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Supplementary information

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Supplementary Information

Synthesis of azetidines via visible-light-mediated intermolecular [2+2] photocycloadditions

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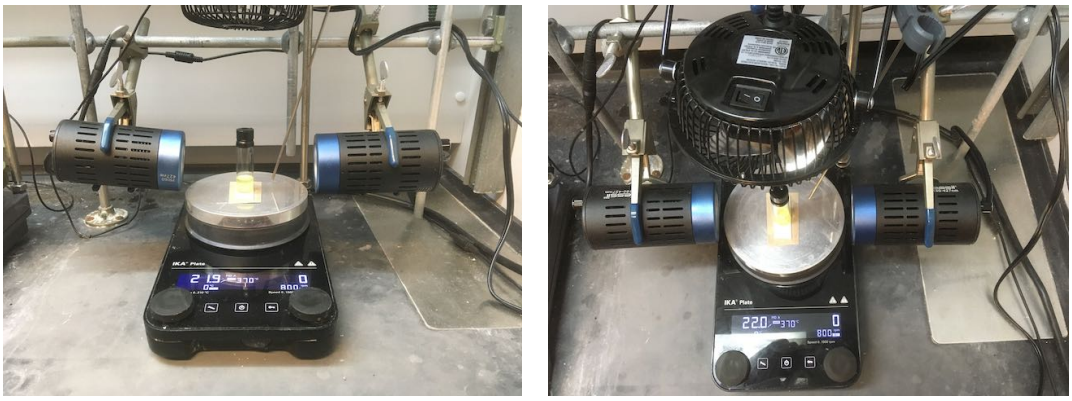
1) General Information

General Laboratory Procedures. All air- or moisture-sensitive reaction were carried out in flame-dried glassware under an atmosphere of nitrogen. Thin-layer chromatography (TLC) was performed on *Merck* silica gel 60 F_{254} plates using UV light (254 or 366 nm), $KMnO_4$ or CAM stain for visualization. Flash chromatography was performed using silica gel Silia Flash® 40-63 micron (230-400 mesh) from Silicycle unless noted.

Materials and Instrumentation. All chemicals were purchased from Sigma-Aldrich, Alfa Aesar, Acros Organics, Oakwood, TCI America, Frontier Scientific, Matrix Scientific, Ark Pharm, and Chem Impex International, and were used as received unless otherwise stated. THF, CH_2Cl_2, Et_2O, MeOH, MeCN and DMF were dried by being passed through a column of activated alumina under argon using a JC-Meyer Solvent Systems. $[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$ (**11**•PF_6) was prepared according to a literature procedure.[1] All other photocatalysts including *fac*-$[Ir(dFppy)_3]$ (**18**) were purchased from Sigma-Aldrich and used as received. 2-(3-phenylpropoxy)acetaldehyde *O*-methyl oxime (**16**)[2], 3-phenylisoxazol-5(4*H*)-one (**A1**)[3], 5,5-dimethyl-3-phenyl-1-tosyl-4,5-dihydro-1*H*-pyrazole (**A2**)[4] and (5,5-dimethyl-4,5-dihydroisoxazol-3-yl)methanol (**70**)[5] were prepared according to literature procedures. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on Varian MR400, Varian vnmrs 500, Varian Inova 500, and Varian vnmrs 700 spectrometers and are referenced to residual protic NMR solvent ($CDCl_3$: δ 7.26 ppm). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad), coupling constant (Hz), integration. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on Varian vnmrs 500 and Varian vnmrs 700 spectrometers and are referenced to the carbon resonances of the NMR solvent ($CDCl_3$: δ 77.16 ppm). High-resolution mass spectrometry (MS) data was recorded at the Mass Spectrometry Facility at the Department of Chemistry of the University of Michigan in Ann Arbor, MI on an Agilent 6230 TOF HPLC-MS (ESI) or Micromass AutoSpec Ultima Magnetic Sector mass spectrometer (ESI, EI). Infrared (IR) spectra were obtained using a Thermo-Nicolet IS-50 spectrometer. IR data are represented as frequency of absorption (cm^{-1}). Stereochemistry indicators with asterisk (*R**, *S**) were used to indicate relative stereochemistry of diastereomers.

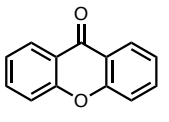
Photochemical setup: Visible light-mediated reactions were carried out using two 40 W PR160-427 Kessil lights (100% intensity) that were placed at both sides of the reaction vessel at a distance of approximately 10 cm. The reactor temperature was monitored throughout the reaction with a temperature probe placed adjacent to the reaction vessel and maintained at 35 ºC by cooling with a fan positioned above the reaction.



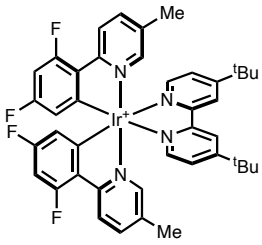
Supplementary Figure 1: Photochemical setup for [2+2] photocycloaddition.

Abbreviations used: aq. = aqueous, Boc_2O = di-*tert*-butyl dicarbonate, Cbz =carboxybenzyl, CbzCl =benzyl chloroformate, d.r. =diastereomeric ratio, DMAP = 4-dimethylaminopyridine, DMF = dimethylformamide, DMSO = dimethyl sulfoxide, EDC • HCl = *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride, EI = electron ionization, EWG = electron-withdrawing group, ESI = electrospray ionization, E_T = triplet energy, Et_2O = diethyl ether, Et_3N = triethylamine, EtOAc = ethyl acetate, GP = general procedure, HRMS = high-res mass spec, IR = infrared, K_{SV} = Stern-Volmer quenching constant, MeCN = acetonitrile, $MgSO_4$ =magnesium sulfate, MS = mass spec, *n*-Bu = *n*-butyl, Na_2SO_4 = sodium sulfate, NaOH = sodium hydroxide, NCS = *N*-chlorosuccinimide, NMR = nuclear magnetic resonance, *p*-TsCl = 4-toluenesulfonyl chloride, *p*-TsOH = *para*-toluenesulfonic acid, r.r. = regioisomer ratio, Raney-Ni = Raney-nickel, sat. = saturated, SCE = saturated calomel electrode, SmI_2 = samarium(II) iodide, TFA = trifluoroacetic acid, THF = tetrahydrofuran, TLC = thin-layer chromatography, xs = excess.

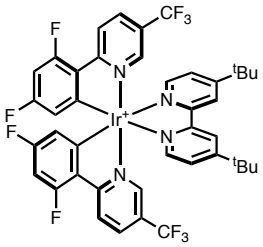
2) Photocatalyst Overview



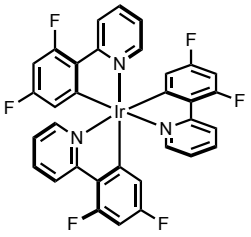
xanthone
E_T = 74.3 kcal mol^{-1}
$E_{1/2}^{(M+/M^*)}$ = –1.42 V
$E_{1/2}^{(M^*/M-)}$ = +1.57 V



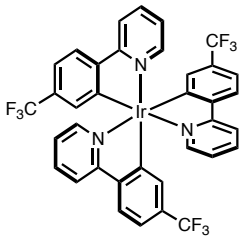
[Ir(dF(Me)ppy)$_2$(dtbbpy)]PF$_6$
E_T = 60.2 kcal mol^{-1}
$E_{1/2}^{(M+/M^*)}$ = –0.92 V
$E_{1/2}^{(M^*/M-)}$ = +0.97 V



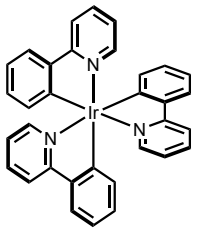
[Ir(dF(CF$_3$)ppy)$_2$(dtbbpy)]PF$_6$
E_T = 60.1 kcal mol^{-1}
$E_{1/2}^{(M+/M^*)}$ = –0.89 V
$E_{1/2}^{(M^*/M-)}$ = +1.21 V



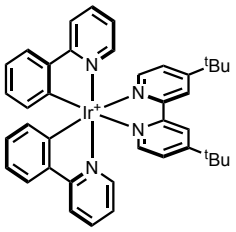
***fac*-[Ir(dFppy)$_3$]**
E_T = 60.1 kcal mol^{-1}
$E_{1/2}^{(M+/M^*)}$ = –1.28 V
$E_{1/2}^{(M^*/M-)}$ = +0.36 V



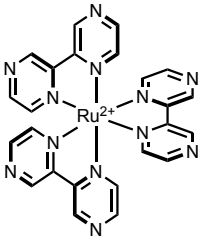
***fac*-[Ir(4'-CF$_3$-ppy)$_3$]**
E_T = 56.4 kcal mol^{-1}
$E_{1/2}^{(M+/M^*)}$ = –1.70 V
$E_{1/2}^{(M^*/M-)}$ = +0.59 V



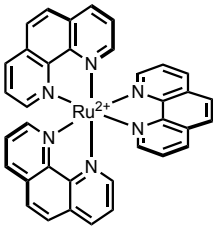
***fac*-[Ir(ppy)$_3$]**
E_T = 55.2 kcal mol^{-1}
$E_{1/2}^{(M+/M^*)}$ = –1.73 V
$E_{1/2}^{(M^*/M-)}$ = +0.31 V



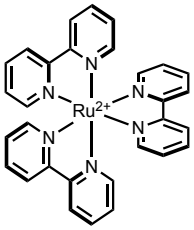
[Ir(ppy)$_2$(dtbbpy)]PF$_6$
E_T = 49.2 kcal mol^{-1}
$E_{1/2}^{(M+/M^*)}$ = –0.96 V
$E_{1/2}^{(M^*/M-)}$ = +0.66 V



[Ru(bpz)$_3$](PF$_6$)$_2$
E_T = 48.4 kcal mol^{-1}
$E_{1/2}^{(M+/M^*)}$ = –0.26 V
$E_{1/2}^{(M^*/M-)}$ = +1.45 V



[Ru(phen)$_3$](PF$_6$)$_2$
E_T = 46.9 kcal mol^{-1}
$E_{1/2}^{(M+/M^*)}$ = –0.87 V
$E_{1/2}^{(M^*/M-)}$= +0.82 V

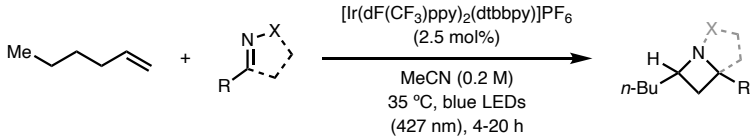


[Ru(bpy)$_3$](PF$_6$)$_2$
E_T = 46.5 kcal mol^{-1}
$E_{1/2}^{(M+/M^*)}$ = –0.81 V
$E_{1/2}^{(M^*/M-)}$ = +0.77 V

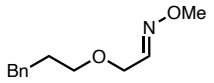
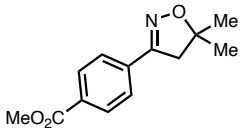
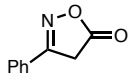
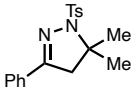
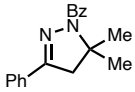
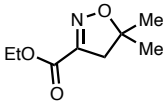
Supplementary Figure 2: Overview of photocatalysts used in this study. All potentials (given versus the saturated calomel electrode (SCE)) and triplet state energy (E_T) values were obtained from the literature.[19,20]

3) Substrate Evaluation for Photochemical [2+2] Cycloaddition

A 1-dram vial was charged with the corresponding substrate (0.1 mmol, 1.0 equiv.), $[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$ (3 mg, 2.5 mol%) and MeCN (0.5 mL). The vial was subsequently sealed with a septum-equipped cap and the reaction mixture degassed by sparging with nitrogen gas for 5 min. Then, 1-hexene (67 µL, 0.54 mmol, 5.0 equiv.) was added via syringe, the vial sealed with electrical tape and the reaction stirred under irradiation with blue LED lights (427 nm) at ambient temperature (fan cooling) for 4-20 h. The solvent was removed *in vacuo* and crude reaction mixture purified by flash column chromatography.



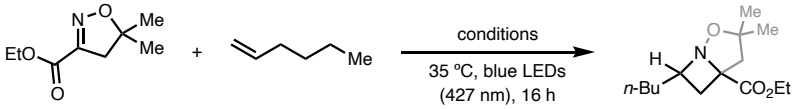
Supplementary Table 1. Substrate Evaluation

Entry	Substrate		Reaction time (h)	Quenching percentage (%)[a]	Yield (%)
1		**16**	18	24	0[b]
2		**17**	18	97	0[b]
3		**A1**	4	59	0[c]
4		**A2**	4	88	0[c]
5		**A3**	18	96	0[b]
6		**14**	18	54	60

[a]calculated using the following equation: $100(1-I/I_0)$ (I: luminescence of $[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$ in the presence of quencher; I_0: luminescence of $[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$ in the absence of 2500 equiv. of substrate).[21] 190 µL of a 0.11 mM stock solution of catalyst in MeCN and the respective amount of a 50-60 mM stock solution of substrate (2500 equiv.) were added to a 4-mL volumetric flask and the volume adjusted with MeCN. The solution was transferred to a 1-cm cuvette, which was sealed with a septum-equipped cap and the solution degassed by sparging for 15 min with argon gas, before measuring the luminescence using a PTI quantaMaster fluorimeter (Horiba) (excitation at 420 nm; luminescence was observed at 427 nm); [b]no reaction was observed; [c]rapid decomposition of the substrate was observed.

4) Reaction Optimization of Photochemical [2+2] Cycloaddition

A 1-dram vial was charged with **14** (17 mg, 0.1 mmol, 1.0 equiv.), photocatalyst and solvent. The vial was subsequently sealed with a septum-equipped cap and the reaction mixture degassed by sparging with nitrogen gas for 5 min. Then, 1-hexene was added via syringe, the vial sealed with electrical tape and the reaction stirred under irradiation with blue LED lights (427 nm) at ambient temperature (fan cooling) for 16 h. The solvent was removed *in vacuo* and the crude reaction mixture analyzed by ^{1}H NMR using mesitylene as internal standard.



14 **15**

Supplementary Table 2. Photocatalyst evaluation

Entry	Photocatalyst	Yield (%)	d.r.	r.r.	Conversion (%)
1	xanthone[a]	54	4:1	16:1	70
2[a]	$[Ir(dF(Me)ppy)_2(dtbbpy)]PF_6$	54	>20:1	9:1	>95
3[a]	$[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$	69	9:1	13:1	>95
4[a]	*fac*-$[Ir(dFppy)_3]$ (**18**)	94	3:1	>20:1	>95
5	*fac*-$[Ir(4'\text{-}CF_3\text{-}ppy)_3]$	8	3:1	>20:1	9
6	*fac*-$[Ir(ppy)_3]$	0	–	–	<5
7	$[Ir(ppy)_2(dtbbpy)]PF_6$	0	–	–	<5
8	$[Ru(bpz)_3](PF_6)_2$	0	–	–	<5
9	$[Ru(phen)_3](PF_6)_2$	0	–	–	<5
10	$[Ru(bpy)_3](PF_6)_2$	0	–	–	<5

Conditions: Reactions performed with 0.5 mmol 1-hexene (5.0 equiv.) and 2.5 mol% photocatalyst in MeCN (1 mL) for 16 h. d.r. = diastereomer ratio; r.r. = regioisomer ratio; [a]run with 20 mol% catalyst under UV light irradiation (365 nm). [a]for further information regarding the decreased yields of **15** in entries 2+3, see Supplementary Figure 12.

Supplementary Table 3. Solvent evaluation

Entry	Solvent	Yield (%)	d.r.	r.r.	Conversion (%)
1	acetonitrile	94	3:1	>20:1	>95
2	CH_2Cl_2	>95	3:1	>20:1	>95
3	1,2-dichloroethane	>95	3:1	19:1	>95
4	THF	50	3:1	11:1	>95
5	ethyl acetate	89	3:1	16:1	>95
6	methanol	89	2:1	17:1	94
7	toluene	91	4:1	16:1	>95
8	acetone	92	3:1	18:1	>95
9	1,4-dioxane	94	3:1	>20:1	>95
10	DMF	94	3:1	>20:1	>95
11	DMSO	84	2:1	19:1	>95

Conditions: Reactions performed with 0.5 mmol 1-hexene (5.0 equiv.) and 2.5 mol% *fac*-$[Ir(dFppy)_3]$ in the corresponding solvents (1 mL) for 16 h. d.r. = diastereomer ratio; r.r. = regioisomer ratio.

Supplementary Table 4. Reaction concentration evaluation

Entry	Concentration (M)	Yield (%)	d.r.	r.r.	Conversion (%)
1	0.05	94	3:1	>20:1	>95
2	0.10	94	3:1	>20:1	>95
3	0.25	93	3:1	>20:1	>95
4	0.50	90	3:1	19:1	>95
5	no solvent (neat)	10	–	–	12

Conditions: Reactions performed with 0.5 mmol 1-hexene (5.0 equiv.) and 2.5 mol% *fac*-[Ir(dFppy)$_3$] in MeCN (x mL) for 16 h. d.r. = diastereomer ratio; r.r. = regioisomer ratio.

Supplementary Table 5. Alkene equivalents evaluation

Entry	Equivalents (alkene)	Yield (%)	d.r.	r.r.	Conversion (%)
1	1.1	75	3:1	18:1	79
2	1.5	93	3:1	>20:1	>95
3	2.0	92	3:1	19:1	>95
4	5.0	94	3:1	>20:1	>95

Conditions: Reactions performed with x mmol 1-hexene (x equiv.) and 2.5 mol% *fac*-[Ir(dFppy)$_3$] in MeCN (1 mL) for 16 h. d.r. = diastereomer ratio; r.r. = regioisomer ratio.

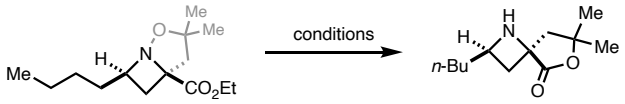
Supplementary Table 6. Catalyst loading evaluation

Entry	Catalyst loading (mol%)	Yield (%)	d.r.	r.r.	Conversion (%)
1	0.1	88	3:1	19:1	>95
2	0.5	86	3:1	17:1	>95
3	1.0	91	3:1	19:1	>95
4	2.5	93	3:1	>20:1	>95

Conditions: Reactions performed with 0.15 mmol 1-hexene (1.5 equiv.) and x mol% *fac*-[Ir(dFppy)$_3$] in MeCN (1 mL) for 16 h. d.r. = diastereomer ratio; r.r. = regioisomer ratio.

