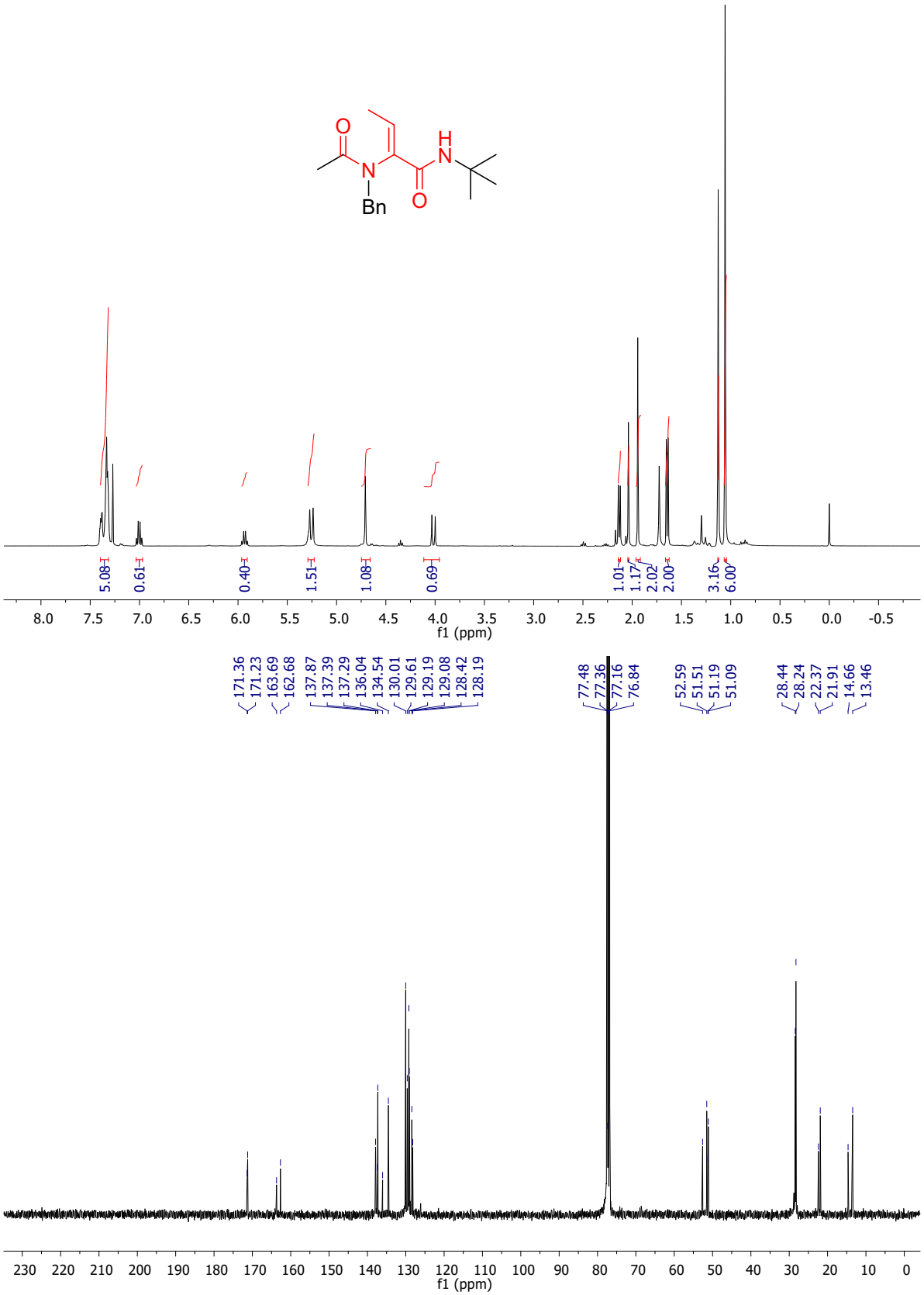


FIGURE 1. ^{1}H and ^{13}C NMR spectra in $CDCl_3$ of **1a**.

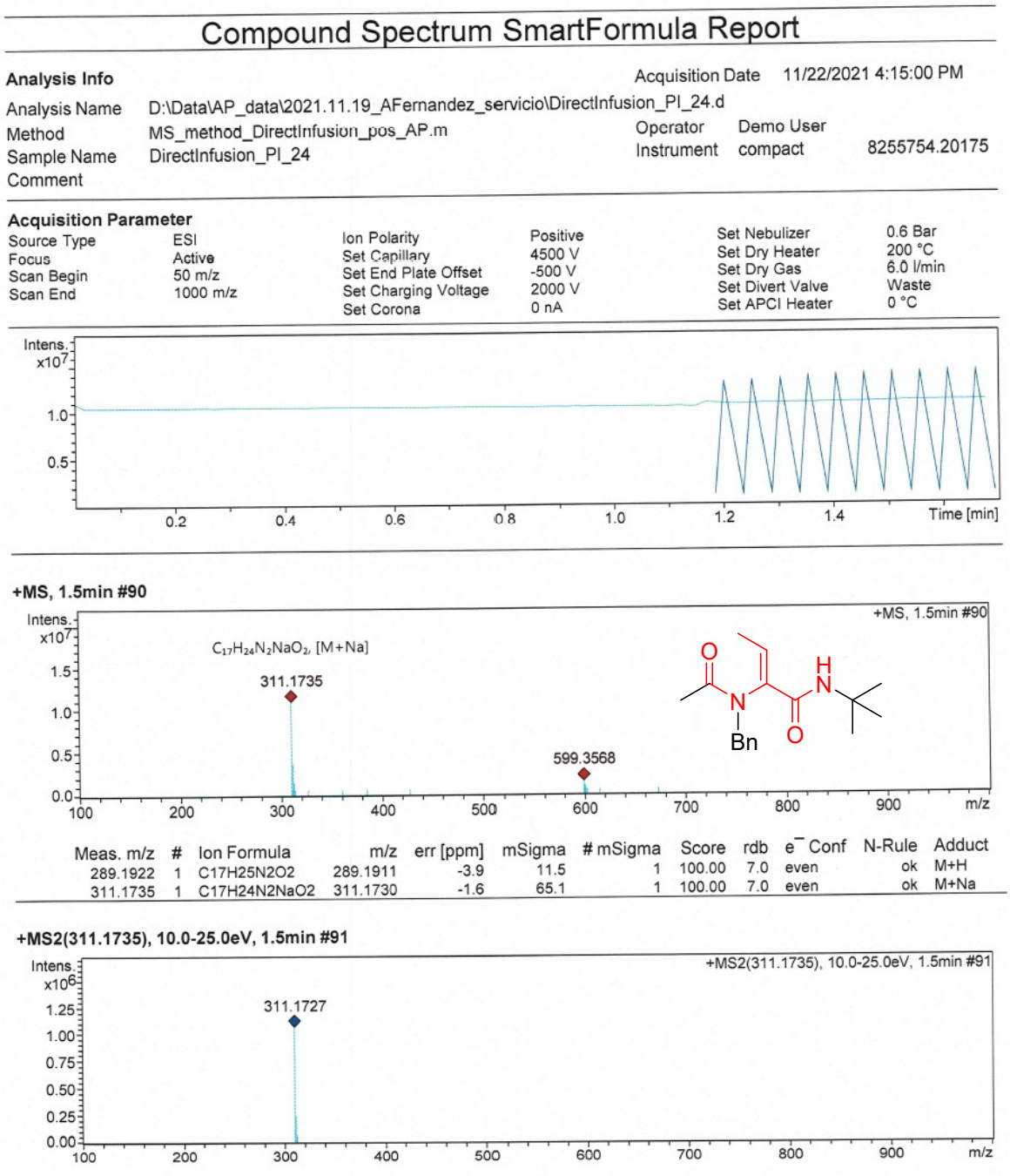
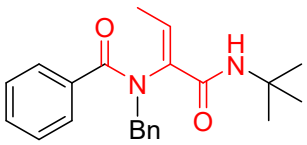


FIGURE 2- HRMS (ESI-FT-ICR) m/z spectra of **1a**.



(Z)-N-benzyl-N-(1-(tert-butylamino)-1-oxobut-2-en-2-yl)benzamide (1b)

2-(phenylselanyl)propanal (43 mg, 0.2 mmol, 1 equiv.), benzylamine (22 µL, 0.2 mmol), benzoic acid (24 mg, 0.2 mmol), and terbutyl isocyanide (23 µL, 0.2 mmol) were dissolved in 1mL of 2-MeTHF and reacted according to the general Ugi-4CR/oxidative-elimination procedure (A). Flash column chromatography purification (Hex/EtOAc from 4:1 to 1:1 v/v) afforded compound ***1b*** (56 mg, 80%) as a yellow sticky oil. R_f = 0.55 (Hex/EtOAc 1:1 v/v). A mixture of rotamers in a 9:1 ratio was observed by NMR analysis.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (m, 5H), 7.39 – 7.30 (m, 5H), 6.64 (q, J = 7.2 Hz, 1H), 5.41 (bs, 1H, NH), 5.21 (d, J = 13.7 Hz, 1H), 4.43 (d, J = 12.7 Hz, 1H), 1.47 (d, J = 5.5 Hz, 3H), 1.06 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 162.8, 137.5, 136.9, 135.5, 133.3, 131.6, 130.6, 130.0, 129.0, 128.8, 128.6, 128.4, 128.0, 127.7, 127.4, 127.0, 52.2, 51.1, 44.2, 28.2, 13.8.

HRMS (ESI-FT-ICR) m/z: 351.2073 $[M+H]^+$; calcd. for $C_{22}H_{27}N_2O_2$: 351.2073.

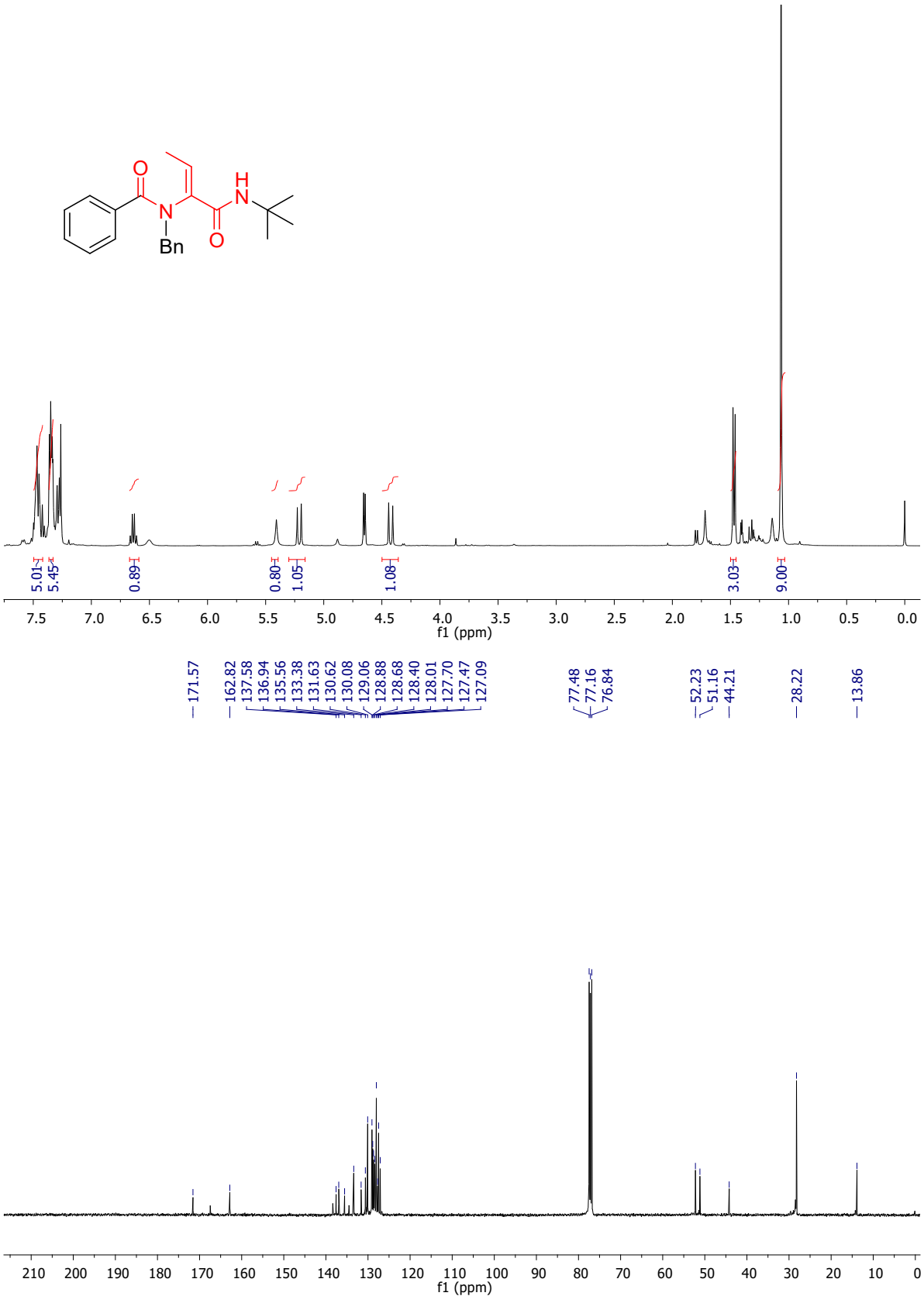


FIGURE 3. ^{1}H and ^{13}C NMR spectra in $CDCl_3$ of **1b**.

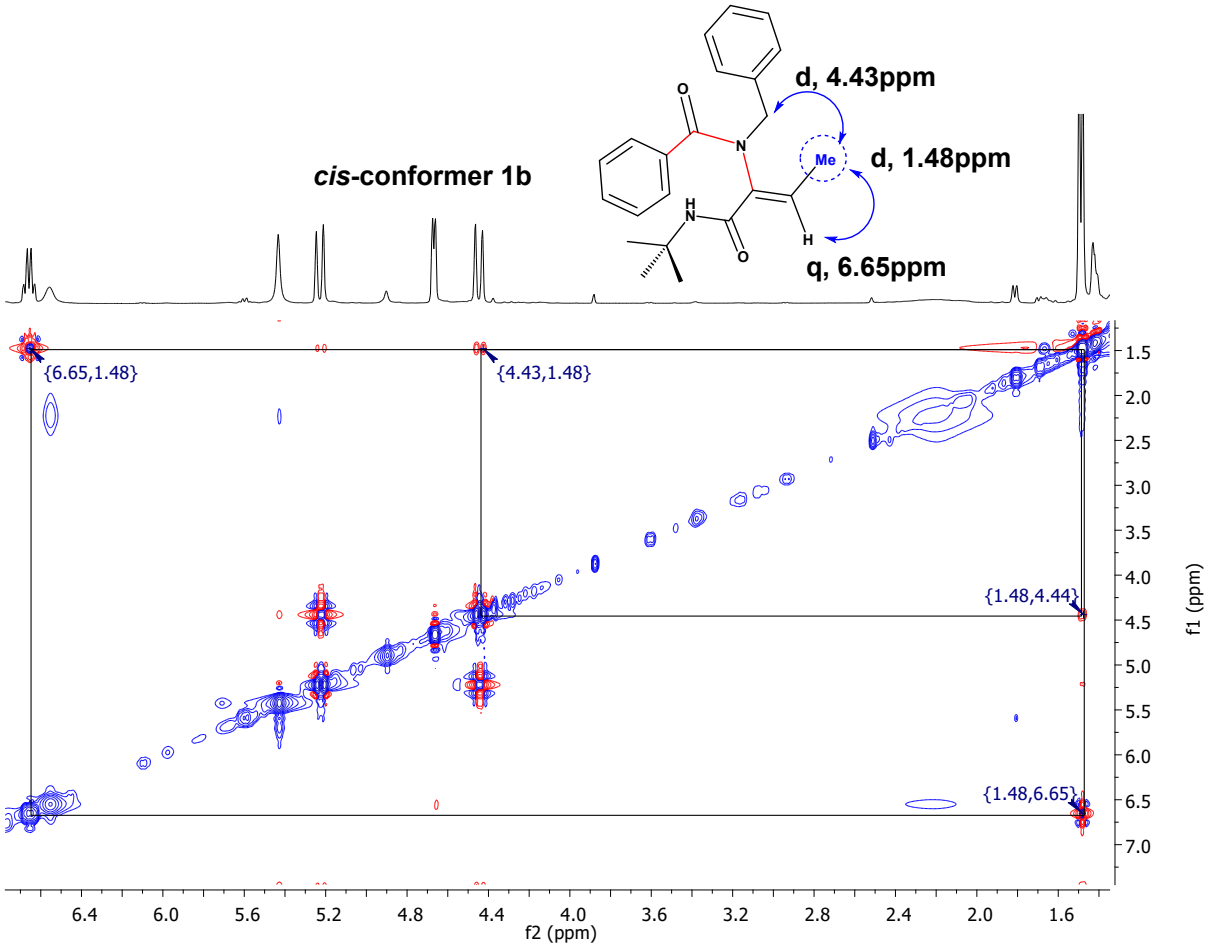
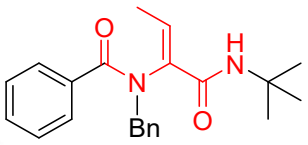


FIGURE 4. 400 MHz nuclear Overhauser effect (NOE) correlation spectrum of *cis*-conformer 1b indicating the NOE interaction between the Me group at 1.48 ppm with Benzyl CH_2 (4.41 ppm) and with α-H at 6.65ppm.



Compound Spectrum SmartFormula Report

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Acquisition Parameter

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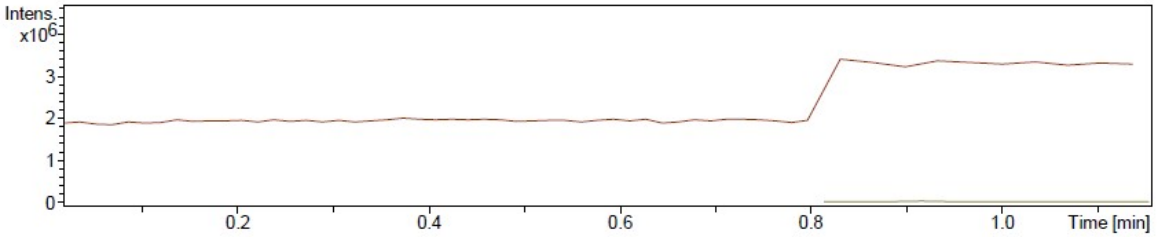

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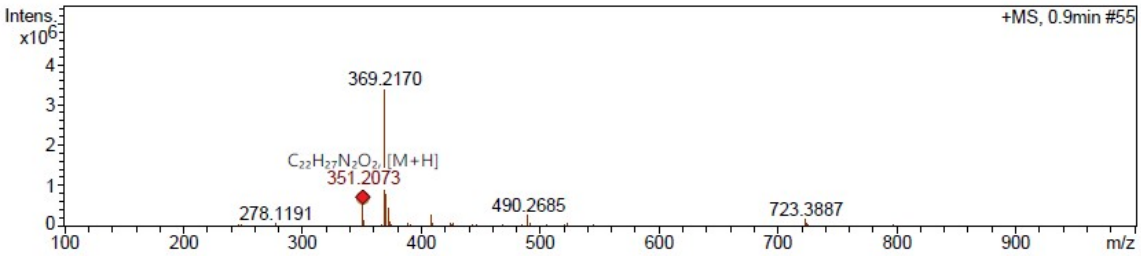

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e¯ Conf	N-Rule	Adduct
351.2073	1	C22H27N2O2	351.2067	-1.8	10.1	1	100.00	11.0	even	ok	M+H

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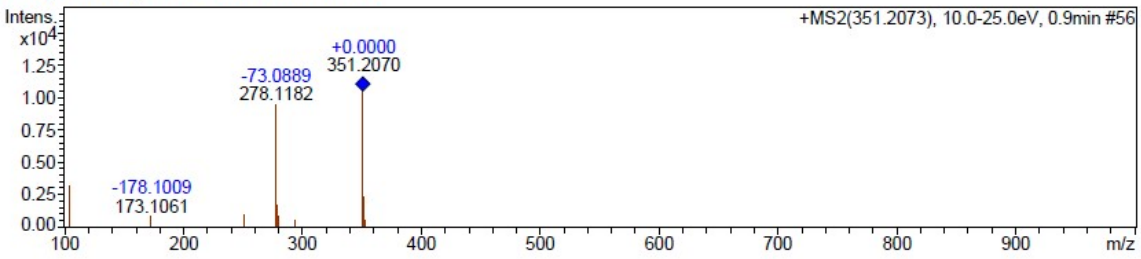
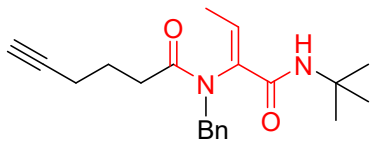


FIGURE 5- HRMS (ESI-FT-ICR) m/z spectra of **1b**.



(Z)-N-benzyl-N-(1-(tert-butylamino)-1-oxobut-2-en-2-yl)hex-5-ynamide (1c)

2-(phenylselanyl)propanal (43 mg, 0.2 mmol, 1 equiv.), benzylamine (22 µL, 0.2 mmol), hex-5-ynoic acid (22 µL, 0.2 mmol), and terbutyl isocyanide (23 µL, 0.2 mmol) were dissolved in 1mL of 2-MeTHF and reacted according to the general Ugi-4CR/oxidative elimination procedure (A). Flash column chromatography purification (Hex/EtOAc from 4:1 to 1:1 v/v) afforded compound ***1c*** (58 mg, 85%) as a light-yellow sticky oil. R_f = 0.50 (Hex/EtOAc 1:1 v/v). A mixture of rotamers in a 3:2 ratio was observed by NMR analysis.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.28 (m, 5H), 7.03, 5.92 (2xq, J = 7.3 Hz, 1H), 5.29 (d, J = 13.6 Hz, 1H), 5.26, 470 (2xbs, 1H, NH), 3.99 (d, J = 13.6 Hz, 1H), 2.39 (t, J = 7.2 Hz, 1H), 2.30 – 2.20 (m, 3H), 2.15, 1.65 (2xd, J = 7.4 Hz, 3H), 1.93 – 1.82 (m, 3H), 1.13, 1.05 (2xs, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 172.9, 163.6, 162.6, 138.5, 137.3, 137.3, 136.6, 135.2, 134.7, 130.0, 129.6, 129.1, 129.0, 128.4, 128.1, 83.7, 83.6, 69.2, 69.1, 52.7, 51.7, 51.1, 51.0, 32.5, 32.1, 28.4, 28.1, 24.0, 23.7, 17.9, 14.7, 13.5.

