Supporting Information

N-Alkenylation of Hydroxamic Acid Derivatives with Ethynyl Benziodoxolone to Synthesize *cis*-Enamides Through Vinyl Benziodoxolones

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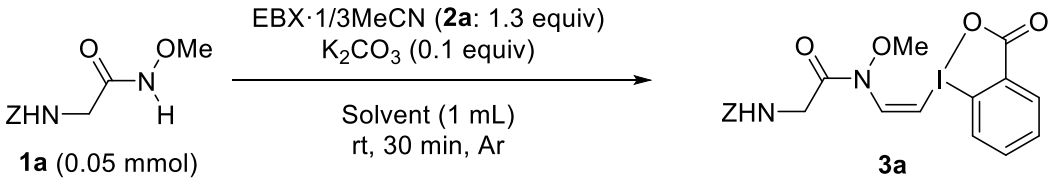
1. General information

All reactants and reagents including dry solvents were obtained from commercial suppliers and used as received. ^{1}H NMR and ^{13}C NMR spectra were obtained on a JEOL ECA 500 spectrometer (500 MHz for ^{1}H NMR, 125 MHz for ^{13}C NMR) and JEOL ECZ 400 spectrometer (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR). Chemical shifts (δ) are expressed in parts per million and are internally referenced [0.00 ppm (tetramethylsilane), 2.50 ppm (DMSO-d_6), 3.31 ppm (MeOH-d_4), and 2.05 ppm (acetone-d_6) for ^{1}H NMR; 77.0 ppm ($CHCl_3$), 39.51 ppm (DMSO-d_6), and 49.15 ppm (MeOH-d_4) for ^{13}C NMR]. The following abbreviations were used to express the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, sept = septet, non = nonet, m = multiplet, brs = broad singlet, dd = doublet of doublets, td = triplet of doublets, dt = doublet of triplets. High-resolution mass spectra (HRMS) were obtained on a JEOL JMS-T100TD and was reported as m/z (relative intensity). Analytical thin-layer chromatography (TLC) was carried out using 0.25 mm commercial silica gel plates (Merck silica gel 60 F254). Flash column chromatography was performed with Kanto silica gel 60N (Spherical, Neutral, 63-210 μm). Visualization of the developed chromatogram was performed by UV lamp (254 nm) and *p*-anisaldehyde or basic potassium permanganate stain.

2. Optimization of the reaction conditions

Table S1. Examination of solvent.



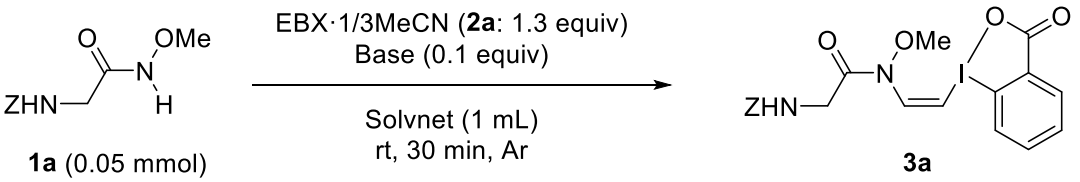
1a (0.05 mmol) **3a**

Entry	Sovent	Yields (%)[a]	
		3a	**1a**
1	MeOH	40	52
2	EtOH	32	40
3	TFE	10	90
4	1-propanol	39	61
5	IPA	53	22
6	HFIP	27	73
7	^{n}BuOH	8	35
8	^{t}BuOH	54	33
9	THF	0	16
10	^{t}BuOMe	23	53
11	$(MeOCH_2)_2$	62	13
12	MeCN	31	15
13	DCE	28	26
14	$CHCl_3$	58	37
15	toluene	44	22
16	EtOAc	1	5
17	acetone	24	15
18	DMF	7	27
19	MeOH:H_2O = 9:1	34	21
20	EtOH:H_2O = 9:1	49	51
21	TFE:H_2O = 9:1	39	61
22	1-propanol:H_2O = 9:1	24	40
23	IPA:H_2O = 9:1	38	62
24	HFIP:H_2O = 9:1	28	61
25	^{t}BuOH:H_2O = 9:1	47	50
26	^{t}BuOMe:H_2O = 9:1	14	56
27	$(MeOCH_2)_2$:H_2O = 9:1	49	28

28	MeCN:H_2O = 9:1	41	49
29	DCE:H_2O = 9:1	62	38
30	DCM:H_2O = 9:1	34	35
31	$CHCl_3$:H_2O = 9:1	24	30
32	toluene:H_2O = 9:1	1	43
33	acetone:H_2O = 9:1	24	46
34	MeCN:IPA = 1:1	37	26
35	DCE:IPA = 1:1	42	25

[a] Reaction conditions: **1a** (0.05 mmol), **2a** (1.3 equiv), K_2CO_3 (0.1 equiv), solvent (1 mL), rt, 30 min, argon. Yields were determined by ^1H NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard.

Table S2. Examination of base.



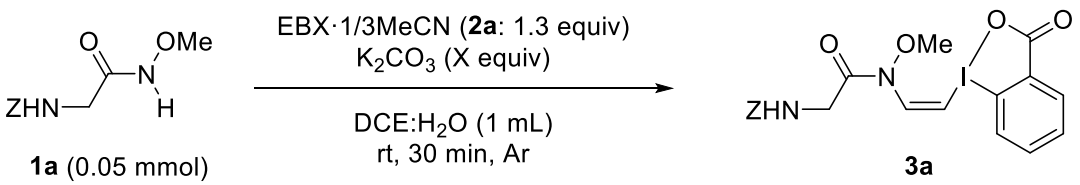
1a (0.05 mmol) **3a**

Entry	Base	Solvent	Yields (%)[a]	
			3a	**1a**
1	none	DCE:H_2O = 9:1	28	55
2	Na_2CO_3	DCE:H_2O = 9:1	50	39
3	K_2CO_3	DCE:H_2O = 9:1	62	38
4	Cs_2CO_3	DCE:H_2O = 9:1	51	49
5	$NaHCO_3$	DCE:H_2O = 9:1	39	40
6	$NaHCO_3$ (0.5 equiv)	DCE:H_2O = 9:1	41	55
7	K_3PO_4	DCE:H_2O = 9:1	53	45
8	TEA	DCE:H_2O = 9:1	47	33
9	pyridine	DCE:H_2O = 9:1	38	14
10	DBU	DCE:H_2O = 9:1	47	43
11	none	$CHCl_3$	25	57
12	Na_2CO_3	$CHCl_3$	14	70
13	K_2CO_3	$CHCl_3$	58	37
14	Cs_2CO_3	$CHCl_3$	48	36

15	$NaHCO_3$	$CHCl_3$	38	51
16	K_3PO_4	$CHCl_3$	39	32
17	TEA	$CHCl_3$	44	48
18	pyridine	$CHCl_3$	57	43
19	DBU	$CHCl_3$	50	45
20	none	IPA	30	70
21	Na_2CO_3	IPA	22	67
22	K_2CO_3	IPA	53	22
23	Cs_2CO_3	IPA	49	41
24	$NaHCO_3$	IPA	41	57
25	$NaHCO_3$ (0.5 equiv)	IPA	38	62
26	K_3PO_4	IPA	62	34
27	TEA	IPA	37	46
28	pyridine	IPA	58	35
29	DBU	IPA	48	52
30	none	$(MeOCH_2)_2$	9	52
31	Na_2CO_3	$(MeOCH_2)_2$	31	14
32	K_2CO_3	$(MeOCH_2)_2$	62	13
33	Cs_2CO_3	$(MeOCH_2)_2$	30	34
34	$NaHCO_3$	$(MeOCH_2)_2$	33	26
35	K_3PO_4	$(MeOCH_2)_2$	63	5
36	TEA	$(MeOCH_2)_2$	31	17
37	pyridine	$(MeOCH_2)_2$	29	40
38	DBU	$(MeOCH_2)_2$	50	16

[a] Reaction conditions: **1a** (0.05 mmol), **2a** (1.3 equiv), base (0.1 equiv), solvent (1 mL), rt, 30 min, argon. Yields were determined by ^1H NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard.

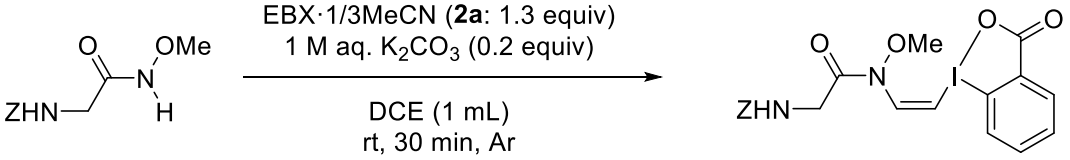
Table S3. Examination of detailed conditions.



Entry	DCE:H_2O	X	Yields (%)[a]	
			3a	**1a**
1[b]	1000:10	0.2	72	24
2[c]	995:5	0.2	72	23
3	990:10	0.1	61	21
4[d]	990:10	0.2	72	19
5	990:10	0.3	64	27
6	990:10	0.5	63	32
7	990:10	1.0	32	44
8[e]	980:20	0.2	53	36
9	970:30	0.2	44	36
10	950:50	0.1	34	62
11	950:50	0.2	38	52
12	950:50	0.3	42	25
13	950:50	0.5	58	45
14	900:100	none	28	55
15	900:100	0.1	62	38
16	900:100	0.2	38	65
17	900:100	0.3	31	56
18	900:100	0.5	58	42
19	900:100	1.0	52	38
20	800:200	0.1	46	37
21	800:200	0.5	43	27
22	800:200	1.0	43	35
23	500:500	0.1	27	45
24	500:500	0.5	44	40
25	500:500	1.0	36	35

[a] Reaction conditions: **1a** (0.05 mmol), **2a** (1.3 equiv), K_2CO_3 (0.1 equiv), DCE:H_2O (1 mL), rt, 30 min, argon. Yields were determined by ^1H NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard. [b] 1 M aq. K_2CO_3 (10 μL, 0.2 equiv) and DCE (1 mL) were uesd. [c] 2 M aq. K_2CO_3 (5 μL, 0.2 equiv) and DCE (995 μL) were uesd. [d] 1 M aq. K_2CO_3 (10 μL, 0.2 equiv) and DCE (990 μL) were uesd. [e] 0.5 M aq. K_2CO_3 (20 μL, 0.2 equiv) and DCE (980 μL) were uesd.

Table S4 Investigation of the various conditions.



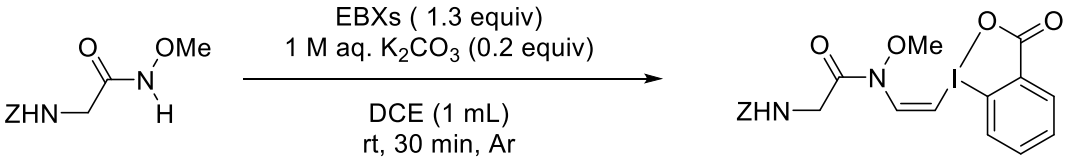
1a (0.05 mmol) **3a**

Entry	Chenge from the above conditions	Yields (%)[a]	
		3a	**1a**
1	with brown flask	72	24
2	Irradiated with a fluorescent lamp	70	28
3	Air, instead of Ar	72	28
4	1 h	68	20
5	0 °C	36	67
6	0 °C, 1 h	56	26
7	0 °C, 3 h	59	28
8	35 °C	50	26
9	added 18-crown-6 (0.4 equiv) before 1 M aq. K_2CO_3 was added	38	41
10	1 h, 1 M aq. K_2CO_3 (0.2 + 0.2 equiv) (added another 1 M aq. K_2CO_3 (0.2 equiv) after sterring for 30 minutes)	69	19
11	1 h, **2a** (1.3 + 1.3 equiv) (added another **2a** (1.3 equiv) after sterring for 30 minutes)	48	21
12[b]	0.1 mmol	(84)	-

[a] Reaction conditions: **1** (0.05 mmol), **2a** (1.3 equiv), 1 M aq. K_2CO_3 (10 μL: 0.2 equiv), DCE (1 mL), rt, 30 min, argon. Yields were determined by ^1H NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard. [b] **1** (0.1 mmol), 1 M aq. K_2CO_3 (20 μL: 0.2 equiv), DCE (2 mL) was used.

3. Investigation of the EBX reagents and amide structure

Table S5 Investigation of the EBX reagents.

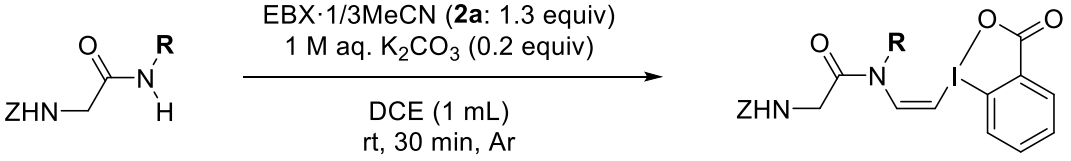


1a (0.05 mmol) **3a**

Entry	EBXs (X equiv)	Yields (%)[a]	
		3a	**1a**
1	EBX·1/3MeCN (**2a**: 1.1 equiv)	66	25
2	EBX·1/3MeCN (**2a**: 1.5 equiv)	60	31
3	EBX·1/6$CHCl_3$ (1.3 equiv)	62	27
4	EBX·1/6EtOAc (1.3 equiv)	68	23
5	EBX·H_2O (1.3 equiv)	61	22
6	TMS-EBX (1.3 equiv)	0	56

[a] Reaction conditions: **1** (0.05 mmol), EBXs (1.3 equiv), 1 M aq. K_2CO_3 (10 μL: 0.2 equiv), DCE (1 mL), rt, 30 min, argon. Yields were determined by ^1H NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard.

Table S6 Investigation of the various amides.



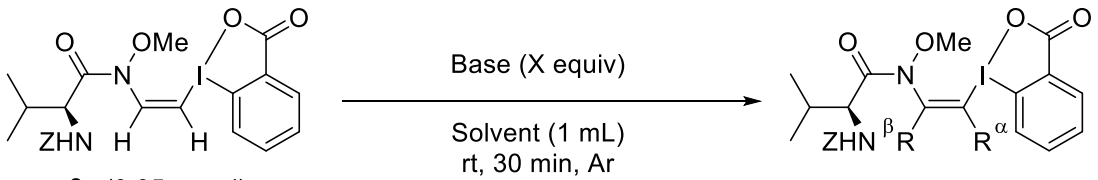
1' (0.05 mmol) **3a'**

Entry	**R**	Yields (%)[a]	
		3a'	**1'**
1	Ph	0	52
2	Me	0	85
3	H	0	20
4	OH	0	20
5	OPiv	0	62

[a] Reaction conditions: **1'** (0.05 mmol), **2a** (1.3 equiv), 1 M aq. K_2CO_3 (10 μL: 0.2 equiv), DCE (1 mL), rt, 30 min, argon. Yields were determined by ^1H NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard.

4. Mechanistic study

Table S7 H-D exchange reaction.



3z (0.05 mmol)

R = H or D

Entry	Base (X equiv)	Solvent	Yields (%)[a]
1	1 M K_2CO_3 in D_2O (0.2 equiv)	DCE	60; α: <5%D, β: <5%D
2	K_2CO_3 (0.2 equiv)	DCE:D_2O = 9:1	60; α: 9%D, β: <5%D
3	K_2CO_3 (0.1 equiv)	acetone:D_2O = 9:1	57; α: <5%D, β: 9%D
4	DBU (0.2 equiv)	MeCN:D_2O = 9:1	56; α: <5%D, β: <5%D

[a] Reaction conditions: **3z** (0.05 mmol), base (X equiv), solvent (1 mL), rt, 30 min, argon. Yields were determined by ^1H NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard.

5. X-ray crystallography of EBX·H_2O complex and 3l

Crystal samples were cut from the grown crystals and mounted on the MicroMount™. Measurements were carried out on a Rigaku/MSC Mercury CCD using a graphite-monochromator with Mo Kα radiation (λ = 0.71073 Å for EBX-H_2O and **3l**). The structure was solved by direct methods (SIR97,[S1] SIR2014[S2]) and refined by full-matrix least-squares procedures (SHELXL2014/7)[S3] using the Yadokari-XG.[S4] The crystal data are shown in Tables S6-9.

S1. A. Altomare, M. C. Burla, M. Camalli, G. L. Cascarano, C. Giacovazzo, A. Guagliardi, A. G. G. Moliterni, G. Polidori and R. Spagna, *J. Appl. Cryst.*, 1999, **32**, 115–119.

S2. M. C. Burla, R. Caliandro, B. Carrozzini, G. L. Cascarano, C. Cuocci, C. Giacovazzo, M. Mallamo, A. Mazzone and G. Polidori, *J. Appl. Cryst.*, 2015, **48**, 306–309.

S3. G. M. Sheldrick, SHELXL-2014/7: Program for the Solution of Crystal Structures, University of Göttingen, Göttingen, Germany, 2014.

S4. Yadokari-XG, Software for Crystal Structure Analyses, K. Wakita (2001); Release of Software (Yadokari-XG 2009) for Crystal Structure Analyses, C. Kabuto, S. Akine, T. Nemoto and E. Kwon, *J. Cryst. Soc. Jpn.*, 2009, **51**, 218–224.

Van der Waals volumes and radii, see: A. Bondi, *J. Phys. Chem.*, 1964, **68**, 441−451; R. S. Rowland and R. Taylor, *J. Phys. Chem.*, 1996, **100**, 7384–7391.

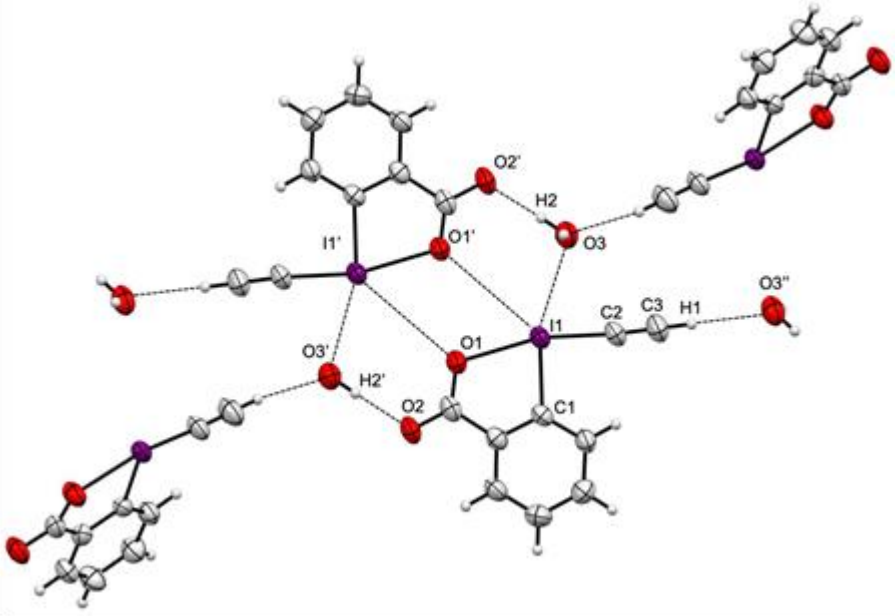


Fig. S1 ORTEP drawing of EBX-H_2O (thermal ellipsoids set at 50% probability). Selected bond lengths [Å] and angles [°]: I1−C1, 2.125(2); I1−C2, 2.055(3); I1−O1, 2.363(2); C2−C3, 1.157(5); C3−H1, 0.930; I1···O3, 2.923(3); I1···O1', 3.632(2); H1···O3'', 2.288; H2'···O2, 1.87(5); C1−I1−O1, 75.29(9); C1−I1−C2, 90.8(1); C2−I1−O1, 166.1(1); C1−I1···O3, 163.10(8); C1−I1···O1', 132.90(8); C3−H1···O3'', 171.0; O3'−H2'···O2, 179(5).

The complex adopts a distorted pentagonal planar geometry around the iodine atom due to the root-mean-square deviation of 0.144Å (I1, C1, C2, O3, O1', and O1) from their least-square plane and the sum of the iodine-centered bond angles of Σ°I1=361.2°. The nearly linear C1–I1···O3 angle (163.10(8)°) and the relatively strong I1···O3 contact (2.923(3)Å) are indicative of the presence of hypervalent secondary interaction. The dimer of EBX is linked with the adjacent dimers via hydrogen bonds, each of which involves an acidic acetylenic hydrogen atom and water oxygen. The H1···O3'' distance of 2.288 Å is shorter than their combined contact radii (2.72Å), and the C3-H1···O3'' bond shows a nearly linear conformation with an angle of 171.0°. The ratio of isotropic displacement parameters of EBX-H_2O (U(C3)/U(C2)=1.30) is larger than that of EBX-MeCN (U(C3)/U(C2)=1.19), which supports the weaker H1···O3'' hydrogen bond than that of EBX-MeCN (EBX-MeCN makes rigid honeycomb structure through acidic acetylenic hydrogen atom of an EBX), since hydrogen bonding reduces the thermal vibrations of the engaged residues.

Reduction of Thermal Vibrations by C-H···X Hydrogen Bonding, see: T. Steiner, *J. Chem. Soc., Chem. Commun.*, 1994, 101−102.

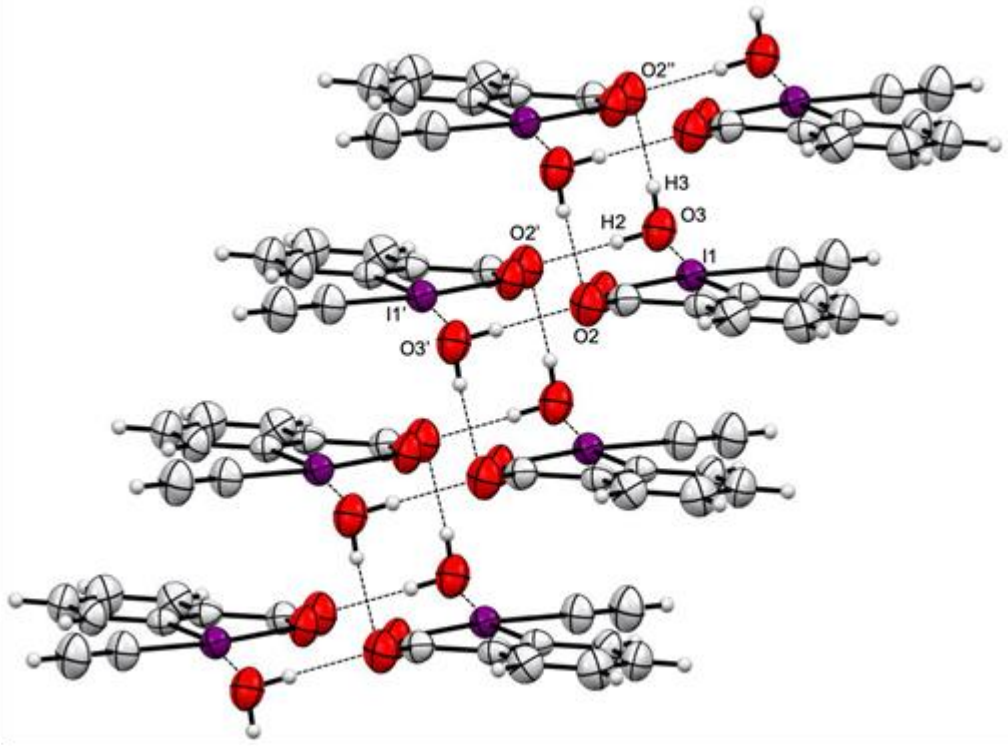


Fig. S2 ORTEP drawing of EBX-H_2O (thermal ellipsoids set at 50% probability). Side view. Selected bond lengths [Å] and angles [°]: H3−O2'', 2.02(5); O3−H3···O2'', 168(5). The hydrogen of water molecule makes a hydrogen bond to the carbonyl oxygen of an EBX from other layer, with a H3···O2'' distance of 2.02 Å, which is shorter than the sum of the van der Waals radii (2.72 Å).

Table S6 Experimental details of single crystal X-ray structural analysis of EBX·H_2O.

	(20190828)
Crystal data	
Chemical formula	$C_9H_7IO_3$
M_r	290.05
Crystal system, space group	Monoclinic, $P2_1/n$
Temperature (K)	293
a, b, c (Å)	12.4119 (4), 4.1382 (1), 18.5166 (6)
β (°)	94.868 (3)
V (Å^3)	947.64 (5)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	3.35
Crystal size (mm)	0.37 × 0.06 × 0.03
Data collection	
Diffractometer	Rigaku Mercury CCD (2x2 bin mode)
Absorption correction	Numerical
T_{min}, T_{max}	0.618, 0.949
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	8188, 2173, 1822
R_{int}	0.024
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.650
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.022, 0.051, 1.06
No. of reflections	2173
No. of parameters	124

No. of restraints	3
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.73, -0.36

Computer programs: *CrystalClear*-SM Expert 2.0 r16 (Rigaku, 2014), *SHELXL2014*/7 (Sheldrick, 2014).

Table S7 Selected geometric parameters (Å, º) of EBX·H_2O single crystal.

I1—C8	2.054 (3)	C2—C3	1.396 (4)
I1—C1	2.126 (3)	C2—C7	1.492 (4)
I1—O1	2.363 (2)	C3—C4	1.369 (5)
O1—C7	1.276 (4)	C4—C5	1.386 (5)
O2—C7	1.239 (4)	C5—C6	1.386 (5)
C1—C6	1.375 (4)	C8—C9	1.158 (4)
C1—C2	1.385 (4)		
C8—I1—C1	90.82 (11)	C3—C2—C7	121.8 (3)
C8—I1—O1	166.07 (10)	C4—C3—C2	120.4 (3)
C1—I1—O1	75.29 (9)	C3—C4—C5	120.3 (3)
C7—O1—I1	113.42 (19)	C4—C5—C6	120.8 (3)
C6—C1—C2	123.0 (3)	C1—C6—C5	117.7 (3)
C6—C1—I1	122.2 (2)	O2—C7—O1	124.9 (3)
C2—C1—I1	114.8 (2)	O2—C7—C2	119.4 (3)
C1—C2—C3	117.9 (3)	O1—C7—C2	115.8 (3)
C1—C2—C7	120.3 (3)	C9—C8—I1	175.3 (3)
C6—C1—C2—C3	-0.1 (4)	I1—C1—C6—C5	179.2 (2)
I1—C1—C2—C3	-179.0 (2)	C4—C5—C6—C1	-0.4 (5)
C6—C1—C2—C7	-179.1 (3)	I1—O1—C7—O2	174.3 (3)
I1—C1—C2—C7	2.0 (3)	I1—O1—C7—C2	-5.9 (3)
C1—C2—C3—C4	-0.1 (5)	C1—C2—C7—O2	-177.2 (3)
C7—C2—C3—C4	178.9 (3)	C3—C2—C7—O2	3.9 (4)

C2—C3—C4—C5	0.1 (5)	C1—C2—C7—O1	3.1 (4)
C3—C4—C5—C6	0.2 (5)	C3—C2—C7—O1	-175.9 (3)
C2—C1—C6—C5	0.4 (4)		

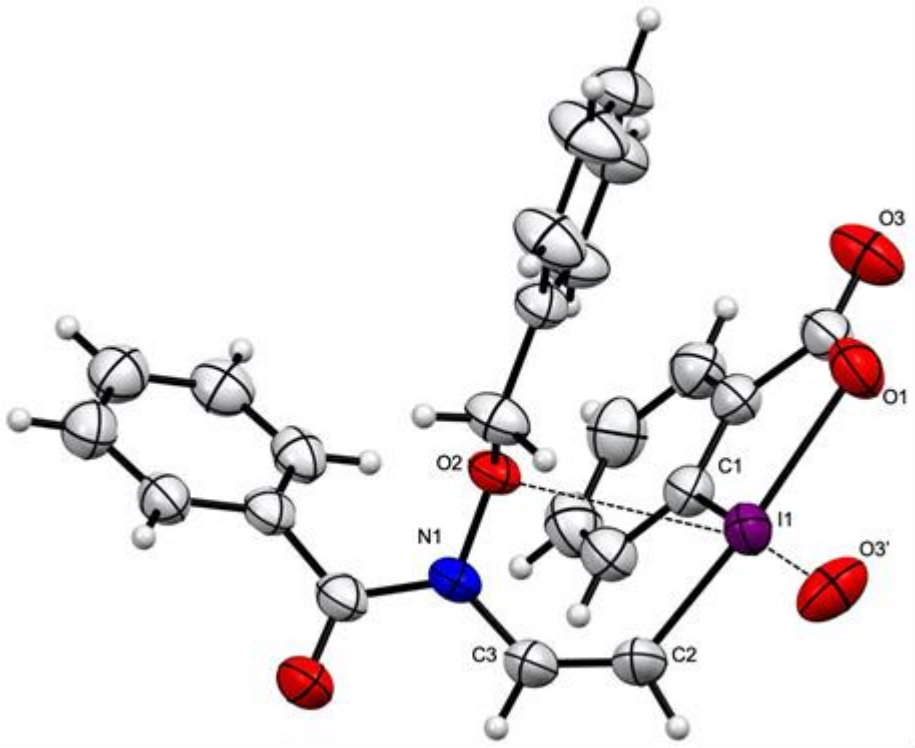


Fig. S3 ORTEP drawing of **3l** (thermal ellipsoids set at 50% probability). Selected bond lengths [Å] and angles [°]: I1−C1, 2.129(3); I1−C2, 2.106(2); I1−O1, 2.468(2); C2−C3, 1.317(4); I1···O2, 3.147(2); I1···O3', 2.780(2); C1−I1−O1, 74.01(8); C1−I1−C2, 96.48(9); C2−I1−O1, 170.41(8); C1−I1···O2, 71.51(7) ; C1−I1···O3', 176.45(8); C1−I1−C2−C3, -66.1(3); I1−C2−C3−N1, 5.6(4). The complex adopts a distorted square-planar geometry around the iodine atom due to the root-mean-square deviation of 0.042 Å (I1, C1, C2, O1, and O3') from their least-squares plane and the sum of the iodine-centered bond angles of Σ°I1 = 360.06°.

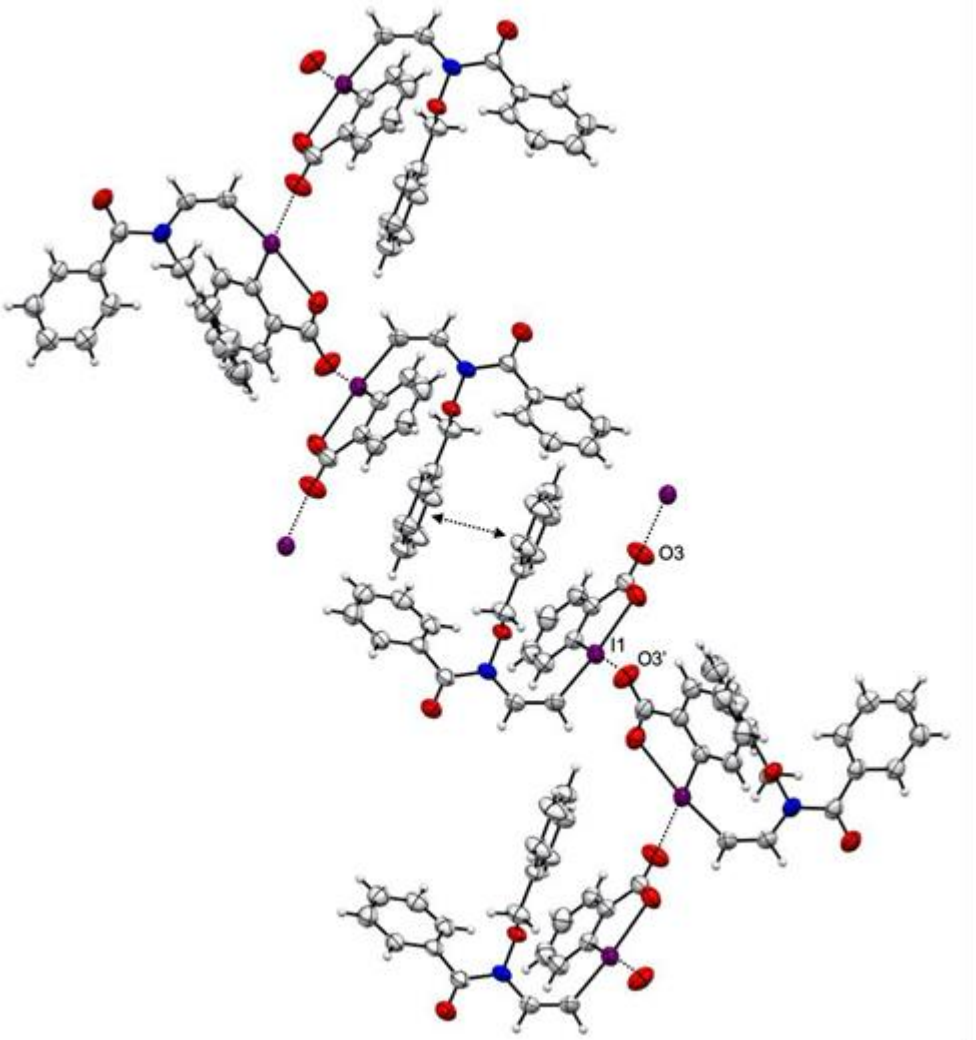


Fig. S4 ORTEP drawing of **3l** (thermal ellipsoids set at 50% probability). Wide view: Through secondary bonding (I1···O3'), **3l** forms a zigzag structure. Distance between benzene rings of benzyl group is ca. 3.64 Å, which are longer than the sum of the corresponding van der Waals radii (3.4 Å for C and C).

Table S8 Experimental details of single crystal X-ray structural analysis of **3l**.

	(200915)
Crystal data	
Chemical formula	$C_{23}H_{18}INO_4$
M_r	499.28
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	293

a, *b*, *c* (Å)	8.9812 (3), 10.2319 (3), 22.2899 (6)
β (°)	96.794 (3)
V (Å^3)	2033.94 (11)
Z	4
Radiation type	Mo *K*α
μ (mm^{-1})	1.60
Crystal size (mm)	0.70 × 0.25 × 0.25
Data collection	
Diffractometer	Mercury (2x2 bin mode)
Absorption correction	Multi-scan
T_{min}, T_{max}	0.651, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	26961, 4676, 4084
R_{int}	0.030
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.650
Refinement	
$R[F^2 > 2s(F^2)]$, $wR(F^2)$, S	0.025, 0.078, 1.15
No. of reflections	4676
No. of parameters	270
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.43, -0.42

Computer programs: *CrystalClear* (Rigaku/MSC Inc., 2006), *SHELXL2014*/7 (Sheldrick, 2014).

Table S9 Selected geometric parameters (Å, º) of **3l** single crystal.

I1—C8	2.106 (2)	C6—C7	1.374 (4)

I1—C3	2.128 (2)	C8—C9	1.317 (3)
I1—O1	2.4679 (18)	C10—C11	1.493 (3)
O1—C1	1.254 (3)	C11—C12	1.377 (4)
O2—C1	1.239 (3)	C11—C16	1.378 (4)
O3—N1	1.395 (2)	C12—C13	1.376 (4)
O3—C10	1.444 (3)	C13—C14	1.358 (5)
O4—C17	1.210 (3)	C14—C15	1.363 (4)
N1—C9	1.378 (3)	C15—C16	1.379 (4)
N1—C17	1.388 (3)	C17—C18	1.487 (4)
C1—C2	1.508 (4)	C18—C19	1.390 (3)
C2—C4	1.386 (4)	C18—C23	1.391 (3)
C2—C3	1.391 (3)	C19—C20	1.378 (4)
C3—C7	1.383 (3)	C20—C21	1.381 (4)
C4—C5	1.383 (4)	C21—C22	1.377 (4)
C5—C6	1.384 (4)	C22—C23	1.378 (4)
C8—I1—C3	96.48 (10)	C8—C9—N1	130.0 (2)
C8—I1—O1	170.41 (9)	O3—C10—C11	108.64 (19)
C3—I1—O1	74.01 (8)	C12—C11—C16	118.6 (2)
C1—O1—I1	112.63 (16)	C12—C11—C10	117.8 (2)
N1—O3—C10	109.17 (17)	C16—C11—C10	123.6 (2)
C9—N1—C17	123.4 (2)	C13—C12—C11	120.0 (3)
C9—N1—O3	117.98 (18)	C14—C13—C12	121.1 (3)
C17—N1—O3	118.63 (19)	C13—C14—C15	119.5 (3)
O2—C1—O1	125.7 (3)	C14—C15—C16	120.2 (3)
O2—C1—C2	118.3 (3)	C11—C16—C15	120.6 (2)
O1—C1—C2	116.0 (2)	O4—C17—N1	119.4 (2)
C4—C2—C3	117.4 (2)	O4—C17—C18	122.4 (2)
C4—C2—C1	121.3 (2)	N1—C17—C18	118.1 (2)
C3—C2—C1	121.2 (2)	C19—C18—C23	119.6 (2)
C7—C3—C2	122.0 (2)	C19—C18—C17	117.4 (2)

C7—C3—I1	121.95 (19)	C23—C18—C17	122.5 (2)
C2—C3—I1	116.03 (17)	C20—C19—C18	120.1 (2)
C5—C4—C2	121.3 (3)	C19—C20—C21	120.0 (3)
C4—C5—C6	119.7 (3)	C22—C21—C20	120.1 (3)
C7—C6—C5	120.3 (3)	C21—C22—C23	120.4 (3)
C6—C7—C3	119.1 (3)	C22—C23—C18	119.7 (2)
C9—C8—I1	130.5 (2)		
C10—O3—N1—C9	-94.3 (3)	C16—C11—C12—C13	1.1 (5)
C10—O3—N1—C17	85.3 (3)	C10—C11—C12—C13	-179.4 (3)
I1—O1—C1—O2	179.3 (2)	C11—C12—C13—C14	-1.4 (6)
I1—O1—C1—C2	-2.0 (3)	C12—C13—C14—C15	0.5 (6)
O2—C1—C2—C4	-0.4 (4)	C13—C14—C15—C16	0.5 (5)
O1—C1—C2—C4	-179.2 (2)	C12—C11—C16—C15	-0.1 (4)
O2—C1—C2—C3	178.7 (2)	C10—C11—C16—C15	-179.5 (3)
O1—C1—C2—C3	-0.1 (4)	C14—C15—C16—C11	-0.8 (5)
C4—C2—C3—C7	1.8 (4)	C9—N1—C17—O4	17.2 (4)
C1—C2—C3—C7	-177.4 (2)	O3—N1—C17—O4	-162.4 (2)
C4—C2—C3—I1	-178.31 (18)	C9—N1—C17—C18	-159.8 (2)
C1—C2—C3—I1	2.5 (3)	O3—N1—C17—C18	20.6 (3)
C3—C2—C4—C5	-1.7 (4)	O4—C17—C18—C19	33.3 (3)
C1—C2—C4—C5	177.4 (2)	N1—C17—C18—C19	-149.8 (2)
C2—C4—C5—C6	0.3 (4)	O4—C17—C18—C23	-138.2 (3)
C4—C5—C6—C7	1.2 (4)	N1—C17—C18—C23	38.7 (3)
C5—C6—C7—C3	-1.1 (4)	C23—C18—C19—C20	-1.0 (3)
C2—C3—C7—C6	-0.4 (4)	C17—C18—C19—C20	-172.8 (2)
I1—C3—C7—C6	179.7 (2)	C18—C19—C20—C21	1.4 (4)
I1—C8—C9—N1	5.6 (5)	C19—C20—C21—C22	-0.4 (4)
C17—N1—C9—C8	171.2 (3)	C20—C21—C22—C23	-0.9 (4)
O3—N1—C9—C8	-9.2 (4)	C21—C22—C23—C18	1.3 (4)
N1—O3—C10—C11	179.18 (19)	C19—C18—C23—C22	-0.3 (3)

O3—C10—C11—C12	179.5 (2)	C17—C18—C23—C22	171.0 (2)
O3—C10—C11—C16	-1.1 (4)		

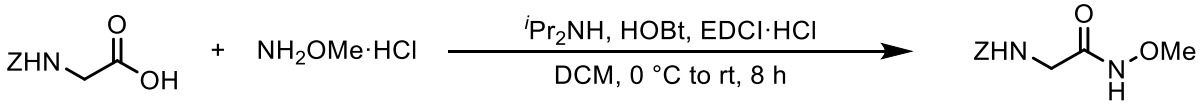
6. Experimental procedure and characterizations

The synthesis of **2a**, EBX·1/6$CHCl_3$, EBX·1/6EtOAc, TMS-EBX, Ph-EBX, *n*-Bu-EBX and their precursors had already described in our previous papers.[1,2]

1b,[3] **1c**,[4] **1d**,[3] **1e**,[4] **1f-1j**[3] ware synthesized according to the reported procedures.

Procedure A: Preparation of *N*-methoxy amides

Cbz-Glycine-*N*-methoxyamide (1a)



Following a reported procedure,[1] Cbz-glycine (2.0 g, 10 mmol, 1.0 equiv), *O*-methylhydroxylamine hydrochloride (835.2 mg, 10 mmol, 1.0 equiv) and $^{i}Pr_2NH$ (3.5 mL, 25 mmol, 2.5 equiv) were stirred in DCM (50 mL) under 0 °C for 15 min. Without changing temperature, HOBt (1.6 g, 12 mmol, 1.2 equiv) was added, and 30 min later, EDCI·HCl (2.9 g, 15 mmol, 1.5 equiv) was added. The mixture was stirred under 0 °C for 3 h and under room temperature for another 5 h. Then to the mixture was added water. After separation, organic layer was washed with brine and dried over Na_2SO_4. Solvent was removed under reduced pressure, affording the crude product, which was purified by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford Cbz-glycine-*N*-methoxyamide (**1a**: 1.39 g, 58%).

Rf: 0.42 ($CHCl_3$: MeOH = 20 : 1).

Physical state: Colorless solid.

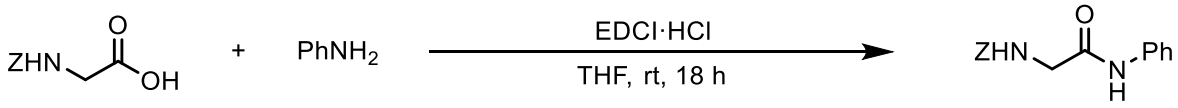
^{1}H NMR (500 MHz, DMSO-d_6): δ 11.17 (s, 1H), 7.52 (t, *J* = 5.73 Hz, 1H), 7.39-7.29 (m, 5H), 5.03 (s, 2H), 3.57 (s, 3H), 3.51 (d, *J* = 6.30 Hz, 2H).

^{13}C NMR (125 MHz, DMSO-d_6): δ 166.2, 156.6, 137.1, 128.5, 127.9, 127.9, 65.6, 63.3, 41.5.

HRMS (DART, positive): calcd for $C_{11}H_{15}N_2O_4$ $[M + H]^+$ 239.10318, Found 239.10385.

CAS Registry Number: 16975-15-8

Cbz-Glycine-*N*-phenylamide (S1a)[5]



Follwing a reported procedure,[6] EDCI·HCl (766 mg, 4 mmol, 2 equiv) was added to THF (10 mL) solution of Cbz-glycine (418 mg, 2 mmol, 1 equiv) and aniline (182 μL, 2 mmol, 1 equiv), followed by stirring for 6 hours at room temperature. After a reaction mixture was concentrated under reduced pressure, the concentrate was extracted by adding water and ethyl acetate. After an organic layer was washed with brine (two times), and the organic layer was dried over sodium sulfate. After the drying agent was separated by filtration, the filtrate was concentrated under reduced pressure, thereby obtaining

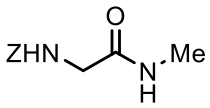
Cbz-glycine-*N*-phenylamide (**S1a**: 536.4 mg, 94%).

Physical state: Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.97-7.80 (brs, 1H), 7.48 (d, *J* = 7.32 Hz, 2H), 7.40-7.29 (m, 7H), 7.13 (t, *J* = 7.32 Hz, 1H), 5.46 (brs, 1H), 5.17 (s, 2H), 4.01 (d, *J* = 5.95 Hz, 2H).

CAS Registry Number: 6833-09-6

Cbz-Glycine-*N*-methylamide (S1b)[7]



Following the **Procedure A**, Cbz-glycine (418.0 mg, 2 mmol) and methylamine hydrochloride (135.0 mg, 2 mmol) were used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford Cbz-glycine-*N*-methylamide (**S1b**: 369.5 mg, 83%).

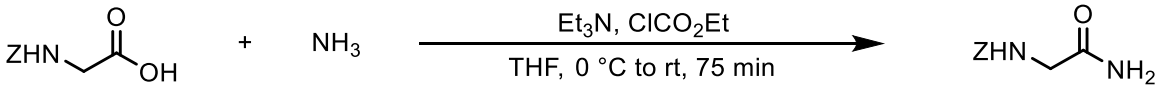
Rf: 0.16 (CH_2Cl_2 : MeOH = 20 : 1).

Physical state: Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39-7.32 (m, 5H), 5.98 (brs, 1H), 5.42-5.28 (brs, 1H), 5.14 (s, 2H), 3.86 (d, *J* = 5.95 Hz, 2H), 2.84 (d, *J* = 4.57 Hz, 3H).

CAS Registry Number: 21855-72-1

Cbz-Glycinamide (S1c)[8]



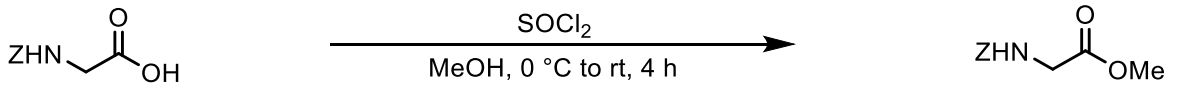
Following a reported procedure,[9] ethyl chloroformate (190 μL, 2 mmol, 1 equiv) was added dropwise to a stirring solution of Cbz-glycine (418.0 mg, 2 mmol, 1 equiv) and triethylamine (279 μL, 2 mmol, 1 equiv) in anhydrous THF (3 mL) at -10 ˚C. The mixture was stirred under nitrogen for 30 minutes and 28% aq. NH_3 (0.5 mL) was then added. After stirring for an additional 45 minutes, the reaction was partitioned between ethyl acetate and water. The organic layer was reserved and the aqueous layer was extracted again with ethyl acetate. The combined organic layers were washed with aqueous sodium hydrogen carbonate, brine, dried with sodium sulfate, and concentrated. The product (**S1c**: 259.6 mg, 62%) was used without further purification.

Physical state: Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41-7.30 (m, 5H), 5.87 (brs, 1H), 5.37 (brs, 2H), 5.14 (s, 2H), 3.91 (d, *J* = 5.73 Hz, 2H).

CAS Registry Number: 949-90-6

Cbz-Glycine methyl ester[10]



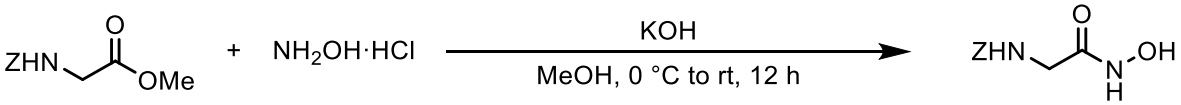
Following a reported procedure,[10] thionyl chloride (1 mL, 14 mmol, 1.4 equiv) was added dropwise to a stirred solution of the Cbz-glycine (2.09 g, 10 mmol, 1 equiv) in methanol (50 mL) at 0 °C. The mixture was stirred for 4 hours until the acid had been consumed. The methanol was removed under reduced pressure. The concentrate was extracted by ethyl acetate and washed with sat. aq. $NaHCO_3$ and brine, then the organic layer was dried over sodium sulfate. After the drying agent was separated by filtration, the filtrate was concentrated under reduced pressure. The pruduct (1.7 g, 76%) was used without further purification.

Physical state: Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42-7.30 (m, 5H), 5.25 (brs, 1H), 5.13 (s, 2H), 4.00 (d, *J* = 5.49 Hz, 2H), 3.76 (s, 3H).

CAS Registry Number:1212-53-9

Cbz-Glycine-*N*-hydroxyamide (S1d)[11]



Following a reported procedure,[12] a methanolic solution of Cbz-glycine methyl ester (1.05 g, 5 mmol, 1 equiv), cooled in an ice bath, was charged with a preformed methanoic slurry of hydroxylamine hydrochloride (1.0 g, 15 mmol, 3 equiv) and KOH (1.7 g, 30 mmol, 6 equiv). The reaction mixture was stirred under argon. When the reaction was complete, as indicated by TLC analysis, the reaction mixture was acidified to an apparent pH of 4 with concentrated HCl. The resulting solution was then concentrated to give a colorless solid. The colorless solid was boiled in EtOAc and filtered. The filtrate was concentrated and the crude was purified by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 10:1) to afford Cbz-glycine-*N*-hydroxyamide (**S1d**: 327.9 mg, 29%).

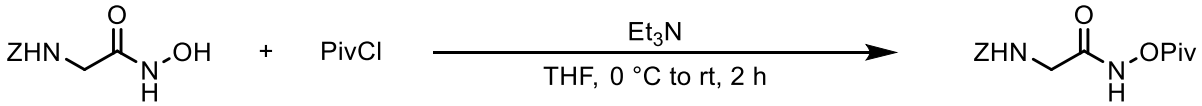
Rf: 0.14 ($CHCl_3$: MeOH = 10 : 1).

Physical state: Colorless solid.

^{1}H NMR (400 MHz, DMSO-d_6): δ 10.54 (s, 1H), 8.82 (s, 1H), 7.57 (s, 1H), 7.39-7.26 (m, 5H), 5.02 (s, 2H), 3.65 (s, 2H).

CAS Registry Number:76960-28-6

Cbz-Glycine-*N*-pivaloxyamide (S1e)



Following a reported procedure,[13] Cbz-glycine-*N*-hydroxyamide (224.2 mg, 1 mmol, 1 equiv) was dissolved in THF (5 mL) at 0 °C, followed by addition of Et_3N (210 μL, 1.5 mmol, 1.5 equiv) and PivCl (133 μL, 1.1 mmol, 1.1 equiv). The reaction was allowed to warm to room temperature, stirring until completed conversion. After that, the mixture was diluted with EtOAc, and washed with water and brine. The organic layer was then dried over anhydrous Na_2SO_4, solids were filtered, and the filtrate was concentrated by rotary evaporation. The crude was purified by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford Cbz-glycine-*N*-pivaloxyamide (**S1e**: 101.7 mg, 33%).

Rf: 0.37 ($CHCl_3$: MeOH = 20 : 1).

Physical state: Colorless oil.

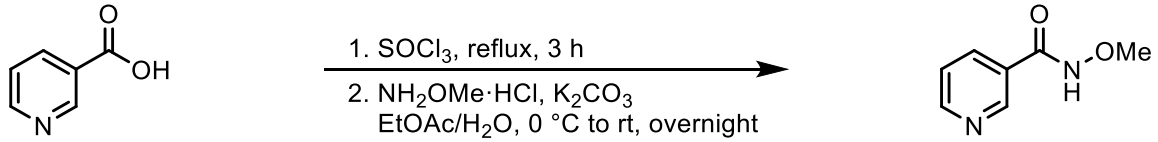
^{1}H NMR (500 MHz, $CDCl_3$): δ 9.53 (brs, 1H), 7.37-7.34 (m, 5H), 5.43 (brs, 1H), 5.15 (s, 2H), 3.97 (d, *J* = 4.58 Hz, 2H), 1.31 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 176.2, 167.1, 156.9, 135.8, 128.5, 128.3, 128.1, 67.4, 42.5, 38.3, 26.9.

HRMS (DART, positive): calcd for $C_{15}H_{21}N_2O_5$ $[M + H]^+$ 309.14505, Found 309.14481.

Procedure B: Preparation of *N*-methoxyamides

***N*-Methoxy-3-pyridinecarboxamide (1k)**[14]



Following a reported procedure,[3,15] nicotinic acid (246.2 mg, 2.0 mmol, 1.0 equiv) was refluxed in thionyl chloride (2 mL) for 3 h, and then the solution was cooled to room temperature, and the remaining thionyl chloride was evaporated to afford 3-pyridinecarbonyl chloride hydrochloride, which was used without further purification.

To a solution of K_2CO_3 (830 mg, 6.0 mmol, 3.0 equiv) in a mixture of EtOAc/H_2O (20 mL, 2:1) was added *O*-methylhydroxylamine hydrochloride (200 mg, 2.4 mmol, 1.2 equiv). The resulting solution was cooled to 0 °C, followed by dropwise addition of the above acid chloride. The reaction mixture was warmed to room temperature and stirred for overnight. The organic phase was separated and the aqueous phase was extracted with EtOAc. The combined organic layer was washed with brine and dried over Na_2SO_4. The organic layer was filtered, and evaporated under reduced pressure. The product (**1k**: 103.8 mg, 34%) was used without further purification.

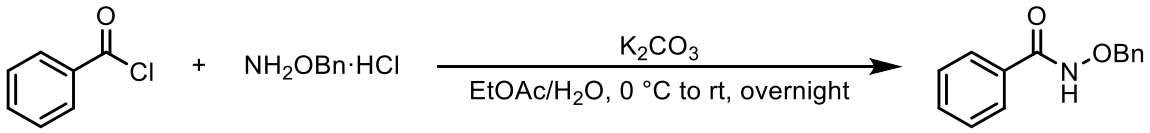
Physical state: Brown oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.42 (brs, 1H), 8.94 (s, 1H), 8.75 (s, 1H), 8.14 (d, *J* = 7.78 Hz, 1H), 7.47-7.39 (m, 1H), 3.91 (s, 3H).

CAS Registry Number: 37140-90-2

Procedure C: Preparation of *N*-alkyloxyamides

***N*-Benzyloxybenzamide (1l)**[16]



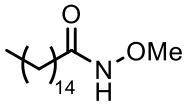
Following a reported procedure,[3] to a solution of K_2CO_3 (553 mg, 4.0 mmol, 2.0 equiv) in a mixture of EtOAc/H_2O (20 mL, 2:1) was added *O*-benzylhydroxylamine hydrochloride (383 mg, 2.4 mmol, 1.2 equiv). The resulting solution was cooled to 0 °C, followed by dropwise addition of the benzoyl chloride (232 μL, 2.0 mmol, 1.0 equiv). The reaction mixture was warmed to room temperature and stirred for overnight. The organic phase was separated and the aqueous phase was extracted with EtOAc. The combined organic layer was washed with brine and dried over Na_2SO_4. The organic layer was filtered, and evaporated under reduced pressure. The product (**1l**: 452.5 mg, quantitative yield) was used without further purification.

Physical state: Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.45 (brs, 1H), 7.66 (d, *J* = 6.87 Hz, 2H), 7.52 (t, *J* = 7.45 Hz, 1H), 7.46 (dd, *J* = 7.45, 1.72 Hz, 2H), 7.44-7.36 (m, 6H), 5.05 (s, 2H).

CAS Registry Number: 3532-25-0

***N*-Methoxyhexadecanamide (1m)**[17]



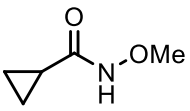
Following the **Procedure B**, palmitic acid (512.8 mg, 2 mmol) and K_2CO_3 (553 mg, 4 mmol) were used. The product (**1m**: 519.9 mg, 91%) was used without further purification.

Physical state: Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.15 (brs, 1H), 3.77 (s, 3H), 2.51-5.31 (m, 0.7H (minor rotamer)), 2.18-2.00 (m, 1.3H (major rotamer)), 1.75-1.53 (m, 2H), 1.47-1.15 (m, 24H), 0.88 (t, *J* = 6.87 Hz, 3H).

CAS Registry Number: 337962-52-4

***N*-Methoxycyclopropanecarboxamide (1n)**[18]



Following the **Procedure A**, cycloporopanecarboxylic acid (187 μL, 2 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 10:1) to afford *N*-methoxycyclopropanecarboxamide (**1n**: 81.7 mg, 35%).

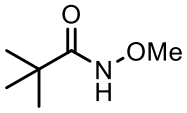
Rf: 0.24 ($CHCl_3$: MeOH = 20 : 1).

Physical state: Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.16 (brs, 1H), 3.79 (s, 3H), 1.37-1.15 (m, 1H), 1.13-1.01 (m, 2H), 0.97-0.73 (m, 2H).

CAS Registry Number: 93630-17-2

***N*-Methoxy-2,2-dimethylpropanamide (1o)**[19]



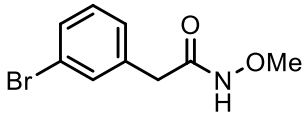
Following the **Procedure C**, pivaloyl chloride (241 μL, 2 mmol) and *O*-methylhydroxylamine hydrochloride (200 mg, 2.4 mmol) were used. The product (**1o**: 229.5 mg, 87%) was used without further purification.

Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.29 (brs, 1H), 3.77 (s, 3H), 1.21 (s, 9H).

CAS Registry Number: 64214-63-7

2-(3-Bromophenyl)-*N*-methoxyacetamide (1p)



Following the **Procedure B**, 2-(3-bromophenyl)acetic acid (430.1 mg, 2 mmol) and K_2CO_3 (553 mg, 4 mmol) were used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 10:1) to afford 2-(3-bromophenyl)-*N*-methoxyacetamide (**1p**: 431.6 mg, 88%).

Rf: 0.33 ($CHCl_3$: MeOH = 20 : 1).

Physical state: Colorless solid.

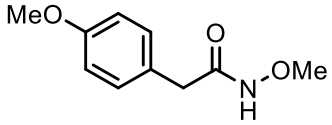
^{1}H NMR (500 MHz, DMSO-d_6): δ 11.32 (s, 1H), 7.48-7.42 (m, 2H), 7.31-7.23 (m, 2H), 3.57 (s, 3H), 3.30 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.0, 136.0, 132.1, 130.5, 130.4, 127.8, 122.8, 64.5, 40.1.

HRMS (DART, positive): calcd for $C_9H_{11}BrNO_2$ $[M + H]^+$ 243.99732, Found 243.99671.

CAS Registry Number: 1467949-96-7

***N*-Methoxy-2-(4-methoxyphenyl)acetamide (1q)**[20]



Following the **Procedure B**, 2-(4-methoxyphenyl)acetic acid (332.4 mg, 2 mmol) and K_2CO_3 (553 mg, 4 mmol) were used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 10:1) to afford *N*-methoxy-2-(4-methoxyphenyl)acetamide (**1q**: 256.5 mg, 66%).

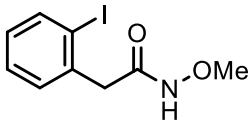
Rf: 0.30 ($CHCl_3$: MeOH = 10 : 1).

Physical state: Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.93 (brs, 1H), 7.19 (d, *J* = 8.23 Hz, 2H), 6.91-6.85 (m, 2H), 3.81 (s, 3H), 3.72 (s, 3H), 3.49 (s, 2H).

CAS Registry Number: 112403-98-2

2-(2-Iodophenyl)-*N*-methoxyacetamide (1r)[21]



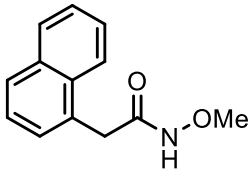
Following the **Procedure B**, 2-(2-iodophenyl)acetic acid (524.1 mg, 2 mmol) and K_2CO_3 (553 mg, 4 mmol) were used. The product (**1r**: 390.1 mg, 67%) was used without further purification.

Physical state: Colorless solid.

^{1}H NMR (400 MHz, DMSO-d_6): δ 11.26 (brs, 1H), 7.79 (dd, *J* = 7.78, 0.91 Hz, 1H), 7.34-7.25 (m, 2H), 6.97 (td, *J* = 7.32, 1.83 Hz, 1H), 3.57 (s, 3H), 3.46 (s, 2H).

CAS Registry Number: 121989-41-1

***N*-Methoxy-1-naphthaleneacetamide (1s)**



Following the **Procedure B**, 1-naphthaleneacetic acid (372.4 mg, 2 mmol) and K_2CO_3 (553 mg, 4 mmol) were used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford *N*-methoxy-1-naphthaleneacetamide (**1s**: 96.3 mg, 22%).

Rf: 0.33 ($CHCl_3$: MeOH = 20 : 1).

Physical state: Colorless solid.

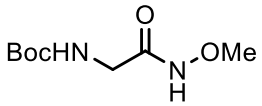
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (brs, 1H), 7.96 (d, *J* = 7.78 Hz, 1H), 7.88 (d, *J* = 8.69 Hz, 1H), 7.83 (d, *J* = 7.78 Hz, 1H), 7.59-7.48 (m, 2H), 7.47-7.37 (m, 2H), 4.19 (brs, 0.2H (minor rotamer)), 4.00 (s, 1.8H (major rotamer)), 3.64 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4, 133.9, 131.8, 129.6, 128.8, 128.7, 128.2, 126.9, 126.3, 125.6, 123.5, 64.3, 39.3.

HRMS (DART, positive): calcd for $C_{13}H_{14}NO_2$ $[M + H]^+$ 216.10245 Found 216.10150.

CAS Registry Number: 113519-25-8

Boc-Glycine-*N*-methoxyamide (1t)[22]



Following the **Procedure A**, Boc-glycine (350.4 mg, 2 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 10:1) to afford Boc-glycine-*N*-methoxyamide (**1t**: 196.4 mg, 48%).

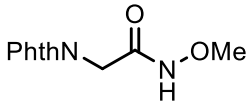
Rf: 0.24 ($CHCl_3$: MeOH = 10 : 1).

Physical state: Colorless oil.

^{1}H NMR (400 MHz, MeOH-d_4): δ 3.69 (s, 3H), 3.65 (s, 2H), 1.45 (s, 9H).

CAS Registry Number: 120939-89-1

Phth-Glycine-*N*-methoxyamide (1u)[23]



Following the **Procedure A**, Phth-glycine (410.3 mg, 2 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford Phth-glycine-*N*-methoxyamide (**1u**: 174.6 mg, 37%).

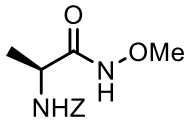
Rf: 0.19 ($CHCl_3$: MeOH = 20 : 1).

Physical state: Colorless solid.

^{1}H NMR (500 MHz, DMSO-d_6): δ 11.50 (s, 1H), 7.95-7.85 (m, 4H), 4.13 (s, 2H), 3.59 (s, 3H).

CAS Registry Number: 817556-29-9

Cbz-L-Alanine-*N*-methoxyamide (1x)[24]



Following the **Procedure A**, Cbz-L-alanine (446.5 g, 2 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford Cbz-L-alanine-*N*-methoxyamide (**1x**: 263.7 mg, 52%).

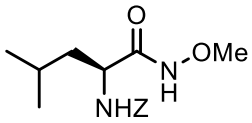
Rf: 0.27 ($CHCl_3$: MeOH = 20 : 1).

Physical state: Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.93 (brs, 1H), 7.40-7.29 (m, 5H), 5.26-5.05 (m, 1H), 5.11 (d, *J* = 4.12 Hz, 2H), 4.20-4.05 (m, 1H), 3.75 (s, 3H), 1.39 (d, *J* = 6.86 Hz, 3H).

CAS Registry Number: 16707-91-8

Cbz-L-Leucine-*N*-methoxyamide (1y)[25]



Following the **Procedure A**, Cbz-L-leucine (1.32 g, 5 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford Cbz-L-leucine-*N*-methoxyamide (**1y**: 220.9 mg, 38%).

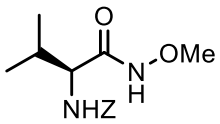
Rf: 0.35 ($CHCl_3$: MeOH = 20 : 1).

Physical state: Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.26 (brs, 1H), 7.39-7.29 (m, 5H), 5.31 (d, *J* = 8.02 Hz, 1H), 5.09 (q, *J* = 11.07 Hz, 2H), 4.11-4.03 (m, 1H), 3.74 (s, 3H), 1.70-1.61 (m, 2H), 1.60-1.47 (m, 1H), 0.93 (d, *J* = 6.3 Hz, 6H).

CAS Registry Number: 1610455-77-0

Cbz-L-Valine-*N*-methoxyamide (1z)[24]



Following the **Procedure A**, Cbz-L-valine (502.6 mg, 2 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 10:1) to afford Cbz-L-valine-*N*-methoxyamide (**1z**: 452.8 mg, 81%).

Rf: 0.22 ($CHCl_3$: MeOH = 10 : 1).

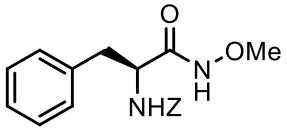
Physical state: Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.01 (brs, 1H), 7.43-7.29 (m, 5H), 5.38 (d, *J* = 8.69 Hz, 1H), 5.10 (s, 2H), 3.76 (s, 3H),

2.19-2.00 (m, 1H), 0.97 (d, *J* = 6.40 Hz, 3H), 0.96 (d, *J* = 6.40 Hz, 3H).

CAS Registry Number: 2504956-94-7

Cbz-L-Phenylalanine-*N*-methoxyamide (1aa)[26]



Following the **Procedure A**, Cbz-L-phenylalanine (598.7 mg, 2 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford Cbz-L-phenylalanine-*N*-methoxyamide (**1aa**: 613.0 mg, 93%).

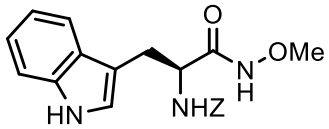
Rf: 0.35 ($CHCl_3$: MeOH = 20 : 1).

Physical state: Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44 (brs, 1H), 7.39-7.25 (m, 8H), 7.20 (d, *J* = 6.86 Hz, 2H), 5.33 (brs, 1H), 5.08 (s, 2H), 4.31-4.17 (m, 1H), 3.61 (s, 3H), 3.15-2.98 (m, 2H).

CAS Registry Number: 923570-05-2

Cbz-L-Tryptophan-*N*-methoxyamide (1ab)



Following the **Procedure A**, Cbz-L-tryptophan (676.7g, 2 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 10:1) to afford Cbz-L-tryptophan-*N*-methoxyamide (**1ab**: 616.0 mg, 84%).

Rf: 0.34 ($CHCl_3$: MeOH = 10 : 1).

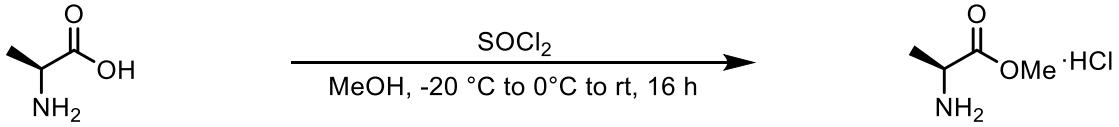
Physical state: Pale yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.69 (brs, 1H), 8.21 (brs, 1H), 7.62 (d, *J* = 7.45 Hz, 1H), 7.38-7.28 (m, 6H), 7.19 (t, *J* = 7.45 Hz, 1H), 7.10 (t, *J* = 7.45 Hz, 1H), 6.99 (s, 1H), 5.54 (d, *J* = 7.45 Hz, 1H), 5.04 (s, 2H), 4.38 (d, *J* = 5.73 Hz, 1H), 3.50 (s, 3H), 3.26 (dd, *J* = 14.32, 5.73 Hz, 1H), 3.15 (dd, *J* = 14.32, 8.02 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.0, 156.0, 136.1, 135.9, 128.5, 128.3, 128.0, 127.1, 123.4, 122.3, 119.8, 118.7, 111.3, 109.9, 67.1, 64.2, 53.2, 28.3.