5) Reaction Optimization of *N–O* bond cleavage of Azetidine Products

General procedure for hydrogenolysis reactions: A 1-dram vial was charged with *exo*-**15** (10 mg, 0.04 mmol, 1.0 equiv.), reagents and solvent (1 mL). The vial was subsequently sealed with a septum-equipped cap and reaction mixture sparged with hydrogen gas for 5-10 min, before being stirred at the corresponding temperature for 24 h under a hydrogen atmosphere (balloon, 1 atm). The reaction mixture was filtered through celite, the filter cake washed with CH_2Cl_2 and the filtrate concentrated *in vacuo*. The residue was taken up in CH_2Cl_2 and water and the aqueous layer brought to pH 10-11 with 2 M NaOH (aq.). Next, the organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (2x). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude reaction mixture was analyzed by ^1H NMR to determine yield and conversion using mesitylene as internal standard.



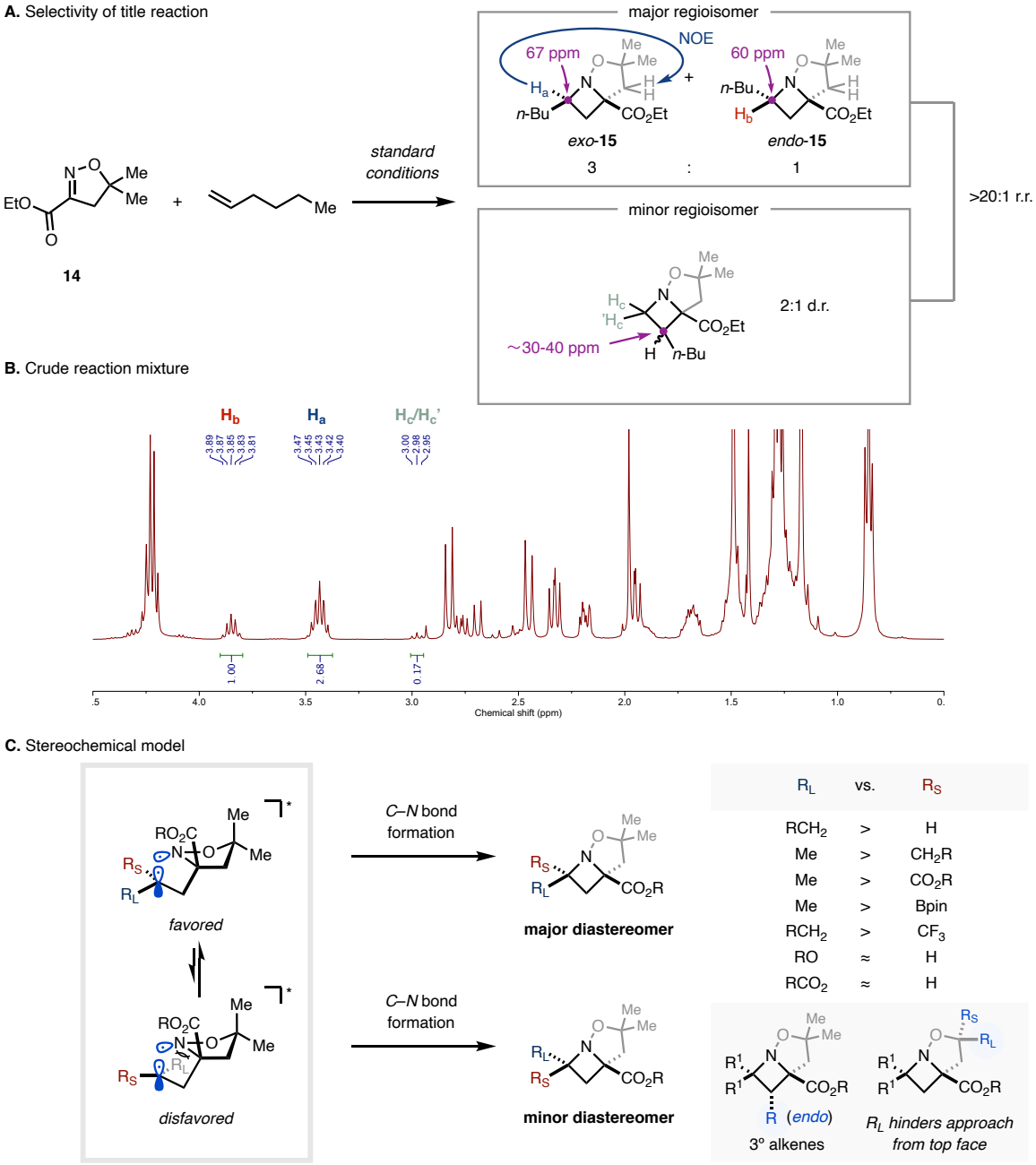
exo-**15** **59**

Supplementary Table 7. Reaction Optimization for *N–O* bond cleavage

Entry	Reagents (mol%)	Solvent	Temperature (ºC)	Yield (%)	Conversion (%)
1	Zn (xs)	HCl (aq.)/THF	80	0	>95
2	Zn (xs)	AcOH	60	38	53
3	Pd/C (20)	EtOH	40	12	11
4	$Pd(OH)_2$ (20), H_2 (1 atm)	EtOH	40	23	16
5	Raney-Ni, H_2 (1 atm)	EtOH	40	58	67
6	PtO_2 (20), H_2 (1 atm)	EtOH	40	0	<5
7	Ru/C (20), H_2 (1 atm)	EtOH	40	12	17
8	$Pd(OH)_2$ (50), H_2 (1 atm)	EtOH	40	27	39
9	$Pd(OH)_2$ (20), H_2 (4 atm)	EtOH	60	16	46
10	$Pd(OH)_2$ (20), H_2 (1 atm)	EtOH	78	14	>95
11	$Pd(OH)_2$ (20), H_2 (1 atm)	EtOH/H_2O (1:1)	40	4	28
12	$Pd(OH)_2$ (20), H_2 (1 atm)	DMF	40	0	<5
13	$Pd(OH)_2$ (20), H_2 (1 atm)	acetone	40	0	51
14	$Pd(OH)_2$ (20), H_2 (1 atm)	H_2O/AcOH (1:1)	40	0	>95
15	$Pd(OH)_2$ (20), H_2 (1 atm)	EtOH/H_2O/AcOH	40	61	>95
16	**$Pd(OH)_2$ (20), H_2 (1 atm) *p*-TsOH (2.0 equiv.)**	**EtOH**	**40**	**85**	**87**
17	$Pd(OH)_2$ (20), H_2 (1 atm) oxalic acid (2.0 equiv.)	EtOH	40	14	40
18	$Pd(OH)_2$ (20), H_2 (1 atm) TFA (3.4 equiv.)	EtOH	40	33	61
19	$Pd(OH)_2$ (20), H_2 (1 atm) HCl (aq., 2.6 equiv.)	EtOH	40	79	80

Conditions: Reactions performed with 0.04 mmol *exo*-**15** for 24 h. xs = excess; TFA = trifluoroacetic acid; yields and conversion were determined from the crude reaction mixture using mesitylene as internal standard.

6) Stereo- and Regiochemistry of Azetidine Products



Supplementary Figure 3: Determination of stereo- and regiochemistry of azetidines products via NMR analysis **A.** Selectivity of title reaction **B.** Representative ^{1}H NMR spectrum of crude reaction mixture **C.** Stereochemical model. R_L = larger substituent; R_S = smaller substituent

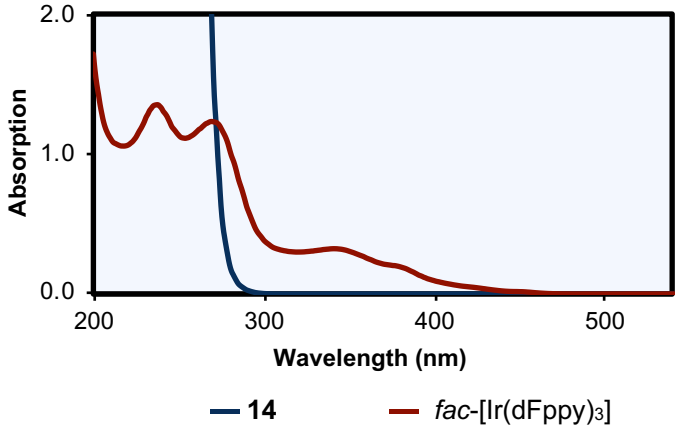
Diastereomer and regioisomer ratios of the developed intermolecular aza Paternò-Büchi reaction were determined by ^{1}H NMR analysis of the crude reaction mixture (Supplementary Fig. 3B). The reaction exhibits high regioselectivity (8:1 to >20:1 r.r.) for the azetidine product, in which the more substituted side of the alkene adds to the 2-isoxazoline nitrogen. For mono- and 1,1-disubstituted alkenes the major diastereomer is typically the *exo*-isomer in which the larger substituent (R_L) ends up opposite to the isoxazolidine ring with diastereoselectivities between 1:1 to >10:1. For

tertiary alkenes, the additional substituent was found to preferentially add *endo* during the cycloaddition process. Furthermore, in the case of monosubstituted 2-isoxazoline substrates, the cycloaddition occurs at the least hindered face (Supplementary Figure 3C). The regio- and stereochemical assignments for azetidine products were based on 1D NMR (^{1}H, ^{13}C), 2D NMR (gCOSY, gHMBCAD, gHSQCAD) and ^{1}H NMR NOE analysis (Supplementary Fig. 3A). Specifically, the regiochemistry was typically assigned according to the ^{13}C NMR shift of the carbon signals adjacent to the azetidine nitrogen. The stereochemistry of the azetidine products was assigned based on NOE correlations of characteristic ^{1}H NMR signals. For example, in the case of products arising from the reaction with primary alkenes (e.g. **15**), a strong NOE correlation was observed for proton H_a with the methylene group in the backbone of the substrate, which was not observed for the corresponding other diastereomer. Representative 1D, 2D NMR and NOE spectra for **15** are provided in section 10 (NMR spectra). The regio- and stereochemical assignments based on NMR analysis were further confirmed by the X-ray crystallographic analyses of compounds **44**, **46** and **59**.

7) Mechanistic Investigations

UV/Vis Absorption Spectra

UV/Vis absorption specta were recorded on a Varian Cary 50 UV/Vis spectrophotometer. Samples were prepared in MeCN with **14** (2.5 mM) and *fac*-[Ir(dFppy)$_3$] (0.025 mM). The photocatalyst is the only species absorbing at 427 nm.

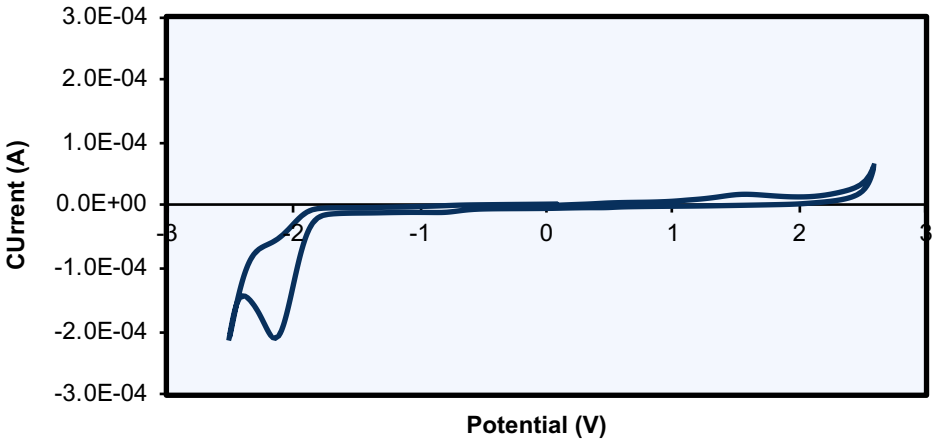


Supplementary Figure 4: UV/vis absorption spectra of *fac*-[Ir(dFppy)$_3$] (red line) and **14** (blue line).

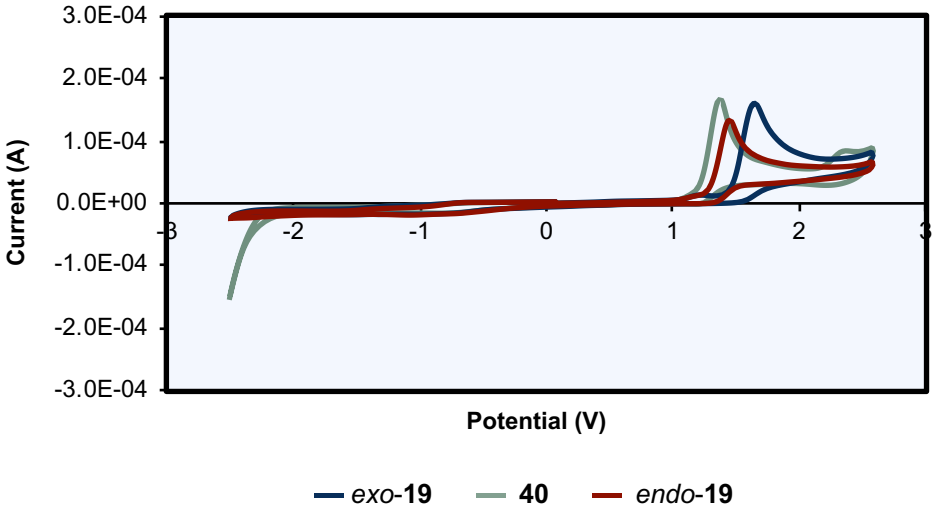
Electrochemical Measurements

Cyclic voltammetry was performed on a CHI620E electrochemical analyzer (CH instruments) using a 3-mL five-neck electrochemical cell equipped with a glassy carbon working electrode, a platinum counter or auxiliary electrode and an Ag/AgCl (3 M KCl) reference electrode. The experimental setup was calibrated using ferrocene (Fc^{+}/Fc) prior to each experiment. Samples were prepared with 0.03 mmol substrate in 3 mL *n*-Bu_4NPF_6 electrolyte (0.1 M in MeCN) and degassed prior to use by sparging with argon gas for 10 min. Data acquisition was performed at a scan rate of 100 mV/s

and the potential ($E_{p/2}$) determined according to literature procedures.[6] All potentials are reported versus the saturated calomel electrode (SCE). The cyclic voltammogram for 2-isoxazoline **14** shows an irreversible reduction process at $E_{p/2}$ = –2.01 V (vs. SCE) and a weak oxidation process at approximately E = 1.57 V (Supplementary Figure 5). The excited state redox potentials of the photocatalyst *fac*-[Ir(dFppy)$_3$] used in this study are not sufficient to oxidize or reduce 2-isoxazoline **14** indicating that a single-electron transfer mechanism is unlikely.



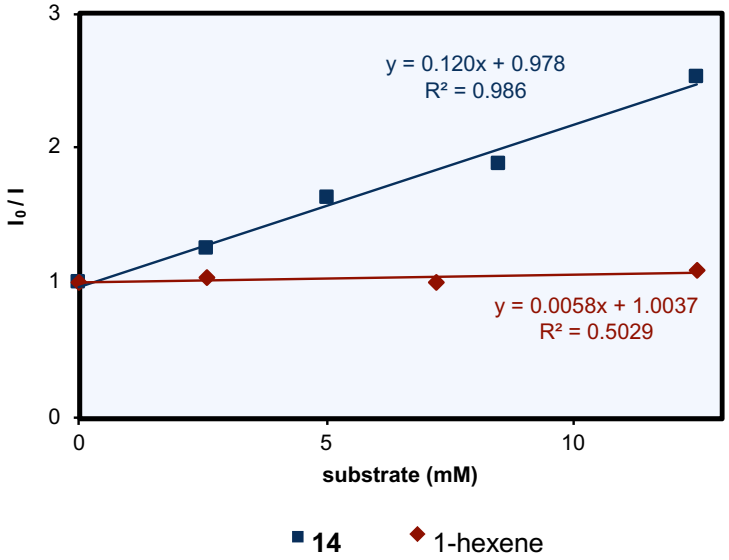
Supplementary Figure 5: Cyclic voltammogram of **14** (blue line). **14** shows an irreversible reduction process at $E_{p/2}$ = –2.01 V (vs. SCE) and a weak oxidation process at approximately 1.57 V.



Supplementary Figure 6: Cyclic voltammogram of *exo*-**19** (blue line), **40** (green line) and *endo*-**19** (red line). The compounds show an irreversible oxidation process at $E_{p/2}$ (*exo*-**19**)= +1.51 V, $E_{p/2}$ (**40**)= +1.25 V and $E_{p/2}$ (*endo*-**19**)= +1.33 V, respectively. (vs. SCE).

Stern-Volmer Quenching Studies

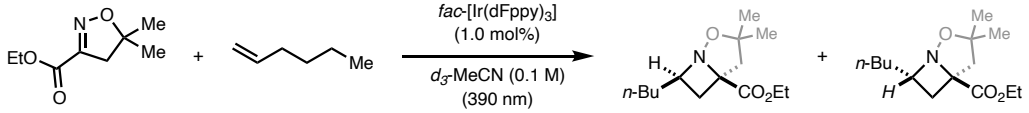
Samples for the quenching study were prepared using stock solutions of **14** (103 mM), 1-hexene (103 mM) and *fac*-[Ir(dFppy)$_3$] (0.05 mM) in dry MeCN. To a 4-mL volumetric flask was added *fac*-[Ir(dFppy)$_3$] (572 µL) and the respective amount of quencher (for **14**: 0 µL, 100 µL, 195 µL, 332 µL, 488 µL; for 1-hexene: 0 µL; 100 µL, 280 µL, 485 µL) and the volume adjusted to 4 mL with dry MeCN. The solution was transferred to a 1-cm quartz cuvette, which was sealed with a septum-equipped cap and degassed by sparging with nitrogen gas for 15 min. Emission spectra were recorded using a PTI quantaMaster fluorimeter (Horiba) with an excitation wavelength of 420 nm. Emission was observed at 480 nm and the ratio of I_0/I plotted as a function of the quencher concentration (I_0: emission intensity without quencher; I: emission intensity with quencher). The Stern-Volmer analysis shows that 2-isoxazoline **14** is a quencher of the photocatalyst *fac*-[Ir(dFppy)$_3$] with a quenching rate K_{SV} = 0.12 mM^{-1}, while 1-hexene does not quench the photocatalyst.