HRMS (ESI-FT-ICR) m/z: 341.2220 $[M+H]^+$; calcd. for $C_{21}H_{29}N_2O_2$: 341.2229.

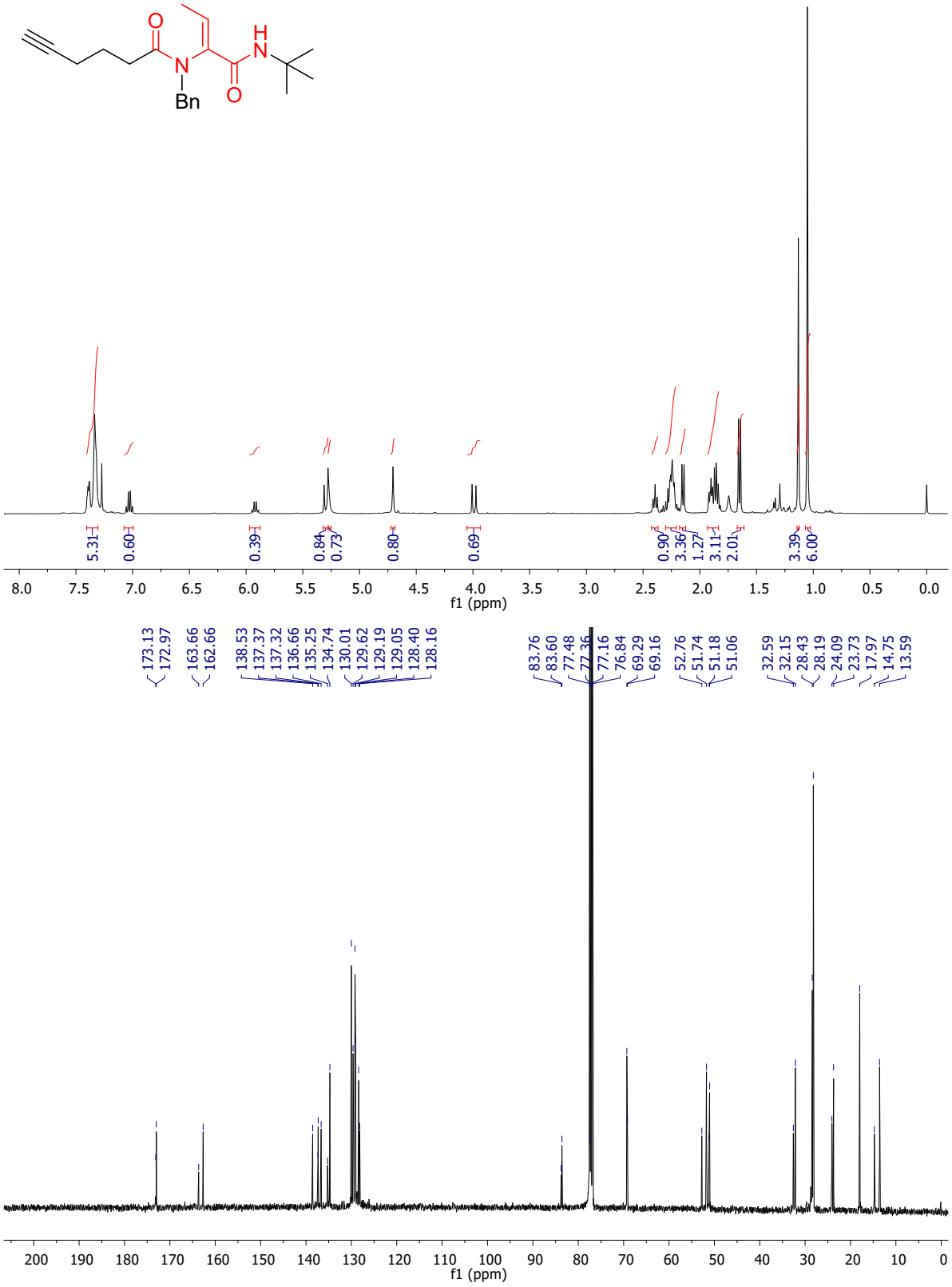
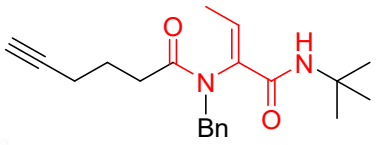


FIGURE 6. ^{1}H and ^{13}C NMR spectra in $CDCl_3$ of **1c**.



Compound Spectrum SmartFormula Report

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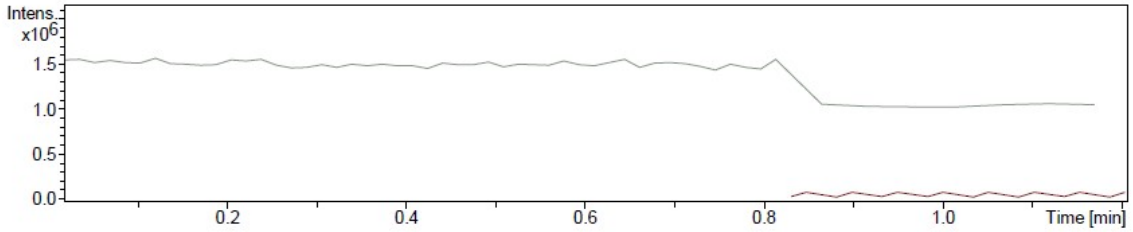

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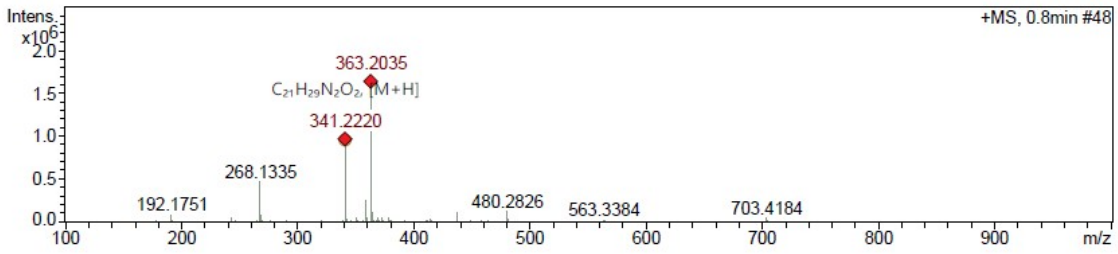

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule	Adduct
341.2220	1	C21H29N2O2	341.2224	0.9	7.7	1	100.00	9.0	even	ok	M+H

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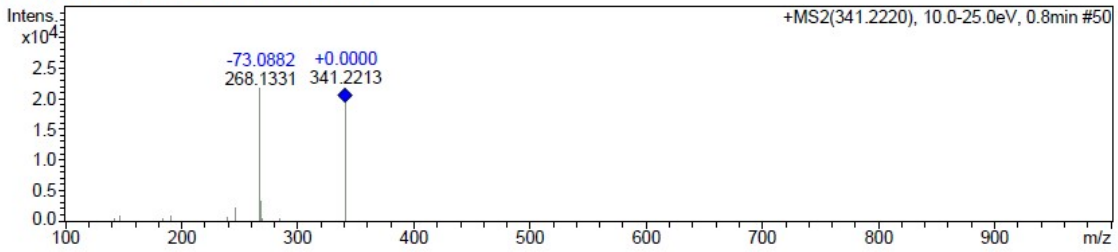
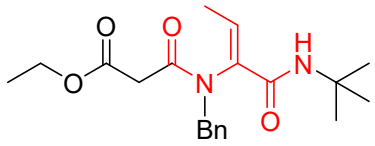


FIGURE 7- HRMS (ESI-FT-ICR) m/z spectra of **1c**.



Ethyl (Z)-3-(benzyl(1-(tert-butylamino)-1-oxobut-2-en-2-yl)amino)-3-oxopropanoate (1d)

2-(phenylselanyl)propanal (43 mg, 0.2 mmol, 1 equiv.), benzylamine (22 µL, 0.2 mmol), 3-ethoxy-3-oxopropanoic acid (24 µL, 0.2 mmol), and terbutyl isocyanide (23 µL, 0.2 mmol) were dissolved in 1mL of 2-MeTHF and reacted according to the general Ugi-4CR/oxidative elimination procedure (A). Flash column chromatography purification (Hex/EtOAc from 4:1 to 1:1 v/v) afforded compound ***1d*** (55 mg, 76%) as a colorless sticky oil. R_f= 0.35 (Hex/EtOAc 1:1 v/v). A mixture of rotamers in a 1:1 ratio was observed by NMR analysis.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.38 (m, 1H), 7.32 (m, 4H), 7.01, 5.79 (2xq, J = 7.3 Hz, 1H), 5.84, 5.73 (2xbs, 1H, NH), 5.02 (d, J = 13.7 Hz, 1H), 4.69, 3.45 (2xs, 2H), 4.31 (d, J = 13.6 Hz, 1H), 4.22 – 4.14 (m, 2H), 3.35 (d, J = 15.9 Hz, 1H), 3.22 (d, J = 15.8 Hz, 1H), 2.07, 1.54 (2xd, J = 7.2 Hz, 3H), 1.33 (d, J = 4.8 Hz, 2H), 1.27 (2×t, J = 7.1 Hz, 3H), 1.21, 1.12 (2xs, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 167.9, 167.0, 166.9, 163.1, 162.2, 138.8, 136.6, 136.5, 135.6, 130.0, 129.5, 129.0, 128.8, 128.7, 128.4, 128.1, 127.6, 61.7, 51.9, 51.5, 51.4, 51.3, 41.1, 40.5, 29.6, 28.4, 28.1, 14.6, 14.2, 13.4.

HRMS (ESI-FT-ICR) m/z: 361.2125 $[M+H]^+$; calcd. for $C_{20}H_{29}N_2O_4$: 361.2127.

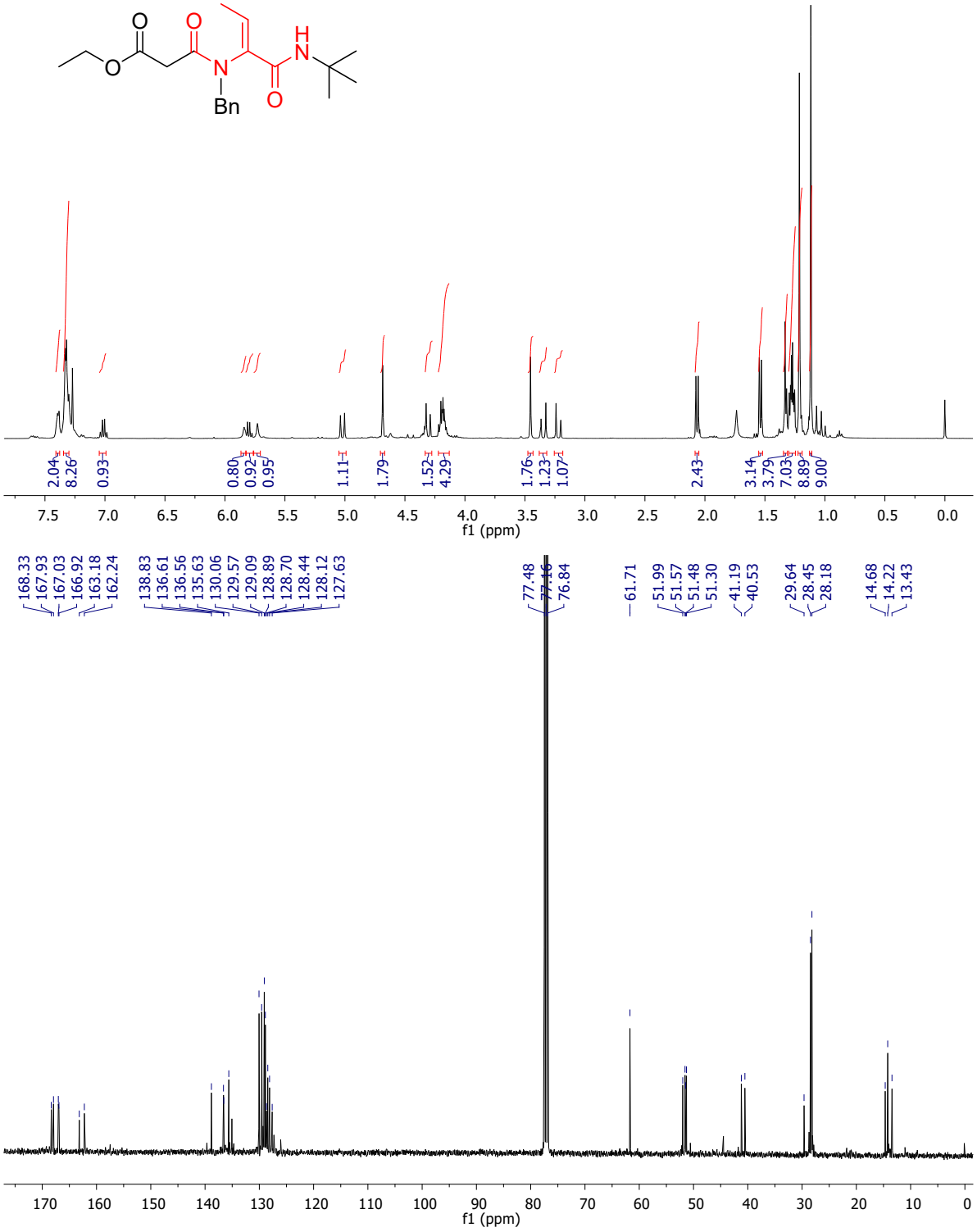
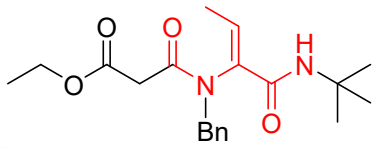


FIGURE 8. ^{1}H and ^{13}C NMR spectra in $CDCl_3$ of **1d**.



Compound Spectrum SmartFormula Report

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Sample Name	DirectInfusion_PI_45	Instrument	compact 8255754.20175
Comment			

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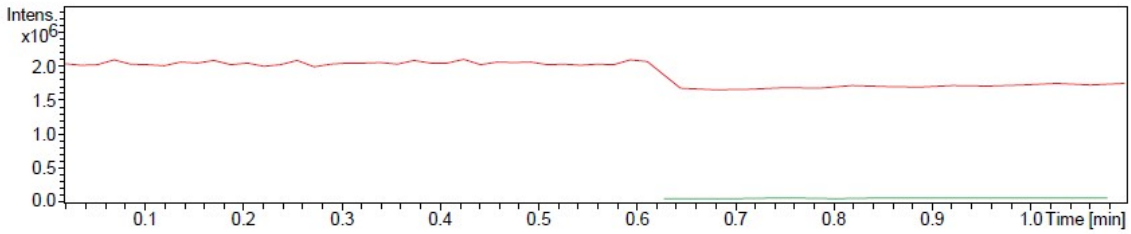

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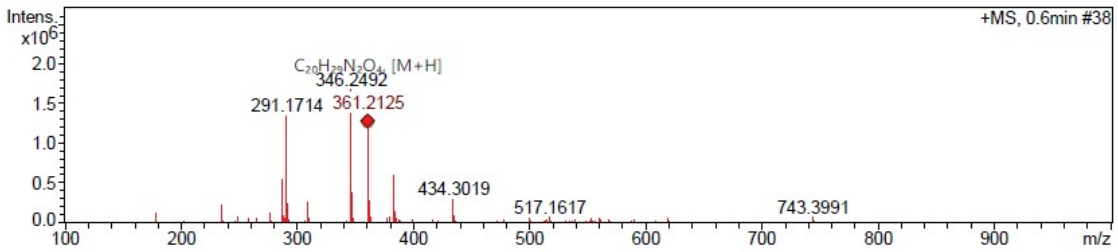

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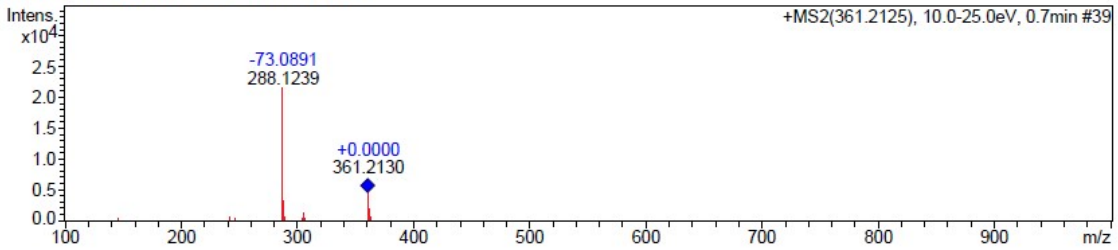
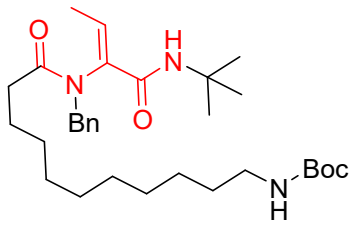


FIGURE 9- HRMS (ESI-FT-ICR) m/z spectra of **1d**.



tert-butyl (Z)-(11-(benzyl(1-(tert-butylamino)-1-oxobut-2-en-2-yl)amino)-11-oxoundecyl)carbamate (1e)

2-(phenylselanyl)propanal (43 mg, 0.2 mmol, 1 equiv.), benzylamine (22 µL, 0.2 mmol), 11-((tert-butoxycarbonyl)amino)undecanoic acid (60 mg, 0.2 mmol), and terbutyl isocyanide (23 µL, 0.2 mmol) were dissolved in 1mL of 2-MeTHF and reacted according to the general Ugi-4CR/oxidative elimination procedure (A). Flash column chromatography purification (Hex/EtOAc from 4:1 to 1:1 v/v) afforded compound ***1e*** (69 mg, 65%) as a colorless sticky oil. R_f = 0.55 (Hex/EtOAc 1:1 v/v). A mixture of rotamers in a 1:0.5 ratio was observed by NMR analysis.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (m, 2H), 7.33 (m, 3H), 7.01, 5.91 (2xq, J = 7.4 Hz, 1H), 5.33 (d, J = 13.6 Hz, 1H), 5.25 (s, 1H), 4.71 (s, 1H), 3.95 (d, J = 13.6 Hz, 1H), 3.09 (m, 2H), 2.22 (t, J = 7.4 Hz, 1H), 2.15, 1.65 (2xd, J = 7.2 Hz, 3H), 1.65 – 1.55 (m, 1H), 1.42, 1.27 (2xm, 22H), 1.11, 1.03 (2xs, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 173.9, 163.8, 162.8, 156.1, 138.4, 137.5, 137.5, 136.9, 135.4, 134.4, 130.0, 129.6, 129.2, 129.0, 128.3, 128.1, 79.1, 52.8, 51.7, 51.1, 51.0, 40.7, 34.2, 33.7, 30.1, 29.5, 29.5, 29.3, 28.5, 28.4, 28.1, 26.9, 25.4, 25.2, 14.7, 13.6.

HRMS (ESI-FT-ICR) m/z: 530.3953 $[M+H]^+$; calcd. for $C_{31}H_{52}N_3O_4$: 530.3958.

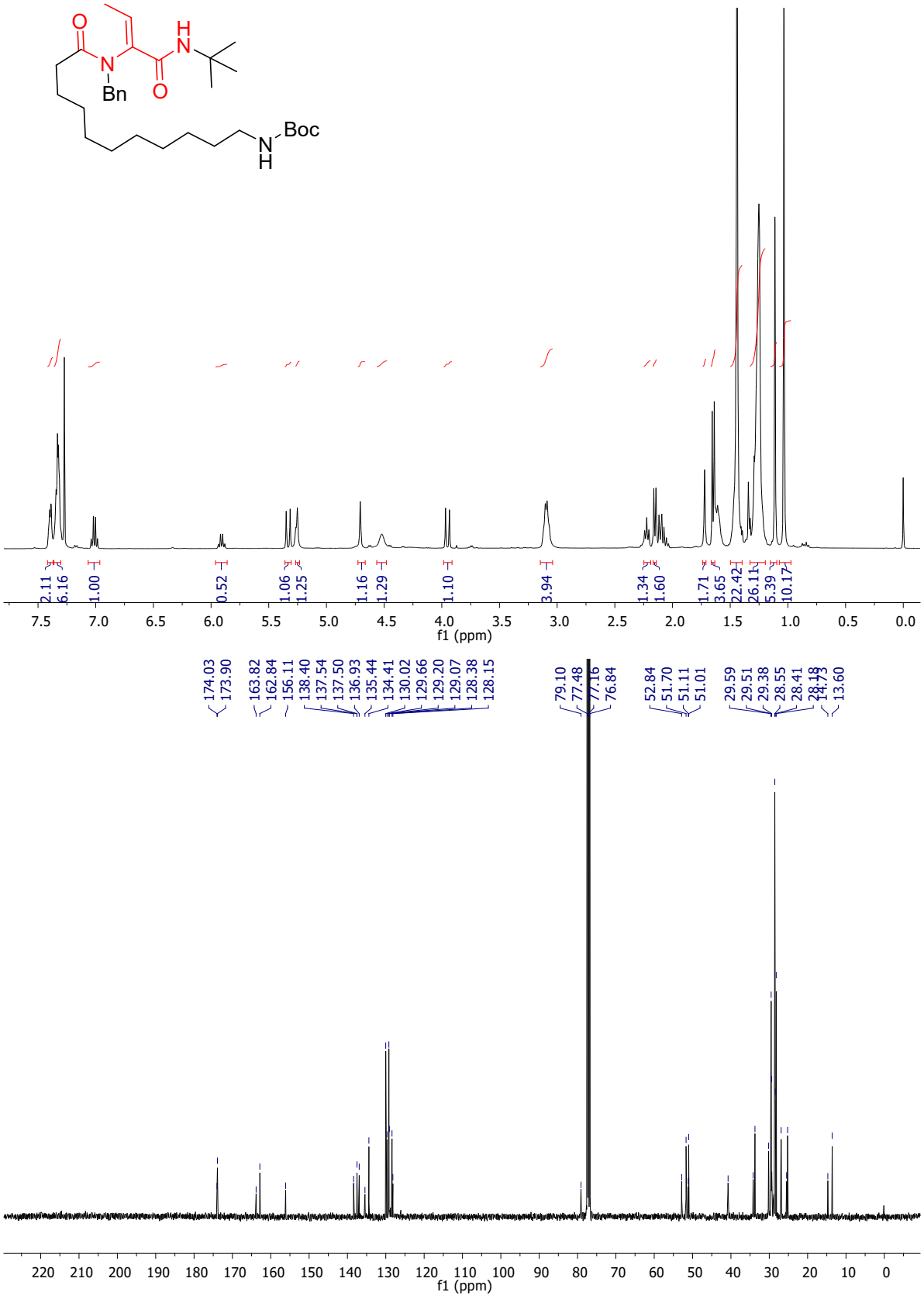


FIGURE 10. ^{1}H and ^{13}C NMR spectra in $CDCl_3$ of **1e**.