HRMS (DART, positive): calcd for $C_{20}H_{22}N_3O_4$ $[M + H]^+$ 368.16103, Found 368.16339.

L-Alanine methyl ester hydrochloride[27]



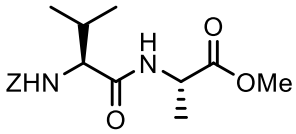
Following a reported procedure,[28] L-alanine (890.9 mg, 10 mmol, 1.0 eq.) was dissolved in methanol (10 mL) and cooled to -20 °C (ice/NaCl). To this suspension, thionyl chloride (762 μL, 10.5 mmol, 1.05 eq.) was added dropwise. The reaction mixture was stirred at 0 °C for 1 h, then at room temperature for 16 h. The reaction mixture was concentrated under vacuum. The obtained colorless solid was washed with diethyl ether and then dried under vacuum to afford L-alanine methyl ester hydrochloride (1.3 g, 93%).

Physical state: Colorless solid.

^{1}H NMR (500 MHz, DMSO-d_6): δ 8.51 (brs, 3H), 4.07 (q, *J* = 7.45 Hz, 1H), 3.74 (s, 3H), 1.41 (d, *J* = 7.45 Hz, 3H).

CAS Registry Number: 2491-20-5

Cbz-L-Valyl-L-alanine methyl ester[29]



Following the **Procedure A**, Cbz-L-valine (1.256 g, 5 mmol) and L-alanine methyl ester hydrochloride (697.9 mg, 5 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford Cbz-L-valyl-L-alanine methyl ester (1.534 g, 91%).

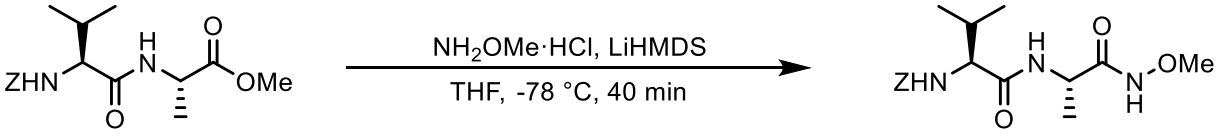
Rf: 0.53 ($CHCl_3$: MeOH = 20 : 1).

Physical state: Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40-7.29 (m, 5H), 6.34 (d, *J* = 6.86 Hz, 1H), 5.36 (d, *J* = 8.69 Hz, 1H), 5.11 (s, 2H), 4.58 (quint, *J* = 7.32 Hz, 1H), 4.02 (dd, *J* = 8.69, 6.40 Hz, 1H), 3.75 (s, 3H), 2.12 (sext, *J* = 6.86 Hz, 1H), 1.41 (d, *J* = 7.32 Hz, 3H), 0.98 (d, *J* = 6.86 Hz, 3H), 0.93 (d, *J* = 6.86 Hz, 3H).

CAS Registry Number: 4817-92-9

Cbz-L-Valyl-L-alanine-*N*-methoxyamide (1ac)



Following a reported procedure,[30] a stirred suspension of *O*-methylhydroxylamine hydrochloride (167.0 mg, 2 mmol, 1 equiv) in dry THF (10 mL) at -78 °C under Ar atmosphere was treated with a 1 M THF solution of LiHMDS (10.2 mL, 10.2 mmol, 5.1 equiv). After 10 min a solution of Cbz-L-valyl-L-alanine methyl ester (672.8 mg, 2 mmol, 1 equiv) in dry THF (7

mL) was added. After the total consumption of the starting material was determined by TLC, the reaction was quenched with a saturated aqueous solution of NH_4Cl, warmed to room temperature, and extracted with EtOAc. The collected organic layers were dried (Na_2SO_4), filtered, and concentrated under reduced pressure, and the crude was purified by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford Cbz-L-valyl-L-alanine-*N*-methoxyamide (**1ac**: 291.2 mg, 41%).

Rf: 0.40 ($CHCl_3$: MeOH = 20 : 1).

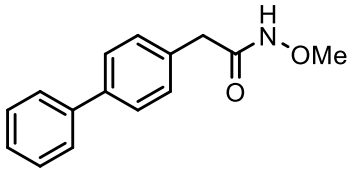
Physical state: Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.27 (brs, 1H), 7.44-7.31 (m, 5H), 6.40 (brs, 1H), 5.28 (brs, 1H), 5.12 (s, 2H), 4.37 (brs, 1H), 3.97 (brs, 1H), 3.75 (s, 3H), 2.18-2.07 (m, 1H), 1.39 (d, *J* = 6.87 Hz, 3H), 0.96 (d, *J* = 6.30 Hz, 3H), 0.92 (d, *J* = 6.87 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 171.0, 168.9, 156.2, 137.1, 128.5, 127.9, 127.7, 65.5, 63.2, 59.9, 45.9, 30.5, 19.2, 18.1, 18.1.

HRMS (DART, positive): calcd for $C_{17}H_{26}N_3O_5$ $[M + H]^+$ 352.18725, Found 352.18696.

2-[(1,1'-Biphenyl)-4-yl]-*N*-methoxyacetamide (1ad)



Following the **Procedure A**, 2-[(1,1'-biphenyl)-4-yl]acetic acid (212.3 mg, 1 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 10:1) to afford 2-[(1,1'-biphenyl)-4-yl]-*N*-methoxyacetamide (**1ad**: 192.1 mg, 80%).

Rf: 0.54 ($CHCl_3$: MeOH = 10 : 1).

Physical state: Colorless solid.

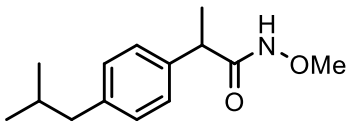
^{1}H NMR (500 MHz, DMSO-d_6): δ 11.34 (s, 1H), 7.64 (d, *J* = 8.02 Hz, 2H), 7.60 (d, *J* = 8.59 Hz, 2H), 7.45 (t, *J* = 7.45 Hz, 2H), 7.37-7.31 (m, 3H), 3.59 (s, 3H), 3.33 (s, 2H).

^{13}C NMR (100 MHz, MeOH-d_4): δ 170.7, 142.2, 141.5, 135.3, 130.7, 130.0, 128.5, 128.3, 128.1, 64.5, 40.4.

HRMS (DART, positive): calcd for $C_{15}H_{16}NO_2$ $[M + H]^+$ 242.11810, Found 242.11729.

CAS Registry Number: 153720-56-0

***N*-Methoxy-2-[4-(2-methylpropyl)phenyl]propanamide (1ae)**[31]



Following the **Procedure A**, 2-[4-(2-methylpropyl)phenyl]propanoic acid (212.3 mg, 1 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 10:1) to afford *N*-methoxy-2-[4-(2-methylpropyl)phenyl]propanamide (**1ae**: 232.8 mg, 99%).

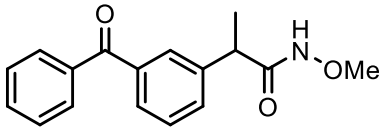
Rf: 0.58 ($CHCl_3$: MeOH = 10 : 1).

Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (brs, 1H), 7.19 (d, *J* = 8.23 Hz, 2H), 7.11 (d, *J* = 8.23 Hz, 2H), 3.69 (s, 3H), 3.56-3.34 (m, 1H), 2.45 (d, *J* = 7.32 Hz, 2H), 1.92-1.77 (m, 1H), 1.52 (d, *J* = 6.86 Hz, 3H), 0.90 (d, *J* = 6.86 Hz, 6H).

CAS Registry Number: 127946-61-6

2-(3-Benzoylphenyl)-*N*-methoxypropanamide (1af)



Following the **Procedure A**, 2-(3-benzoylphenyl)propanoic acid (254.3 mg, 1 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 10:1) to afford 2-(3-benzoylphenyl)-*N*-methoxypropanamide (**1af**: 50.4 mg, 18%).

Rf: 0.36 ($CHCl_3$: MeOH = 10 : 1).

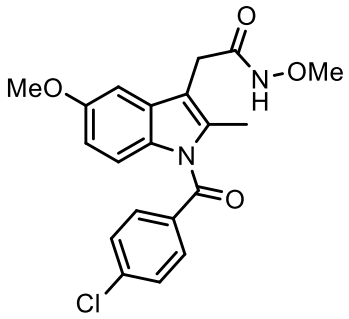
Physical state: Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.38 (brs, 1H), 7.79 (dd, *J* = 8.59, 1.15 Hz, 2H), 7.75 (s, 1H), 7.67 (dt, *J* = 7.45, 1.15 Hz, 1H), 7.63-7.57 (m, 2H), 7.49 (t, *J* = 7.45 Hz, 2H), 7.45 (t, *J* = 7.45 Hz, 1H), 3.72 (s, 3H), 3.54 (brs, 1H), 1.56 (d, *J* = 6.87 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 196.6, 171.4, 140.8, 138.0, 137.3, 132.7, 131.4, 130.1, 129.4, 129.0, 128.8, 128.4, 64.4, 44.0, 18.5.

HRMS (DART, positive): calcd for $C_{17}H_{18}NO_3$ $[M + H]^+$ 284.12867, Found 284.12894.

1-(4-Chlorobenzoyl)-*N*,5-dimethoxy-2-methyl-1*H*-indole-3-acetamide (1ag)[32]



Following the **Procedure A**, 1-(4-chlorobenzoyl)-*N*,5-dimethoxy-2-methyl-1*H*-indole-3-acetic acid (357.8 mg, 1 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 10:1) to afford 1-(4-chlorobenzoyl)-*N*,5-dimethoxy-2-methyl-1*H*-indole-3-acetamide (**1ag**: 305.2 mg, 79%).

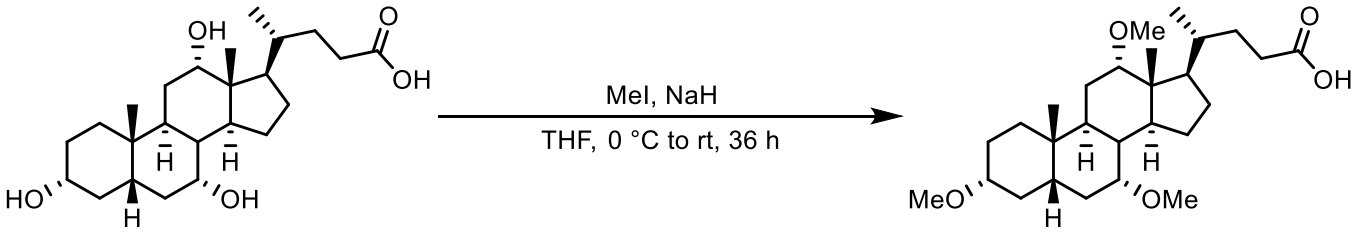
Rf: 0.49 ($CHCl_3$: MeOH = 10 : 1).

Physical state: Colorless solid.

^{1}H NMR (500 MHz, DMSO-d_6): δ 11.32 (s, 1H), 7.69 (d, *J* = 8.59 Hz, 2H), 7.64 (d, *J* = 8.59 Hz, 2H), 7.10 (s, 1H), 6.85 (d, *J* = 9.16 Hz, 1H), 6.70 (dd, *J* = 8.88, 2.58 Hz, 1H), 3.76 (s, 3H), 3.58 (s, 3H), 3.41, (s, 2H), 2.23 (s, 3H).

CAS Registry Number: 127080-14-2

(*R*)-4-[(3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,7,12-Trimethoxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]-phenanthren-17-yl]pentanoic acid[33]



Following a reported procedure,[33] to a suspension of NaH (1.0 g of a 60 % suspension in mineral oil, 25 mmol, 5 equiv) in 40 mL of dry tetrahydrofuran at 0 °C, was added via cannula a solution of commercially available cholic acid (2.04 g, 5 mmol, 1 equiv) in 20 mL of dry tetrahydrofuran. The resulting solution was stirred at 0 °C for 10 min. and then was added methyl iodide (731 μL, 11.75 mmol, 2.35 equiv). The reaction mixture was stirred for 18 h at ambient temperature and then was added a second portion of NaH (0.8 g, 20 mmol, 4 equiv), followed by more methyl iodide (622 μL, 10 mmol, 2 equiv). The reaction was stirred for an additional 18h at ambient temperature. The reaction mixture was quenched by slow addition of methanol then concentrated using rotary evaporation. The resulting mixture was diluted with ethyl acetate and poured on a saturated aqueous solution of NH_4Cl. The aqueous layer was then extracted with ethyl acetate. The combined organics were washed with brine, dried over Na_2SO_4 and filtered. The solvent was then removed by rotary evaporation and the product was purified by flash column chromatography on silica gel (hexane:EtOAc = 7:3) to afford (*R*)-4-[(3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,7,12-trimethoxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl]pentanoic acid (1.44 g, 64%).

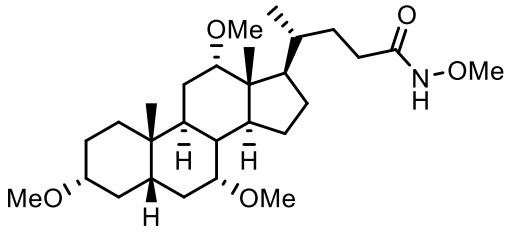
Rf: 0.4 (hexane:EtOAc = 7:3).

Physical state: Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.36 (s, 1H), 3.33 (s, 3H), 3.26 (s, 3H), 3.21 (s, 3H), 3.14 (d, *J* = 2.86 Hz, 1H), 3.04-2.96 (m, 1H), 2.46-2.37 (m, 1H), 2.31-2.23 (m, 1H), 2.19 (q, *J* = 12.41 Hz, 1H), 2.13-2.02 (m, 2H), 1.94 (q, *J* = 9.55 Hz, 1H), 1.90-1.72 (m, 6H), 1.71-1.65 (m, 1H), 1.62-1.56 (m, 1H), 1.56-1.14 (m, 9H), 1.06-0.85 (m, 8H), 0.65 (s, 3H).

CAS Registry Number: 117832-92-5

(*R*)-*N*-Methoxy-4-[(3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,7,12-trimethoxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl]pentanamide (1ah)



Following the **Procedure A**, (*R*)-4-[(3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,7,12-trimethoxy-10,13-dimethylhexadeca hydro-1*H*-cyclopenta[*a*]phenanthren-17-yl]pentanoic acid (450.7 mg, 1 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*R*)-*N*-methoxy-4-[(3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,7,12-trimethoxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl]pentanamide (**1ah**: 378.0 mg, 77%).

Rf: 0.53 ($CHCl_3$: MeOH = 20 : 1).

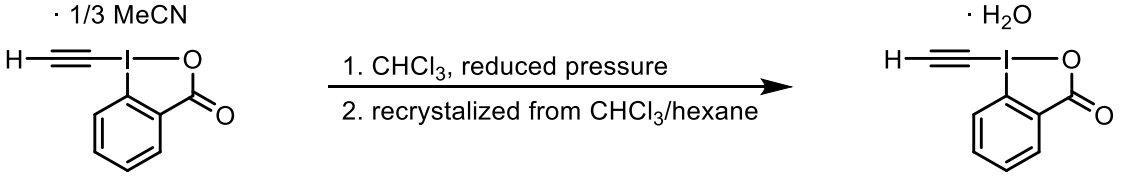
Physical state: Colorless solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (brs, 1H), 3.77 (s, 3H), 3.35 (s, 1H), 3.33 (s, 3H), 3.25 (s, 3H), 3.21 (s, 3H), 3.14 (d, *J* = 2.74 Hz, 1H), 3.05-2.94 (m, 1H), 2.24-1.99 (m, 4H), 1.98-1.87 (m, 1H), 1.86-1.65 (m, 7H), 1.61-1.12 (m, 10H), 1.08-0.87 (m, 8H), 0.65 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.8, 82.0, 80.7, 76.9, 64.5, 55.8, 55.6, 55.4, 46.1, 45.9, 42.7, 41.9, 39.6, 35.2, 34.9, 34.9, 34.4, 31.2, 29.7, 27.9, 27.7, 27.3, 26.7, 23.1, 22.8, 21.9, 17.4, 12.4.

HRMS (DART, positive): calcd for $C_{28}H_{50}NO_5$ $[M + H]^+$ 480.36890, Found 480.36491.

Ethynyl-1,2-benziodoxol-3-(1*H*)-one-H_2O complex



Ethynyl-1,2-benziodoxol-3-(1*H*)-one-MeCN complex (142.9 mg, 0.5 mmol, 1 equiv) was completely dissolved in $CHCl_3$ (16 mL). Then the solvent was slowly removed by rotary evaporation, and ethynyl-1,2-benziodoxol-3-(1*H*)-one-$CHCl_3$ complex was obtained. The solid was recrystallized from wet $CHCl_3$/hexane to afford ethynyl-1,2-benziodoxol-3-(1*H*)-one-H_2O complex (111.5 mg, 77%).

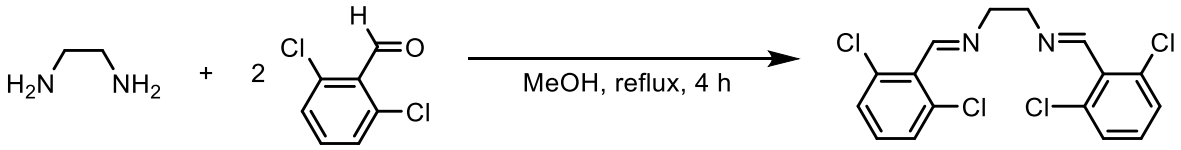
Physical state: Colorless solid.

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.28 (d, *J* = 8.23 Hz, 1H), 8.12 (dd, *J* = 7.32, 1.83 Hz, 1H), 7.90 (td, *J* = 7.32, 1.83 Hz, 1H), 7.80 (t, *J* = 7.32 Hz, 1H), 4.67 (s, 1H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 166.3, 135.1, 132.0, 131.4, 131.4, 127.5, 115.5, 97.6, 46.8.

Elemental analysis: Anal. Calcd for $C_9H_7IO_3$: C, 37.27; H, 2.43, Found: C, 37.05; H, 2.37.

***N*,*N'*-Bis(2,6-dichlorobenzylidene)ethylenediamine (Ligand A)**[34]



Following a reported procedure,[35] 1,2-ethanediamine (67 μL, 1.0 mmol, 1 equiv) and 2,6-dichlorobenzaldehyde (350.0 mg, 2.00 mmol, 1 equiv) were dissolved in methanol (10 mL) and stirred under reflux for 4 h to produce a precipitate. The reaction mixture was cooled down to room temperature and the Schiff base was isolated by filtration and purified by recrystallization from dichloromethane/hexane (**Ligand A**: 351.3 mg, 95%).

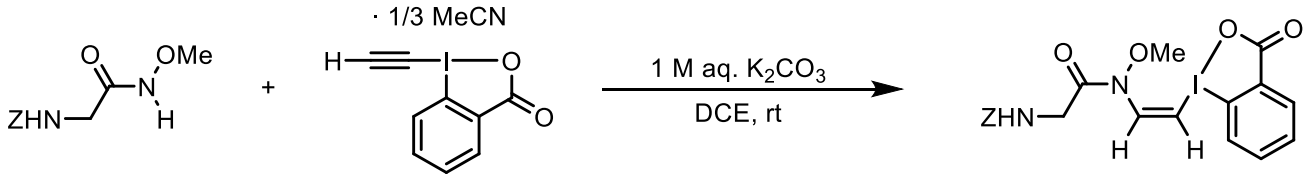
Physical state: Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.52 (s, 2H), 7.32 (d, *J* = 8.69 Hz, 4H), 7.20 (t, *J* = 8.69 Hz, 2H), 4.14 (s, 4H).

CAS Registry Number: 157982-81-5

Procedure D: Synthesis of *cis*-*β*-amide-VBXs

(*Z*)-*N*-(1-Vin-2-yl)-Cbz-glycine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3a)



To a stirred solution of Cbz-glycine-*N*-methoxyamide (**1a**: 23.8 mg, 0.1 mmol, 1.0 equiv) in 1,2-dichloroethane (2 mL) under argon was added 1 M aq. K_2CO_3 (20 μL, 0.02 mmol, 0.2 equiv) at rt. After 5 min, ethynyl-1,2-benziodoxol-3-(1*H*)-one-MeCN complex (**2a**: 37.1 mg, 0.13 mmol, 1.3 equiv) was added one portion. After 30 min, the reaction mixture was diluted with $CHCl_3$. The solution was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude

produst was purified by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-Cbz- glycine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (**3a**: 42.8 mg, 84%).

Rf: 0.17 ($CHCl_3$: MeOH = 20 : 1).

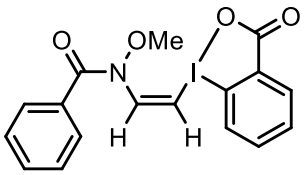
Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$:CD_3OD = 10:1): δ 8.39-8.28 (m, 1H), 7.88 (d, *J* = 8.02 Hz, 1H), 7.73-7.52 (m, 3H), 7.40-7.24 (m, 5H), 6.32 (brs, 1H), 6.06 (d, *J* = 7.45 Hz, 1H), 5.13 (s, 2H), 4.27 (s, 1.7H (major rotamer)), 4.21 (s, 0.3H (minor rotamer)), 3.87 (s, 2.6H (major rotamer)), 3.74 (s, 0.4H (minor rotamer)).

^{13}C NMR (125 MHz, $CDCl_3$:CD_3OD = 10:1): δ 169.6, 167.8, 156.9, 136.0, 134.3, 133.9, 132.9, 132.6, 130.7, 128.3, 128.0, 127.8, 126.2, 114.4, 79.5, 67.0, 64.5, 42.2.

HRMS (ESI, positive): calcd for $C_{20}H_{19}IN_2NaO_6$ $[M + Na]^+$ 533.01855, Found 533.02133.

(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxybenzamide-1,2-benziodoxol-3-(1*H*)-one (3b)



Following the **Procedure D**, *N*-methoxybenzamide (**1b**: 15.1 mg, 0.1 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-*N*-methoxybenzamide-1,2-benziodoxol-3-(1*H*)-one (**3b**: 33.1 mg, 78%).

1 mmol scale reaction

To a stirred solution of *N*-methoxybenzamide (**1b**: 151.2 mg, 1.0 mmol, 1.0 equiv) in 1,2-dichloroethane (20 mL) under argon was added 1 M aq. K_2CO_3 (0.2 mL, 0.2 mmol, 0.2 equiv) at rt. After 5 min, ethynyl-1,2-benziodoxol-3-(1*H*)-one-MeCN complex (**2a**: 371.5 mg, 1.3 mmol, 1.3 equiv) was added one portion. After 24 h, the reaction mixture was diluted with $CHCl_3$. The solution was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude was purified by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-*N*-methoxybenzamide-1,2-benziodoxol-3-(1*H*)-one (**3b**: 309.1 mg, 73%).

Rf: 0.35 ($CHCl_3$: MeOH = 10 : 1).

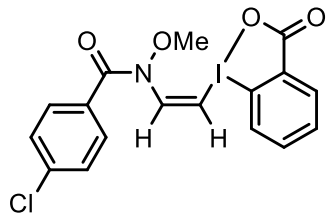
Physical state: Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.49-8.44 (m, 1H), 8.26 (d, *J* = 8.02 Hz, 1H), 7.76 (d, *J* = 7.45 Hz, 2H), 7.69-7.64 (m, 3H), 7.62-7.58 (m, 1H), 7.49 (t, *J* = 8.02 Hz, 2H), 5.89 (d, *J* = 8.02 Hz, 1H), 3.61 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 167.0, 166.9, 134.5, 133.5, 133.5, 132.7, 132.7, 130.7, 130.5, 129.0, 128.5, 125.8, 114.7, 76.5, 64.0.

HRMS (ESI, positive): calcd for $C_{17}H_{14}INNaO_4$ $[M + Na]^+$ 445.98652, Found 445.98408.

(*Z*)-*N*-(1-Vin-2-yl)-4-chloro-*N*-methoxybenzamide-1,2-benziodoxol-3-(1*H*)-one (3c)



Following the **Procedure D**, 4-chloro-*N*-methoxybenzamide (**1c**: 18.6 mg, 0.1 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-4-chloro-*N*-methoxybenzamide-1,2-benziodoxol-3-(1*H*)-one (**3c**: 31.9 mg, 70%).

Rf: 0.13 ($CHCl_3$: MeOH = 20 : 1).

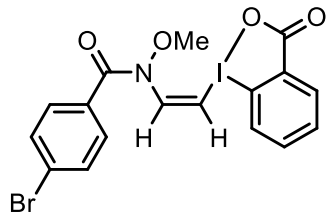
Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.45 (brs, 1H), 8.27 (d, *J* = 8.02 Hz, 1H), 7.75 (d, *J* = 8.59 Hz, 1H), 7.66 (brs, 3H), 7.56 (d, *J* = 8.59 Hz, 2H), 5.97 (d, *J* = 8.59 Hz, 1H), 3.61 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 167.0, 165.9, 139.4, 134.2, 133.6, 133.5, 133.0, 130.7, 130.7, 129.0, 128.9, 125.7, 114.7, 77.4, 64.3.

HRMS (ESI, positive): calcd for $C_{17}H_{13}ClINNaO_4$ $[M + Na]^+$ 479.94755, Found 479.94617.

(*Z*)-*N*-(1-Vin-2-yl)-4-bromo-*N*-methoxybenzamide-1,2-benziodoxol-3-(1*H*)-one (3d)



Following the **Procedure D**, 4-bromo-*N*-methoxybenzamide (**1d**: 23.0 mg, 0.1 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-4-bromo-*N*-methoxybenzamide-1,2-benziodoxol-3-(1*H*)-one (**3d**: 37.5 mg, 75%).

Rf: 0.32 ($CHCl_3$: MeOH = 10 : 1).

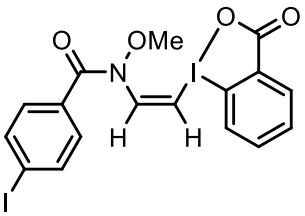
Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.49-8.43 (m, 1H), 8.25 (d, *J* = 8.59 Hz, 1H), 8.72-8.59 (m, 7H), 5.95 (d, *J* = 8.59 Hz, 1H), 3.61 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 166.8, 166.0, 134.2, 133.7, 133.5, 133.1, 132.0, 130.9, 130.8, 129.3, 128.0, 125.5, 114.6, 77.4, 64.3.

HRMS (ESI, positive): calcd for $C_{17}H_{13}BrINNaO_4$ $[M + Na]^+$ 523.89703, Found 523.89644.

(*Z*)-*N*-(1-Vin-2-yl)-4-iodo-*N*-methoxybenzamide-1,2-benziodoxol-3-(1*H*)-one (3e)



Following the **Procedure D**, 4-iodo-*N*-methoxybenzamide (**1e**: 27.7 mg, 0.1 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-4-iodo-*N*-methoxybenzamide-1,2-benziodoxol-3-(1*H*)-one (**3e**: 44.0 mg, 80%).

Rf: 0.21 ($CHCl_3$: MeOH = 10 : 1).

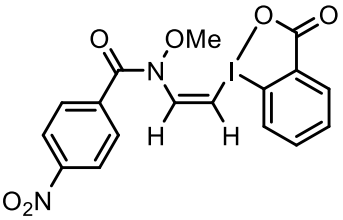
Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.51-8.44 (m, 1H), 8.25 (d, *J* = 8.02 Hz, 1H), 7.85 (d, *J* = 8.59 Hz, 2H), 7.70-7.61 (m, 3H), 7.51 (d, *J* = 8.59 Hz, 2H), 5.94 (d, *J* = 8.02 Hz, 1H), 3.61 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 167.0, 166.3, 137.9, 134.1, 133.5, 132.9, 130.7, 130.5, 130.0, 125.8, 114.8, 100.4, 77.56, 64.3 (*one carbon aromatic signal not resolved*).

HRMS (ESI, positive): calcd for $C_{17}H_{13}I_2NNaO_4$ $[M + Na]^+$ 571.88316, Found 571.87946.

(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxy-4-nitrobenzamide-1,2-benziodoxol-3-(1*H*)-one (3f)



Following the **Procedure D**, *N*-methoxy-4-nitorbenzamide (**1f**: 19.6 mg, 0.1 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-*N*-methoxy-4-nitrobenzamide-1,2-benziodoxol-3-(1*H*)-one (**3f**: 28.3 mg, 64%).

Rf: 0.27 ($CHCl_3$: MeOH = 10 : 1).

Physical state: Colorless oil.

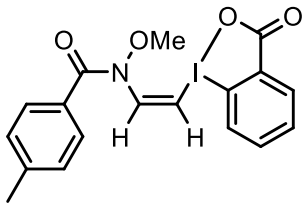
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.46-8.39 (m, 1H), 8.32 (d, *J* = 8.59 Hz, 1H), 8.25 (d, *J* = 6.87 Hz, 1H), 7.95 (d, *J* = 8.59 Hz, 2H), 7.70-7.62 (m, 3H), 6.13 (d, *J* = 8.59 Hz, 1H), 3.62 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 167.0, 165.3, 149.9, 136.4, 133.7, 133.6, 133.5, 133.0, 130.9, 130.3, 125.7, 123.7, 114.8,

79.7, 64.6.

HRMS (ESI, positive): calcd for $C_{17}H_{13}IN_2NaO_6$ $[M + Na]^+$ 490.97160, Found 490.97586.

(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxy-4-methylbenzamide-1,2-benziodoxol-3-(1*H*)-one (3g)



Following the **Procedure D**, *N*-methoxy-4-methylbenzamide (**1g**: 16.5 mg, 0.1 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-*N*-methoxy-4-methylbenzamide-1,2-benziodoxol-3-(1*H*)-one (**3g**: 37.9 mg, 87%).

Rf: 0.23 ($CHCl_3$: MeOH = 10 : 1).

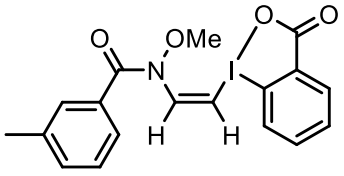
Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.50-8.46 (m, 1H), 8.27 (d, *J* = 8.59 Hz, 1H), 7.69 (d, *J* = 8.02 Hz, 2H), 7.68-7.64 (m, 3H), 7.28 (d, *J* = 8.02 Hz, 2H), 5.84 (d, *J* = 8.59 Hz, 1H), 3.60 (s, 3H), 2.44 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 166.9, 166.8, 143.9, 134.9, 133.6, 133.1, 130.8, 129.3, 127.6, 125.4, 114.6, 75.7, 64.0, 21.7 (*two carbon aromatic signal not resolved*).

HRMS (ESI, positive): calcd for $C_{18}H_{16}INNaO_4$ $[M + Na]^+$ 460.00217, Found 460.00025.

(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxy-3-methylbenzamide-1,2-benziodoxol-3-(1*H*)-one (3h)



Following the **Procedure D**, *N*-methoxy-3-methylbenzamide (**1h**: 16.5 mg, 0.1 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-*N*-methoxy-3-methylbenzamide-1,2-benziodoxol-3-(1*H*)-one (**3h**: 37.9 mg, 87%).

Rf: 0.25 ($CHCl_3$: MeOH = 10 : 1).

Physical state: Colorless oil.

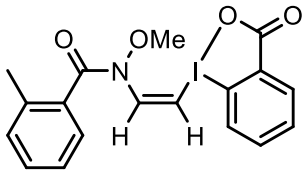
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.51-8.46 (m, 1H), 8.23 (d, *J* = 8.59 Hz, 1H), 7.70-7.62 (m, 3H), 7.57-7.53 (m, 2H), 7.43-7.34 (m, 2H), 5.84 (d, *J* = 8.59 Hz, 1H), 3.61 (s, 3H), 2.42 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 167.2, 166.7, 138.7, 134.8, 133.7, 133.6, 133.6, 133.2, 130.9, 130.6, 129.6, 128.5, 126.1,

125.4, 114.6, 75.9, 64.1, 21.3.

HRMS (ESI, positive): calcd for $C_{18}H_{16}INNaO_4$ $[M + Na]^+$ 460.00217, Found 459.99983.

(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxy-2-methylbenzamide-1,2-benziodoxol-3-(1*H*)-one (3i)



Following the **Procedure D**, *N*-methoxy-2-methylbenzamide (**1i**: 16.5 mg, 0.1 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-*N*-methoxy-2-methylbenzamide-1,2-benziodoxol-3-(1*H*)-one (**3i**: 33.3 mg, 76%).

Rf: 0.24 ($CHCl_3$: MeOH = 10 : 1).

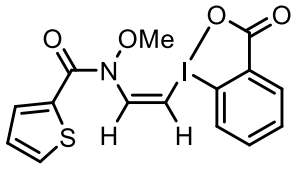
Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.41 (s, 1H), 8.05 (brs, 1H), 7.69-7.57 (m, 3H), 7.43 (t, *J* = 7.45 Hz, 1H), 7.36-7.31 (m, 1H), 7.29 (d, *J* = 7.45 Hz, 2H), 5.84 (brs, 1H), 3.65 (brs, 3H), 2.33 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 167.6, 167.0, 142.2, 135.9, 133.5, 133.5, 132.8, 131.5, 131.1, 130.8, 130.6, 127.2, 125.8, 125.7, 114.7, 64.0, 19.3 (*one carbon vinylic signal not resolved*).

HRMS (ESI, positive): calcd for $C_{18}H_{16}INNaO_4$ $[M + Na]^+$ 460.00217, Found 460.00109.

(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxy-2-thiophenecarboxamide-1,2-benziodoxol-3-(1*H*)-one (3j)



Following the **Procedure D**, *N*-methoxy-2-thiophenecarboxamide (**1j**: 15.7 mg, 0.1 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-*N*-methoxy-2-thiophenecarboxamide-1,2-benziodoxol-3-(1*H*)-one (**3j**: 40.9 mg, 95%).

Rf: 0.24 ($CHCl_3$: MeOH = 10 : 1).

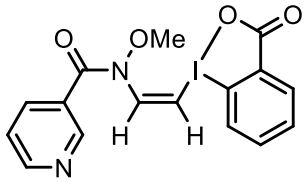
Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.50-8.44 (m, 1H), 8.18 (d, *J* = 8.59 Hz, 1H), 8.10 (dd, *J* = 4.01, 1.15 Hz, 1H), 7.76 (dd, *J* = 4.87, 1.15 Hz, 1H), 7.69-7.61 (m, 3H), 7.22-7.19 (m, 1H), 6.04 (d, *J* = 8.59 Hz, 1H), 3.86 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 167.0, 160.0, 137.0, 135.5, 134.4, 133.6, 132.9, 130.6, 130.6, 127.8, 125.9, 114.9, 79.8, 64.9.

HRMS (ESI, positive): calcd for $C_{15}H_{12}INNaO_4S$ $[M + Na]^+$ 451.94294, Found 451.94394.

(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxy-3-pyridinecarboxamide-1,2-benziodoxol-3-(1*H*)-one (3k)



Following the **Procedure D**, *N*-methoxy-3-pyridinecarboxamide (**1k**: 15.2 mg, 0.1 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 10:1) to afford (*Z*)-*N*-(1-vin-2-yl)-*N*-methoxy-3-pyridinecarboxamide-1,2-benziodoxol-3-(1*H*)-one (**3k**: 13.3 mg, 31%).

Rf: 0.18 ($CHCl_3$: MeOH = 10 : 1).

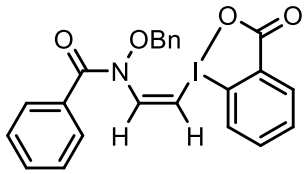
Physical state: Brown oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.00 (s, 1H), 8.80 (s, 1H), 8.41 (m, 1H), 8.28 (d, *J* = 8.02 Hz, 1H), 8.09 (d, *J* = 8.02 Hz, 1H), 7.68-7.60 (m, 3H), 7.47-7.41 (m, 1H), 6.12 (d, *J* = 8.02 Hz, 1H), 3.63 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 167.1, 165.1, 153.2, 149.9, 136.7, 133.6, 133.5, 132.9, 130.7, 126.9, 125.9, 123.3, 114.8, 78.8, 64.45 (*one carbon aromatic signal not resolved*).

HRMS (ESI, positive): calcd for $C_{16}H_{13}IN_2NaO_4$ $[M + Na]^+$ 446.98177, Found 446.98214.

(*Z*)-*N*-(1-Vin-2-yl)-*N*-benzyloxybenzamide-1,2-benziodoxol-3-(1*H*)-one (3l)



Following the **Procedure D**, *N*-benzyloxybenzamide (**1l**: 22.8 mg, 0.1 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-*N*-benzyloxybenzamide-1,2-benziodoxol-3-(1*H*)-one (**3l**: 44.6 mg, 89%). A single crystal of the product used for single crystal X-ray structural analysis was obtained by recrystalization from hot MeCN.

1mmol scale reaction

N-Benzyloxybenzamide (**1l**: 227.3 mg, 1 mmol) was used and the reaction time was 24 h. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-*N*-benzyloxybenzamide-1,2-benziodoxol-3-(1*H*)-one (**3l**: 472.3 mg, 95%).

Rf: 0.39 ($CHCl_3$: MeOH = 10 : 1).

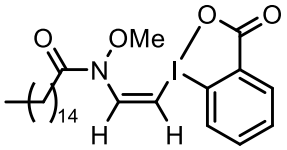
Physical state: Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.45-8.39 (m, 1H), 8.14 (d, *J* = 8.02 Hz, 1H), 7.67-7.60 (m, 4H), 7.60-7.54 (m, 2H), 7.44 (t, *J* = 8.02 Hz, 2H), 7.24 (t, *J* = 7.45 Hz, 1H), 7.15 (t, *J* = 7.45 Hz, 1H), 6.89 (d, *J* = 7.45 Hz, 2H), 5.96 (d, *J* = 8.02 Hz, 1H), 4.76 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.0, 166.8, 135.8, 133.5, 133.0, 132.6, 131.4, 131.0, 130.8, 130.0, 129.8, 128.8, 128.5, 125.7, 115.1, 79.2, 79.1 (*one carbon aromatic signal not resolved*).

HRMS (ESI, positive): calcd for $C_{23}H_{18}INNaO_4$ $[M + Na]^+$ 522.01782, Found 522.01619.

(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxyhexadecanamide-1,2-benziodoxol-3-(1*H*)-one (3m)



Following the **Procedure D**, *N*-methoxyhexadecanamide (**1m**: 28.6 mg, 0.1 mmol) was used and the reaction time was 24 h. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-*N*-methoxyhexadecanamide-1,2-benziodoxol-3-(1*H*)-one (**3m**: 31.9 mg, 57%).

Rf: 0.28 ($CHCl_3$: MeOH = 10 : 1).

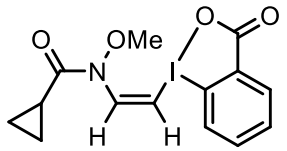
Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.48-8.42 (m, 1H), 8.00 (d, *J* = 8.02 Hz, 1H), 7.67-7.61 (m, 2H), 7.60-7.57 (m, 1H), 5.89 (d, *J* = 8.02 Hz, 1H), 3.82 (s, 3H), 2.57 (t, *J* = 7.45 Hz, 2H), 1.67 (quint, *J* = 7.45 Hz, 2H), 1.37-1.22 (m, 24H), 0.88 (t, *J* = 6.87 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 173.1, 166.8, 134.1, 133.6, 133.5, 133.0, 125.5, 114.7, 77.9, 64.4, 32.2, 31.9, 29.6, 29.6, 29.6, 29.4, 29.3, 29.3, 29.1, 24.0, 22.7, 14.1.

HRMS (ESI, positive): calcd for $C_{26}H_{40}INNaO_4$ $[M + Na]^+$ 580.18997, Found 580.19300.

(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxycyclopropanecarboxamide-1,2-benziodoxol-3-(1*H*)-one (3n)



Following the **Procedure D**, *N*-methoxycyclopropanecarboxamide (**1n**: 11.5 mg, 0.1 mmol) was used and the reaction time was 12 h. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-*N*-methoxycyclopropanecarboxamide-1,2-benziodoxol-3-(1*H*)-one (**3n**: 29.7 mg, 77%).

Rf: 0.17 ($CHCl_3$: MeOH = 20 : 1).

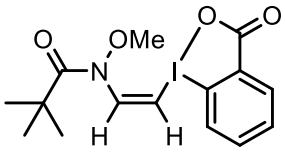
Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.48-8.42 (m, 1H), 8.09 (d, *J* = 8.59 Hz, 1H), 7.69-7.59 (m, 3H), 5.81 (d, *J* = 8.59 Hz, 1H), 3.91 (s, 3H), 2.29-2.31 (m, 1H), 1.22-1.17 (m, 2H), 1.13-1.07 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 173.2, 167.0, 133.9, 133.6, 133.5, 133.0, 130.7, 125.6, 114.6, 75.5, 64.6, 10.6, 10.4.

HRMS (ESI, positive): calcd for $C_{14}H_{14}INNaO_4$ $[M + Na]^+$ 409.98652, Found 409.98619.

(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxy-2,2-dimethylpropanamide-1,2-benziodoxol-3-(1*H*)-one (3o)



Following the **Procedure D**, *N*-methoxy-2,2-dimethylpropanamide (**1o**: 13.1 mg, 0.1 mmol) was used and the reaction time was 24 h. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-*N*-methoxy-2,2-dimethylpropanamide-1,2-benziodoxol-3-(1*H*)-one (**3o**: 20.0 mg, 50%).

Rf: 0.30 ($CHCl_3$: MeOH = 10 : 1).

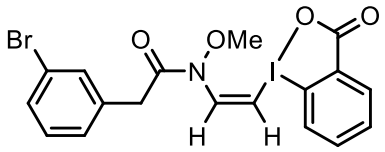
Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.45-8.38 (m, 1H), 7.64 (d, *J* = 8.02 Hz, 1H), 8.62-8.57 (m, 3H), 6.27 (d, *J* = 8.02 Hz, 1H), 3.81 (s, 3H), 1.30 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 178.4, 167.3, 137.2, 133.8, 133.5, 133.0, 130.6, 126.3, 115.1, 86.1, 64.1, 40.7, 26.8.

HRMS (ESI, positive): calcd for $C_{15}H_{18}INNaO_4$ $[M + Na]^+$ 426.01782, Found 426.01845.

(*Z*)-*N*-(1-Vin-2-yl)-2-(3-bromophenyl)-*N*-methoxyacetamide-1,2-benziodoxol-3-(1*H*)-one (3p)



Following the **Procedure D**, 2-(3-bromophenyl)-*N*-methoxyacetamide (**1p**: 24.4 mg, 0.1 mmol) was used and the reaction time was 3 h. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-2-(3-bromophenyl)-*N*-methoxyacetamide-1,2-benziodoxol-3-(1*H*)-one (**3p**: 29.2 mg, 57%).

Rf: 0.38 ($CHCl_3$: MeOH = 10 : 1).

Physical state: Colorless oil.

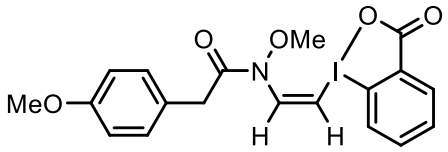
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.40 (dd, *J* = 7.75, 1.72 Hz, 1H), 7.97 (d, *J* = 8.02 Hz, 1H), 7.61 (td, *J* = 7.16, 1.15 Hz, 1H),

7.57 (td, *J* = 8.02,1.72 Hz, 1H), 7.52 (d, *J* = 8.02 Hz, 1H), 7.44-7.40 (m, 2H), 7.22-7.16 (m, 2H), 6.03 (d, *J* = 8.02 Hz, 1H), 3.88 (s, 2H), 3.83 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.3, 167.1, 134.5, 134.0, 133.6, 133.4, 132.9, 132.4, 130.8, 130.7, 130.3, 128.2, 125.8, 122.7, 114.8, 80.0, 64.7, 38.7.

HRMS (ESI, positive): calcd for $C_{18}H_{15}BrINNaO_4$ $[M + Na]^+$ 537.91268, Found 537.91425.

(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxy-2-(4-methoxyphenyl)acetamide-1,2-benziodoxol-3-(1*H*)-one (3q)



Following the **Procedure D**, *N*-methoxy-2-(4-methoxyphenyl)acetamide (**1q**: 19.5 mg, 0.1 mmol) was used and the reaction time was 3 h. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-*N*-methoxy-2-(4-methoxyphenyl)acetamide-1,2-benziodoxol-3-(1*H*)-one (**3q**: 36.7 mg, 79%).

Rf: 0.36 ($CHCl_3$: MeOH = 10 : 1).

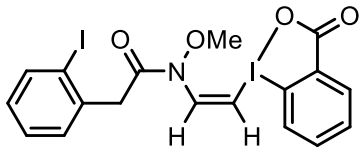
Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.38 (d, *J* = 7.45 Hz, 1H), 7.95 (d, *J* = 8.02 Hz, 1H), 7.59 (t, *J* = 6.87 Hz, 1H), 7.56-7.49 (m, 2H), 7.15 (d, *J* = 8.59 Hz, 2H), 6.84 (d, *J* = 8.59 Hz, 2H), 6.01 (d, *J* = 8.02 Hz, 1H), 3.83 (s, 2H), 3.78 (s, 6H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.3, 167.1, 158.9, 134.2, 133.5, 133.4, 132.8, 130.5, 130.4, 125.9, 124.2, 114.8, 114.2, 79.6, 64.6, 55.2, 38.4.

HRMS (ESI, positive): calcd for $C_{19}H_{18}INNaO_5$ $[M + Na]^+$ 490.01273, Found 490.00987.

(*Z*)-*N*-(1-Vin-2-yl)-2-(2-iodophenyl)-*N*-methoxyacetamide-1,2-benziodoxol-3-(1*H*)-one (3r)



Following the **Procedure D**, 2-(2-iodophenyl)-*N*-methoxyacetamide (**1r**: 29.1 mg, 0.1 mmol) was used and the reaction time was 3 h. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-2-(2-iodophenyl)-*N*-methoxyacetamide-1,2-benziodoxol-3-(1*H*)-one (**3r**: 36.1 mg, 64%).

Rf: 0.29 ($CHCl_3$: MeOH = 10 : 1).

Physical state: Colorless oil.

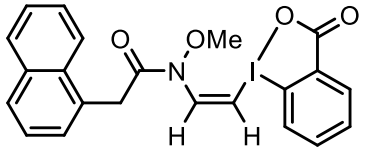
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44-8.39 (m, 1H), 7.96 (d, *J* = 8.02 Hz, 1H), 7.86 (d, *J* = 8.02 Hz, 1H), 7.66-7.57 (m, 3H),

7.35 (t, *J* = 7.45 Hz, 1H), 7.26 (d, *J* = 8.02 Hz, 1H), 7.02 (t, *J* = 8.02 Hz, 1H), 6.05 (d, *J* = 8.02 Hz, 1H), 4.07 (s, 2H), 3.94 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.1, 167.0, 139.5, 136.2, 134.3, 133.6, 133.6, 132.9, 130.9, 130.7, 129.4, 128.7, 125.9, 114.9, 101.2, 80.3, 64.8, 44.6.

HRMS (ESI, positive): calcd for $C_{18}H_{15}I_2NNaO_4$ $[M + Na]^+$ 585.89881, Found 585.89993.

(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxy-1-naphthaleneacetamide-1,2-benziodoxol-3-(1*H*)-one (3s)



Following the **Procedure D**, *N*-methoxy-1-naphthaleneacetamide (**1s**: 21.5 mg, 0.1 mmol) was used and the reaction time was 3 h. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-*N*-methoxy-1-naphthaleneacetamide-1,2-benziodoxol-3-(1*H*)-one (**3s**: 34.0 mg, 70%).

Rf: 0.31 ($CHCl_3$: MeOH = 10 : 1).

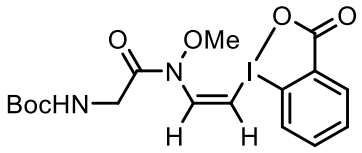
Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.43-8.38 (m, 1H), 7.94 (d, *J* = 8.59 Hz, 1H), 7.89-7.84 (m, 2H), 7.81 (d, *J* = 8.02 Hz, 1H), 7.62-7.57 (m, 1H), 7.55-7.47 (m, 4H), 7.41 (t, *J* = 8.02 Hz, 1H), 7.38-7.35 (m, 1H), 5.96 (d, *J* = 8.02 Hz, 1H), 4.33 (s, 2H), 3.79 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.9, 167.0, 134.2, 133.8, 133.5, 132.8, 131.9, 130.6, 128.9, 128.9, 128.5, 128.2, 126.7, 126.0, 125.8, 125.4, 123.2, 114.8, 80.0, 64.7, 36.8 (*one carbon aromatic signal not resolved*).

HRMS (ESI, positive): calcd for $C_{22}H_{18}INNaO_4$ $[M + Na]^+$ 510.01782, Found 510.01620.

(*Z*)-*N*-(1-Vin-2-yl)-Boc-glycine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3t)



Following the **Procedure D**, Boc-glycine-*N*-methoxyamide (**1t**: 20.4 mg, 0.1 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-Boc-glycine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (**3t**) with 2-iodobenzoic acid as an impurity (19.6 mg; **3t**(37% yield):2-iodobenzoic acid = 82:18).

Rf: 0.26 ($CHCl_3$: MeOH = 10 : 1).

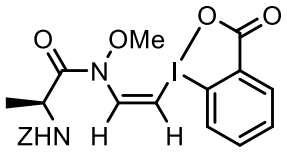
Physical state: Colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$:MeOH-d_4 = 10:1): δ 8.40-8.33 (m, 1H), 7.93 (d, *J* = 8.23 Hz, 1H), 7.71-7.65 (m, 2H), 7.65-7.59 (m, 1H), 6.05 (d, *J* = 8.23 Hz, 1H), 4.21 (s, 2H), 3.89 (s, 3H), 1.47 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$:MeOH-d_4 = 10:1): δ 169.9, 167.8, 156.2, 141.1, 134.3, 134.0, 132.8, 130.9, 126.1, 114.3, 80.4, 79.0, 64.6, 41.9, 28.1.

HRMS (ESI, positive): calcd for $C_{17}H_{21}IN_2NaO_6$ $[M + Na]^+$ 499.03420, Found 499.03472.

(*Z*)-*N*-(1-Vin-2-yl)-Cbz-L-alanine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3x)



Following the **Procedure D**, Cbz-L-alanine-*N*-methoxyamide (**1x**: 25.2 mg, 0.1 mmol) was used. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-Cbz-L-alanine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (**3x**: 19.6 mg, 41%).

Rf: 0.31 ($CHCl_3$: MeOH = 10 : 1).

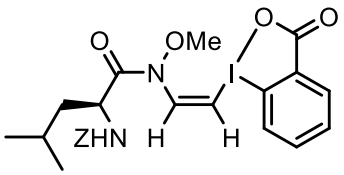
Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.45(dd, *J* = 6.87, 2.27 Hz, 1H), 7.96 (d. *J* = 8.59 Hz, 1H), 7.68-7.60 (m, 2H), 7.59-7.53 (m, 1H), 7.39-7.29 (m, 5H), 6.02 (d, *J* = 6.02 Hz, 1H), 5.43 (d, *J* = 7.45 Hz, 1H), 5.15 (d, *J* = 12.32 Hz, 1H), 5.11 (d, *J* = 12.32 Hz, 1H), 4.78 (quint, *J* = 6.87 Hz, 1H), 3.96 (s, 3H), 1.36 (d, *J* = 6.87 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 172.9, 167.1, 156.0, 141.0, 135.9, 133.5, 133.5, 132.9, 130.6, 128.5, 128.2, 128.0, 125.9, 114.8, 80.4, 67.1, 64.9, 47.7, 17.7.

HRMS (ESI, positive): calcd for $C_{21}H_{21}IN_2NaO_6$ $[M + Na]^+$ 547.03420, Found 547.03415.

(*Z*)-*N*-(1-Vin-2-yl)-Cbz-L-leucine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3y)



Following the **Procedure D**, Cbz-L-leucine-*N*-methoxyamide (**1y**: 29.4 mg, 0.1 mmol) was used and the reaction time was 24 h. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-Cbz-L-leucine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (**3y**: 40.1 mg, 71%).

Rf: 0.29 ($CHCl_3$: MeOH = 10 : 1).

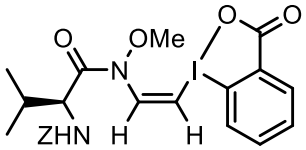
Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44-8.36 (m, 1H), 7.99 (d, *J* = 8.02 Hz, 1H), 7.65-7.53 (m, 3H), 7.39-7.29 (m, 5H), 6.08 (d, *J* = 8.02 Hz, 1H), 5.48 (brs, 1H), 5.12 (d, *J* = 12.03 Hz, 1H), 5.07 (d, *J* = 12.03 Hz, 1H), 4.80-8.70 (m, 1H), 3.97 (s, 3H), 1.78-1.64 (m, 1H), 1.54-1.42 (m, 1H), 1.42-1.30 (m, 1H), 0.90-0.82 (m, 6H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 172.9, 167.1, 156.3, 141.0, 135.8, 133.5, 133.3, 132.9, 130.5, 128.5, 128.2, 127.9, 125.9, 114.9, 80.0, 67.1, 64.8, 50.3, 40.9, 24.7, 23.0, 21.1.

HRMS (ESI, positive): calcd for $C_{24}H_{27}IN_2NaO_6$ $[M + Na]^+$ 589.08115, Found 589.08263.

(*Z*)-*N*-(1-Vin-2-yl)-Cbz-L-valine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3z)



Following the **Procedure D**, Cbz-L-valine-*N*-methoxyamide (**1z**: 28.0 mg, 0.1 mmol) was used and the reaction time was 24 h. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-Cbz-L-valine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (**3z**: 33.3 mg, 60%).

1mmol reaction

Cbz-L-Valine-*N*-methoxyamide (**1z**: 280.3 mg, 1 mmol) was used and the reaction time was 24 h. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-Cbz-L-valine *N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (**3z**: 456.8 mg, 83%).

Rf: 0.29 ($CHCl_3$: MeOH = 10 : 1).

Physical state: Colorless solid.

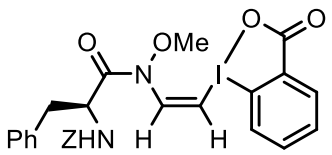
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.41 (dd, *J* = 7.45, 1.75 Hz, 1H), 8.01 (d, *J* = 8.01 Hz, 1H), 7.66-7.53 (m, 3H), 7.39-7.29 (m, 5H), 6.07 (d, *J* = 8.02 Hz, 1H), 5.42 (d, *J* = 8.02 Hz, 1H), 5.13 (d, *J* = 12.03 Hz, 1H), 5.07 (d, *J* = 12.03 Hz, 1H), 4.71-4.59 (m, 1H), 3.98 (s, 3H), 2.04-1.84 (m, 1H), 0.95 (d, *J* = 6.30 Hz, 3H), 0.92 (d, *J* = 6.87 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.0, 167.0, 156.5, 141.1, 135.8, 133.5, 133.1, 133.0, 130.7, 128.6, 128.3, 128.1, 125.7, 114.7, 80.2, 67.3, 64.8, 56.3, 30.9, 19.2, 17.5.

HRMS (ESI, positive): calcd for $C_{23}H_{25}IN_2NaO_6$ $[M + Na]^+$ 575.06550, Found 575.06471.

$[\alpha]_D^{22}$ = +154.8 (*c* = 0.1 in MeOH).

(*Z*)-*N*-(1-Vin-2-yl)-Cbz-L-phenylalanine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3aa)



Following the **Procedure D**, Cbz-L-phenylalanine-*N*-methoxyamide (**1aa**: 32.8 mg, 0.1 mmol) was used and the reaction time was 24 h. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-Cbz-L-phenylalanine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (**3aa**) with 2-iodobenzoic acid as an impurity (40.7 mg; **3aa**(61% yield):2-iodobenzoic aicd = 80:20).

Rf: 0.31 ($CHCl_3$: MeOH = 10 : 1).

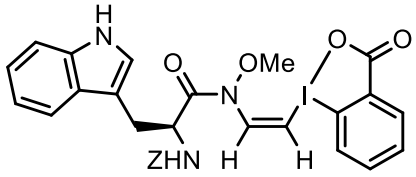
Physical state: Colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50-8.43 (m, 1H), 7.89 (d, *J* = 8.23 Hz, 1H), 7.66-7.62 (m, 2H), 7.54 (d, *J* = 6.86 Hz, 1H), 7.39-7.22 (m, 8H), 7.12 (d, *J* = 5.95 Hz, 2H), 5.96 (d, *J* = 7.78 Hz, 1H), 5.43 (d, *J* = 6.40 Hz, 1H), 5.14-5.00 (m, 3H), 3.87 (s, 3H), 2.99 (d, *J* = 6.86 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9, 167.1, 156.0, 141.1, 135.8, 134.8, 133.6, 132.9, 132.2, 130.7, 129.3, 128.7, 128.5, 128.2, 128.0, 127.5, 125.8, 114.7, 80.5, 67.2, 64.7, 52.7, 38.3.

HRMS (ESI, positive): calcd for $C_{27}H_{25}IN_2NaO_6$ $[M + Na]^+$ 623.06550, Found 623.06651.

(*Z*)-*N*-(1-Vin-2-yl)-Cbz-L-tryptophan-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3ab)



Following the **Procedure D**, Cbz-L-tryptophan-*N*-methoxyamide (**1ab**: 36.7 mg, 0.1 mmol) was used and the reaction time was 24 h. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-Cbz-L-tryptophan-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (**3ab**: 36.6 mg, 57%).

Rf: 0.32 ($CHCl_3$: MeOH = 10 : 1).

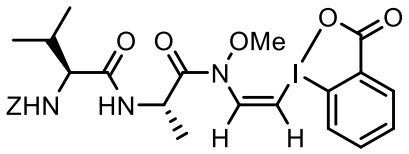
Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.34 (brs, 1H), 8.42 (brs, 1H), 7.76 (brs, 1H), 7.63-7.53 (m, 2H), 7.50-7.38 (m, 3H), 7.38-7.32 (m, 5H), 7.16-7.00 (m, 3H), 5.77 (brs, 1H), 5.56 (brs, 1H), 5.16-5.03 (m, 3H), 3.66 (s, 3H), 3.31-3.13 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.8, 167.4, 156.0, 136.3, 135.9, 133.5, 133.3, 132.8, 130.6, 128.5, 128.2, 128.0, 127.2, 125.8, 124.1, 122.0, 119.5, 118.2, 114.5, 112.1, 108.2, 79.8, 67.2, 64.2, 52.4, 28.8 (*one carbon aromatic signal not resolved*).

HRMS (ESI, positive): calcd for $C_{29}H_{26}IN_3NaO_6$ $[M + Na]^+$ 662.07640, Found 662.07786.

(*Z*)-*N*-(1-Vin-2-yl)-Cbz-L-valyl-L-alanine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3ac)



Following the **Procedure D**, Cbz-L-valyl-L-alanine-*N*-methoxyamide (**1ac**: 35.1 mg, 0.1 mmol) and 2-propanol instead of 1,2-dichloroethane were used and the reaction time was 24 h. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-Cbz-L-valyl-L-alanine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (**3ac**: 27.1 mg, 43%). When EBX·H_2O complex (37.7 mg, 0.13 mmol, 1.3 equiv) instead of EBX·1/3MeCN was used, the desired compound (**3ac**: 25.4 mg, 41%) was obrained.

Rf: 0.22 ($CHCl_3$: MeOH = 10 : 1).

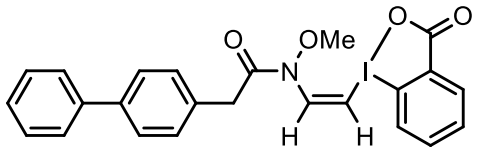
Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.50-8.41 (m, 1H), 7.94 (d, *J* = 8.02 Hz, 1H), 7.70-7.61 (m, 2H), 7.61-7.52 (m, 1H), 7.40-7.26 (m, 5H), 6.80 (brs, 1H), 5.98 (brs, 1H), 5.50 (brs, 1H), 5.08 (s, 2H), 4.97-4.86 (m, 1H), 4.14-4.04 (m, 1H), 3.95 (s, 3H), 2.22-2.07 (m, 1H), 1.39 (d, *J* = 6.87 Hz, 3H), 1.00 (d, *J* = 6.30 Hz, 3H), 0.95 (d, *J* = 6.30 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 172.4, 172.0, 167.1, 156.5, 141.3, 136.2, 133.7, 133.4, 133.0, 130.8, 128.5, 128.1, 127.9, 125.8, 114.7, 80.1, 66.9, 64.9, 60.1, 46.2, 31.1, 19.2, 17.8, 17.0.

HRMS (ESI, positive): calcd for $C_{26}H_{30}IN_3NaO_7$ $[M + Na]^+$ 646.10261, Found 646.10501.

(*Z*)-*N*-(1-Vin-2-yl)-2-[(1,1'-biphenyl)-4-yl]-*N*-methoxyacetamide-1,2-benziodoxol-3-(1*H*)-one (3ad)



Following the **Procedure D**, 2-[(1,1'-biphenyl)-4-yl]-*N*-methoxyacetamide (**1ad**: 24.1 mg, 0.1 mmol) was used and the reaction time was 24 h. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-2-[(1,1'-biphenyl)-4-yl]-*N*-methoxyacetamide-1,2-benziodoxol-3-(1*H*)-one (**3ad**: 36.7 mg, 71%).

Rf: 0.15 ($CHCl_3$: MeOH = 20 : 1).

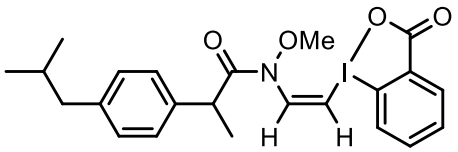
Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.45 (d, *J* = 7.45 Hz, 1H), 7.98 (d, *J* = 8.59 Hz, 1H), 7.63-7.51 (m, 7H), 7.45 (t, *J* =8.02 Hz, 2H), 7.39-7.31 (m, 3H), 5.96 (d, *J* = 8.02 Hz, 1H), 3.95 (s, 2H), 3.82 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.0, 166.9, 140.5, 140.3, 134.1, 133.6, 133.0, 131.2, 130.7, 129.8, 128.8, 127.5, 127.5, 127.0, 125.6, 114.8, 79.8, 64.7, 39.0.

HRMS (ESI, positive): calcd for $C_{24}H_{20}INNaO_4$ $[M + Na]^+$ 536.03347, Found 536.03324.

(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxy-2-[4-(2-methylpropyl)phenyl]propanamide-1,2-benziodoxol-3-(1*H*)-one (3ae)



Following the **Procedure D**, *N*-methoxy-2-[4-(2-methylpropyl)phenyl]propanamide (**1ae**: 23.5 mg, 0.1 mmol) was used and the reaction time was 24 h. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-*N*-methoxy-2-[4-(2-methylpropyl)phenyl]propanamide-1,2-benziodoxol-3-(1*H*)-one (**3ae**: 36.7 mg, 71%).

Rf: 0.36 ($CHCl_3$: MeOH = 10 : 1).

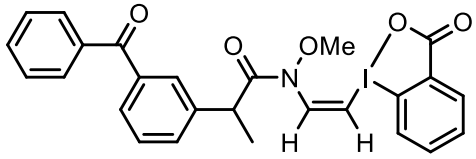
Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.38 (d, *J* = 7.45 Hz, 1H), 7.90 (d, *J* = 8.02 Hz, 1H), 7.57 (t, *J* = 7.45 Hz, 1H), 7.54-7.45 (m, 2H), 7.16 (d, *J* = 7.45 Hz, 2 H), 7.09 (d, *J* = 7.45 Hz, 2H), 6.01 (brs, 1H), 4.16 (d, *J* = 5.73 Hz, 1H), 3.51 (s, 3H), 2.44 (d, *J* = 6.87 Hz, 2H), 1.83 (non, *J* = 6.87 Hz, 1H), 1.49 (d, *J* = 6.87 Hz, 3H), 0.88 (d, *J* = 6.30 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 174.3, 167.1, 141.1, 136.6, 134.7, 133.4, 132.8, 130.5, 129.7, 127.1, 125.8, 114.8, 80.4, 64.4, 44.9, 42.2, 30.0, 22.3, 22.3, 19.5 (*one carbon aromatic signal not resolved*).

HRMS (ESI, positive): calcd for $C_{23}H_{26}INNaO_4$ $[M + Na]^+$ 530.08042, Found 530.07990.

(*Z*)-*N*-(1-Vin-2-yl)-2-(3-benzoylphenyl)-*N*-methoxypropanamide-1,2-benziodoxol-3-(1*H*)-one (3af)



Following the **Procedure D**, 2-(3-benzoylphenyl)-*N*-methoxypropanamide (**1af**: 28.3 mg, 0.1 mmol) was used and the reaction time was 24 h. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-2-(3-benzoylphenyl)-*N*-methoxypropanamide-1,2-benziodoxol-3-(1*H*)-one (**3af**: 38.5 mg, 69%).

Rf: 0.10 ($CHCl_3$: MeOH = 20 : 1).

Physical state: Colorless oil.

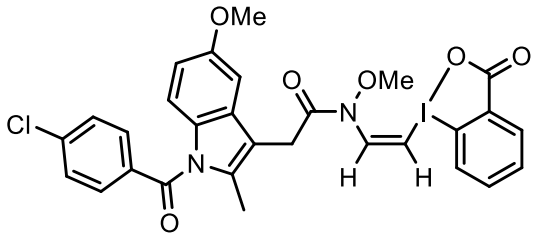
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.34 (d, *J* = 7.45 Hz, 1H), 7.93 (d, *J* = 8.02 Hz, 1H), 7.74-7.70 (m, 3H), 7.66 (d, *J* = 7.45 Hz, 1H), 7.59 (t, *J* = 7.45 Hz, 1H), 7.56-7.53 (m, 1H), 7.52-7.41 (m, 6H), 6.06 (d, *J* = 5.73 Hz, 1H), 4.25 (q, *J* = 6.87 Hz, 1H), 3.67 (s, 3H), 1.54 (d, *J* = 7.45 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 196.1, 173.6, 167.2, 141.0, 139.8, 138.2, 137.1, 134.3, 133.5, 132.8, 132.7, 131.3, 130.5,

129.9, 129.4, 129.0, 128.9, 128.3, 125.8, 114.8, 80.6, 64.7, 42.3, 19.4.

HRMS (ESI, positive): calcd for $C_{26}H_{22}INNaO_5$ $[M + Na]^+$ 578.04403, Found 578.04262.