[**14**] (mM)	I_0 / I
0.0	1.0
2.6	1.3
5.0	1.6
8.5	1.9
12.5	2.5
[1-hexene] (mM)	I_0 / I
0.0	1.0
2.6	1.0
7.2	1.0
12.5	1.1

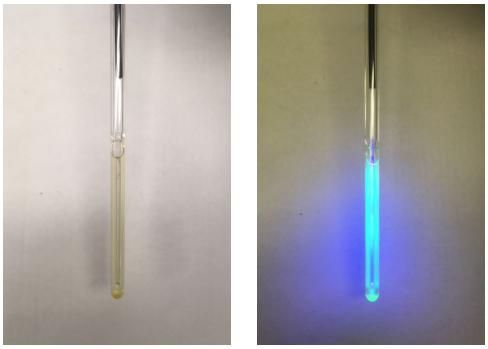
Supplementary Figure 7: Stern-Volmer quenching study. Data was obtained for **14** (blue squares) and 1-hexene (red diamonds) using *fac*-[Ir(dFppy)$_3$]. The data was fitted through linear regression for **14** (y = 0.120*x* + 0.978; R^2 = 0.986; blue line) and 1-hexene (*y* = 0.0058*x* + 1.004; R^2 = 0.503; red line).

In Situ ^{1}H NMR Experiment



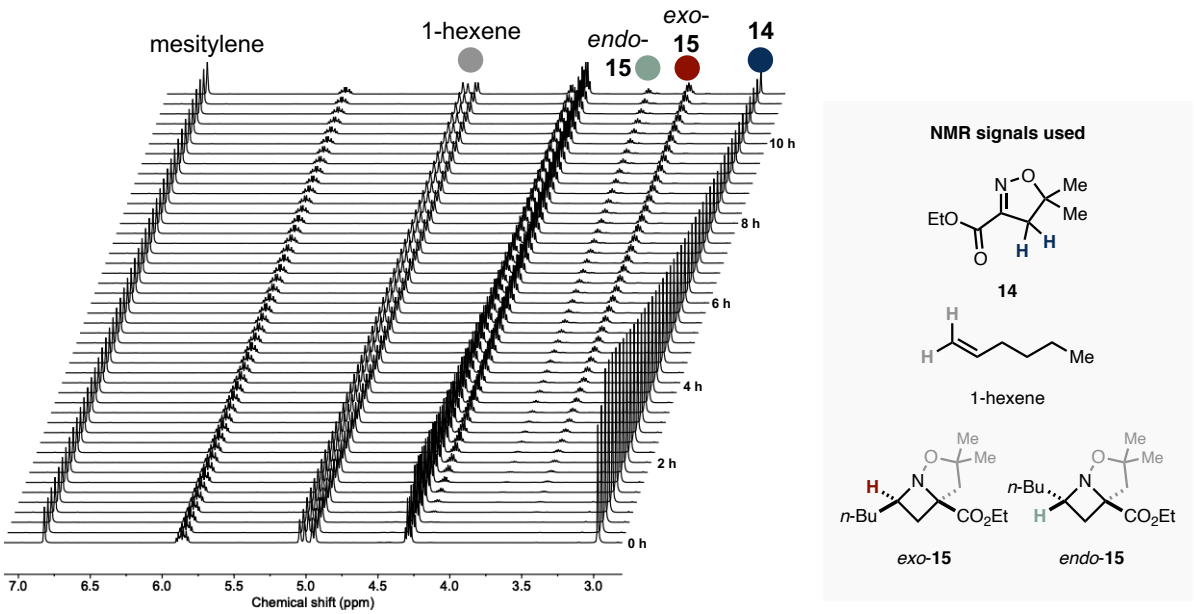
14 1-hexene *exo*-**15** *endo*-**15**

A 1-dram vial was charged with **14** (34 mg, 0.2 mmol, 1.0 equiv.), *fac*-[Ir(dFppy)$_3$] (2 mg, 1 mol%) and d_3-MeCN (2 mL). The mixture was homogenized by sonicating for 1 min. Then, mesitylene (~5 µL) and 1-hexene (37 µL, 0.3 mmol, 1.5 equiv.) were added. The reaction was carried out with a LED NMR setup by Goldstone Scientific (Mic-LED-NMR). A volume of 600 µL of the prepared solution was transferred to a 5 mm thin-wall NMR tube, which was fitted with a coaxial glass insert containing a fiber-optic cable and the tube sealed with a cap and parafilm. The sample was inserted into a Varian vnmrs 500 and the reaction mixture irradiated through the fiber-optic cable with a LED light (390 nm) at ambient temperature. Concentrations of all reactants and products were monitored by ^{1}H NMR in 15 min increments in reference to mesitylene as internal standard. After a reaction time of 11.5 h the reaction reached 84% conversion with 81% yield of product. The product diastereomer ratio was found to be constant (d.r. = 2.9) during the course of the reaction.

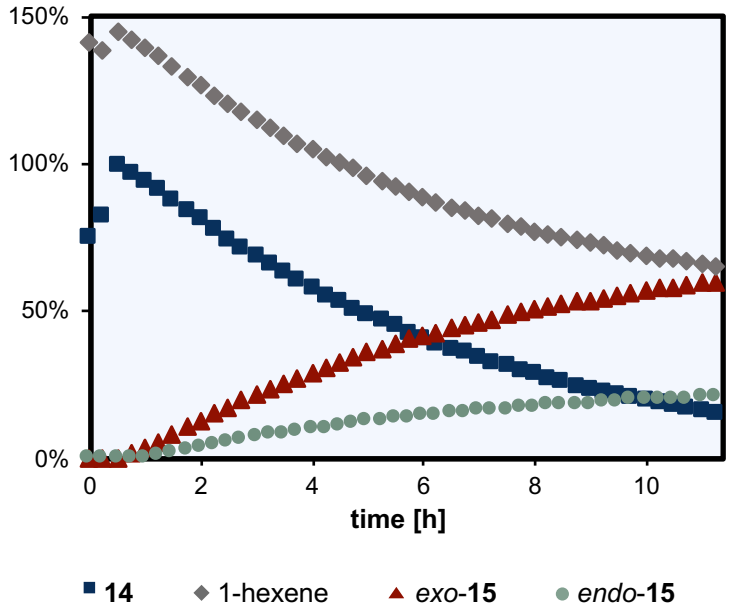


Supplementary Figure 8: Reaction mixture in NMR tube containing the glass insert and fiber-optic cable. Left: Reaction mixture with LED light turned off. Right: Reaction mixture with LED light turned on.

A. Stacked NMR data of the kinetic experiment



B. ^{1}H NMR time study of title reaction



Supplementary Figure 9: *In situ* ^{1}H NMR time study of title reaction **A.** Stacked NMR data of the kinetic experiments **B.** 2-Isoxazoline **14** (blue squares) was reacted with 1-hexene (grey diamonds) under standard conditions and the formation of *exo*-**15** (red triangles) and *endo*-**15** (green circles) observed.

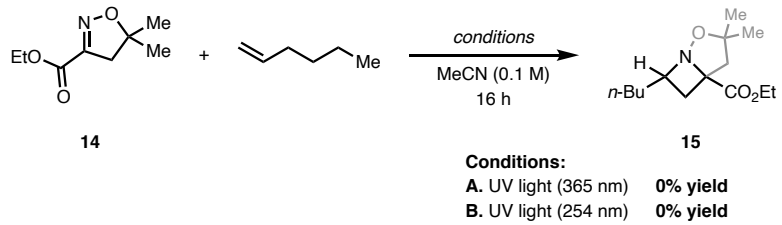
Supplementary Table 8. ^{1}H NMR time study

time [h]	**14** (%)	1-hexene (%)	*exo*-**15** (%)	*endo*-**15** (%)
0.00	76	142	0	0
0.25	83	139	0	0
0.50	100	145	0	0
0.75	98	143	2	0
1.00	95	140	4	1
1.25	92	137	6	2
1.50	88	133	8	3
1.75	85	130	11	3
2.00	82	127	13	4
2.25	78	124	16	5
2.50	75	121	18	6
2.75	72	118	20	7
3.00	69	115	22	7
3.25	66	113	24	8
3.50	64	110	26	9
3.75	61	107	28	10
4.00	58	105	30	10
4.25	56	103	32	11
4.50	54	101	33	12
4.75	51	99	35	12
5.00	49	96	37	13
5.25	47	94	38	13
5.50	45	93	39	14
5.75	43	91	41	14
6.00	41	89	42	15
6.25	40	88	43	15
6.50	38	86	45	16
6.75	36	85	46	16
7.00	35	83	47	16
7.25	33	82	48	17
7.50	32	80	49	17
7.75	30	79	50	17
8.00	29	78	51	18
8.25	28	77	52	18
8.50	26	76	53	18
8.75	25	74	54	19
9.00	24	73	54	19
9.25	23	72	55	19
9.50	22	71	56	20
9.75	21	70	57	20
10.00	20	70	58	20
10.25	19	69	58	20
10.50	18	68	59	21
10.75	17	67	59	21
11.00	17	67	60	21
11.25	16	66	60	21

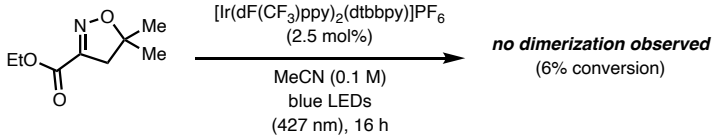
Data was obtained from the integration of the ^{1}H NMR signals as indicated in Supplementary Figure 9A using mesitylene as an internal standard. A percentage of 100% is equivalent to a concentration of 0.1 M.

Control Reactions

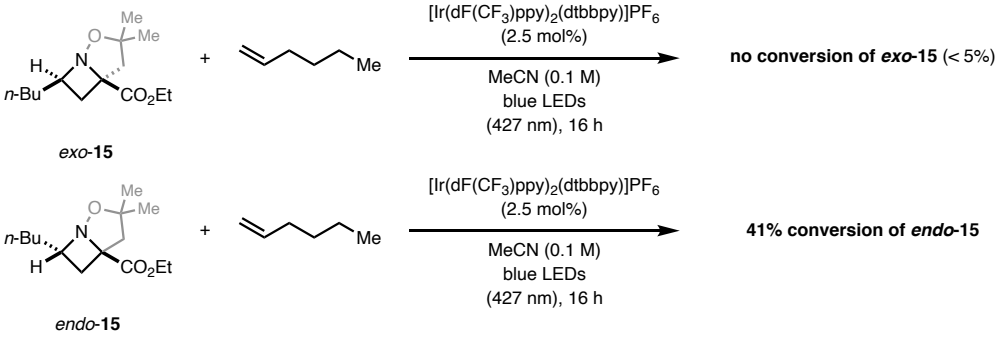
General procedure: A 1-dram vial was charged with substrate (0.1 mmol, 1.0 equiv.), photocatalyst (1-2.5 mol%) and MeCN (1 mL). The vial was subsequently sealed with a septum-equipped cap and the reaction mixture degassed by sparging with nitrogen gas for 5 min. Then, 1-hexene was added via syringe, the vial sealed with electrical tape and the reaction stirred under irradiation with blue LED lights (427 nm) at ambient temperature (fan cooling) for 16-18 h. The solvent was removed *in vacuo* and the crude reaction mixture analyzed by ^{1}H NMR using mesitylene as internal standard.



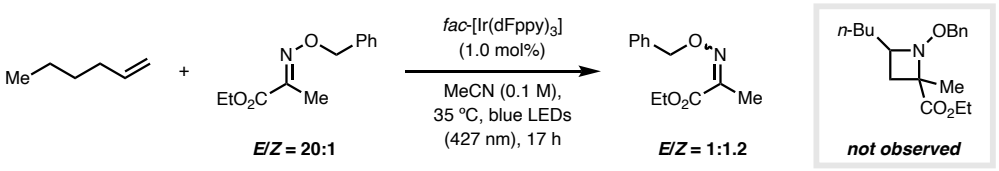
Supplementary Figure 10: Light/catalyst control reactions. No product formation was observed in the absence of photocatalyst or light.



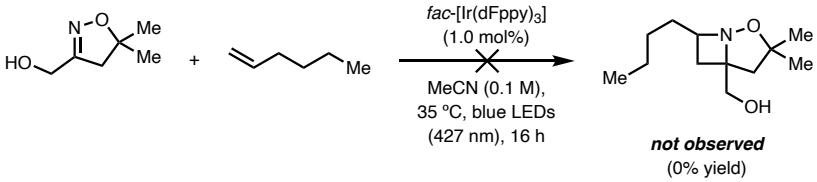
Supplementary Figure 11: Control reaction with 2-isoxazoline **14**. The 2-isoxazolines used in this study do not undergo undesired side reactions, such as dimerization.



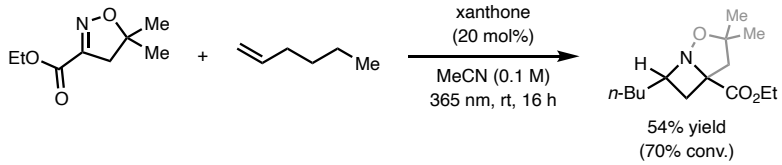
Supplementary Figure 12: Control reactions with both azetidine diastereomers **15**. The minor diastereomer *endo*-**15** decomposes under the reaction conditions using [Ir(dF(CF$_3$)ppy)$_2$(dtbbpy)]PF$_6$ as photocatalyst. No distinct decomposition products could be detected. This reactivity is likely due to an undesired single-electron oxidation of the azetidine, as indicated by the lower redox potential of *endo*-diastereomers of similar azetidines, for example *endo*-/*exo*- **19** (Supplementary Figure 6). This decomposition process is likely responsible for the diminished yields with strongly oxidizing catalysts such as [Ir(dF(Me)ppy)$_2$(dtbbpy)]PF$_6$ and [Ir(dF(CF$_3$)ppy)$_2$(dtbbpy)]PF$_6$ (Supplementary Table 2, entries 2+3).



Supplementary Figure 13: Control reaction with acyclic oxime **71**. No [2+2] cycloaddition product was observed under standard conditions, showing that a cyclic oxime (2-isoxazoline) is required for reactivity. Oxime isomerization of **71** (*E*/*Z* = 20:1 to 1:1.2) indicates that triplet sensitization of the substrate by the photocatalyst takes place under the reaction conditions. In contrast, no isomerization was observed when the reaction was conducted in the absence of photocatalyst.

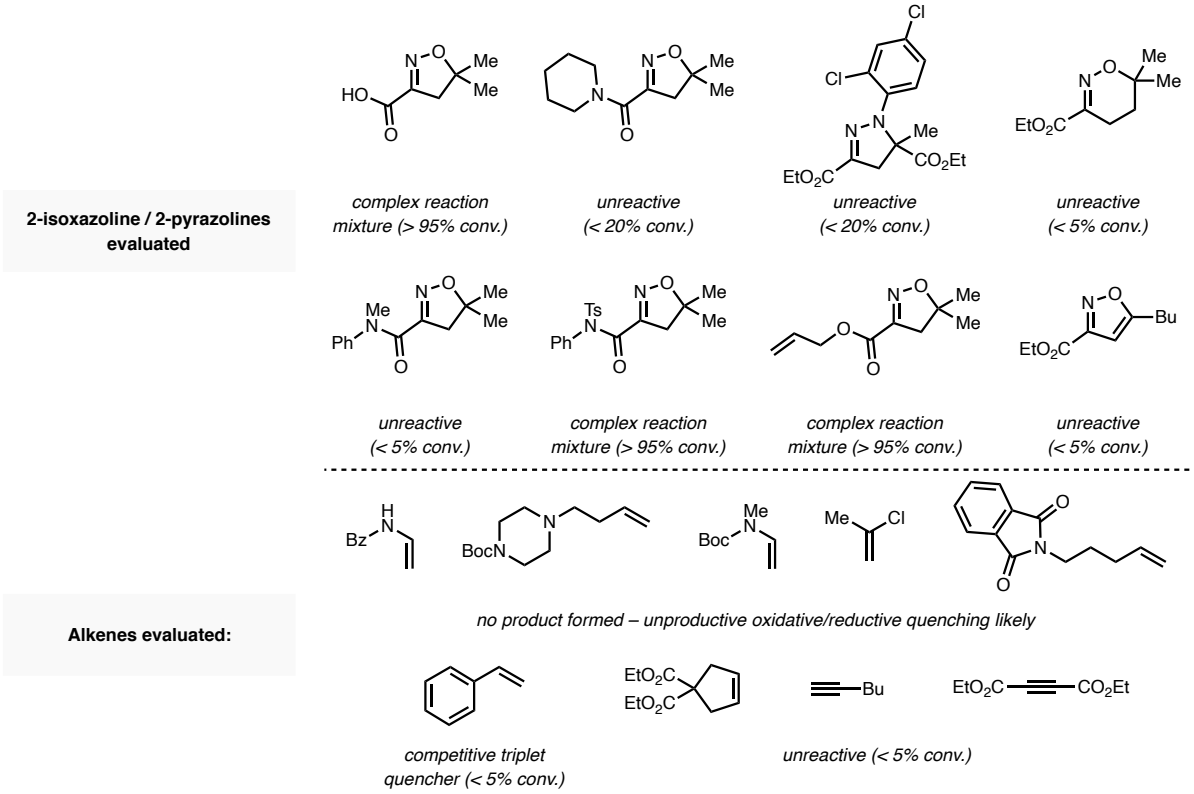


Supplementary Figure 14: Control reaction with 2-isoxazoline **70**. No [2+2] cycloaddition product was observed when 2-isoxazoline **70** was reacted under standard conditions. This highlights that the ester moiety (**14**) is necessary for reactivity.



Supplementary Figure 15: Control reaction with 2-isoxazoline **14**. The aza Paternò-Büchi reaction can be carried out with organic triplet sensitizers such as xanthone.

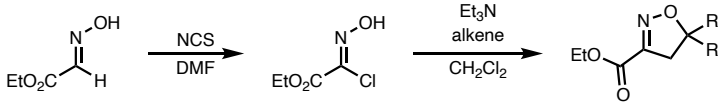
Other Evaluated Substrates in the Photochemical [2+2] Cycloaddition



Supplementary Figure 16: Additional substrates evaluated in the developed intermolecular aza Paternò-Büchi reaction.