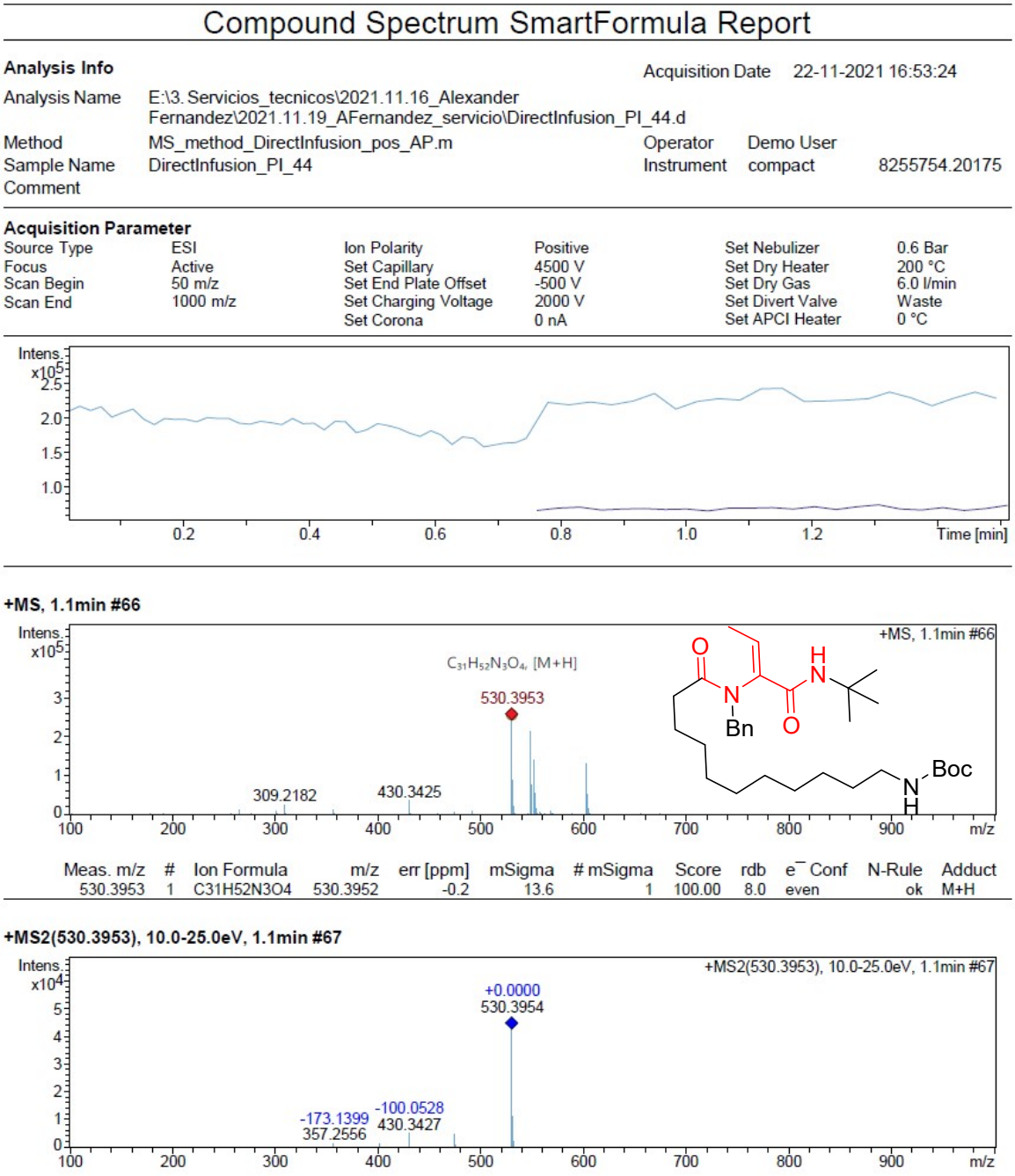
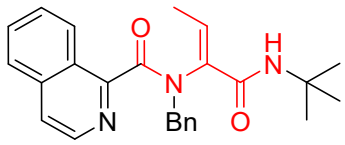


FIGURE 11- HRMS (ESI-FT-ICR) m/z spectra of **1e**.



(Z)-N-benzyl-N-(1-(tert-butylamino)-1-oxobut-2-en-2-yl)isoquinoline-1-carboxamide (1f)

2-(phenylselanyl)propanal (43 mg, 0.2 mmol, 1 equiv.), benzylamine (22 µL, 0.2 mmol), isoquinoline-1-carboxylic acid (35 mg, 0.2 mmol), and terbutyl isocyanide (23 µL, 0.2 mmol) were dissolved in 1mL of 2-MeTHF and reacted according to the general Ugi-4CR/oxidative elimination procedure (A). Flash column chromatography purification (Hex/EtOAc from 4:1 to 1:1 v/v) afforded compound ***1f*** (57 mg, 71%) as a colorless sticky oil. R_f = 0.30 (Hex/EtOAc 1:1 v/v). A mixture of rotamers in a 1:1 ratio was observed by NMR analysis.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (dd, *J* = 14.4, 5.7 Hz, 2H), 8.20 (d, *J* = 7.9 Hz, 1H), 7.83 (dd, *J* = 11.7, 8.3 Hz, 2H), 7.75 – 7.64 (m, 5H), 7.60 – 7.53 (m, 5H), 7.39 – 7.29 (m, 7H), 6.26 (q, *J* = 7.2 Hz, 1H), 5.12 (d, *J* = 13.7 Hz, 1H), 4.89 (q, *J* = 7.2 Hz, 1H), 4.62 (d, *J* = 13.7 Hz, 1H), 1.42 (s, 9H), 1.34 (s, 9H), 1.27 (d, *J* = 5.6 Hz, 3H), 0.94 (d, *J* = 5.9 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 167.8, 164.3, 164.3, 155.3, 154.0, 140.2, 140.0, 137.2, 137.2, 136.7, 136.6, 136.5, 136.4, 136.1, 133.7, 131.5, 131.1, 130.7, 130.3, 129.6, 129.0, 128.7, 128.6, 128.5, 128.5, 128.4, 128.1, 128.0, 127.7, 127.2, 127.1, 126.5, 126.3, 125.5, 122.8, 122.5, 122.3, 51.2, 51.1, 51.0, 50.0, 28.8, 28.6, 13.5, 13.3.

HRMS (ESI-FT-ICR) *m/z*: 402.2169 $[M+H]^+$; calcd. for $C_{25}H_{28}N_3O_2$: 402.2182.

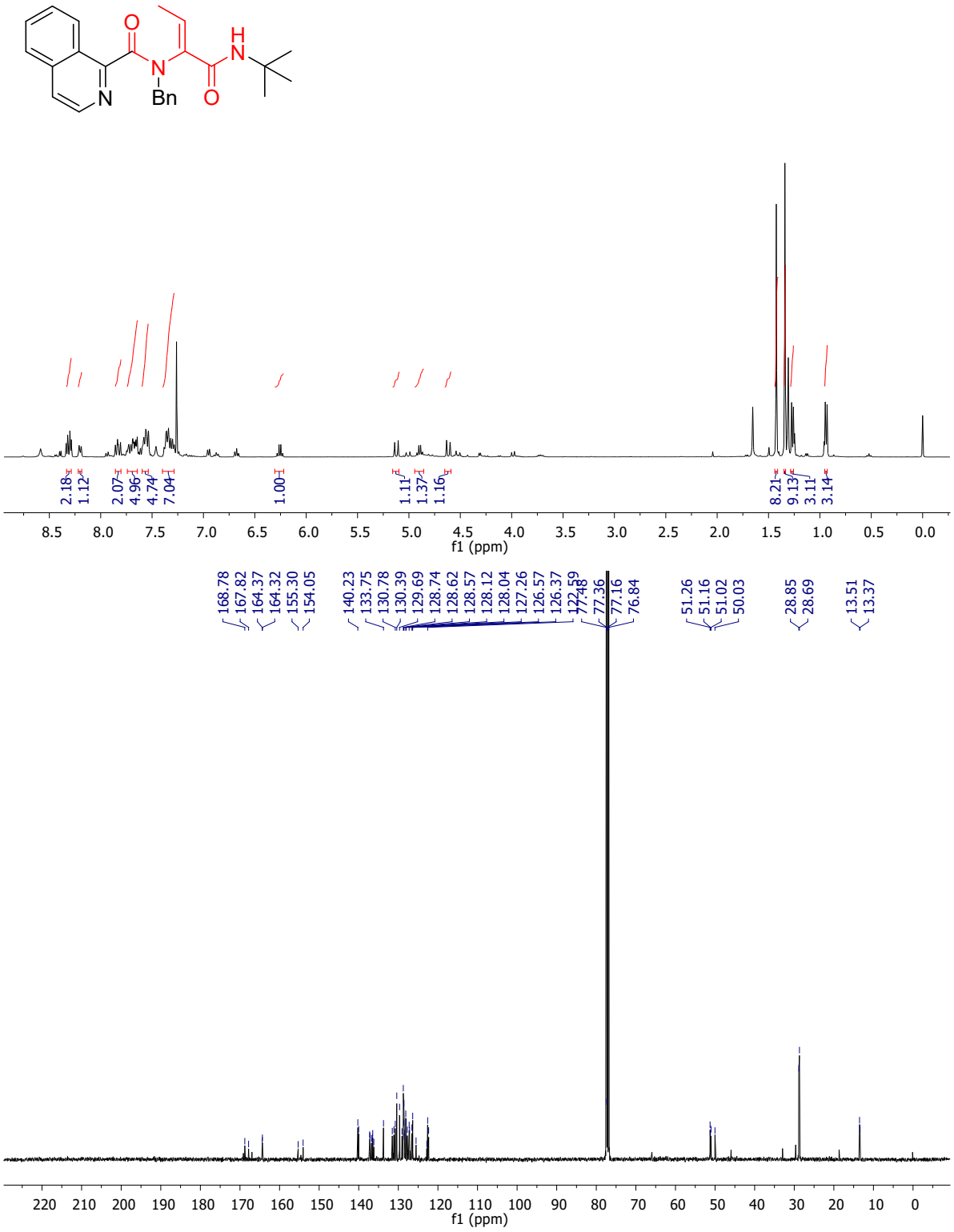
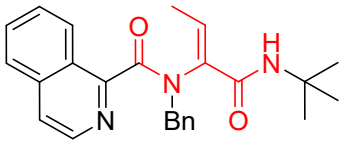


FIGURE 12. ^{1}H and ^{13}C NMR spectra in $CDCl_3$ of **1f**.



Compound Spectrum SmartFormula Report

Analysis Info

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Method	MS_method_DirectInfusion_pos_AP.m			Operator	Demo User
Sample Name	DirectInfusion_PI_46			Instrument	compact 8255754.20175
Comment					

Acquisition Parameter

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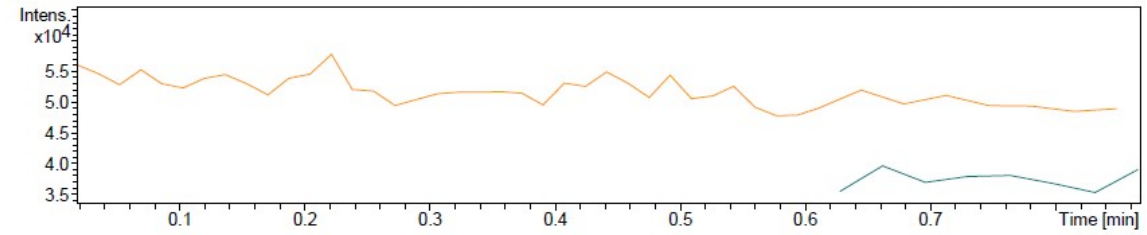
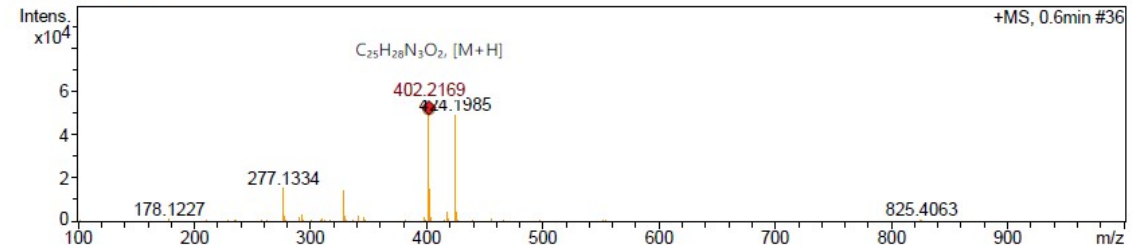
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



+MS, 0.6min #36



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule	Adduct
402.2169	1	C25H28N3O2	402.2176	1.8	8.6	1	100.00	14.0	even	ok	M+H

+MS2(402.2169), 10.0-25.0eV, 0.6min #37

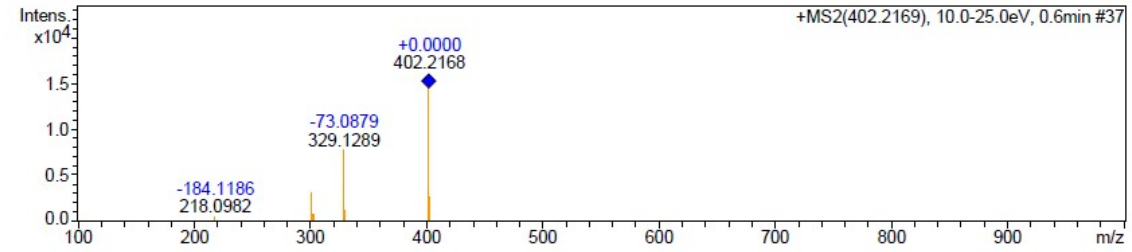
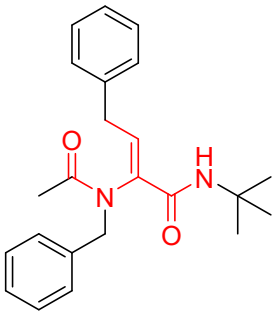


FIGURE 13- HRMS (ESI-FT-ICR) m/z spectra of **1f**.



(Z)-2-(N-benzylacetamido)-N-(tert-butyl)-4-phenylbut-2-enamide (1g)

3-phenyl-2-(phenylselanyl)propanal (58 mg, 0.2 mmol, 1 equiv.), benzylamine (22 µL, 0.2 mmol), acetic acid (11 µL, 0.2 mmol), and terbutyl isocyanide (23 µL, 0.2 mmol) were dissolved in 1mL of 2-MeTHF and reacted according to the general Ugi-4CR/oxidative-elimination procedure (A). Flash column chromatography purification (Hex/EtOAc from 4:1 to 1:1 v/v) afforded compound ***1***g (57 mg, 71%) as a colorless sticky oil. R_f= 0.30 (Hex/EtOAc 1:1 v/v). A mixture of rotamers in a 1:1 ratio was observed by NMR analysis.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (m, 2H), 7.36 – 7.25 (m, 13H), 7.20 – 7.06 (m, 5H), 5.97 (t, J = 7.9 Hz, 1H), 5.41 (d, J = 13.8 Hz, 1H), 5.29 (bs, 2H, NH), 4.04 (d, J = 13.7 Hz, 1H), 4.00 (d, J = 7.8 Hz, 2H), 3.38 (d, J = 7.8 Hz, 2H), 2.07 (s, 3H), 1.97 (s, 3H), 1.16 (s, 9H), 1.06 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 167.8, 164.3, 164.3, 155.3, 154.0, 140.2, 140.0, 137.2, 137.2, 136.7, 136.6, 136.5, 136.4, 136.1, 133.7, 131.5, 131.1, 130.7, 130.3, 129.6, 129.0, 128.7, 128.6, 128.5, 128.5, 128.4, 128.1, 128.0, 127.7, 127.2, 127.1, 126.5, 126.3, 125.5, 122.8, 122.5, 122.3, 51.2, 51.1, 51.0, 50.0, 28.8, 28.6, 13.5, 13.3.

HRMS (ESI-FT-ICR) m/z: 365.2237 $[M+H]^+$; calcd. for $C_{23}H_{29}N_2O_2$: 365.2229.

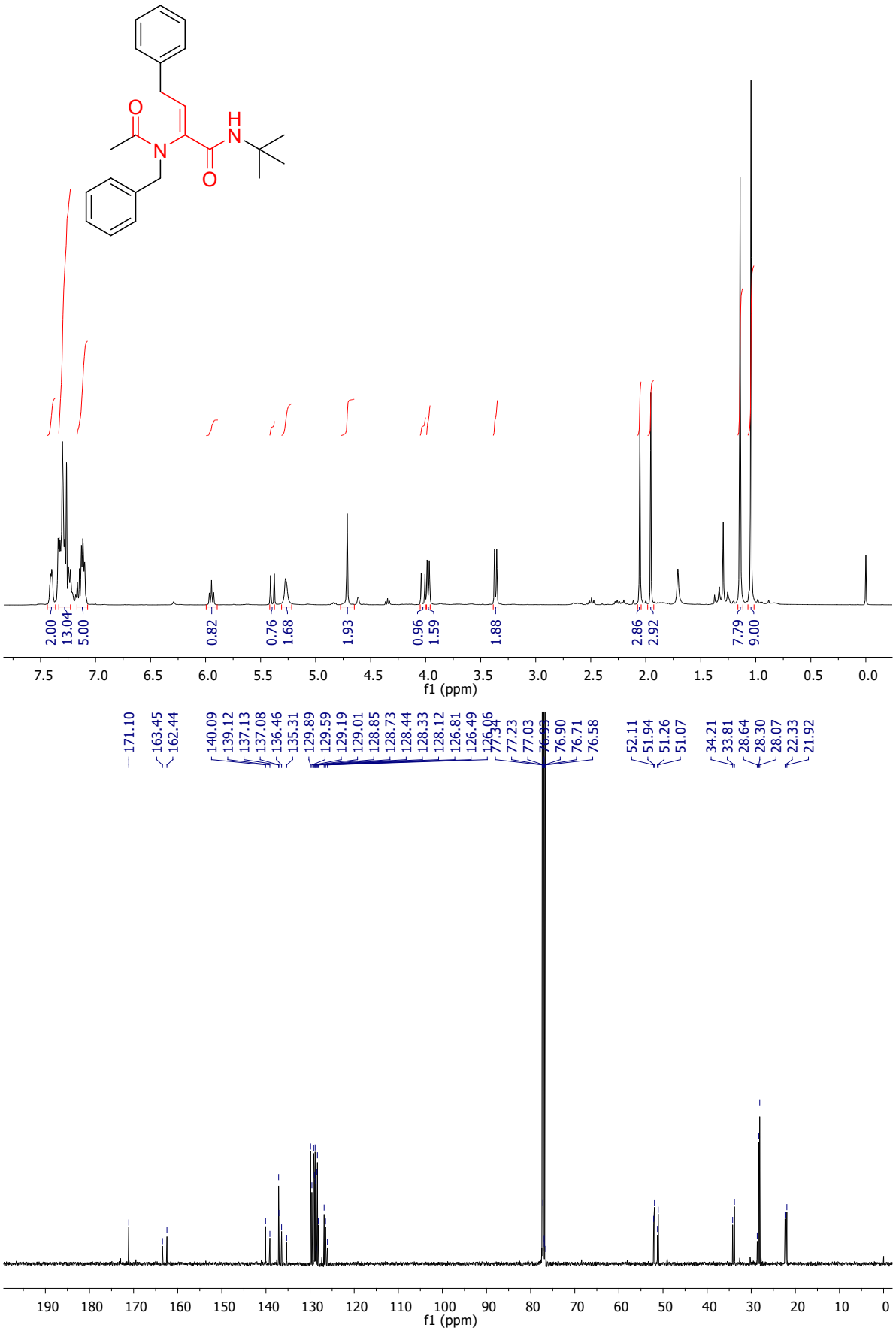
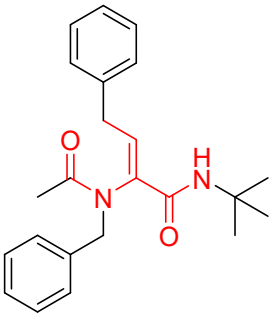


FIGURE 14. ^{1}H and ^{13}C NMR spectra in $CDCl_3$ of **1*g***.