(*Z*)-*N*-(1-Vin-2-yl)-1-(4-chlorobenzoyl)-*N*,5-dimethoxy-2-methyl-1*H*-indole-3-acetamide-1,2-benziodoxol-3-(1*H*)-one (3ag)



Following the **Procedure D**, 1-(4-chlorobenzoyl)-*N*,5-dimethoxy-2-methyl-1*H*-indole-3-acetamide (**1ag**: 38.9 mg, 0.1 mmol) was used and the reaction time was 24 h. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford (*Z*)-*N*-(1-vin-2-yl)-1-(4-chlorobenzoyl)-*N*,5-dimethoxy-2-methyl-1*H*-indole-3-acetamide-1,2-benziodoxol-3-(1*H*)-one (**3ag**: 43.1 mg, 65%).

Rf: 0.10 ($CHCl_3$: MeOH = 20 : 1).

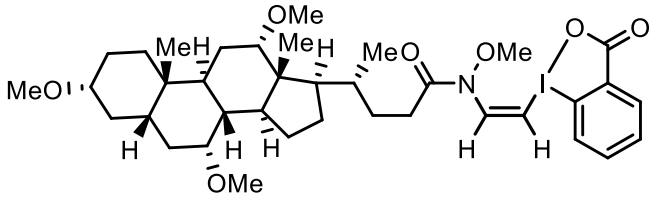
Physical state: Yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.46 (d, *J* = 8.02 Hz, 1H), 7.95 (d, *J* = 8.59 Hz, 1H), 7.69-7.62 (m, 3H), 7.59-7.52 (m, 2H), 7.48 (dt, *J* = 8.59, 2.29 Hz, 2H), 6.91 (d, *J* = 2.86 Hz, 1H), 6.84 (d, *J* = 9.16 Hz, 1H), 6.68 (dd, *J* = 9.16, 2.86 Hz, 1H), 5.97 (d, *J* = 8.59 Hz, 1H), 3.96 (s, 2H), 3.89 (s, 3H), 3.82 (s, 3H), 2.37 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ. 170.0, 168.2, 167.0, 156.0, 139.5, 136.5, 134.2, 133.6, 133.5, 133.4, 133.0, 131.2, 130.8, 130.7, 130.3, 129.2, 125.6, 115.0, 114.8, 111.5, 110.6, 101.4, 80.3, 64.7, 55.7, 28.9, 13.5.

HRMS (ESI, positive): calcd for $C_{29}H_{24}ClIN_2NaO_6$ $[M + Na]^+$ 681.02653, Found 681.02816.

(*Z*)-*N*-(1-Vin-2-yl)-(*R*)-*N*-methoxy-4-[(3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,7,12-trimethoxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl]pentanamide-1,2-benziodoxol-3-(1*H*)-one (3ah)



Following the **Procedure D**, (*R*)-*N*-methoxy-4-[(3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,7,12-trimethoxy-10,13-dimethyl hexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl]pentanamide (**1ah**: 31.4 mg, 0.1 mmol) was used and the reaction time was 24 h. Purification by flash column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$:MeOH = 20:1) to afford

(*Z*)-*N*-(1-vin-2-yl)-(*R*)-*N*-methoxy-4-[(3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,7,12-trimethoxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl]pentanamide-1,2-benziodoxol-3-(1*H*)-one (**3ah**: 18.7 mg, 32%).

Rf: 0.39 ($CHCl_3$: MeOH = 10 : 1).

Physical state: Colorless oil.

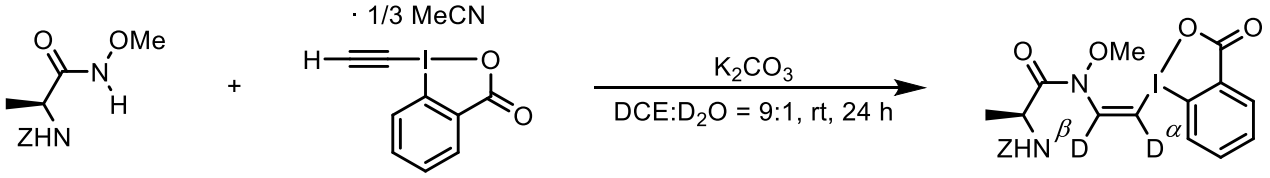
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.45-8.38 (m, 1H), 8.02 (d, *J* = 8.02 Hz, 1H), 7.67-7.57 (m, 3H), 5.95 (d, *J* = 8.59 Hz, 1H), 3.84 (s, 3H), 3.36 (s, 1H), 3.33 (s, 3H), 3.25 (s, 3H), 3.21 (s, 3H), 3.15 (s, 1H), 3.05-2.95 (m, 1H), 2.64-2.55 (m, 1H), 2.53-2.44 (m, 1H), 2.18 (q, *J* = 12.60 Hz, 1H), 2.13-1.99 (m, 2H), 1.98-1.89 (m, 1H), 1.87-1.41 (m, 11H), 1.38-1.14 (m, 5H), 1.09-0.99 (m, 1H), 0.98-0.87 (m, 7H), 0.66 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 173.6, 167.0, 141.0, 134.1, 133.5, 132.8, 130.6, 125.7, 114.7, 81.8, 80.6, 77.7, 76.8, 64.4, 55.7, 55.6, 55.3, 46.0, 45.9, 42.6, 41.8, 39.4, 35.1, 34.8, 34.7, 34.3, 30.1, 28.8, 27.8, 27.7, 27.2, 26.6, 23.0, 22.7, 21.8, 17.4, 12.4.

HRMS (ESI, positive): calcd for $C_{37}H_{54}INNaO_7$ $[M + Na]^+$ 774.28426, Found 774.28165.

Procedure E: Synthesis of di-deuterated *cis*-*β*-amide-VBXs

(*Z*)-*N*-(1,2-d_2-1-Vin-2-yl)-Cbz-L-alanine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3x-d_2)



To a stirred solution of Cbz-L-alanine-*N*-methoxyamide (**1x**: 12.6 mg, 0.05 mmol, 1.0 equiv) in dry 1,2-dichloroethane (0.9 mL) and D_2O (0.1 mL) under argon was added K_2CO_3 (1.4 mg, 0.01 mmol, 0.2 equiv) at rt. After 5 min, ethynyl-1,2-benziodoxol-3-(1*H*)-one-MeCN complex (**2a**: 18.6 mg, 0.065 mmol, 1.3 equiv) was added one portion. After 24 h, $CHCl_3$ was added to the reaction mixture. The solution was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by preparative TLC ($CHCl_3$: MeOH = 10 : 1) to afford (*Z*)-*N*-(1,2-d_2-1-vin-2-yl)-Cbz-L-alanine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (**3x**-d_2: 21.4 mg, 81%, *α*: 94%D, *β*: 97%D).

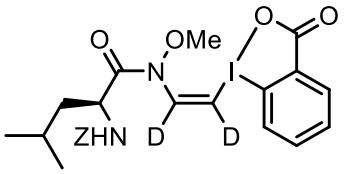
Rf: 0.26 ($CHCl_3$: MeOH = 10 : 1).

Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.49-8.41 (m, 1H), 7.97 (s, 0.03H), 7.68-7.60 (m, 2H), 7.59-7.53 (m, 1H), 7.40-7.28 (m, 5H), 6.01 (s, 0.06H), 5.45 (d, *J* = 6.30 Hz, 1H), 5.14 (d, *J* = 12.03 Hz, 1H), 5.17 (d, *J* = 12.03 Hz, 1H), 4.78 (quint, *J* = 7.45 Hz, 1H), 3.96 (s, 3H), 1.36 (d, *J* = 7.45 Hz, 3H).

HRMS (ESI, positive): calcd for $C_{21}H_{19}D_2IN_2NaO_6$ $[M + Na]^+$ 549.04675, Found 549.04390.

(*Z*)-*N*-(1,2-d_2-1-Vin-2-yl)-Cbz-L-leucine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3y-d_2)



Following the **Procedure E**, Cbz-L-leucine-*N*-methoxyamide (**1y**: 14.7 mg, 0.05 mmol) was used. Purification by preparative TLC ($CHCl_3$: MeOH = 10 : 1) to afford (*Z*)-*N*-(1,2-d_2-1-vin-2-yl)-Cbz-L-leucine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (**3y**-d_2: 23.7 mg, 83%, α: 97%D, β: 98%D).

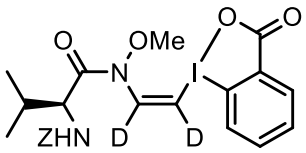
Rf: 0.30 ($CHCl_3$: MeOH = 10 : 1).

Physical state: Colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55-8.37 (m, 1H), 7.99 (s, 0.02H), 7.70-7.52 (m, 3H), 7.41-7.28 (m, 5H), 5.98 (s, 0.03H), 5.27 (d, *J* = 7.78 Hz, 1H), 5.14 (d, *J* = 12.12 Hz, 1H), 5.07 (d, *J* = 12.12 Hz, 1H), 4.83-4.72 (m, 1H), 3.98 (s, 3H), 1.77-1.66 (m, 1H), 1.54-1.36 (m, 2H), 0.93-0.88 (m, 6H).

HRMS (ESI, positive): calcd for $C_{24}H_{25}D_2IN_2NaO_6$ $[M + Na]^+$ 591.09370, Found 591.09159.

(*Z*)-*N*-(1,2-d_2-1-Vin-2-yl)-Cbz-L-valine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3z-d_2)



Following the **Procedure E**, Cbz-L-valine-*N*-methoxyamide (**1z**: 14.0 mg, 0.05 mmol) was used. Purification by preparative TLC ($CHCl_3$: MeOH = 10 : 1) to afford (*Z*)-*N*-(1,2-d_2-1-vin-2-yl)-Cbz-L-valine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (**3z**-d_2: 20.4 mg, 74%, α: 94%D, β: 97%D).

1 mmol scale reaction

To a stirred solution of Cbz-L-valine-*N*-methoxyamide (**1z**: 280.3 mg, 1.0 mmol, 1.0 equiv) in 1,2-dichloroethane (18 mL) and D_2O (2 mL) under argon was added K_2CO_3 (27.6 mg, 0.2 mmol, 0.2 equiv) at rt. After 5 min, ethynyl-1,2-benziodoxol-3-(1*H*)-one-MeCN complex (**2a**: 371.5 mg, 1.3 mmol, 1.3 equiv) was added one portion. After 24 h, $CHCl_3$ was added to the reaction mixture and the layers ware separated. The aqueous layer was the extracted with $CHCl_3$. The organic layers ware combined, dried over Na_2SO_4 and filtered and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (only $CHCl_3$ to $CHCl_3$/MeOH = 20 : 1) to afford (*Z*)-*N*-(1,2-d_2-1-vin-2-yl)-Cbz-L-valine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (**3z**-d_2: 546.6 mg, 99%, α: 97%D, β: 98%D).

Rf: 0.32 ($CHCl_3$: MeOH = 10 : 1).

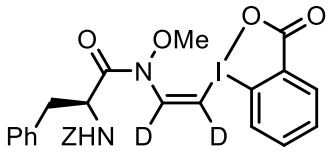
Physical state: Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.53-8.40 (m, 1H), 8.01 (s, 0.02H), 7.69-7.59 (m, 2H), 7.59-7.53 (m, 1H), 7.41-7.28 (m, 5H), 6.00 (s, 0.03H), 5.33 (d, *J* = 9.17 Hz, 1H), 5.14 (d, *J* = 12.03 Hz, 1H), 5.07 (d, *J* = 12.03 Hz, 1H), 4.70-4.60 (m, 1H), 3.98 (s, 3H), 2.04-1.91 (m, 1H), 0.96 (d, *J* = 6.87 Hz, 3H), 0.93 (d, *J* = 6.87 Hz, 3H).

HRMS (ESI, positive): calcd for $C_{23}H_{23}D_2IN_2NaO_6$ $[M + Na]^+$ 577.07805, Found 577.08134.

$[\alpha]_D^{22}$ = +157.5 (*c* = 0.1 in MeOH).

(*Z*)-*N*-(1,2-d_2-1-Vin-2-yl)-Cbz-L-phenylalanine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3aa-d_2)



Following the **Procedure E**, Cbz-L-phenylalanine-*N*-methoxyamide (**1aa**: 16.4 mg, 0.05 mmol) was used. Purification by preparative TLC ($CHCl_3$: MeOH = 10 : 1) to afford (*Z*)-*N*-(1,2-d_2-1-vin-2-yl)-Cbz-L-phenylalanine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (**3aa**-d_2: 19.3 mg, 64%, *α*: 94%D, *β*: 97%D).

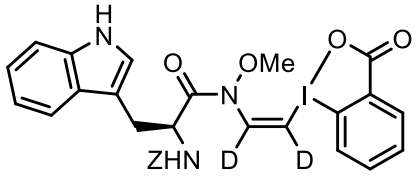
Rf: 0.27 ($CHCl_3$: MeOH = 10 : 1).

Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.51-8.42 (m, 1H), 7.88 (s, 0.03H), 7.68-7.60 (m, 2H), 7.53 (d, *J* = 6.87 Hz, 1H), 7.39-7.23 (m, 8H), 7.12 (d, *J* = 7.12 Hz, 2H), 5.94 (s, 0.06H), 5.41 (d, *J* = 7.45 Hz, 1H), 5.14-5.01 (m, 3H), 3.86 (s, 3H), 2.99 (d, *J* = 6.87 Hz, 2H).

HRMS (ESI, positive): calcd for $C_{27}H_{24}D_2IN_2O_6$ $[M + H]^+$ 603.09611, Found 603.09503.

(*Z*)-*N*-(1,2-d_2-1-Vin-2-yl)-Cbz-L-tryptophan-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3ab-d_2)



Following the **Procedure E**, Cbz-L-tryptophan-*N*-methoxyamide (**1ad**: 18.4 mg, 0.05 mmol) was used. Purification by preparative TLC ($CHCl_3$: MeOH = 10 : 1) to afford (*Z*)-*N*-(1,2-d_2-1-vin-2-yl)-Cbz-L-tryptophan-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (**3ab**-d_2: 23.9 mg, 75%, *α*: 93%D, *β*: 93%D).

Rf: 0.27 ($CHCl_3$: MeOH = 10 : 1).

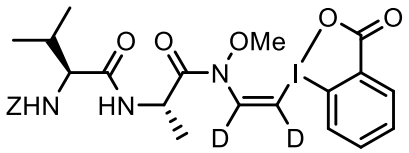
Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.49 (brs, 1H), 8.47-8.32 (m, 1H), 7.72 (s, 0.07H), 7.63-7.52 (m, 2H), 7.48-7.38 (m, 3H),

7.38-7.29 (m, 5H), 7.17-7.06 (m, 2H), 7.06-6.98 (m, 1H), 5.73 (s, 0.07H), 5.61 (brs, 1H), 5.17-5.01 (m, 3H), 3.64 (s, 3H), 3.28-3.12 (m, 2H).

HRMS (ESI, positive): calcd for $C_{29}H_{24}D_2IN_3NaO_6$ $[M + Na]^+$ 664.08895, Found 664.08955.

(*Z*)-*N*-(1,2-*d*$_2$-1-Vin-2-yl)-Cbz-L-valyl-L-alanine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3ac-*d*$_2$)



Following the **Procedure E**, Cbz-L-valyl-L-alanine-*N*-methoxyamide (**1ac**: 16.8 mg, 0.05 mmol) was used. Purification by preparative TLC ($CHCl_3$: MeOH = 10 : 1) to afford (*Z*)-*N*-(1,2-*d*$_2$-1-vin-2-yl)-Cbz-L-valyl-L-alanine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (**3ac**-*d*$_2$: 10.3 mg, 33%, *α*: 92%D, *β*: 97%D).

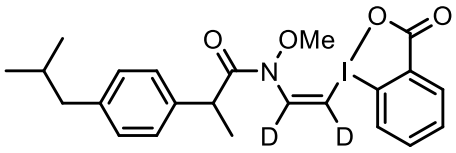
Rf: 0.20 ($CHCl_3$: MeOH = 10 : 1).

Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.48-8.40 (m, 1H), 7.95 (s, 0.03H), 7.68-7.60 (m, 2H), 7.60-7.52 (m, 1H), 7.40-7.26 (m, 5H), 6.97 (brs, 1H), 5.98 (s, 0.08H), 5.59 (brs, 1H), 5.08 (s, 2H), 4.92 (t, *J* = 6.30 Hz, 1H), 4.11 (t, *J* = 6.87 Hz, 1H), 3.95 (s, 3H), 2.23-2.10 (m, 1H), 1.38 (d, *J* = 6.87 Hz, 3H), 1.00 (d, *J* = 6.87 Hz, 3H), 0.95 (d, *J* = 6.87 Hz, 3H).

HRMS (ESI, positive): calcd for $C_{26}H_{28}D_2IN_3NaO_7$ $[M + Na]^+$ 648.11517, Found 648.11124.

(*Z*)-*N*-(1,2-*d*$_2$-1-Vin-2-yl)-*N*-methoxy-2-[4-(2-methylpropyl)phenyl]propanamide-1,2-benziodoxol-3-(1*H*)-one (3ae-*d*$_2$)



Following the **Procedure E**, *N*-methoxy-2-[4-(2-methylpropyl)phenyl]propanamide (**1ae**: 11.8 mg, 0.05 mmol) was used. Purification by preparative TLC ($CHCl_3$: MeOH = 20 : 1) to afford (*Z*)-*N*-(1,2-*d*$_2$-1-vin-2-yl)-*N*-methoxy-2-[4-(2-methylpropyl)phenyl]propenamide-1,2-benziodoxol-3-(1*H*)-one (**3ae**-*d*$_2$: 16.3 mg, 64%, *α*: 96%D, *β*: 96%D).

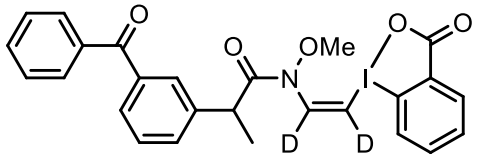
Rf: 0.33 ($CHCl_3$: MeOH = 10 : 1).

Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.41 (dd, *J* = 7.45, 1.72 Hz, 1H), 7.89 (s, 0.04H), 7.62-7.57 (m, 1H), 7.56-7.46 (m, 2H), 7.16 (d, *J* = 8.59 Hz, 2H), 7.10 (d, *J* = 8.59 Hz, 2H), 5.96 (s, 0.04H), 4.16 (d, *J* = 5.16 Hz, 1H), 3.50 (s, 3H), 2.44 (d, *J* = 6.87 Hz, 2H), 1.83 (non, *J* = 6.87 Hz, 1H), 1.48 (d, *J* = 6.87 Hz, 3H), 0.88 (d, *J* = 6.30 Hz, 6H).

HRMS (ESI, positive): calcd for $C_{23}H_{25}D_2INO_4$ $[M + H]^+$ 510.11103, Found 510.11100.

(*Z*)-*N*-(1,2-d_2-1-Vin-2-yl)-2-(3-benzoylphenyl)-*N*-methoxypropanamide-1,2-benziodoxol-3-(1*H*)-one (3af-d_2)



Following the **Procedure E**, 2-(3-benzoylphenyl)-*N*-methoxypropanamide (**1af**: 14.2 mg, 0.05 mmol) was used. Purification by preparative TLC ($CHCl_3$: MeOH = 20 : 1) to afford (*Z*)-*N*-(1,2-d_2-1-vin-2-yl)-*N*-methoxy-2-(3-benzoylphenyl)propenamide-1,2-benziodoxol-3-(1*H*)-one (**3af**-d_2: 23.0 mg, 83%, α: 94%D, β: 95%D).

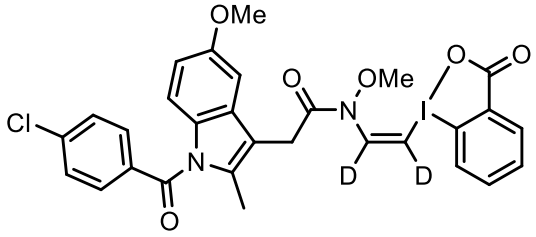
Rf: 0.10 ($CHCl_3$: MeOH = 20 : 1).

Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.39 (d, *J* = 6.30 Hz, 1H), 7.91 (s, 0.05H), 7.77-7.70 (m, 3H), 7.67 (d, *J* = 8.02 Hz, 1H), 7.64-7.55 (m, 2H), 7.55-7.41 (m, 6H), 6.00 (s, 0.06H), 4.26 (d, *J* = 6.87 Hz, 1H), 3.66 (s, 3H), 1.55 (d, *J* = 6.87 Hz, 3H).

HRMS (ESI, positive): calcd for $C_{26}H_{20}D_2INNaO_5$ $[M + Na]^+$ 580.05659, Found 580.05424.

(*Z*)-*N*-(1,2-d_2-1-Vin-2-yl)-1-(4-chlorobenzoyl)-*N*,5-dimethoxy-2-methyl-1*H*-indole-3-acetamide-1,2-benziodoxol-3-(1*H*)-one (3ag-d_2)



Following the **Procedure E**, 1-(4-chlorobenzoyl)-*N*,5-dimethoxy-2-methyl-1*H*-indole-3-acetamide (**1ag**: 19.4 mg, 0.05 mmol) was used. Purification by preparative TLC ($CHCl_3$: MeOH = 20 : 1) to afford (*Z*)-*N*-(1,2-d_2-1-vin-2-yl)-1-(4-chlorobenzoyl)-*N*,5-dimethoxy-2-methyl-1*H*-indole-3-acetamide-1,2-benziodoxol-3-(1*H*)-one (**3ag**-d_2: 27.5 mg, 83%, α: 94%D, β: 97%D).

Rf: 0.10 ($CHCl_3$: MeOH = 20 : 1).

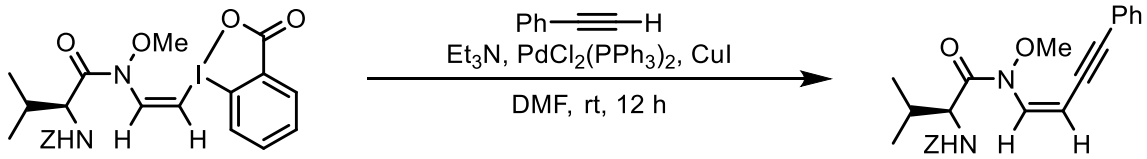
Physical state: yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42 (d, *J* = 7.45 Hz, 1H), 7.95 (s, 0.03H), 7.67-7.63 (m, 2H), 7.63-7.58 (m, 1H), 7.55-7.51 (m, 2H), 7.50-7.46 (m, 2H), 6.91 (d, *J* = 2.29 Hz, 1H), 6.85 (d, *J* = 9.17 Hz, 1H), 6.68 (dd, *J* = 9.16, 2.29 Hz, 1H), 5.99 (s, 0.06H), 3.96 (s, 2H), 3.89 (s, 3H), 3.81 (s, 3H), 2.35 (s, 3H).

HRMS (ESI, positive): calcd for $C_{29}H_{22}D_2ClIN_2NaO_6$ $[M + Na]^+$ 683.03908, Found 683.03877.

Procedure F: Sonogashira coupling using VBX

Cbz-L-Valine-(*Z*)-*N*-methoxy-*N*-(4-phenylbut-1-en-3-yn-1-yl)amide (4z)



Following a reported procedure,[36] (*Z*)-*N*-(1-vin-2-yl)-Cbz-L-valine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (**3z**: 27.6 mg, 0.05 mmol, 1 equiv), $PdCl_2(PPh_3)_2$ (1.8 mg, 2.5 μmol, 5 mol%), CuI (1.9 mg, 0.01 mmol, 20 mol%), TEA (7 μL, 0.05 mmol, 1 equiv.) and ethynylbenzene (16 μL, 0.15 mmol, 3 equiv.) were added to a flame-dried vial. Upon sealing and oxygen removing under vacuum, the vial was backfilled with Ar (process repeated for three cycles). Dry DMF (1.00 mL) was added under Ar atmosphere and the reaction was left stirring at room temperature for 12 hours. Then the reaction was stopped, EtOAc (10 mL) was added and the organic layer was washed with brine (3x30 mL). The solvent was removed under reduced pressure and the crude product was purified by preparative TLC (hexane:EtOAc = 4:1 to only toluene). Cbz-L-valine-(*Z*)-*N*-methoxy-*N*-(4-phenylbut-1-en-3-yn-1-yl)amide (**4z**: 11.6 mg, 57%) was obtained.

Rf: 0.42 (hexane : EtOAc = 4 : 1).

Physical state: Brown oil.

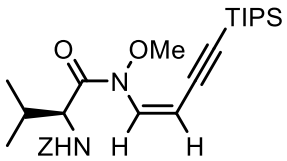
^{1}H NMR (500 MHz, acetone-d_6): δ 7.48 (d, *J* = 7.45 Hz, 2H), 7.41-7.34 (m, 7H), 7.34-7.28 (m, 1H), 7.16 (d, *J* = 10.31 Hz, 1H), 6.65 (d, *J* = 8.02 Hz, 1H), 5.22 (d, *J* = 10.31 Hz, 1H), 5.11 (d, *J* = 12.60 Hz, 1H), 5.07 (d, *J* = 12.60 Hz, 1H), 4.72 (t, *J* = 6.87 Hz, 1H), 4.11 (s, 3H), 2.18-2.10 (m, 1H), 1.02 (d, *J* = 6.87 Hz, 3H), 1.00 (d, *J* = 6.87 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ. 170.2, 156.5, 136.1, 131.2, 128.6, 128.4, 128.2, 128.1, 126.6, 123.5, 93.4, 89.1, 85.6, 67.1, 64.5, 55.9, 31.1, 19.6, 17.0 (*one carbon aromatic or vinylic signal not resolved*).

HRMS (DART, positive): calcd for $C_{24}H_{27}N_2O_4$ $[M + H]^+$ 407.19708, Found 407.19359.

$[\alpha]_D^{22}$ = +208.6 (*c* = 0.1 in MeOH).

Cbz-L-Valine-(*Z*)-*N*-methoxy-*N*-[4-(triisopropylsilyl)but-1-en-3-yn-1-yl]amide (5z)



Following the **Procedure F**, (triisopropylsilyl)acetylene (33 μL, 0.15 mmol) was used. Purification by preparative TLC (hexane:EtOAc = 4:1) to afford Cbz-L-valine-(*Z*)-*N*-methoxy-*N*-[4-(triisopropylsilyl)but-1-en-3-yn-1-yl]amide (**5z**: 14.4 mg, 59%).

Rf: 0.51 (hexane : EtOAc = 4 : 1).

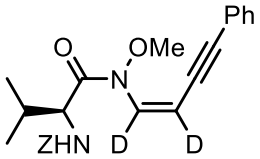
Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40-7.30 (m, 5H), 6.99 (d, *J* = 9.74 Hz, 1H), 5.36 (d, *J* = 9.74 Hz, 1H), 5.14 (d, *J* = 12.32 Hz, 1H), 5.07 (d, *J* = 12.32 Hz, 1H), 5.03 (d, *J* = 9.74 Hz, 1H), 4.74 (dd, *J* = 9.74, 5.73 Hz, 1H), 3.93 (s, 3H), 2.13-2.02 (m, 1H), 1.09 (s, 21H), 1.01 (d, *J* = 6.87 Hz, 3H), 0.91 (d, *J* = 6.87 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ. 170.2, 156.5, 136.1, 128.5, 128.2, 128.1, 126.9, 102.1, 96.0, 90.1, 67.0, 64.4, 55.7, 31.3, 19.3, 18.6, 17.3, 11.4.

HRMS (ESI, positive): calcd for $C_{27}H_{42}N_2NaO_4Si$ $[M + Na]^+$ 509.28115, Found 509.27996.

Cbz-L-Valine-(*Z*)-*N*-methoxy-*N*-(1,2-d_2-4-phenylbut-1-en-3-yn-1-yl)amide (4z-d_2)



Following the **Procedure F**, (*Z*)-*N*-(1,2-d_2-1-vin-2-yl)-Cbz-L-valine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (**3z**-d_2 (*α*: 97%D, *β*: 98%D): 27.7 mg, 0.05 mmol) was used. Purification by preparative TLC (hexane:EtOAc = 4:1 to only toluene) to afford Cbz-L-valine-(*Z*)-*N*-methoxy-*N*-(1,2-d_2-4-phenylbut-1-en-3-yn-1-yl)amide (**4z-d_2**: 13.4 mg, 66%, *α*: 97%D, *β*: 96%D).

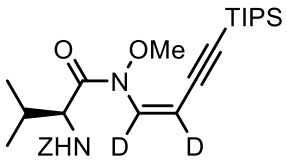
Rf: 0.42 (hexane : EtOAc = 4 : 1).

Physical state: Brown oil.

^{1}H NMR (500 MHz, acetone-d_6): δ 7.48 (d, *J* = 7.45 Hz, 2H), 7.42-7.34 (m, 7H), 7.34-7.30 (m, 1H), 7.16 (s, 0.04H), 6.66 (d, *J* = 8.59 Hz, 1H), 5.22 (s, 0.03H), 5.14 (d, *J* = 12.60 Hz, 1H), 5.08 (d, *J* = 12.60 Hz, 1H), 4.72 (t, *J* = 7.45 Hz, 1H), 4.12 (s, 3H), 2.18-2.10 (m, 1H), 1.02 (d, *J* = 6.87 Hz, 3H), 0.99 (d, *J* = 6.87 Hz, 3H).

HRMS (DART, positive): calcd for $C_{24}H_{25}D_2N_2O_4$ $[M + H]^+$ 409.20964, Found 409.21107.

Cbz-L-Valine-(*Z*)-*N*-methoxy-*N*-[1,2-d_2-4-(triisopropylsilyl)but-1-en-3-yn-1-yl]amide (5z-d_2)



Following the **Procedure F**, (*Z*)-*N*-(1,2-d_2-1-vin-2-yl)-Cbz-L-valine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (**3z**-d_2 (*α*: 97%D, *β*: 98%D): 27.7 mg, 0.05 mmol) and (triisopropylsilyl)acetylene (33 μL, 0.15 mmol) was used. Purification by preparative TLC (hexane:EtOAc = 4:1) to afford Cbz-L-valine-(*Z*)-*N*-methoxy-*N*-[1,2-d_2-4-(triisopropylsilyl)but-1-en-3-yn-1-yl]amide (**5z**-d_2: 12.8 mg, 52%, *α*: 96%D, *β*: 97%D).

Rf: 0.50 (hexane : EtOAc = 4 : 1).

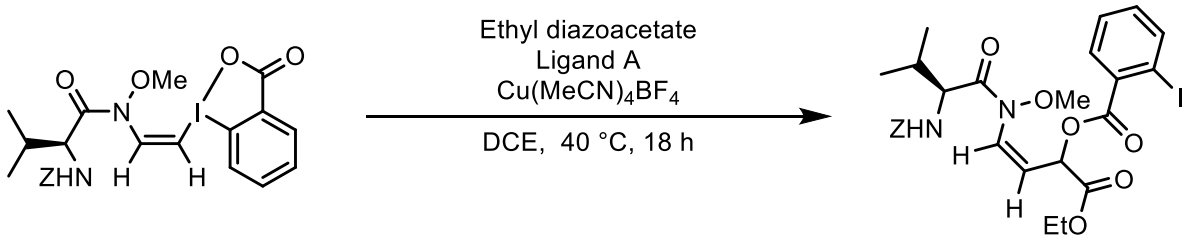
Physical state: Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39-7.29 (m, 5H), 6.99 (s, 0.03H), 5.36 (d, *J* = 9.74 Hz, 1H), 5.14 (d, *J* = 12.32 Hz, 1H), 5.07 (d, *J* = 12.32 Hz, 1H), 5.02 (s, 0.04H), 4.74 (dd, *J* = 9.74, 5.73 Hz, 1H), 3.93 (s, 3H), 2.14-2.02 (m, 1H), 1.09 (s, 21H), 1.01 (d, *J* = 6.30 Hz, 3H), 0.91 (d, *J* = 6.87 Hz, 3H).

HRMS (ESI, positive): calcd for $C_{27}H_{40}D_2N_2O_4Si$ $[M + Na]^+$ 511.29371, Found 511.29425.

Procedure G: Oxyvinylation of diazo compound

Cbz-L-Valine-(*Z*)-*N*-methoxy-*N*-[4-ethoxy-3-(2-iodobenzoyl)oxy-4-oxobut-1-en-1-yl]amide (6z)



Following a reported procedure,[37] under argon atmosphere, a catalytic solution was prepared by mixing $Cu(CH_3CN)_4BF_4$ (2.5 mg, 0.008 mmol) and *N*,*N'*-bis(2,6-dichlorobenzylidene)ethylenediamine (ligand A) (3.7 mg, 0.01 mmol) in DCE (1.0 mL) at rt for 1 h. 0.25 mL of the catalytic solution was then added to a suspension of (*Z*)-*N*-(1-vin-2-yl)-Cbz-L-valine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (**3z**: 27.6 mg, 0.05 mmol, 1 equiv) and 15% ethyl diazoacetate in toluene (85 μL, 0.1 mmol, 2 equiv) in DCE (1 mL). The reaction mixture was stirred at 40 °C. After 18 h, the solvent was removed under reduced pressure and the resulting crude oil was purified by preparative TLC (hexane:EtOAc = 4:1) directly without further work-up to afford Cbz-L-valine-(*Z*)-*N*-methoxy-*N*-[4-ethoxy-3-(2- iodobenzoyl)oxy-4-oxobut-1-en-1-yl]amide (**6z**: 20.4 mg, 64%, dr = 1.0:1.0).

Rf: 0.27 (hexane : EtOAc = 4 : 1).

Physical state: Colorless oil.

^{1}H NMR (500 MHz, acetone-d_6): δ 8.09 (dd, *J* = 8.02, 1.15 Hz, 0.5H), 8.07 (dd, *J* = 8.02, 1.15 Hz, 0.5H), 7.93 (d, *J* = 6.30 Hz, 0.5H), 7.87 (d, *J* = 6.30 Hz, 0.5H), 7.60-7.53 (m, 1H), 7.39-7.29 (m, 6H), 7.01 (d, *J* = 9.17 Hz, 1H), 6.68 (d, *J* = 8.59 Hz, 0.5H), 6.61 (d, *J* = 6.87 Hz, 0.5H), 6.48 (d, *J* = 10.31 Hz, 0.5H), 6.39 (d, *J* = 8.59 Hz, 0.5H), 5.26-5.18 (m, 0.5H), 5.17-5.12 (m, 0.5H), 5.11 (d, *J* = 12.32 Hz, 1H), 5.06 (d, *J* = 12.32 Hz, 1H), 4.72-4.60 (m, 1H), 4.27 (q, *J* = 6.87 Hz, 1H), 4.20 (q, *J* = 6.87 Hz, 1H), 4.04 (s, 1.5H), 4.00 (s, 1.5H), 2.15-2.09 (m, 0.5H), 2.04-1.96 (m, 0.5H), 1.29 (t, *J* = 6.87 Hz, 1.5H), 1.24 (t, *J* = 6.87 Hz, 1.5H), 1.06-1.01 (m, 3H), 0.94-0.89 (m, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ. 171.1, 171.0, 168.6, 168.4, 165.6, 165.2, 156.5, 141.4, 141.4, 136.1, 134.1, 133.8, 133.1, 133.0, 131.4, 131.4, 128.5, 128.2, 128.0, 128.0, 127.9, 124.4, 123.3, 105.6, 105.2, 94.4, 94.2, 68.9, 68.8, 67.1, 63.6, 63.2, 62.0, 61.9, 55.8, 55.8, 31.4, 31.2, 19.4, 19.2, 17.5, 17.2, 14.1, 14.0.

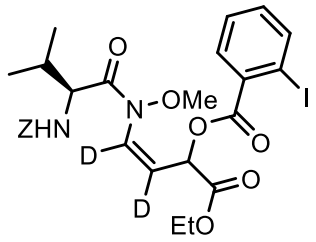
HRMS (ESI, positive): calcd for $C_{27}H_{31}IN_2NaO_8$ $[M + Na]^+$ 661.10228, Found 661.10190.

$[\alpha]_D^{22}$ = +33.0(*c* = 0.1 in MeOH).

When using (*S*,*S*)-(-)-2,2'-isopropylidenebis(4-*tert*-butyl-2-oxazoline) (Ligand B) (2.9 mg, 0.01 mmol) instead of Ligand A, the desired compound (**6z**: 19.8 mg, 62%, dr = 1.2:1.0) was obtainded.

^{1}H NMR (400 MHz, acetone-d_6): δ 8.09 (d, *J* = 7.78 Hz, 0.55H), 8.08 (d, *J* = 7.78 Hz, 0.45H), 7.94 (d, *J* = 7.78 Hz, 0.55H), 7.88 (d, *J* = 7.78 Hz, 0.45H), 7.61-7.53 (m, 1H), 7.39-7.31 (m, 6H), 7.02 (d, *J* = 9.61 Hz, 1H), 6.70 (d, *J* = 8.23 Hz, 0.55H), 6.64 (d, *J* = 7.78 Hz, 0.45H), 6.49 (d, *J* = 10.06 Hz, 0.55H), 6.40 (d, *J* = 8.69 Hz, 0.45H), 5.27-5.19 (m, 0.45H), 5.19-5.13 (m, 0.55H), 5.11 (d, *J* = 12.32 Hz, 1H), 5.06 (d, *J* = 12.32 Hz, 1H), 4.74-4.53 (m, 1H), 4.30-4.18 (m, 2H), 4.05 (s, 1.36H), 4.00 (s, 1.64H), 2.15-2.09 (m, 0.55H), 2.04-1.96 (m, 0.45H), 1.30 (t, *J* = 7.09 Hz, 1.36H), 1.24 (t, *J* = 7.09 Hz, 1.64H), 1.06-1.02 (m, 3.27H), 0.94-0.90 (m, 2.73H).

Cbz-L-Valine-(*Z*)-*N*-methoxy-*N*-[1,2-d_2-4-ethoxy-3-(2-iodobenzoyl)oxy-4-oxobut-1-en-1-yl]amide (6z-d_2)



Following the **Procedure G**, (*Z*)-*N*-(1,2-d_2-1-vin-2-yl)-Cbz-L-valine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (**3z**-d_2 (*α*: 97%D, *β*: 98%D): 27.7 mg, 0.05 mmol) was used. Purification by preparative TLC (hexane:EtOAc = 4:1) to afford Cbz-L-valine-(*Z*)-*N*- methoxy-*N*-[1,2-d_2-4-(triisopropylsilyl)but-1-en-3-yn-1-yl]amide (**6z**-d_2: 20.3 mg, 63%, dr = 1.0:1.0, *α*: 96%D, *β*: 98%D).

Rf: 0.30 (hexane : EtOAc = 4 : 1).

Physical state: Colorless oil.

^{1}H NMR (500 MHz, acetone-d_6): δ 8.09 (d, *J* = 8.02 Hz, 0.5H), 8.07 (d, *J* = 8.02 Hz, 0.5H), 7.93 (d, *J* = 7.45 Hz, 0.5H), 7.87 (d, *J* = 7.45 Hz, 0.5H), 7.60-7.53 (m, 1H), 7.40-7.28 (m, 6H), 7.01 (s, 0.02H), 6.68 (d, *J* = 8.59 Hz, 0.5H), 6.61 (d, *J* = 6.87 Hz, 0.5H), 6.48 (s, 0.5 H), 6.39 (s, 0.5H), 5.22 (s, 0.02H), 5.15 (s, 0.02H), 5.10 (d, *J* = 12.60 Hz, 1H), 5.06 (d, *J* = 12.60 Hz, 1H), 4.72-4.60 (m, 1H), 4.27 (q, *J* = 6.87 Hz, 1H), 4.20 (q, *J* = 6.87 Hz, 1H), 4.04 (s, 1.5H), 4.00 (s, 1.5H), 2.15-2.08 (m, 0.5H), 2.04-1.95 (m, 0.5H), 1.29 (t, *J* = 6.87 Hz, 1H), 1.24 (t, *J* = 6.87 Hz, 1H), 1.06-1.00 (m, 3H), 0.94-0.88 (m, 3H).

HRMS (ESI, positive): calcd for $C_{27}H_{29}D_2N_2NaO_8$ $[M + Na]^+$ 663.11483, Found 663.11629.

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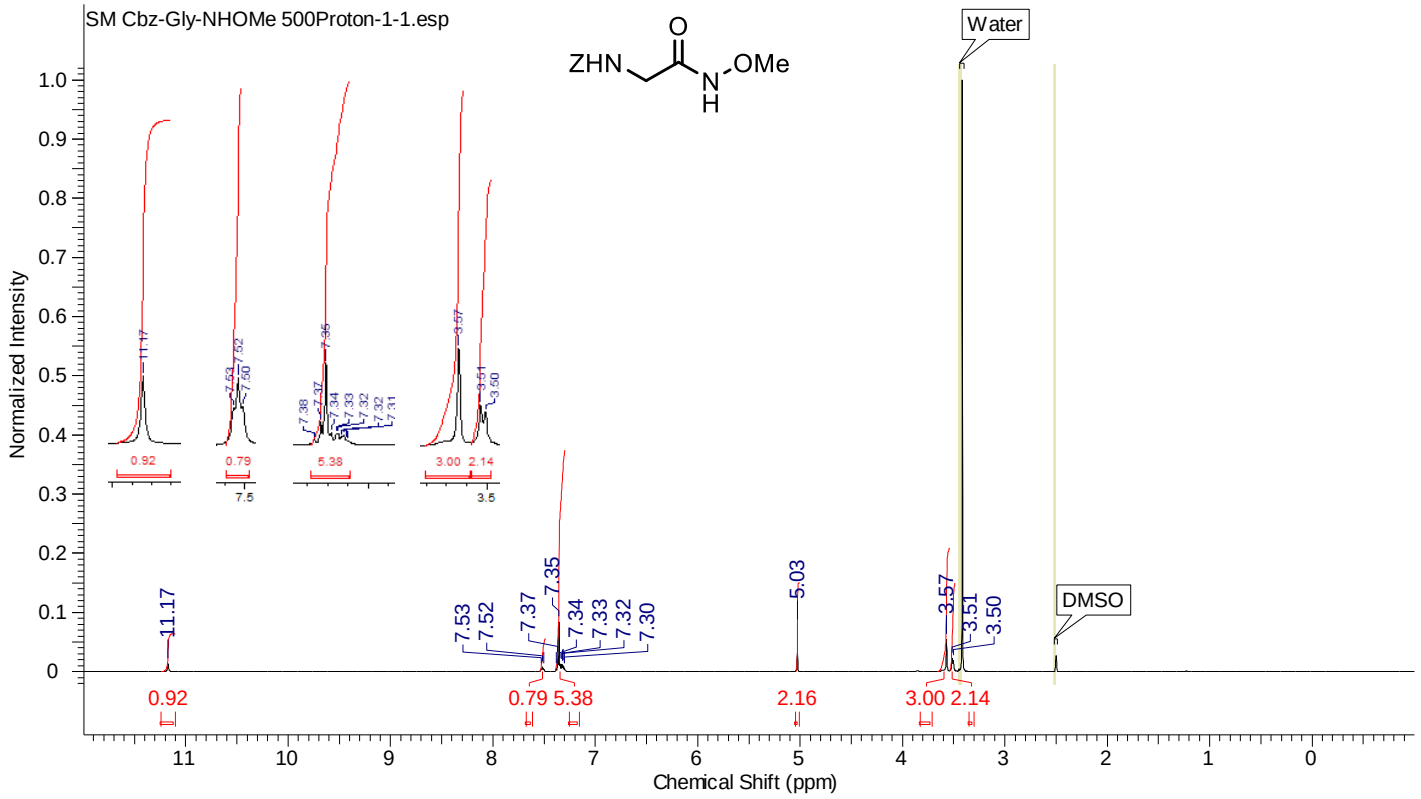
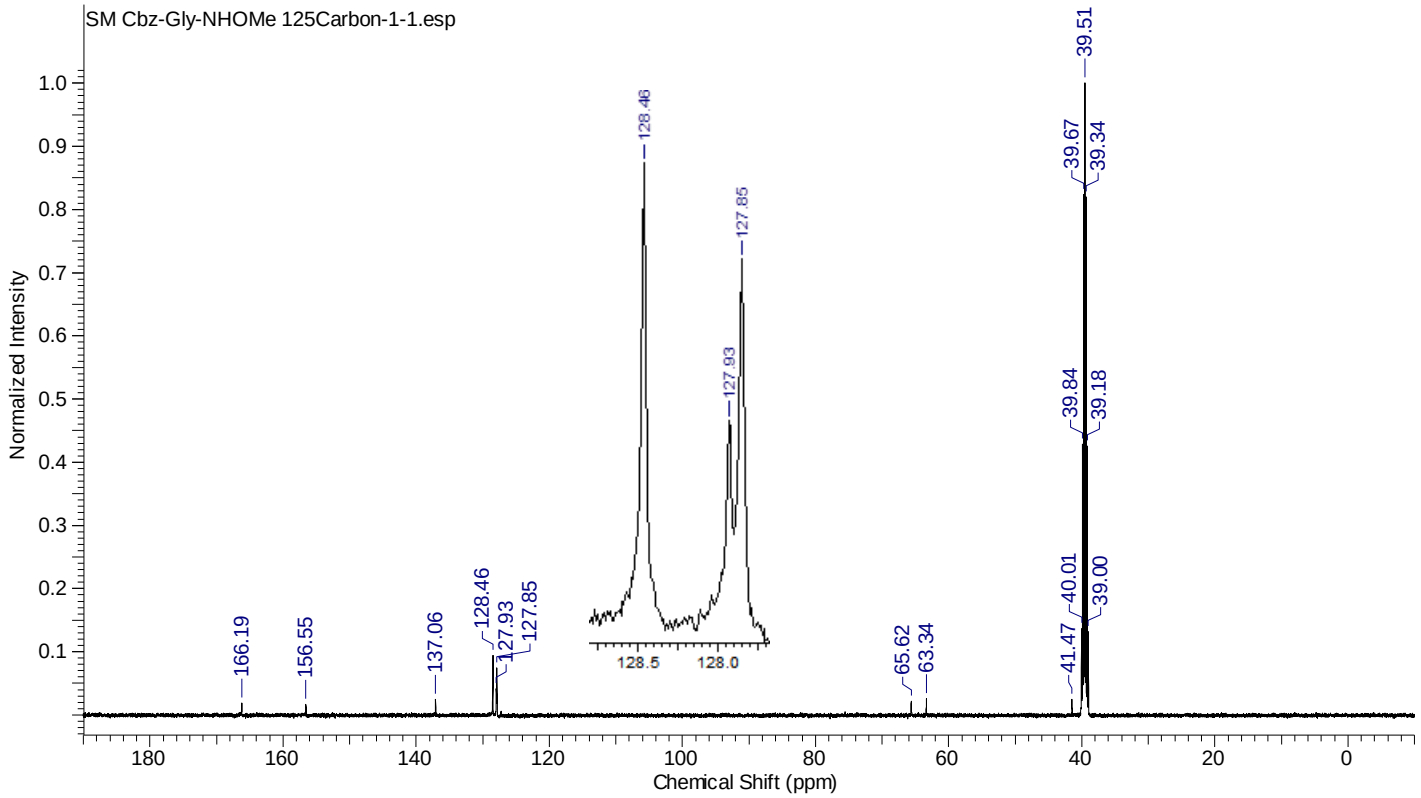
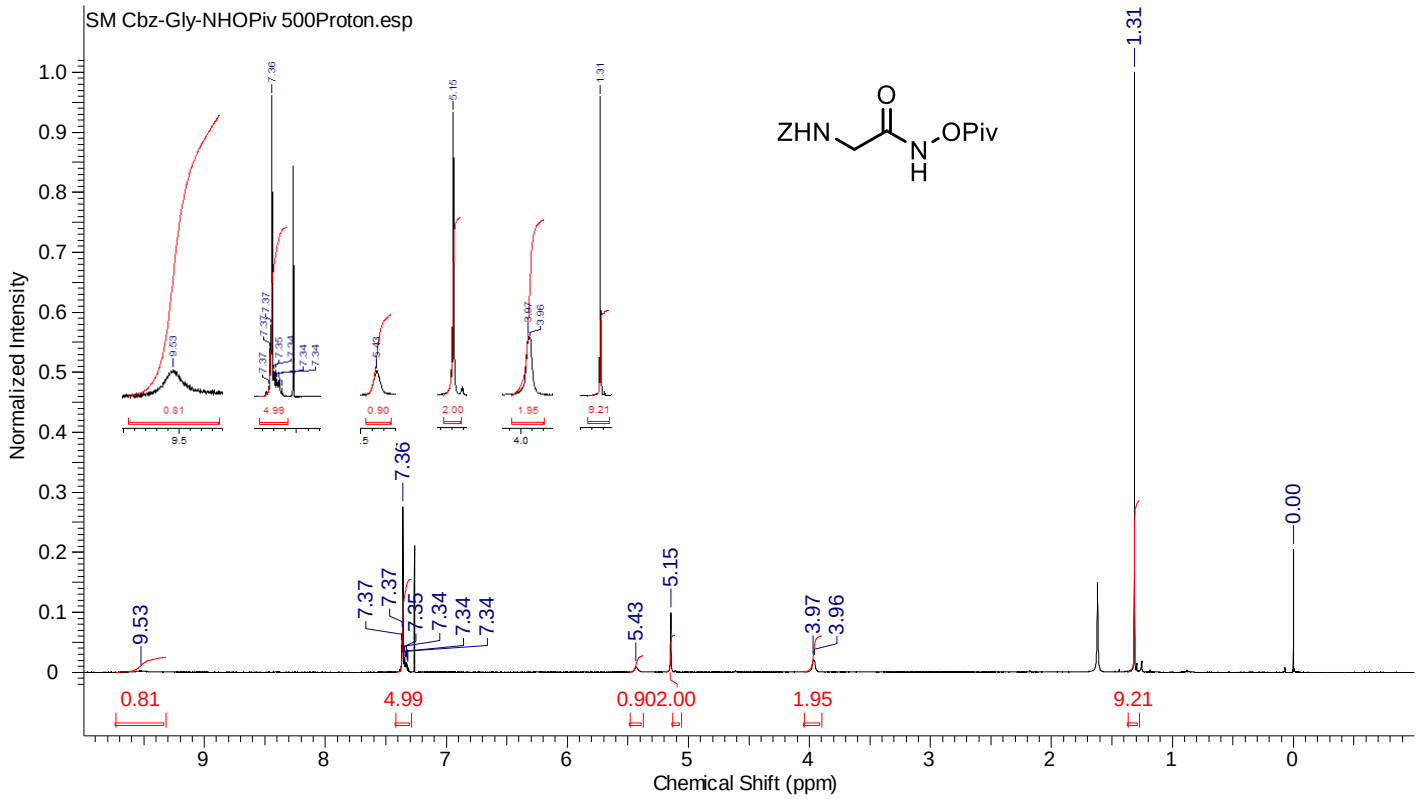
8. ^{1}H NMR and ^{13}C NMR spectra

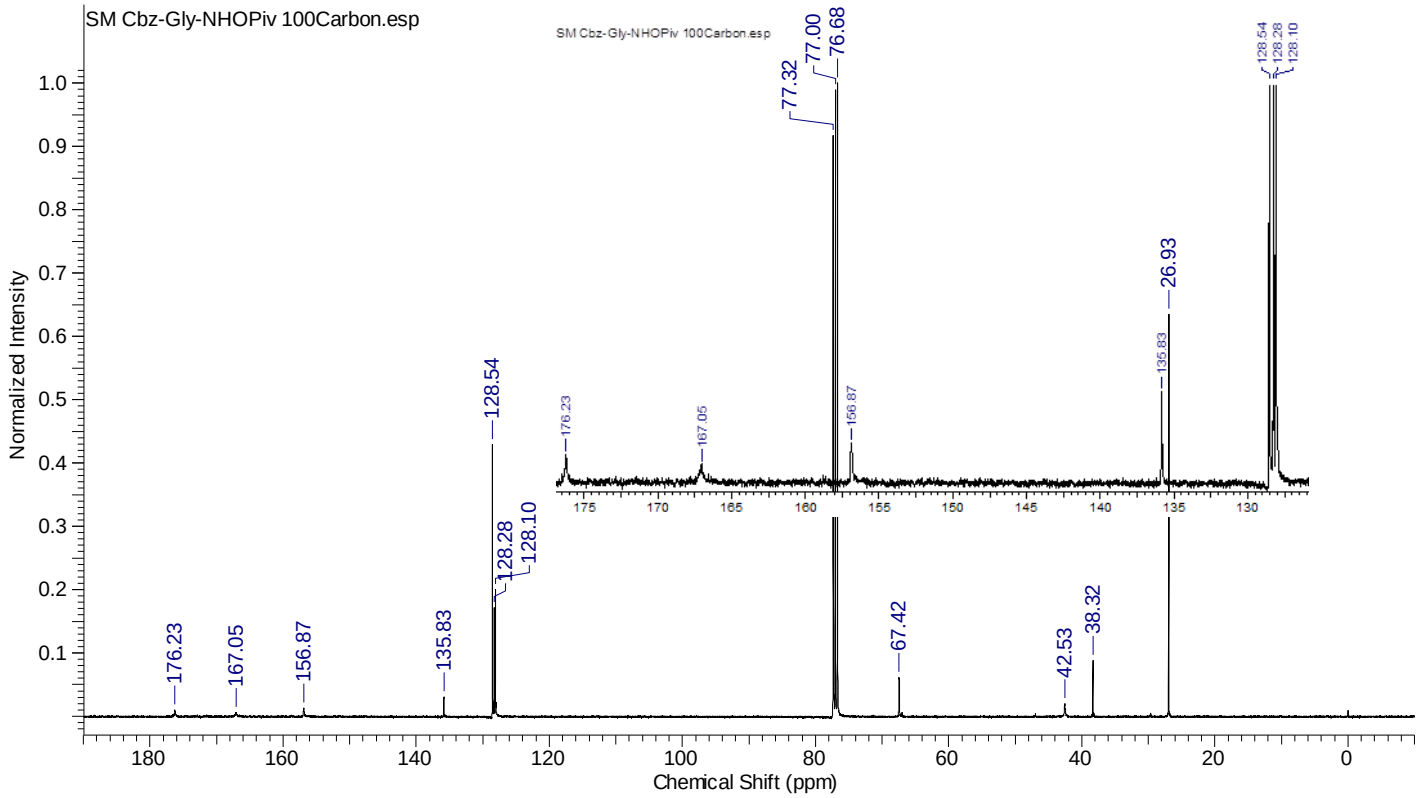
Cbz-Glycine-*N*-methoxyamide (1a)



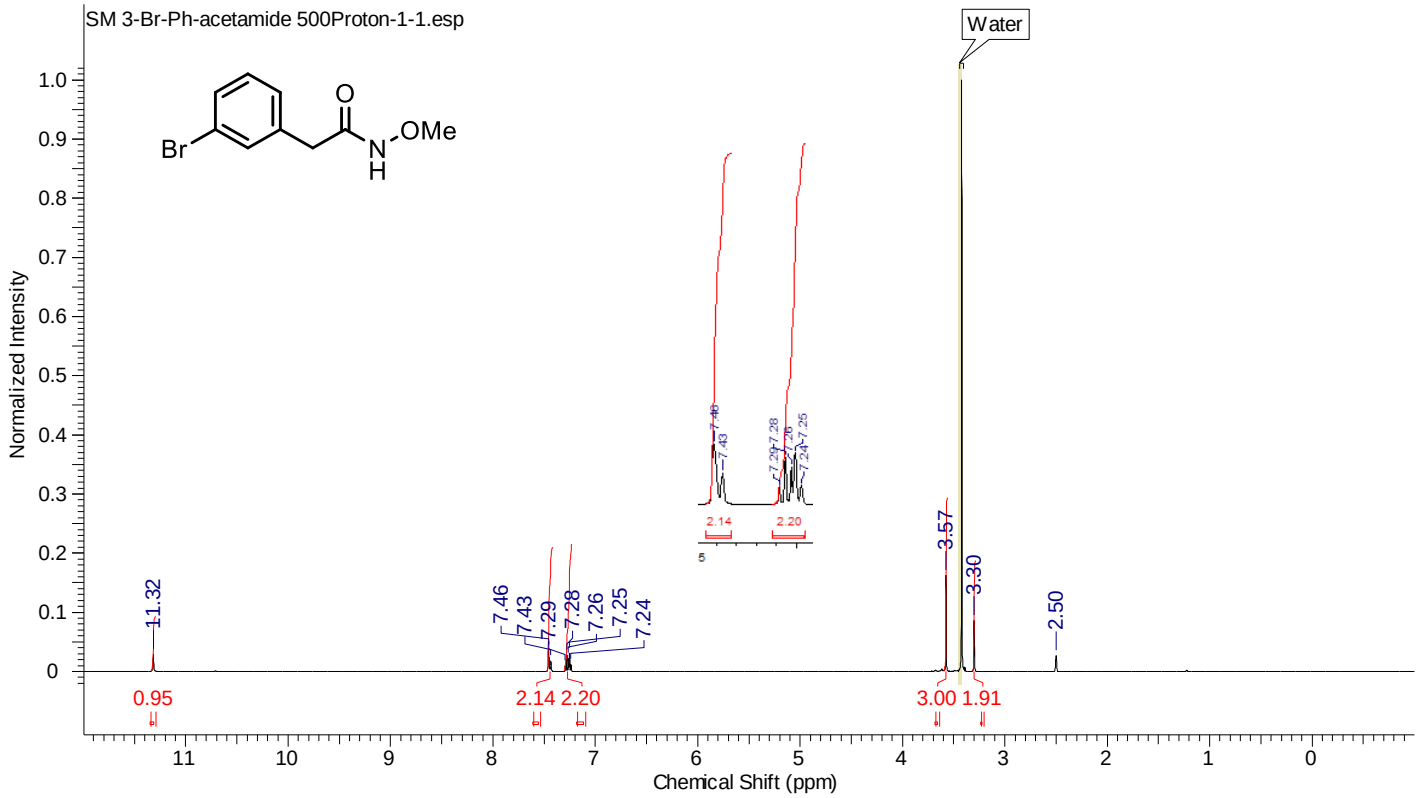


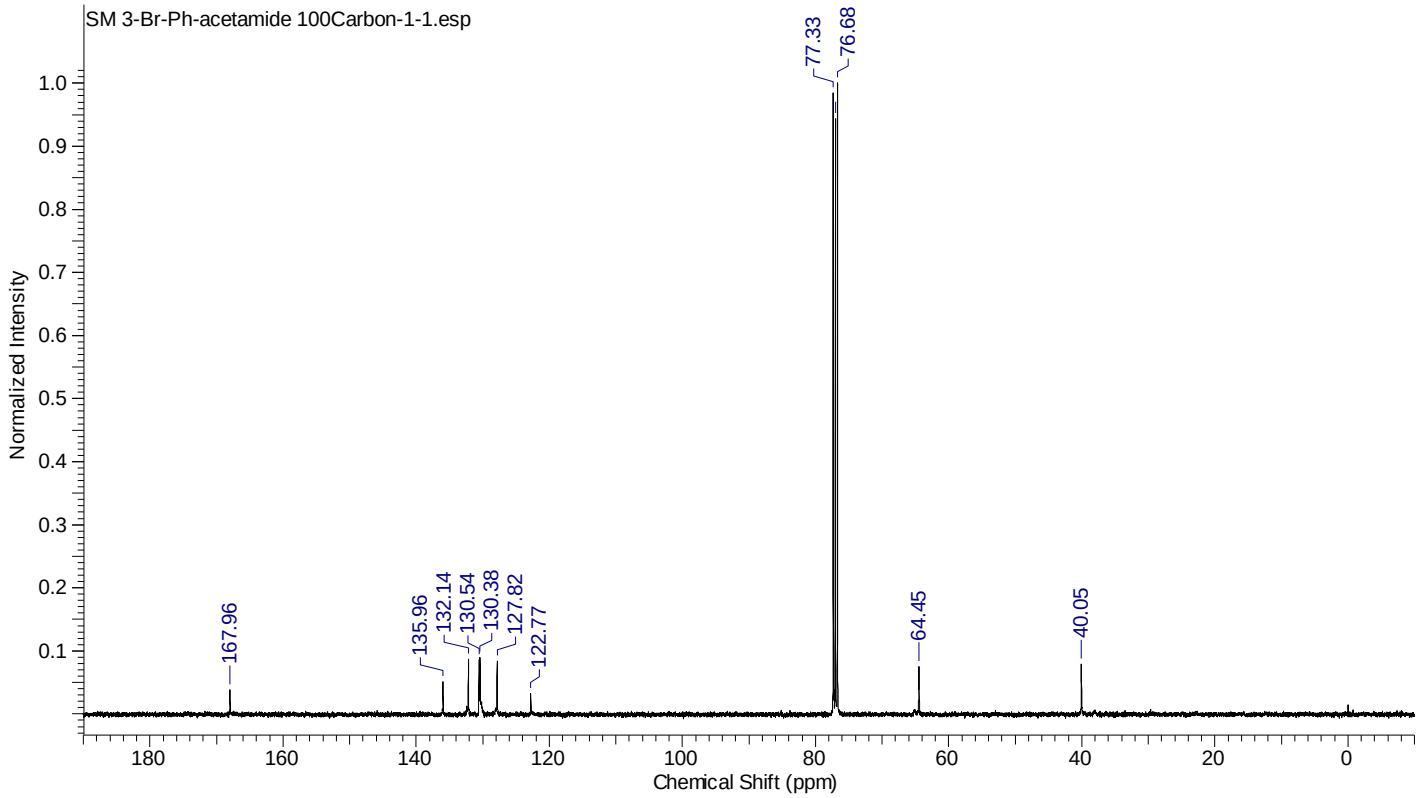
Cbz-Glycine-*N*-pivaloxyamide (S1e)



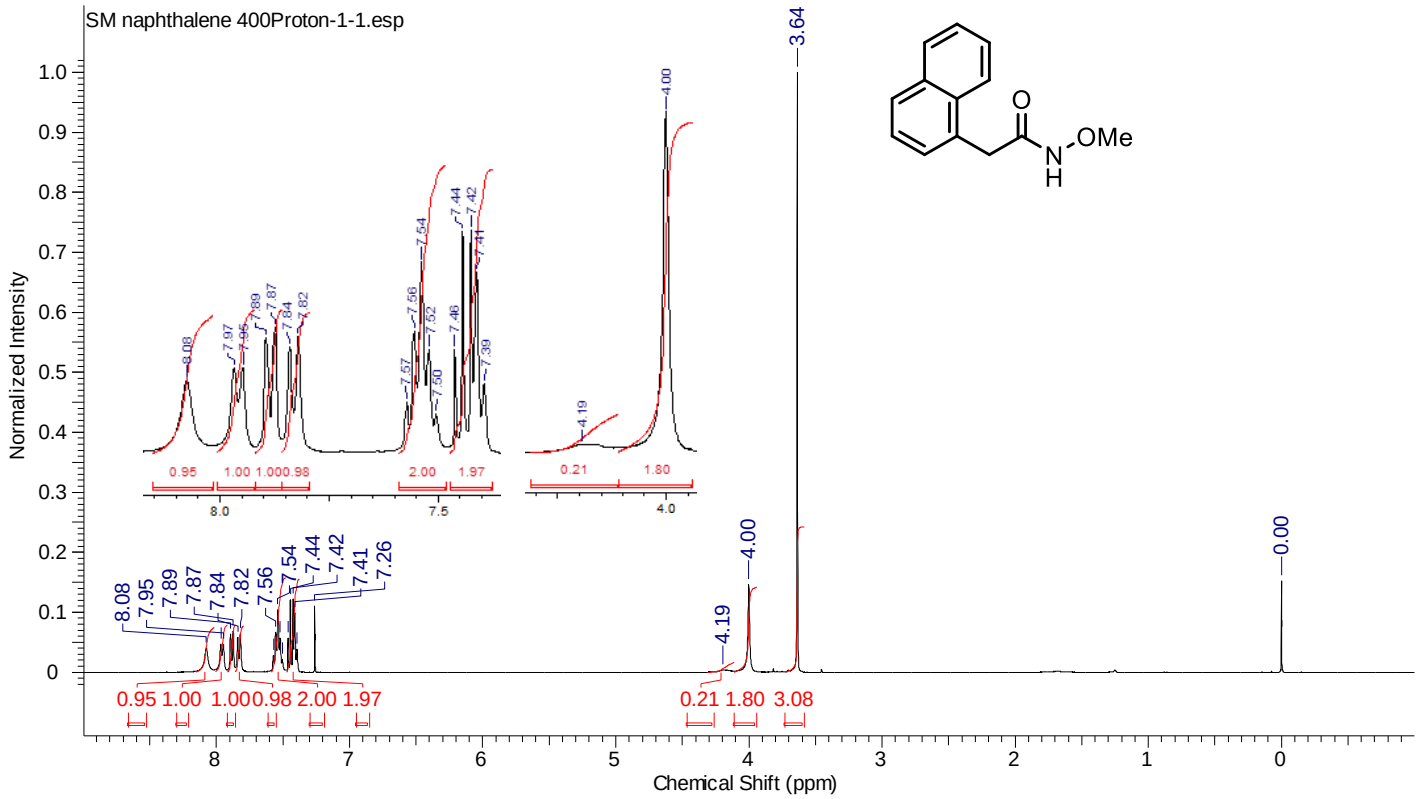


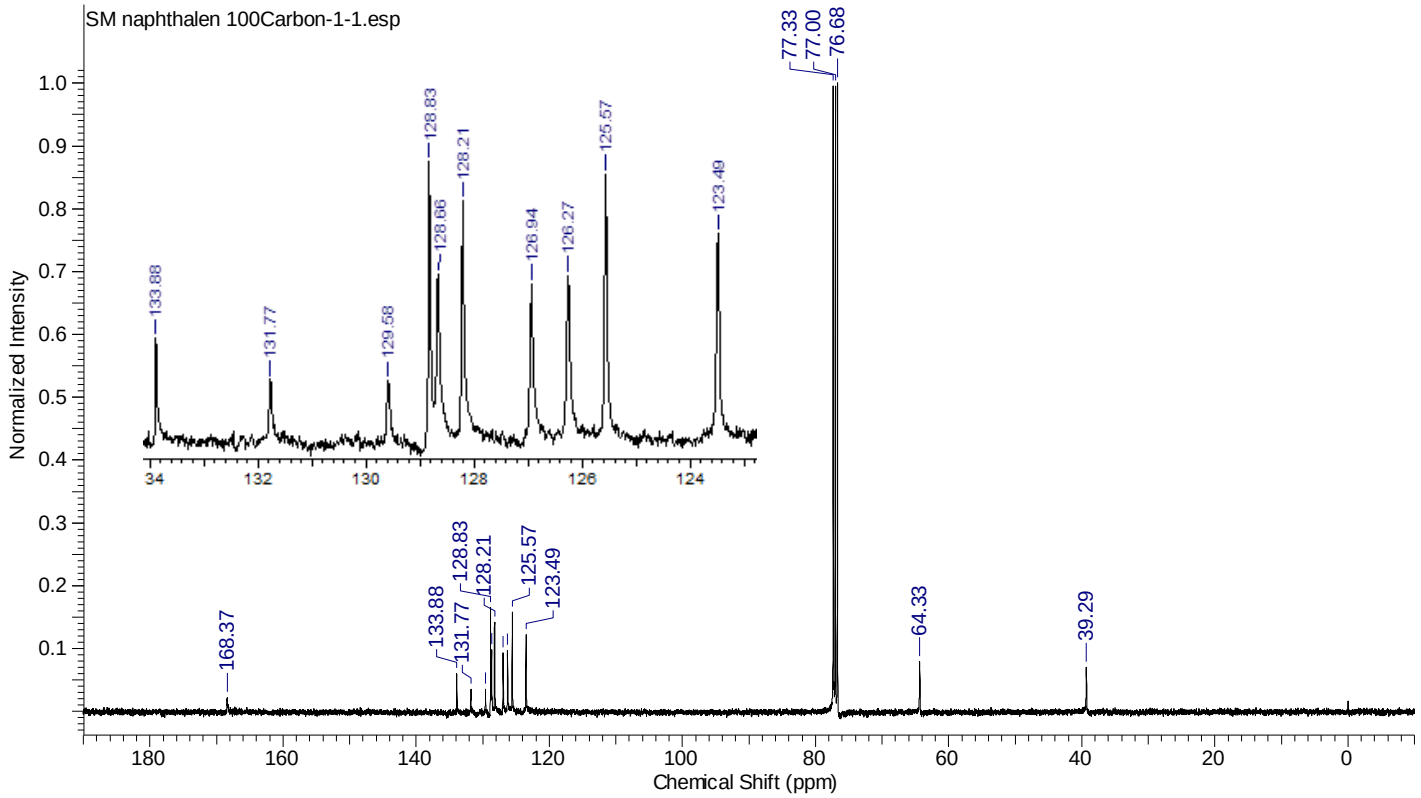
2-(3-Bromophenyl)-*N*-methoxyacetamide (1p)