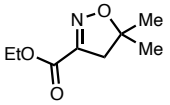
8) Experimental Procedures

General Procedure for Synthesis of 2-Isoxazolines via (3+2) Cycloaddition (GP-1)



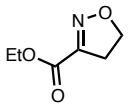
A round-bottom flask equipped with a magnetic stir bar was charged with ethyl 2-(hydroxyimino)acetate[7] (1.0 equiv.) and DMF (0.5 M). *N*-chlorosuccinimide (1.0 equiv.) was added and the resulting mixture stirred at 60 ºC for 2 h. After cooling to rt, the reaction mixture was partitioned between water and EtOAc. The organic layer was separated, and the aqueous layer extracted with EtOAc (2x). The combined organic layers were washed with water (2x), brine, dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford ethyl 2-chloro-2-(hydroxyimino)acetate as colorless solid.

A round-bottom flask containing ethyl 2-chloro-2-(hydroxyimino)acetate was equipped with a magnetic stir bar, charged with the corresponding alkene (1.5-33.4 equiv.) and CH_2Cl_2 (0.3 M), and subsequently sealed with a rubber septum. Next, Et_3N (1.0 equiv.) was added dropwise over 2-4 h using a syrringe pump, and, after completion of addition, the reaction stirred for additional 0.5-12 h. The resulting reaction mixture was washed with 0.5 M HCl (aq.) and the aqueous layer extracted with CH_2Cl_2 (2x). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude mixture was purified by flash column chromatography to afford the pure title compound.
Note: For cyclic 2-isoxazolines **S30**, **S40** and **S62**, the alkene was added by sparging the solution with the corresponding gaseous alkene after sealing the flask with a rubber septum, and the reaction carried out under an atmosphere of the alkene. The amount of added alkene was determined by weighing the gas container before and after addition of alkene.



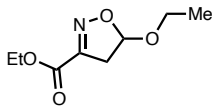
Ethyl 5,5-dimethyl-4,5-dihydroisoxazole-3-carboxylate (14): Prepared according to GP-1 using ethyl 2-(hydroxyimino)acetate[7] (5.00 g, 42.7 mmol, 1.0 equiv.), *N*-chlorosuccinimide (5.70 g, 42.7 mmol, 1.0 equiv.), Et_3N (6.0 mL, 42.7 mmol, 1.0 equiv.) and 2-methylpropene (24.0 g, 427 mmol, 10.0 equiv.). Purification by flash column chromatography (5-20% EtOAc/hexanes) afforded the pure title compound as colorless low-melting solid (4.62 g, 63%). Spectroscopic data were consistent with those reported in the literature.[5]

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.34 (q, *J* = 7.1 Hz, 2H), 2.96 (s, 2H), 1.46 (s, 6H), 1.37 (t, *J* = 7.1 Hz, 3H).



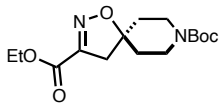
Ethyl 4,5-dihydroisoxazole-3-carboxylate (S19): Prepared according to GP-1 using ethyl 2-(hydroxyimino)acetate[7] (750 mg, 6.4 mmol, 1.0 equiv.), *N*-chlorosuccinimide (855 mg, 6.4 mmol, 1.0 equiv.), Et_3N (0.89 mL, 6.4 mmol, 1.0 equiv.) and ethylene (6.00 g, 214 mmol, 33.4 equiv.). Purification by flash column chromatography (5-35% EtOAc/hexanes) afforded the pure title compound as colorless oil (600 mg, 65%).

^{1}H NMR (700 MHz, $CDCl_3$): δ 4.54 (t, *J* = 10.7 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.21 (t, *J* = 10.7 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H).; **^{13}C NMR** (176 MHz, $CDCl_3$): δ 160.8, 151.9, 71.4, 62.2, 33.9, 14.2; **IR** (cm^{-1}): 2984, 2361, 2338, 1715, 1685, 1587, 1404, 1333, 1254, 1118, 1017, 916, 858, 818, 748; **HRMS**: *m*/*z* calculated for $C_6H_{10}NO_3^+$ $[M+H]^+$: 144.0655; found: 144.0656.



Ethyl 5-ethoxy-4,5-dihydroisoxazole-3-carboxylate (S23): Prepared according to GP-1 using ethyl 2-(hydroxyimino)acetate[7] (293 mg, 2.5 mmol, 1.0 equiv.), *N*-chlorosuccinimide (334 mg, 2.5 mmol, 1.0 equiv.), Et_3N (0.35 mL, 2.5 mmol, 1.0 equiv.) and ethyl vinyl ether (1.2 mL, 12.5 mmol, 5.0 equiv.). Purification by flash column chromatography (2-15% EtOAc/hexanes) afforded the pure title compound as colorless oil (328 mg, 70%).

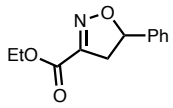
^{1}H NMR (500 MHz, $CDCl_3$): δ 5.70 (d, *J* = 6.9 Hz, 1H), 4.36 (q, *J* = 6.7 Hz, 2H), 3.90 (p, *J* = 7.4 Hz, 1H), 3.61 (p, *J* = 7.5 Hz, 1H), 3.23 (dd, *J* = 18.4, 6.9 Hz, 1H), 3.08 (d, *J* = 18.4 Hz, 1H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.22 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 160.4, 152.0, 105.0, 64.5, 62.2, 40.3, 15.1, 14.2; **IR** (cm^{-1}): 2981, 2361, 2338, 1718, 1589, 1374, 1339, 1260, 1190, 1130, 1090, 1017, 904, 850, 761, 741; **HRMS**: *m*/*z* calculated for $C_8H_{14}NO_4^+$ $[M+H]^+$: 188.0917; found: 188.0916.



8-(*Tert*-butyl) 3-ethyl 1-oxa-2,8-diazaspiro[4.5]dec-2-ene-3,8-dicarboxylate (S21): Prepared according to GP-1 using ethyl 2-(hydroxyimino)acetate[7] (293 mg, 2.5 mmol, 1.0 equiv.), *N*-chlorosuccinimide (334 mg, 2.5 mmol, 1.0 equiv.), Et_3N (0.35 mL, 2.5 mmol, 1.0 equiv.) and *tert*-butyl 4-methylenepiperidine-1-carboxylate[8]

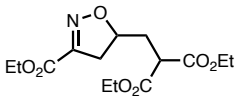
(740 mg, 3.8 mmol, 1.5 equiv.). Purification by flash column chromatography (7-40% EtOAc/hexanes) afforded the pure title compound as colorless solid (463 mg, 59%).

^{1}H NMR (700 MHz, $CDCl_3$): δ 4.35 (q, *J* = 7.1 Hz, 2H), 3.65 (b, 2H), 3.49 – 3.39 (m, 2H), 2.96 (s, 2H), 1.88 (d, *J* = 13.3 Hz, 2H), 1.70 (t, *J* = 9.0 Hz, 2H), 1.46 (s, 9H), 1.37 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 160.9, 154.7, 151.2, 88.0, 79.9, 62.2, 43.8, 40.7, 35.8, 28.5, 14.2; **IR** (cm^{-1}): 2979, 2927, 2361, 2338, 1734, 1695, 1429, 1366, 1152, 1110, 1077, 949, 855, 749; **HRMS**: *m*/*z* calculated for $C_{15}H_{24}N_2NaO_5^+$ $[M+Na]^+$: 335.1577; found: 335.1581.



Ethyl 5-phenyl-4,5-dihydroisoxazole-3-carboxylate (S22): Prepared according to GP-1 using ethyl 2-(hydroxyimino)acetate[7] (293 mg, 2.5 mmol, 1.0 equiv.), *N*-chlorosuccinimide (334 mg, 2.5 mmol, 1.0 equiv.), Et_3N (0.35 mL, 2.5 mmol, 1.0 equiv.) and styrene (0.57 mL, 5.0 mmol, 2.0 equiv.). Purification by flash column chromatography (7-40% EtOAc/hexanes) afforded the pure title compound as colorless oil (413 mg, 75%).

^{1}H NMR (700 MHz, $CDCl_3$): δ 7.42 – 7.37 (m, 2H), 7.37 – 7.31 (m, 3H), 5.79 (dd, *J* = 11.6, 8.9 Hz, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 3.64 (dd, *J* = 17.8, 11.6 Hz, 1H), 3.22 (dd, *J* = 17.8, 8.9 Hz, 1H), 1.38 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 160.7, 151.3, 139.6, 129.0, 128.8, 126.0, 85.1, 62.3, 41.6, 14.2; **IR** (cm^{-1}): 2983, 2361, 2338, 1717, 1588, 1379, 1333, 1243, 1119, 1016, 921, 860, 745, 698; **HRMS**: *m*/*z* calculated for $C_{12}H_{14}NO_3^+$ $[M+H]^+$: 220.0968; found: 220.0970.

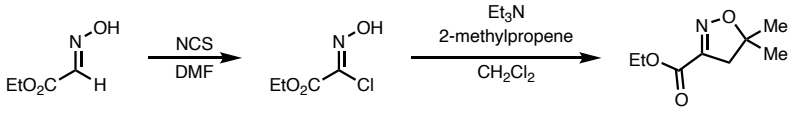


Diethyl 2-((3-(ethoxycarbonyl)-4,5-dihydroisoxazol-5-yl)methyl)malonate (S24): Prepared according to GP-1 using ethyl 2-(hydroxyimino)acetate[7] (293 mg, 2.5 mmol, 1.0 equiv.), *N*-chlorosuccinimide (334 mg, 2.5 mmol, 1.0 equiv.), Et_3N (0.35 mL, 2.5 mmol, 1.0 equiv.) and diethyl allylmalonate (0.99 mL, 5.0 mmol, 2.0 equiv.). Purification by flash column chromatography (5-40% EtOAc/hexanes) afforded the pure title compound as colorless oil (571 mg, 72%).

^{1}H NMR (700 MHz, $CDCl_3$): δ 4.90 – 4.83 (m, 1H), 4.35 (qd, *J* = 7.1, 1.4 Hz, 2H), 4.28 – 4.17 (m, 4H), 3.63 (dd, *J* = 8.8, 5.8 Hz, 1H), 3.33 (dd, *J* = 17.6, 10.9 Hz, 1H), 2.89 (dd, *J* = 17.6, 7.4 Hz, 1H), 2.28 – 2.18 (m, 2H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.28 (dt, *J* = 10.3, 7.1 Hz, 6H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 168.9, 168.8, 160.6, 151.6, 81.1, 62.3, 61.9 (2C), 48.4, 39.2, 34.3, 14.23, 14.15, 14.1; **IR** (cm^{-1}): 2983, 1721, 1590,

1446, 1370, 1239, 1175, 1149, 1018, 924, 859, 793, 748; **HRMS**: *m*/*z* calculated for $C_{14}H_{21}NNaO_7^+$ [M+Na]$^+$: 338.1210; found: 338.1214.

Procedure for 10 g Scale Synthesis of 14



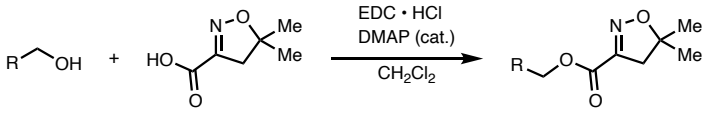
To a 250-mL round-bottom flask equipped with a magnetic stir bar containing ethyl 2-(hydroxyimino)acetate[7] (10.00 g, 85.4 mmol, 1.0 equiv.) and DMF (100 mL) was added *N*-chlorosuccinimide, and the resulting mixture heated at 60 ºC for 3.5 h. After cooling to rt, the reaction mixture was diluted with water (300 mL) and extracted with Et_2O (3x 200 mL). The combined organic layers were washed with water (200 mL) and brine (200 mL), then dried over $MgSO_4$, filtered and concentrated in vacuo to afford ethyl 2-chloro-2-(hydroxyimino)acetate as white solid.

Supplementary Figure 17. Experimental setup for scale-up synthesis of **14**.

Next, a 1-L three-neck round-bottom flask was equipped with a magnetic stir bar, nitrogen gas inlet and a condenser, which was cooled to –78 ºC and connected to a lecture bottle containing 2-methylpropene. The three-neck flask was cooled to approximately –20 ºC and 2-methylpropene gas (56 g, 998 mmol, 11.7 equiv.) was condensed into the flask. Ethyl 2-chloro-2-(hydroxyimino)acetate was added as solution in CH_2Cl_2 (300 mL) and the resulting mixture warmed up to 0 ºC with an ice bath. The ice bath was removed and Et_3N (12.0 mL, 85.4 mmol, 1.0 equiv.) was subsequently added dropwise using a syrringe pump over 6 h. After stirring for 10 h at rt, water (100 mL) was added, the organic layer separated and the aqueous layer extracted with CH_2Cl_2 (2x 50 mL). The combined organic layers were washed with brine (100 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (0-10% EtOAc/hexanes) afforded the pure title compound as colorless, low-melting solid (9.89 g, 68%). Spectroscopic data were consistent with those reported in the literature.[5]

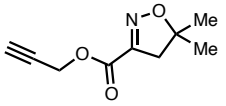
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.34 (q, *J* = 7.1 Hz, 2H), 2.96 (s, 2H), 1.46 (s, 6H), 1.37 (t, *J* = 7.1 Hz, 3H).

General Procedure for Synthesis of 2-Isoxazolines from A4 (GP-2)



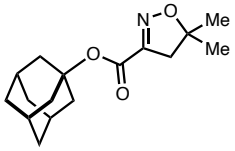
A4

To a round-bottom flask equipped with a magnetic stir bar containing **A4** (1.0 equiv.) and CH_2Cl_2 (0.1 M) were added the corresponding alcohol (1.0-2.0 equiv.) EDC • HCl (1.2 equiv.) and DMAP (0.2 equiv.). The resulting reaction mixture was stirred at rt until complete as judged by TLC analysis (6-24 h). Then, 1 M HCl (aq.) was added, the organic layer separated, and the aqueous layer extracted with CH_2Cl_2 (3x). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography to afford the pure title compound.



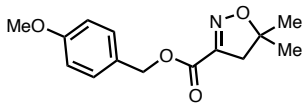
Prop-2-yn-1-yl 5,5-dimethyl-4,5-dihydroisoxazole-3-carboxylate (S25): Prepared according to GP-2 using **A4** (150 mg, 1.1 mmol, 1.0 equiv.), propargyl alcohol (0.12 mL, 2.1 mmol, 2.0 equiv.), EDC • HCl (241 mg, 1.3 mmol, 1.2 equiv.) and DMAP (26 mg, 0.2 mmol, 0.2 equiv.) with a reaction time of 6 h. Purification by flash column chromatography (5-30% EtOAc/hexanes) afforded the pure title compound as colorless oil (167 mg, 88%)

^{1}H NMR (700 MHz, $CDCl_3$): δ 4.87 (d, *J* = 2.5 Hz, 2H), 2.98 (s, 2H), 2.52 (t, *J* = 2.5 Hz, 1H), 1.47 (s, 6H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 160.4, 150.4, 89.1, 76.9, 75.9, 53.1, 45.1, 27.3; **IR** (cm^{-1}): 3279, 2977, 2362, 2337, 1723, 1581, 1437, 1380, 1338, 1285, 1230, 1118, 942, 742, 668; **HRMS**: *m*/*z* calculated for $C_9H_{12}NO_3^+$ $[M+H]^+$: 182.0812; found: 182.0809.



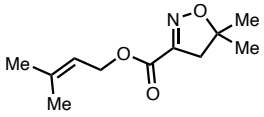
Adamantan-1-yl 5,5-dimethyl-4,5-dihydroisoxazole-3-carboxylate (S26): Prepared according to GP-2 using **A4** (150 mg, 1.1 mmol, 1.0 equiv.), 1-adamantanol (191 mg, 1.3 mmol, 1.2 equiv.), EDC • HCl (241 mg, 1.3 mmol, 1.2 equiv.) and DMAP (26 mg, 0.2 mmol, 0.2 equiv.) with a reaction time of 24 h. Purification by flash column chromatography (1-10% EtOAc/hexanes) afforded the pure title compound as white solid (143 mg, 49%).

^{1}H NMR (700 MHz, $CDCl_3$): δ 2.92 (s, 2H), 2.20 (s, 9H), 1.73 – 1.64 (m, 6H), 1.44 (s, 6H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 160.0, 152.4, 88.2, 83.4, 45.6, 41.4, 36.2, 31.1, 27.4; **IR** (cm^{-1}): 2912, 2856, 2362, 2337, 1724, 1577, 1457, 1344, 1279, 1235, 1054, 954, 741; **HRMS**: *m*/*z* calculated for $C_{16}H_{23}NNaO_3^+$ $[M+Na]^+$: 300.1570; found: 300.1571.



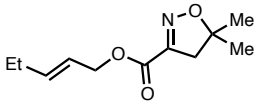
4-Methoxybenzyl 5,5-dimethyl-4,5-dihydroisoxazole-3-carboxylate (S27): Prepared according to GP-2 using **A4** (100 mg, 0.7 mmol, 1.0 equiv.), 4-methoxybenzyl alcohol (97 mg, 0.7 mmol, 1.0 equiv.), EDC • HCl (148 mg, 0.8 mmol, 1.1 equiv.) and DMAP (17 mg, 0.1 mmol, 0.2 equiv.) with a reaction time of 24 h. Purification by flash column chromatography (5-30% EtOAc/hexanes) afforded the pure title compound as colorless oil (135 mg, 73%).

^{1}H NMR (700 MHz, $CDCl_3$): δ 7.36 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 5.24 (s, 2H), 3.81 (s, 3H), 2.95 (s, 2H), 1.44 (s, 6H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 161.0, 159.9, 151.0, 130.6, 127.2, 114.0, 88.6, 67.3, 55.3, 45.2, 27.3; **IR** (cm^{-1}): 2959, 2836, 2361, 2338, 1712, 1513, 1298, 1234, 1179, 1121, 1092, 1033, 925, 851, 832, 768, 759; **HRMS**: *m*/*z* calculated for $C_{14}H_{17}NO_4^+$ $[M]^+$: 263.1152; found: 263.1158.



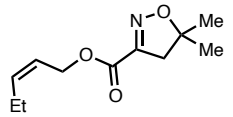
3-Methylbut-2-en-1-yl 5,5-dimethyl-4,5-dihydroisoxazole-3-carboxylate (S28): Prepared according to GP-2 using **A4** (143 mg, 1.0 mmol, 1.0 equiv.), 3-methyl-2-buten-1-ol (0.20 mL, 2.0 mmol, 2.0 equiv.), EDC • HCl (230 mg, 1.2 mmol, 1.2 equiv.) and DMAP (24 mg, 0.2 mmol, 0.2 equiv.) with a reaction time of 6 h. Purification by flash column chromatography (2-15% EtOAc/hexanes) afforded the pure title compound as colorless oil (198 mg, 94%).