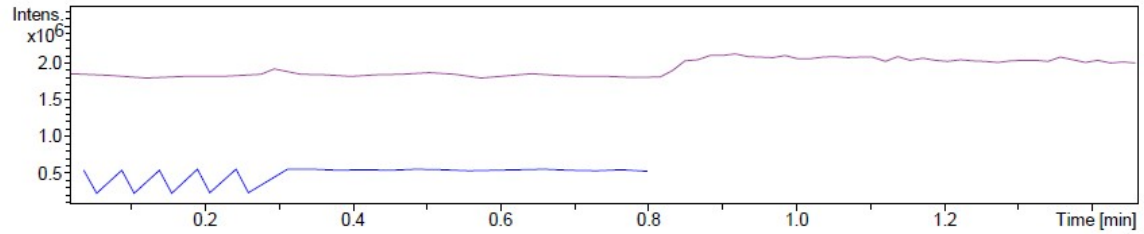
Compound Spectrum SmartFormula Report

Analysis Info

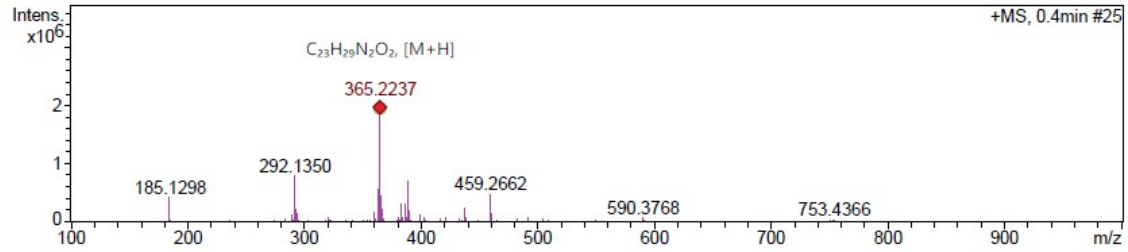
Analysis Name	E:\3. Servicios_tecnicos\2021.11.16_Alexander Fernandez\2021.11.19_AFernandez_servicio\DirectInfusion_PI_25.d	Acquisition Date	22-11-2021 16:20:30
Method	MS_method_DirectInfusion_pos_AP.m	Operator	Demo User
Sample Name	DirectInfusion_PI_25	Instrument	compact 8255754.20175
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.6 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	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



+MS, 0.4min #25



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule	Adduct
365.2237	1	C23H29N2O2	365.2224	-3.7	45.0	1	100.00	11.0	even	ok	M+H

+MS2(365.2237), 10.0-25.0eV, 0.5min #26

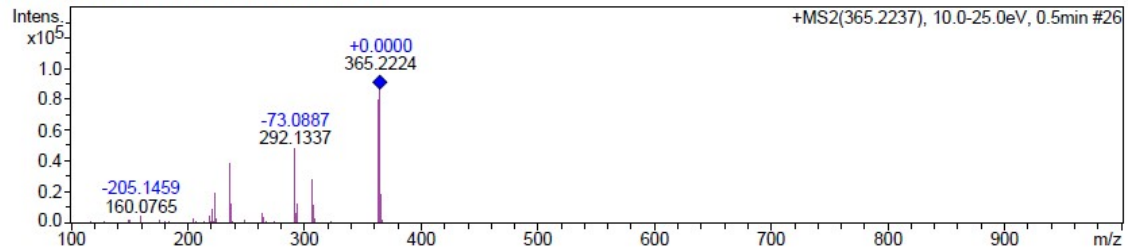
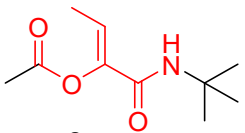
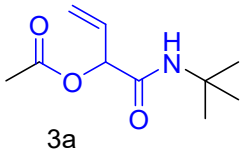


FIGURE 15- HRMS (ESI-FT-ICR) m/z spectra of **1g**.



2a



3a

(Z)-1-(tert-butylamino)-1-oxobut-2-en-2-yl acetate (2a)

1-(tert-butylamino)-1-oxobut-3-en-2-yl acetate (3a)

2-(phenylselanyl)propanal (43 mg, 0.2 mmol, 1 equiv.), acetic acid (11 µL, 0.2 mmol), and terbutyl isocyanide (23 µL, 0.2 mmol) were dissolved in 1mL of THF and reacted according to the general P-3CR/oxidative-elimination procedure (B). Flash column chromatography purification (Hex/EtOAc from 4:1 to 1:1 v/v) afforded compounds 2a and 3***a*** (17 mg, 43%) as a yellow sticky oil. R_f = 0.55 (Hex/EtOAc 1:1 v/v). A mixture of compounds 2a and 3***a*** in a 1:0.7 ratio was observed by NMR analysis.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.41 (q, J = 7.2 Hz, 1H), 5.95 (ddd, J = 16.9, 10.5, 6.0 Hz, 1H), 5.81 (bs, 1H, NH), 5.70 (bs, 1H), 5.47 (d, J = 6.0 Hz, 1H), 5.39 (d, J = 17.3 Hz, 1H), 5.32 (d, J = 10.5 Hz, 1H), 2.27 (s, 3H), 2.18 (s, 3H), 1.64 (d, J = 7.2 Hz, 3H), 1.37 (s, 9H), 1.36 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 167.8, 167.0, 161.2, 142.3, 132.1, 121.2, 118.9, 74.8, 51.5, 51.4, 28.7, 21.0, 20.6, 11.6.

HRMS (ESI-FT-ICR) m/z: 200.1288 $[M+H]^+$; calcd. for $C_{10}H_{18}NO_3$: 200.1287.

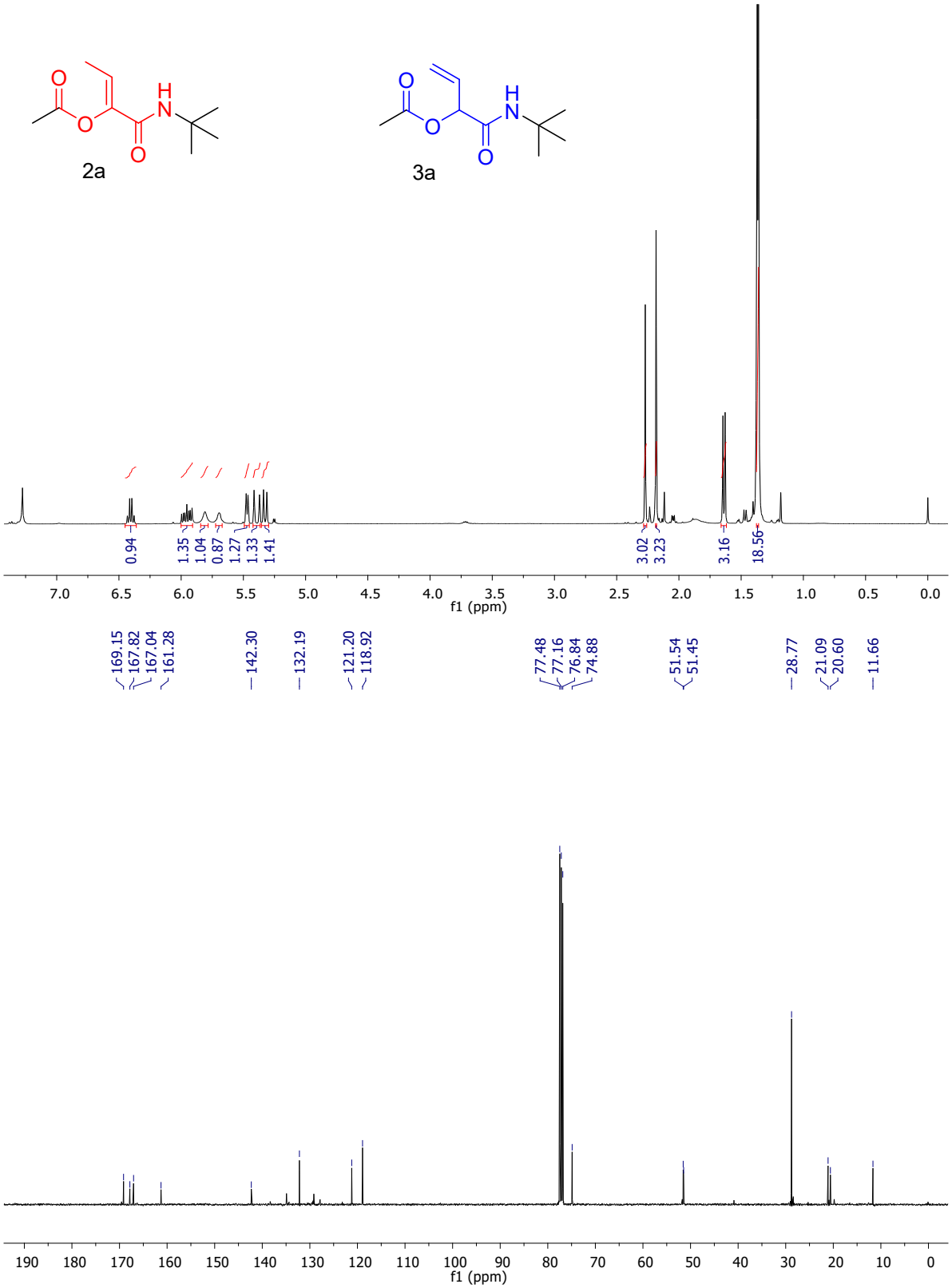


FIGURE 16. ^{1}H and ^{13}C NMR spectra in $CDCl_3$ of ***2a*** and ***3a***.

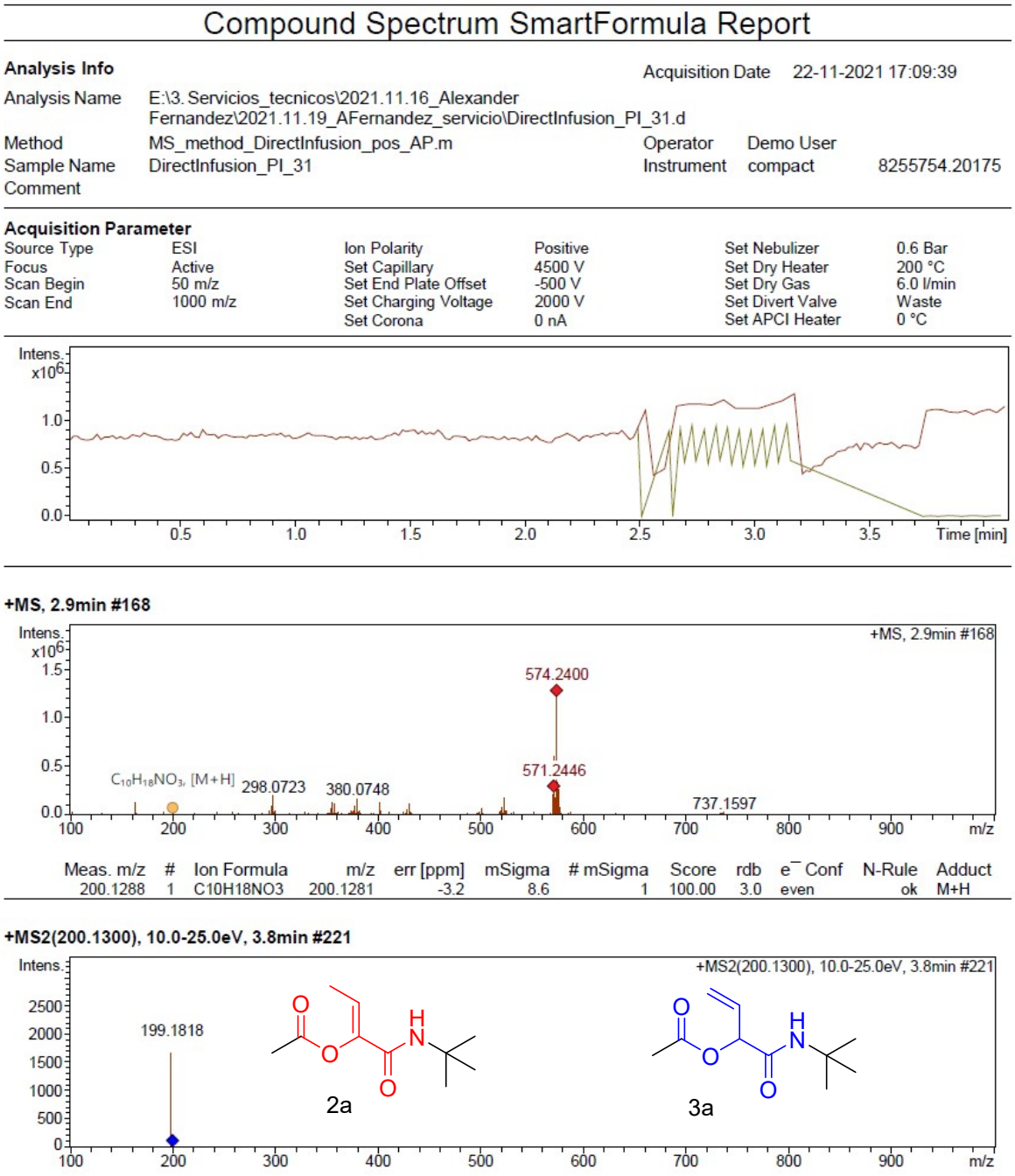
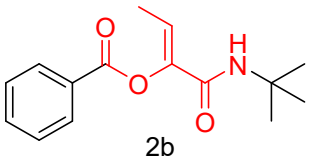
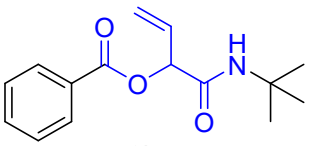


FIGURE 17- HRMS (ESI-FT-ICR) m/z spectra of **2a** and **3a**.



2b



3b

(Z)-1-(tert-butylamino)-1-oxobut-2-en-2-yl benzoate (2b)

1-(tert-butylamino)-1-oxobut-3-en-2-yl benzoate (3b)

2-(phenylselanyl)propanal (43 mg, 0.2 mmol, 1 equiv.), benzoic acid (24 mg, 0.2 mmol), and terbutyl isocyanide (23 µL, 0.2 mmol) were dissolved in 1mL of THF and reacted according to the general P-3CR/oxidative-elimination procedure (B). Flash column chromatography purification (Hex/EtOAc from 4:1 to 1:1 v/v) afforded compounds 2***b*** and 3***b*** (28 mg, 54%) as a colorless sticky oil. R_f = 0.50 (Hex/EtOAc 1:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 7.2 Hz, 2H), 8.10 (d, J = 7.2 Hz, 2H), 7.69 – 7.60 (m, 2H), 7.55 – 7.47 (m, 4H), 6.59 (q, J = 7.2 Hz, 1H), 6.10 (ddd, J = 16.9, 10.6, 5.7 Hz, 1H), 5.91 (bs, 1H, NH), 5.77 (bs, 1H, NH), 5.75 (d, J = 6.0 Hz, 1H), 5.48 (d, J = 17.3 Hz, 1H), 5.37 (d, J = 10.5 Hz, 1H), 1.68 (d, J = 7.2 Hz, 3H), 1.37 (s, 9H), 1.36 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 164.8, 163.6, 161.2, 142.2, 134.1, 133.7, 132.1, 130.3, 129.8, 129.4, 128.9, 128.9, 128.8, 128.8, 128.6, 121.8, 118.7, 76.8, 75.1, 51.5, 51.4, 28.8, 28.7, 11.8.

HRMS (ESI-FT-ICR) m/z: 284.1254 $[M+Na]^+$; calcd. for $C_{15}H_{19}NNaO_3$: 284.1263.

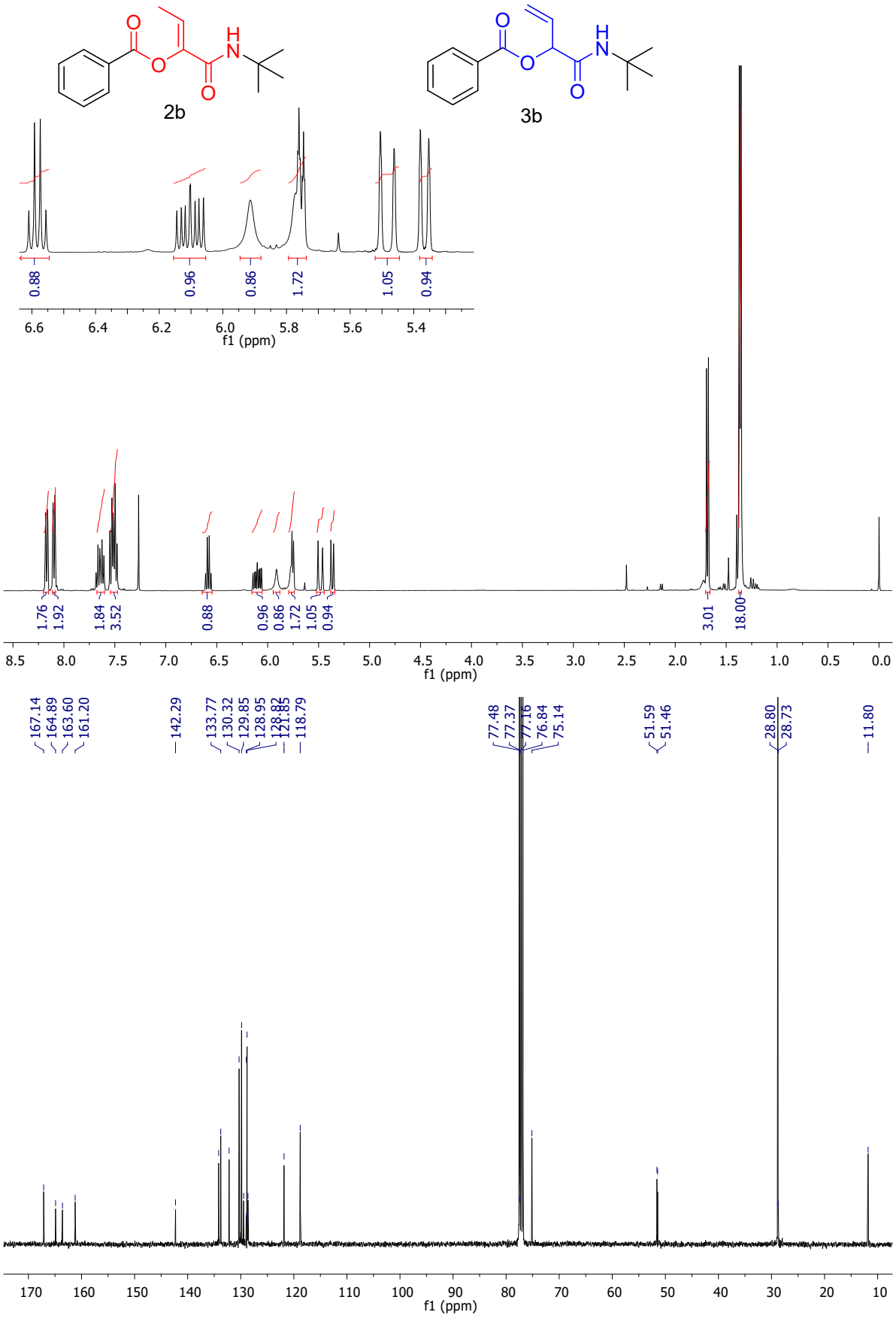


FIGURE 18. ^{1}H and ^{13}C NMR spectra in $CDCl_3$ of ***2b*** and ***3b***.

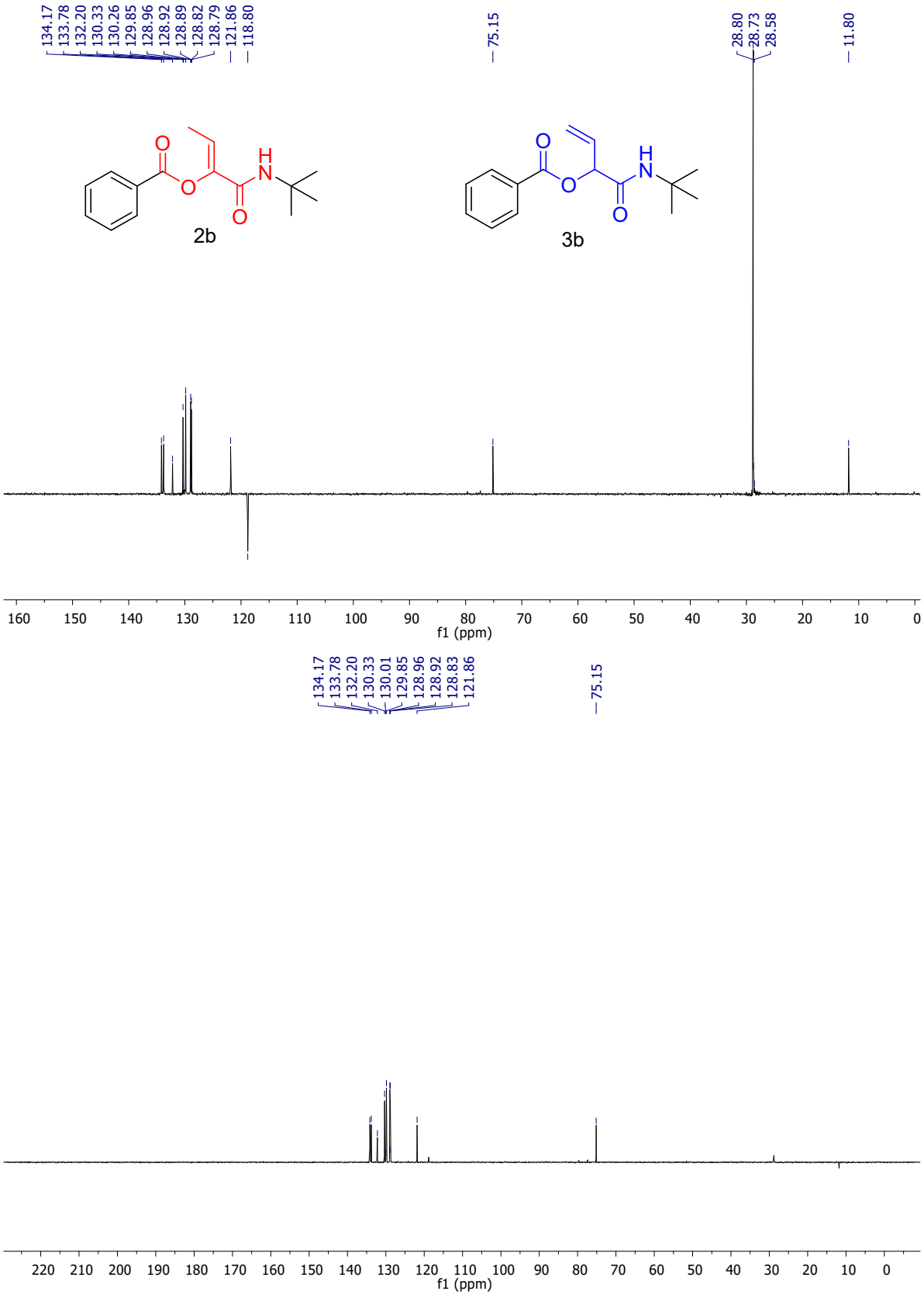


FIGURE 19. DEPT 135° and DEPT 90° spectra in $CDCl_3$ of ***2b*** and ***3b***.