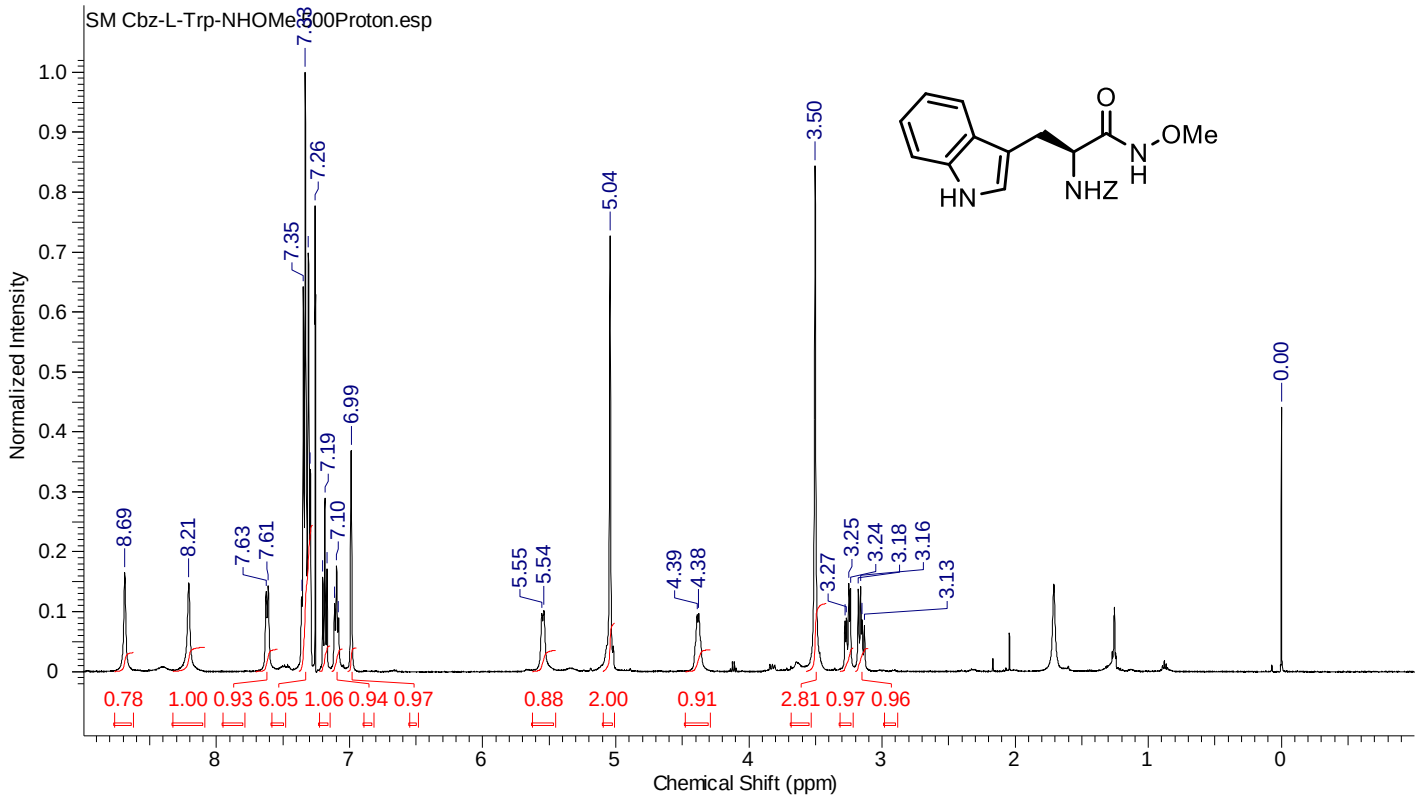


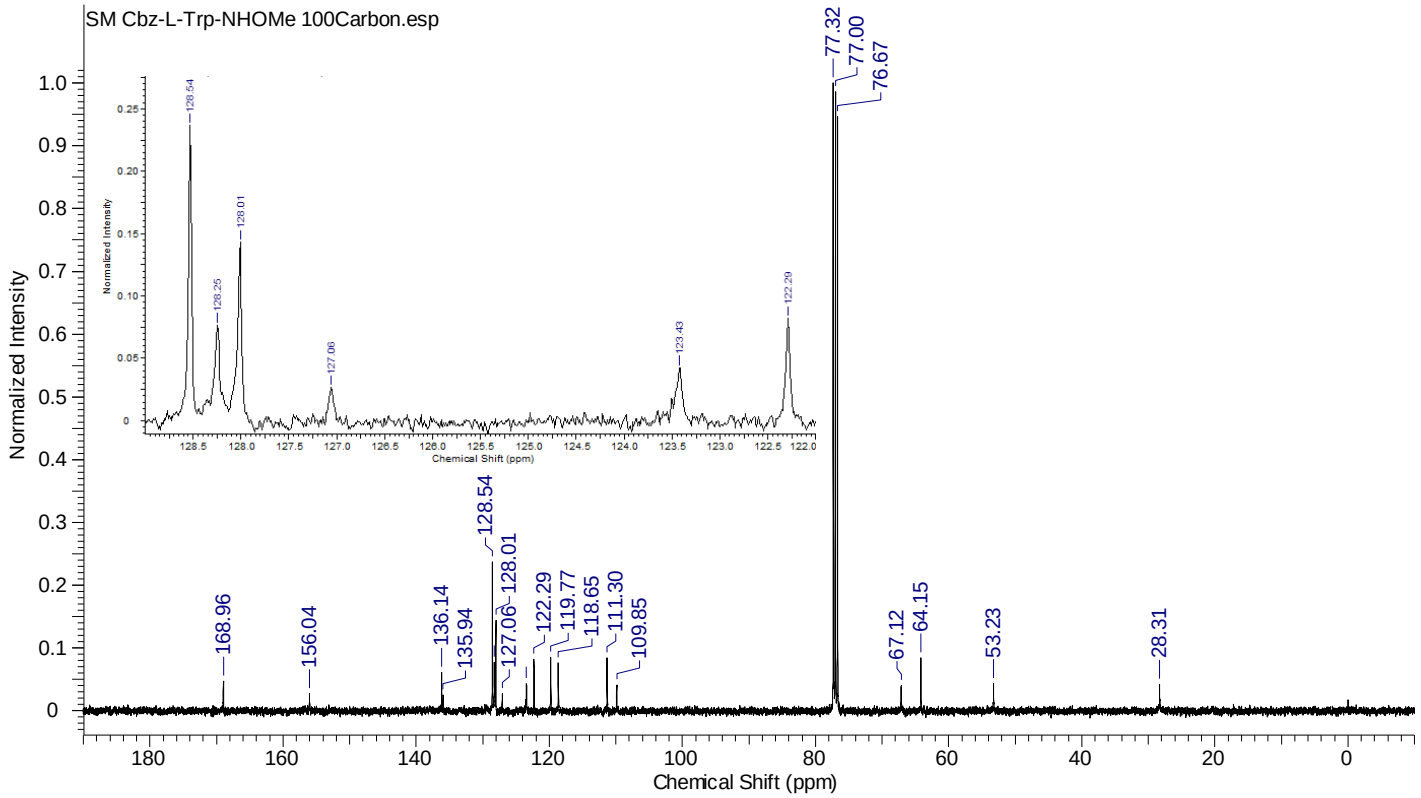
_N_-Methoxy-1-naphthaleneacetamide (1s)



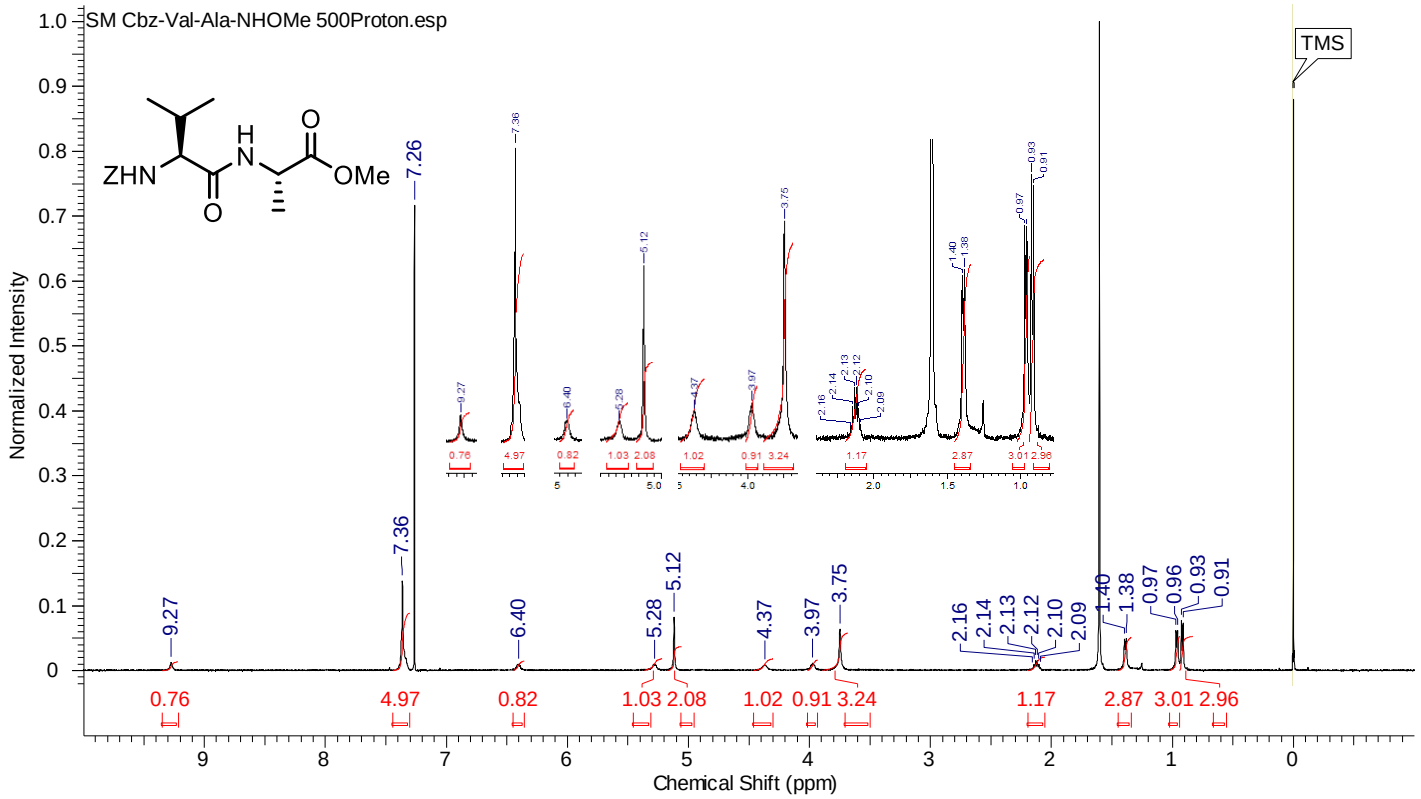


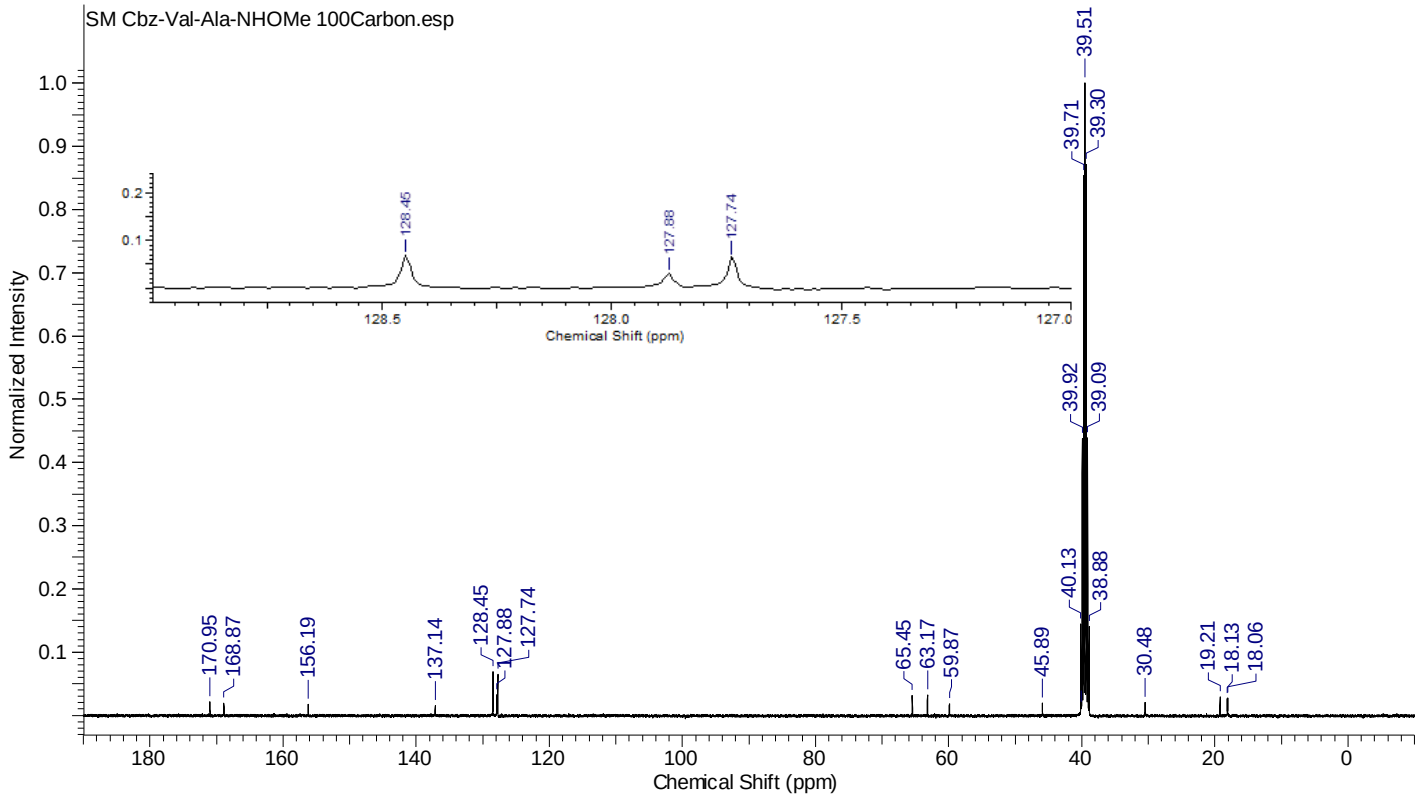
Cbz-L-Tryptophan-*N*-methoxyamide (1ab)



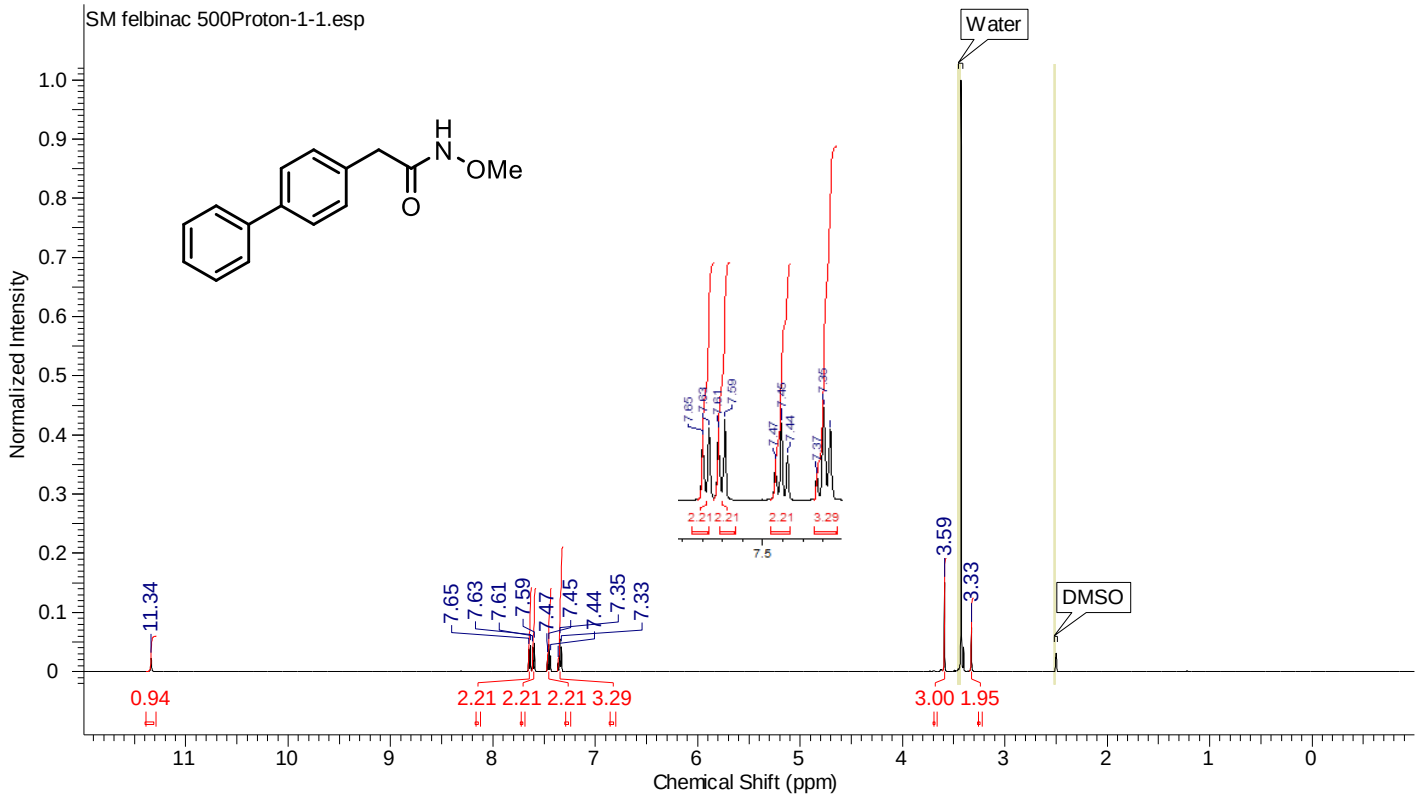


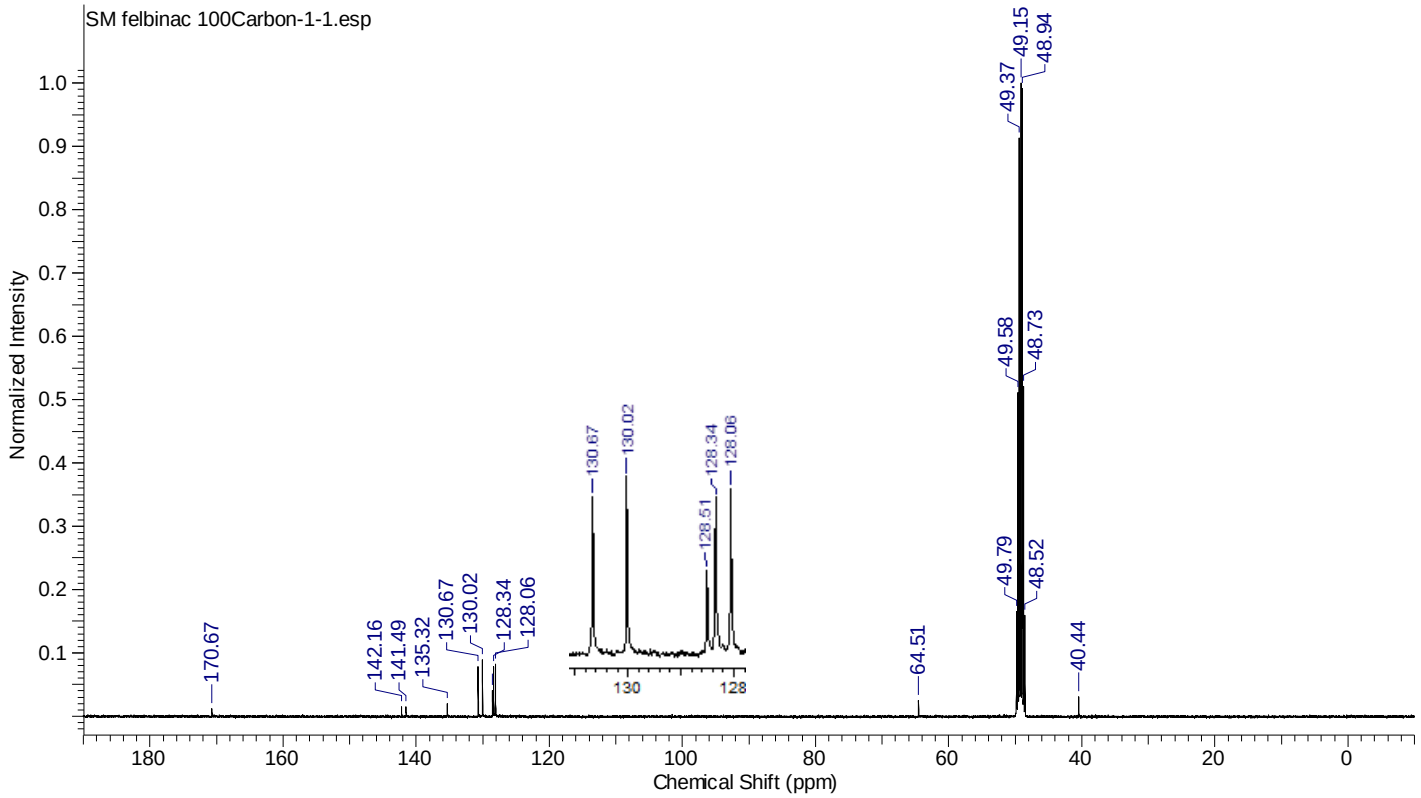
Cbz-L-Valyl-L-alanine-*N*-methoxyamide (1ac)



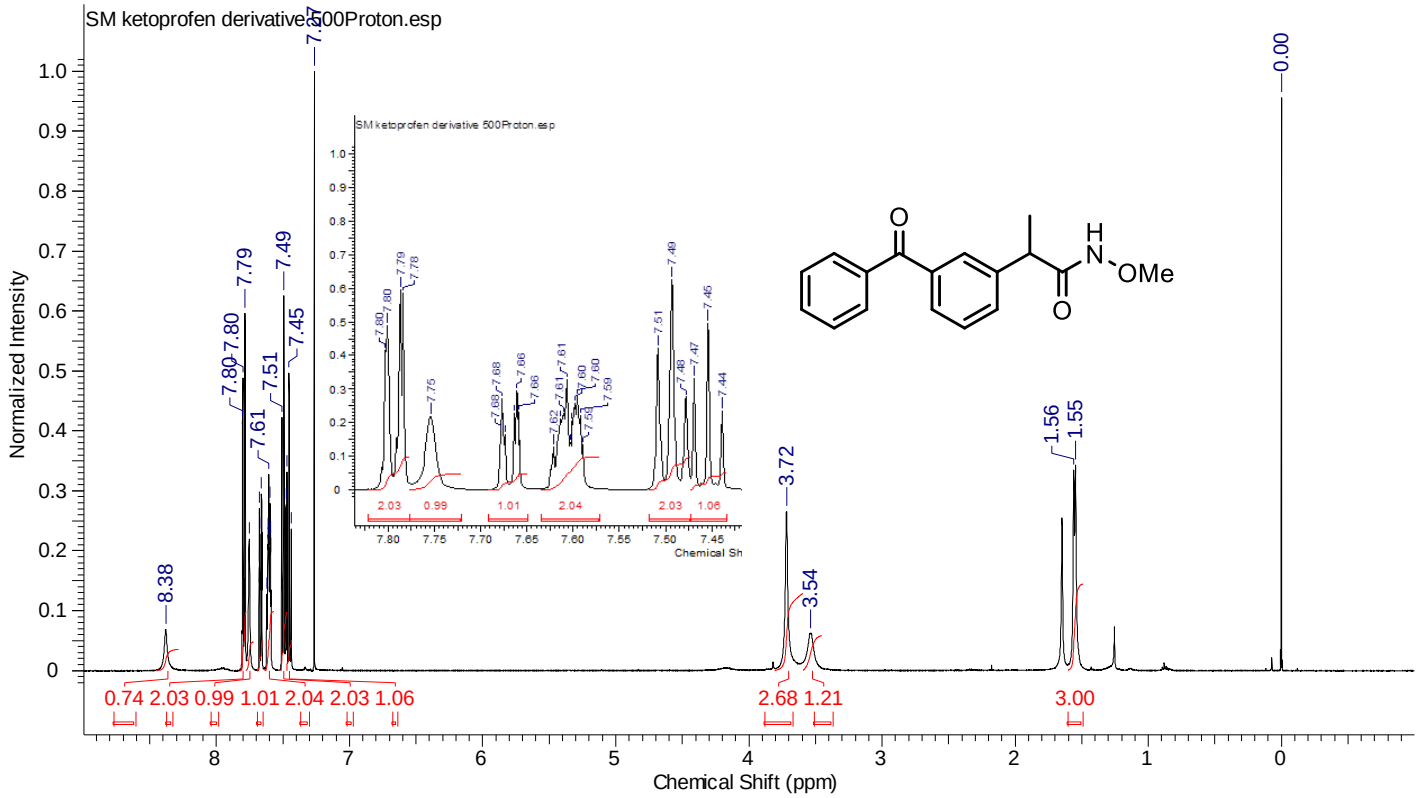


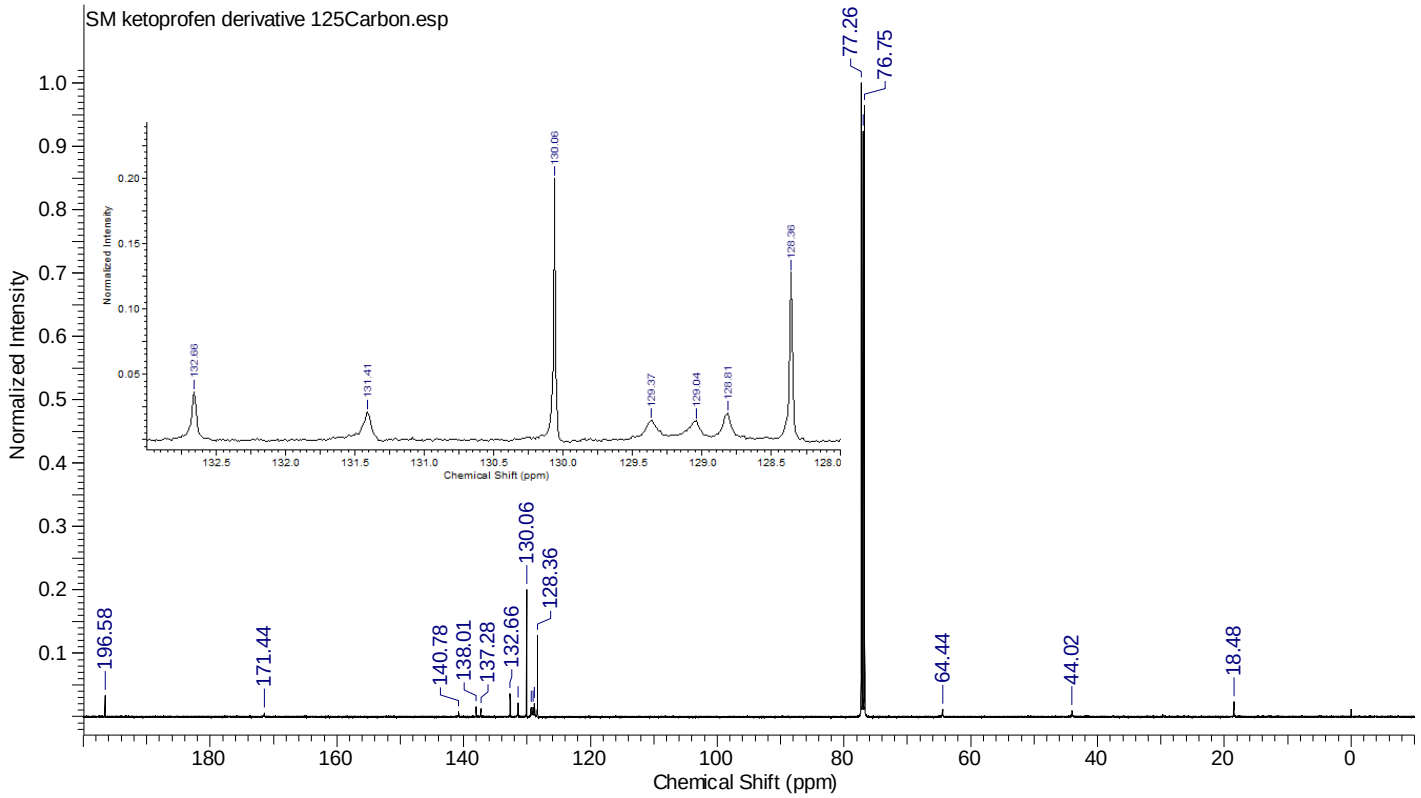
2-[(1,1'-Biphenyl)-4-yl]-*N*-methoxyacetamide (1ad)



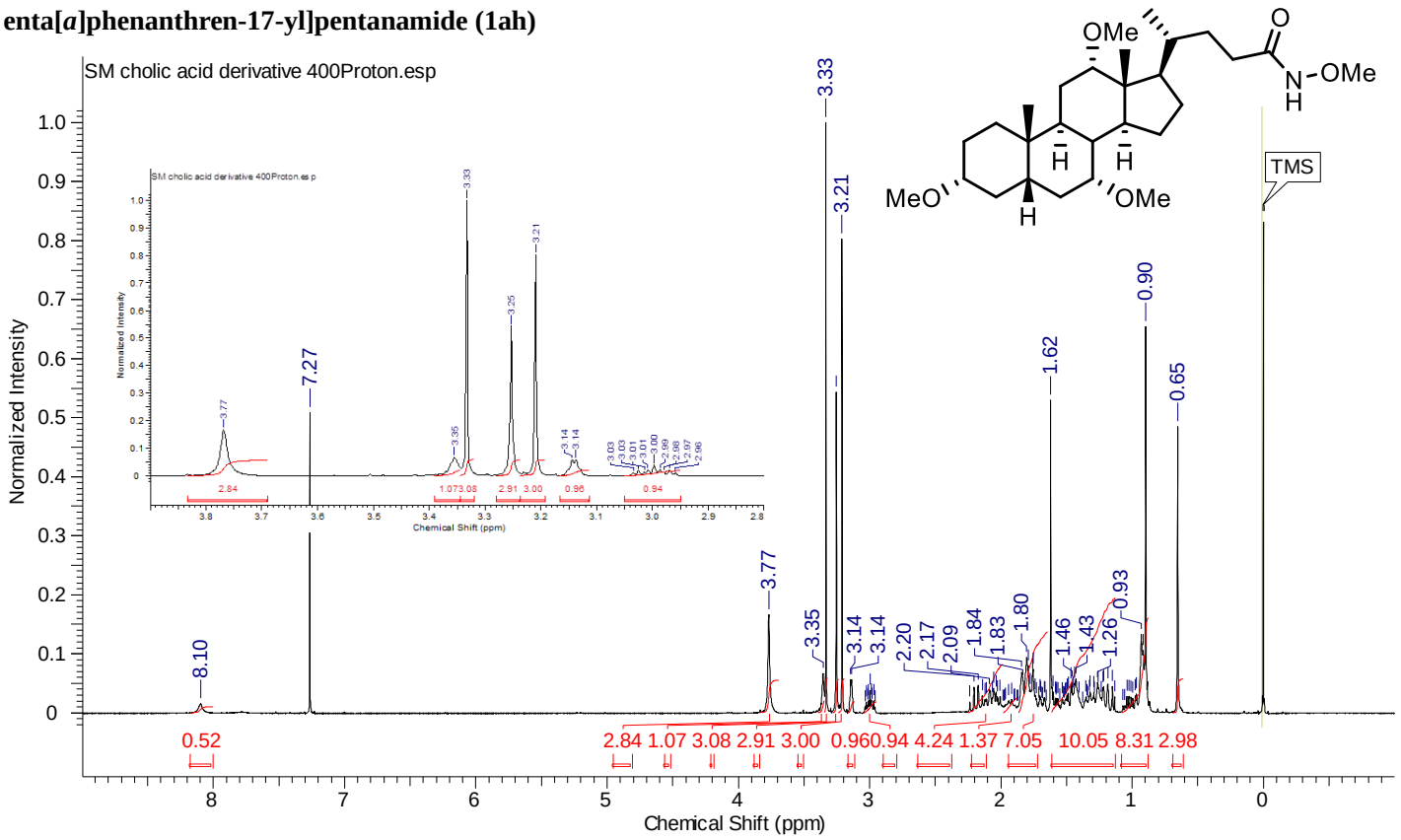


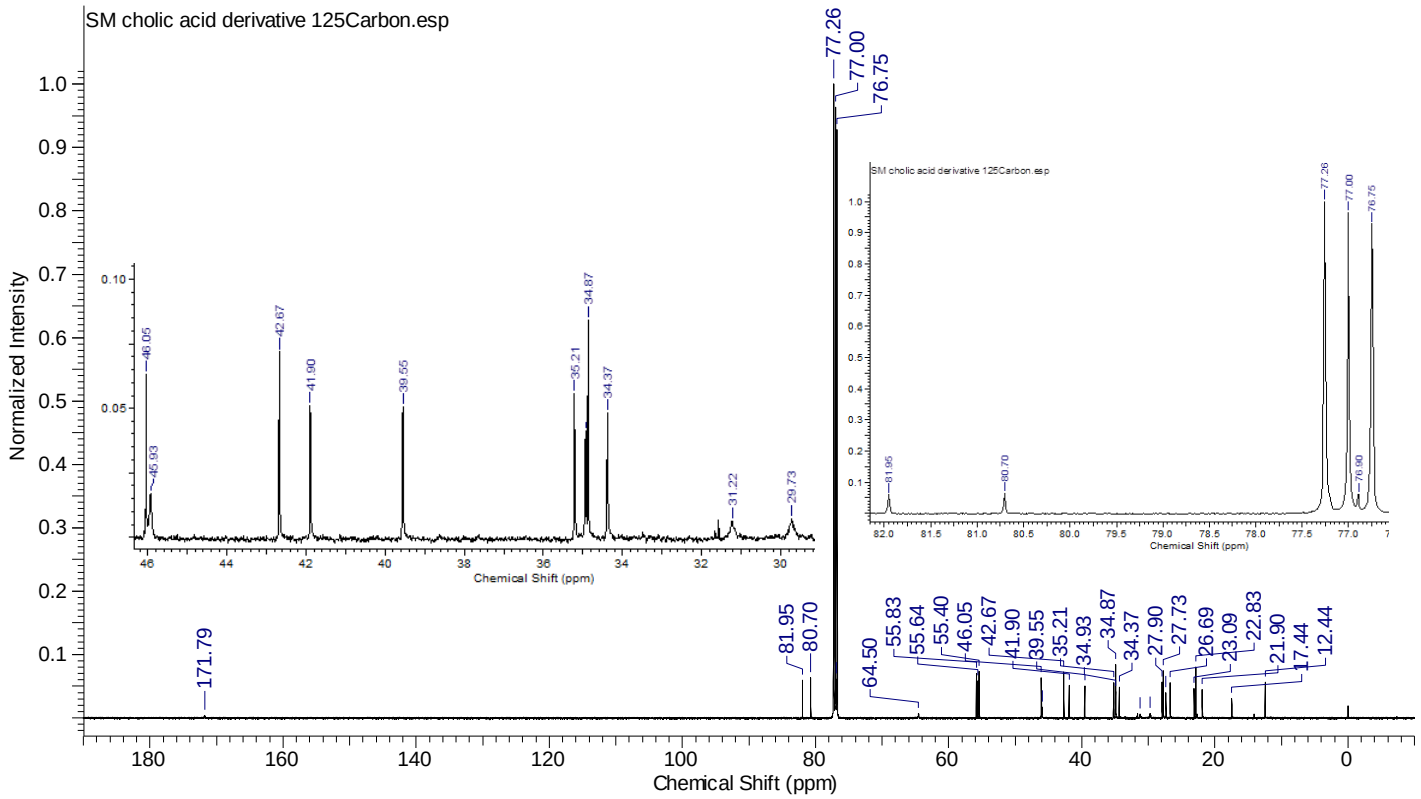
2-(3-Benzoylphenyl)-*N*-methoxypropanamide (1af)



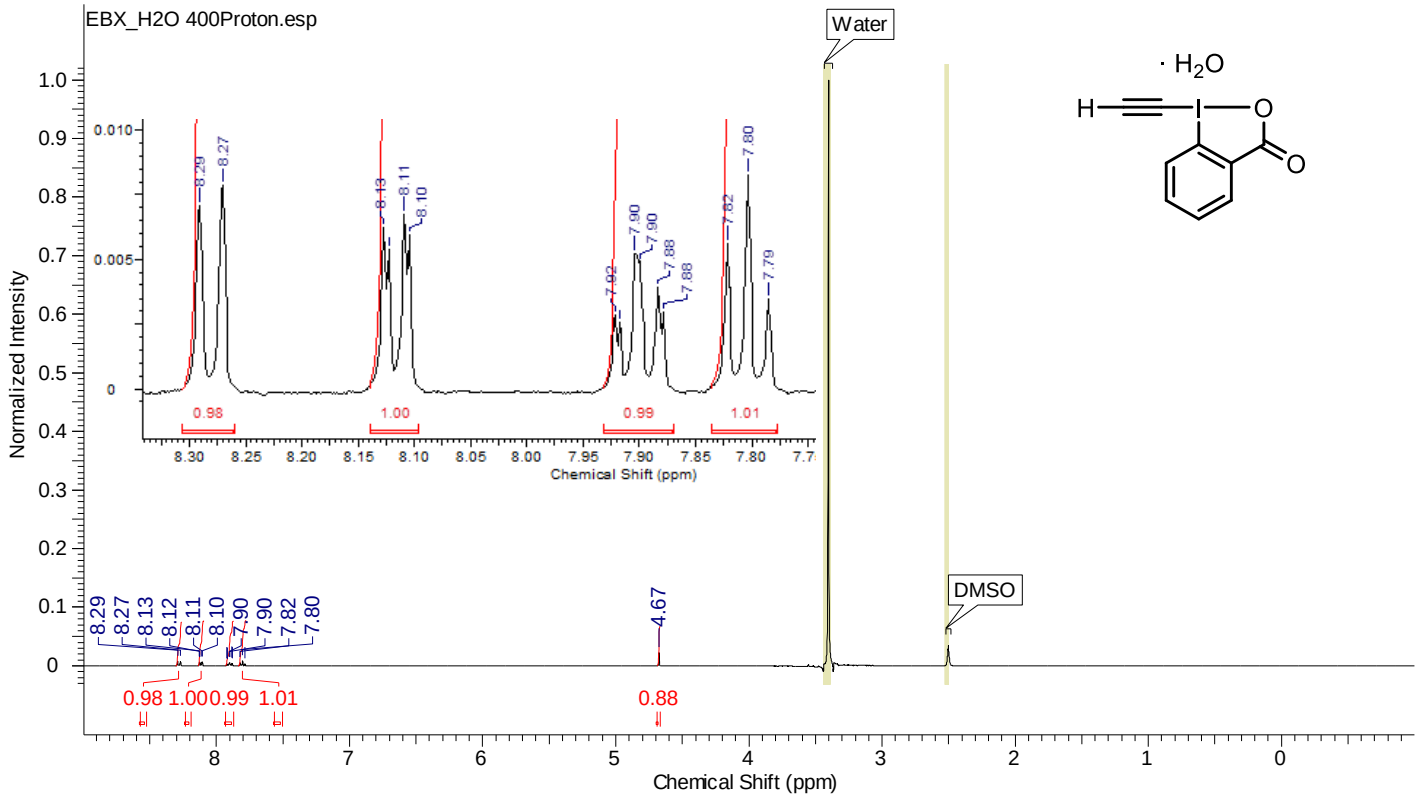


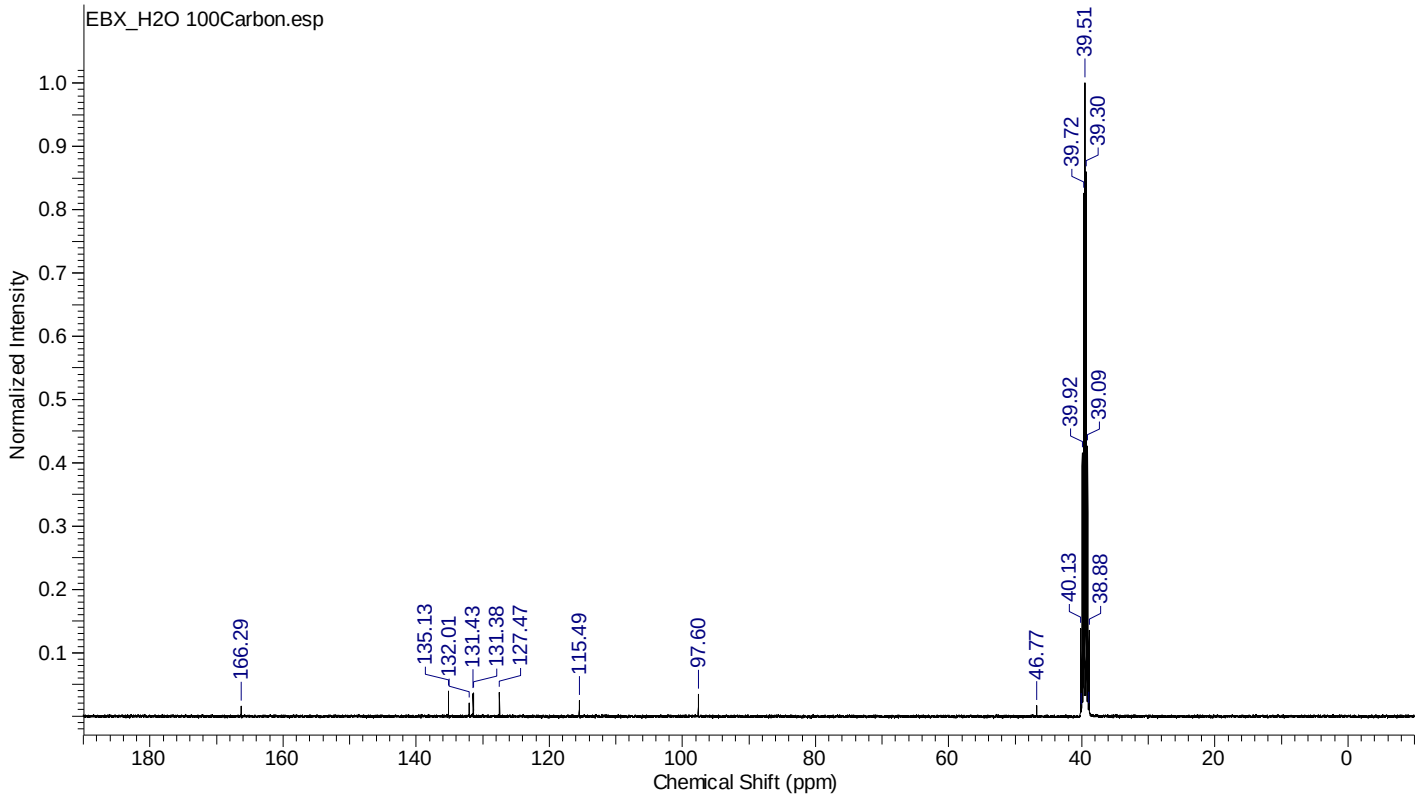
(*R*)-*N*-Methoxy-4-[(3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,7,12-trimethoxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl]pentanamide (1ah)



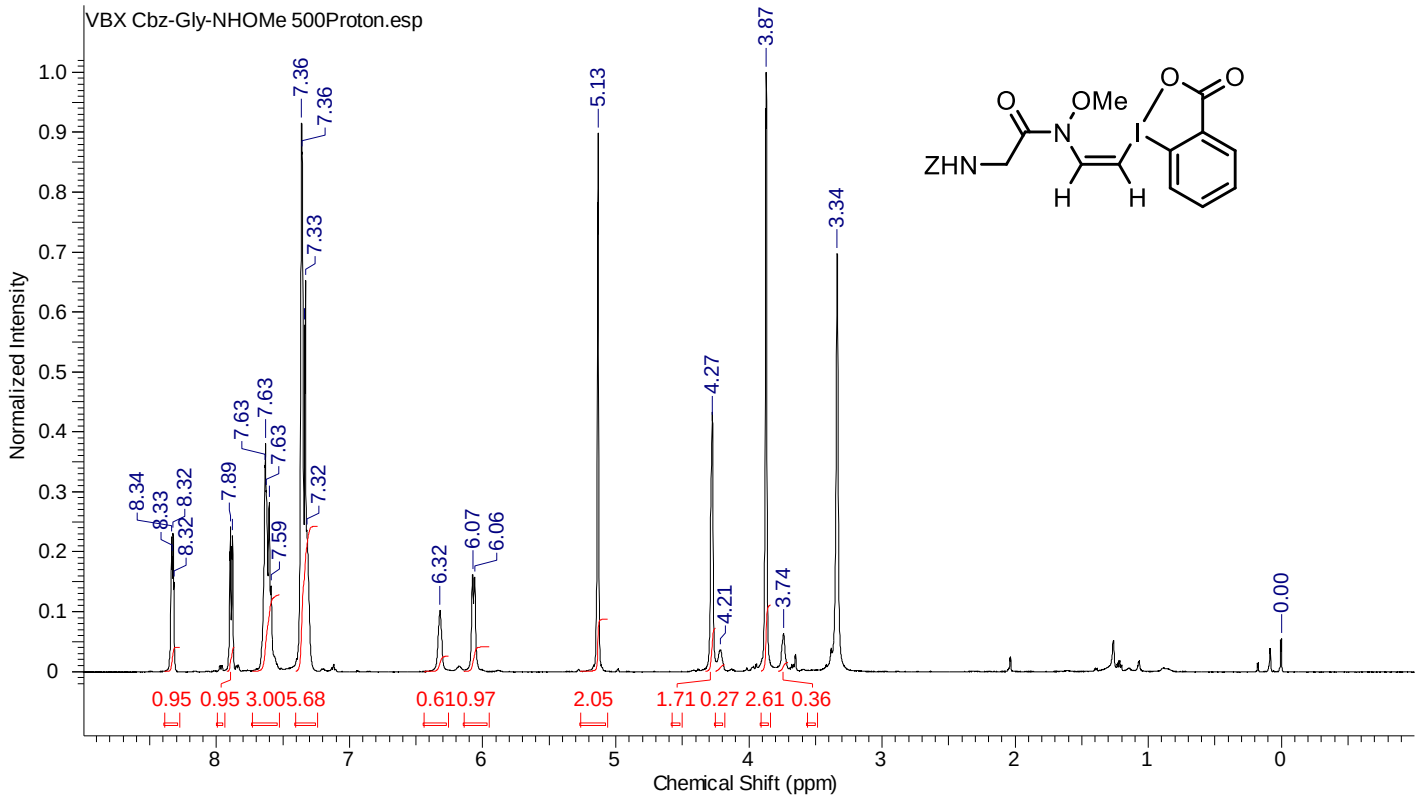


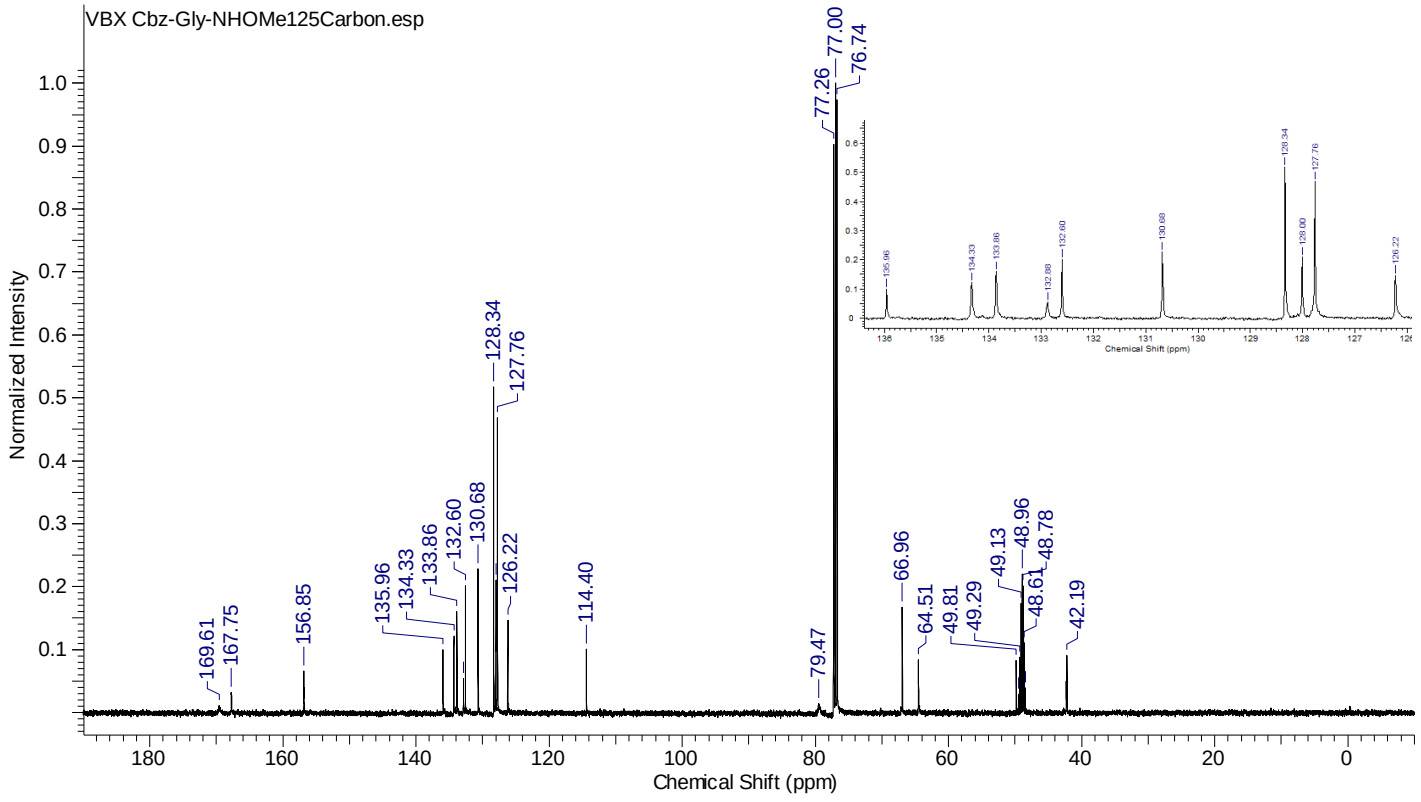
Ethynyl-1,2-benziodoxol-3(1*H*)-one-H_2O complex



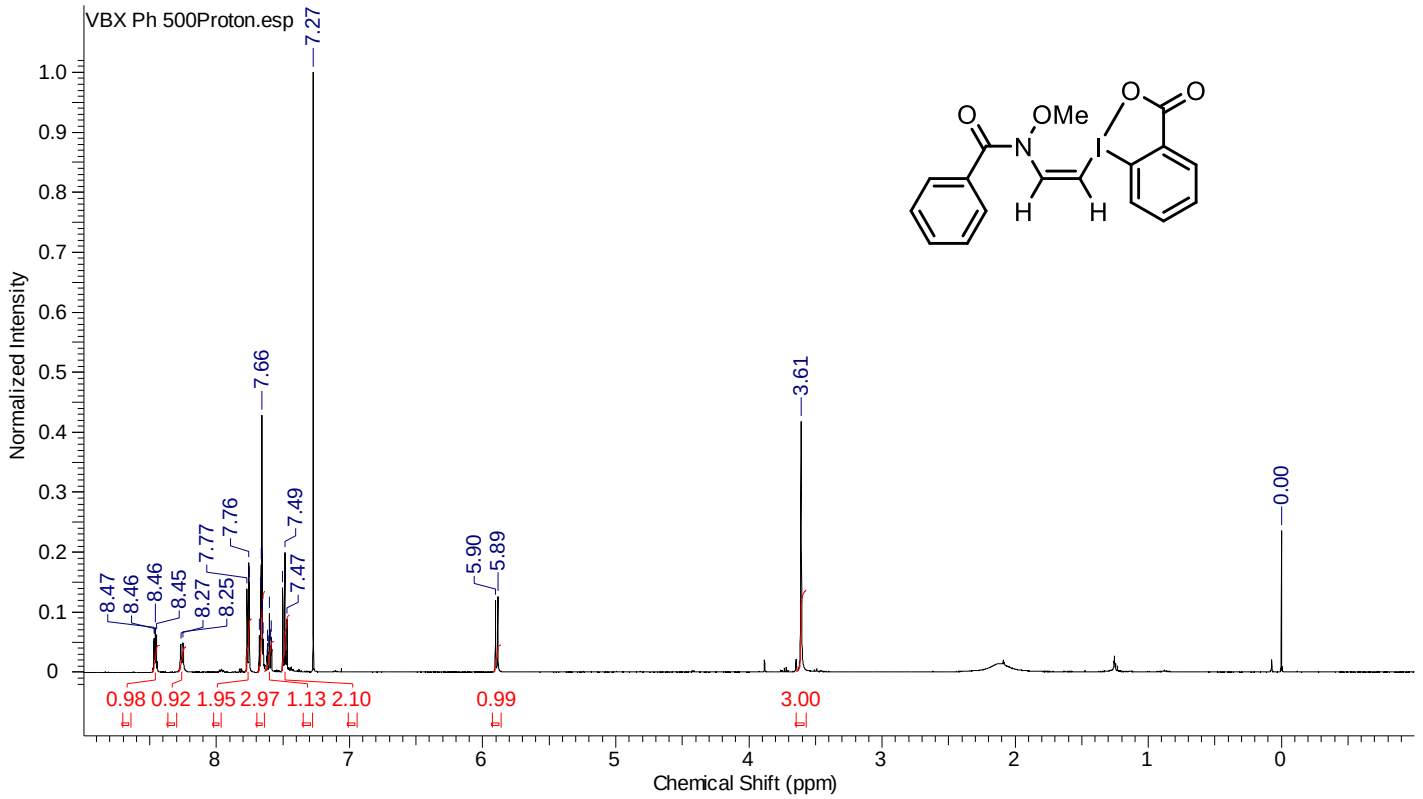


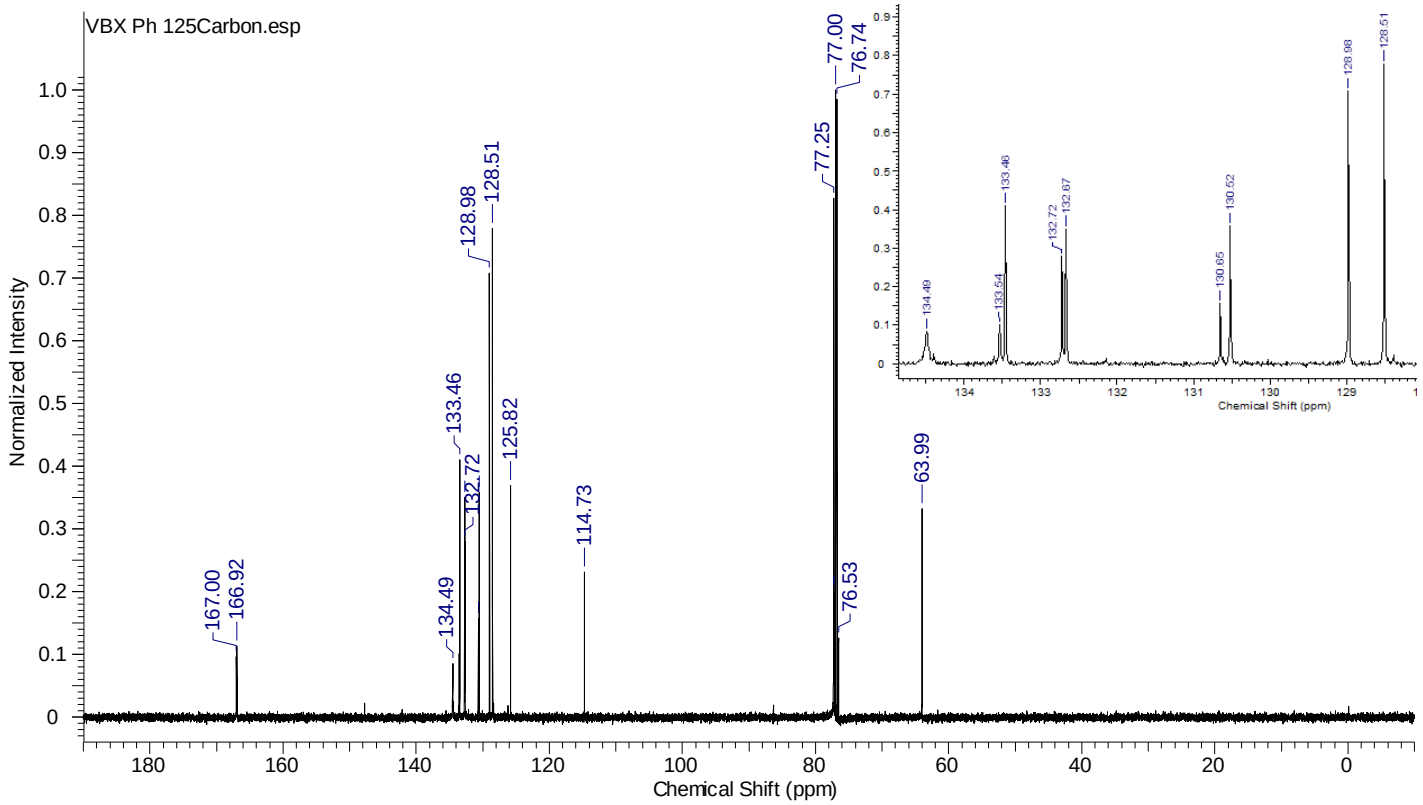
(*Z*)-*N*-(1-Vin-2-yl)-Cbz-glycine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3a)



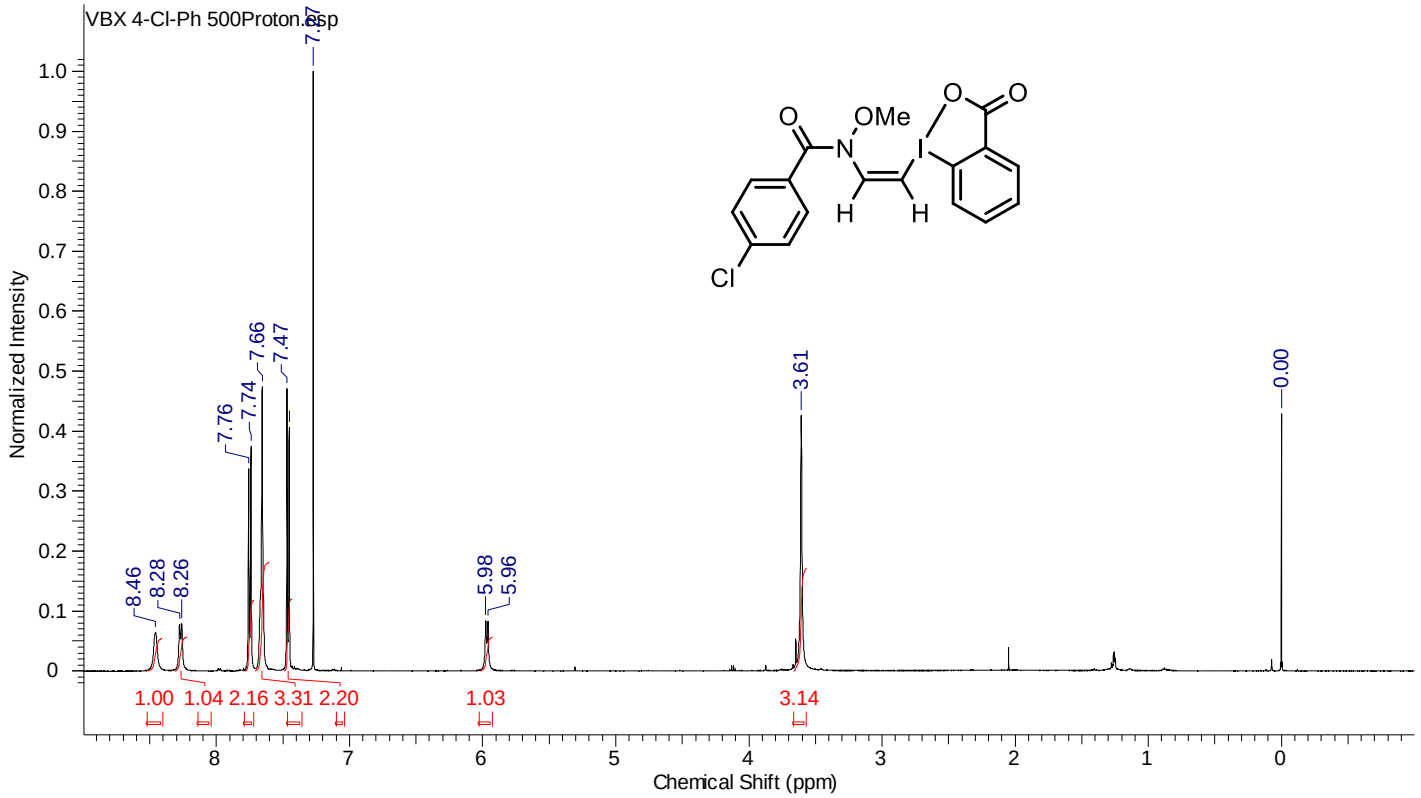


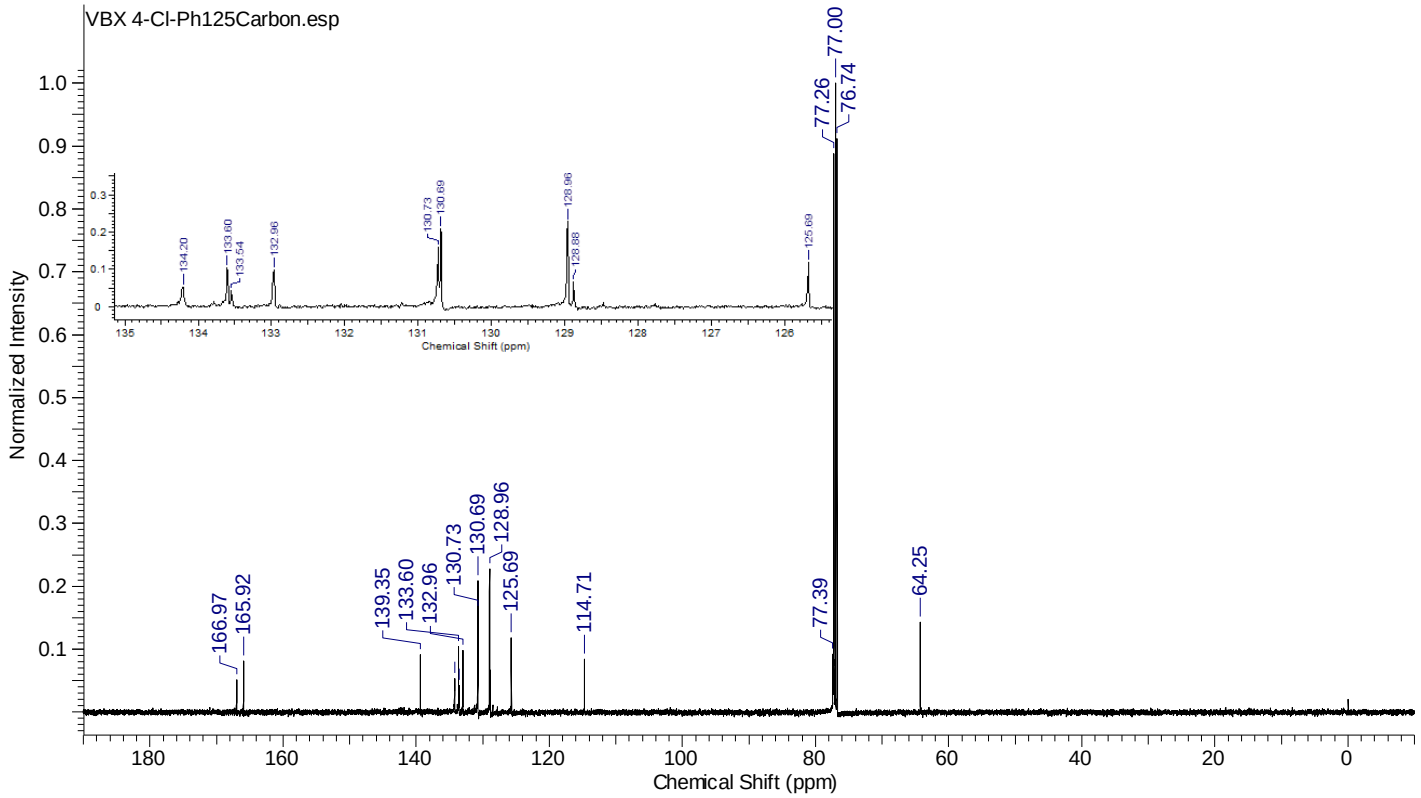
(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxybenzamide-1,2-benziodoxol-3-(1*H*)-one (3b)