^{1}H NMR (700 MHz, $CDCl_3$): δ 5.39 (t, *J* = 7.3 Hz, 1H), 4.75 (d, *J* = 7.4 Hz, 2H), 2.94 (d, *J* = 1.0 Hz, 2H), 1.74 (d, *J* = 16.9 Hz, 6H), 1.44 (s, 6H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 161.2, 151.2, 140.3, 117.9, 88.5, 62.8, 45.3, 27.3, 25.9, 18.2; **IR** (cm^{-1}): 2975, 2934, 1713, 1583, 1440, 1400, 1286, 1231, 1123, 940, 731; **HRMS**: *m*/*z* calculated for $C_{11}H_{17}NNaO_3^+$ $[M+Na]^+$: 234.1101; found: 234.1101.



(*E*)-Pent-2-en-1-yl 5,5-dimethyl-4,5-dihydroisoxazole-3-carboxylate (*E*-72): Prepared according to GP-2 using **A4** (143 mg, 1.0 mmol, 1.0 equiv.), *trans*-2-Penten-1-ol (0.20 mL, 2.0 mmol, 2.0 equiv.), EDC • HCl (230 mg, 1.2 mmol, 1.2 equiv.) and DMAP (24 mg, 0.2 mmol, 0.2 equiv.) with a reaction time of 18 h. Purification by flash column chromatography (2-15% EtOAc/hexanes) afforded the pure title compound as colorless oil (184 mg, 87%).

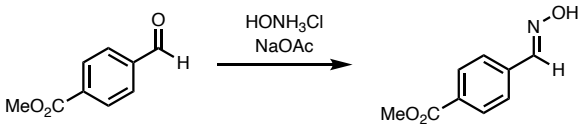
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.94 – 5.85 (m, 1H), 5.67 – 5.56 (m, 1H), 4.71 (d, *J* = 6.6 Hz, 2H), 2.96 (s, 2H), 2.08 (p, *J* = 7.1 Hz, 2H), 1.46 (s, 6H), 1.00 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 161.0, 151.1, 139.5, 122.0, 88.6, 66.7, 45.3, 27.3, 25.4, 13.1; **IR** (cm^{-1}): 2969, 2935, 1714, 1583, 1440, 1372, 1285, 1231, 1121, 938, 765, 745; **HRMS**: *m*/*z* calculated for $C_{11}H_{17}NNaO_3^+$ $[M+Na]^+$: 234.1101; found: 234.1100.



(*Z*)-Pent-2-en-1-yl 5,5-dimethyl-4,5-dihydroisoxazole-3-carboxylate (*Z*-72): Prepared according to GP-2 using **A4** (143 mg, 1.0 mmol, 1.0 equiv.), *cis*-2-Penten-1-ol (0.20 mL, 2.0 mmol, 2.0 equiv.), EDC • HCl (230 mg, 1.2 mmol, 1.2 equiv.) and DMAP (24 mg, 0.2 mmol, 0.2 equiv.) with a reaction time of 18 h. Purification by flash column chromatography (2-15% EtOAc/hexanes) afforded the pure title compound as colorless oil (195 mg, 92%).

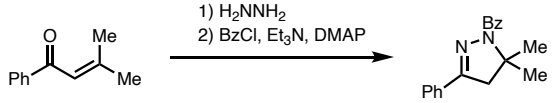
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.74 – 5.65 (m, 1H), 5.61 – 5.52 (m, 1H), 4.82 (d, *J* = 6.9 Hz, 2H), 2.96 (s, 2H), 2.15 (p, *J* = 7.3 Hz, 2H), 1.46 (s, 6H), 1.00 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 161.1, 151.0, 138.0, 121.9, 88.6, 61.6, 45.3, 27.3, 21.0, 14.1; **IR** (cm^{-1}): 2971, 2876, 1715, 1583, 1390, 1371, 1336, 1286, 1230, 1120, 939, 765, 745; **HRMS**: *m*/*z* calculated for $C_{11}H_{17}NNaO_3^+$ $[M+Na]^+$: 234.1101; found: 234.1103.

Miscellaneous Procedures

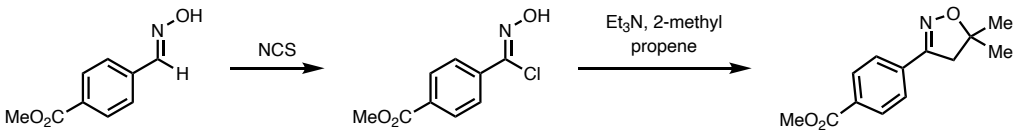


Methyl (*E*)-4-((hydroxyimino)methyl)benzoate (S17): A 50-mL round-bottom flask equipped with a magnetic stir bar was charged with methyl 4-formylbenzoate (1.00 g, 6.1 mmol, 1.0 equiv.) and MeOH (20 mL). Sodium acetate (1.50 g, 18.3 mmol, 3.0 equiv.) and hydroxylamine hydrochloride (466 mg, 6.7 mmol, 1.1 equiv.) were added sequentially and the resulting mixture stirred at rt for 18 h. $NaHCO_3$ (aq., sat.) was added and the organic solvent removed *in vacuo*. The residue was diluted with water and extracted with EtOAc (3x). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*, then dried using high-vac to afford the pure title compound as white solid. Spectroscopic data were consistent with those reported in the literature.[9]

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (s, 1H), 8.05 (d, *J* = 8.0 Hz, 2H), 7.65 (d, *J* = 8.1 Hz, 2H), 7.51 (s, 1H), 3.93 (d, *J* = 2.1 Hz, 3H).

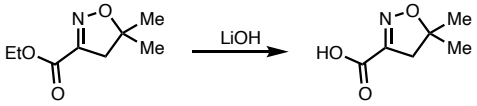


(5,5-Dimethyl-3-phenyl-4,5-dihydro-1*H*-pyrazol-1-yl)(phenyl)methanone (A3): A 25-mL round-bottom flask was charged with 3-methyl-1-phenylbut-2-en-1-one[10] (500 mg, 3.1 mmol, 1.0 equiv.) and EtOH (12 mL). Hydrazine hydrate (1.4 mL, 15.6 mmol, 5.0 equiv.) was added and the resulting reaction mixture heated at 70 ºC for 6 h. After cooling to rt the solvent was removed *in vacuo* and the resulting residue taken up in EtOAc. The organic layer was washed with NH_4Cl (aq., sat.) and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford 5,5-dimethyl-3-phenyl-4,5-dihydro-1*H*-pyrazole. The crude compound was dissolved in CH_2Cl_2 (15 mL) and benzoyl chloride (0.54 mL, 4.7 mmol, 1.5 equiv.), Et_3N (0.65 mL, 4.7 mmol, 1.5 equiv.) and DMAP (76 mg, 0.6 mmol, 0.2 equiv.) were sequentially added. After stirring the reaction mixture for 18 h at rt, the mixture was diluted with CH_2Cl_2 and washed with 1 M HCl (aq.) and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (2-20% EtOAc/hexanes) afforded the pure title compound as off-white solid (235 mg, 27%). Spectroscopic data were found consistent with those reported in the literature.[11]



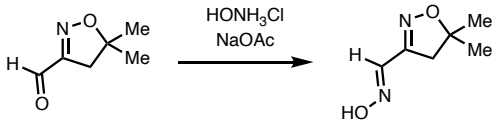
Methyl 4-(5,5-dimethyl-4,5-dihydroisoxazol-3-yl)benzoate (17): To a 25-mL round-bottom flask equipped with a magnetic stir bar containing **S17** (544 mg, 3.0 mmol, 1.0 equiv.) and DMF (10 mL) was added *N*-chlorosuccinimide (405 mg, 3.0 mmol, 1.0 equiv.). After heating for 2 h at 60 ºC, the reaction mixture was poured onto ice water. The white precipitate was collected by filtration to afford methyl (*Z*)-4-(chloro(hydroxyimino)methyl)benzoate, which was subsequently added to a 100-mL round-bottom flask and dissolved in CH_2Cl_2 (30 mL). The flask was sealed with a rubber septum and the solution sparged with 2-methyl propene for 20 min. Next, Et_3N (0.47 mL, 3.3 mmol, 1.1 equiv.) was added dropwise over 2 h using a syrringe pump and the reaction stirred for additional 0.5 h at rt under an atmosphere of 2-methylpropene. The reaction mixture was diluted with CH_2Cl_2 and washed with 0.2 M HCl (aq.) and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatograpny (5-30% EtOAc/hexanes) afforded the pure title compound as white solid (448 mg, 63%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, *J* = 8.5 Hz, 2H), 7.71 (d, *J* = 8.5 Hz, 2H), 3.93 (s, 3H), 3.12 (s, 2H), 1.51 (s, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 166.7, 155.7, 134.7, 131.1, 130.0, 126.4, 85.9, 52.4, 46.6, 27.5; **IR** (cm^{-1}): 2972, 1709, 1609, 1588, 1436, 1370, 1274, 1101, 960, 904, 860, 770, 693; **HRMS**: *m*/*z* calculated for $C_{13}H_{16}NO_3^+$ $[M+H]^+$: 234.1125; found: 234.1125.



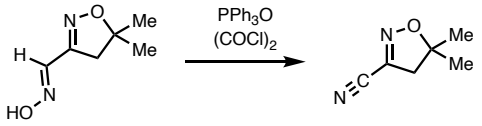
5,5-Dimethyl-4,5-dihydroisoxazole-3-carboxylic acid (A4): To a 50-mL round-bottom flask equipped with a magnetic stir bar was added **14** (1.00 g, 5.8 mmol, 1.0 equiv.) and a 3:1 mixture of methanol/H_2O (20 mL). Lithium hydroxide monohydrate (270 mg, 6.4 mmol, 1.1 equiv.) was added and the reaction mixture stirred for 12 h at rt. Next, the solution was acidified with 1 M HCl (aq.) and subsequently extracted with CH_2Cl_2 (10x). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*, then dried using high-vac to afford the pure title compound as white solid (773 mg, 92%).

^{1}H NMR (700 MHz, $CDCl_3$): δ 2.98 (s, 2H), 1.49 (s, 6H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 164.2, 150.7, 90.2, 44.5, 27.4; **IR** (cm^{-1}): 3381, 2978, 1704, 1587, 1439, 1289, 1240, 1139, 1020, 949, 724; **HRMS**: *m*/*z* calculated for $C_6H_{10}NO_3^+$ $[M+H]^+$: 144.0655; found: 144.0655.



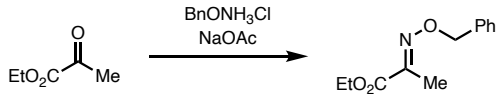
5,5-Dimethyl-4,5-dihydroisoxazole-3-carbaldehyde oxime (S29a): A 25-mL round-bottom flask equipped with a magnetic stir bar was charged with 5,5-dimethyl-4,5-dihydroisoxazole-3-carbaldehyde[5] (160 mg, 1.3 mmol, 1.0 equiv.). MeOH (10 mL) was added, followed by sequential addition of hydroxylamine hydrochloride (175 mg, 2.5 mmol, 2.0 equiv.) and sodium acetate (413 mg, 5.0 mmol, 4.0 equiv.). After stirring for 16 h at rt, the mixture mixture was concentrated *in vacuo*. The residue was diluted with $NaHCO_3$ (aq., sat.) and extracted with EtOAc (3x). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*, then dried using high-vac to afford the pure title compound as white solid (123 mg, 69%; 4:1 mixture of oxime isomers).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.48 (s, 1H; minor), 8.07 (s, 4H; major), 8.04 (s, 4H; major), 7.40 (s, 1H; minor), 3.25 (s, 2H; minor), 2.91 (s, 8H; major), 1.44 (d, J = 1.7 Hz, 30H; major+minor); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 154.0, 143.8 (2C), 139.6, 87.1, 86.5, 48.5, 44.5, 27.2, 27.1; **IR** (cm^{-1}): 3245, 3179, 3089, 2999, 2982, 2937, 2859, 1467, 1432, 1369, 1292, 1154, 907, 855, 760, 730; **HRMS**: *m*/*z* calculated for $C_6H_{11}N_2O_2^+$ $[M+H]^+$: 143.0815; found: 143.0815.



5,5-Dimethyl-4,5-dihydroisoxazole-3-carbonitrile (S29): Adapted from a literature procedure procedure with minor modifications.[12] To a 10-mL round-bottom flask equipped with a magnetic stir bar containing a solution of triphenylphosphine (22 mg, 0.08 mmol, 0.1 equiv.) in EtOAc (2 mL) was added oxalyl chloride (0.1 mL, 1.2 mmol, 1.5 equiv.) dropwise. After stirring for 5 min at rt, a solution of **S29a** (110 mg, 0.8 mmol, 1.0 equiv.) in EtOAc (1 mL) was added dropwise over 0.5 h. The reaction mixture was stirred for 1 h at rt, after which it was concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (10-20% Et_2O/pentane) to afford the pure title compound as colorless oil (77 mg, 80%).

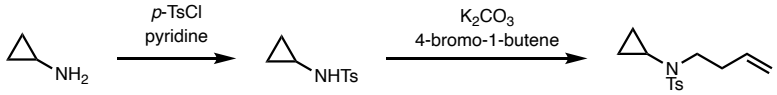
^{1}H NMR (500 MHz, $CDCl_3$): δ 2.93 (s, 2H), 1.49 (s, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 133.9, 111.6, 89.6, 46.9, 27.1; **IR** (cm^{-1}): 2982, 2236, 1555, 1462, 1374, 1324, 1263, 1150, 964, 827, 782, 663; **HRMS**: *m*/*z* calculated for $C_6H_8N_2O^+$ $[M]^+$: 124.0637; found: 124.0642.



Ethyl 2-((benzyloxy)imino)propanoate (*E*-71): To a 25-mL round-bottom flask equipped with a magnetic stir bar was added ethyl pyruvate (0.20 mL, 1.8 mmol, 1.0 equiv.) and EtOH (10 mL). After sequential addition of sodium acetate (591 mg, 7.2 mmol, 4.0 equiv.) and *O*-benzylhydroxylamine hydrochloride (575 mg, 3.6 mmol, 2.0 equiv.), the reaction was stirred for 14 h at rt. Next, $NaHCO_3$ (aq., sat.) was added and the organic solvent removed *in vacuo*. Water was added to the remaining residue and the mixture extracted with EtOAc (3x). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (2-10% EtOAc/hexanes) afforded the pure title compound as colorless oil (338 mg, 85%; *E*/*Z* = 20:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40 – 7.31 (m, 5H), 5.31 (s, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 2.09 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 163.9, 149.6, 136.8, 128.6, 128.4, 128.3, 77.7, 61.9, 14.3, 11.8; **IR** (cm^{-1}): 2982, 1715, 1613, 1497, 1454, 1366, 1317, 1148, 1009, 955, 923, 855, 754, 715, 696; **HRMS**: *m*/*z* calculated for $C_{12}H_{15}NNaO_3^+$ $[M+Na]^+$: 244.0944; found: 244.0946.

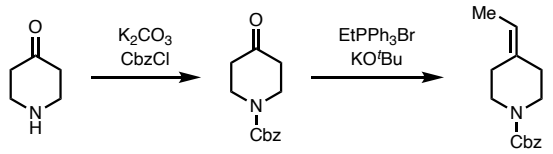
Synthesis of Alkene Starting Materials



***N*-(But-3-en-1-yl)-*N*-cyclopropyl-4-methylbenzenesulfonamide (S34):** A 10-mL round-bottom flask equipped with a magnetic stir bar was charged with cyclopropylamine (0.21 mL, 3.0 mmol, 1.0 equiv.) and water (3 mL). Pyridine (0.29 mL, 3.6 mmol, 1.2 equiv.) and 4-toluenesulfonyl chloride (636 mg, 3.3 mmol, 1.1 equiv.) were added sequentially and the reaction stirred for 1 h at rt. The resulting precipitate was collected by filtration and washed with water to afford *N*-cyclopropyl-4-methylbenzenesulfonamide as orange solid. The compound was dissolved in DMF (10 mL) followed by addition of K_2CO_3 (1.26 g, 9.1 mmol, 3.0 equiv.) and 4-bromo-1-butene (0.46 mL, 4.6 mmol, 1.5 equiv.). After stirring the reaction for 6 h at 80 ºC, the mixture was allowed to cool down to rt and diluted with water. After extracting with EtOAc (3x) the combined organic layers were washed with water (2x) and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (2-20% EtOAc/hexanes) afforded the product as colorless oil (150 mg, 19%).

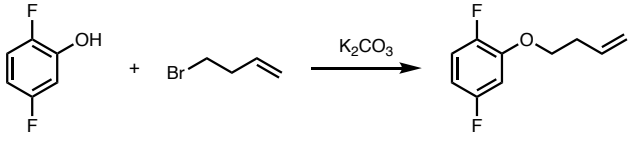
^{1}H NMR (700 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 5.74 (ddt, *J* = 17.1, 10.2, 6.8 Hz, 1H), 5.07 – 5.01 (m, 2H), 3.26 – 3.22 (m, 2H), 2.43 (s,

3H), 2.35 (q, *J* = 7.0 Hz, 2H), 2.04 (h, *J* = 6.9, 3.7 Hz, 1H), 0.87 – 0.83 (m, 2H), 0.71 – 0.67 (m, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 143.4, 135.8, 135.2, 129.6, 127.7, 116.9, 50.7, 33.1, 30.5, 21.6, 7.5; **IR** (cm^{-1}): 2924, 2361, 2338, 1457, 1341, 1160, 1090, 1028, 992, 916, 862, 814, 711, 691, 654; **HRMS**: *m*/*z* calculated for $C_{14}H_{19}NNaO_2S^+$ $[M+Na]^+$: 288.1029; found: 288.1024.



Benzyl 4-ethylidenepiperidine-1-carboxylate (S48): Benzyl 4-oxopiperidine-1-carboxylate was synthesized from piperidine-4-one hydrochloride (400 mg, 2.6 mmol, 1.0 equiv.) according to a literature procedure[13] and used for the next step without further purification. To a 25-mL round-bottom flask equipped with a magnetic stir bar containing a suspension of ethyltriphenylphosphonium bromide (1.45 g. 3.9 mmol, 1.5 equiv.) in Et_2O (10 mL) was added KO*t*-Bu (438 mg, 3.9 mmol, 1.5 equiv.) at 0 ºC. After stirring the mixture for 0.5 h, a solution of crude benzyl 4-oxopiperidine-1-carboxylate in Et_2O (2 mL) was slowly added and the reaction allowed to warm up to rt. After stirring for 2.5 h at rt, NH_4Cl (aq., sat.) and water were added, the organic layer separated, and the aqueous layer extracted with Et_2O (3x). The combined organic layers were washed with brine, dried over MgSO4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (1-10% EtOAc/hexanes) afforded the pure title compound as colorless oil (455 mg, 71%).