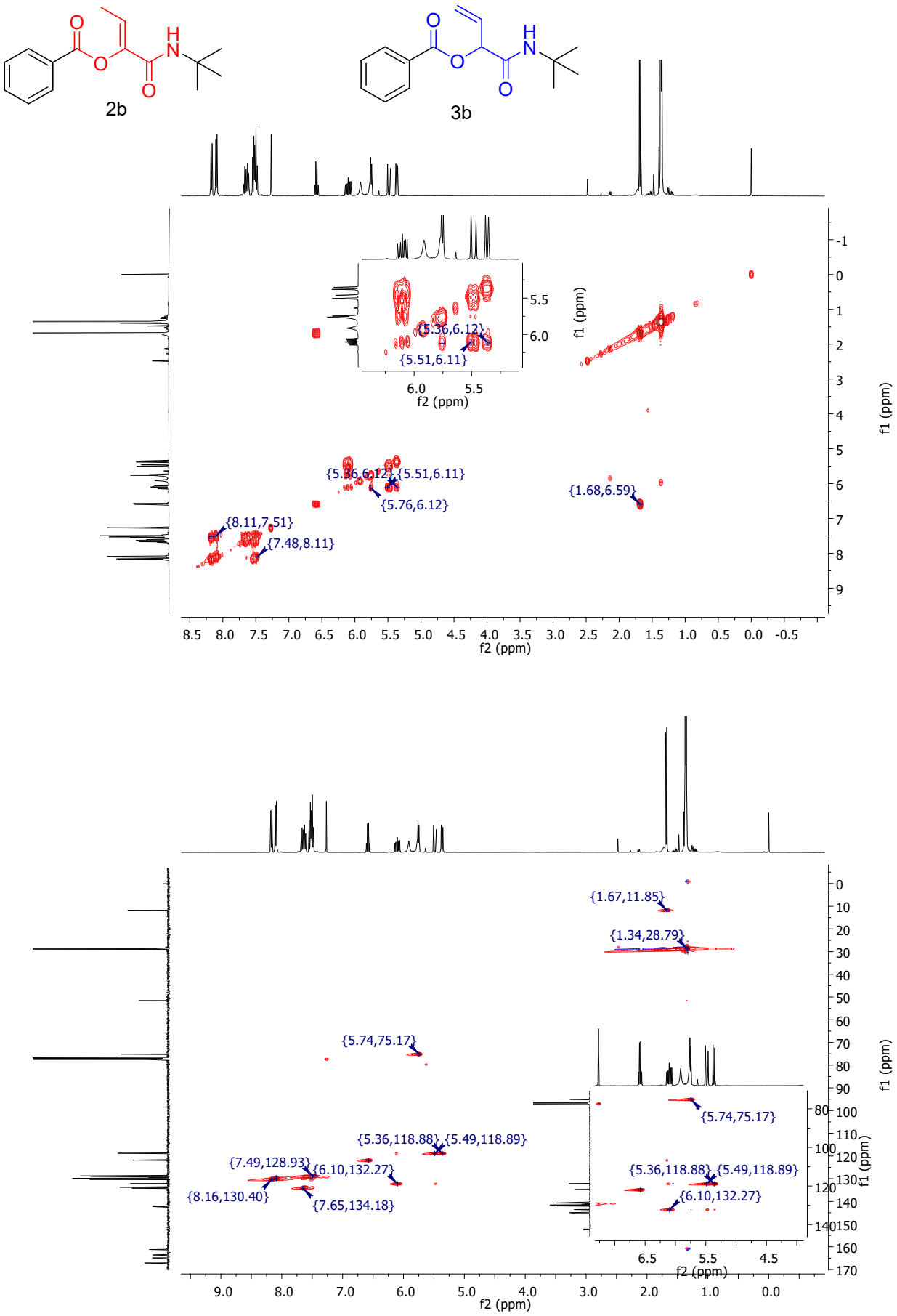


FIGURE 20. COSY and HSQC spectra in $CDCl_3$ of ***2b*** and ***3b***.

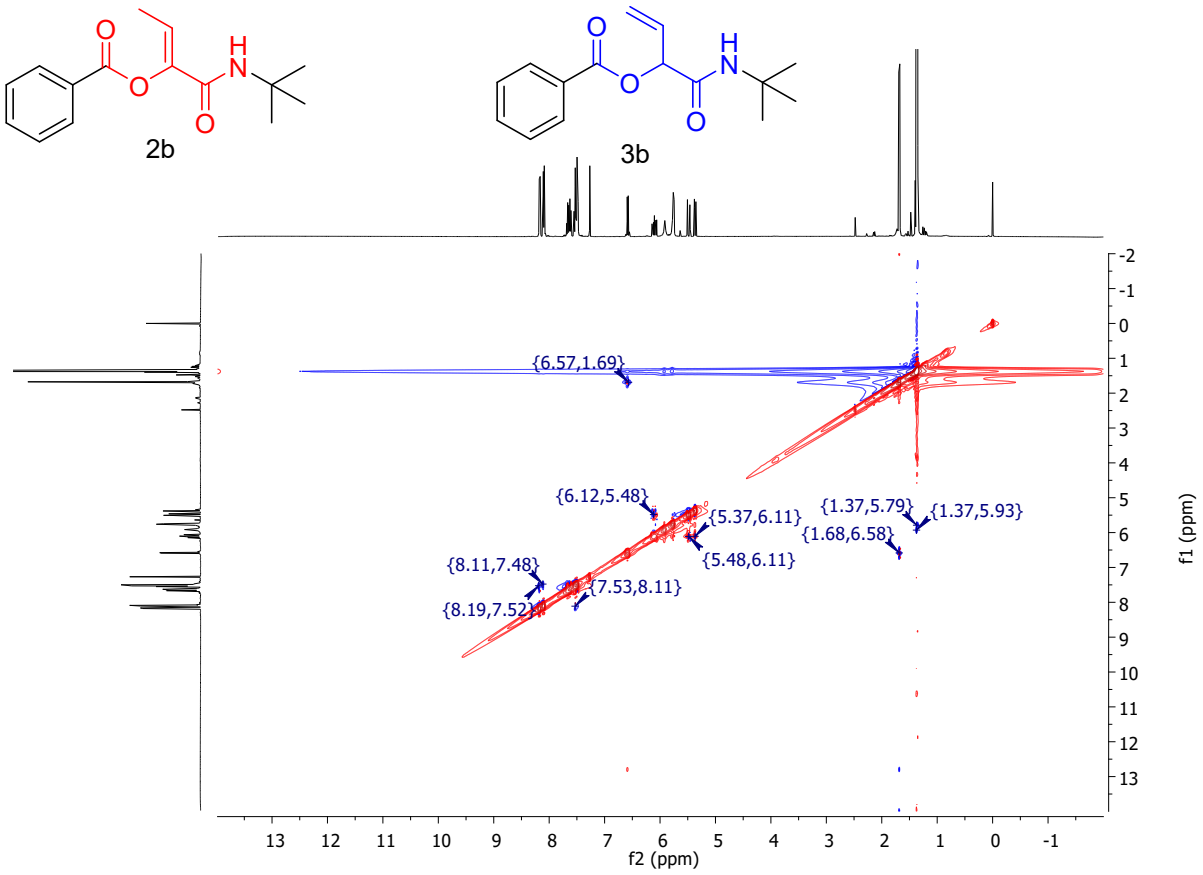
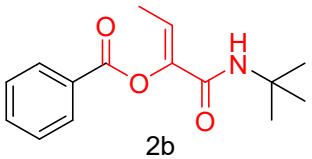
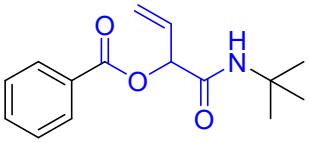


FIGURE 21. NOESY spectra in $CDCl_3$ of ***2b*** and ***3b***.



2b



3b

Compound Spectrum SmartFormula Report

Analysis Info

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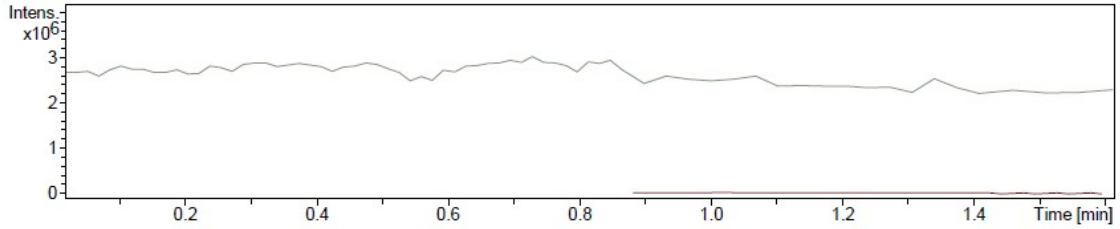
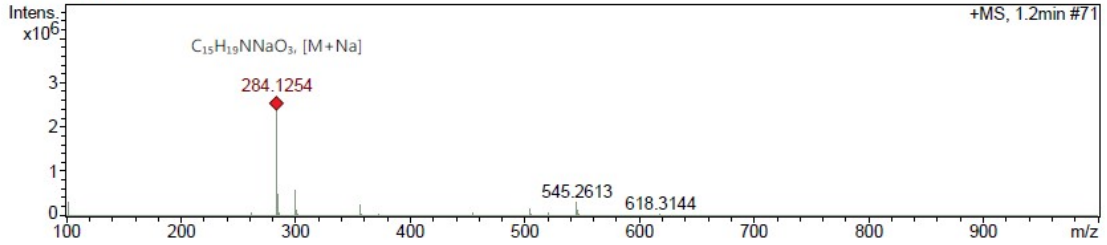
Method	MS_method_DirectInfusion_pos_AP.m	Operator	Demo User
Sample Name	DirectInfusion_PI_35	Instrument	compact 8255754.20175
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.6 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	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



+MS, 1.2min #71



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule	Adduct
284.1254	1	C15H19NNaO3	284.1257	1.2	24.7	1	100.00	7.0	even	ok	M+Na

+MS2(284.1254), 10.0-25.0eV, 1.2min #72

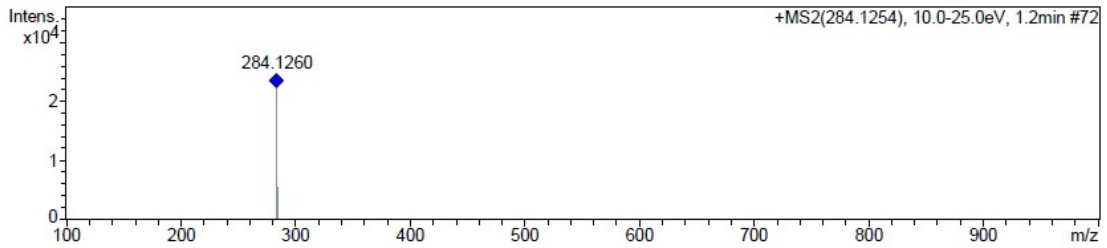
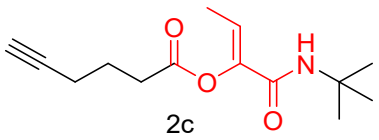
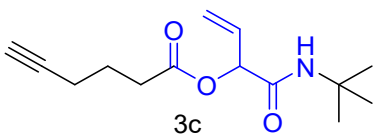


FIGURE 22- HRMS (ESI-FT-ICR) m/z spectra of **2b** and **3b**.



2c



3c

(Z)-1-(tert-butylamino)-1-oxobut-2-en-2-yl hex-5-ynoate (2c)

1-(tert-butylamino)-1-oxobut-3-en-2-yl hex-5-ynoate (3c)

2-(phenylselanyl)propanal (43 mg, 0.2 mmol, 1 equiv.), , hex-5-ynoic acid (22 µL, 0.2 mmol) and terbutyl isocyanide (23 µL, 0.2 mmol) were dissolved in 1mL of THF and reacted according to the general P-3CR/oxidative-elimination procedure (B). Flash column chromatography purification (Hex/EtOAc from 4:1 to 1:1 v/v) afforded compounds 2***c*** and 3c (19 mg, 38%) as a yellow sticky oil. R_f = 0.55 (Hex/EtOAc 1:1 v/v). A mixture of compounds 2***c*** and 3c in a 0.4:1.0 ratio was observed by NMR analysis.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.41 (q, J = 7.2 Hz, 1H), 5.96 (ddd, J = 16.8, 10.5, 6.0 Hz, 1H), 5.82 (bs, 1H, NH), 5.71 (bs, 1H, NH), 5.49 (d, J = 6.0 Hz, 1H), 5.43 – 5.36 (m, 1H), 5.33 (d, J = 10.5 Hz, 1H), 2.70 (t, J = 7.3 Hz, 2H), 2.60 (td, J = 7.2, 1.4 Hz, 2H), 2.37 – 2.28 (m, 3H), 2.04 – 1.84 (m, 5H), 1.63 (d, J = 7.2 Hz, 3H), 1.37 (s, 9H), 1.36 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 170.0, 167.0, 161.2, 142.1, 132.1, 121.2, 118.9, 83.0, 82.8, 74.7, 69.8, 69.6, 51.5, 51.4, 32.8, 32.3, 28.7, 28.7, 23.5, 23.4, 17.8, 17.7, 11.6.

HRMS (ESI-FT-ICR) m/z: 274.1410 $[M+Na]^+$; calcd. for: $C_{14}H_{21}NNaO_3$: 274.1419.

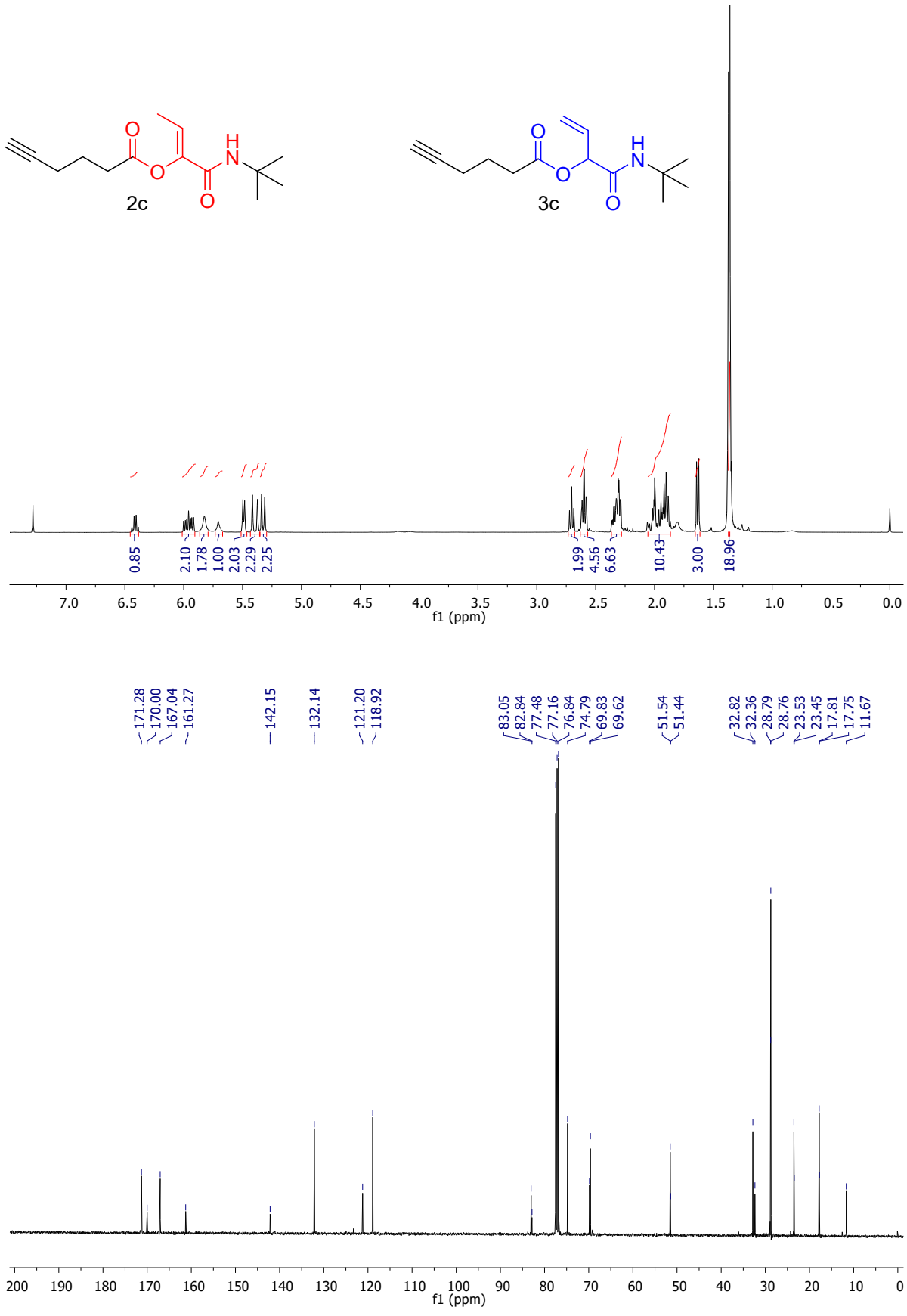


FIGURE 23. ^{1}H and ^{13}C NMR spectra in $CDCl_3$ of ***2c*** and ***3c***.

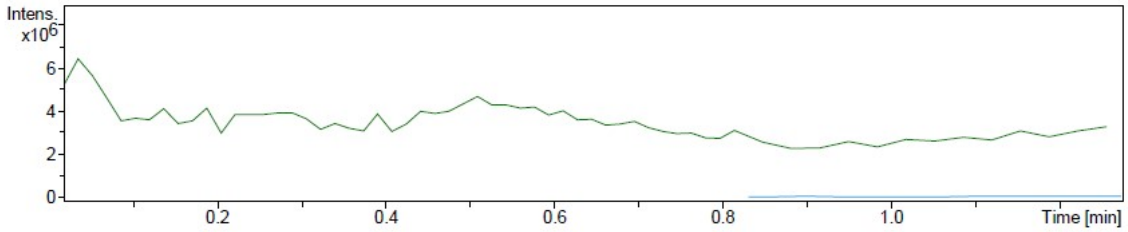
Compound Spectrum SmartFormula Report

Analysis Info

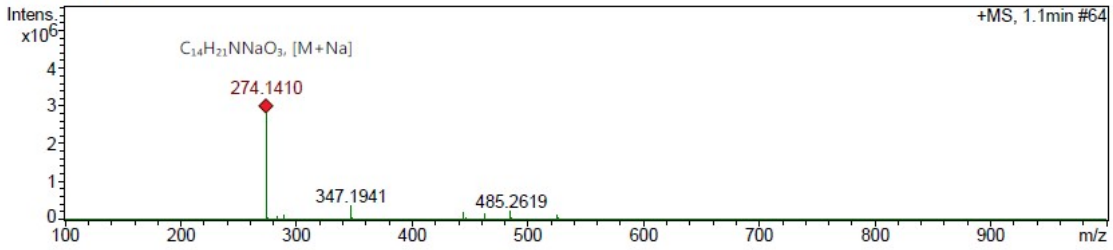
Analysis Name	D:\Data\AP_data\2021.11.19_AFernandez_servicio\DirectInfusion_PI_37b.d	Acquisition Date	11/22/2021 5:59:28 PM
Method	MS_method_DirectInfusion_pos_AP.m	Operator	Demo User
Sample Name	DirectInfusion_PI_37b	Instrument	compact 8255754.20175
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.6 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	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



+MS, 1.1min #64



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule	Adduct
274.1410	1	C14H21NNaO3	274.1414	1.4	5.8	1	100.00	5.0	even	ok	M+Na

+MS2(274.1410), 10.0-25.0eV, 1.1min #65

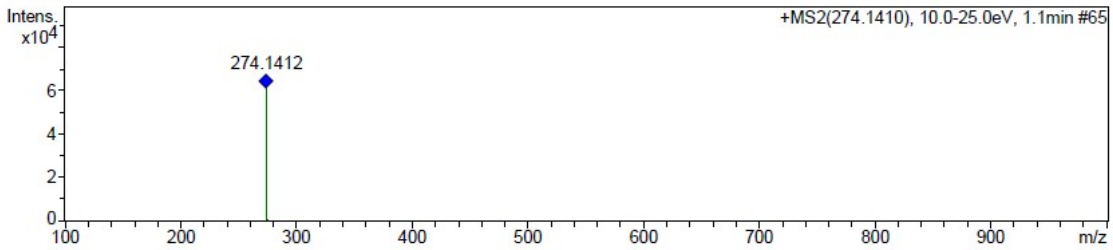
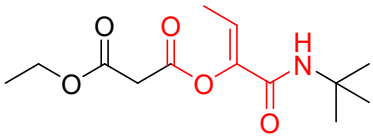
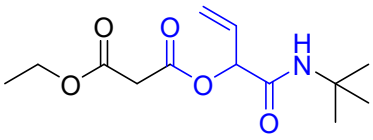


FIGURE 24- HRMS (ESI-FT-ICR) m/z spectra of **2c** and **3c**.



2d



3d

(Z)-1-(tert-butylamino)-1-oxobut-2-en-2-yl ethyl malonate (2d)
1-(tert-butylamino)-1-oxobut-3-en-2-yl ethyl malonate (3d)

2-(phenylselanyl)propanal (43 mg, 0.2 mmol, 1 equiv.), 3-ethoxy-3-oxopropanoic acid (24 µL, 0.2 mmol), and terbutyl isocyanide (23 µL, 0.2 mmol) were dissolved in 1mL of THF and reacted according to the general P-3CR/oxidative-elimination procedure (B). Flash column chromatography purification (Hex/EtOAc from 4:1 to 1:1 v/v) afforded compounds 2***d*** and ***3d*** (26 mg, 48%) as a colorless sticky oil. R_f= 0.25 (Hex/EtOAc 1:1 v/v). A mixture of compounds 2***d*** and ***3d*** in a 0.4:1.0 ratio was observed by NMR analysis.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.65 (q, J = 7.1 Hz, 1H), 5.95 (ddd, J = 16.6, 10.5, 5.9 Hz, 1H), 5.60 (d, J = 5.8 Hz, 1H), 5.39 (d, J = 17.2 Hz, 1H), 5.32 (d, J = 10.5 Hz, 1H), 4.27 – 4.21 (m, 2H), 3.56 (d, J = 16.4 Hz, 2H), 3.45 (d, J = 16.3 Hz, 1H), 1.71 (s, 1H), 1.63 (d, J = 7.3 Hz, 1H), 1.37 (s, 18H), 1.33 (dd, J = 8.2, 3.9 Hz, 4H), 1.31 (t, J = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 167.3, 166.8, 164.6, 163.1, 160.4, 141.7, 135.8, 131.7, 129.5, 122.7, 118.7, 77.4, 77.3, 77.1, 76.8, 75.2, 62.4, 62.1, 51.6, 51.5, 41.3, 41.0, 28.6, 28.6, 14.2, 11.7.