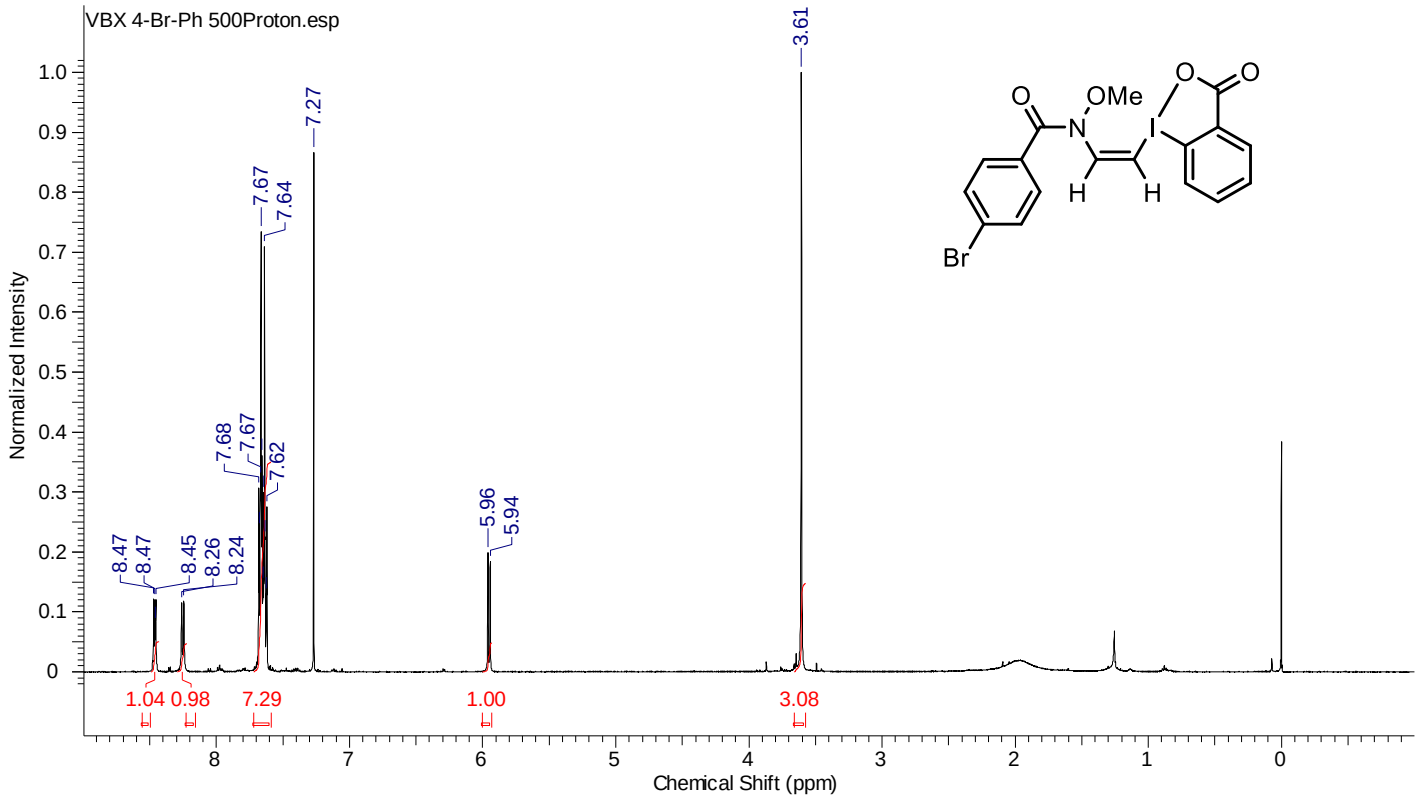


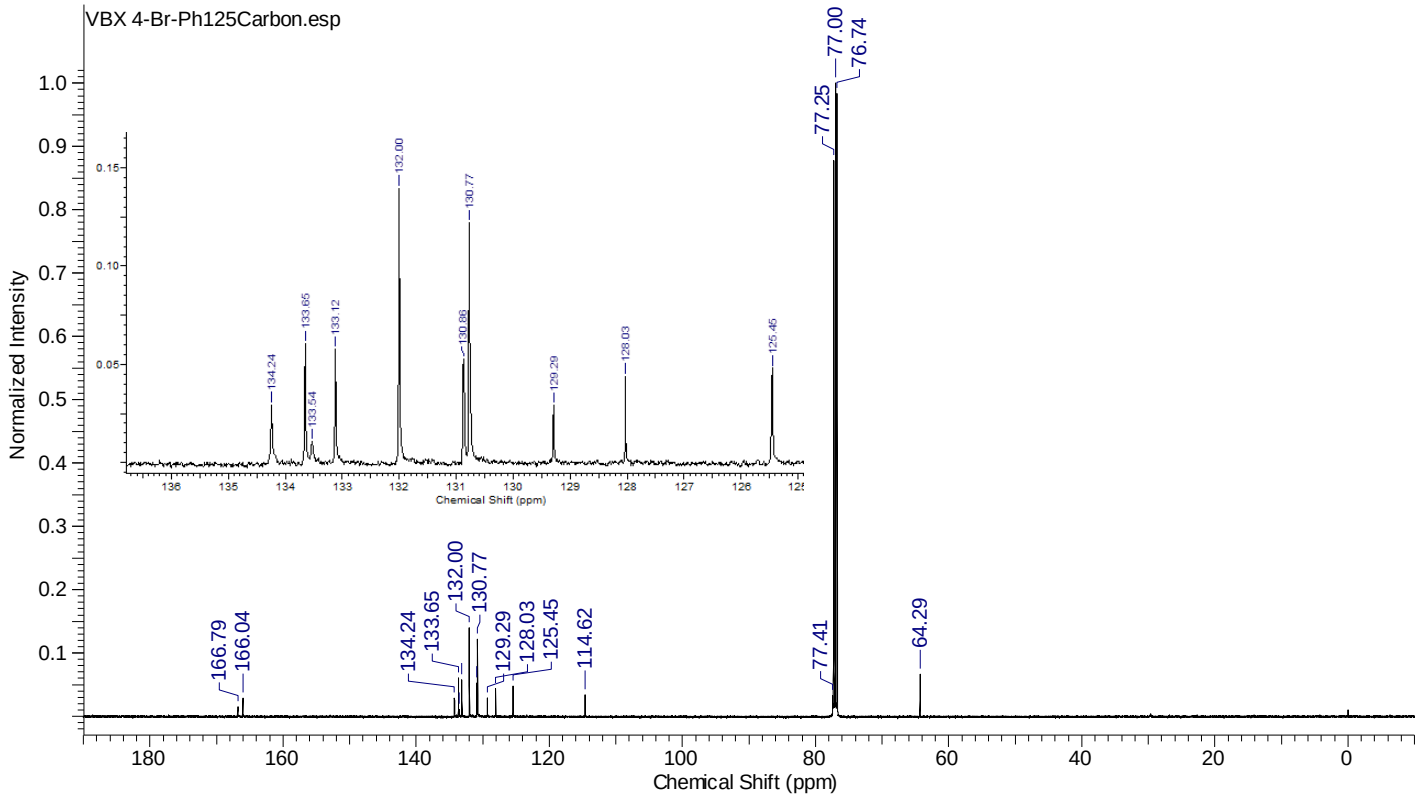
(*Z*)-*N*-(1-Vin-2-yl)-4-chloro-*N*-methoxybenzamide-1,2-benziodoxol-3-(1*H*)-one (3c)



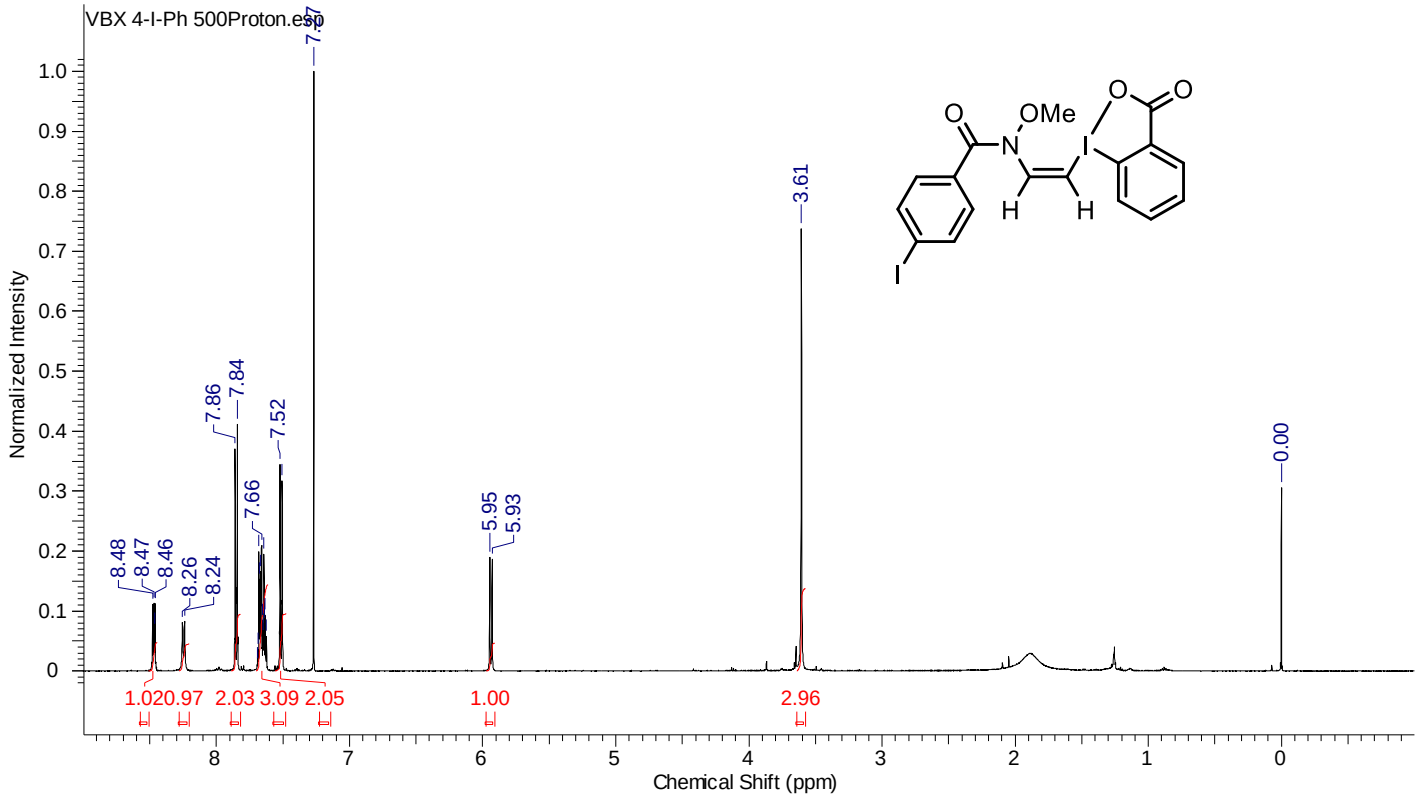


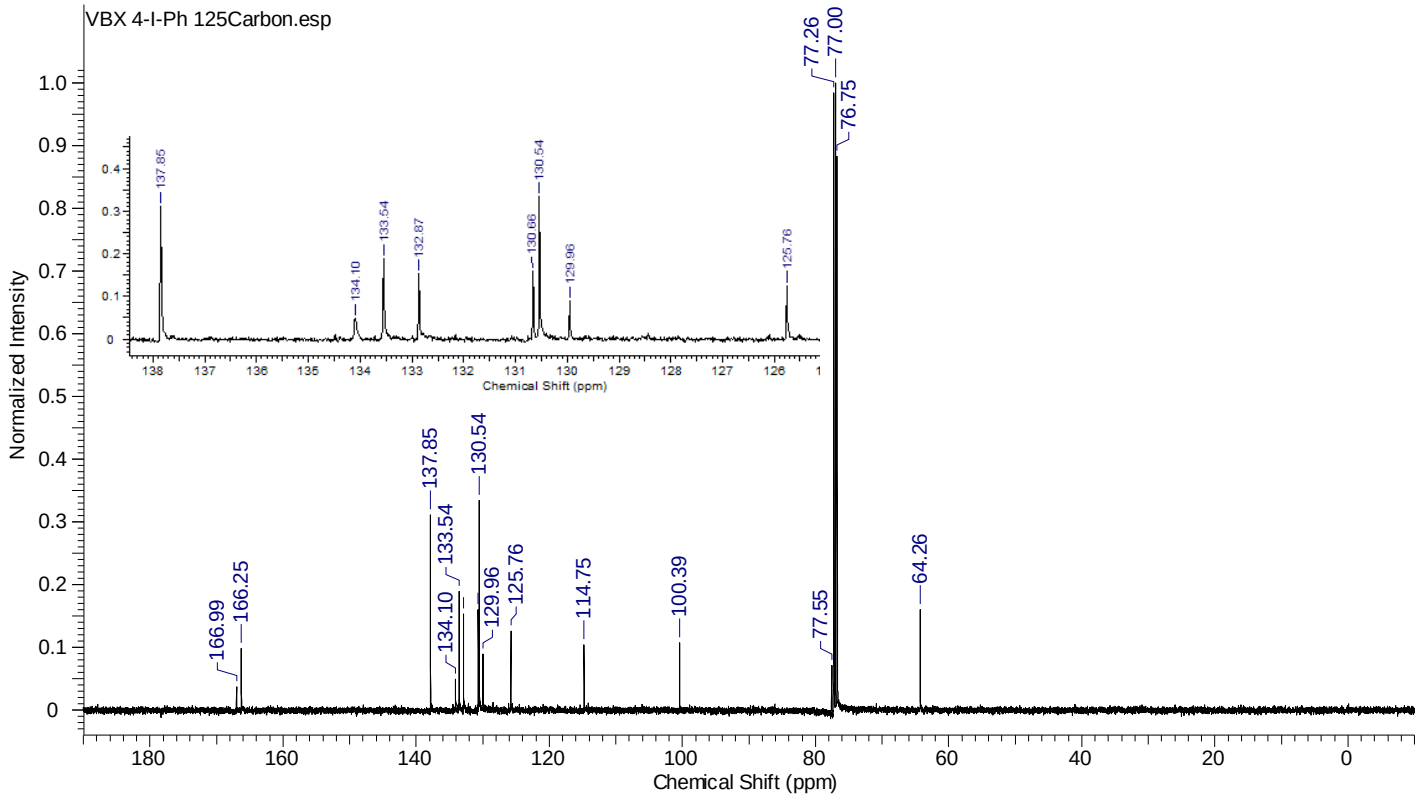
(*Z*)-*N*-(1-Vin-2-yl)-4-bromo-*N*-methoxybenzamide-1,2-benziodoxol-3-(1*H*)-one (3d)



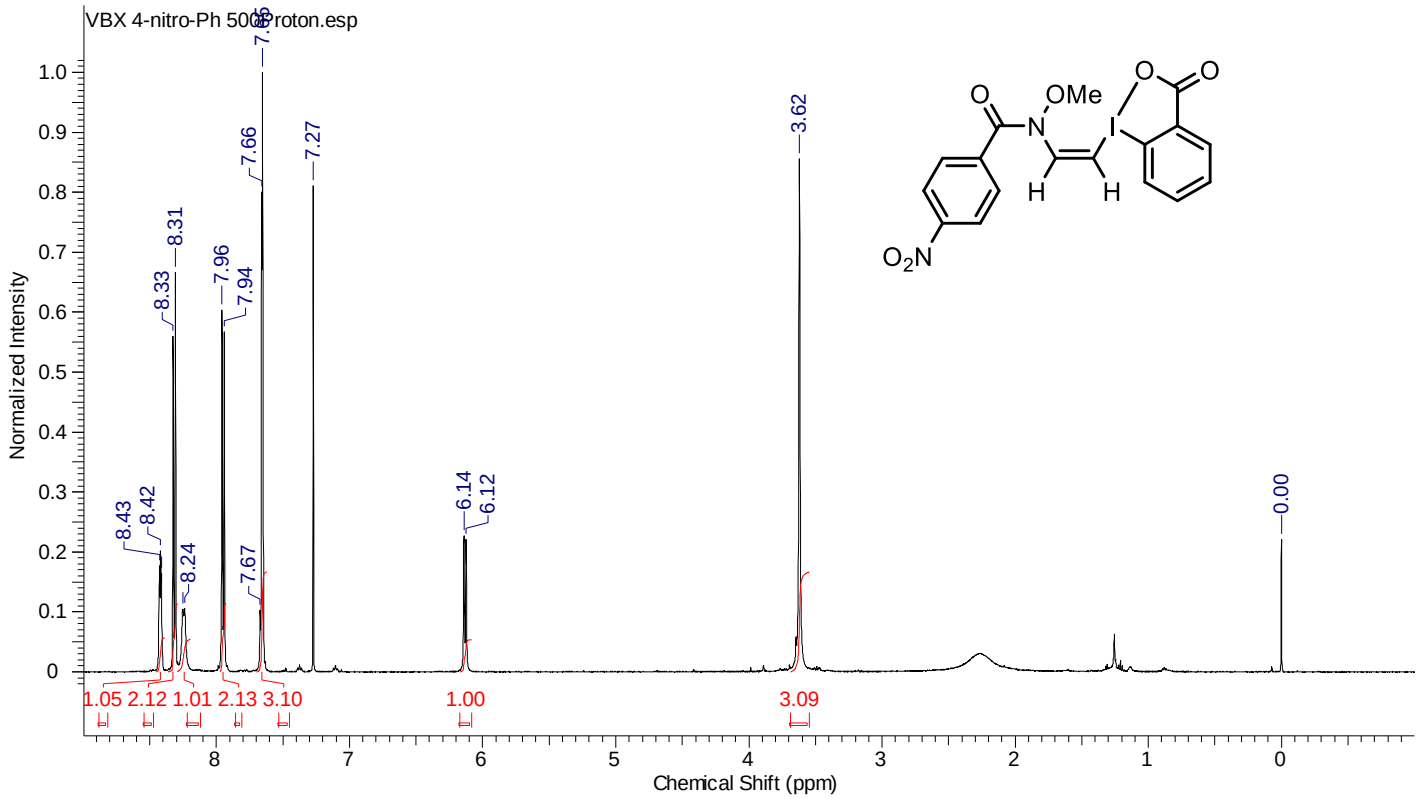


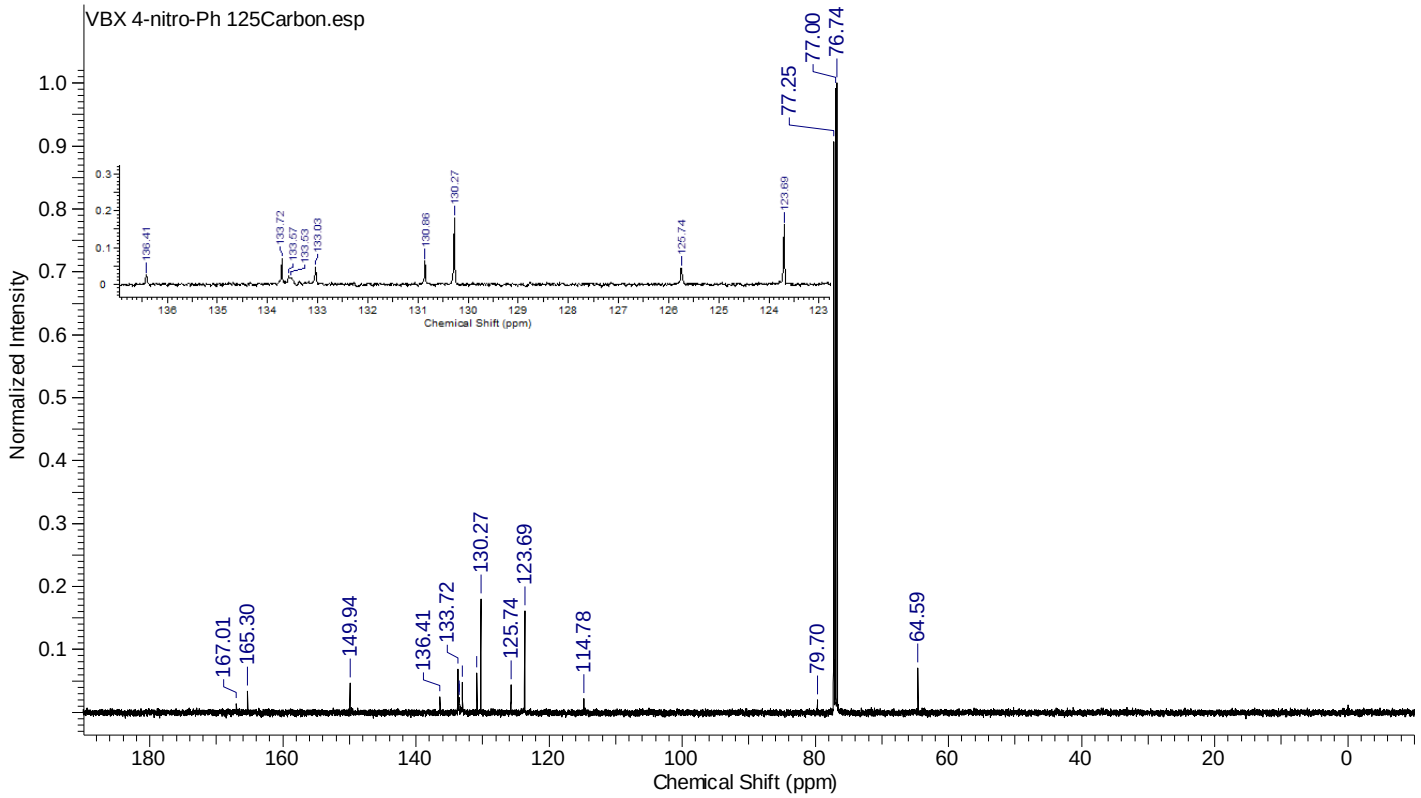
(*Z*)-*N*-(1-Vin-2-yl)-4-iodo-*N*-methoxybenzamide-1,2-benziodoxol-3-(1*H*)-one (3e)



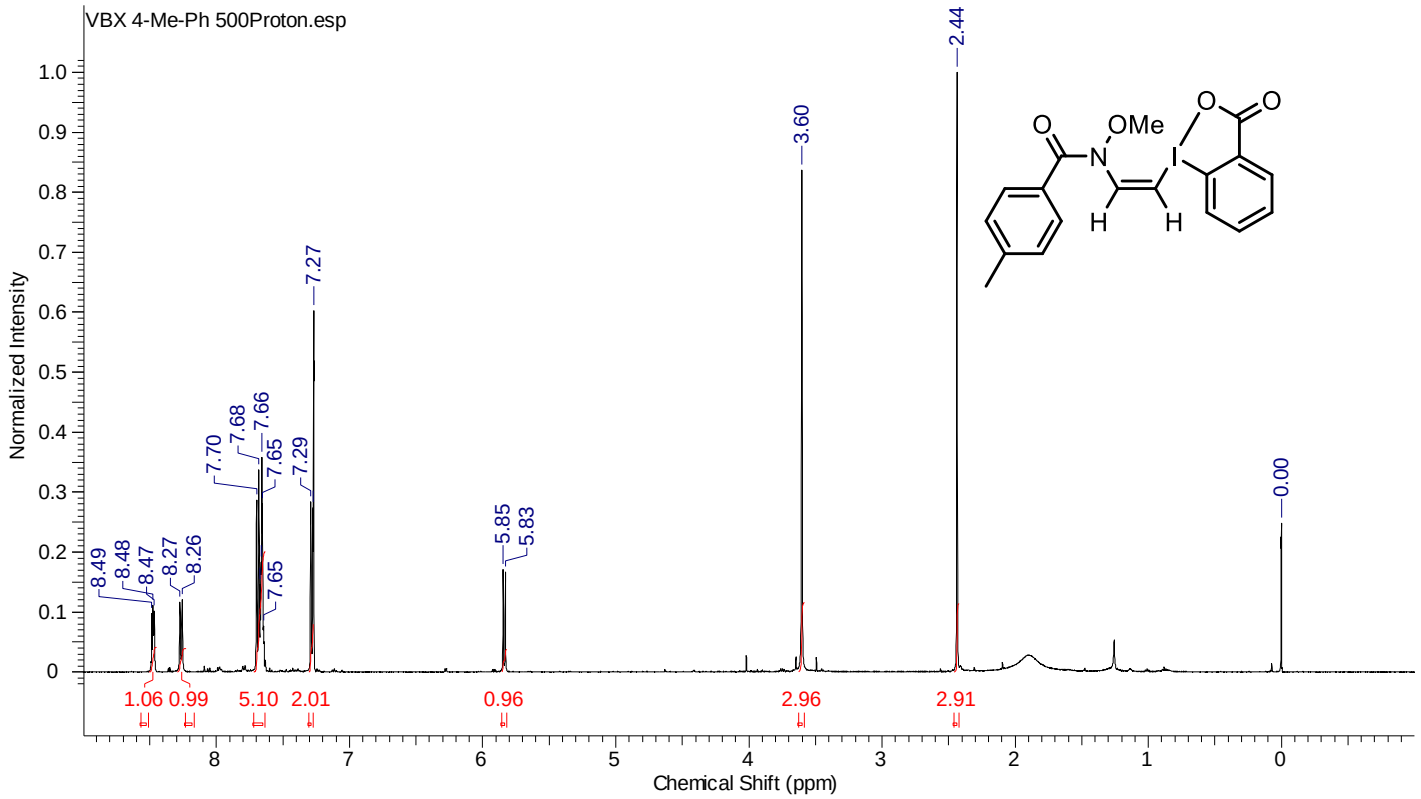


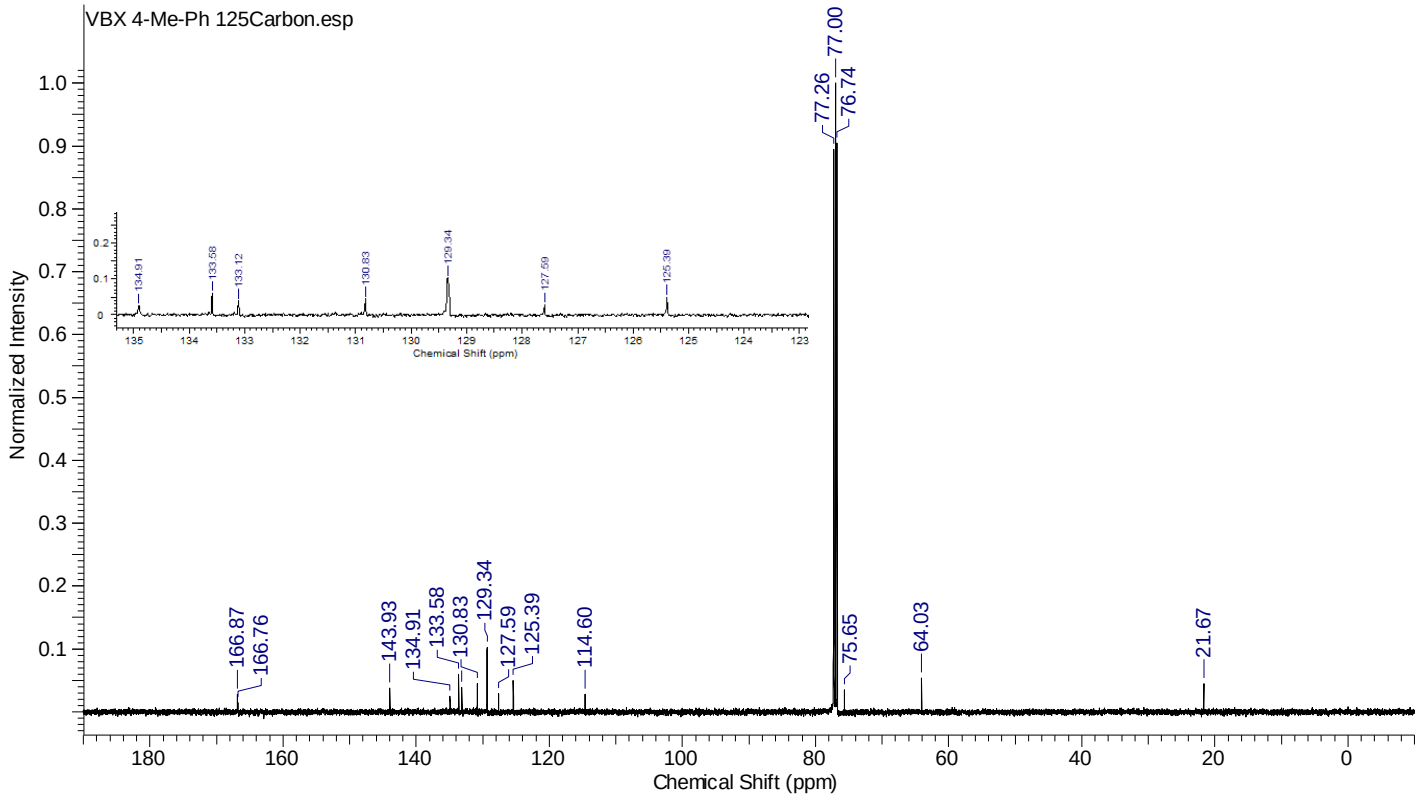
(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxy-4-nitrobenzamide-1,2-benziodoxol-3-(1*H*)-one (3f)



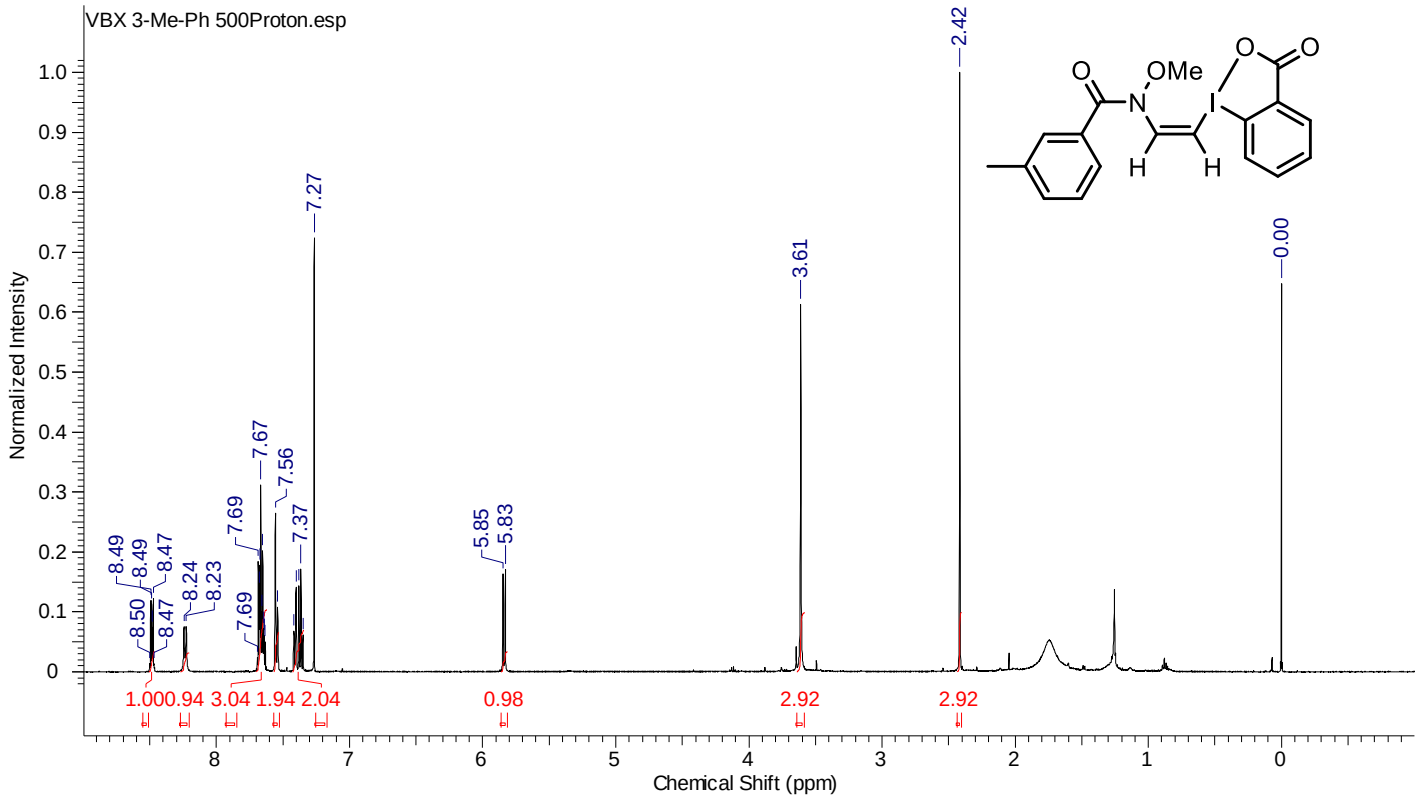


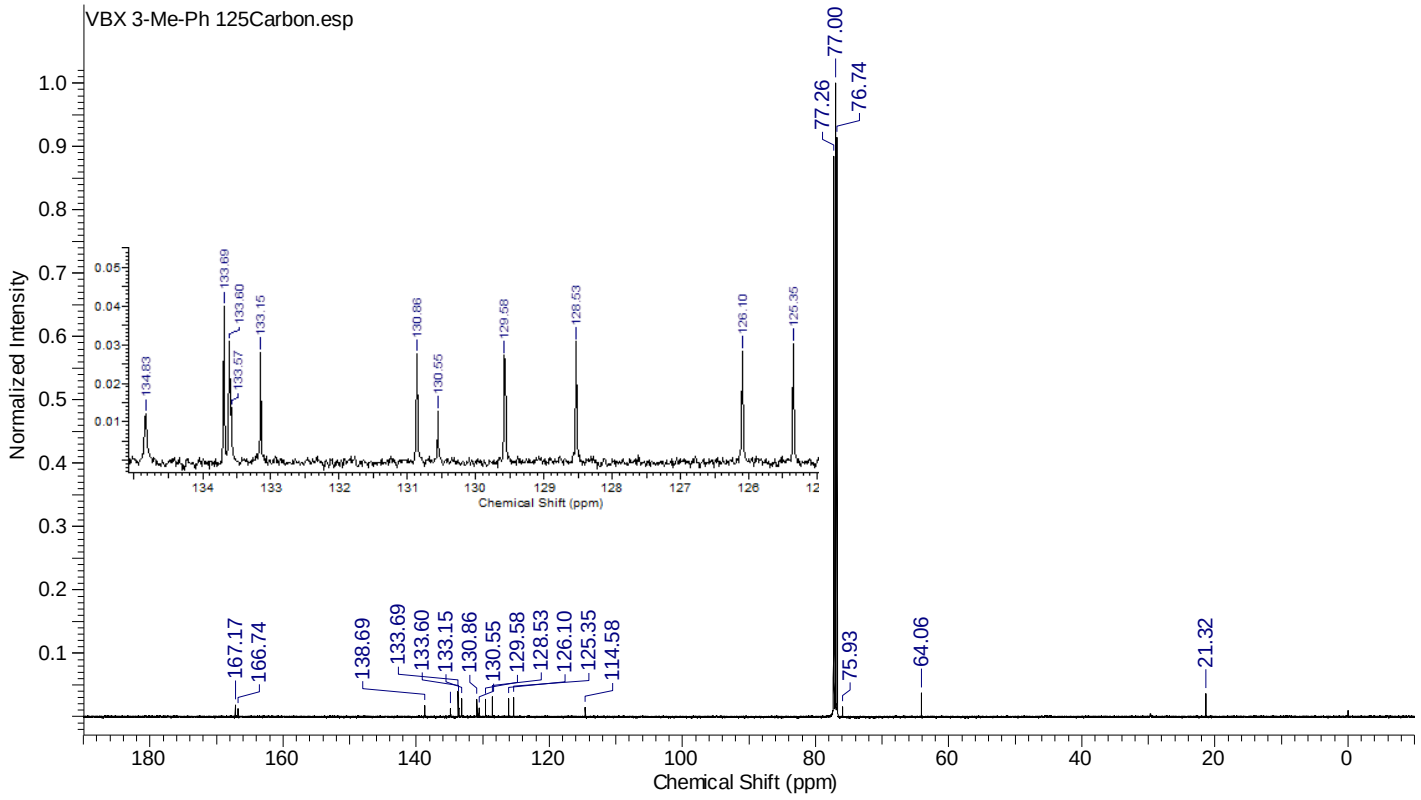
(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxy-4-methylbenzamide-1,2-benziodoxol-3-(1*H*)-one (3g)



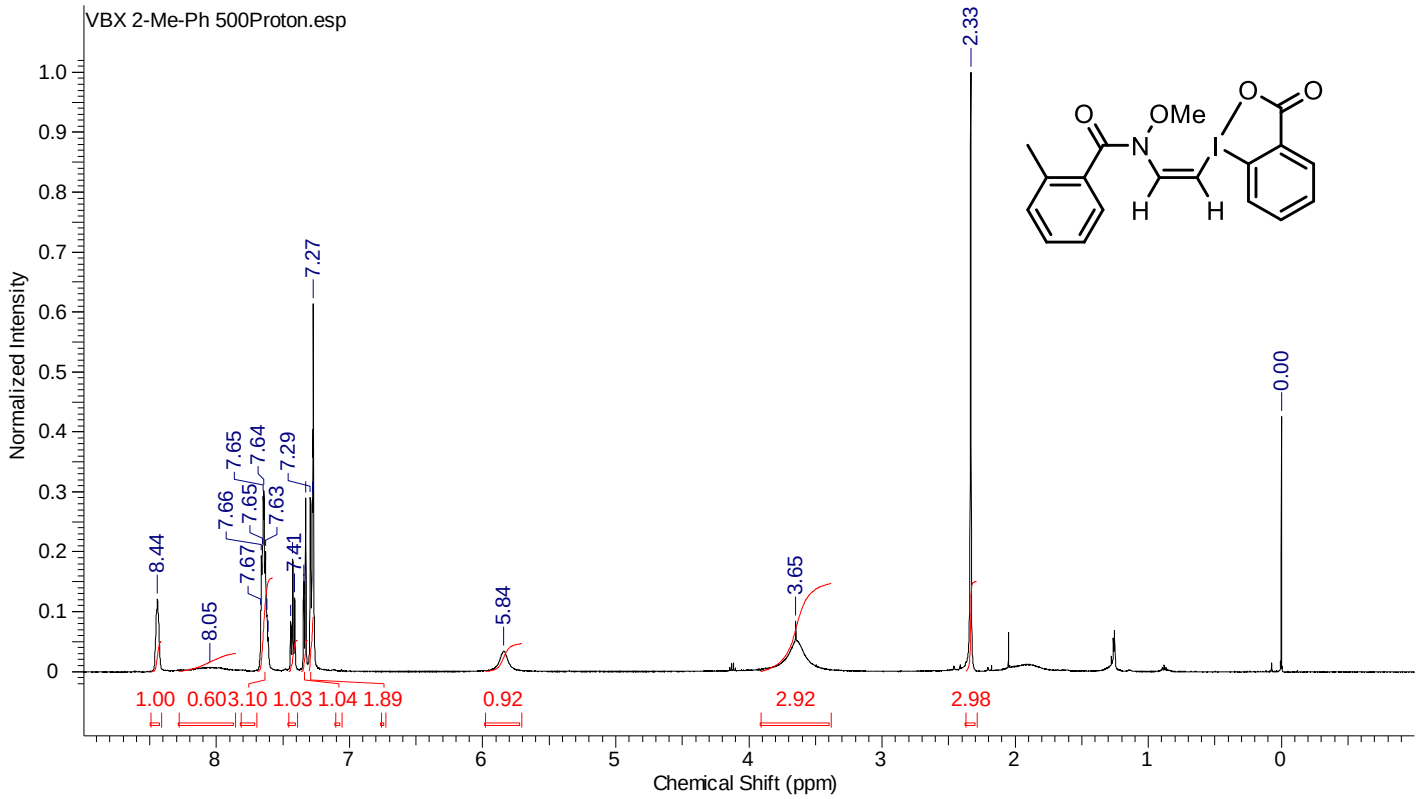


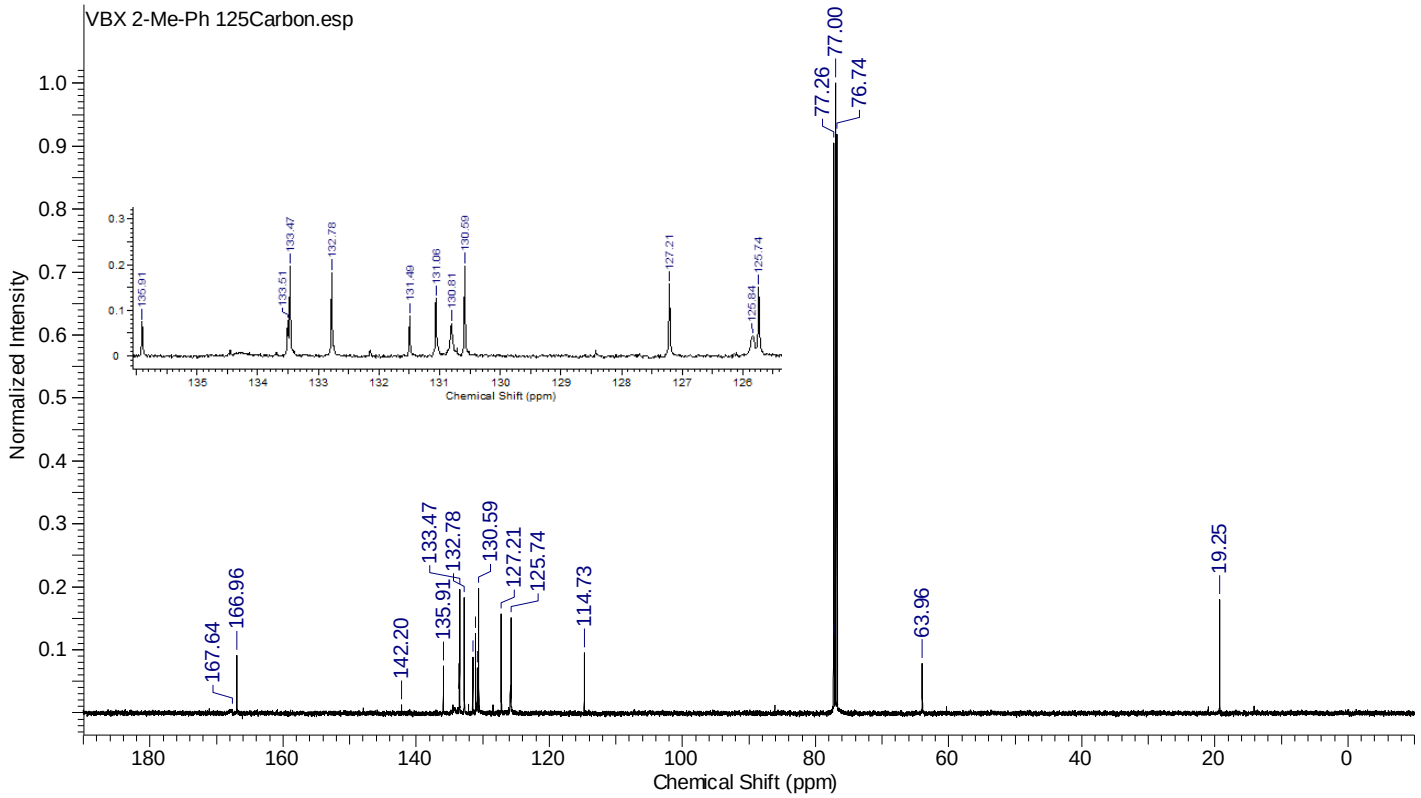
(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxy-3-methylbenzamide-1,2-benziodoxol-3-(1*H*)-one (3h)



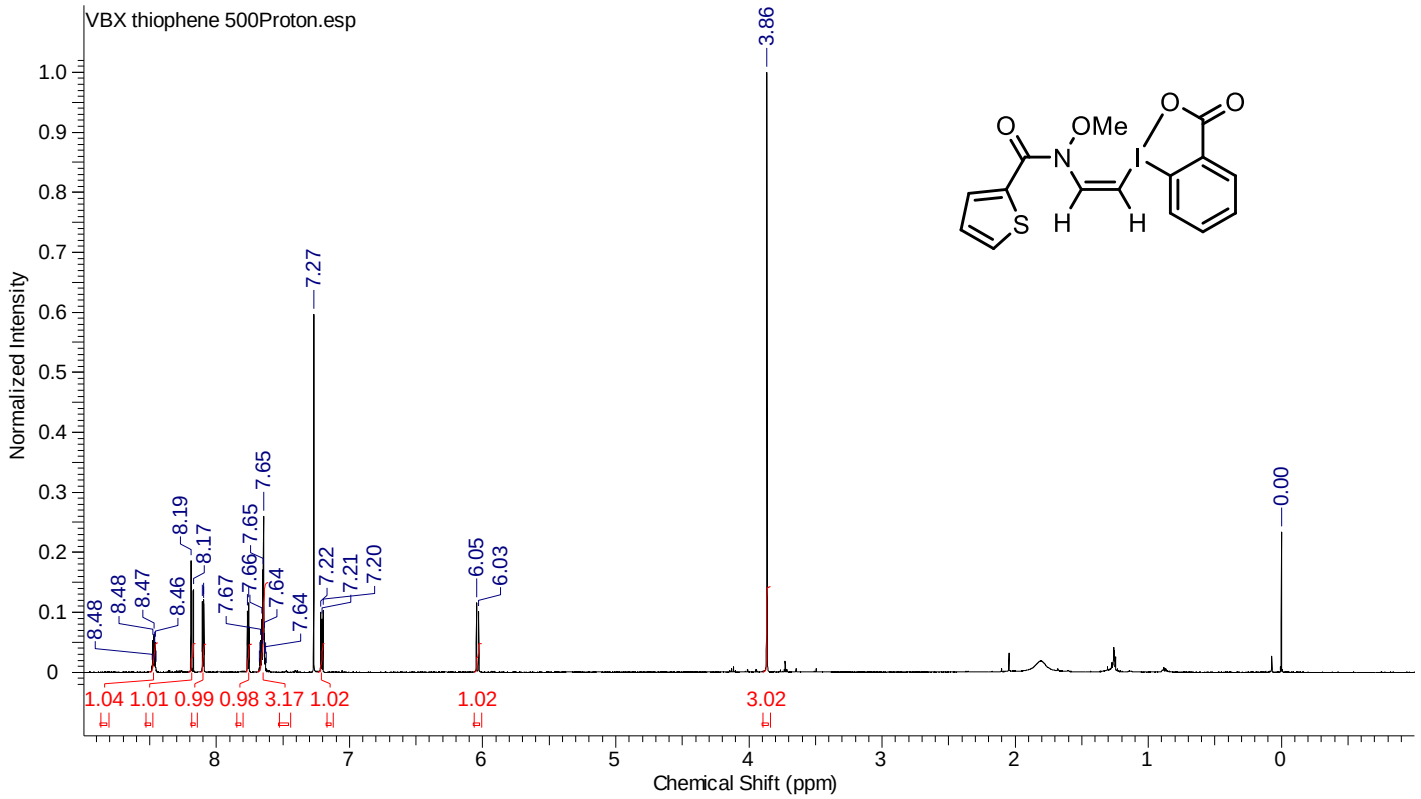


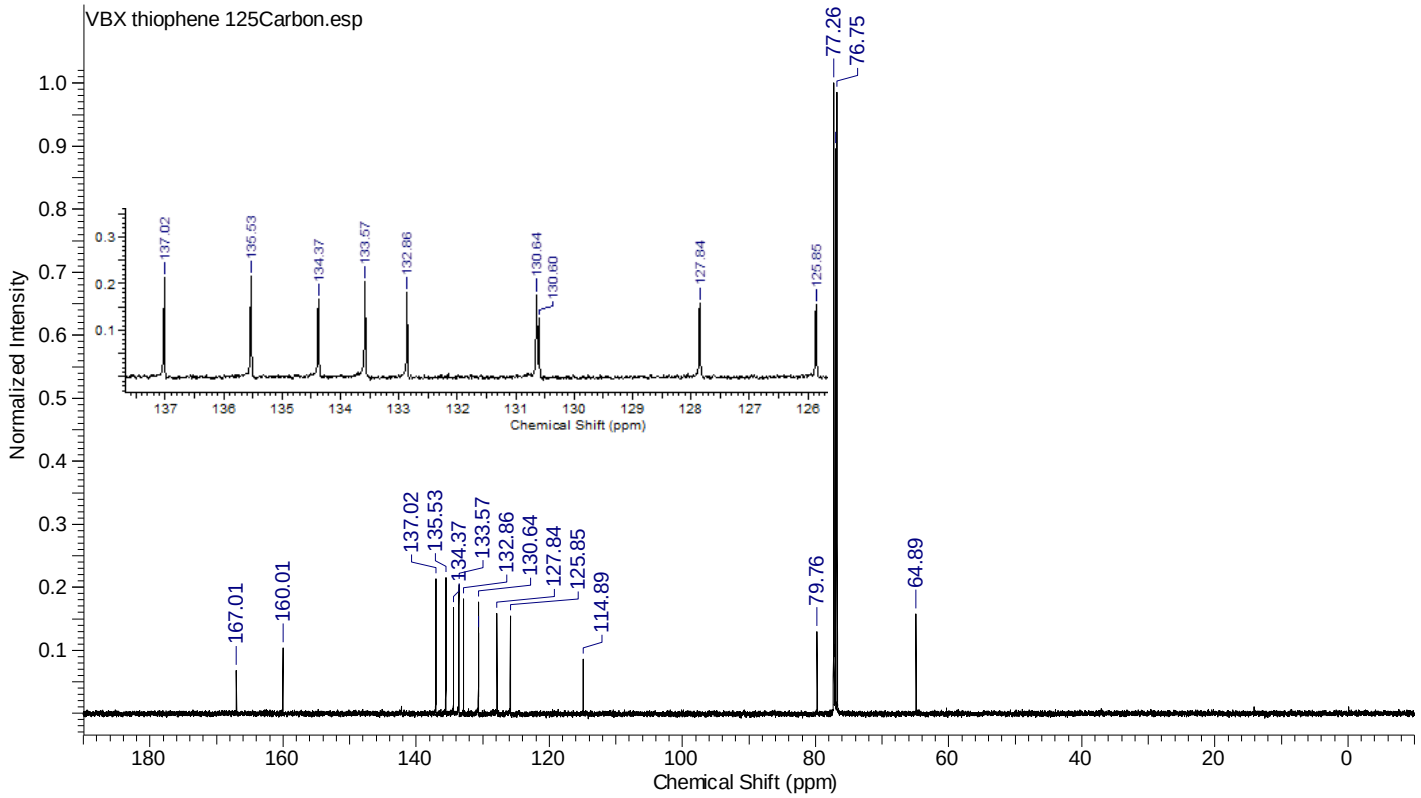
(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxy-2-methylbenzamide-1,2-benziodoxol-3-(1*H*)-one (3i)



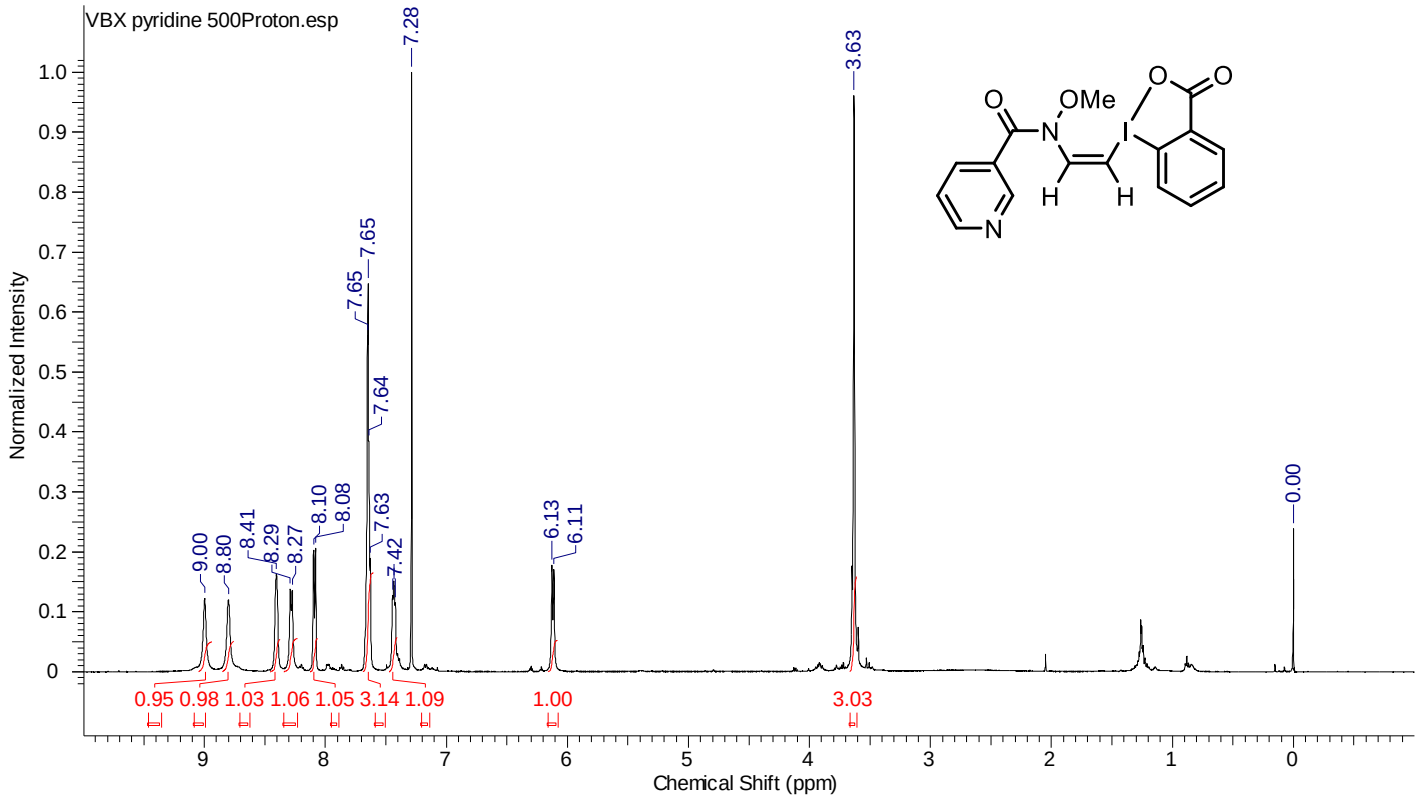


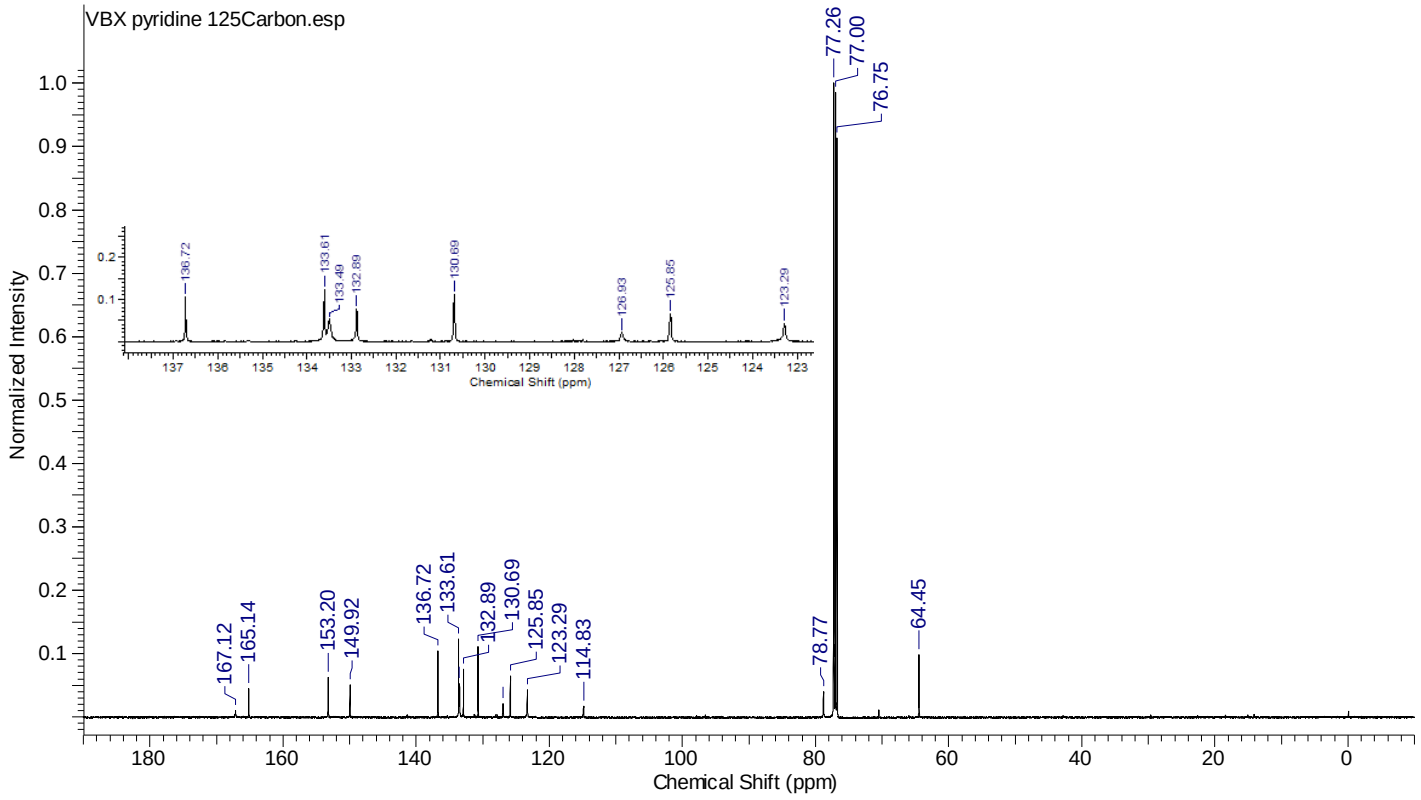
(Z)-*N*-(1-Vin-2-yl)-*N*-methoxy-2-thiophenecarboxamide-1,2-benziodoxol-3-(1*H*)-one (3j)



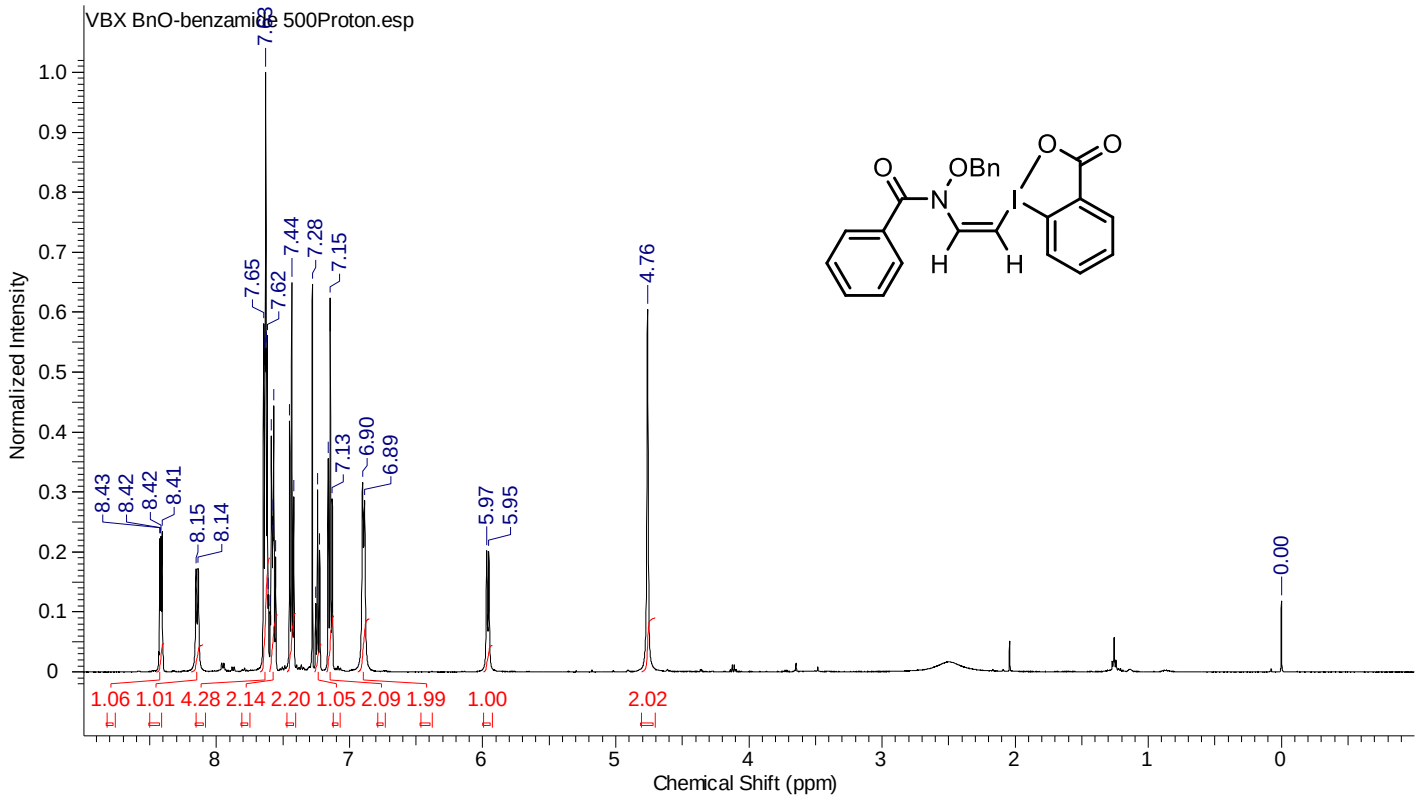


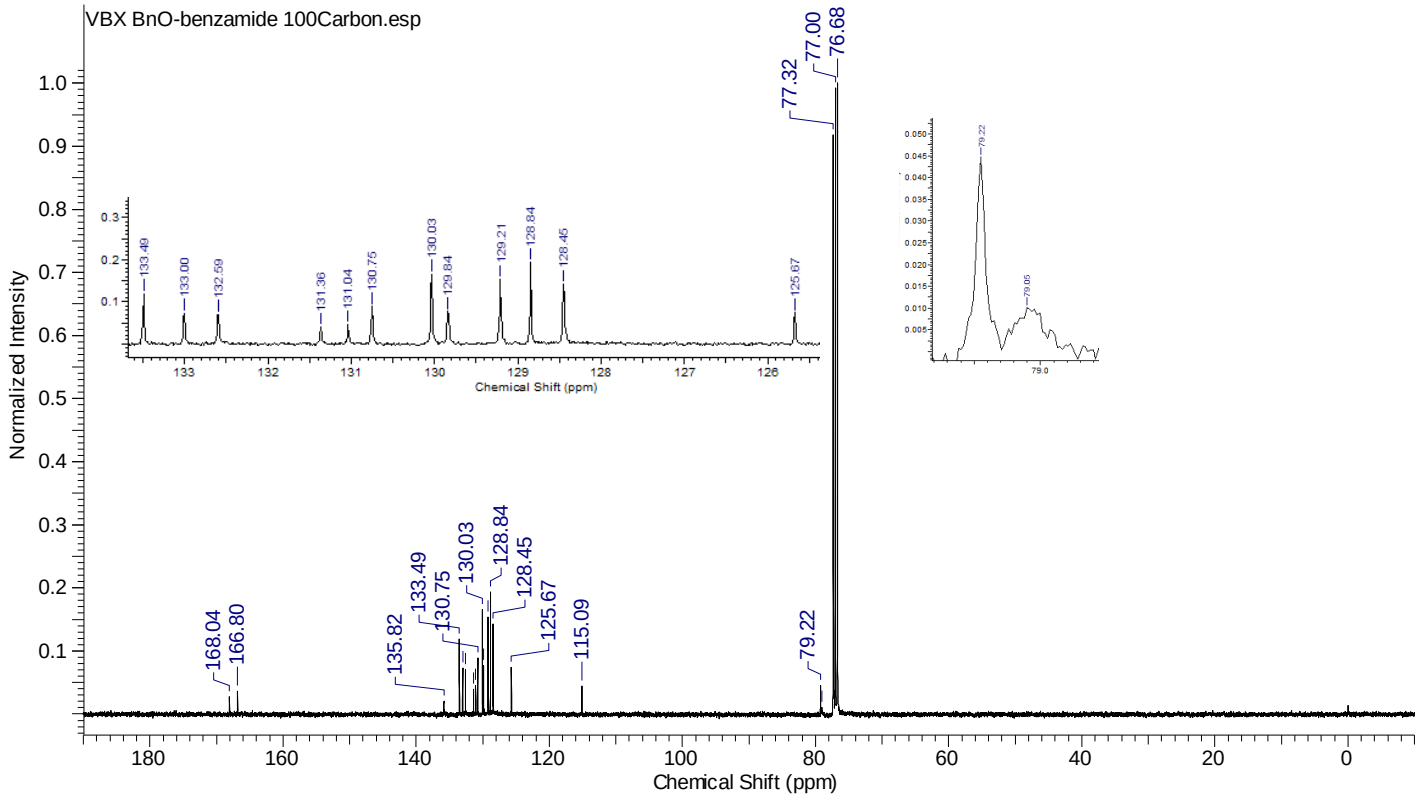
(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxy-3-pyridinecarboxamide-1,2-benziodoxol-3-(1*H*)-one (3k)