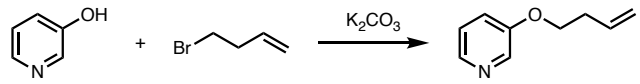
^{1}H NMR (700 MHz, $CDCl_3$): δ 7.39 – 7.29 (m, 5H), 5.29 (q, *J* = 6.5 Hz, 1H), 5.14 (s, 2H), 3.49 – 3.45 (m, 4H), 2.19 (d, *J* = 56.5 Hz, 4H), 1.60 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 155.4, 137.1, 135.1, 128.6, 128.1, 128.0, 118.4, 67.2, 45.9, 44.9, 35.8, 27.9, 12.8; **IR** (cm^{-1}): 2861, 2362, 2337, 1695, 1425, 1363, 1014, 963, 824, 734, 696 ; **HRMS**: *m*/*z* calculated for $C_{15}H_{19}NNaO_2^+$ $[M+Na]^+$: 268.1308; found: 268;1308.



2-(But-3-en-1-yloxy)-1,4-difluorobenzene (S38): A 25-mL round-bottom flask equipped with a magnetic stir bar was charged with 2,5-difluorophenol (325 mg, 2.5 mmol, 1.0 equiv.) and DMF (5 mL). K_2CO_3 (1.04 g, 7.5 mmol, 3.0 equiv.) and 4-bromo-1-butene (0.38 mL, 3.8 mmol, 1.5 equiv.) were added and the resulting heterogeneous mixture stirred for 20 h at 80 ºC. After cooling to rt, the mixture was diluted with water and extracted with EtOAc (3x). The combined organic layers were washed with water (2x) and brine, dried over Na_2SO_4, filtered and concentrated *in*

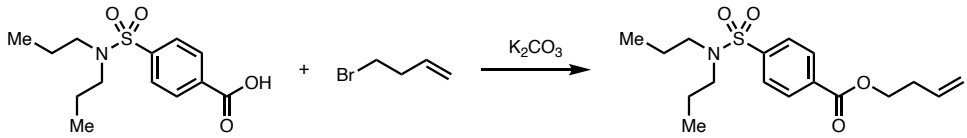
vacuo. Purification by flash column chromatography (1-5% EtOAc/hexanes) afforded the pure title compound as colorless, volatile oil (173 mg, 38%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.05 – 6.96 (m, 1H), 6.73 – 6.65 (m, 1H), 6.61 – 6.53 (m, 1H), 5.90 (ddt, *J* = 17.1, 10.3, 6.7 Hz, 1H), 5.22 – 5.10 (m, 2H), 4.05 (t, *J* = 6.8 Hz, 2H), 2.58 (q, *J* = 6.7 Hz, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 158.9 (dd, *J* = 241.8, 2.5 Hz), 149.1 (dd, *J* = 241.1, 3.3 Hz), 147.7 (dd, *J* = 12.5, 10.5 Hz), 133.9, 117.7, 116.3 (dd, *J* = 20.7, 10.2 Hz), 106.7 (dd, *J* = 23.8, 6.9 Hz), 102.9 (dd, *J* = 27.4, 2.0 Hz), 68.9, 33.5; **IR** (cm^{-1}): 2934, 1626, 1510, 1472, 1432, 1387, 1323, 1286, 1248, 1204, 1157, 1099, 1025, 990, 918, 834, 791, 726; **HRMS**: *m*/*z* calculated for $C_{10}H_{10}F_2O^+$ $[M]^+$: 184.0694; found: 184.0697.



3-(But-3-en-1-yloxy)pyridine (S35): A 25-mL round-bottom flask equipped with a magnetic stir bar was charged with 3-hydroxypyridine (238 mg, 2.5 mmol, 1.0 equiv.) and DMF (5 mL). K_2CO_3 (1.04 g, 7.5 mmol, 3.0 equiv.) and 4-bromo-1-butene (0.38 mL, 3.8 mmol, 1.5 equiv.) were added and the resulting heterogeneous mixture stirred for 20 h at 80 ºC. After cooling to rt, the mixture was diluted with water and extracted with EtOAc (3x). The combined organic layers were washed with water (2x) and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (10-40% EtOAc/hexanes) afforded the pure title compound as orange, volatile oil (70 mg, 19%).

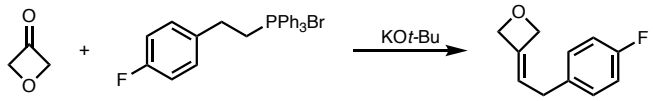
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32 (dd, *J* = 2.7, 1.1 Hz, 1H), 8.21 (dd, *J* = 4.3, 1.8 Hz, 1H), 7.24 – 7.15 (m, 2H), 5.96 – 5.84 (m, 1H), 5.18 (dt, *J* = 17.1, 1.7 Hz, 1H), 5.13 (dt, *J* = 10.3, 1.5 Hz, 1H), 4.06 (t, *J* = 6.7 Hz, 2H), 2.59 – 2.53 (m, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 155.2, 142.2, 138.2, 134.1, 123.9, 121.3, 117.5, 67.6, 33.6; **IR** (cm^{-1}): 2925, 1643, 1586, 1426, 1387, 1231, 1050, 1023, 991, 920, 798, 707; **HRMS**: *m*/*z* calculated for $C_9H_{12}NO^+$ $[M+H]^+$: 150.0913; found: 150.0908.



But-3-en-1-yl 4-(*N*,*N*-dipropylsulfamoyl)benzoate (S36): A 25-mL round-bottom flask equipped with a magnetic stir bar was charged with probenecid (713 mg, 2.5 mmol, 1.0 equiv.) and DMF (5 mL). K_2CO_3 (1.04 g, 7.5 mmol, 3.0 equiv.) and 4-bromo-1-butene (0.38 mL, 3.8 mmol, 1.5 equiv.) were added and the resulting heterogeneous mixture stirred for 2 h at 80 ºC. After cooling to rt, the mixture was diluted with water and extracted with EtOAc (3x). The combined organic layers were

washed with water (2x) and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (2-10% EtOAc/hexanes) afforded the pure title compound as colorless, volatile oil (0.85 g, quant.).

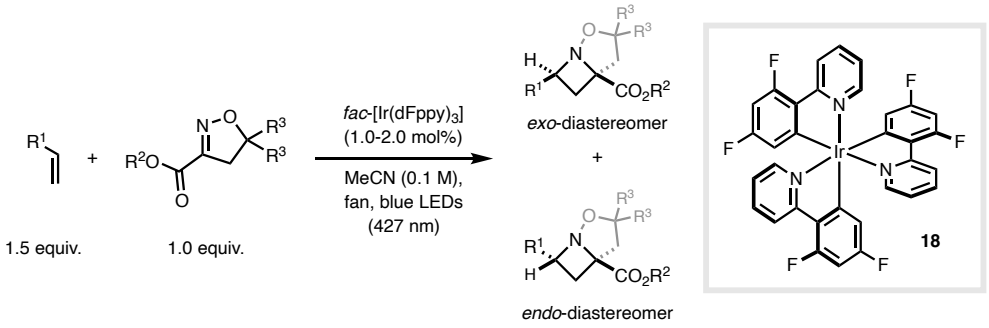
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.3 Hz, 2H), 7.87 (d, *J* = 8.3 Hz, 2H), 5.86 (ddt, *J* = 17.0, 10.3, 6.8 Hz, 1H), 5.15 (dd, *J* = 22.6, 13.7 Hz, 2H), 4.41 (t, *J* = 6.6 Hz, 2H), 3.12 – 3.06 (m, 4H), 2.54 (q, *J* = 6.6 Hz, 2H), 1.54 (dq, *J* = 14.9, 7.3 Hz, 4H), 0.86 (t, *J* = 7.4 Hz, 6H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 165.3, 144.3, 133.9, 133.7, 130.3, 127.1, 117.7, 64.8, 50.0, 33.2, 22.1, 11.3; **IR** (cm^{-1}): 2966, 2876, 1721, 1478, 1342, 1269, 1157, 1105, 1087, 990, 916, 862, 778, 738, 693; **HRMS**: *m*/*z* calculated for $C_{17}H_{26}NO_4S^+$ $[M+H]^+$: 340.1577; found: 340.1581.



3-(2-(4-Fluorophenyl)ethylidene)oxetane (S49): To a 100-mL round bottom flask equipped with a magnetic stir bar containing a suspension of bromo(4-fluorophenethyl)triphenyl-l^5-phosphane[8] (5.88 g, 12.6 mmol, 1.5 equiv.) in Et_2O (40 mL) was added KO*t*-Bu (1.42 g, 12.6 mmol, 1.5 equiv.) at 0 ºC and the reaction mixture stirred for 0.5 h at that temperature. Oxetan-3-one (0.54 mL, 8.4 mmol, 1.0 equiv.) was added dropwise and the resulting mixture allowed to warm up to rt and stirred for 16 h. NH_4Cl (aq., sat.) and water were added, the organic layer separated and the aqueous layer extrated with Et2O (3x). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (5-20% Et_2O/pentane) afforded the pure title compound as pale-yellow oil (688 mg, 46%).

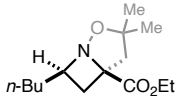
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16 – 7.10 (m, 2H), 7.01 – 6.94 (m, 2H), 5.35 – 5.25 (m, 1H), 5.25 – 5.17 (m, 2H), 5.18 – 5.12 (m, 2H), 3.18 (d, *J* = 7.1 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 161.6 (d, *J* = 243.9 Hz), 135.7, 135.4 (d, *J* = 3.4 Hz), 129.9 (d, *J* = 7.7 Hz), 118.1, 115.4 (d, *J* = 21.1 Hz), 79.5, 78.8, 33.8; **IR** (cm^{-1}): 2862, 1689, 1600, 1508, 1219, 1157, 1094, 1015, 946, 852, 822, 742; **HRMS**: *m*/*z* calculated for $C_{11}H_{11}FO^+$ $[M]^+$: 178.0794; found: 178.0799.

General Procedure for Photochemical [2+2] Cycloaddition (GP-3)



A 3-dram vial equipped with a magnetic stir bar was charged with 2-isoxazoline (0.25 mmol, 1.0 equiv.), alkene (if solid, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (0.2-2 mol%) and MeCN (2.5 mL). The vial was sealed with a septum-equipped cap and the reaction mixture degassed by sparging with nitrogen gas for 10 min. Then, alkene (if liquid, 1.5 equiv.) was added, the vial sealed with electrical tape and the reaction mixture homogenized by sonicating for approximately 30 seconds. Then, the reaction mixture was stirred at ambient temperature (fan cooling) under irradiation with blue LED lights (427 nm). After the indicated time (12-42 h), the reaction mixture was concentrated *in vacuo* and the crude reaction mixture analyzed by ^{1}H NMR to determine the diastereomer (d.r.) and regioisomer (r.r.) ratio, before purification by flash column chromatography to afford the corresponding pure azetidine product (major diastereomer is drawn).

Note: For **30**, **40** and **62**, the alkene was added by sparging the solution with the corresponding gaseous alkene after sealing the vial, and the reaction carried out under an atmosphere of the alkene.

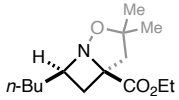


Ethyl 7-butyl-3,3-dimethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (15): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), 1-hexene (47 µL, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 19 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 3:1 and a regioisomer ratio of >20:1. Purification by flash column chromatography (5-40% EtOAc/hexanes) afforded the pure title compound as pale-yellow oil (54 mg, 84% combined yield; d.r. = 3:1). Characterization data for both diastereomers was obtained after separation by flash column chromatography (5-40% EtOAc/hexanes).

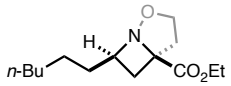
***exo*-Diastereomer (major): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.24 (q, *J* = 7.1 Hz, 2H), 3.46 (p, *J* = 8.4 Hz, 1H), 2.85 (d, *J* = 12.9 Hz, 1H), 2.47 (d, *J* = 12.9 Hz, 1H), 2.35 (dd, *J* = 11.1, 8.7 Hz, 1H), 1.98 (dd, *J* = 11.1, 8.5 Hz, 1H), 1.75 – 1.67 (m, 1H), 1.55 – 1.50 (m, 1H), 1.51 (s, 3H), 1.39 – 1.21 (m, 4H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.20 (s, 3H), 0.88 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 173.0, 87.2, 73.1, 67.4, 61.6, 51.1, 35.2, 30.4, 29.7, 28.5, 27.6, 22.8, 14.3, 14.2; **IR** (cm^{-1}): 2958, 2930, 2872, 1727, 1456, 1367, 1308, 1256, 1215, 1179, 1148, 1045, 864, 779, 733; **HRMS**: *m*/*z* calculated for $C_{14}H_{26}NO_3^+$ $[M+H]^+$: 256.1907; found: 256.1901.

***endo*-Diastereomer (minor): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.27 (qd, *J* = 7.1, 1.4 Hz, 2H), 3.88 (p, *J* = 7.8 Hz, 1H), 2.80 (dd, *J* = 11.6, 7.9 Hz, 1H), 2.72 (d, *J* = 12.4 Hz, 1H), 2.23 – 2.19 (m, 2H), 1.97 – 1.90 (m, 1H), 1.55 – 1.47 (m, 1H), 1.45 (s, 3H), 1.34 – 1.27 (m, 6H), 1.24 – 1.18 (m, 1H), 1.20 (s, 3H), 0.89 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 173.1, 83.6, 72.7, 61.7, 60.6, 52.9, 36.8, 31.3, 28.1, 27.1, 26.0, 22.8, 14.3, 14.1; **IR** (cm^{-1}): 2955, 2930, 2872, 1729, 1457, 1367, 1301, 1254, 1184, 1152, 1020, 924, 863, 785, 730; **HRMS**: *m*/*z* calculated for $C_{14}H_{26}NO_3^+$ $[M+H]^+$: 256.1907; found: 256.1907.

Minor Regioisomer (2:1 mixture of diastereomers A/B): **^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.34 – 4.22 (m, 6H; A+B), 3.86 (dd, *J* = 9.0, 7.7 Hz, 2H; A), 3.54 – 3.47 (m, 2H; B), 3.01 (t, *J* = 9.2 Hz, 2H; A), 2.84 (d, *J* = 12.8 Hz, 1H; B), 2.63 (d, *J* = 12.9 Hz, 2H; A), 2.59 – 2.50 (m, 6H; A+B), 1.59 – 1.45 (m, 15H; A+B), 1.36 – 1.08 (m, 21H; A+B), 1.17 (s, 6H; A), 1.12 (s, 3H; B), 0.90 – 0.85 (m, 9H; A+B); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 173.3, 172.0, 86.2, 86.0, 80.0, 79.1, 62.7, 61.6, 61.4, 60.0, 52.5, 43.9, 39.2, 33.8, 30.6, 30.1, 29.4, 29.1, 29.0, 28.8, 28.4, 28.1, 22.7, 22.6, 14.5, 14.3, 14.10, 14.06; **IR** (cm^{-1}): 2959, 2928, 2859, 1724, 1466, 1368, 1302, 1254, 1183, 1143, 1046, 866, 779, 708; **HRMS**: *m*/*z* calculated for $C_{14}H_{26}NO_3^+$ $[M+H]^+$: 256.1907; found: 256.1901.



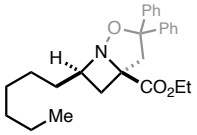
Ethyl 7-butyl-3,3-dimethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (15): Prepared according to GP-3 in a test tube (25x150 mm) using **14** (856 mg, 5.0 mmol, 1.0 equiv.), 1-hexene (0.93 mL, 7.5 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (7.6 mg, 0.2 mol%) and MeCN (15 mL) with a reaction time of 24 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 3:1 and a regioisomer ratio of >20:1. Purification by flash column chromatography (1-10% EtOAc/CH_2Cl_2) afforded the pure title compound as pale-yellow oil (1.14 g, 90% combined yield; d.r. = 3:1). Spectroscopic data was found consistent with that obtained, when conducting the reaction on 0.25 mmol scale.



Ethyl 7-hexyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (19): Prepared according to GP-3 using **S19** (36 mg, 0.25 mmol, 1.0 equiv.), 1-octene (59 µL, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 18 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 1.3:1 and a regioisomer ratio of >20:1. Purification by flash column chromatography (5-30% EtOAc/hexanes) afforded the pure *exo*-diastereomer as pale-yellow oil (34 mg, 53%) and the *endo*-diastereomer as pale-yellow oil (27 mg, 42%).

***exo*-Diastereomer (major): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.34 – 4.17 (m, 4H), 3.37 (p, *J* = 8.4 Hz, 1H), 2.59 (dt, *J* = 12.6, 8.8 Hz, 1H), 2.37 (ddd, *J* = 12.7, 6.8, 3.0 Hz, 1H), 2.27 (d, *J* = 9.1 Hz, 2H), 1.75 – 1.68 (m, 1H), 1.58 – 1.51 (m, 1H), 1.40 – 1.33 (m, 1H), 1.32 – 1.22 (m, 10H), 0.87 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 173.2, 71.6, 67.8, 61.7, 61.6, 39.1, 35.6, 31.9, 29.6, 29.2, 25.3, 22.7, 14.23, 14.16; **IR** (cm^{-1}): 2956, 2927, 2856, 1729, 1454, 1368, 1317, 1268, 1175, 1144, 1029, 907, 862, 725, 671; **HRMS**: *m*/*z* calculated for $C_{14}H_{26}NO_3^+$ $[M+H]^+$: 256.1907; found: 256.1904.

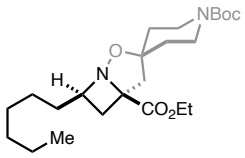
***endo*-Diastereomer (minor): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.32 – 4.17 (m, 4H), 4.00 (p, *J* = 8.4 Hz, 1H), 2.94 (dd, *J* = 12.1, 8.4 Hz, 1H), 2.54 (ddd, *J* = 12.3, 9.5, 7.5 Hz, 1H), 2.26 (ddd, *J* = 12.3, 5.9, 2.8 Hz, 1H), 2.00 (dd, *J* = 12.1, 8.9 Hz, 1H), 1.88 – 1.82 (m, 1H), 1.45 – 1.39 (m, 12H), 0.87 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.8, 73.0, 71.1, 62.7, 61.8, 39.8, 34.3, 31.8, 30.0, 29.3, 26.0, 22.7, 14.24, 14.18; **IR** (cm^{-1}): 2926, 2857, 1729, 1445, 1369, 1320, 1271, 1176, 1140, 1096, 1025, 997, 917, 862, 720; **HRMS**: *m*/*z* calculated for $C_{14}H_{26}NO_3^+$ $[M+H]^+$: 256.1907; found: 256.1905.