HRMS (ESI-FT-ICR) m/z: 272.1501 $[M+H]^+$; calcd. for $C_{13}H_{22}NO_5$: 272.1498.

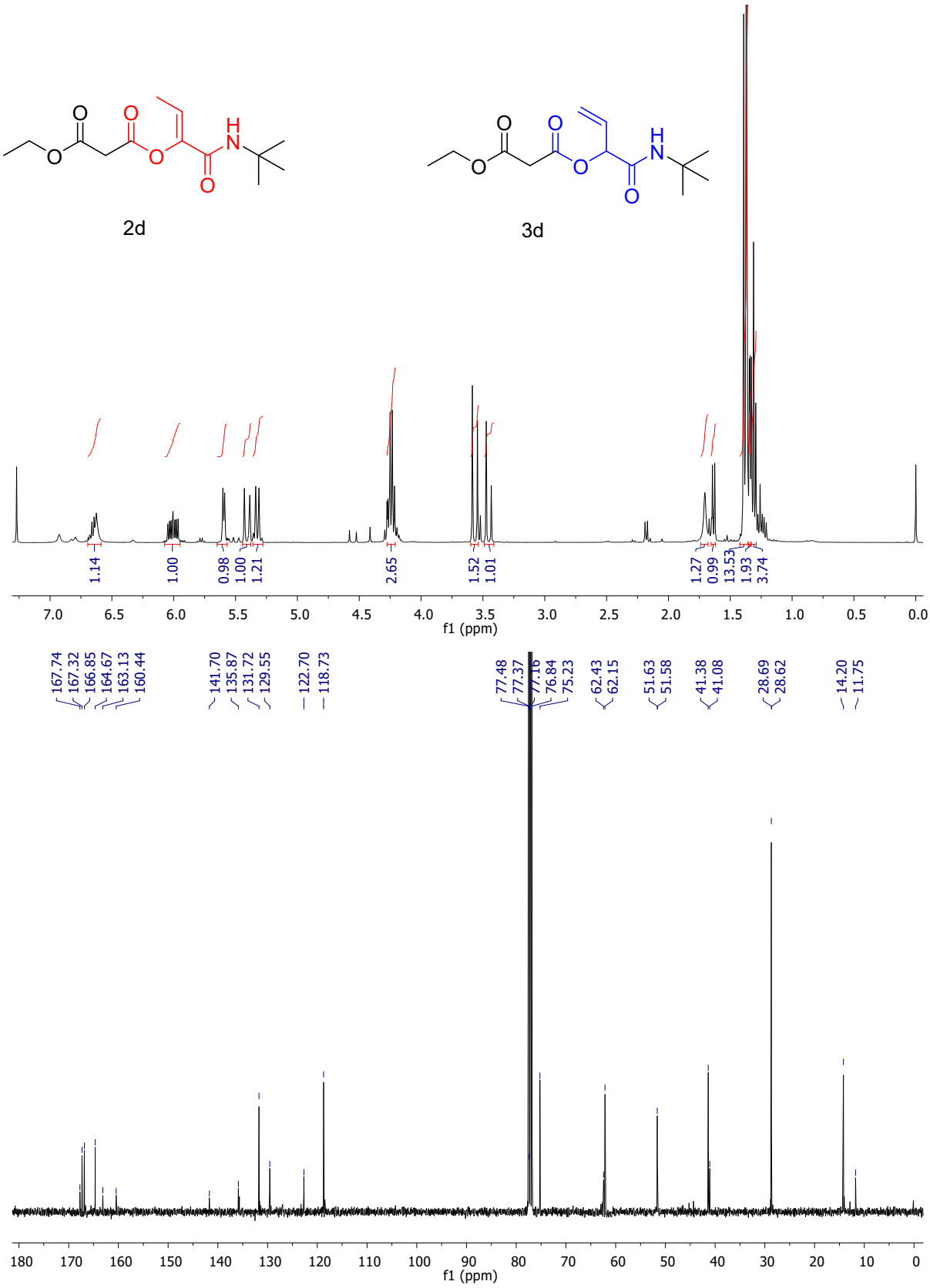
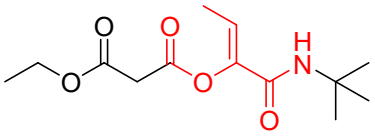
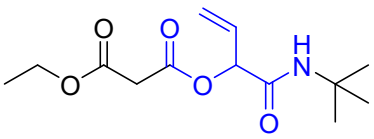


FIGURE 25. ^{1}H and ^{13}C NMR spectra in $CDCl_3$ of ***2d*** and ***3d***.



2d



3d

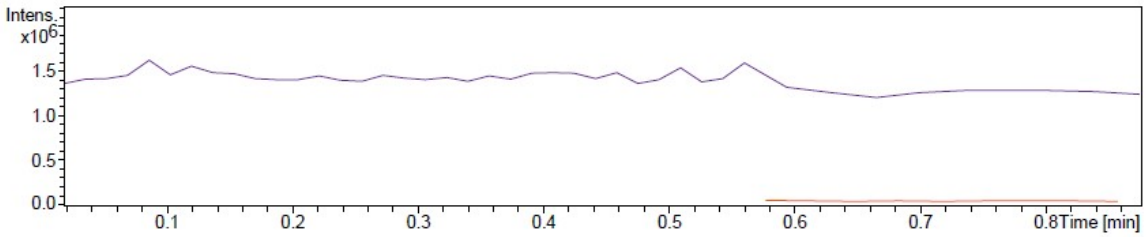
Compound Spectrum SmartFormula Report

Analysis Info

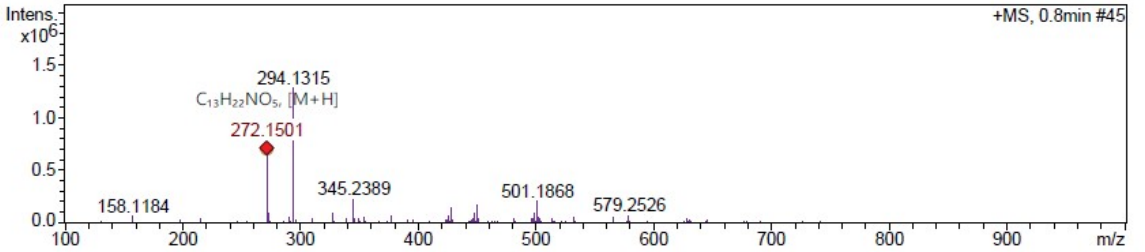
Analysis Name	E:\3. Servicios_tecnicos\2021.11.16_Alexander Fernandez\2021.11.19_AFernandez_servicio\DirectInfusion_PI_39.d	Acquisition Date	22-11-2021 18:04:10
Method	MS_method_DirectInfusion_pos_AP.m	Operator	Demo User
Sample Name	DirectInfusion_PI_39	Instrument	compact 8255754.20175
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.6 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	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



+MS, 0.8min #45



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e¯ Conf	N-Rule	Adduct
272.1501	1	C13H22NO5	272.1492	-3.1	3.6	1	100.00	4.0	even	ok	M+H

+MS2(272.1501), 10.0-25.0eV, 0.8min #46

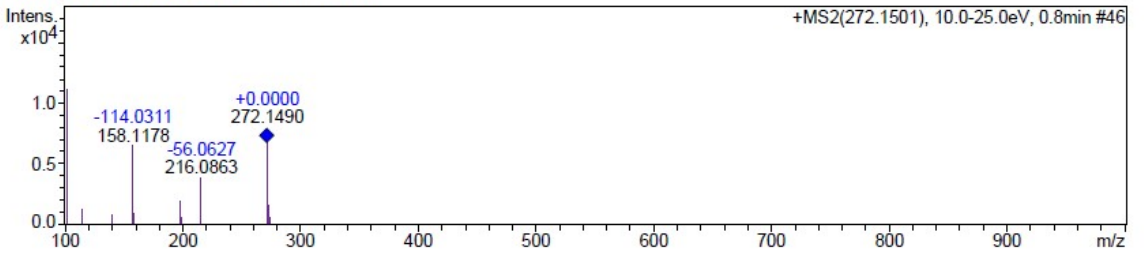
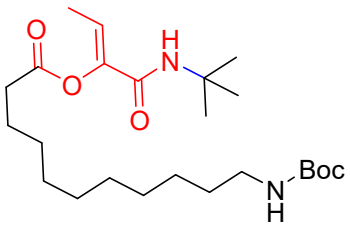
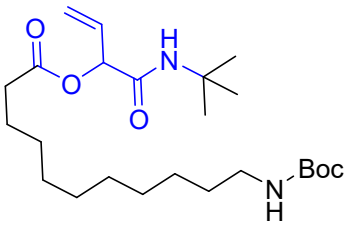


FIGURE 26- HRMS (ESI-FT-ICR) m/z spectra of **2d** and **3d**.



2e



3e

(Z)-1-(tert-butylamino)-1-oxobut-2-en-2-yl 11-((tert-butoxycarbonyl)amino)undecanoate (2e)
1-(tert-butylamino)-1-oxobut-3-en-2-yl 11-((tert-butoxycarbonyl)amino)undecanoate (3e)

2-(phenylselanyl)propanal (43 mg, 0.2 mmol, 1 equiv.), 11-((tert-butoxycarbonyl)amino)undecanoic acid (60 mg, 0.2 mmol), and terbutyl isocyanide (23 µL, 0.2 mmol) were dissolved in 1mL of THF and reacted according to the general P-3CR/oxidative-elimination procedure (B). Flash column chromatography purification (Hex/EtOAc from 9:1 to 1:1 v/v) afforded compounds ***2e*** and ***3e*** (31 mg, 35%) as a yellow sticky oil. R_f = 0.65 (Hex/EtOAc 1:1 v/v). A mixture of compounds ***2e*** and ***3e*** in a 0.44:1.0 (2e:2e´) ratio was observed by NMR analysis.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.43 (q, *J* = 7.1 Hz, 1H), 5.95 (ddd, *J* = 16.6, 10.5, 5.9 Hz, 1H), 5.81 (s, 1H), 5.68 (s, 1H), 5.49 (d, *J* = 5.8 Hz, 1H), 5.37 (d, *J* = 17.2 Hz, 1H), 5.30 (d, *J* = 10.5 Hz, 1H), 4.49 (s, 1H), 3.09 (bs, 3H), 2.51 (t, *J* = 7.5 Hz, 1H), 2.42 (t, *J* = 7.5 Hz, 2H), 1.69 (m, 3H), 1.62 (d, *J* = 7.2 Hz, 2H), 1.44 (s, 18H), 1.35 (s, 18H), 1.27 (s, 18H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 170.6, 167.2, 161.3, 156.1, 142.1, 132.2, 121.3, 118.7, 74.5, 51.4, 51.4, 40.8, 34.4, 34.1, 30.2, 29.5, 29.4, 29.3, 29.3, 29.2, 28.7, 28.5, 26.9, 25.1, 25.0, 11.7.

HRMS (ESI-FT-ICR) *m/z*: 441.3333 $[M+H]^+$; calcd. for $C_{24}H_{45}N_2O_5$: 441.3328.

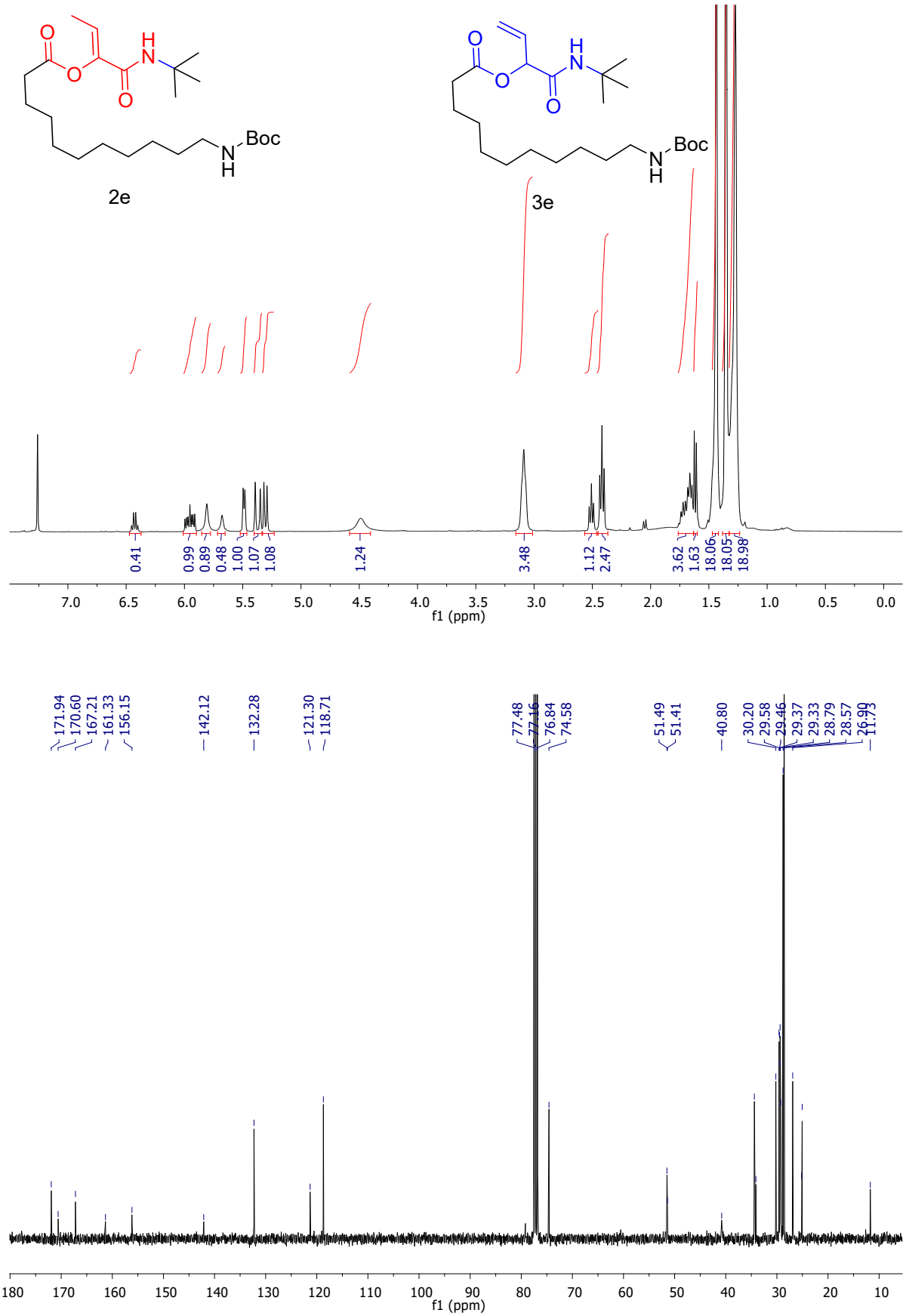
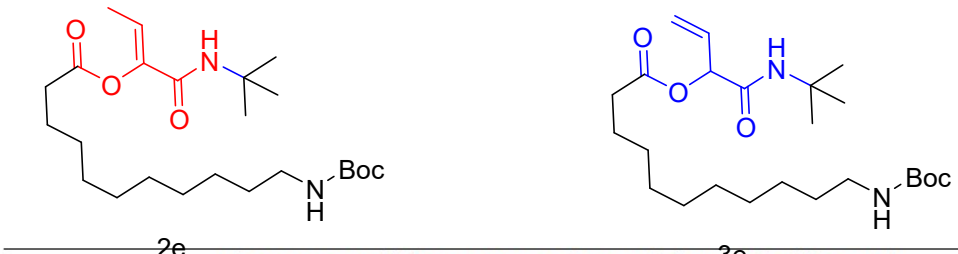


FIGURE 27. ^{1}H and ^{13}C NMR spectra in $CDCl_3$ of ***2e*** and ***3e***.



2e 3e

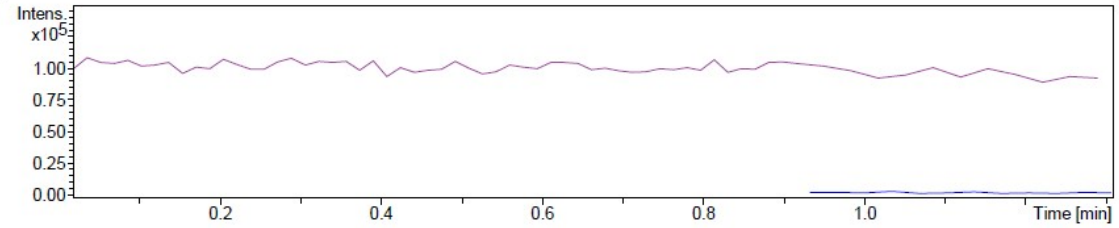
Compound Spectrum SmartFormula Report

Analysis Info

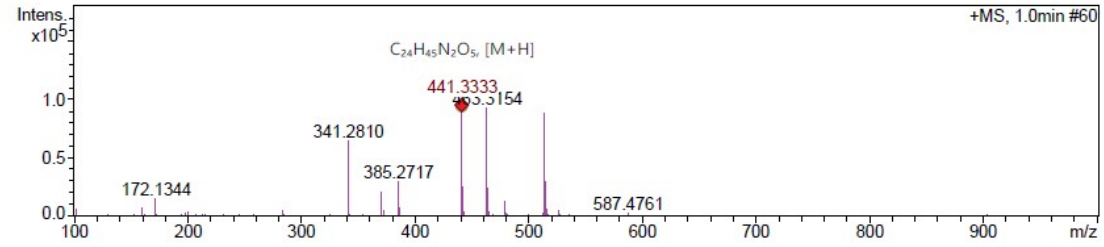
Analysis Name	E:\3. Servicios_tecnicos\2021.11.16_Alexander Fernandez\2021.11.19_AFernandez_servicio\DirectInfusion_PI_38.d	Acquisition Date	22-11-2021 17:50:52
Method	MS_method_DirectInfusion_pos_AP.m	Operator	Demo User
Sample Name	DirectInfusion_PI_38	Instrument	compact 8255754.20175
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.6 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	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



+MS, 1.0min #60



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule	Adduct
441.3333	1	C24H45N2O5	441.3323	-2.3	6.1	1	100.00	4.0	even	ok	M+H

+MS2(441.3333), 10.0-25.0eV, 1.0min #61

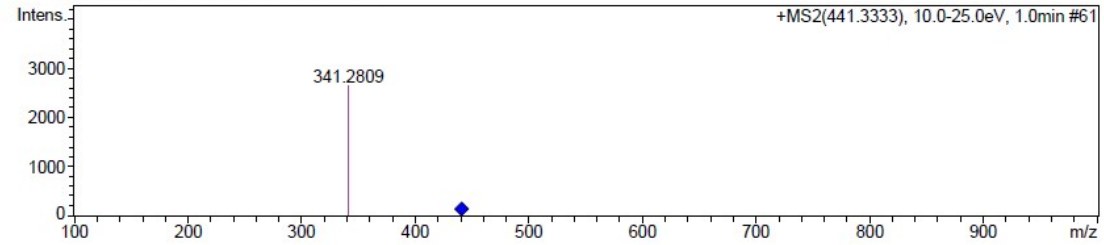
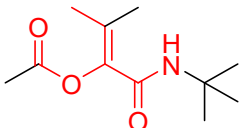
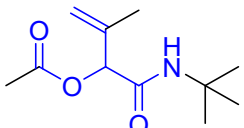


FIGURE 28- HRMS (ESI-FT-ICR) m/z spectra of **2e** and **3e**.



2f



3f

1-(tert-butylamino)-3-methyl-1-oxobut-2-en-2-yl acetate (2f)
1-(tert-butylamino)-3-methyl-1-oxobut-3-en-2-yl acetate (3f)

2-methyl-2-(phenylselanyl)propanal (45 mg, 0.2 mmol, 1 equiv.), acetic acid (11 µL, 0.2 mmol), and terbutyl isocyanide (23 µL, 0.2 mmol) were dissolved in 1mL of THF and reacted according to the general P-3CR/oxidative-elimination procedure (B). Flash column chromatography purification (Hex/EtOAc from 4:1 to 1:1 v/v) afforded compounds 2f and 3f (11 mg, 26%) as a yellow sticky oil. R_f = 0.55 (Hex/EtOAc 1:1 v/v). A mixture of compounds 2f and 3f in 0.6:1 was observed by NMR analysis.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.59 (s, 1H, NH), 5.78 (s, 1H, NH), 5.38 (d, J = 18.2 Hz, 1H), 5.13 (d, J = 13.7 Hz, 1H), 2.15 (s, 3H), 1.76 (s, 3H), 1.35 (s, 18H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 163.9, 139.9, 116.7, 72.8, 52.0, 28.8, 20.9, 18.3.

HRMS (ESI-FT-ICR) m/z: 214.1441 $[M+H]^+$; calcd. for $C_{11}H_{20}NO_3$: 214.1443.