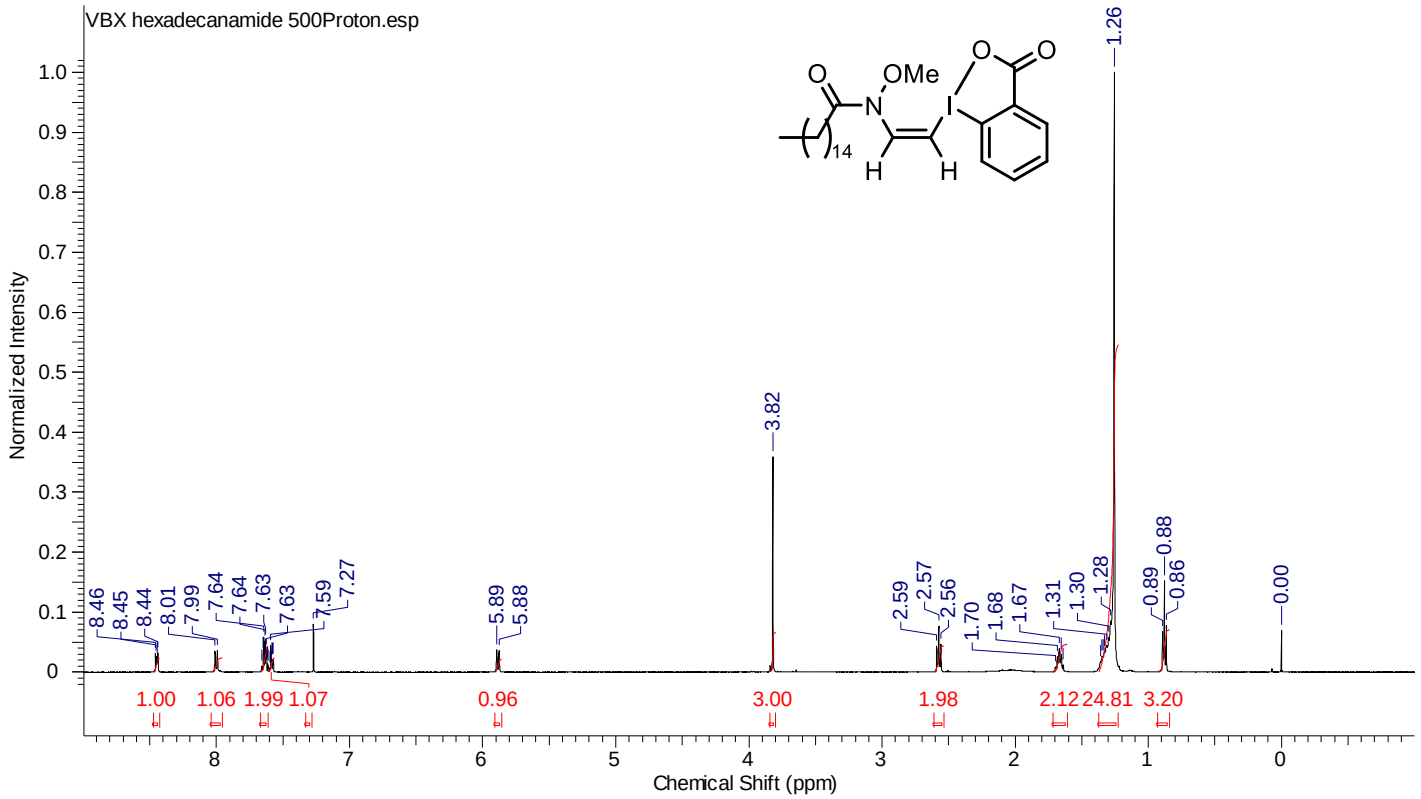


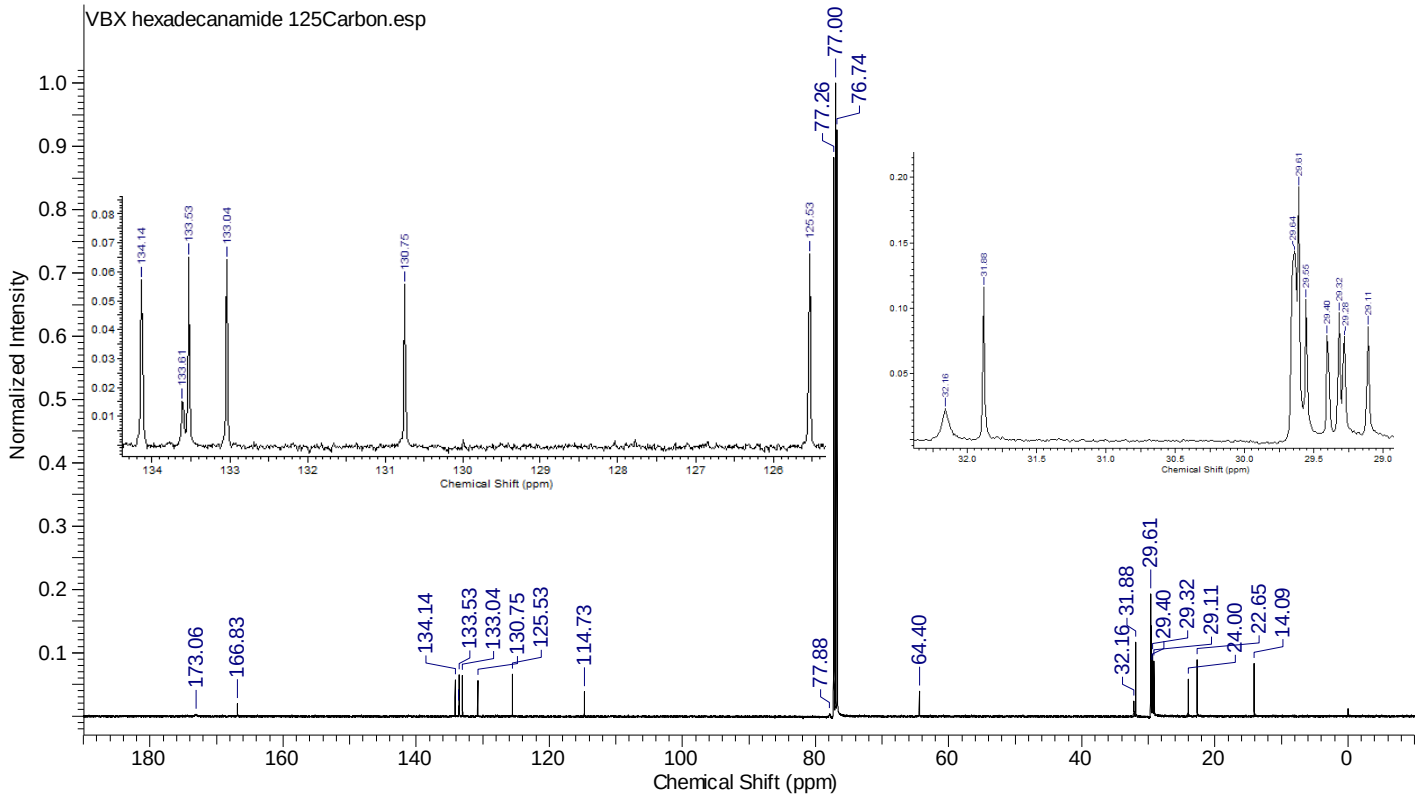
(*Z*)-*N*-(1-Vin-2-yl)-*N*-benzyloxybenzamide-1,2-benziodoxol-3-(1*H*)-one (3l)



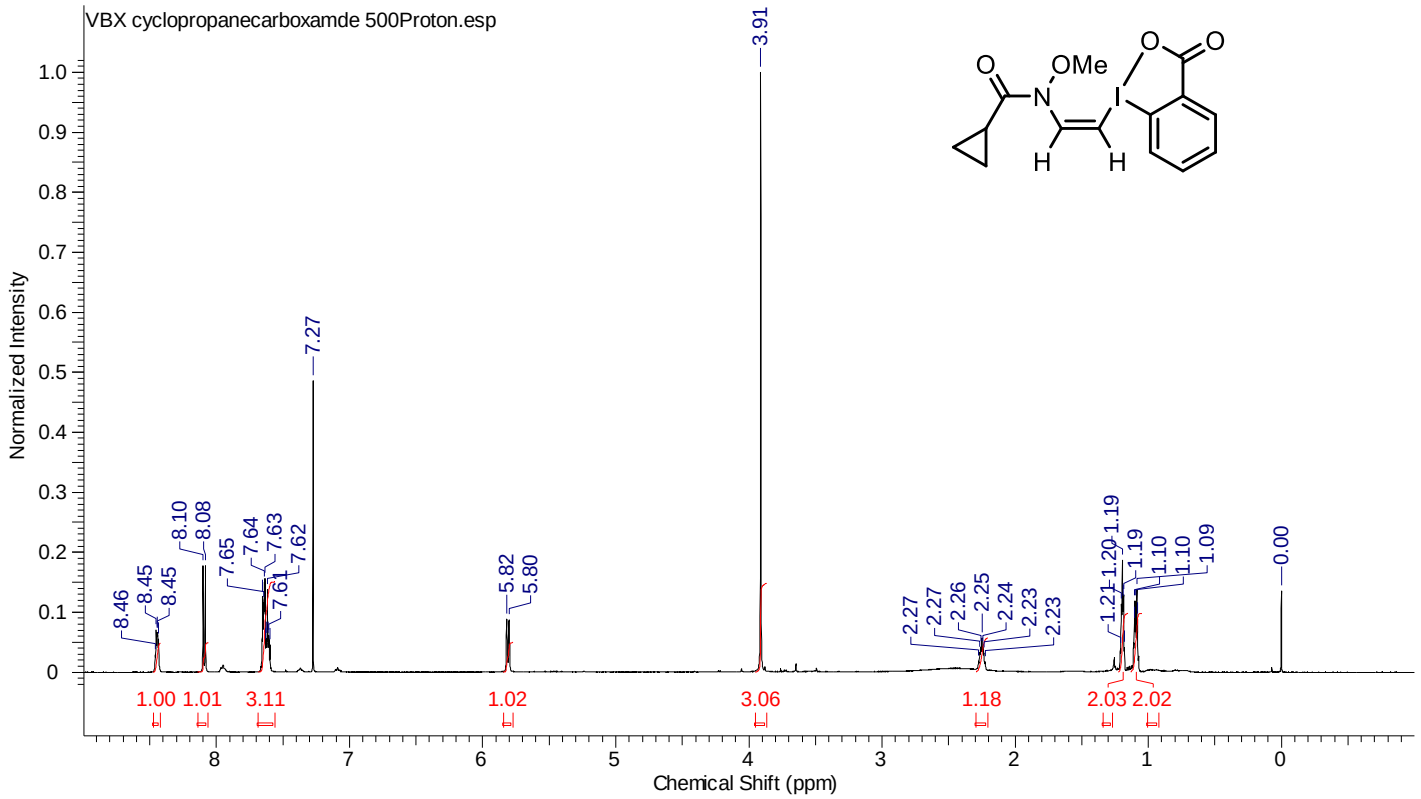


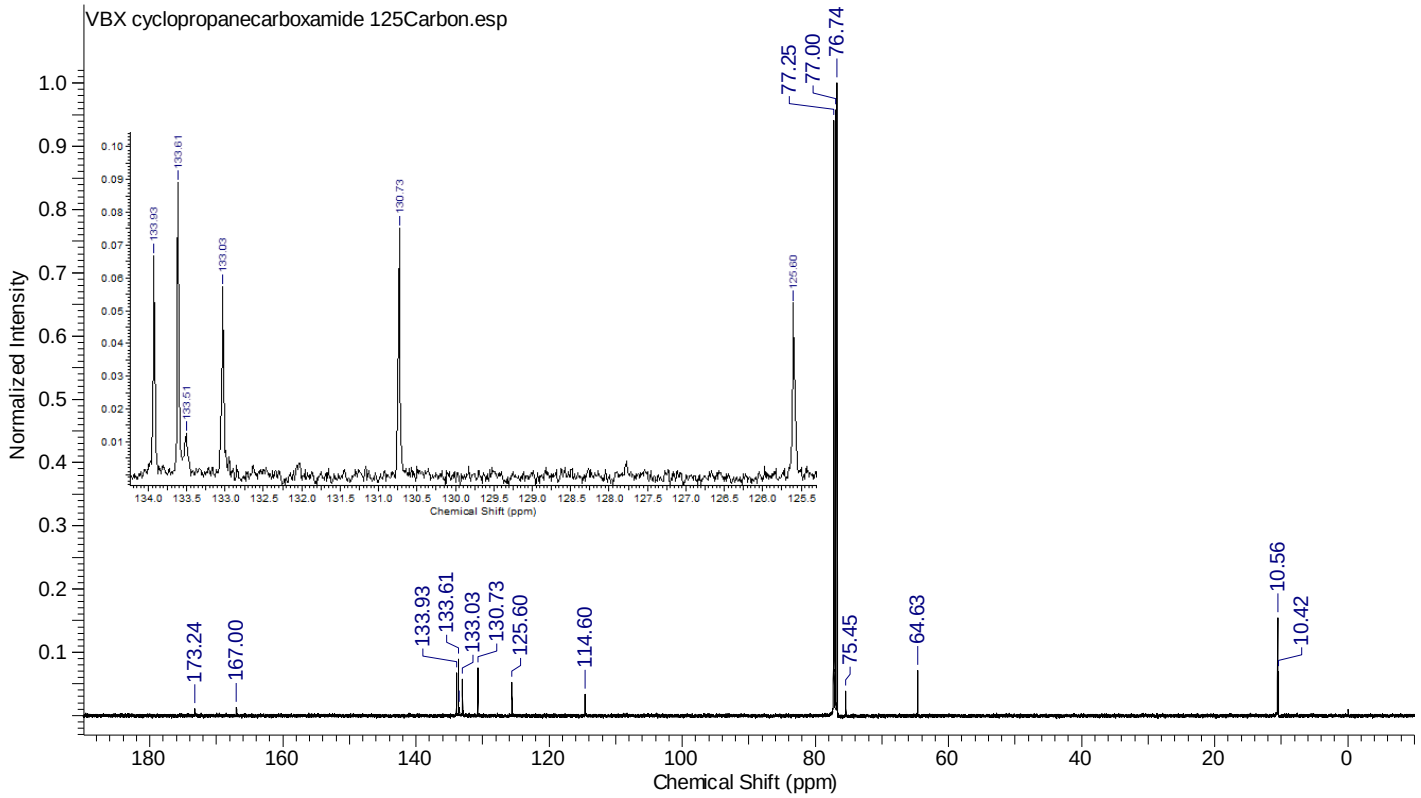
(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxyhexadecanamide-1,2-benziodoxol-3-(1*H*)-one (3m)



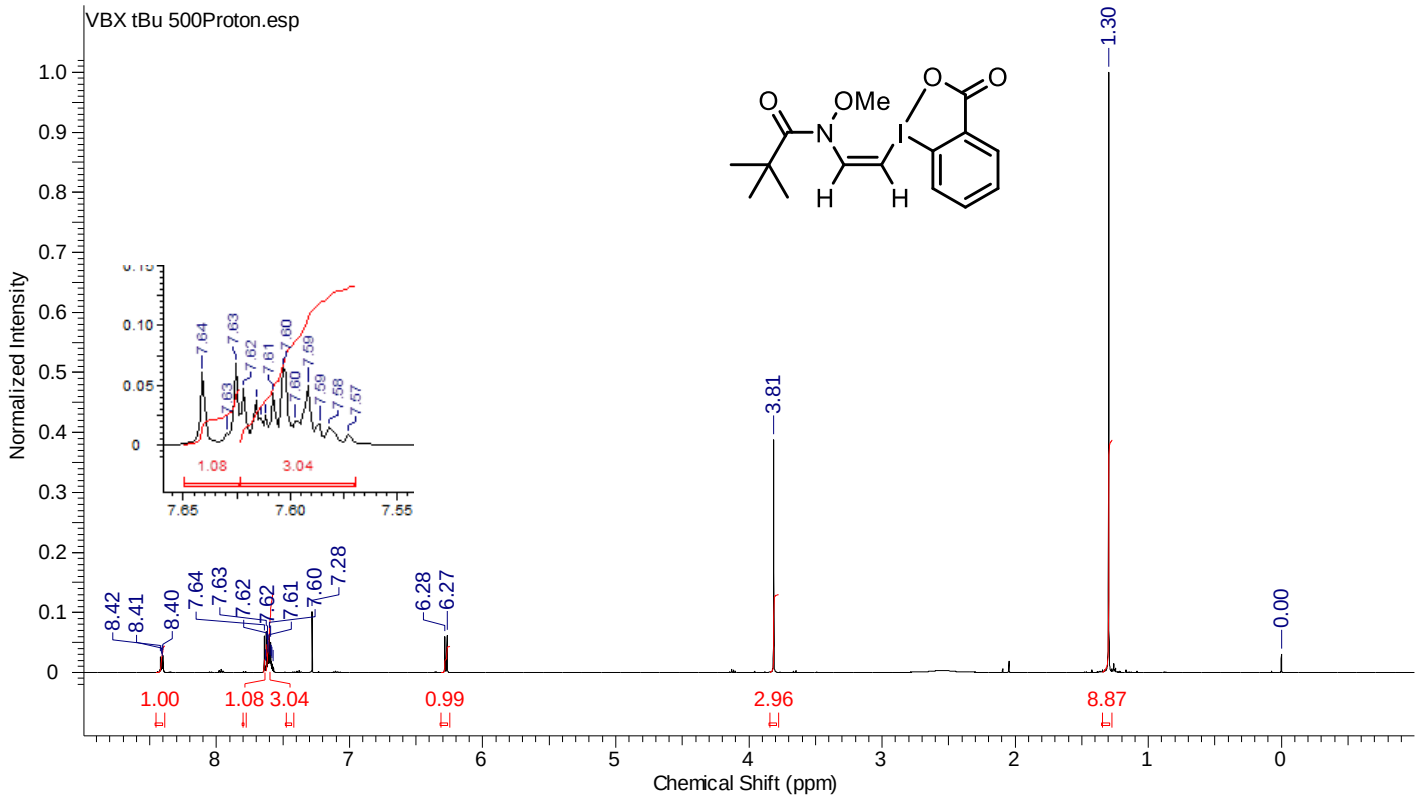


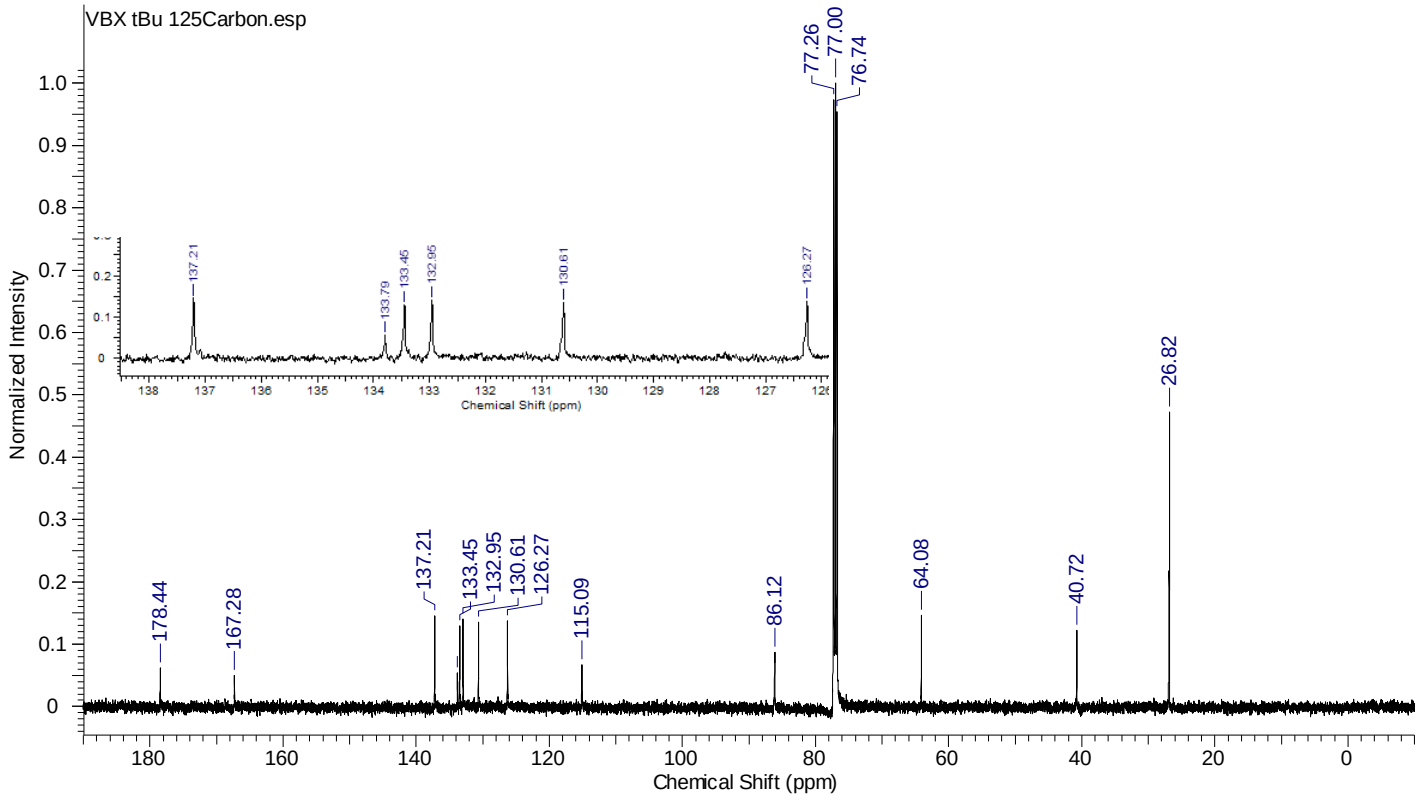
(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxycyclopropanecarboxamide-1,2-benziodoxol-3-(1*H*)-one (3n)



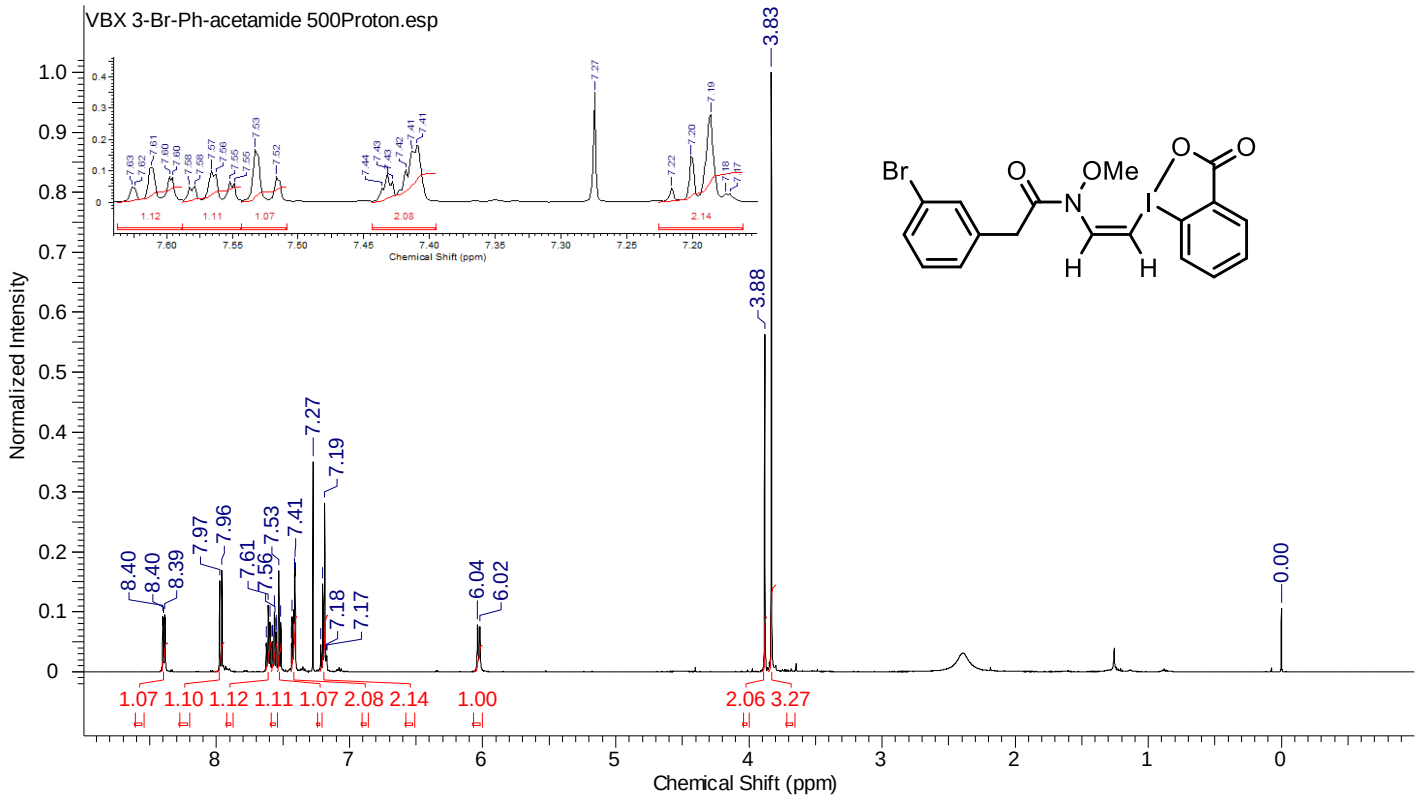


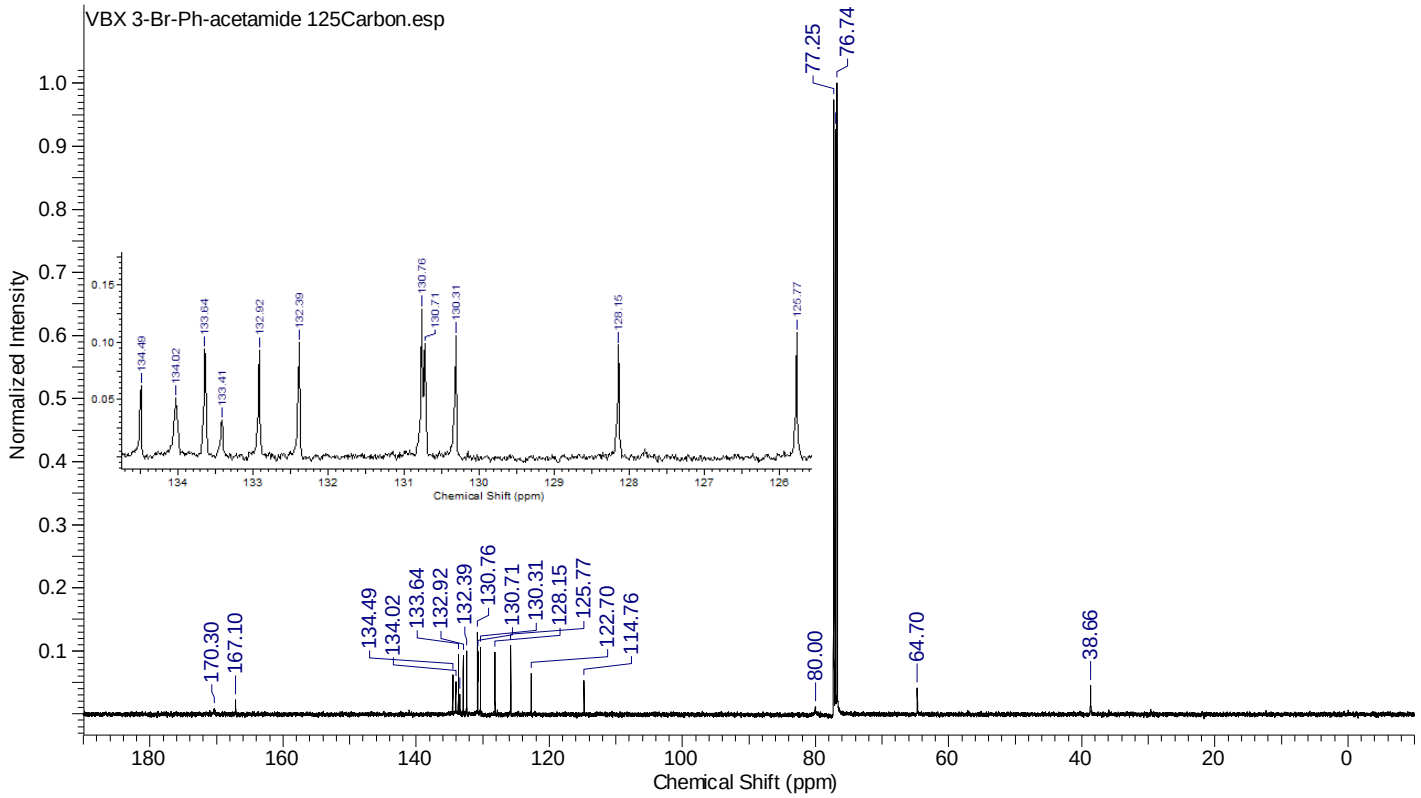
(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxy-2,2-dimethylpropanamide-1,2-benziodoxol-3-(1*H*)-one (3o)



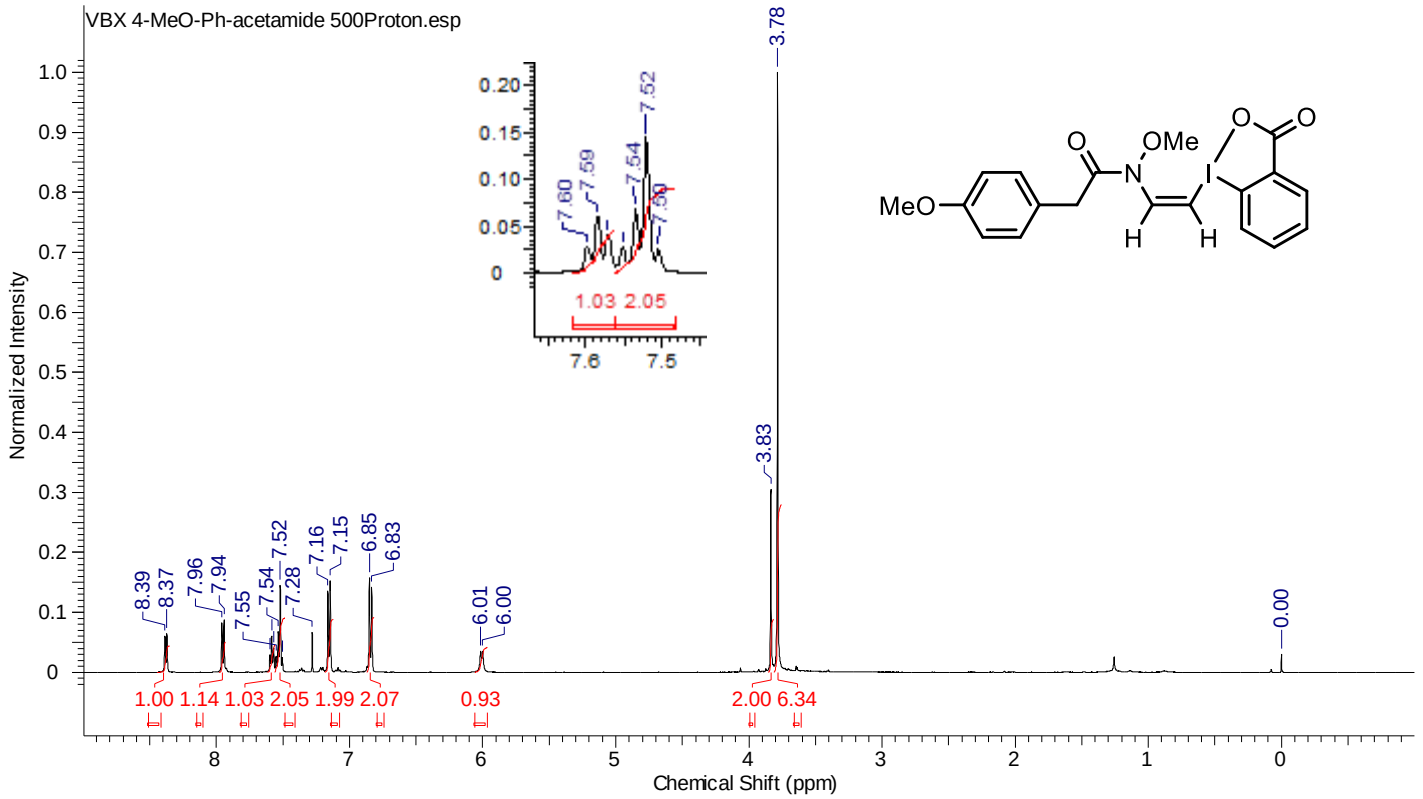


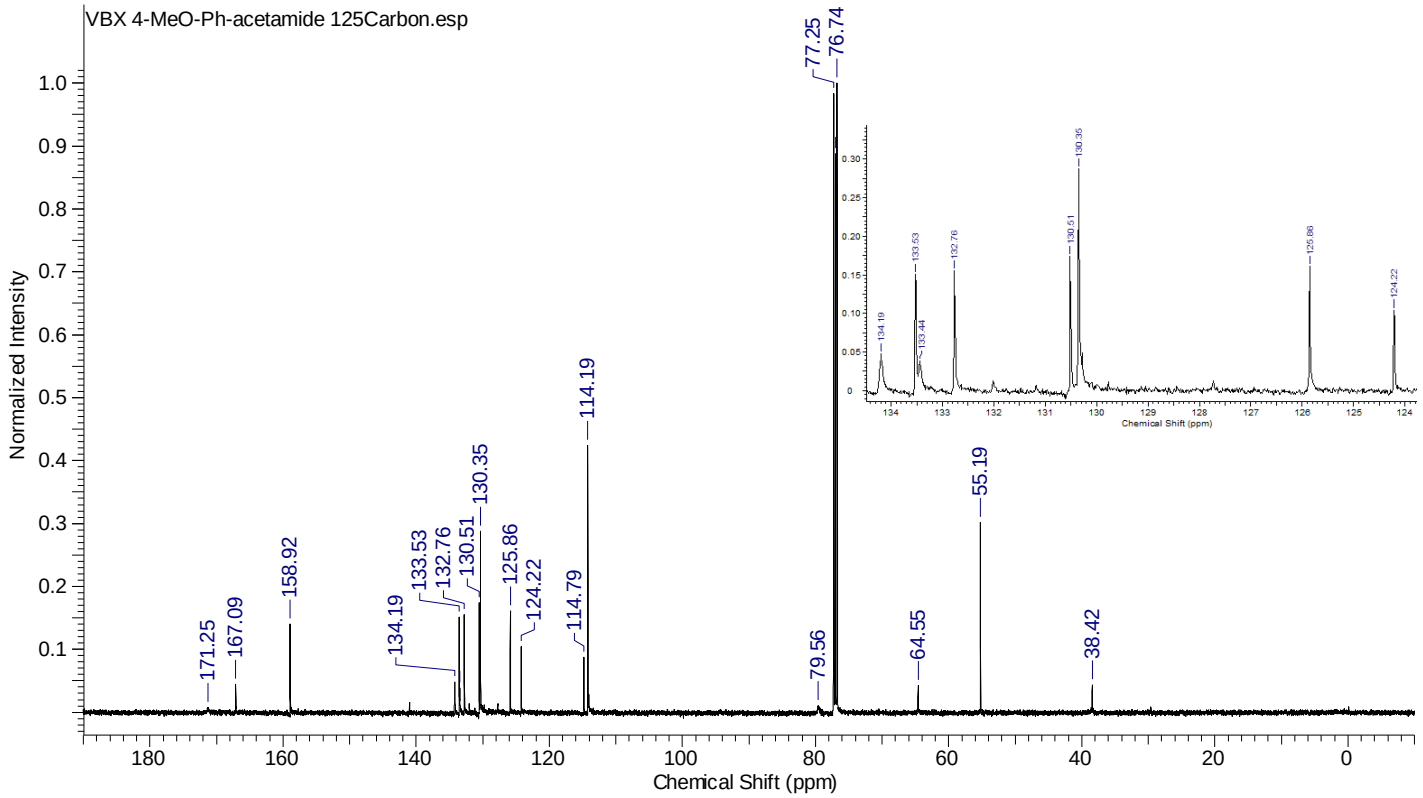
(*Z*)-*N*-(1-Vin-2-yl)-2-(3-bromophenyl)-*N*-methoxyacetamide-1,2-benziodoxol-3-(1*H*)-one (3p)



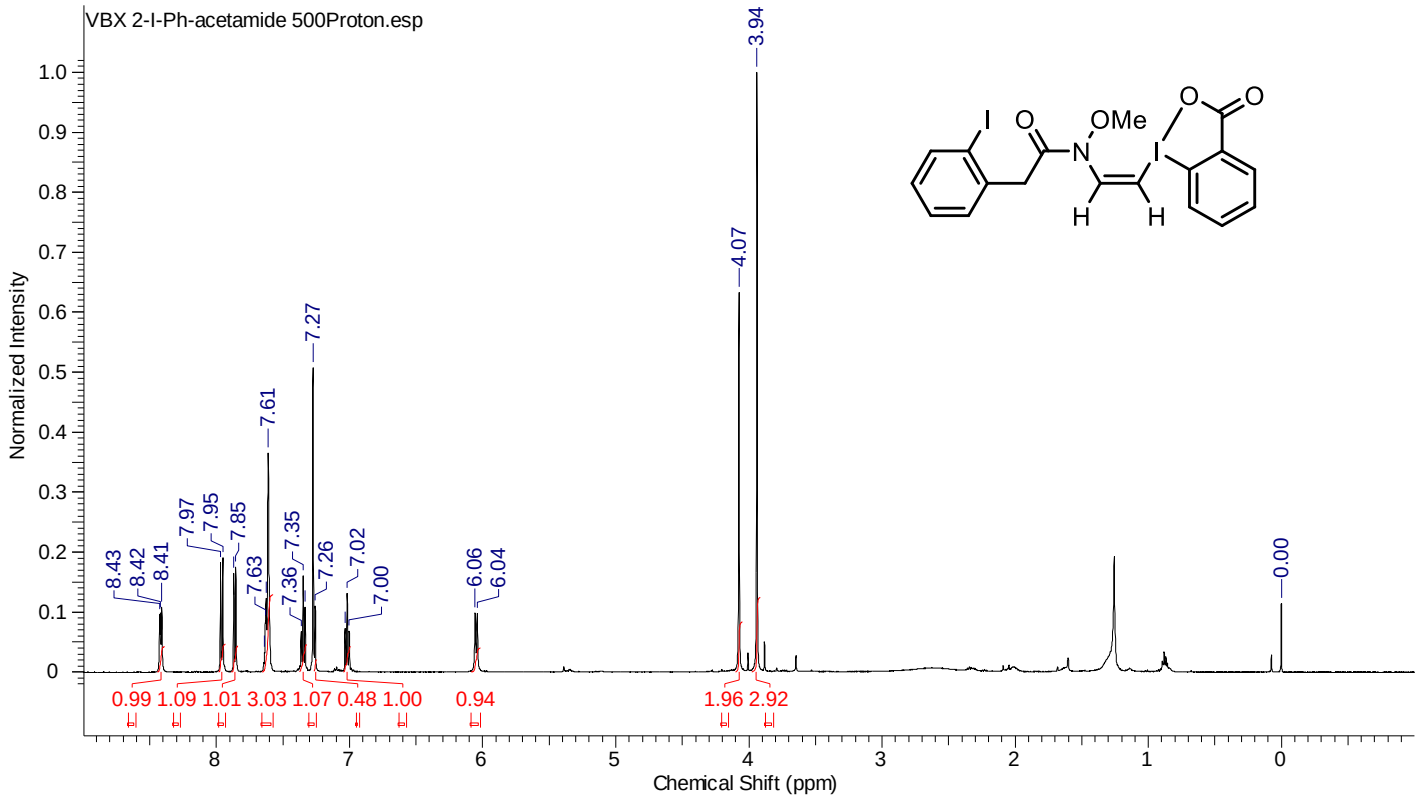


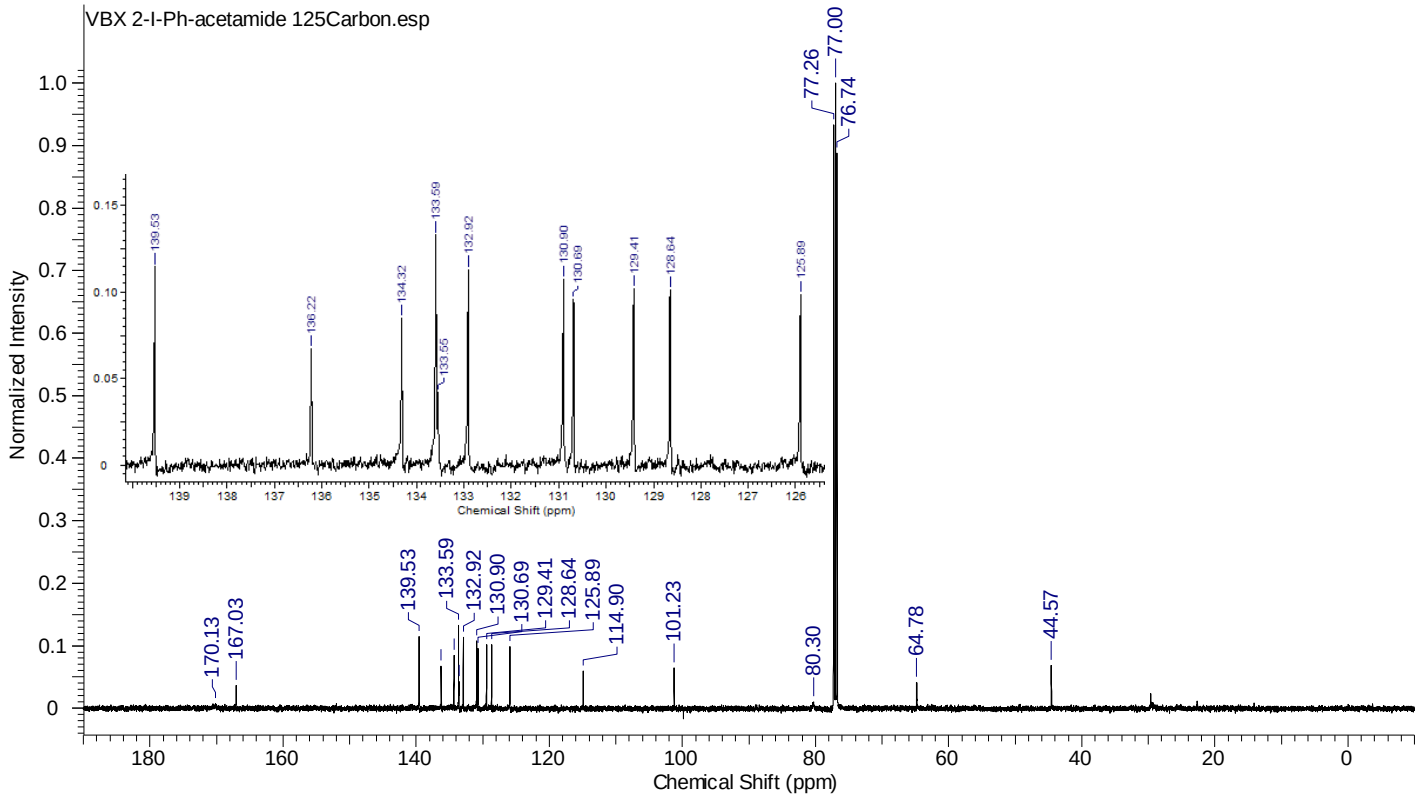
(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxy-2-(4-methoxyphenyl)acetamide-1,2-benziodoxol-3-(1*H*)-one (3q)



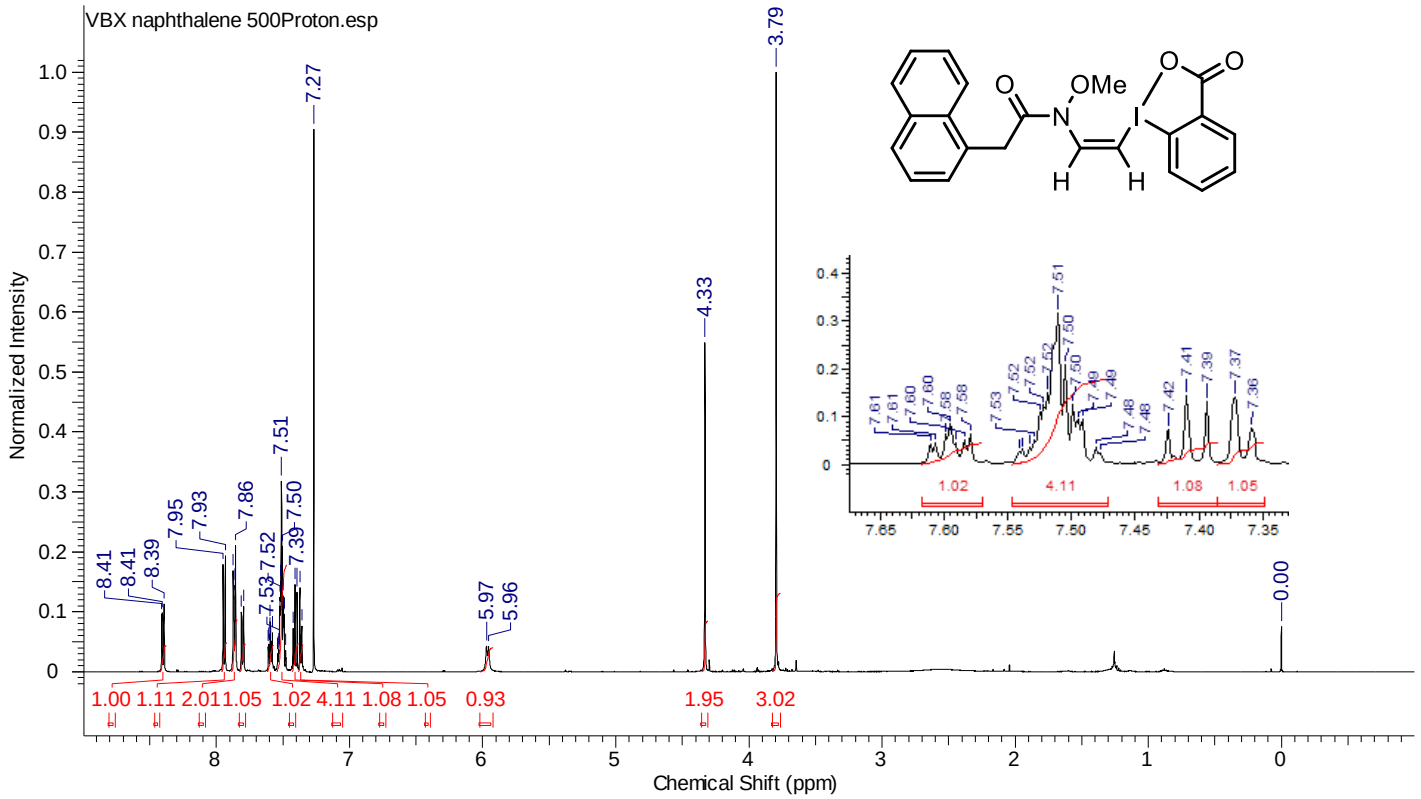


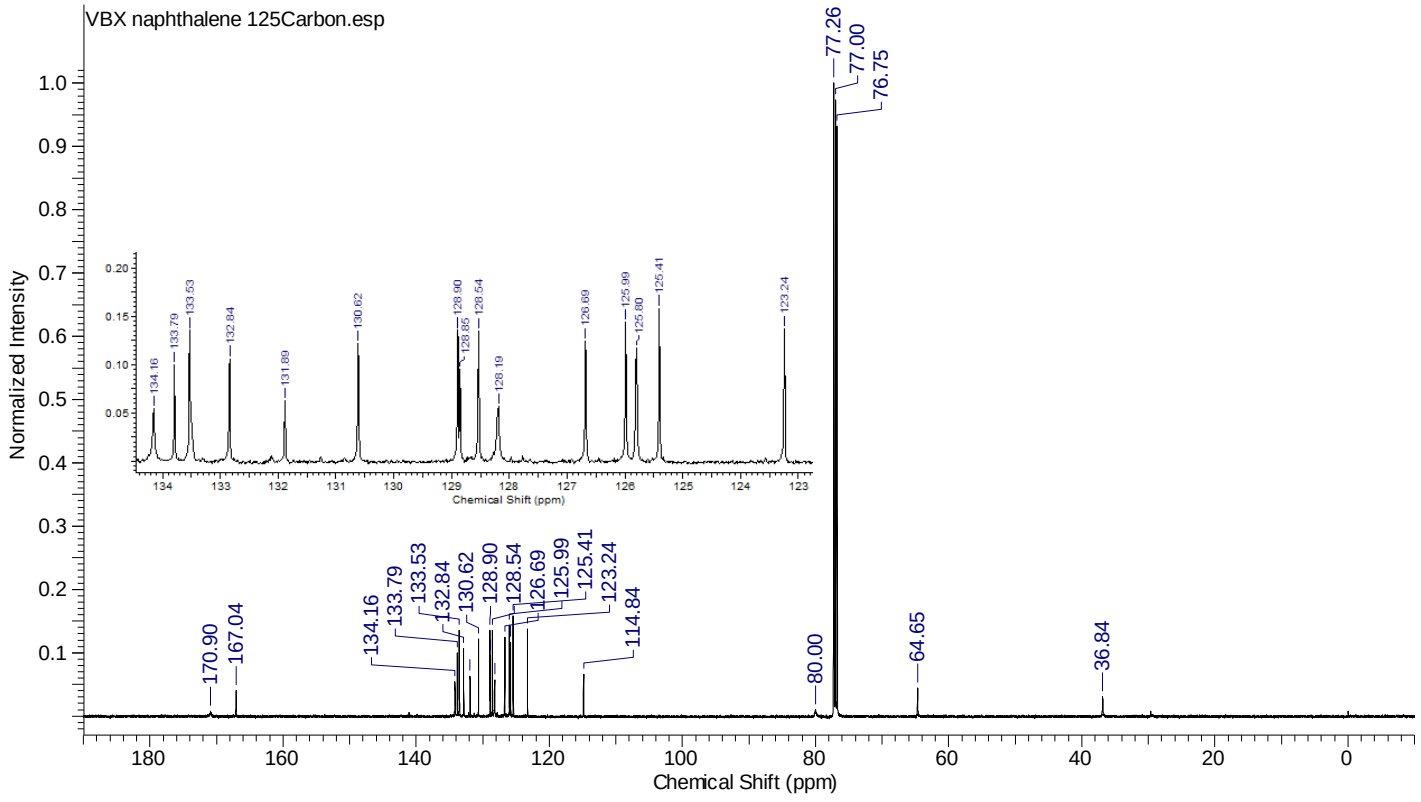
(*Z*)-*N*-(1-Vin-2-yl)-2-(2-iodophenyl)-*N*-methoxyacetamide-1,2-benziodoxol-3-(1*H*)-one (3r)



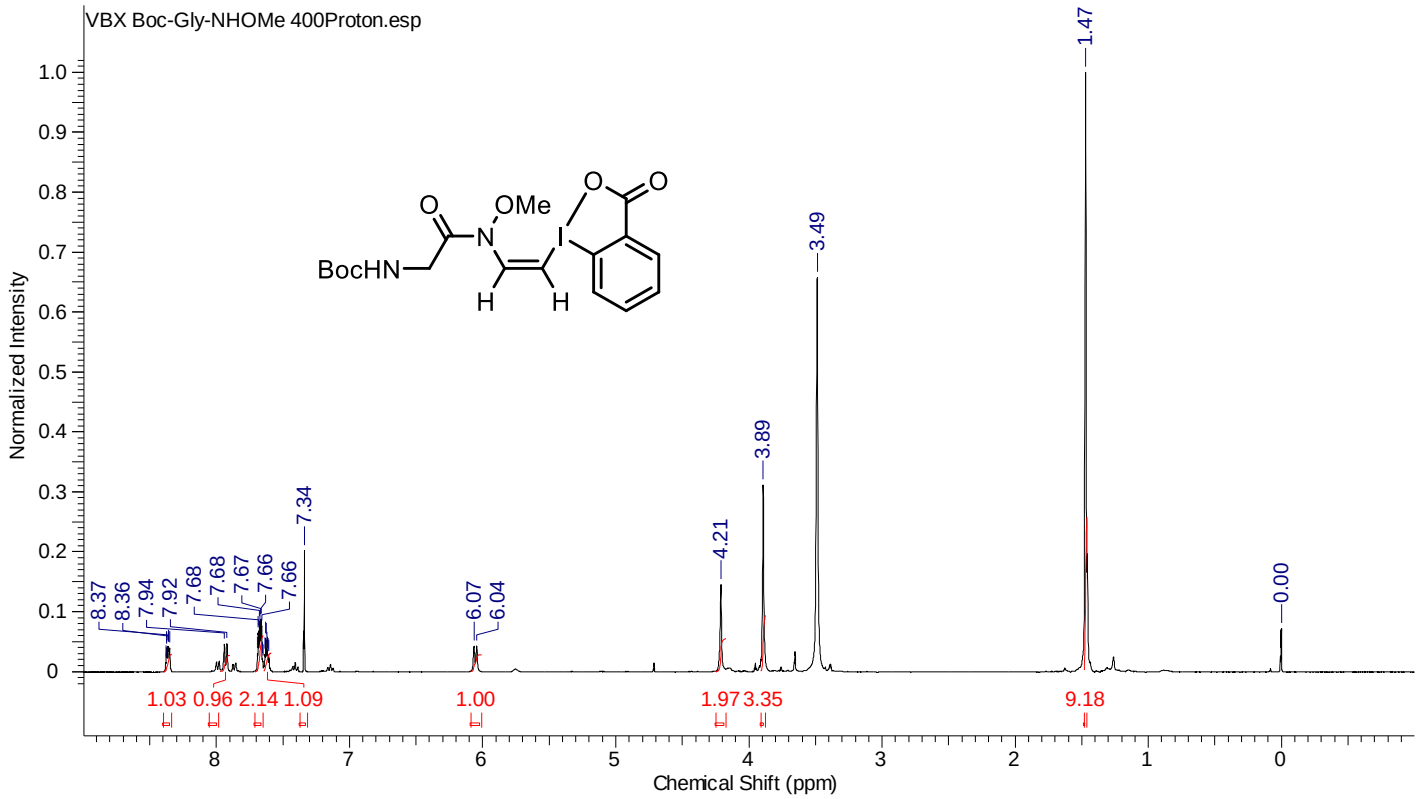


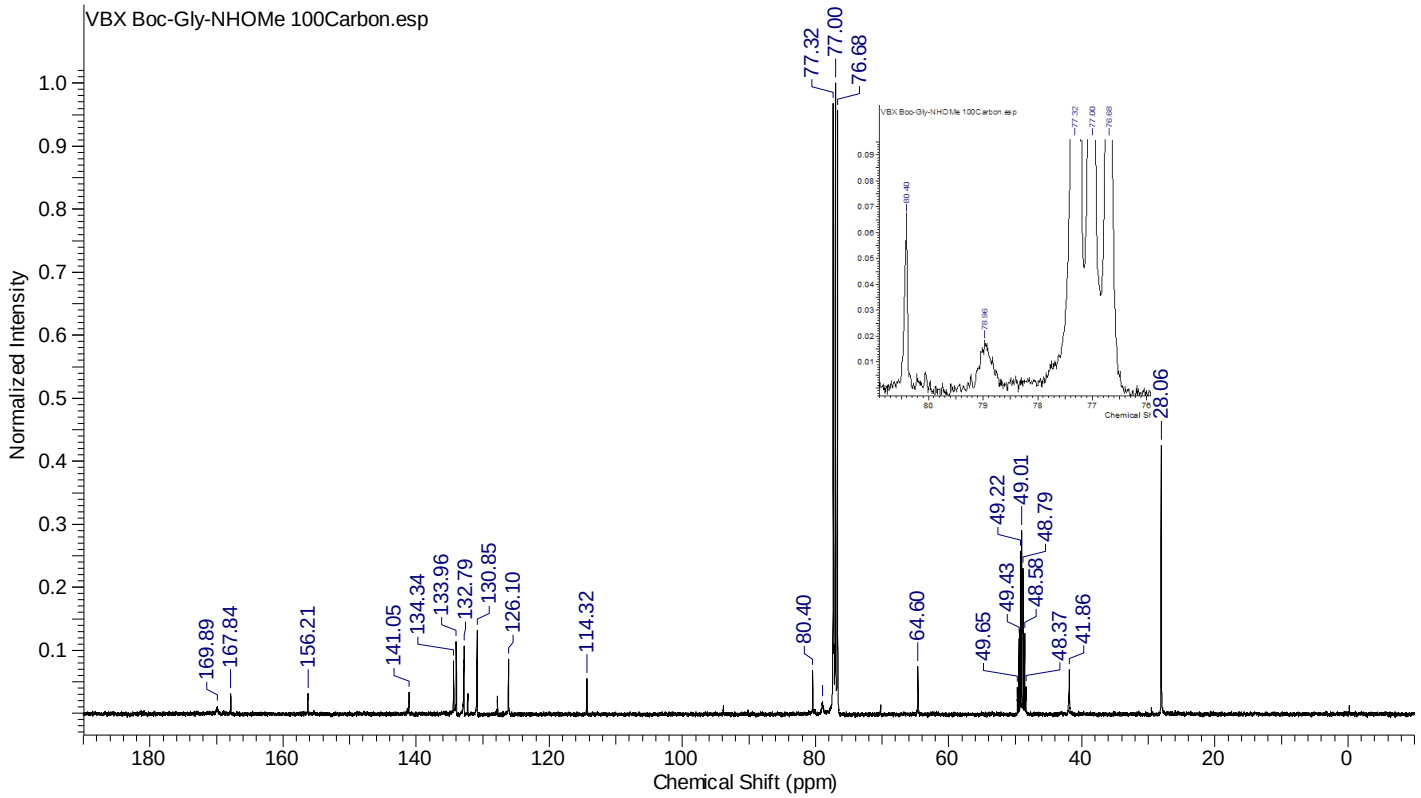
(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxy-1-naphthaleneacetamide-1,2-benziodoxol-3-(1*H*)-one (3s)



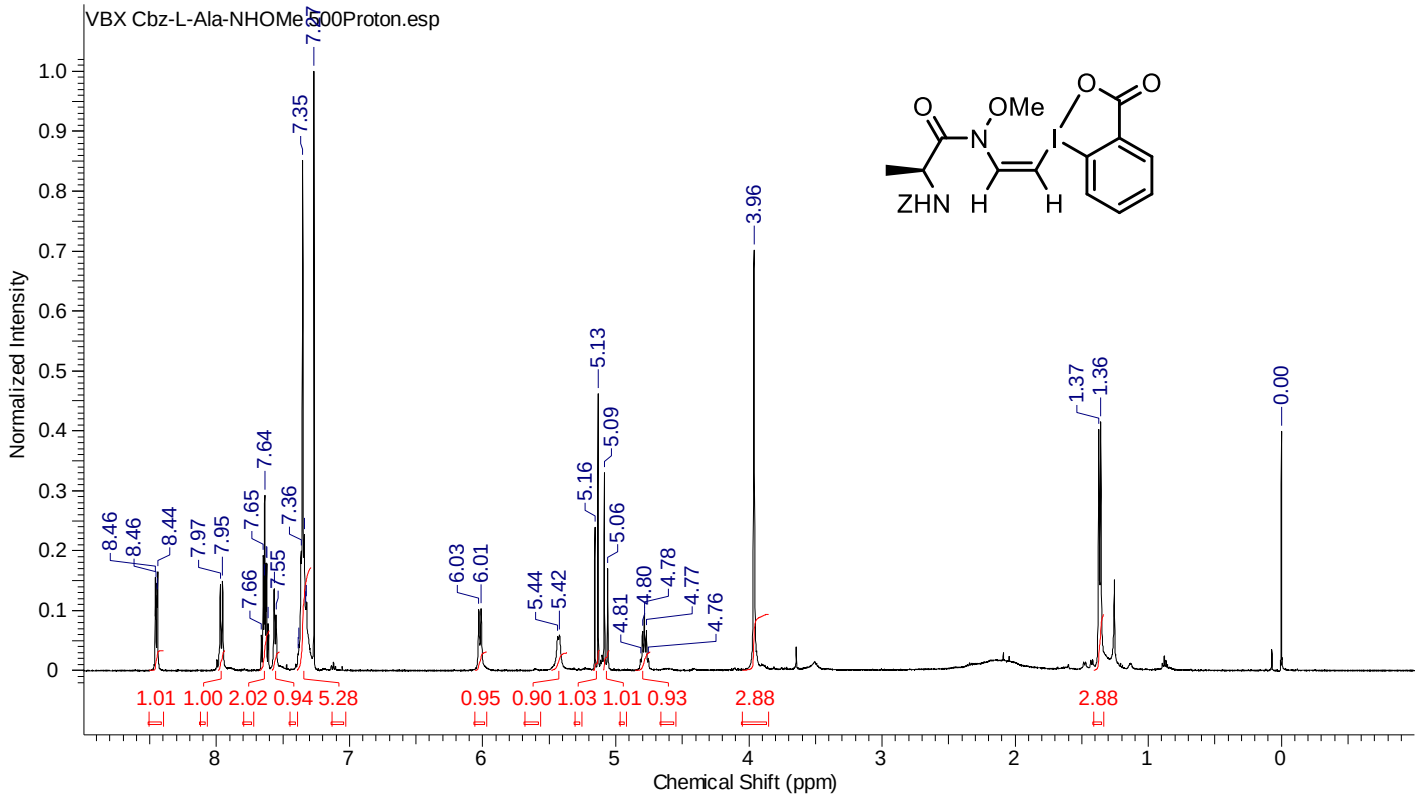


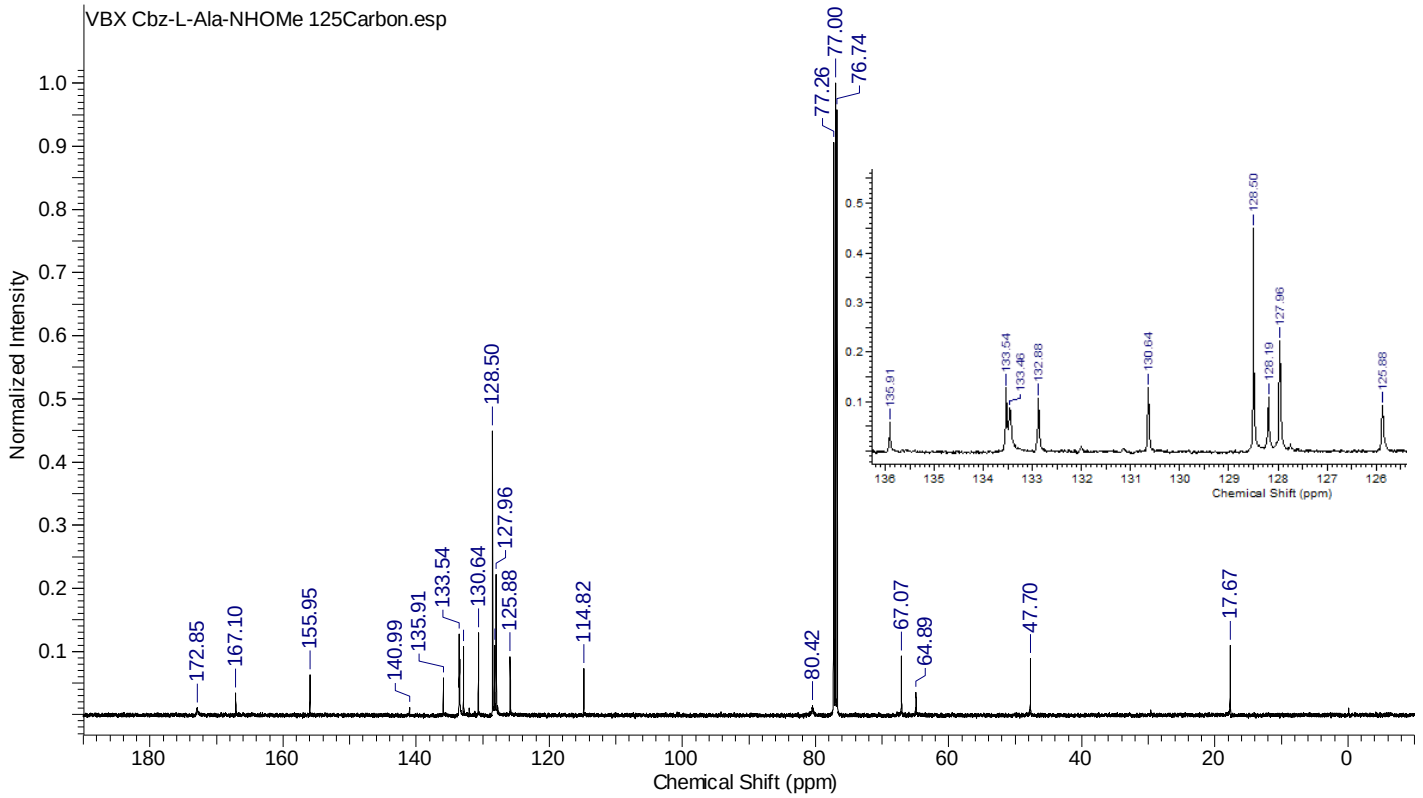
(*Z*)-*N*-(1-Vin-2-yl)-Boc-glycine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3t)