Ethyl 7-hexyl-3,3-diphenyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (20): Prepared according to GP-3 using isoxadifen-ethyl (74 mg, 0.25 mmol, 1.0 equiv.), 1-octene (59 µL, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (3.8 mg, 2 mol%) and MeCN (2.5 mL) with a reaction time of 40 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 2:1 and a regioisomer ratio of 17:1. Purification by flash column chromatography (50-100% CH_2Cl_2/hexanes) afforded the pure title compound as yellow oil (73 mg, 72% combined yield; d.r. = 2:1). Characterization data for both diastereomers was obtained after separation by flash column chromatography (5-40% EtOAc/hexanes).

***exo*-Diastereomer (major): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 7.44 (ddd, *J* = 15.3, 8.4, 1.3 Hz, 4H), 7.32 (t, *J* = 7.7 Hz, 2H), 7.27 – 7.22 (m, 3H), 7.18 – 7.13 (m, 1H), 3.88 (qd, *J* = 7.1, 2.1 Hz, 2H), 3.75 (d, *J* = 12.9 Hz, 1H), 3.58 (p, *J* = 8.0, 7.5 Hz, 1H), 3.24 (d, *J* = 12.9 Hz, 1H), 2.41 (dd, *J* = 11.1, 8.7 Hz, 1H), 1.93 (dd, *J* = 11.1, 8.5 Hz, 1H), 1.86 – 1.78 (m, 1H), 1.58 – 1.51 (m, 1H), 1.45 – 1.37 (m, 1H), 1.31 – 1.23 (m, 7H), 0.99 (t, *J* = 7.1 Hz, 3H), 0.87 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.0, 144.7, 144.6, 128.4, 128.1, 127.5, 127.1, 126.4, 126.2, 93.4, 72.8, 66.8, 61.4, 50.7, 35.5, 31.9, 30.1, 29.2, 25.4, 22.7, 14.2, 14.0; **IR** (cm^{-1}): 2954, 2926, 2855, 1725, 1492, 1447, 1368, 1312, 1222, 1180, 1081, 1031, 911, 862, 778, 749, 697; **HRMS**: *m*/*z* calculated for $C_{26}H_{34}NO_3^+$ $[M+H]^+$: 408.2533; found: 408.2528.

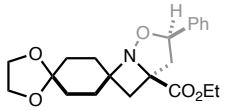
***endo*-Diastereomer (minor): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 7.49 (d, *J* = 7.3 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 2H), 7.30 (t, *J* = 7.7 Hz, 2H), 7.27 – 7.20 (m, 3H), 7.14 (t, *J* = 7.3 Hz, 1H), 4.02 (p, *J* = 7.4 Hz, 1H), 3.92 – 3.81 (m, 3H), 2.98 (d, *J* = 12.5 Hz, 1H), 2.66 (dd, *J* = 11.8, 8.3 Hz, 1H), 2.22 (dd, *J* = 11.8, 6.6 Hz, 1H), 2.07 – 1.99 (m, 1H), 1.52 – 1.40 (m, 2H), 1.31 – 1.17 (m, 7H), 0.95 (t, *J* = 7.1 Hz, 3H), 0.86 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.3, 144.2, 143.3, 128.4, 128.2, 127.4, 127.1, 126.0, 126.0, 90.4, 72.6, 61.7, 61.5, 52.2, 34.7, 32.4, 31.8, 29.3, 26.4, 22.7, 14.2, 14.0; **IR** (cm^{-1}): 2926, 2855, 1724, 1492, 1448, 1368, 1314, 1225, 1180, 1085, 1030, 965, 911, 860, 778, 749, 697; **HRMS**: *m*/*z* calculated for $C_{26}H_{34}NO_3^+$ $[M+H]^+$: 408.2533; found: 408.2528.



1'-(*Tert*-butyl) 5-ethyl 7-hexyl-2-oxa-1-azaspiro[bicyclo[3.2.0]heptane-3,4'-piperidine]-1',5-dicarboxylate (21): Prepared according to GP-3 using **S21** (78 mg, 0.25 mmol, 1.0 equiv.), 1-octene (59 mg, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 19.5 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 3:1 and a regioisomer ratio of 18:1. Purification by flash column chromatography (5-40% EtOAc/hexanes) afforded the pure *exo*-diastereomer as colorless oil (74 mg, 70%) and the *endo*-diastereomer as colorless oil (28 mg, 26%).

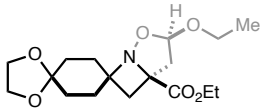
***exo*-Diastereomer (major): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.28 – 4.19 (m, 2H), 3.68 (b, 1H), 3.56 (b, 1H), 3.45 (p, *J* = 8.0 Hz, 1H), 3.31 (m, 2H), 2.89 (d, *J* = 13.1 Hz, 1H), 2.43 (d, *J* = 13.1 Hz, 1H), 2.34 (dd, *J* = 11.1, 8.6 Hz, 1H), 2.02 (dd, *J* = 11.2, 8.5 Hz, 1H), 1.93 – 1.86 (b, 1H), 1.86 – 1.79 (b, 1H), 1.76 – 1.65 (m, 2H), 1.55 – 1.50 (m, 1H), 1.48 – 1.44 (m, 1H), 1.44 (s, 9H), 1.40 – 1.33 (m, 1H), 1.32 – 1.24 (m, 10H), 0.87 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.7, 154.8, 87.1, 79.6, 72.5, 67.6, 61.7, 49.6, 41.5 (2C), 38.9, 36.7, 35.4, 31.9, 30.1, 29.3, 28.6, 25.3, 22.7, 14.3, 14.2; **IR** (cm^{-1}): 2927, 2856, 1729, 1690, 1451, 1419, 1365, 1306, 1277, 1239, 1177, 1146, 1095, 967, 862, 825, 767; **HRMS**: *m*/*z* calculated for $C_{23}H_{41}N_2O_5^+$ $[M+H]^+$: 425.3010; found: 425.3004.

***endo*-Diastereomer (minor): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.26 (q, *J* = 7.1 Hz, 2H), 3.90 (p, *J* = 7.7 Hz, 1H), 3.66 (b, 2H), 3.33 – 3.22 (m, 2H), 2.84 (dd, *J* = 11.7, 7.9 Hz, 1H), 2.74 (d, *J* = 12.6 Hz, 1H), 2.22 (dd, *J* = 11.7, 8.0 Hz, 1H), 2.15 (d, *J* = 12.7 Hz, 1H), 1.97 – 1.91 (m, 1H), 1.86 – 1.72 (m, 3H), 1.51 – 1.42 (m, 10H), 1.42 – 1.21 (m, 12H), 0.88 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.8, 154.9, 83.2, 79.6, 71.9, 61.9, 60.8, 51.4, 41.2 (2C), 36.7, 35.0, 34.7, 31.82, 31.77, 29.3, 28.6, 25.9, 22.7, 14.3, 14.2; **IR** (cm^{-1}): 2927, 2858, 1730, 1691, 1452, 1419, 1365, 1276, 1240, 1177, 1145, 1050, 967, 864, 828, 767; **HRMS**: *m*/*z* calculated for $C_{23}H_{41}N_2O_5^+$ $[M+H]^+$: 425.3010; found: 425.3001.



Ethyl 3-phenyl-4-oxa-5-azadispiro[bicyclo[3.2.0]heptane-6,1'-cyclohexane-4',2''-[1,3]dioxolane]-1-carboxylate (22): Prepared according to GP-3 using **S22** (55 mg, 0.25 mmol, 1.0 equiv.), 8-methylene-1,4-dioxaspiro[4.5]decane[14] (58 mg, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 19.5 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 4:1 and a regioisomer ratio of 18:1. Purification by flash column chromatography (5-30% EtOAc/hexanes) afforded the pure title compound as yellow oil (94 mg, 99% combined yield; d.r. = 4:1). Characterization data was obtained for a 3.8:1 mixture of *exo*/*endo* diastereomers.

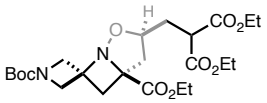
^{1}H NMR (700 MHz, $CDCl_3$): δ 7.45 (d, *J* = 7.2 Hz, 7.6H; major), 7.40 (d, *J* = 7.7 Hz, 2H; minor), 7.36 (t, *J* = 7.5 Hz, 9.6H: major+minor), 7.31 (t, *J* = 7.3 Hz, 4.8H; major+minor), 5.50 (dd, *J* = 10.2, 5.5 Hz, 3.8H; major), 5.19 (dd, *J* = 11.3, 4.9 Hz, 1H; minor), 4.35 – 4.19 (m, 9.6H; major+minor), 3.98 – 3.87 (m, 19.2H; major+minor), 3.08 (dd, *J* = 12.4, 4.9 Hz, 1H; minor), 2.70 (d, *J* = 12.3 Hz, 3.8H: major), 2.65 (dd, *J* = 12.7, 5.5 Hz, 3.8H; major), 2.58 (d, *J* = 12.0 Hz, 1H; minor), 2.50 (dd, *J* = 12.7, 10.2 Hz, 3.8H; major), 2.40 (dd, *J* = 12.4, 11.3 Hz, 1H; minor), 2.31 (d, *J* = 12.3 Hz, 3.8H; major), 2.30 – 2.26 (m, 1H; minor), 2.20 (d, *J* = 12.0 Hz, 1H; minor), 2.15 – 2.08 (m, 3.8H; major+minor), 2.02 – 1.74 (m, 24H; major+minor) 1.62 – 1.53 (m, 9.6H; major+minor), 1.35 (t, *J* = 7.1 Hz, 3H; minor), 1.30 (t, *J* = 7.1 Hz, 11.4H; major); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 173.2, 173.0, 138.4, 137.9, 128.7, 128.6, 128.4, 128.1, 126.8, 126.3, 108.2, 108.1, 84.9, 83.0, 71.7, 69.2, 65.3, 64.47, 64.46, 64.39, 64.35, 63.7, 62.0, 61.9, 49.0, 48.2, 38.7, 36.9, 36.3, 35.8, 31.39, 31.35, 31.3, 30.8, 30.6, 29.6, 14.3, 14.2; **IR** (cm^{-1}): 2951, 1723, 1445, 1375, 1300, 1241, 1180, 1156, 1102, 1032, 946, 926, 885, 751, 730, 699; **HRMS**: *m*/*z* calculated for $C_{21}H_{27}NNaO_5^+$ $[M+Na]^+$: 396.1781; found: 396.1771.



Ethyl 3-ethoxy-4-oxa-5-azadispiro[bicyclo[3.2.0]heptane-6,1'-cyclohexane-4',2''-[1,3]dioxolane]-1-carboxylate (23): Prepared according to GP-3 using **S23** (47 mg, 0.25 mmol, 1.0 equiv.), 8-methylene-1,4-dioxaspiro[4.5]decane[14] (58 mg, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (3.8 mg, 2 mol%) and MeCN (2.5 mL) with a reaction time of 36 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 1.2:1 and a regioisomer ratio of >20:1. Purification by flash column chromatography (10-40% EtOAc/CH_2Cl_2) afforded the pure title compound as pale-yellow oil (63 mg, 74% combined yield; d.r. = 1.2:1). Characterization data for both diastereomers was

obtained after separation by flash column chromatography (20-30% EtOAc/CH_2Cl_2). Characterization data was obtained for a 1.1:1 mixture of *exo*/*endo* diastereomers.

^{1}H NMR (700 MHz, $CDCl_3$): δ 5.44 (dd, *J* = 5.8, 2.0 Hz, 2.1H; major+minor), 4.31 – 4.18 (m, 4.2H; major+minor), 3.96 – 3.88 (m, 8.4H; major+minor), 3.84 – 3.73 (m, 2.1H; major+minor), 3.51 (dq, *J* = 9.6, 7.1 Hz, 1.1H; major), 3.37 (dq, *J* = 9.5, 7.0 Hz, 1H; minor), 3.02 (d, *J* = 13.1 Hz, 1H; minor), 2.84 (dd, *J* = 13.6, 6.2 Hz, 1.1H; major), 2.55 – 2.50 (m, 2.2H; major), 2.48 (dd, *J* = 13.2, 4.9 Hz, 1H; minor), 2.45 (dd, *J* = 13.6, 1.9 Hz, 1.1H; major), 2.27 – 2.19 (m, 2.1H; major+minor), 2.14 (d, *J* = 11.6 Hz, 1H; minor), 2.05 – 1.99 (m, 2H; minor), 1.96 – 1.72 (m, 8.5H; major+minor), 1.67 – 1.60 (m, 1H; minor), 1.59 – 1.45 (m, 4.2H; major+minor), 1.30 (td, *J* = 7.1, 2.4 Hz, 6.3H; major+minor), 1.22 (t, *J* = 7.1 Hz, 3.3H; major), 1.11 (t, *J* = 7.0 Hz, 3H; minor); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 173.1, 172.5, 108.5, 108.3, 108.0, 104.7, 69.6, 67.6, 64.7, 64.6, 64.40, 64.37, 64.35, 64.3, 64.0, 62.6, 61.8, 61.6, 46.8, 46.5, 38.1, 37.4, 36.4, 35.8, 31.4, 30.9 (2C), 30.69, 30.68, 30.1, 15.0, 14.9, 14.24, 14.18; **IR** (cm^{-1}): 2944, 1726, 1444, 1374, 1267, 1225, 1143, 1101, 1033, 993, 945, 925, 882, 771, 713, 662; **HRMS**: *m*/*z* calculated for $C_{17}H_{27}NNaO_6^+$ $[M+Na]^+$: 364.1731; found: 364.1725.

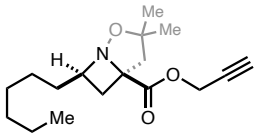


1-(*Tert*-butyl) 1'-ethyl 3'-(3-ethoxy-2-(ethoxycarbonyl)-3-oxopropyl)-4'-oxa-5'-azaspiro[azetidine-3,6'-bicyclo[3.2.0]heptane]-1,1'-dicarboxylate (24): Prepared according to GP-3 using **S24** (79 mg, 0.25 mmol, 1.0 equiv.), *tert*-butyl 3-methyleneazetidine-1-carboxylate[15] (64 mg, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 24 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 3:1 and a regioisomer ratio of >20:1. Purification by flash column chromatography (3-50% EtOAc/CH_2Cl_2) afforded the pure title compound as colorless oil (117 mg, 96% combined yield; d.r. = 3:1). Characterization data for both diastereomers was obtained after separation by flash column chromatography (30-50% EtOAc/hexanes).

***exo*-Diastereomer (major): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.31 (d, *J* = 9.5 Hz, 1H), 4.28 – 4.15 (m, 6H), 4.11 (d, *J* = 9.6 Hz, 1H), 4.00 – 3.94 (m, 1H), 3.88 (d, *J* = 9.6 Hz, 1H), 3.69 (d, *J* = 9.2 Hz, 1H), 3.63 (dd, *J* = 10.1, 4.9 Hz, 1H), 2.94 (d, *J* = 13.2 Hz, 1H), 2.40 (d, *J* = 13.2 Hz, 1H), 2.39 – 2.34 (m, 1H), 2.30 (dd, *J* = 12.7, 5.3 Hz, 1H), 2.21 – 2.11 (m, 2H), 1.40 (s, 9H), 1.28 (q, *J* = 7.2 Hz, 6H), 1.24 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 171.8, 169.2, 169.0, 156.1, 79.9, 79.3, 72.1, 62.5, 62.0, 61.93, 61.86, 61.8, 55.7, 49.1, 43.6, 37.3, 31.7, 28.4, 14.2, 14.14, 14.10; **IR** (cm^{-1}): 2979, 1729, 1700, 1447, 1392, 1367, 1304, 1247, 1203, 1159, 1091, 1025, 961, 930, 860,

771, 732; **HRMS**: *m*/*z* calculated for $C_{23}H_{36}N_2NaO_9^+$ [M+Na]$^+$: 507.2313; found: 507.2314.

***endo*-Diastereomer (minor): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.63 (d, *J* = 9.3 Hz, 1H), 4.31 – 4.13 (m, 7H), 4.05 (d, *J* = 9.9 Hz, 1H), 3.90 (d, *J* = 9.9 Hz, 1H), 3.72 (d, *J* = 9.4 Hz, 1H), 3.56 (dd, *J* = 9.0, 5.8 Hz, 1H), 2.78 (dd, *J* = 12.6, 4.7 Hz, 1H), 2.73 (d, *J* = 12.2 Hz, 1H), 2.45 (d, *J* = 12.2 Hz, 1H), 2.37 (ddd, *J* = 14.1, 9.0, 4.2 Hz, 1H), 2.25 – 2.17 (m, 1H), 1.77 (dd, *J* = 12.7, 11.2 Hz, 1H), 1.43 (s, 9H), 1.30 – 1.25 (m, 9H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 171.4, 169.0, 168.9, 156.2, 81.3, 78.0, 71.1, 63.1, 62.0, 61.89, 61.85, 61.0, 56.0, 49.7, 45.3, 34.11, 31.9, 28.5, 14.20, 14.17, 14.15; **IR** (cm^{-1}): 2979, 1730, 1699, 1447, 1392, 1367, 1329, 1302, 1159, 1093, 1055, 1022, 962, 931, 861, 771, 718; **HRMS**: *m*/*z* calculated for $C_{23}H_{36}N_2NaO_9^+$ [M+Na]$^+$: 507.2313; found: 507.2309.

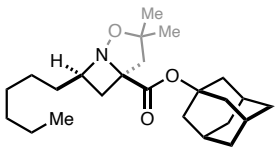


Prop-2-yn-1-yl-7-hexyl-3,3-dimethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (25): Prepared according to GP-3 using **S25** (45 mg, 0.25 mmol, 1.0 equiv.), 1-octene (59 µL, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 20 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 3:1 and a regioisomer ratio of 19:1. Purification by flash column chromatography (5-30% EtOAc/hexanes) afforded the pure exo-diastereomer as pale-yellow oil (31 mg, 43%) and the pure endo-diastereomer as colorless oil (13 mg, 18%).