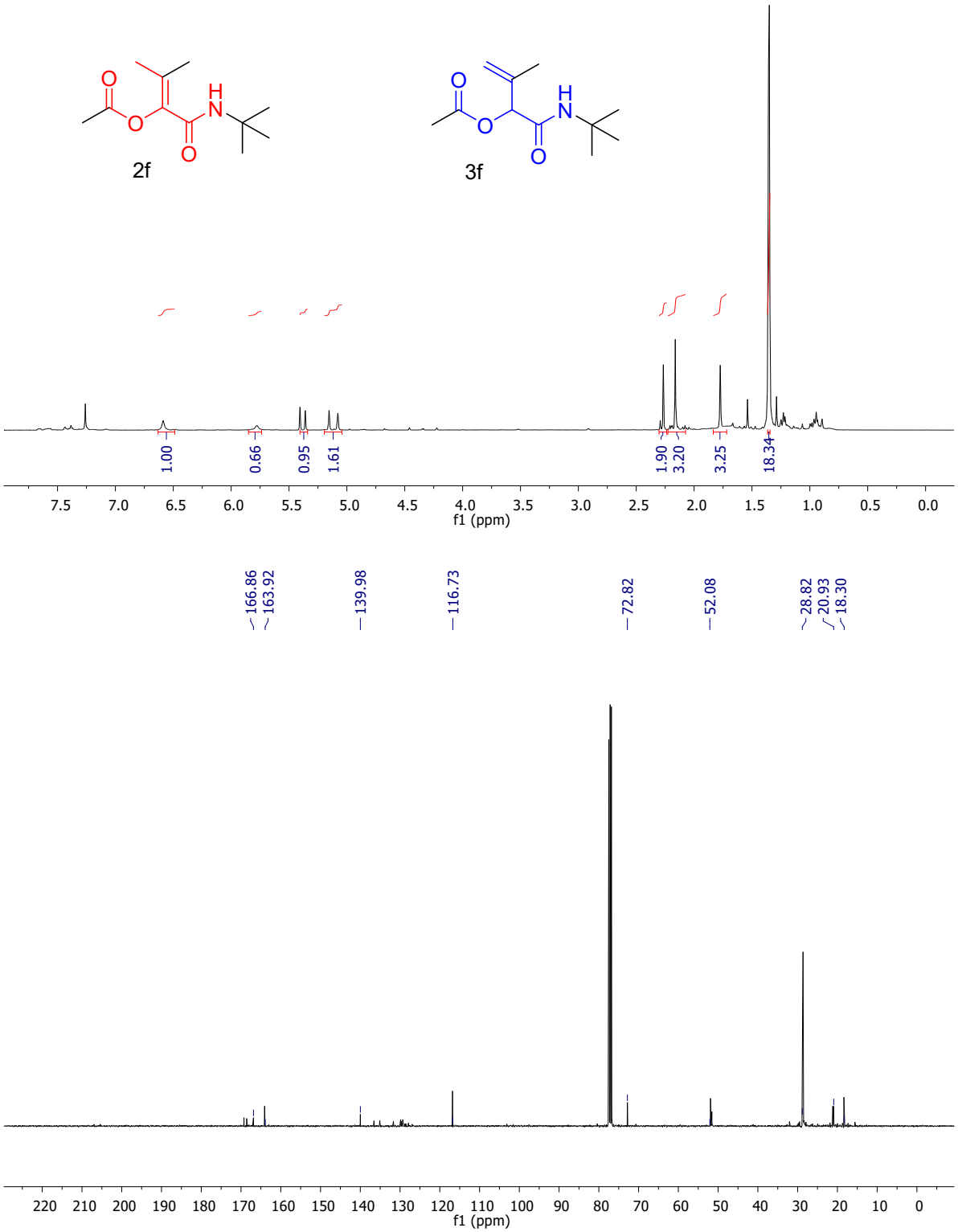
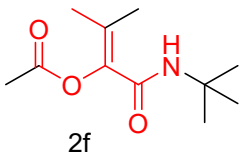
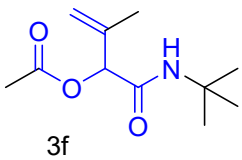


FIGURE 29. ^{1}H and ^{13}C NMR spectra in $CDCl_3$ of ***2f*** and ***3f***.



2f



3f

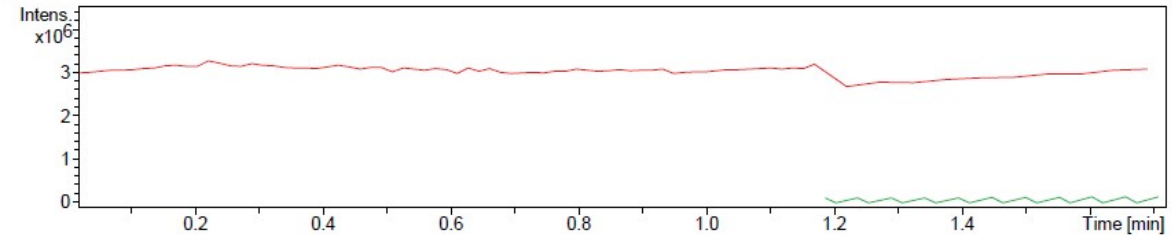
Compound Spectrum SmartFormula Report

Analysis Info

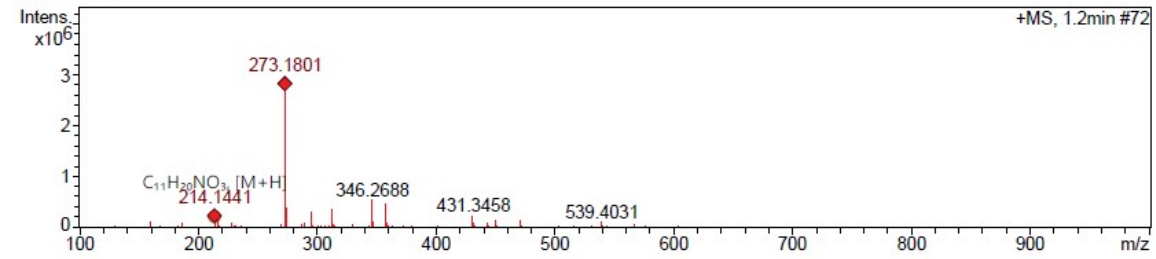
Analysis Name	E:\3. Servicios_tecnicos\2021.11.16_Alexander Fernandez\2021.11.19_AFernandez_servicio\DirectInfusion_PI_78.d	Acquisition Date	23-11-2021 11:47:53
Method	MS_method_DirectInfusion_pos_AP.m	Operator	Demo User
Sample Name	DirectInfusion_PI_78	Instrument	compact 8255754.20175
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.6 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	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



+MS, 1.2min #72



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule	Adduct
214.1441	1	C11H20NO3	214.1438	-1.4	102.0	1	100.00	3.0	even	ok	M+H

+MS2(214.1441), 10.0-25.0eV, 1.3min #74

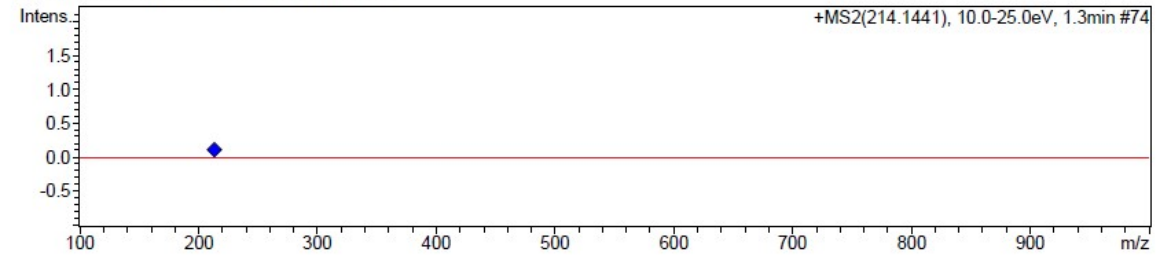
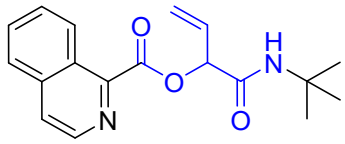


FIGURE 30- HRMS (ESI-FT-ICR) m/z spectra of **2f** and **3f**.



1-(tert-butylamino)-1-oxobut-3-en-2-yl isoquinoline-1-carboxylate (3g)

2-(phenylselanyl)propanal (43 mg, 0.2 mmol, 1 equiv.), isoquinoline-1-carboxylic acid (35 mg, 0.2 mmol), and terbutyl isocyanide (23 µL, 0.2 mmol) were dissolved in 1mL of THF and reacted according to the general P-3CR/oxidative-elimination procedure (B). Flash column chromatography purification (Hex/EtOAc from 9:1 to 1:1 v/v) afforded compound 3f (27.5 mg, 44%) as a yellow sticky oil. R_f = 0.25 (Hex/EtOAc 1:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, J = 8.4 Hz, 1H), 8.62 (d, J = 5.5 Hz, 1H), 7.92 (dd, J = 14.4, 6.8 Hz, 2H), 7.77 (dt, J = 16.1, 7.3 Hz, 2H), 7.30 (b.s, 1H, NH), 6.25 – 6.14 (m, 1H), 5.95 (d, J = 5.6 Hz, 1H), 5.58 (d, J = 17.2 Hz, 1H), 5.41 (d, J = 10.6 Hz, 1H), 1.44 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 164.2, 148.1, 141.5, 137.0, 131.7, 131.0, 129.2, 127.2, 126.9, 126.1, 124.8, 118.9, 76.8, 75.4, 51.5, 28.7.

HRMS (ESI-FT-ICR) m/z: 313.1546 $[M+H]^+$; calcd. for: $C_{18}H_{21}N_2O_3$: 313.1552.

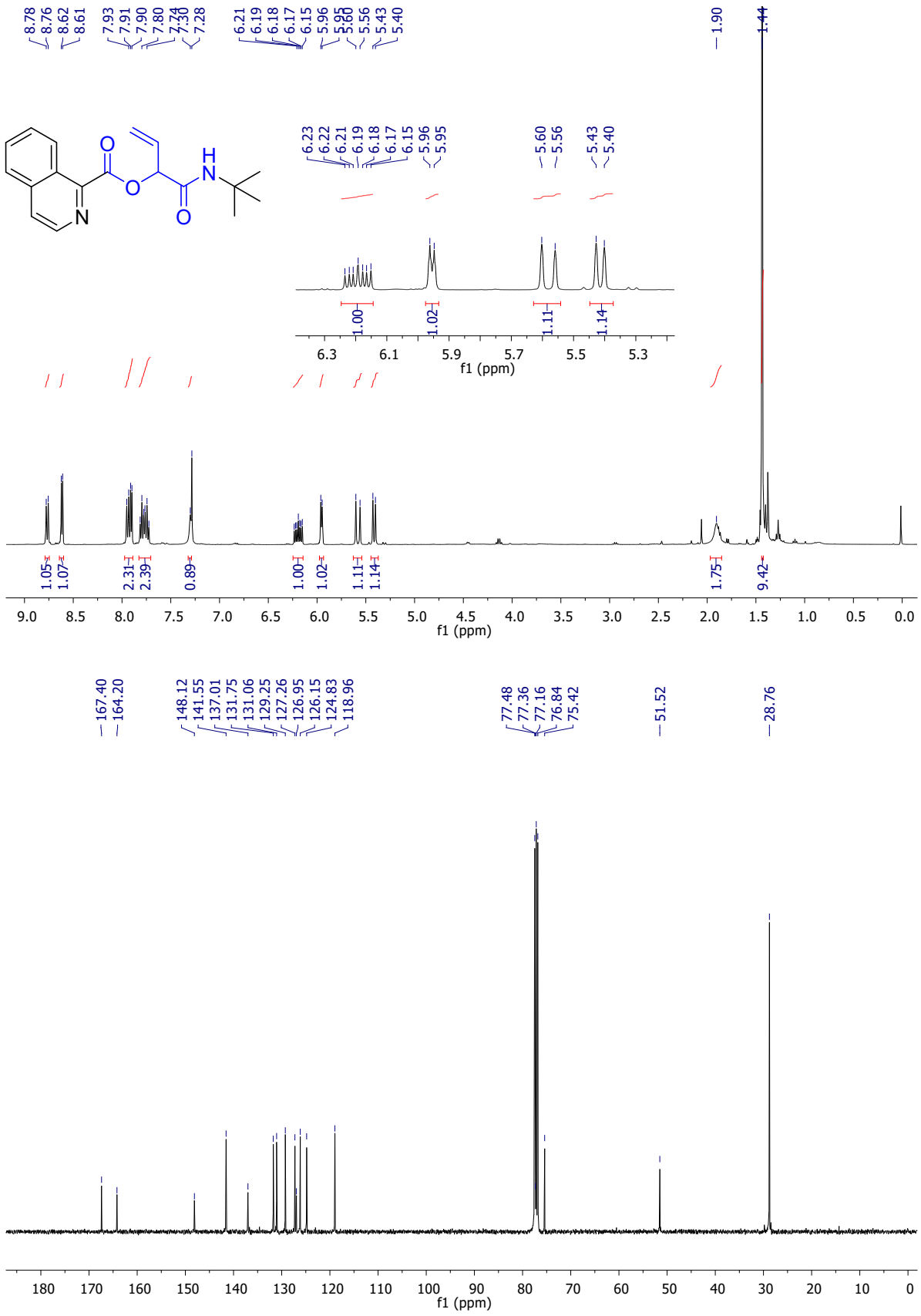
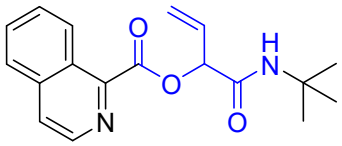


FIGURE 31. ^{1}H and ^{13}C NMR spectra in $CDCl_3$ of ***3g***.



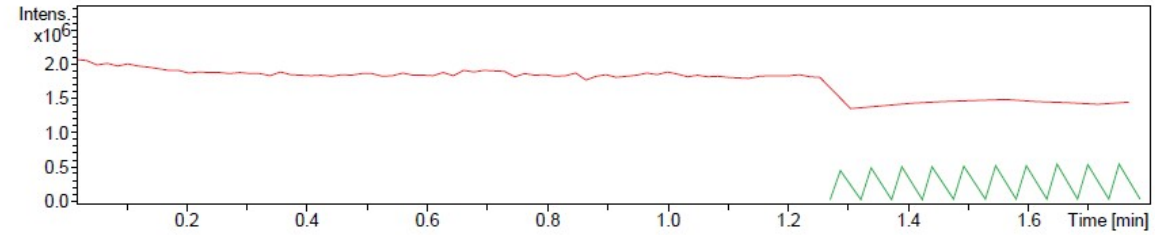
Compound Spectrum SmartFormula Report

Analysis Info

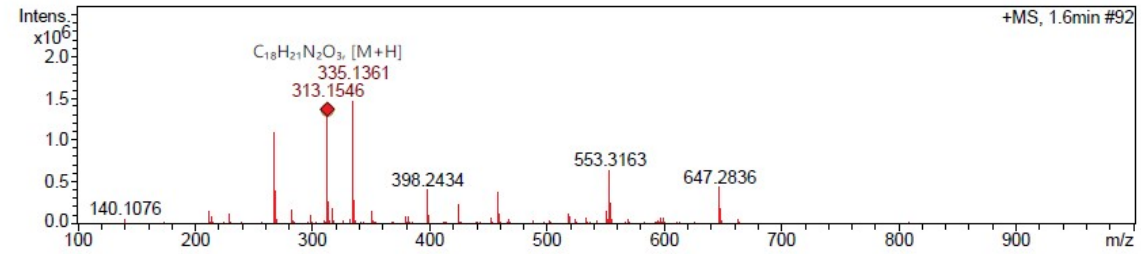
Analysis Name	E:\3. Servicios_tecnicos\2021.11.16_Alexander Fernandez\2021.11.19_AFernandez_servicio\DirectInfusion_PI_40.d	Acquisition Date	23-11-2021 10:53:55
Method	MS_method_DirectInfusion_pos_AP.m	Operator	Demo User
Sample Name	DirectInfusion_PI_40	Instrument	compact 8255754.20175
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.6 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	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



+MS, 1.6min #92



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule	Adduct
313.1546	1	C18H21N2O3	313.1547	0.3	5.1	1	100.00	10.0	even	ok	M+H

+MS2(313.1546), 10.0-25.0eV, 1.6min #94

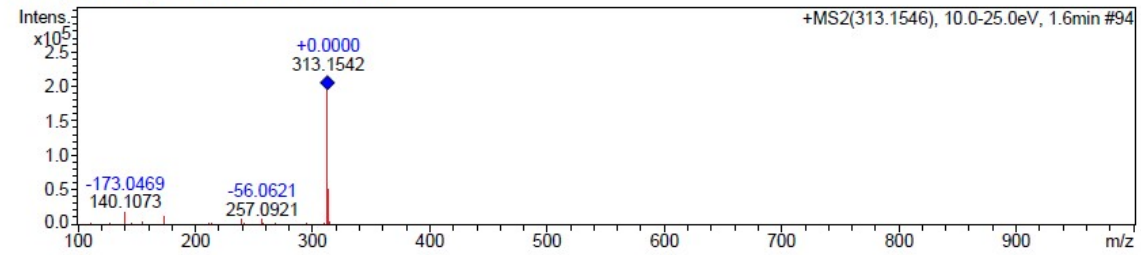
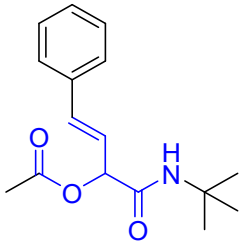


FIGURE 32- HRMS (ESI-FT-ICR) m/z spectra of **3g**.



(E)-1-(tert-butylamino)-1-oxo-4-phenylbut-3-en-2-yl acetate (3h)

3-phenyl-2-(phenylselanyl)propanal (58 mg, 0.2 mmol, 1 equiv.), acetic acid (11 µL, 0.2 mmol), and terbutyl isocyanide (23 µL, 0.2 mmol) were dissolved in 1mL of THF and reacted according to the general P-3CR/oxidative-elimination procedure (B).

Flash column chromatography purification (Hex/EtOAc from 4:1 to 1:1 v/v) afforded compound 3h (30 mg, 55%) as a yellow sticky oil. R_f = 0.60 (Hex/EtOAc 1:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 7.3 Hz, 2H), 7.35 – 7.25 (m, 3H), 6.72 (d, J = 16.0 Hz, 1H), 6.26 (dd, J = 16.0, 6.9 Hz, 1H), 5.85 (s, 1H), 5.62 (dd, J = 7.0, 0.6 Hz, 1H), 2.20 (s, 3H), 1.37 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 167.2, 135.8, 134.7, 128.7, 128.4, 126.9, 122.9, 77.4, 77.1, 76.8, 74.8, 51.6, 28.7, 21.1.

HRMS (ESI-FT-ICR) m/z: 298.1397 $[M+Na]^+$; calcd. for $C_{16}H_{21}NNaO_3$: 298.1419.

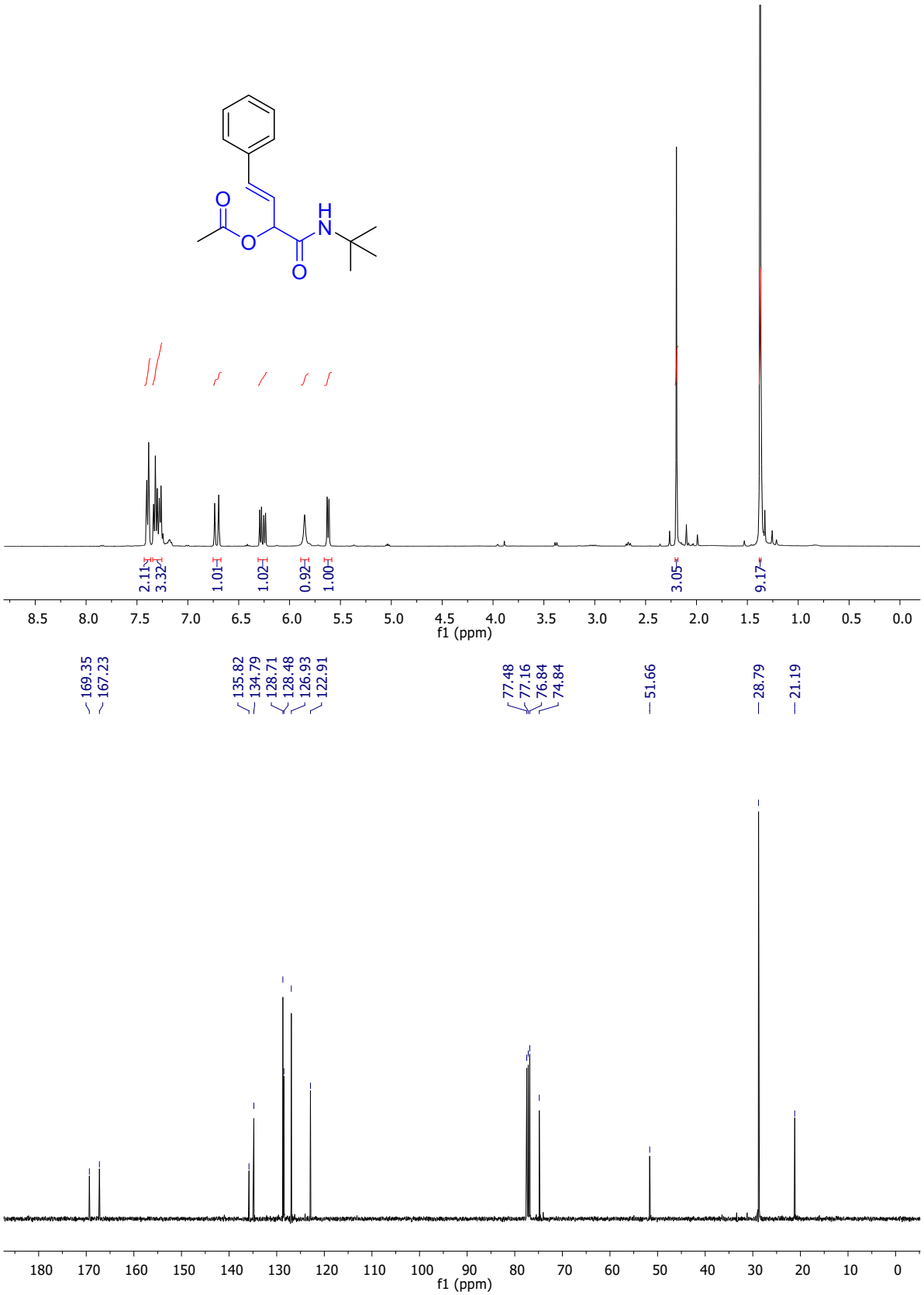
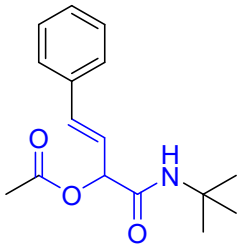


FIGURE 33. ^{1}H and ^{13}C NMR spectra in $CDCl_3$ of ***3h***.