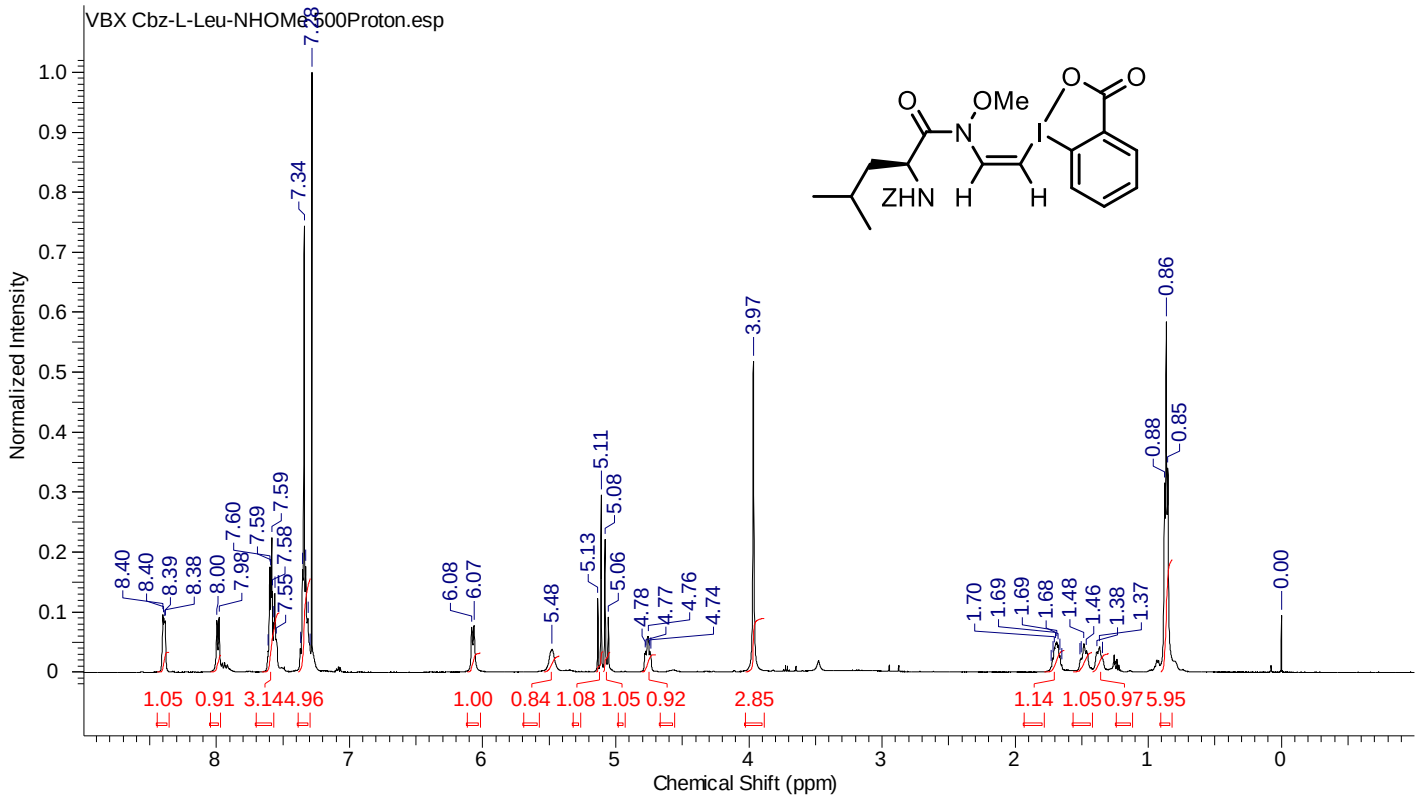


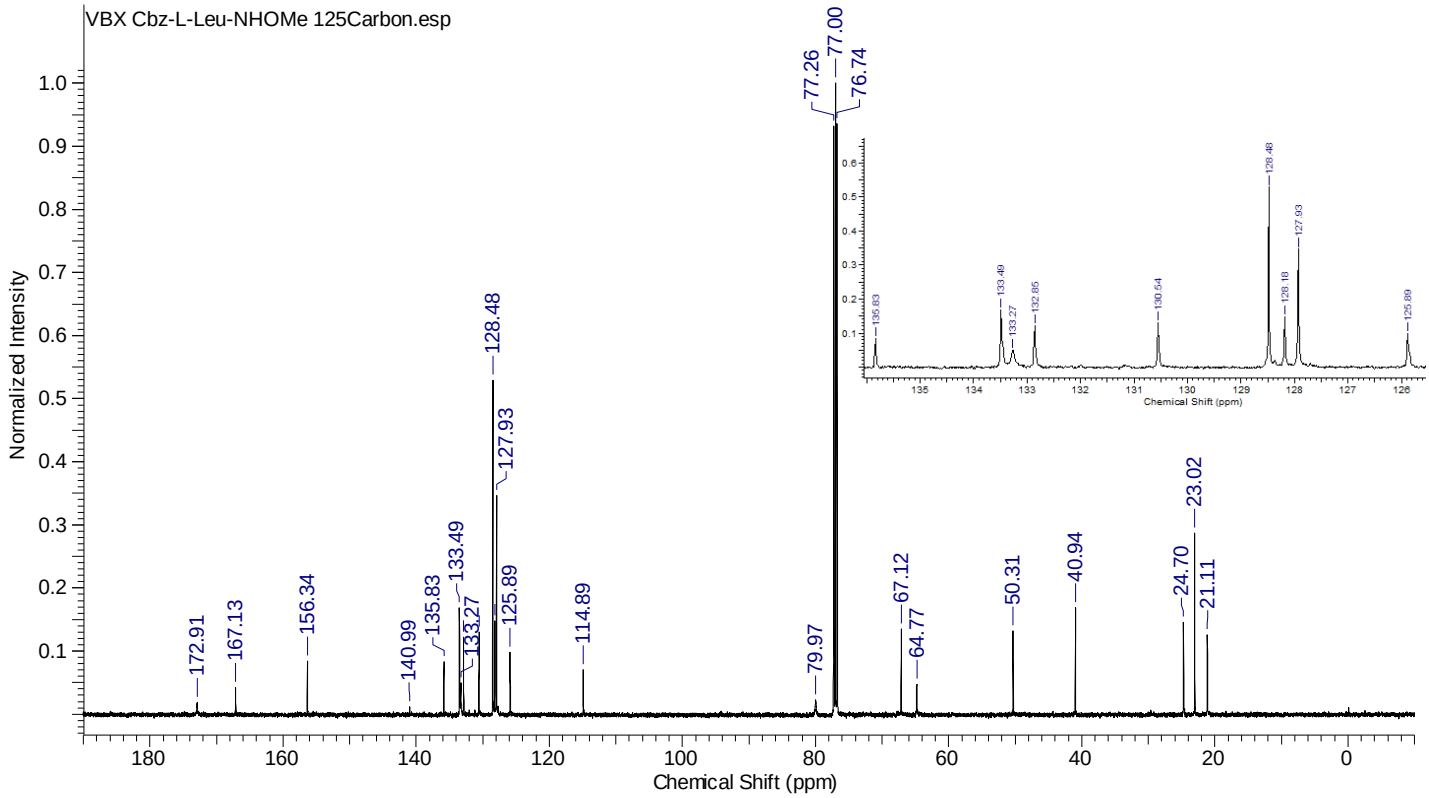
(*Z*)-*N*-(1-Vin-2-yl)-Cbz-L-alanine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3x)



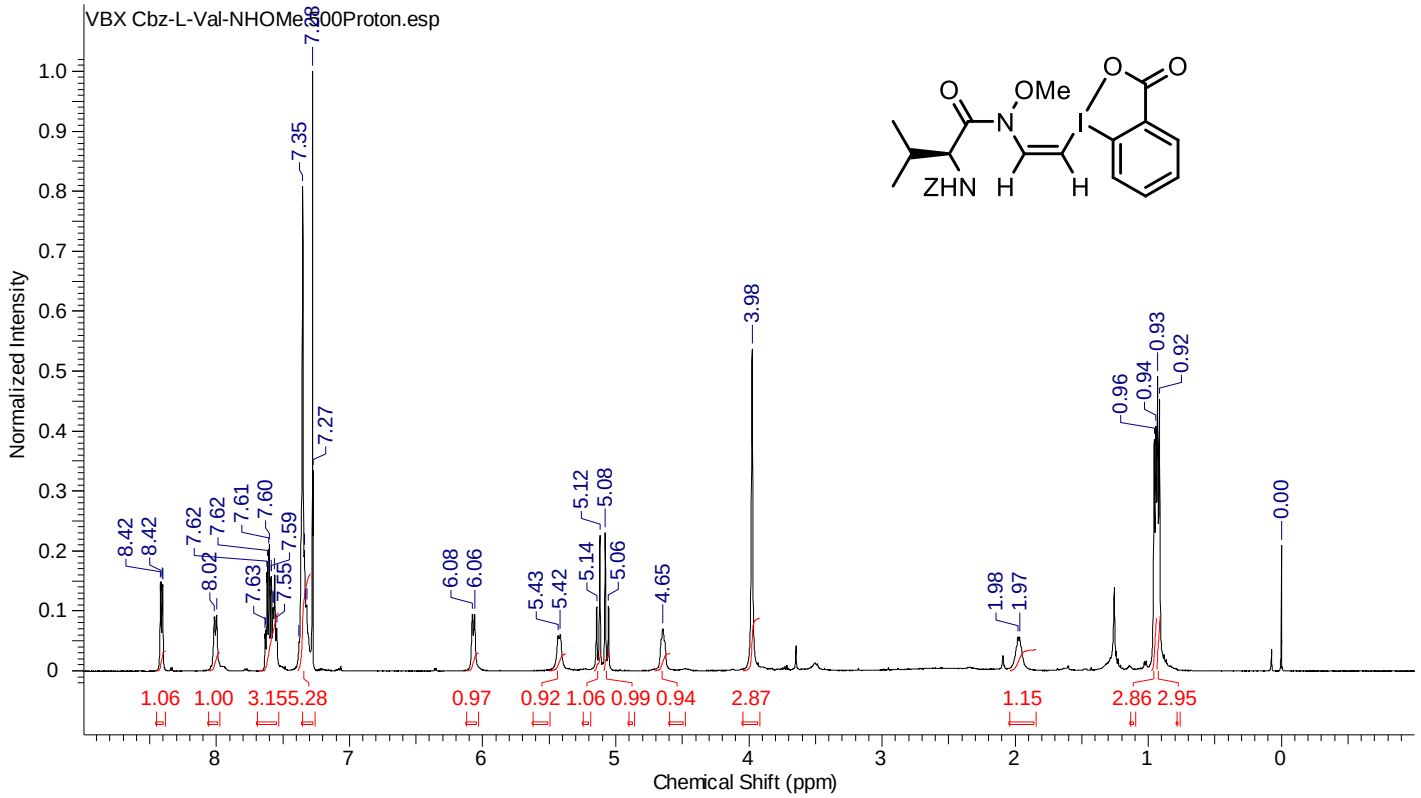


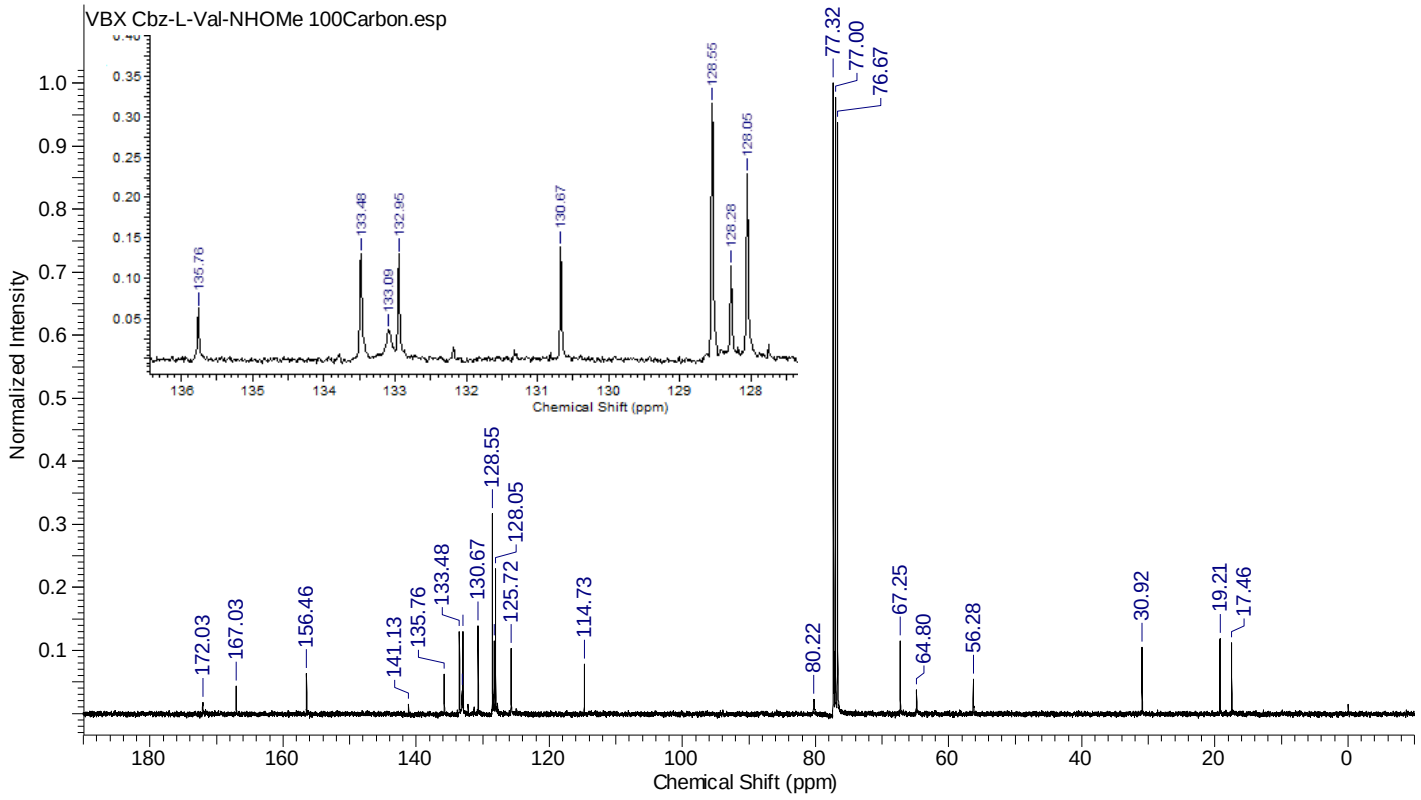
(*Z*)-*N*-(1-Vin-2-yl)-Cbz-L-leucine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3y)



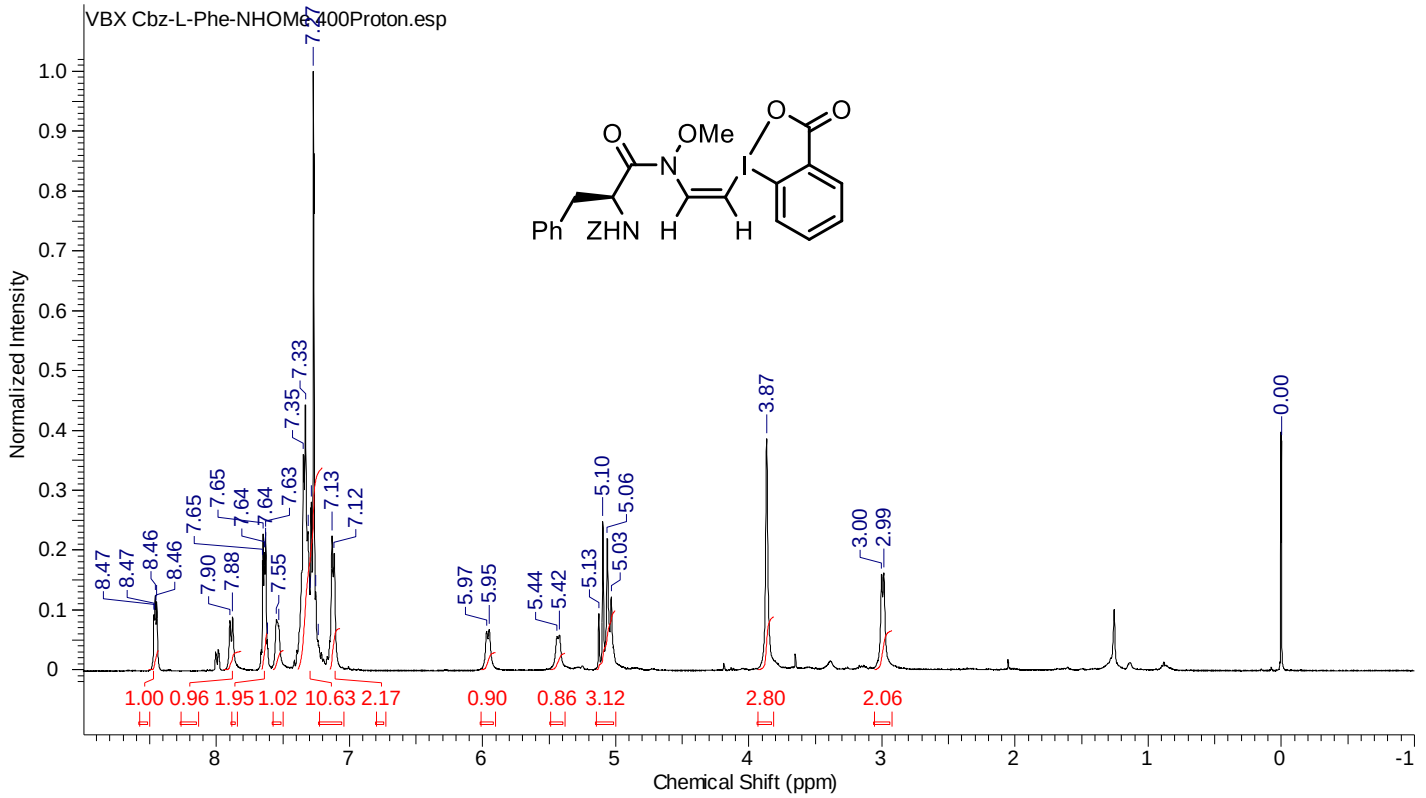


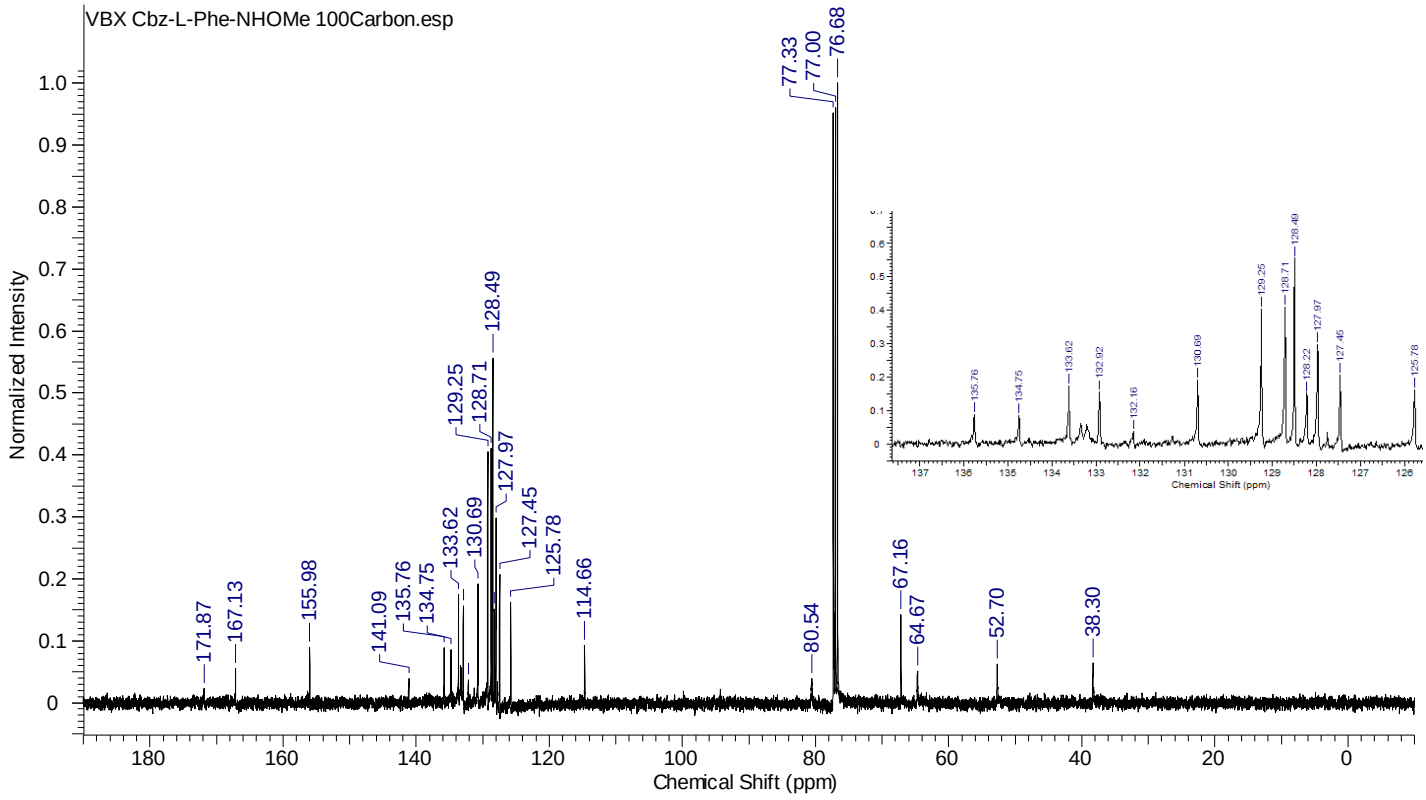
(*Z*)-*N*-(1-Vin-2-yl)-Cbz-L-valine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3z)



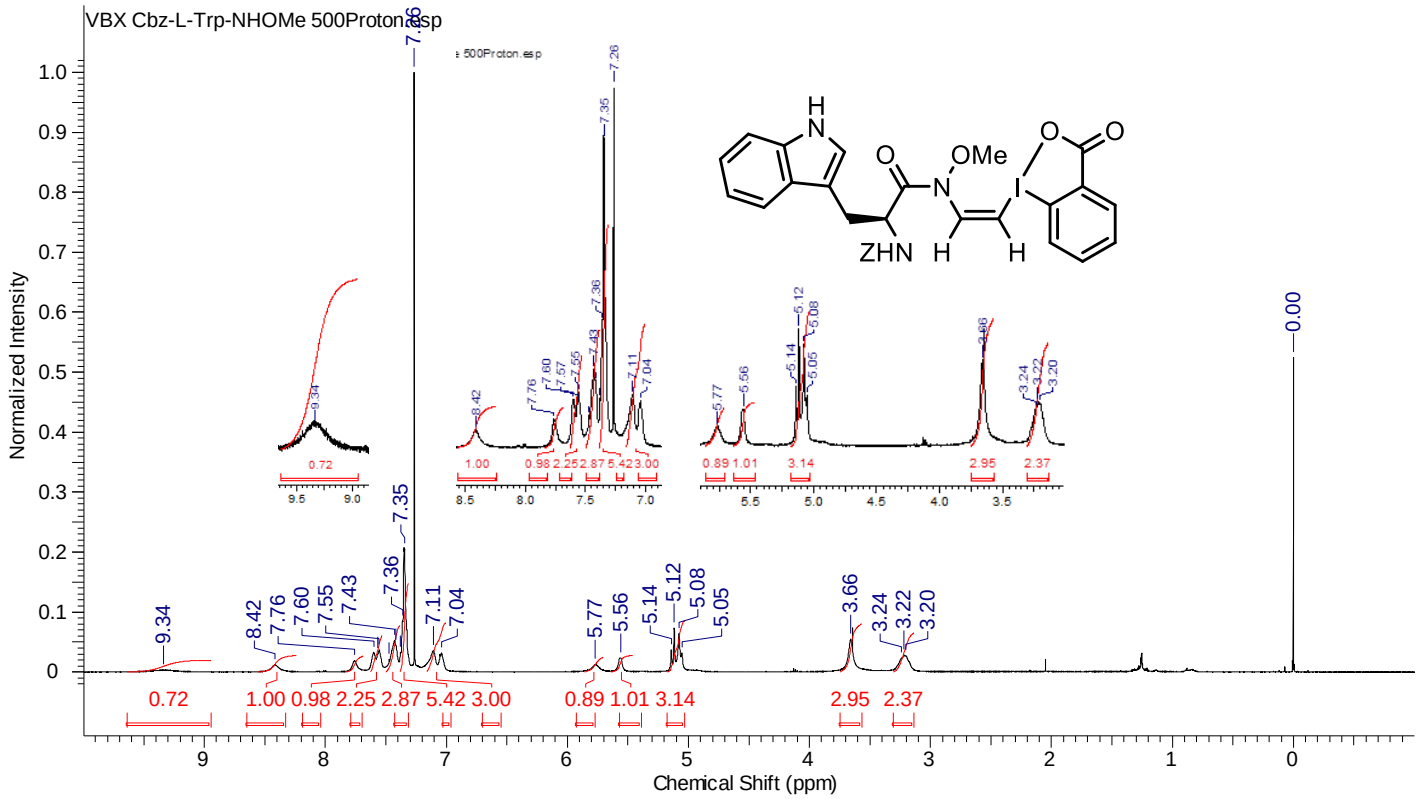


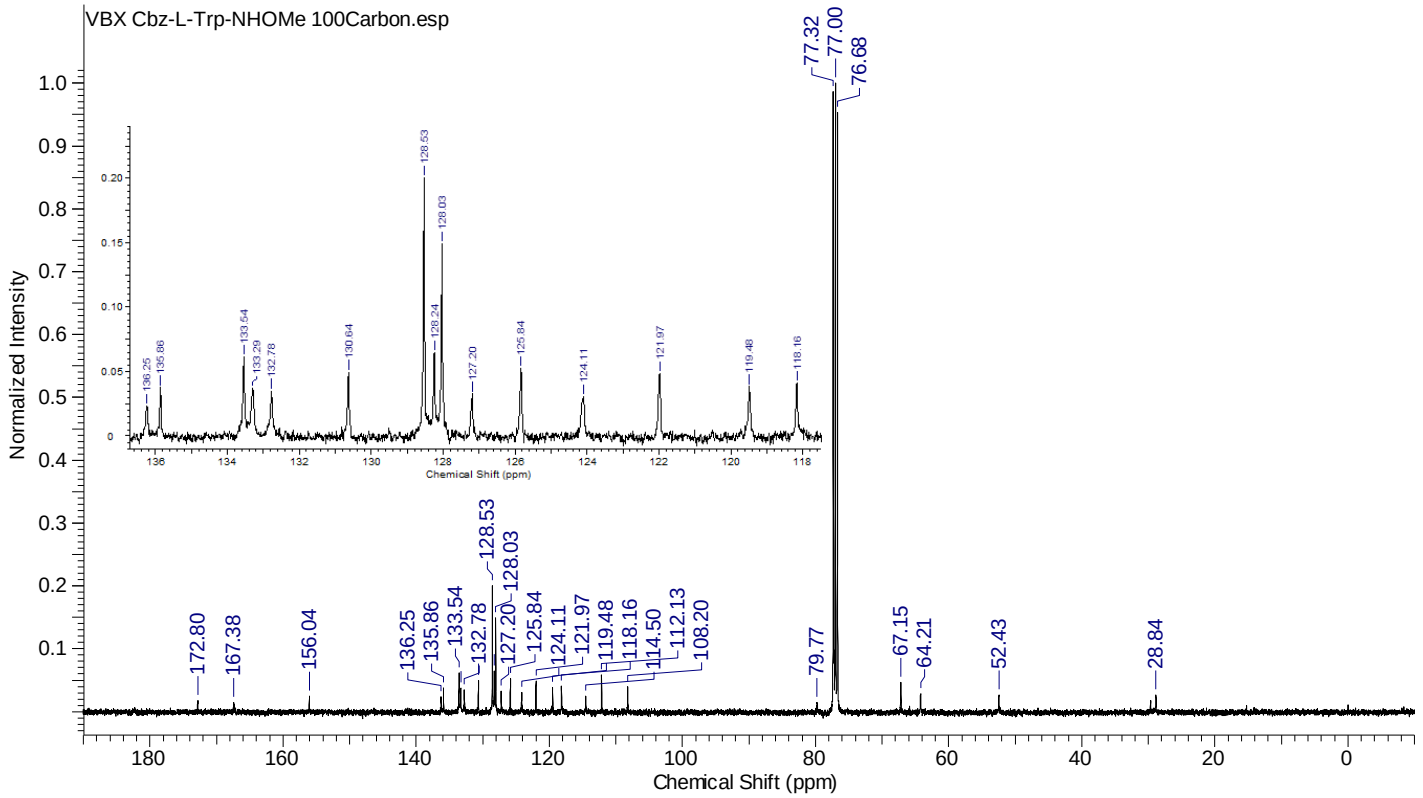
(*Z*)-*N*-(1-Vin-2-yl)-Cbz-L-phenylalanine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3aa)



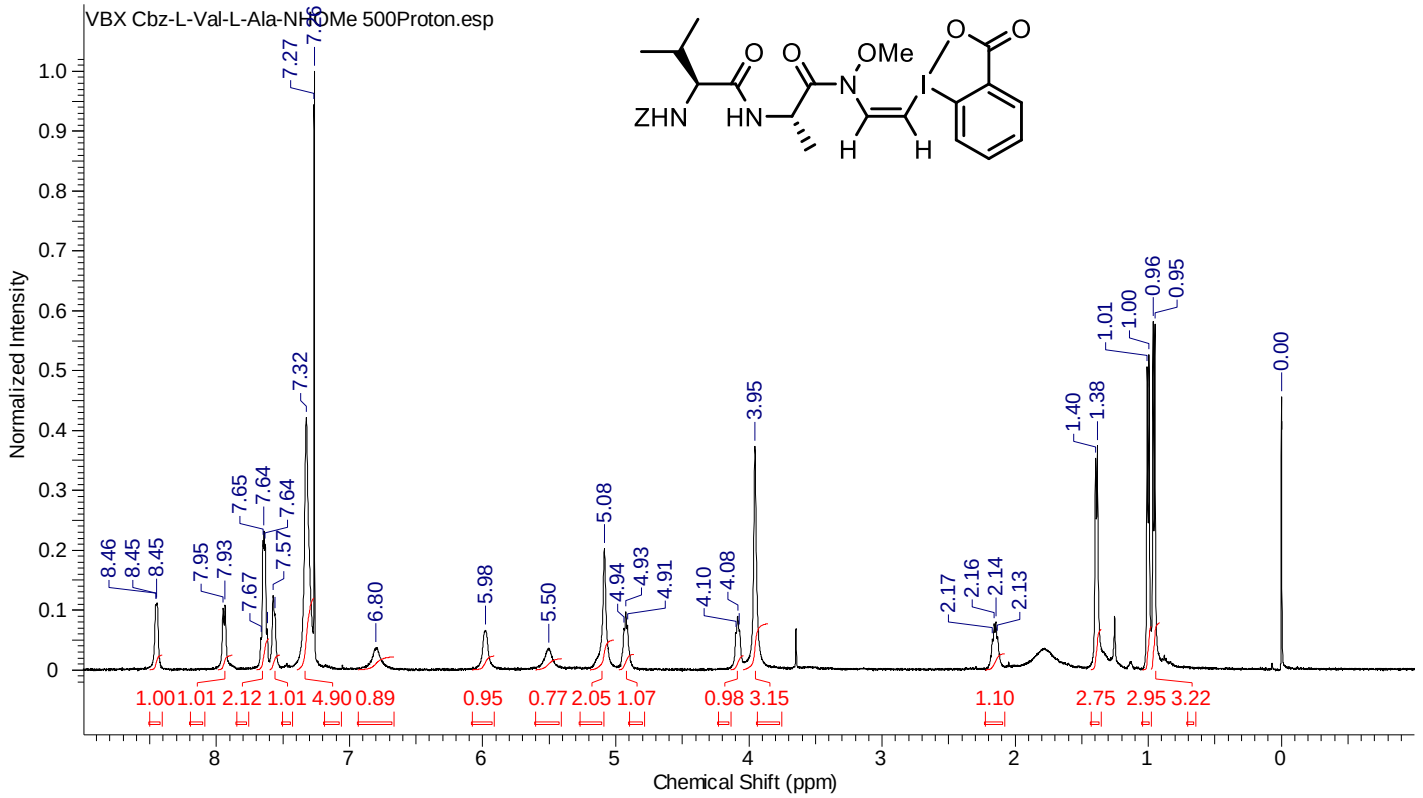


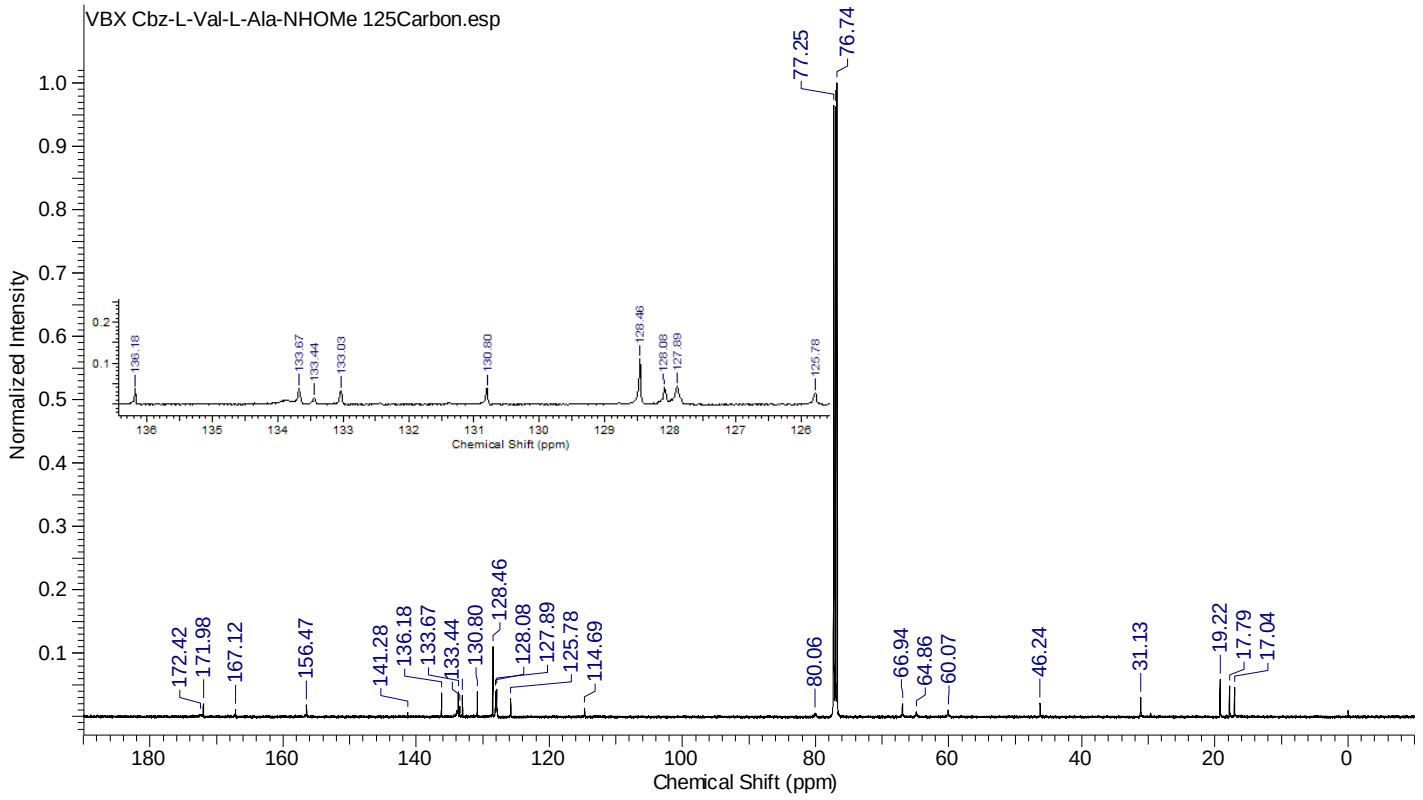
(*Z*)-*N*-(1-Vin-2-yl)-Cbz-L-tryptophan-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3ab)



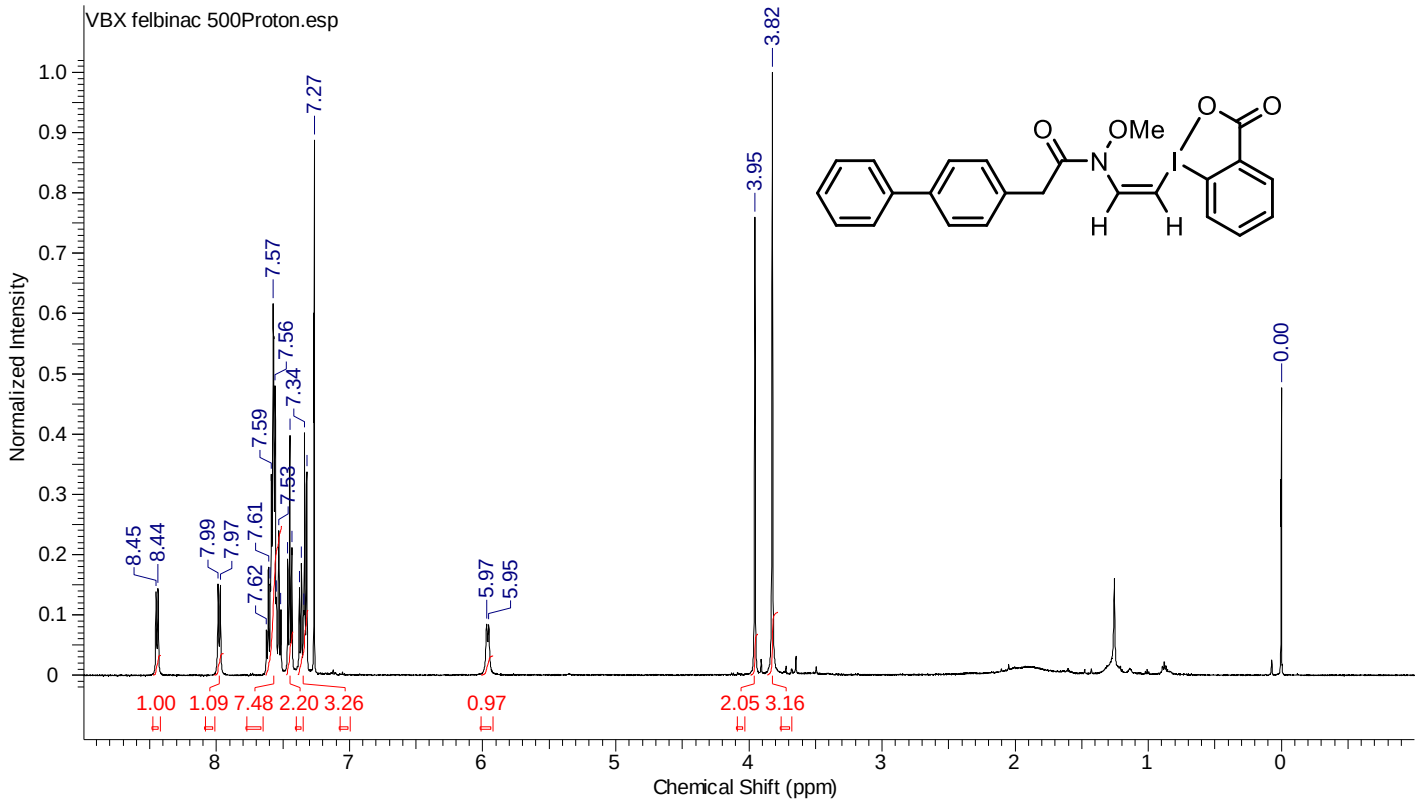


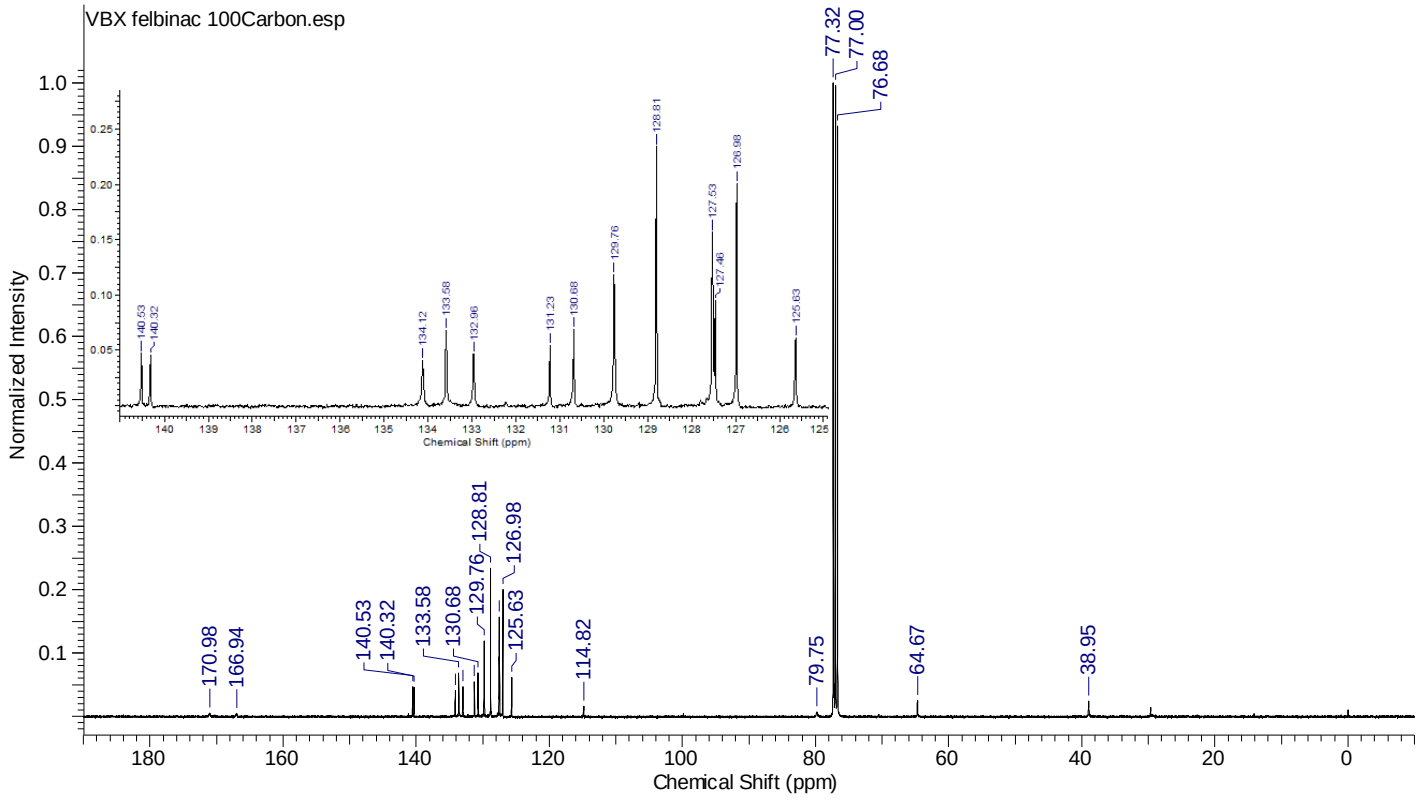
(*Z*)-*N*-(1-Vin-2-yl)-Cbz-L-valyl-L-alanine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3ac)



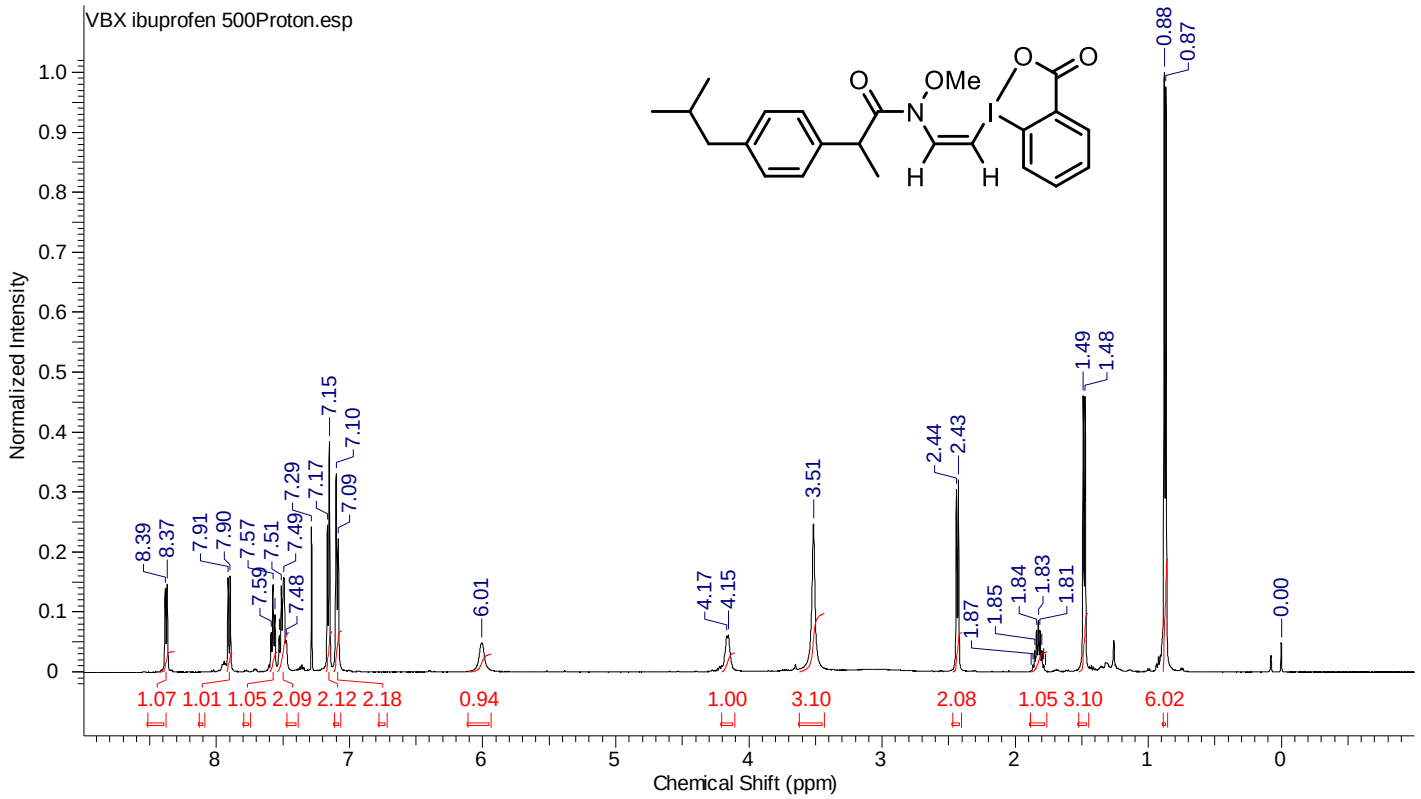


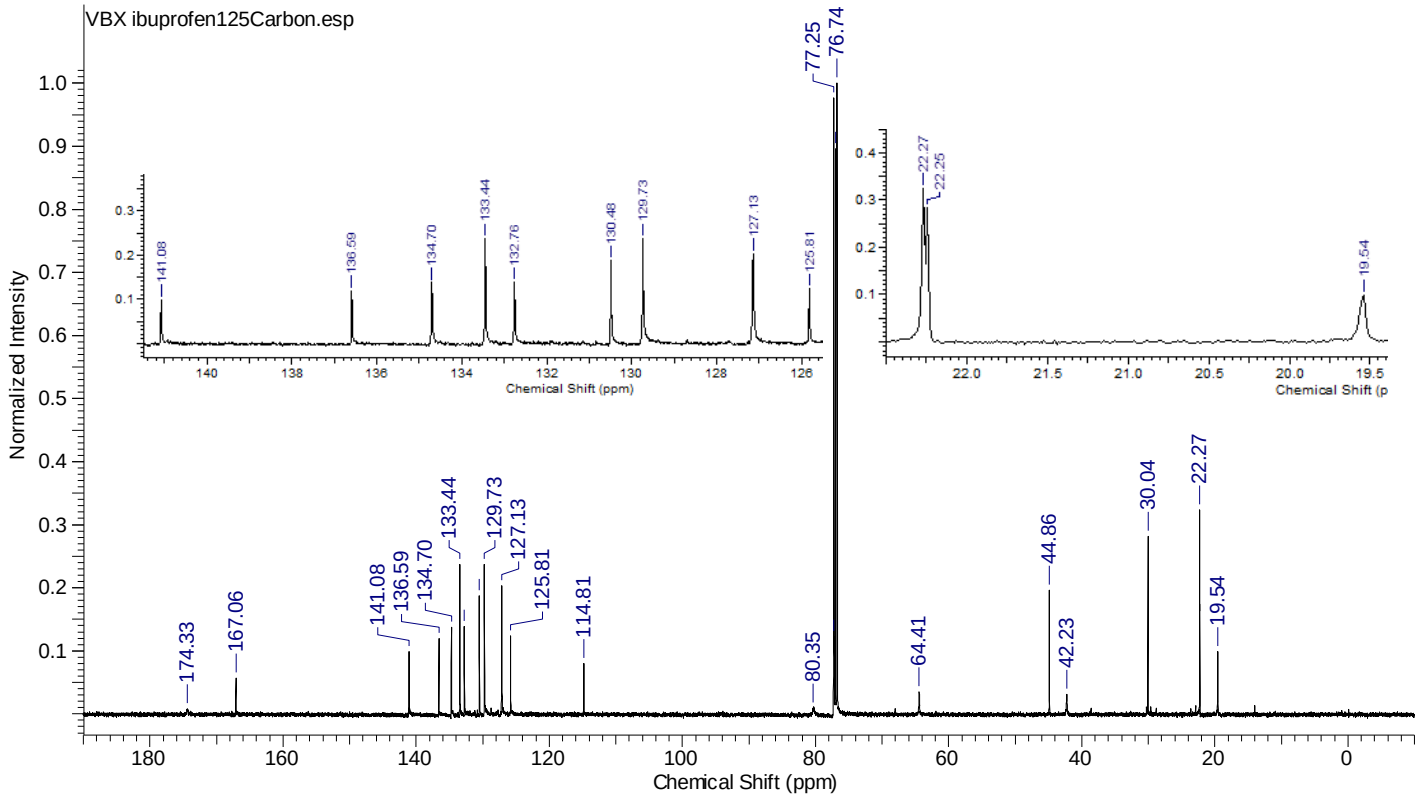
(Z)-*N*-(1-Vin-2-yl)-2-[(1,1'-biphenyl)-4-yl]-*N*-methoxyacetamide-1,2-benziodoxol-3-(1*H*)-one (3ad)



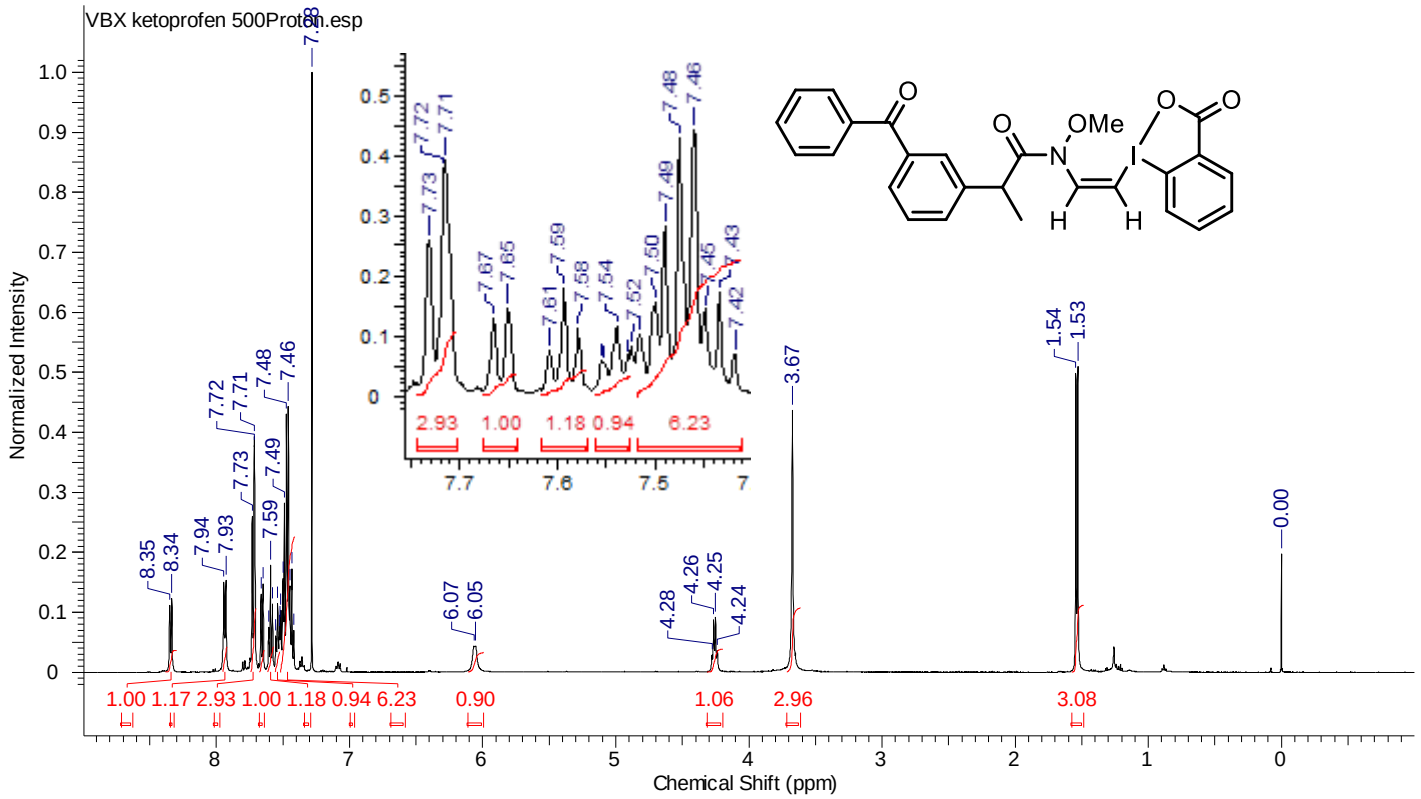


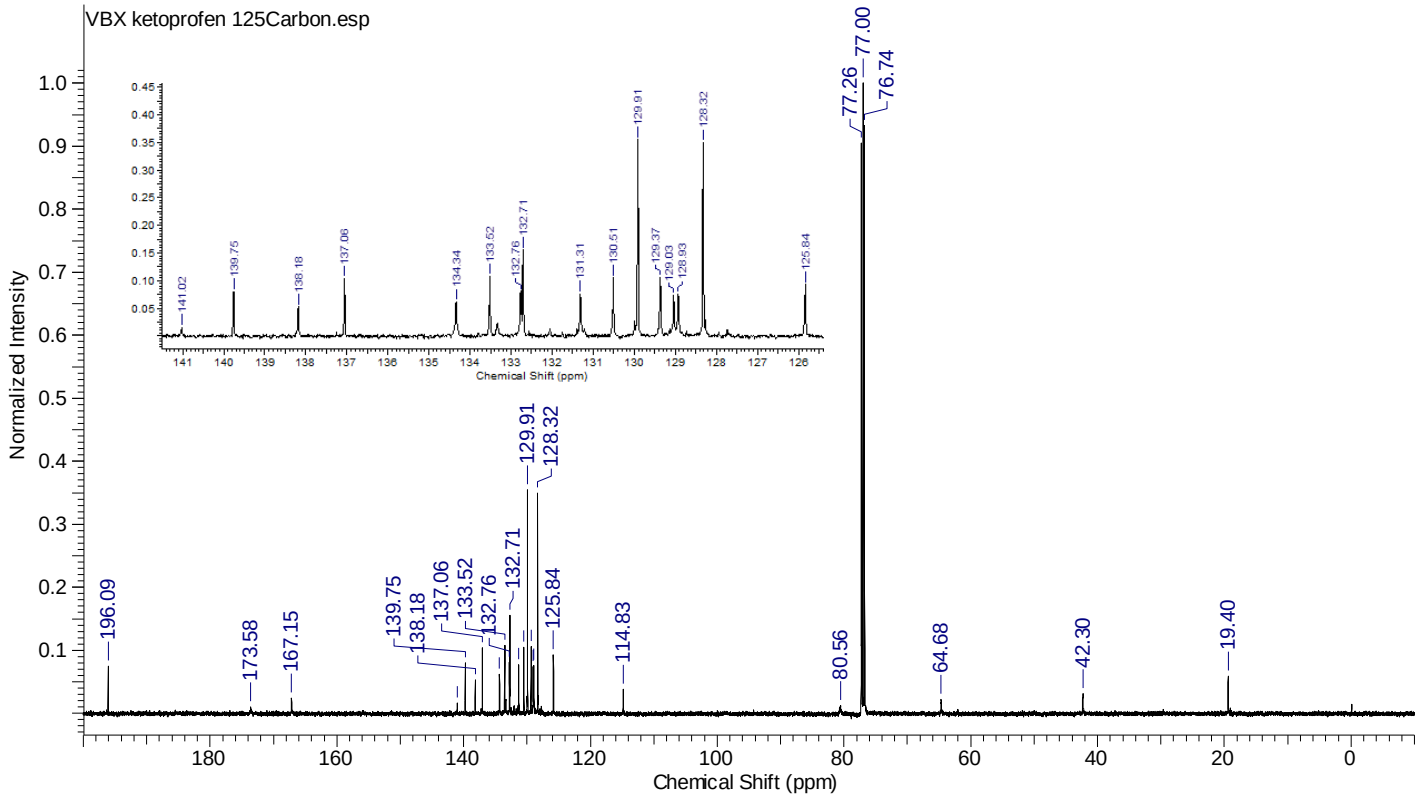
(*Z*)-*N*-(1-Vin-2-yl)-*N*-methoxy-2-[4-(2-methylpropyl)phenyl]propanamide-1,2-benziodoxol-3-(1*H*)-one (3ae)



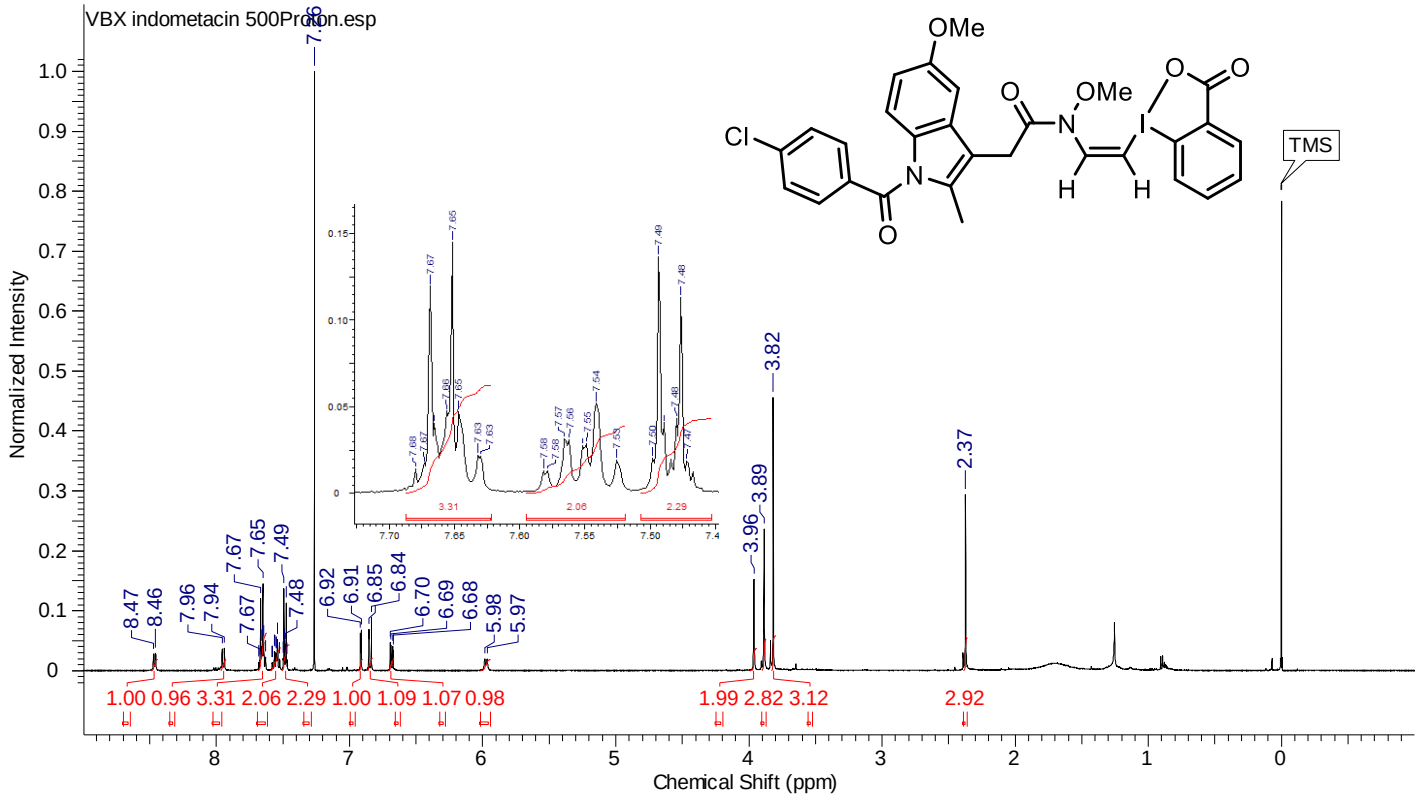


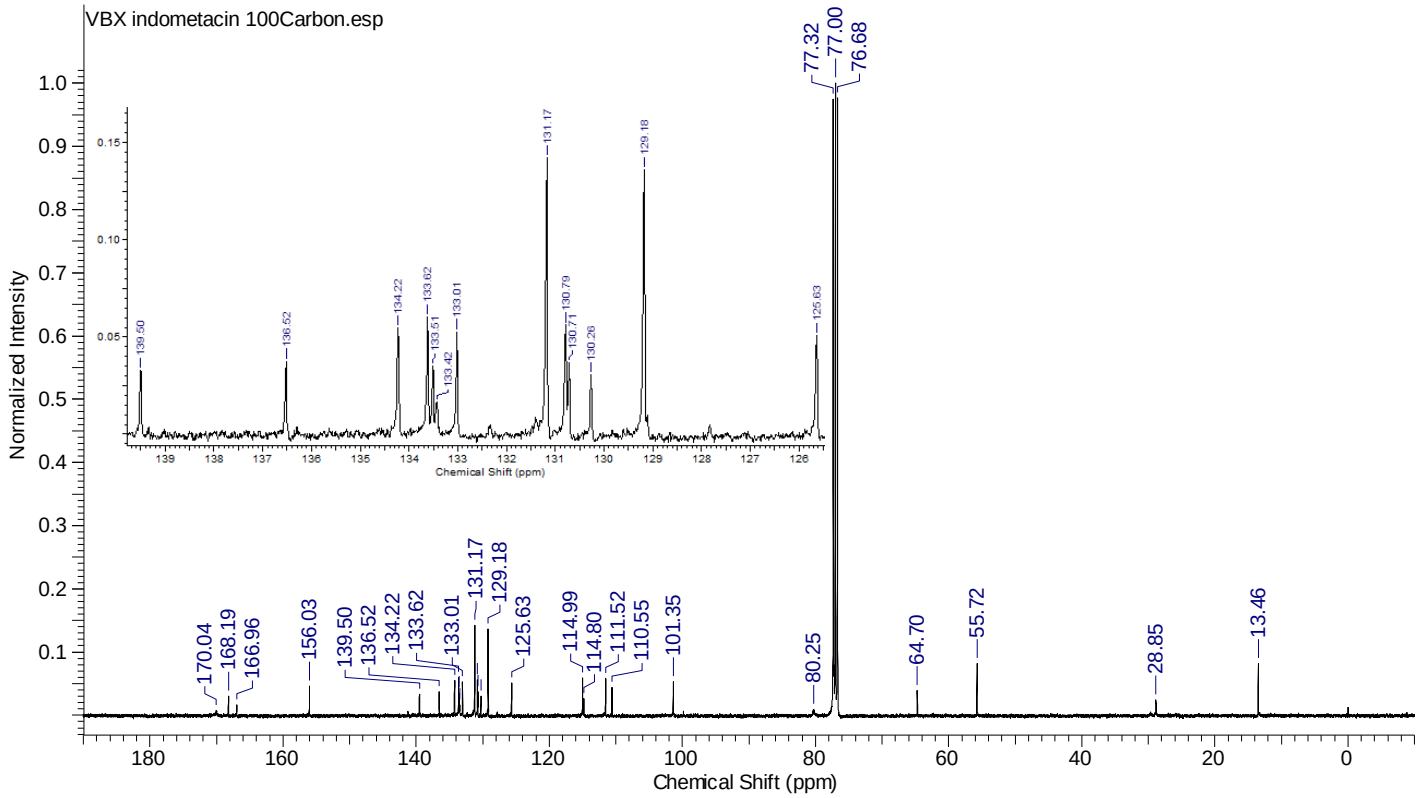
(*Z*)-*N*-(1-Vin-2-yl)-2-(3-benzoylphenyl)-*N*-methoxypropanamide-1,2-benziodoxol-3-(1*H*)-one (3af)



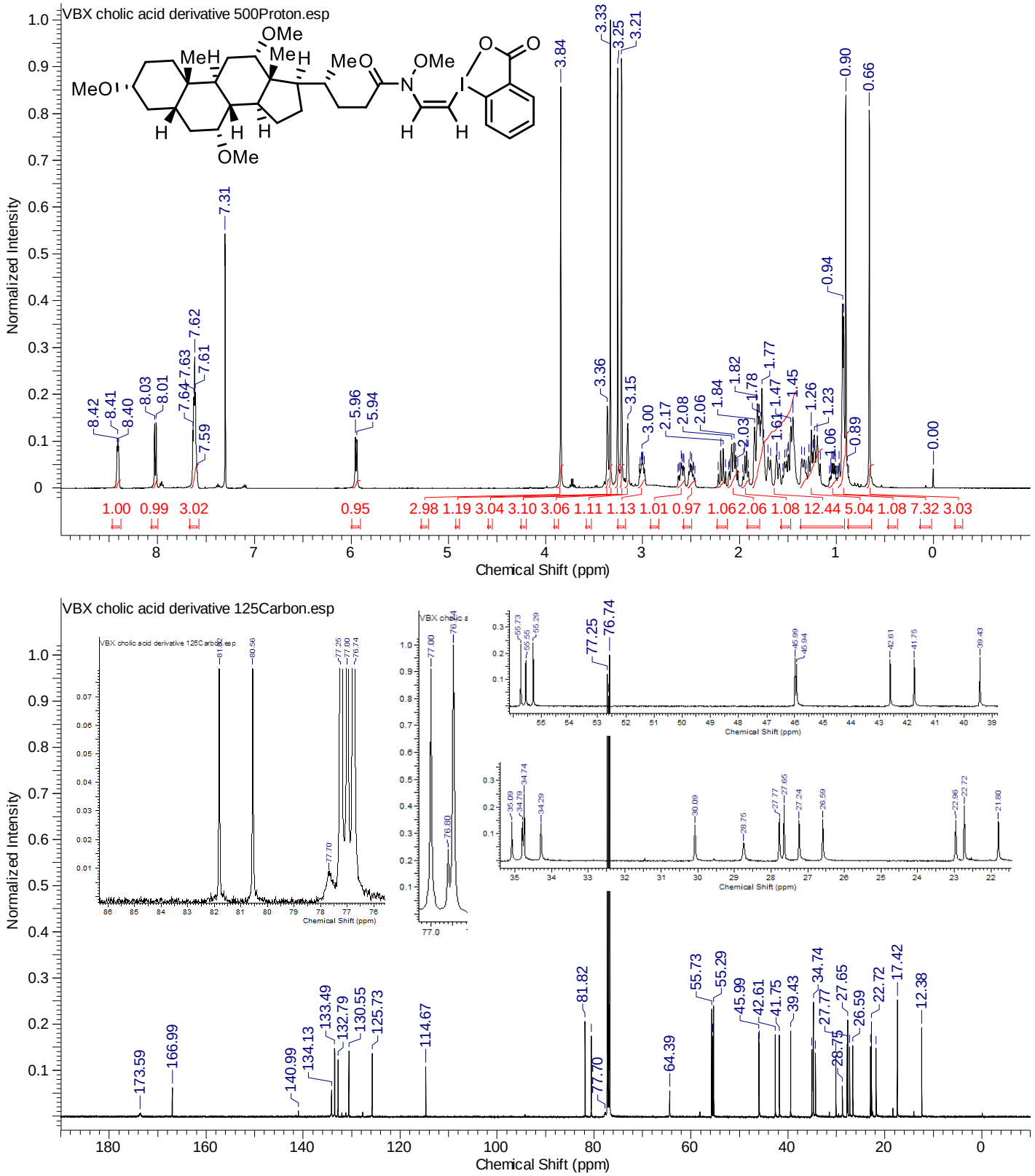


(*Z*)-*N*-(1-Vin-2-yl)-1-(4-chlorobenzoyl)-*N*,5-dimethoxy-2-methyl-1*H*-indole-3-acetamide-1,2-benziodoxol-3-(1*H*)-one (3ag)