Compound Spectrum SmartFormula Report

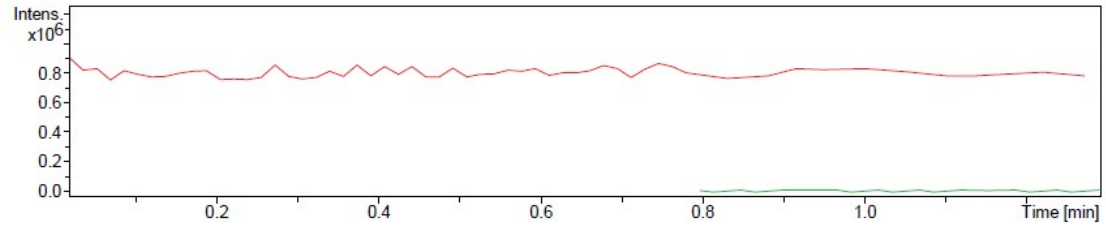
Analysis Info

Analysis Name	D:\Data\AP_data\2021.11.19_AFernandez_servicio\DirectInfusion_PI_71.d		
Method	MS_method_DirectInfusion_pos_AP.m	Operator	Demo User
Sample Name	DirectInfusion_PI_71	Instrument	compact 8255754.20175
Comment			

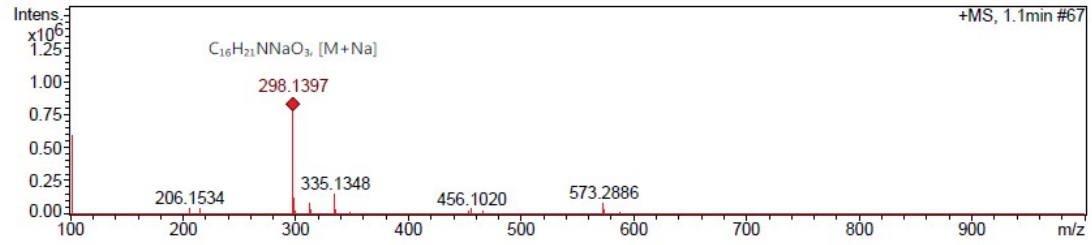
Acquisition Date 11/23/2021 11:41:09 AM

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.6 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	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



+MS, 1.1min #67



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e¯ Conf	N-Rule	Adduct
298.1397	1	C16H21NNaO3	298.1414	5.6	10.1	1	100.00	7.0	even	ok	M+Na

+MS2(298.1397), 10.0-25.0eV, 1.2min #68

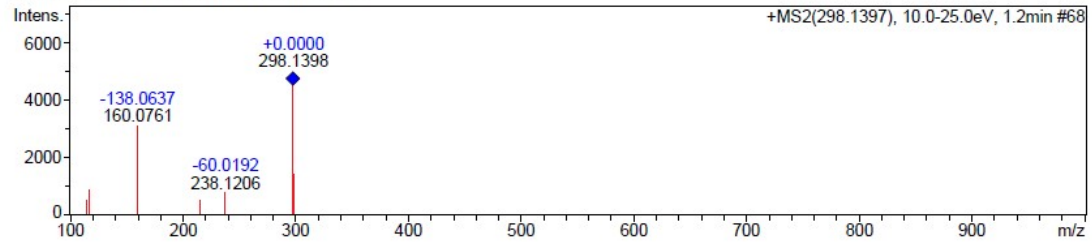
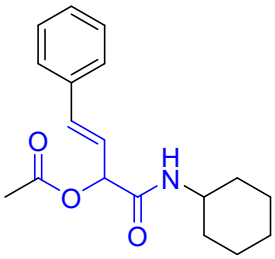


FIGURE 34- HRMS (ESI-FT-ICR) m/z spectra of **3h**.



(E)-1-(cyclohexylamino)-1-oxo-4-phenylbut-3-en-2-yl acetate (3i)

3-phenyl-2-(phenylselanyl)propanal (58 mg, 0.2 mmol, 1 equiv.), acetic acid (11 µL, 0.2 mmol), and cyclohexyl isocyanide (25 µL, 0.2 mmol) were dissolved in 1mL of THF and reacted according to the general P-3CR/oxidative-elimination procedure (B). Flash column chromatography purification (Hex/EtOAc from 4:1 to 1:1 v/v) afforded compound 3i (31 mg, 52%) as a yellow sticky oil. R_f = 0.60 (Hex/EtOAc 1:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.3 Hz, 2H), 7.32 (m, 3H), 6.75 (d, *J* = 16.0 Hz, 1H), 6.29 (dd, *J* = 15.9, 6.8 Hz, 1H), 5.93 (d, *J* = 7.4 Hz, 1H), 5.73 (d, *J* = 6.9 Hz, 1H), 3.90 – 3.75 (m, 1H), 2.26 (d, *J* = 27.4 Hz, 3H), 1.96 (d, *J* = 11.4 Hz, 2H), 1.69 (dd, *J* = 34.5, 12.7 Hz, 4H), 1.47 – 1.15 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 167.1, 135.8, 134.8, 128.7, 128.5, 126.9, 122.8, 74.6, 48.3, 33.1, 25.5, 24.9, 21.2.

HRMS (ESI-FT-ICR) m/z: 324.1549 $[M+Na]^+$; calcd. for $C_{18}H_{23}NNaO_3$: 324.1576

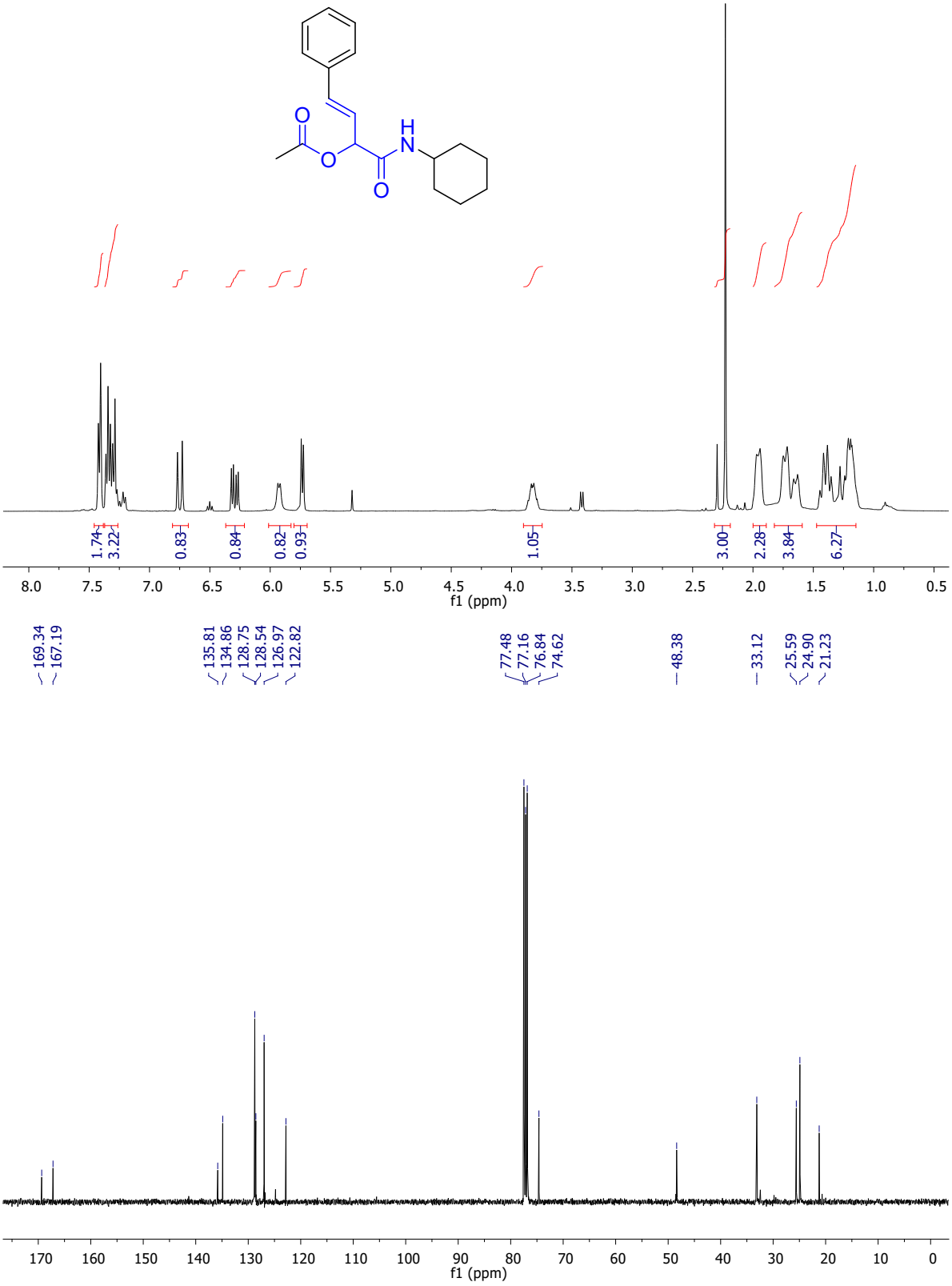


FIGURE 35. ^{1}H and ^{13}C NMR spectra in $CDCl_3$ of ***3i***.

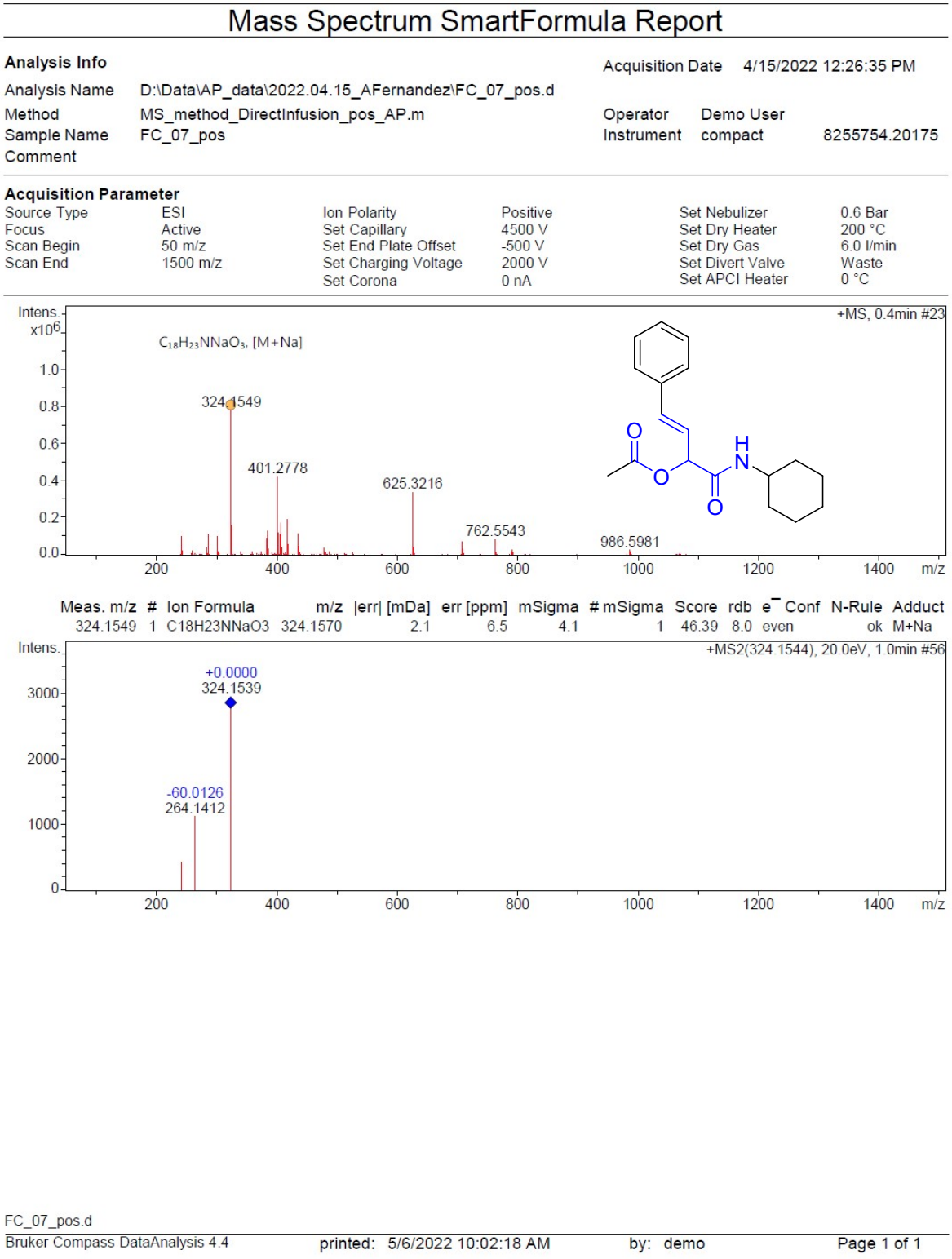
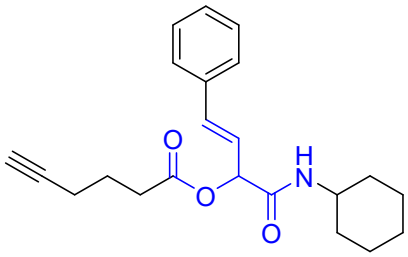


FIGURE 36- HRMS (ESI-FT-ICR) m/z spectra of **3i**.



(E)-1-(cyclohexylamino)-1-oxo-4-phenylbut-3-en-2-yl hex-5-ynoate (3j)

3-phenyl-2-(phenylselanyl)propanal (58 mg, 0.2 mmol, 1 equiv.), hex-5-ynoic acid (22 µL, 0.2 mmol), and cyclohexyl isocyanide (25 µL, 0.2 mmol) were dissolved in 1mL of 2-MeTHF and reacted according to the general P-3CR/oxidative-elimination procedure (B). Flash column chromatography purification (Hex/EtOAc from 4:1 to 1:1 v/v) afforded compound 3j (43mg, 61%) as a yellow sticky oil. R_f = 0.60 (Hex/EtOAc 1:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 7.6 Hz, 2H), 7.39 – 7.23 (m, 3H), 6.75 (d, J = 16.0 Hz, 1H), 6.30 (dd, J = 15.9, 6.8 Hz, 1H), 5.95 (d, J = 7.7 Hz, 1H), 5.76 (d, J = 6.8 Hz, 1H), 3.83 (dd, J = 11.6, 7.2 Hz, 1H), 2.69 – 2.59 (m, 2H), 2.35 (dd, J = 15.0, 8.8 Hz, 2H), 2.01 – 1.84 (m, 4H), 1.81 – 1.59 (m, 4H), 1.44 – 1.12 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 167.1, 135.8, 134.8, 128.7, 128.5, 126.9, 122.7, 83.1, 74.5, 69.7, 48.3, 33.1, 32.8, 25.5, 24.9, 23.5, 17.8.

HRMS (ESI-FT-ICR) m/z: 376.1866 $[M+Na]^+$; calcd. for $C_{22}H_{27}NNaO_3$: 376.1889

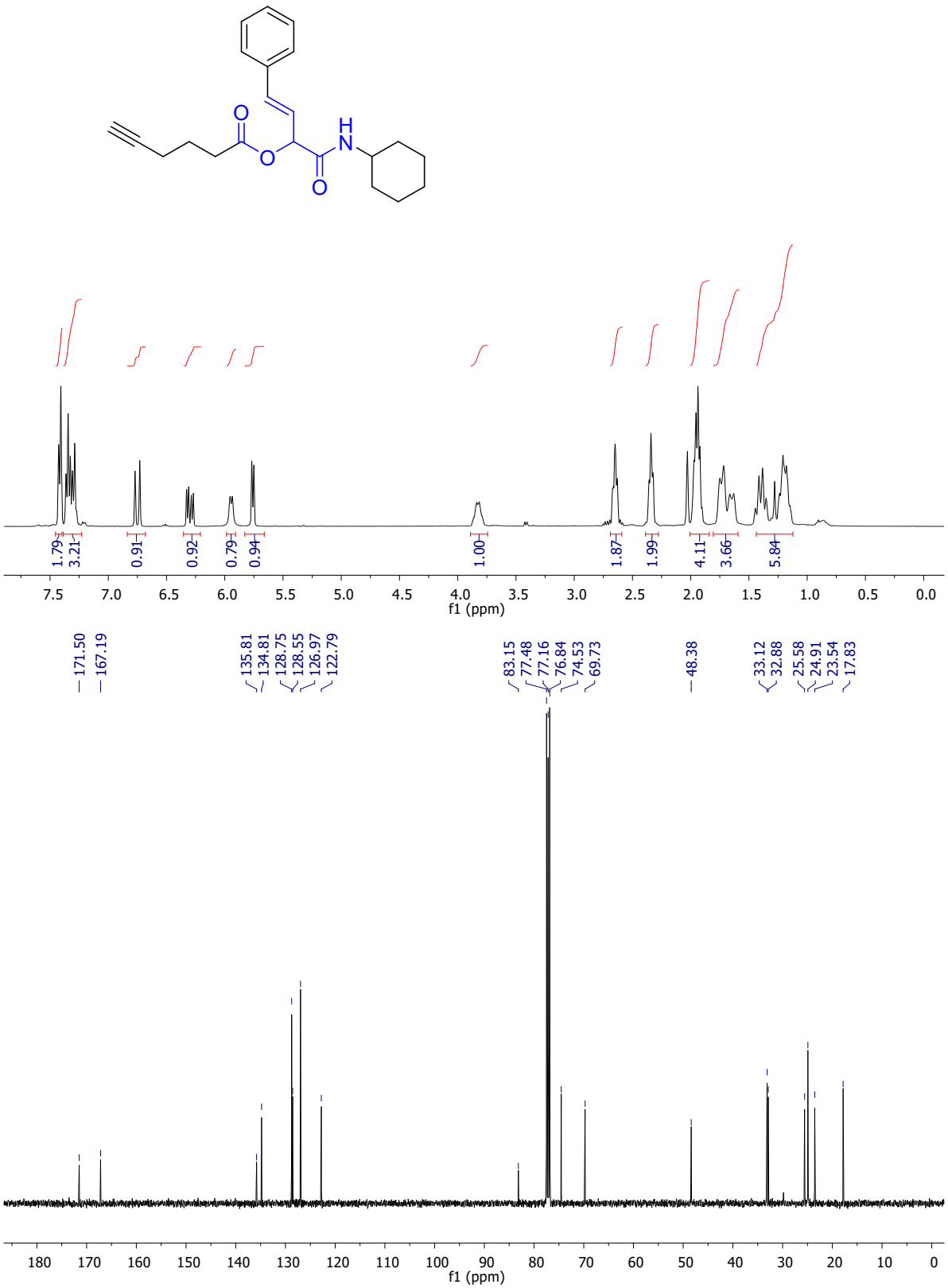


FIGURE 37. ^{1}H and ^{13}C NMR spectra in $CDCl_3$ of 3***j***.

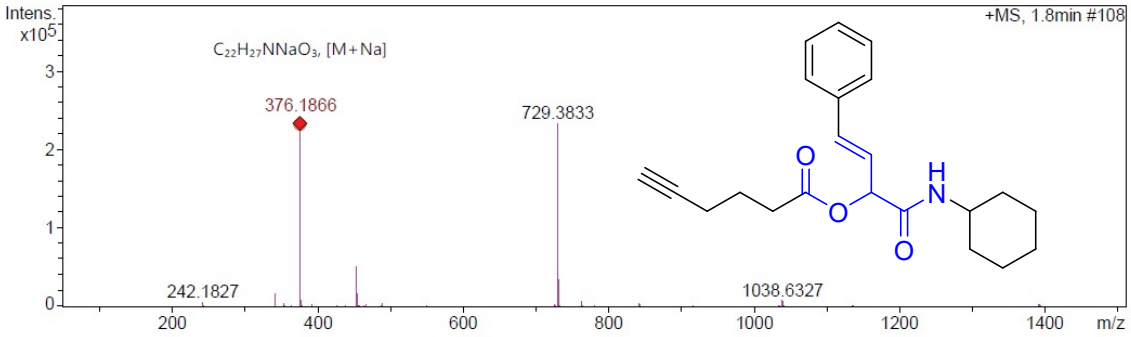
Mass Spectrum SmartFormula Report

Analysis Info

Analysis Name	D:\Data\AP_data\2022.04.15_AFernandez\FC_05_pos.d	Acquisition Date	4/15/2022 12:08:36 PM
Method	MS_method_DirectInfusion_pos_AP.m	Operator	Demo User
Sample Name	FC_05_pos	Instrument	compact 8255754.20175
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.6 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	1500 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



Meas. m/z	#	Ion Formula	m/z	|err| [mDa]	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule	Adduct
376.1866	1	C22H27NNaO3	376.1883	1.7	4.6	4.4	1	67.25	10.0	even	ok	M+Na

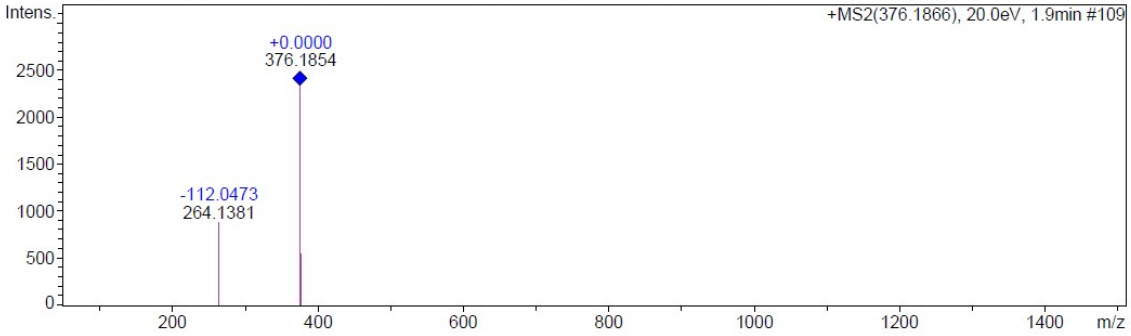


FIGURE 38- HRMS (ESI-FT-ICR) m/z spectra of **3j**.

References

1. W. L. E. Armarego and L. Li, Christina Chai, *Purification of laboratory chemicals (Fifth Edition)*, 2003.
2. G. R. Fulmer, A. J. M. Miller, N. H. Sherden, H. E. Gottlieb, A. Nudelman, B. M. Stoltz, J. E. Bercaw and K. I. Goldberg, *Organometallics*, 2010, **29**, 2176–2179.
3. M. Tiecco, A. Carlone, S. Sternativo, F. Marini, G. Bartoli and P. Melchiorre, *Angew Chem Int Ed.*, 2007, **46**, 6882.