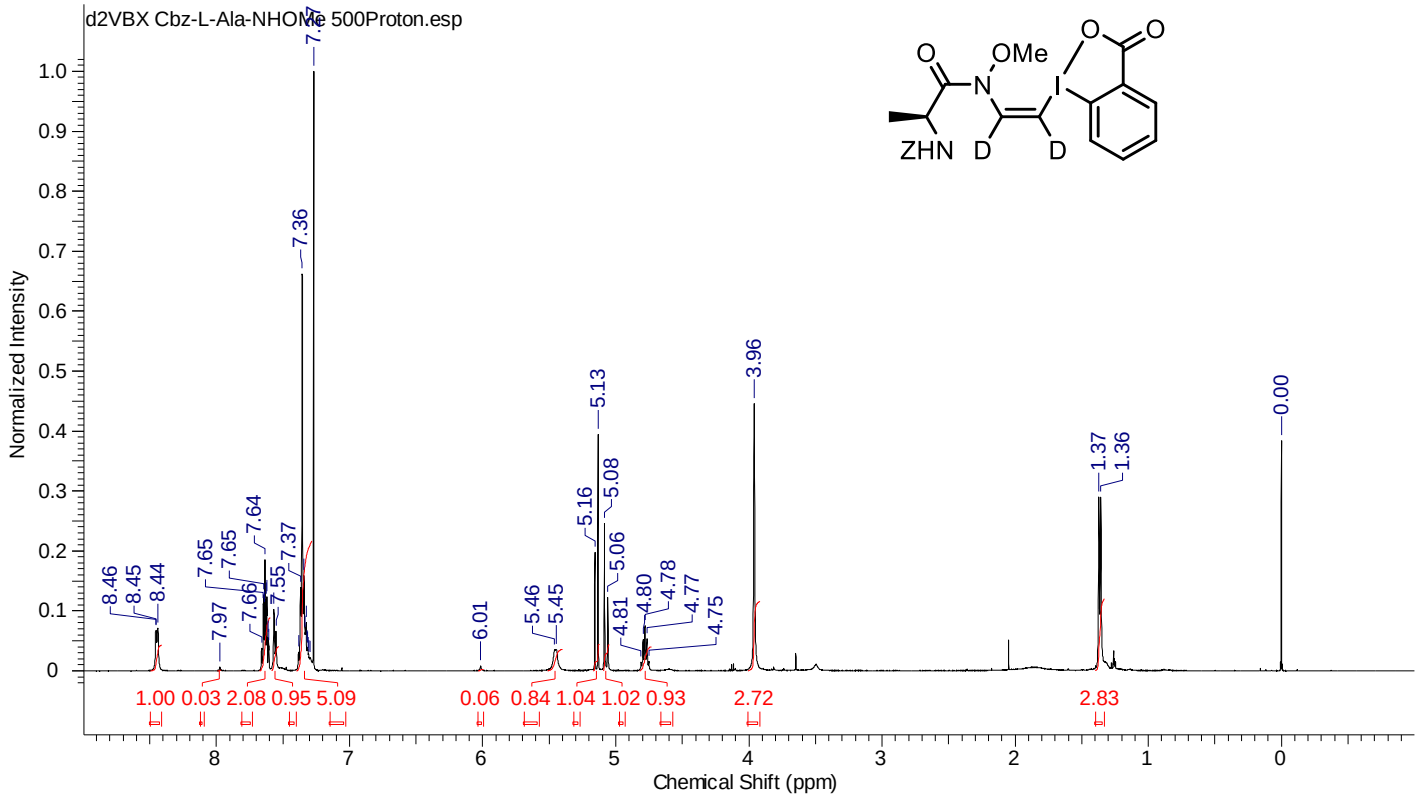




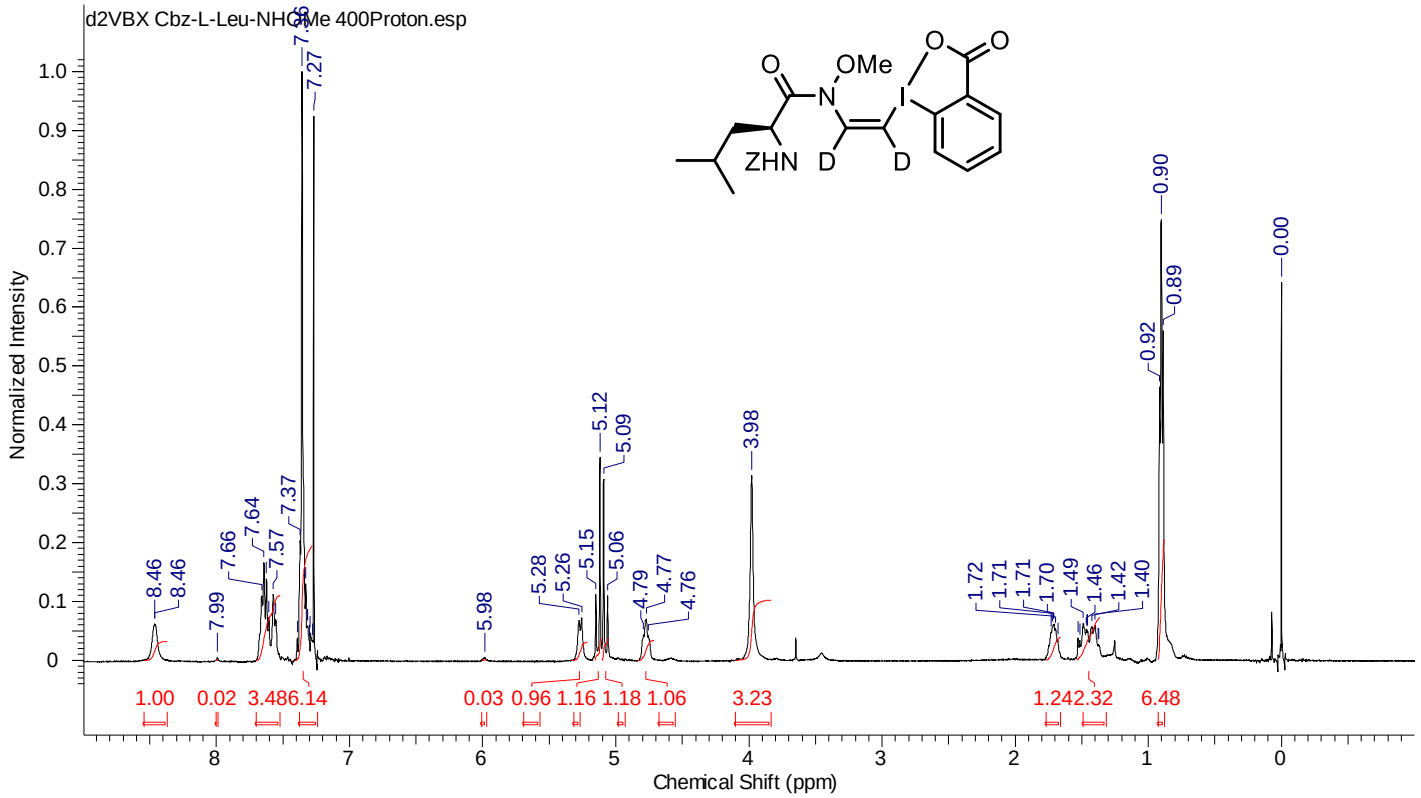
(*Z*)-*N*-(1-Vin-2-yl)-(*R*)-*N*-methoxy-4-[(3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,7,12-trimethoxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl]pentanamide-1,2-benziodoxol-3-(1*H*)-one (3ah)



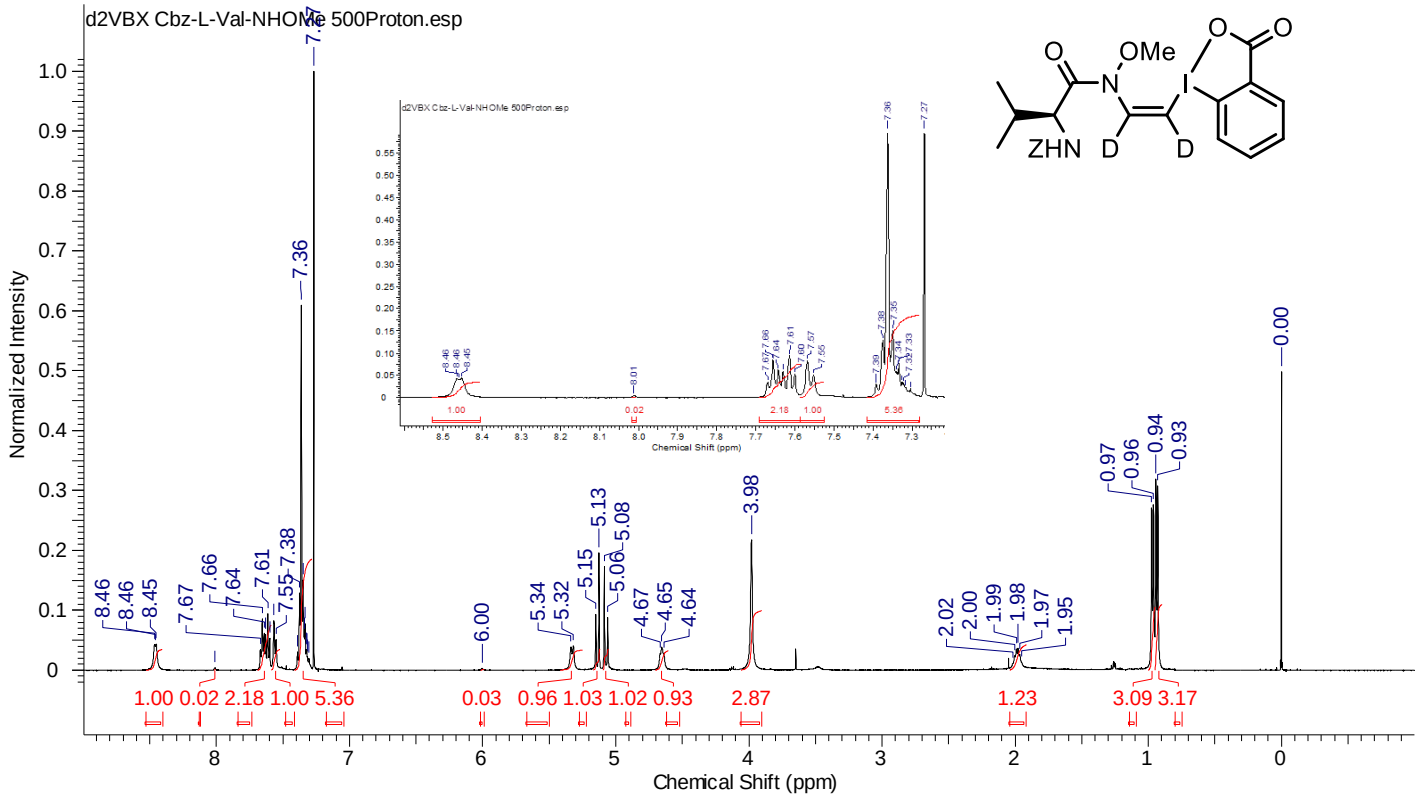
(*Z*)-*N*-(1,2-d_2-1-Vin-2-yl)-Cbz-L-alanine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3x-d_2)



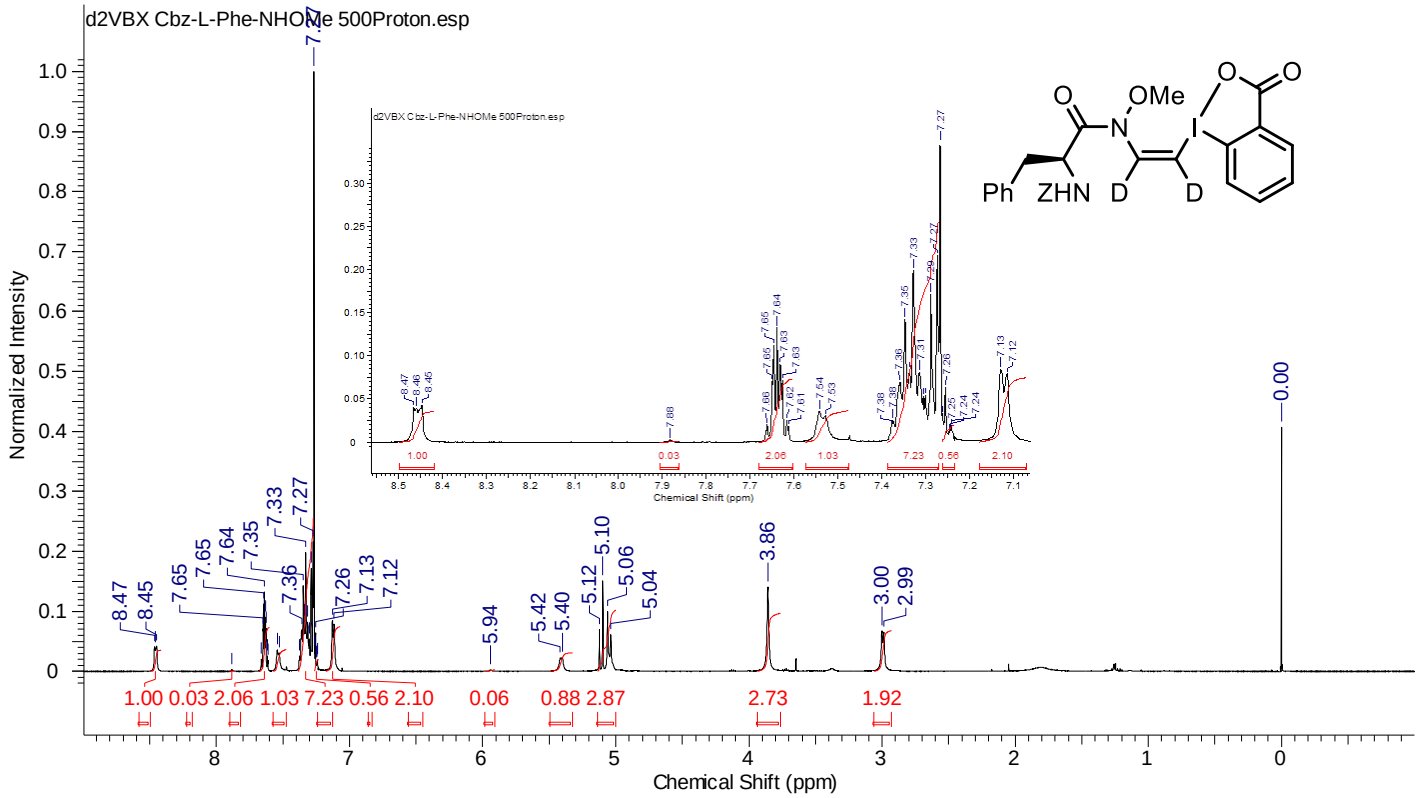
(*Z*)-*N*-(1,2-d_2-1-Vin-2-yl)-Cbz-L-leucine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3y-d_2)



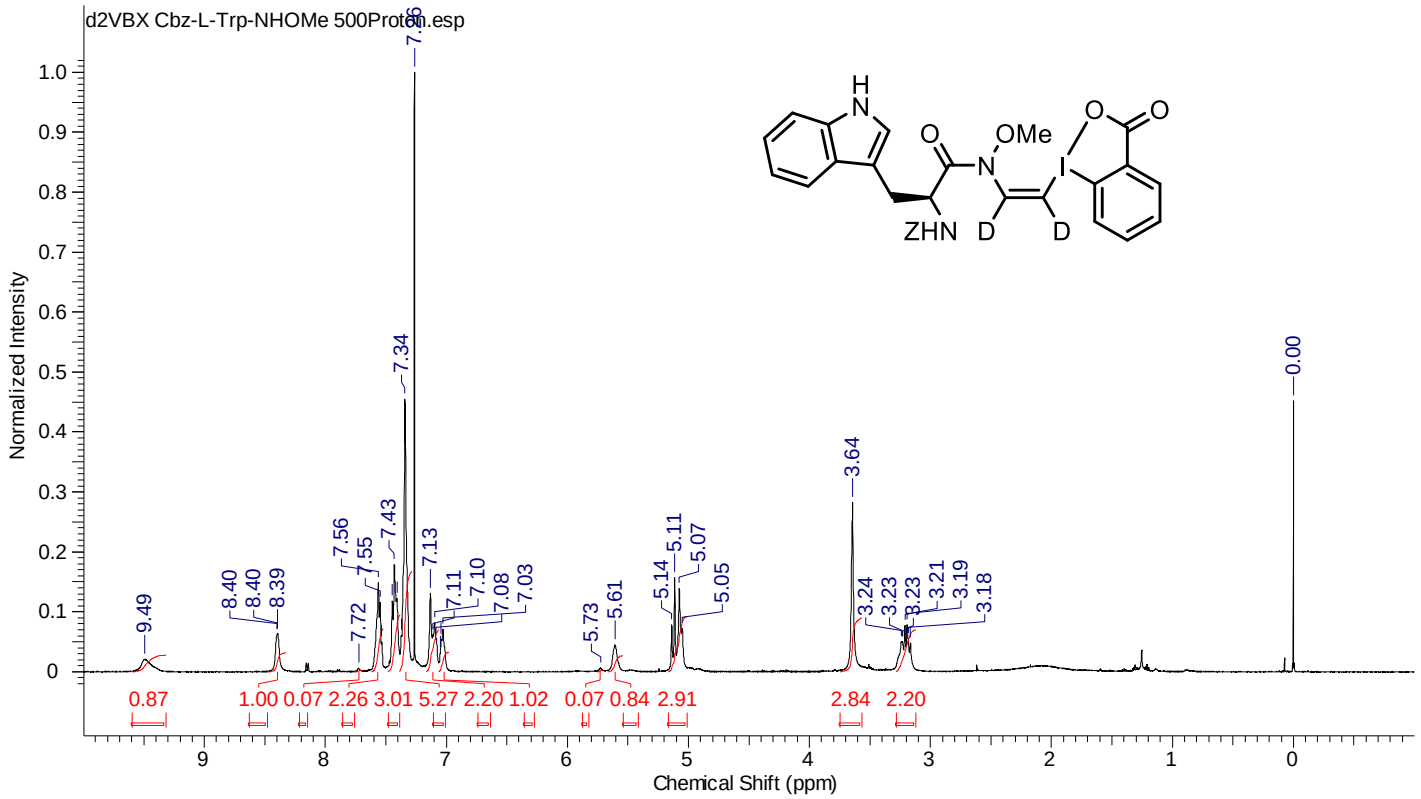
(*Z*)-*N*-(1,2-d_2-1-Vin-2-yl)-Cbz-L-valine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3z-d_2)



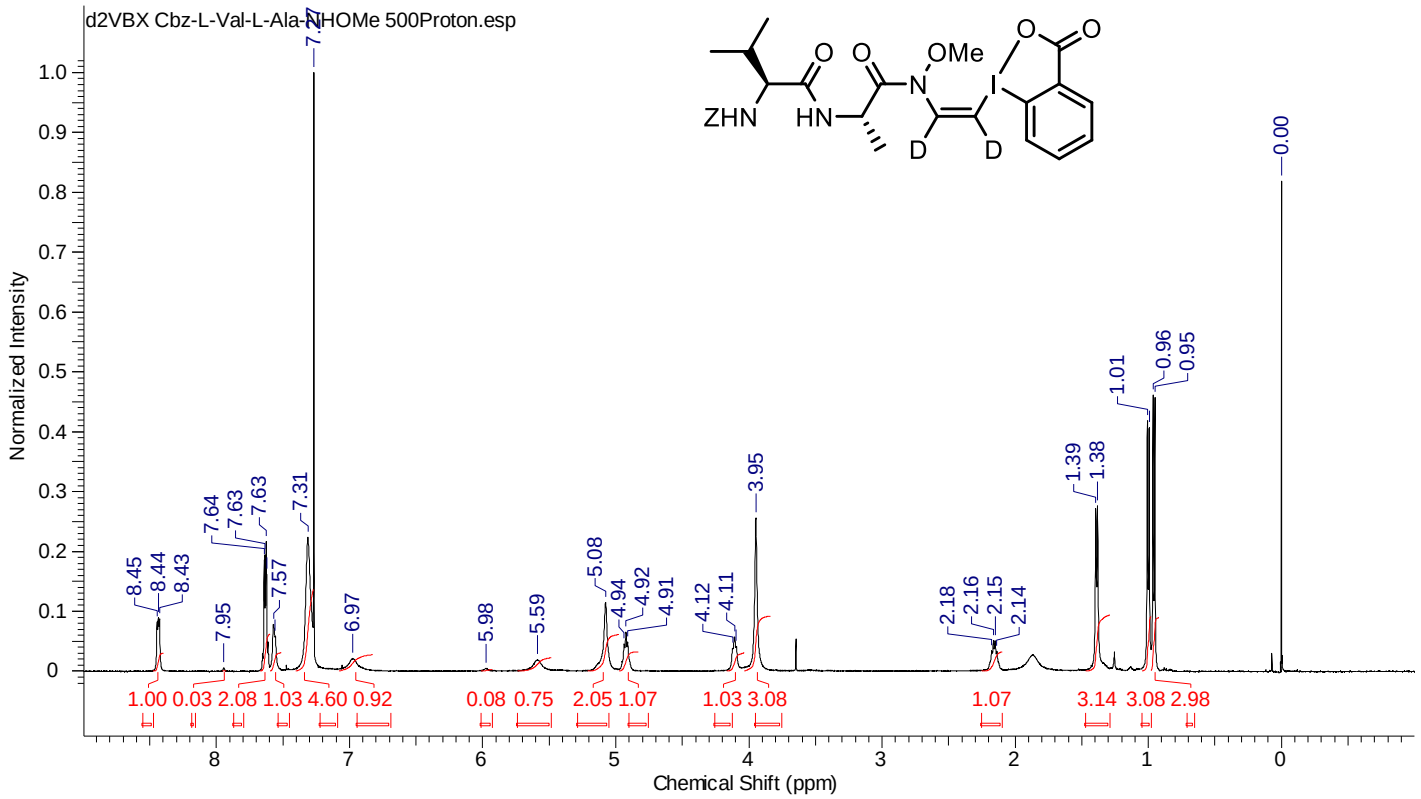
(*Z*)-*N*-(1,2-d_2-1-Vin-2-yl)-Cbz-L-phenylalanine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3aa-d_2)



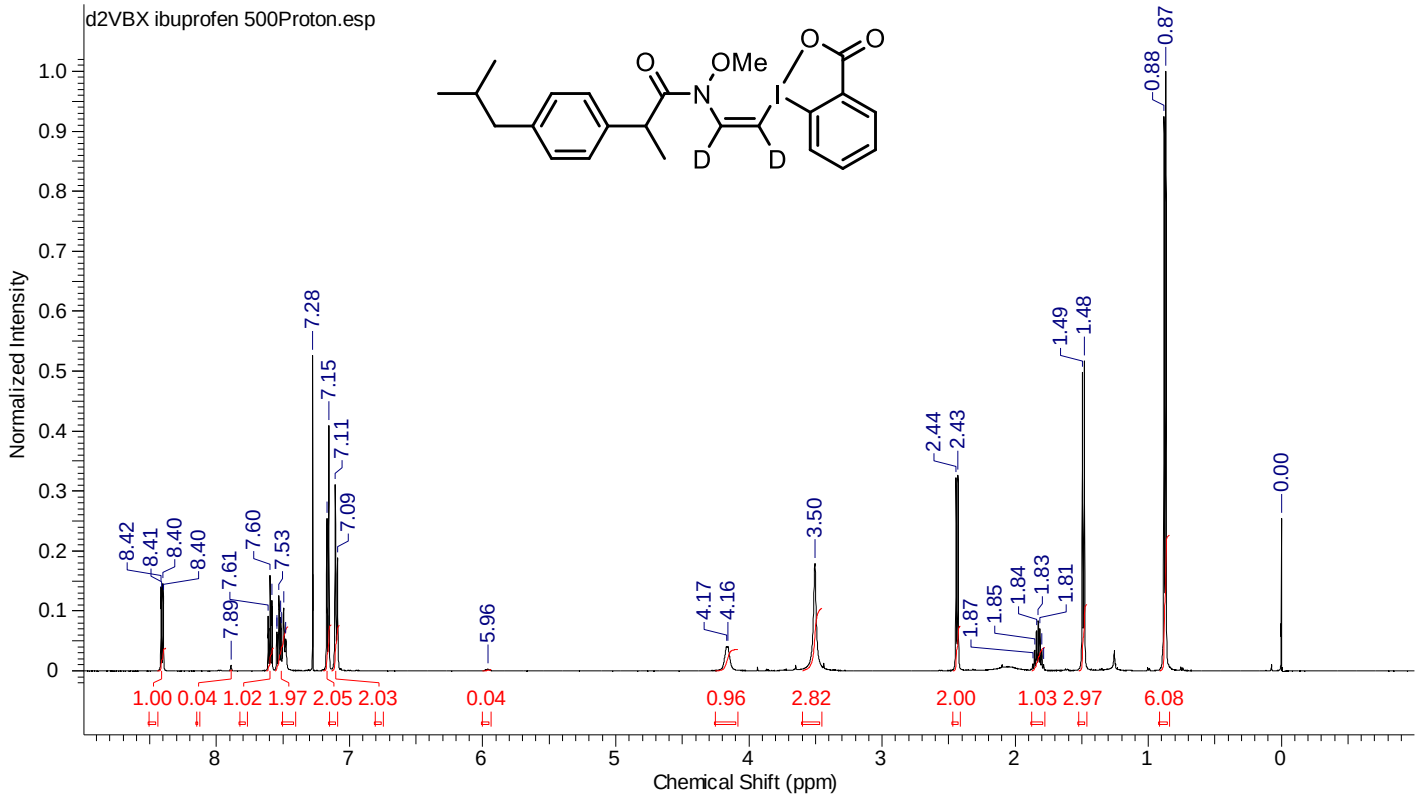
(*Z*)-*N*-(1,2-d_2-1-Vin-2-yl)-Cbz-L-tryptophan-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3ab-d_2)



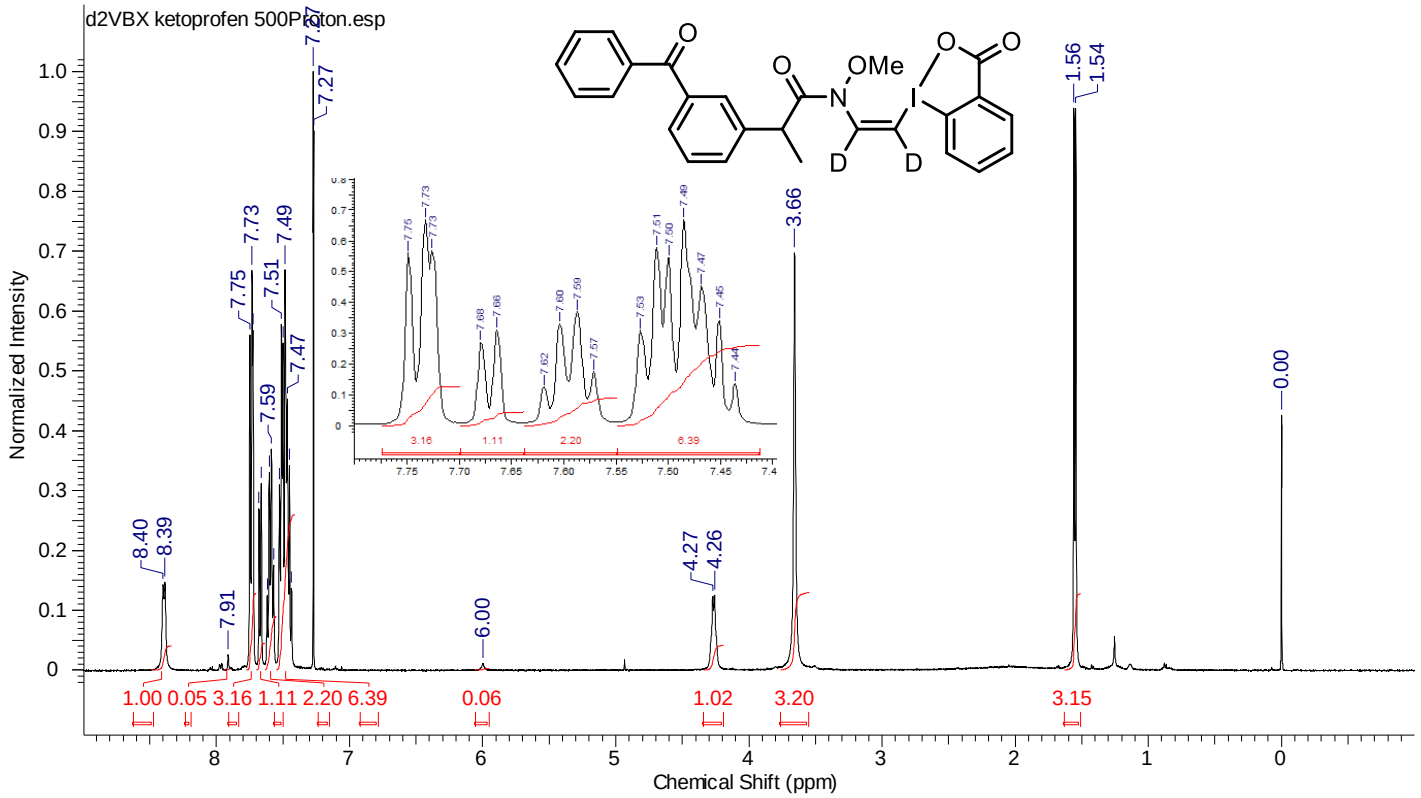
(*Z*)-*N*-(1,2-d_2-1-Vin-2-yl)-Cbz-L-valyl-L-alanine-*N*-methoxyamide-1,2-benziodoxol-3-(1*H*)-one (3ac-d_2)



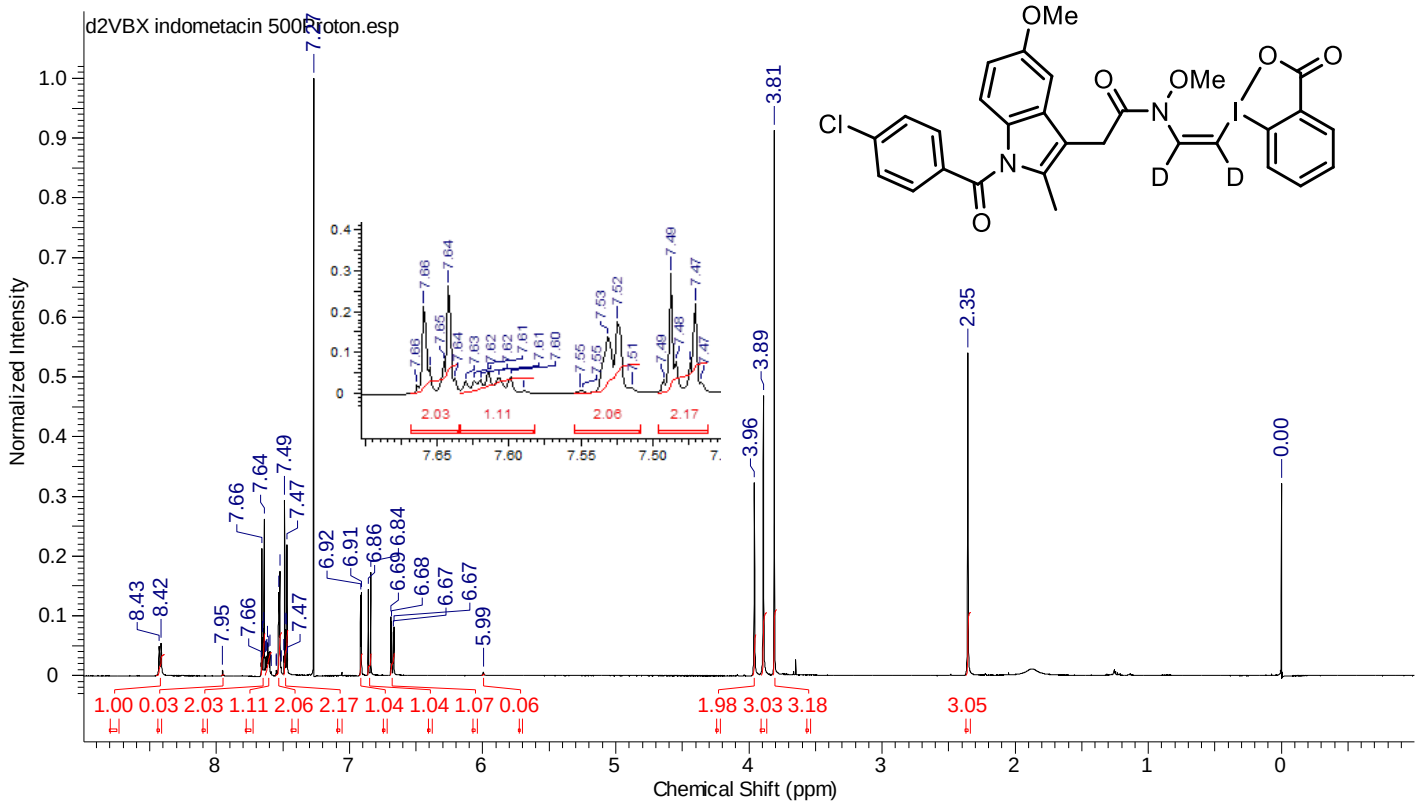
(*Z*)-*N*-(1,2-d_2-1-Vin-2-yl)-*N*-methoxy-2-[4-(2-methylpropyl)phenyl]propanamide-1,2-benziodoxol-3-(1*H*)-one (3ae-d_2)



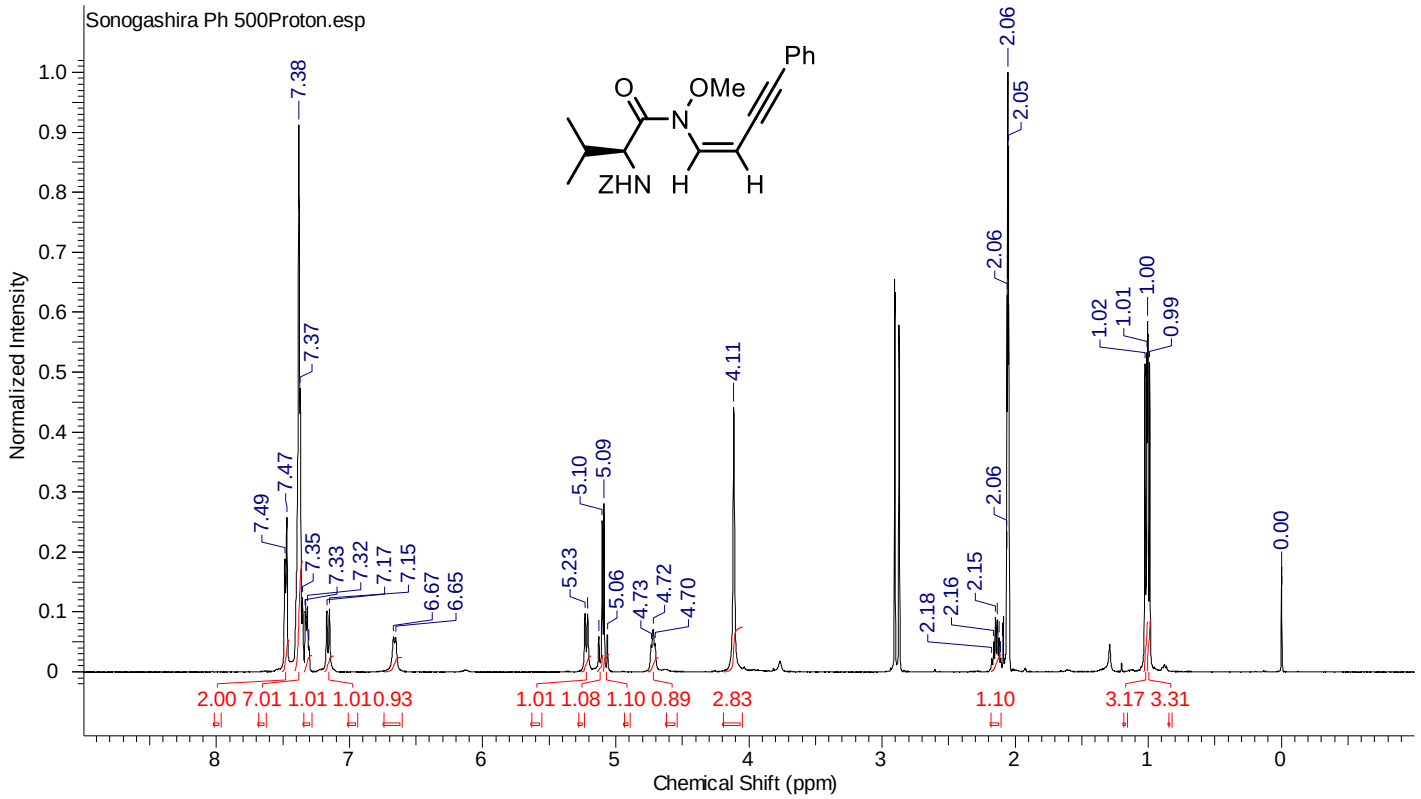
(*Z*)-*N*-(1,2-d_2-1-Vin-2-yl)-2-(3-benzoylphenyl)-*N*-methoxypropanamide-1,2-benziodoxol-3-(1*H*)-one (3af-d_2)

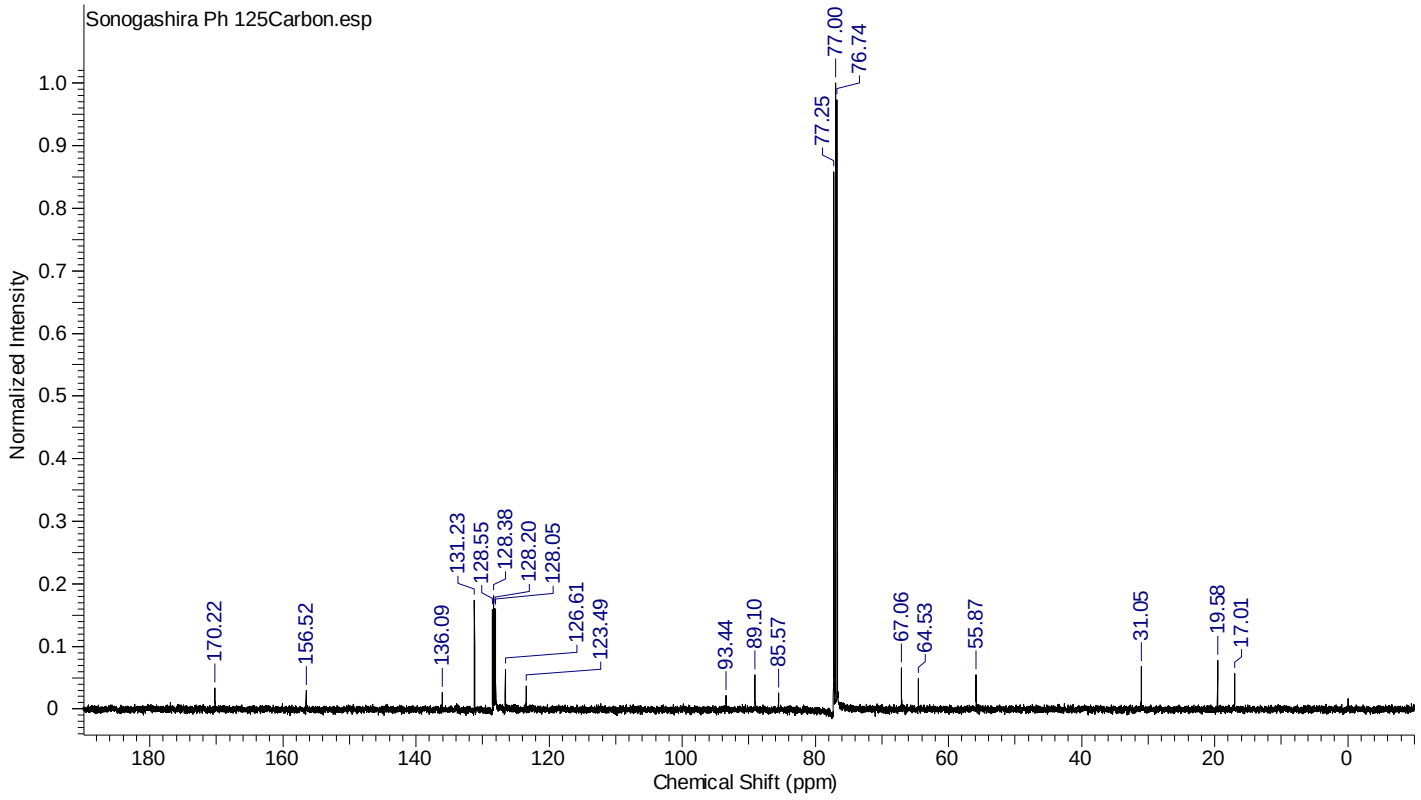


(*Z*)-*N*-(1,2-d_2-1-Vin-2-yl)-1-(4-chlorobenzoyl)-*N*,5-dimethoxy-2-methyl-1*H*-indole-3-acetamide-1,2-benziodoxol-3-(1*H*)-one (3ag-d_2)

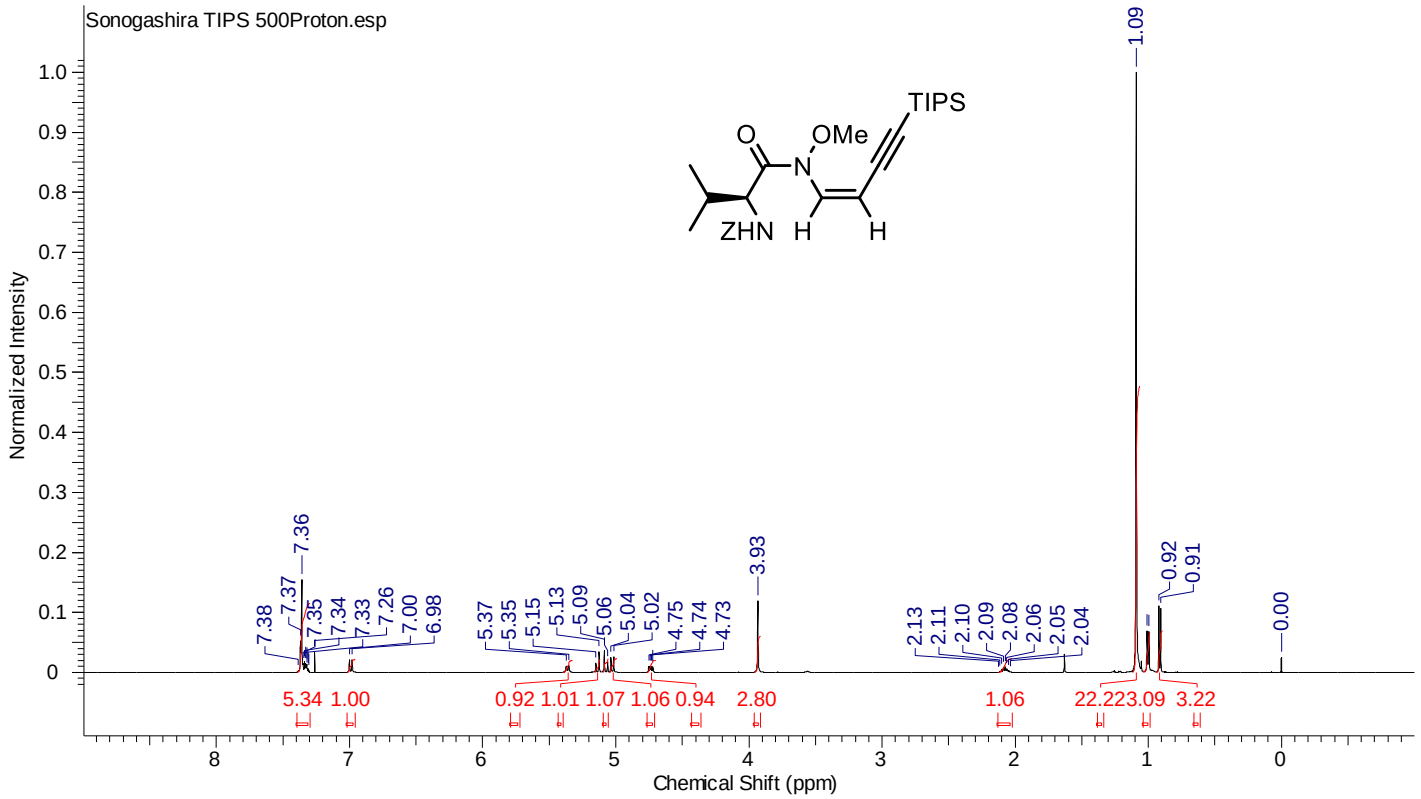


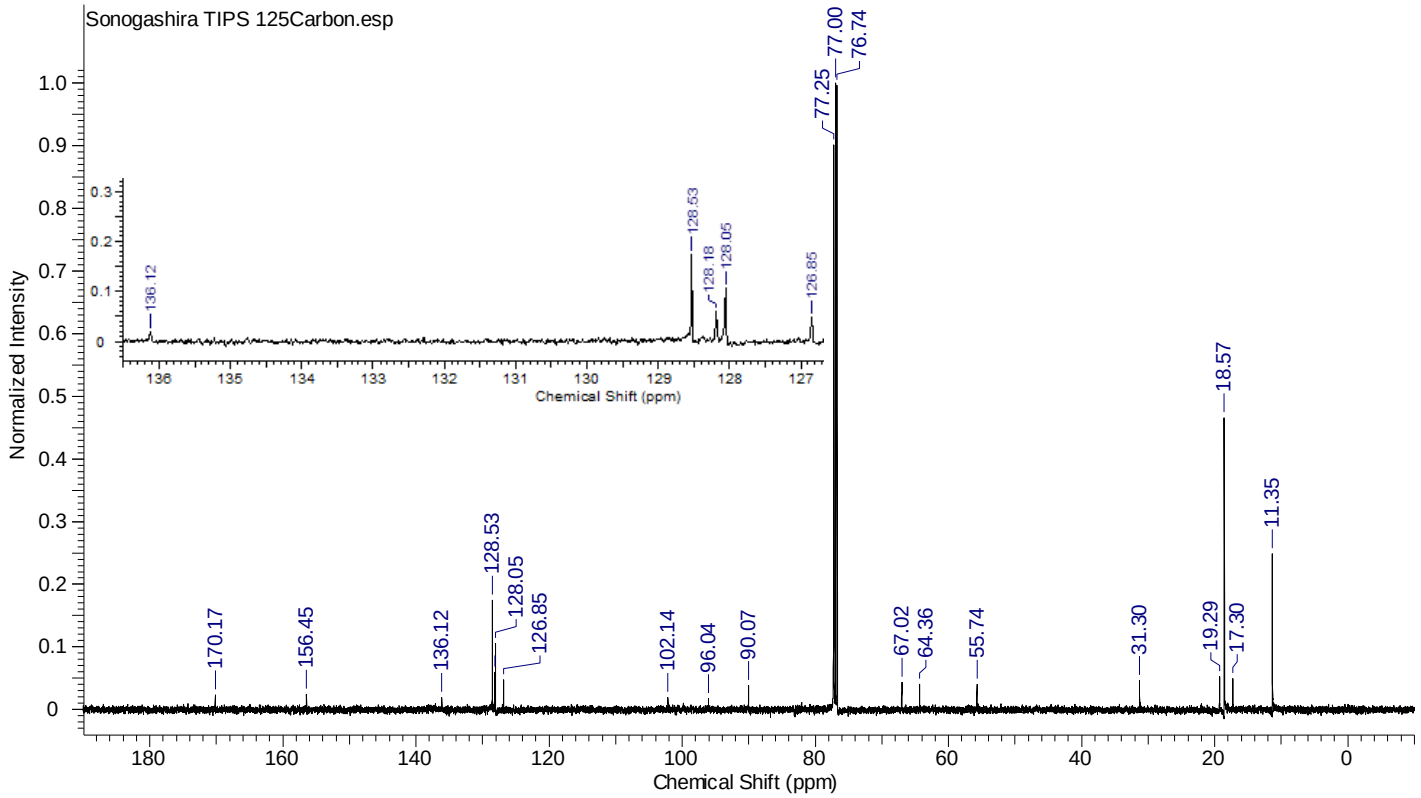
Cbz-L-Valine-(*Z*)-*N*-methoxy-*N*-(4-phenylbut-1-en-3-yn-1-yl)amide (4z)



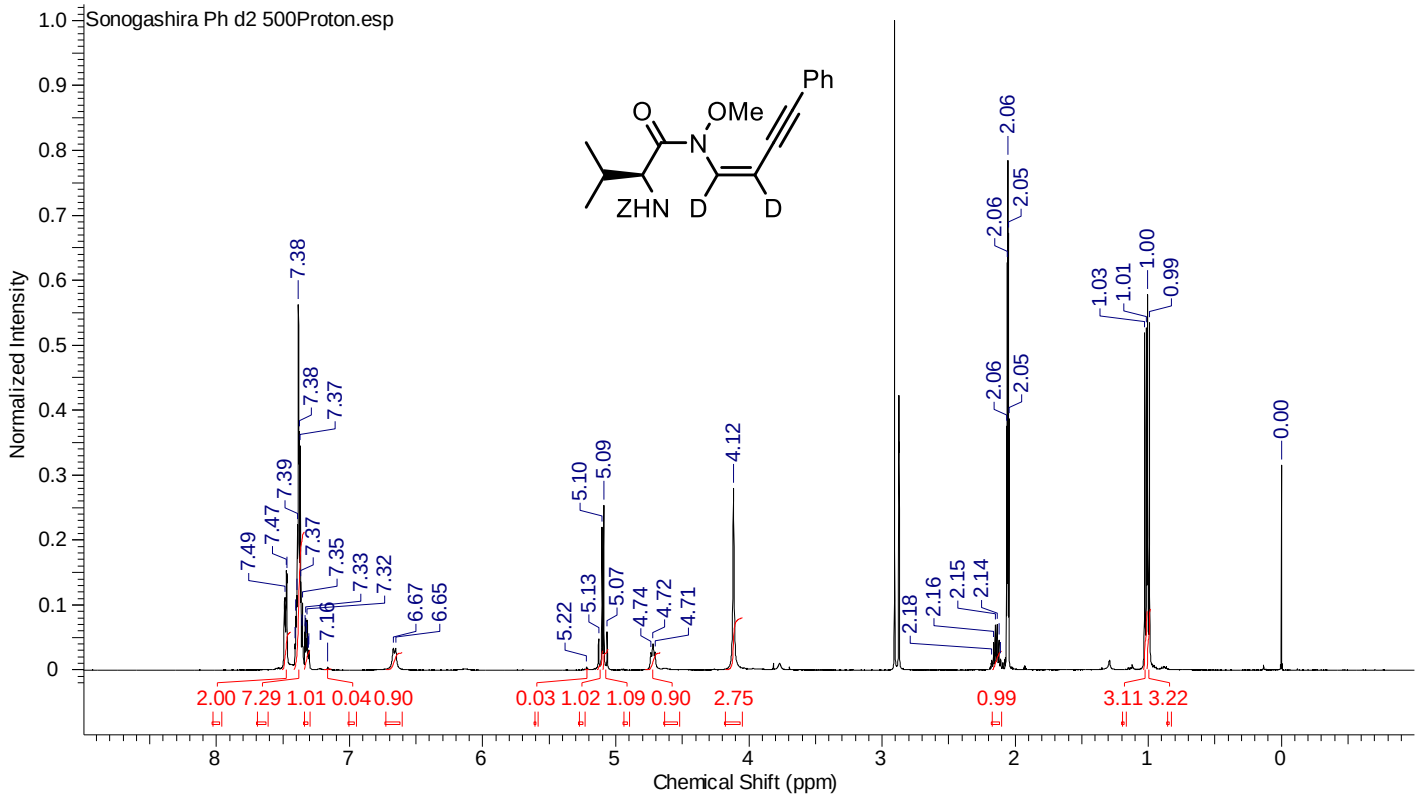


Cbz-L-Valine-(*Z*)-*N*-methoxy-*N*-[4-(triisopropylsilyl)but-1-en-3-yn-1-yl]amide (5z)

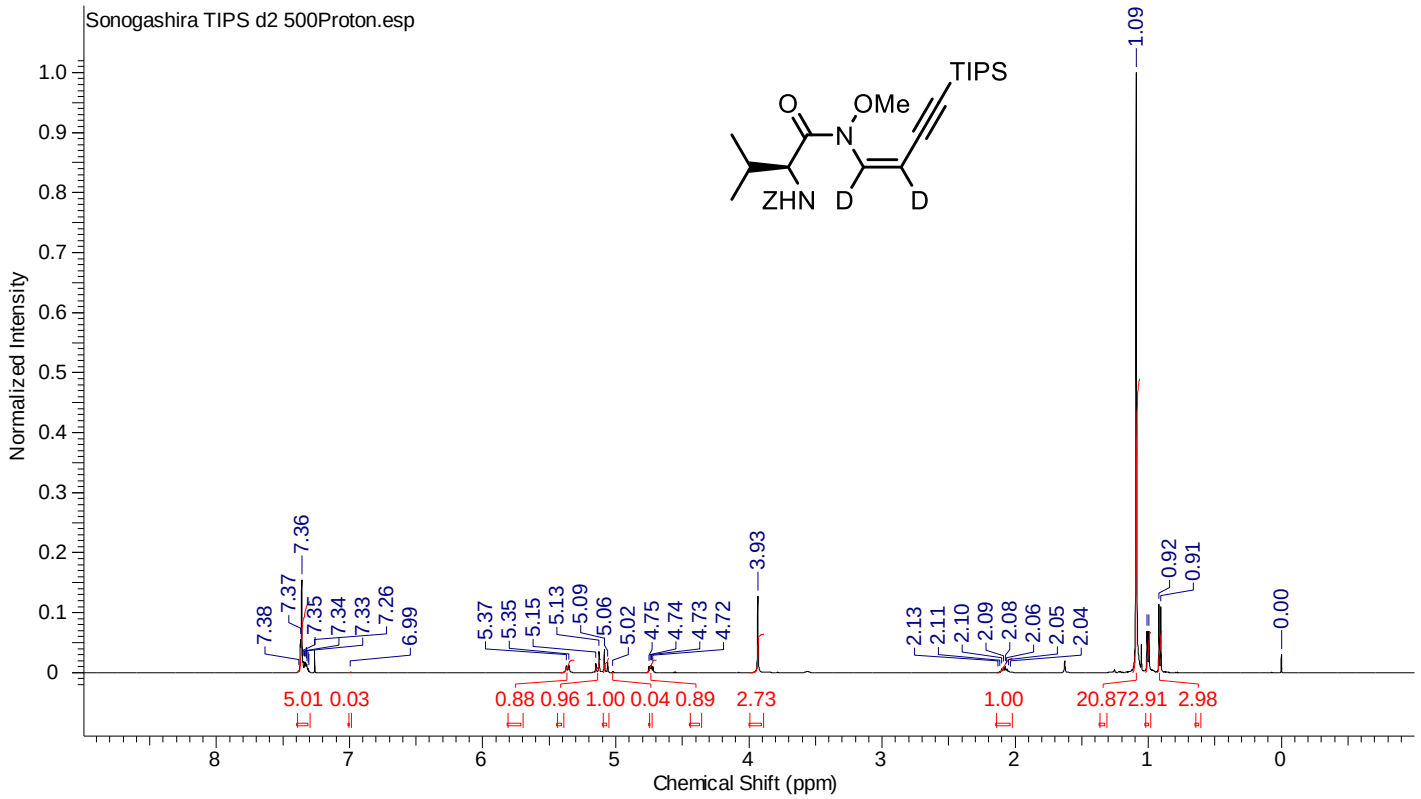




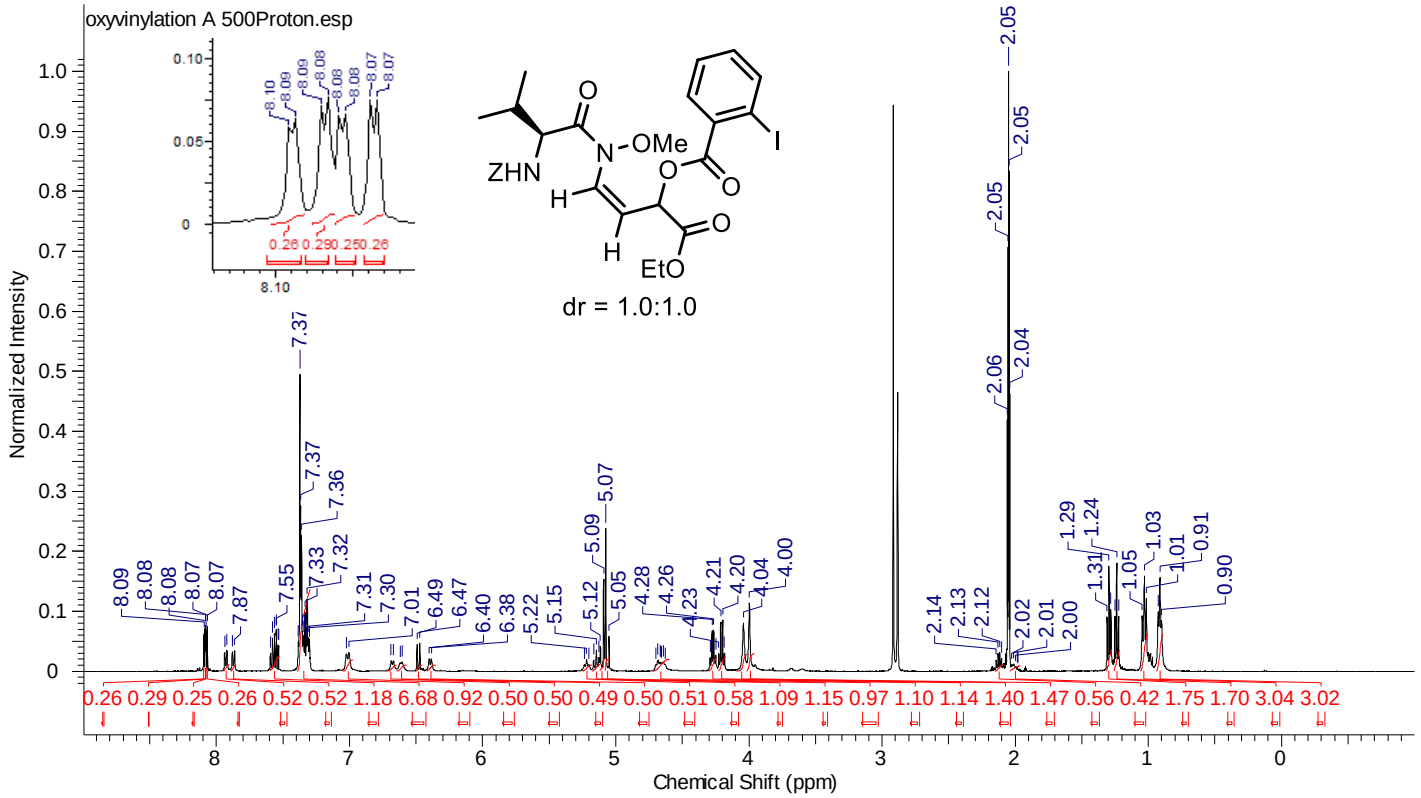
Cbz-L-Valine-(*Z*)-*N*-methoxy-*N*-(1,2-d_2-4-phenylbut-1-en-3-yn-1-yl)amide (4z-d_2)

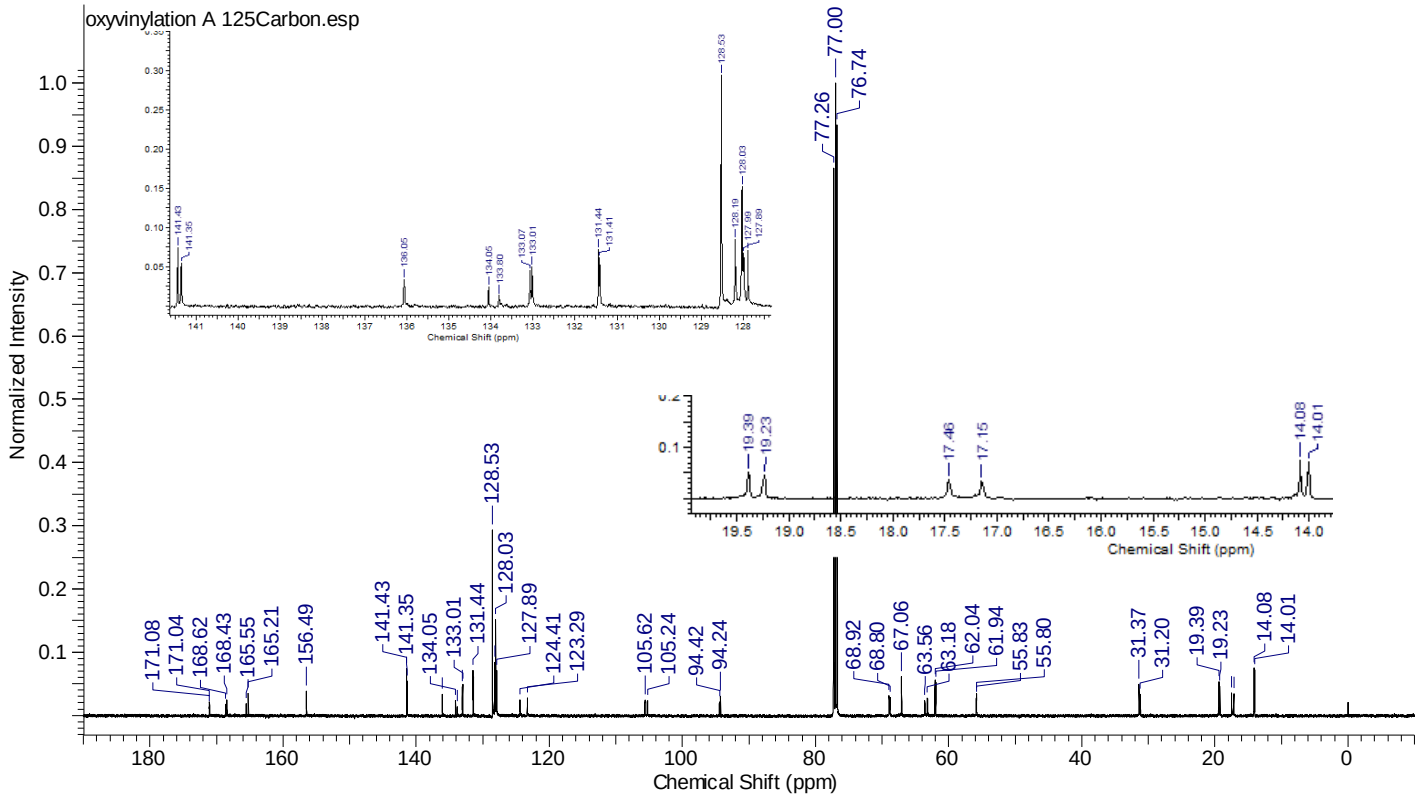


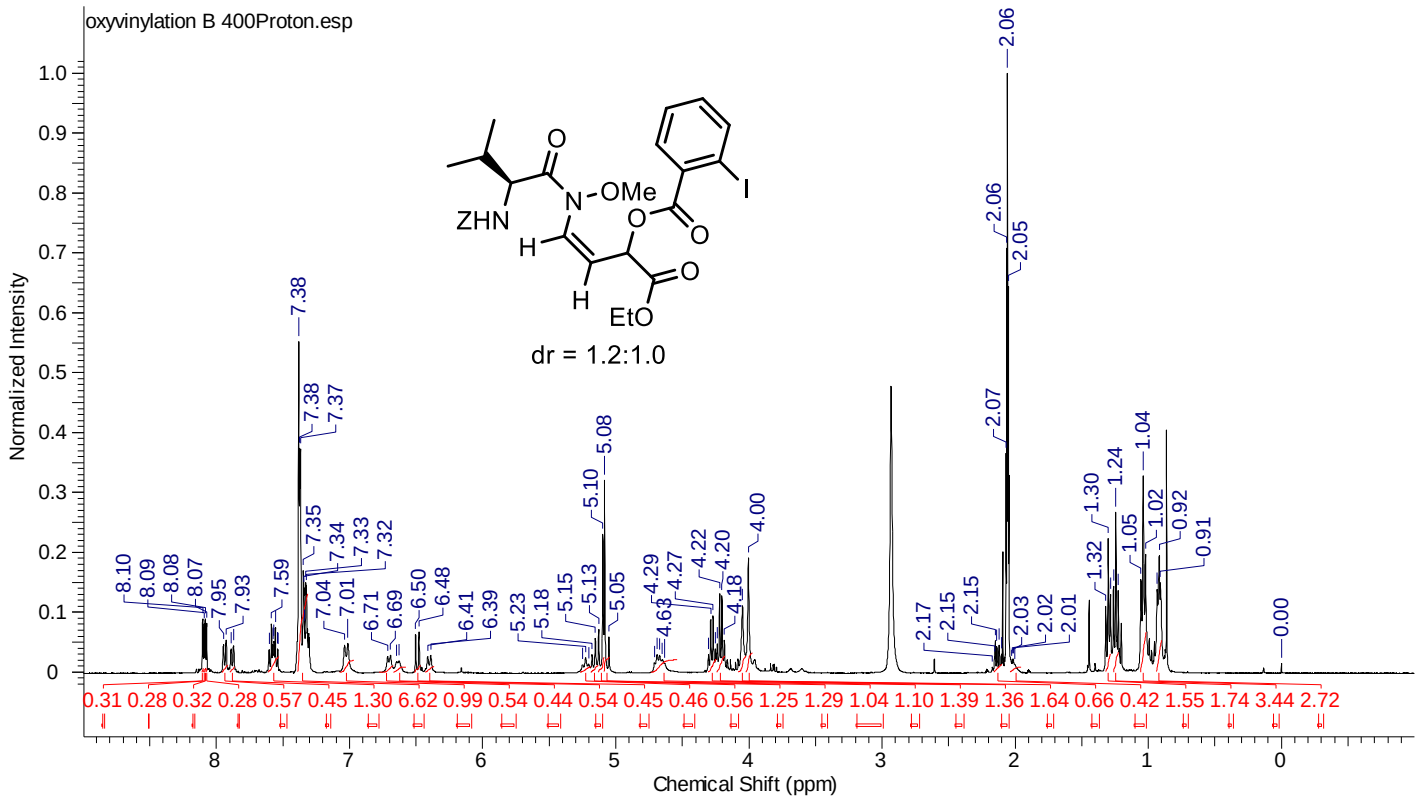
Cbz-L-Valine-(*Z*)-*N*-methoxy-*N*-[1,2-d_2-4-(triisopropylsilyl)but-1-en-3-yn-1-yl]amide (5z-d_2)



Cbz-L-Valine-(*Z*)-*N*-methoxy-*N*-[4-ethoxy-3-(2-iodobenzoyl)oxy-4-oxobut-1-en-1-yl]amide (6z)







Cbz-L-Valine-(*Z*)-*N*-methoxy-*N*-[1,2-d_2-4-ethoxy-3-(2-iodobenzoyl)oxy-4-oxobut-1-en-1-yl]amide (6z-d_2)