***exo*-Diastereomer (major): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.76 (m, 2H), 3.47 (p, *J* = 8.4 Hz, 1H), 2.87 (d, *J* = 13.0 Hz, 1H), 2.49 (d, *J* = 13.0 Hz, 1H), 2.45 (t, *J* = 2.5 Hz, 1H), 2.37 (dd, *J* = 11.1, 8.6 Hz, 1H), 2.00 (dd, *J* = 11.1, 8.4 Hz, 1H), 1.76 – 1.67 (m, 1H), 1.55 – 1.48 (m, 4H), 1.40 – 1.32 (m, 1H), 1.30 – 1.21 (m, 7H), 1.20 (s, 3H), 0.85 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.1, 87.4, 77.4, 75.2, 72.9, 67.5, 52.8, 51.0, 35.5, 31.9, 30.3, 29.7, 29.3, 28.5, 25.4, 22.7, 14.2; **IR** (cm^{-1}): ;**HRMS**: *m*/*z* calculated for $C_{17}H_{28}NO_3^+$ [M+H]$^+$: 294.2064; found: 294.2063.

***endo*-Diastereomer (minor): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.85 – 4.72 (m, 2H), 3.91 (p, *J* = 7.8 Hz, 1H), 2.83 (dd, *J* = 11.7, 8.0 Hz, 1H), 2.75 (d, *J* = 12.5 Hz, 1H), 2.47 (t, *J* = 2.5 Hz, 1H), 2.28 – 2.18 (m, 2H), 1.98 – 1.90 (m, 1H), 1.53 – 1.47 (m, 1H), 1.45 (s, 3H), 1.32 – 1.22 (m, 8H), 1.20 (s, 3H), 0.87 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.3, 83.7, 77.4, 75.3, 72.5, 60.8, 53.0, 52.7, 36.6, 31.8, 31.6, 29.4, 27.1, 25.92, 25.86, 22.7, 14.2; **IR** (cm^{-1}): 2926, 2857, 1738, 1634, 1457, 1368, 1302, 1253,

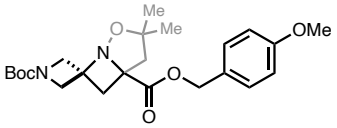
1173, 1147, 1044, 993, 932, 786, 723, 666; **HRMS**: *m*/*z* calculated for $C_{17}H_{28}NO_3^+$ $[M+H]^+$: 294.2064; found: 294.2062.



Adamantan-1-yl-7-hexyl-3,3-dimethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (26): Prepared according to GP-3 using **S26** (69 mg, 0.25 mmol, 1.0 equiv.), 1-octene (59 µL, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 18 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 2:1 and a regioisomer ratio of 19:1. Purification by flash column chromatography (5-15% EtOAc/hexanes) afforded the pure title compound as colorless oil (95 mg, 98% combined yield; d.r. = 2:1). Characterization data for both diastereomers was obtained after separation by flash column chromatography (1-20% EtOAc/hexanes).

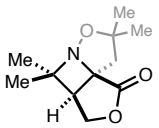
***exo*-Diastereomer (major): ^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.42 (p, *J* = 7.6 Hz, 1H), 2.82 (d, *J* = 12.7 Hz, 1H), 2.40 (d, *J* = 12.8 Hz, 1H), 2.29 (t, *J* = 9.8 Hz, 1H), 2.16 (d, *J* = 7.9 Hz, 9H), 1.97 (t, *J* = 9.6 Hz, 1H), 1.75 – 1.61 (m, 7H), 1.54 – 1.46 (m, 4H), 1.39 – 1.19 (m, 11H), 0.87 (t, *J* = 6.2 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 171.8, 86.9, 81.6, 73.6, 67.1, 51.0, 41.2, 36.2, 35.4, 31.9, 31.0, 30.4, 29.6, 29.3, 28.4, 25.3, 22.7, 14.2; **IR** (cm^{-1}): 2911, 2853, 1720, 1456, 1366, 1326, 1298, 1255, 1186, 1151, 1103, 1055, 967, 872, 778; **HRMS**: *m*/*z* calculated for $C_{24}H_{39}NNaO_3^+$ $[M+Na]^+$: 412.2822; found: 412.2824.

***endo*-Diastereomer (minor): ^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.84 (p, *J* = 7.9 Hz, 1H), 2.79 (dd, *J* = 11.5, 7.8 Hz, 1H), 2.67 (d, *J* = 12.3 Hz, 1H), 2.21 – 2.08 (m, 11H), 1.95 – 1.85 (m, 1H), 1.72 – 1.63 (m, 6H), 1.55 – 1.46 (m, 1H), 1.43 (s, 3H), 1.31 – 1.24 (m, 8H), 1.22 (s, 3H), 0.87 (t, *J* = 6.3 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 171.9, 83.4, 81.8, 73.3, 60.5, 53.0, 41.2, 37.0, 36.3, 31.9, 31.5, 31.0, 29.4, 27.0, 26.1, 25.8, 22.7, 14.2; **IR** (cm^{-1}): 2911. 2852, 1723, 1456, 1366, 1328, 1299, 1253, 1184, 1103, 1055, 967, 875, 729; **HRMS**: *m*/*z* calculated for $C_{24}H_{40}NO_3^+$ $[M+H]^+$: 390.3003; found: 390.3003.



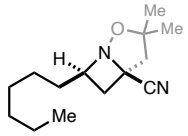
1-(*Tert*-butyl) 1'-(4-methoxybenzyl) 3',3'-dimethyl-4'-oxa-5'-azaspiro[azetidine-3,6'-bicyclo[3.2.0]heptane]-1,1'-dicarboxylate (27): Prepared according to GP-3 using **S27** (66 mg, 0.25 mmol, 1.0 equiv.), *tert*-butyl 3-methyleneazetidine-1-carboxylate[15] (64 mg, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 20 h. ^{1}H NMR analysis of the crude reaction mixture revealed a regioisomer ratio of >20:1. Purification by flash column chromatography (5-20% EtOAc/CH_2Cl_2) afforded the pure title compound as colorless oil (95 mg, 88%).

^{1}H NMR (700 MHz, $CDCl_3$): δ 7.31 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.20 (d, *J* = 11.8 Hz, 1H), 5.13 (d, *J* = 11.9 Hz, 1H), 4.65 (d, *J* = 9.4 Hz, 1H), 4.12 (d, *J* = 9.9 Hz, 1H), 3.87 (d, *J* = 9.9 Hz, 1H), 3.81 (s, 3H), 3.71 (d, *J* = 9.4 Hz, 1H), 2.81 (d, *J* = 12.8 Hz, 1H), 2.60 (d, *J* = 12.0 Hz, 1H), 2.53 (d, *J* = 12.0 Hz, 1H), 1.98 (d, *J* = 12.9 Hz, 1H), 1.42 (d, *J* = 11.5 Hz, 12H), 1.12 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 171.7, 159.9, 156.2, 130.4, 127.5, 114.0, 86.8, 79.7, 71.9, 67.2, 63.0, 61.3, 56.0, 55.3, 50.2, 37.0, 28.4, 27.7, 26.4; **IR** (cm^{-1}): 2976, 2937, 2875, 1740, 1689, 1615, 1586, 1514, 1456, 1410, 1367, 1244, 1214, 1166, 1139, 1096, 1030, 963, 817, 798, 709; **HRMS**: *m*/*z* calculated for $C_{23}H_{33}N_2O_6^+$ [M+H]$^+$: 433.2333; found: 433.2325.



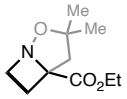
4,4,7,7-Tetramethyltetrahydro-1H,3H-furo[3',4':2,3]azeto[1,2-b]isoxazol-1-one (28): Prepared according to GP-3 using **S28** (53 mg, 0.25 mmol, 1.0 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 12 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of >10:1. Purification by flash column chromatography (2-30% EtOAc/CH_2Cl_2) afforded the pure title compound as white solid (46 mg, 87%).

^{1}H NMR (700 MHz, $CDCl_3$): δ 4.48 (d, *J* = 10.5 Hz, 1H), 4.34 (dd, *J* = 10.4, 8.0 Hz, 1H), 2.91 (d, *J* = 7.8 Hz, 1H), 2.54 (d, *J* = 12.5 Hz, 1H), 2.34 (d, *J* = 12.5 Hz, 1H), 1.50 (s, 3H), 1.42 (s, 3H), 1.38 (s, 3H), 1.35 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 176.7, 86.3, 69.1, 66.8, 63.8, 48.0, 45.3, 27.0, 26.0, 24.58, 24.55; **IR** (cm^{-1}): 2974, 2930, 1771, 1457, 1367, 1288, 1207, 1157, 1131, 1095, 1060, 992, 948, 927, 866, 832, 785, 730, 710, 679; **HRMS**: *m*/*z* calculated for $C_{11}H_{18}NO_3^+$ [M+H]$^+$: 212.1281; found: 212.1277.



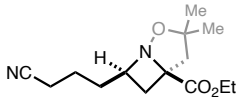
7-Hexyl-3,3-dimethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carbonitrile (29): Prepared according to GP-3 using **S29** (31 mg, 0.25 mmol, 1.0 equiv.), 1-octene (59 µL, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 20 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 2:1 and a regioisomer ratio of >20:1. Purification by flash column chromatography (2-15% EtOAc/hexanes) afforded the pure title compound as colorless oil (52 mg, 88% combined yield; d.r. = 2:1). Characterization data was obtained for a 2.2:1 mixture of diastereomers.

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.99 (p, *J* = 7.7 Hz, 1H; minor), 3.46 (p, *J* = 8.4 Hz, 2.2H; major), 2.93 (dd, *J* = 11.9, 8.1 Hz, 1H; minor), 2.74 (d, *J* = 12.9 Hz, 2.2H; major), 2.65 (d, *J* = 12.6 Hz, 1H; minor), 2.56 (d, *J* = 13.0 Hz, 2.2H; major), 2.50 (dd, *J* = 11.3, 8.7 Hz, 2.2H; major), 2.34 (d, *J* = 12.7 Hz, 1H; minor), 2.29 (dd, *J* = 12.1, 7.3 Hz, 1H; minor), 2.20 (dd, *J* = 11.3, 8.6 Hz, 2.2H; major), 1.95 – 1.87 (m, 1H; minor), 1.76 – 1.65 (m, 2.2H; major), 1.59 – 1.17 (m, 48H; major+minor), 0.86 (t, *J* = 6.7 Hz, 9.6H; major+minor); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 121.0, 120.7, 88.1, 84.8, 69.3, 61.9, 61.3, 61.2, 54.3, 52.4, 36.7, 35.4, 31.8, 31.7, 31.7, 31.3, 29.23, 29.15, 28.4 (2C), 27.1, 25.7, 25.2, 25.1, 22.7 (2C), 14.1 (2C); **IR** (cm^{-1}): 2955, 2925, 2853, 2235, 1468, 1459, 1382, 1368, 1307, 1275, 1226, 1153, 1102, 1006, 970, 858, 824, 804, 722, 685, 646; **HRMS**: *m*/*z* calculated for $C_{14}H_{25}N_2O^+$ [M+H]$^+$: 237.1961; found: 237.1960.



Ethyl 3,3-dimethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (30): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), *fac*-[Ir(dFppy)$_3$] (3.8 mg, 2 mol%) and 1,2-dichloroethane (2.5 mL) with a reaction time of 44 h under an atmosphere of ethylene gas. Purification by flash column chromatography (2-35% EtOAc/CH_2Cl_2) afforded the pure title compound as yellow oil (35 mg, 70%).

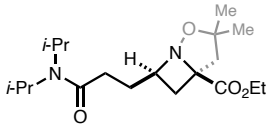
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.26 (qd, *J* = 7.1, 2.5 Hz, 2H), 3.78 (ddd, *J* = 9.7, 8.4, 4.1 Hz, 1H), 3.46 (q, *J* = 9.5 Hz, 1H), 2.85 (d, *J* = 12.9 Hz, 1H), 2.55 (d, *J* = 12.9 Hz, 1H), 2.47 (dt, *J* = 11.3, 8.7 Hz, 1H), 2.29 (ddd, *J* = 11.3, 9.7, 4.1 Hz, 1H), 1.55 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.20 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.7, 87.0, 76.7, 61.6, 55.2, 51.0, 29.5, 28.3, 24.9, 14.2; **IR** (cm^{-1}): 2973, 1725, 1448, 1383, 1313, 1256, 1221, 1179, 1144, 1024, 921, 864, 821, 782, 705, 672; **HRMS**: *m*/*z* calculated for $C_{10}H_{17}NNaO_3^+$ [M+Na]$^+$: 222.1101; found: 222.1099.



Ethyl 7-(3-cyanopropyl)-3,3-dimethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (31): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), 5-hexenenitrile (43 µL, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (3.8 mg, 2 mol%) and MeCN (2.5 mL) with a reaction time of 36 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 2:1 and a regioisomer ratio of 16:1. Purification by flash column chromatography (20-80% EtOAc/hexanes) afforded the pure *exo*-diastereomer as pale-yellow oil (33 mg, 49%) and the pure *endo*-diastereomer as colorless oil (15 mg, 22%).

***exo*-Diastereomer (major): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.26 (q, *J* = 7.0 Hz, 2H), 3.54 – 3.47 (m, 1H), 2.88 (d, *J* = 13.0 Hz, 1H), 2.49 (d, *J* = 13.0 Hz, 1H), 2.47 – 2.35 (m, 3H), 2.04 (dd, *J* = 11.2, 8.5 Hz, 1H), 1.90 – 1.82 (m, 1H), 1.81 – 1.71 (m, 3H), 1.52 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.21 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.6, 119.7, 87.7, 73.2, 66.2, 61.7, 51.0, 33.9, 30.0, 29.8, 28.5, 21.6, 17.1, 14.3; **IR** (cm^{-1}): 2973, 2936, 2245, 1725, 1456, 1384, 1368, 1309, 1256, 1220, 1185, 1148, 1108, 1054, 1022, 861, 779, 729, 676; **HRMS**: *m*/*z* calculated for $C_{14}H_{23}N_2O_3^+$ $[M+H]^+$: 267.1703; found: 267.1703.

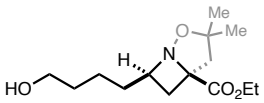
***endo*-Diastereomer (minor): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.28 (q, *J* = 7.0 Hz, 2H), 3.92 (qd, *J* = 8.0, 5.3 Hz, 1H), 2.87 (dd, *J* = 11.8, 7.9 Hz, 1H), 2.74 (d, *J* = 12.4 Hz, 1H), 2.38 (q, *J* = 6.8 Hz, 2H), 2.27 (dd, *J* = 11.8, 8.1 Hz, 1H), 2.21 (d, *J* = 12.5 Hz, 1H), 2.16 – 2.10 (m, 1H), 1.85 – 1.78 (m, 1H), 1.68 – 1.60 (m, 2H), 1.47 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.21 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.7, 119.7, 83.8, 72.5, 61.9, 59.5, 52.9, 36.8, 30.8, 26.9, 26.0, 22.6, 17.3, 14.3; **IR** (cm^{-1}): 2975, 2245, 1726, 1457, 1367, 1303, 1254, 1185, 1152, 1023, 894, 862, 786, 726, 665; **HRMS**: *m*/*z* calculated for for $C_{14}H_{23}N_2O_3^+$ $[M+H]^+$: 267.1703; found: 267.1710.



Ethyl 7-(3-(diisopropylamino)-3-oxopropyl)-3,3-dimethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (32): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), *N*,*N*-diisopropylpent-4-enamide[15] (69 mg, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 24 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 4:1 and a regioisomer ratio of >20:1. Purification by flash column chromatography (30-95% EtOAc/hexanes) afforded the pure *exo*-diastereomer as pale-yellow oil

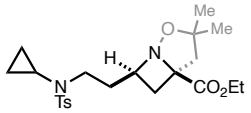
(65 mg, 73%) and the pure *endo*-diastereomer as pale-yellow oil (22 mg, 25%). Characterization data is provided for the *exo*-diastereomer.

***exo*-Diastereomer (major): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.24 (qd, *J* = 7.1, 2.5 Hz, 2H), 4.05 (p, *J* = 6.8 Hz, 1H), 3.58 (qd, *J* = 8.8, 4.1 Hz, 1H), 3.42 (b, 1H), 2.83 (d, *J* = 12.9 Hz, 1H), 2.52 – 2.46 (m, 2H), 2.44 – 2.35 (m, 2H), 2.05 – 1.98 (m, 2H), 1.83 – 1.77 (m, 1H), 1.49 (s, 3H), 1.38 (d, *J* = 6.8 Hz, 6H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.20 (s, 3H), 1.18 (d, *J* = 6.7 Hz, 6H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.9, 171.1, 87.5, 73.3, 66.6, 61.5, 51.1, 48.4, 45.7, 30.4, 30.1, 29.9, 28.7, 21.0, 20.9, 20.8, 14.3; **IR** (cm^{-1}): 2967, 2932, 1727, 1635, 1442, 1368, 1300, 1256, 1214, 1184, 1149, 1107, 1044, 888, 862, 779, 728, 677; **HRMS**: *m*/*z* calculated for $C_{19}H_{35}N_2O_4^+$ $[M+H]^+$: 355.2591; found: 355.2584.



Ethyl 7-(4-hydroxybutyl)-3,3-dimethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (33): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), 5-hexen-1-ol (45 µL, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 20 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 3:1 and a regioisomer ratio of >20:1. Purification by flash column chromatography (30-99% EtOAc/CH_2Cl_2) afforded the pure *exo*-diastereomer as pale-yellow oil (40 mg, 62%) and the pure *endo*-diastereomer as pale-yellow oil (17 mg, 26%).

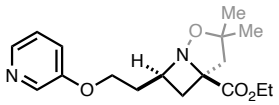
***exo*-Diastereomer (major): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.25 (q, *J* = 7.1 Hz, 2H), 3.65 (td, *J* = 6.5, 2.0 Hz, 2H), 3.49 (qd, *J* = 8.4, 6.1 Hz, 1H), 2.86 (d, *J* = 12.9 Hz, 1H), 2.48 (d, *J* = 12.9 Hz, 1H), 2.37 (dd, *J* = 11.1, 8.7 Hz, 1H), 2.00 (dd, *J* = 11.1, 8.5 Hz, 1H), 1.78 – 1.70 (m, 1H), 1.63 – 1.54 (m, 3H), 1.52 (s, 3H), 1.51 – 1.45 (m, 1H), 1.44 – 1.37 (m, 1H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.20 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.8, 87.3, 73.0, 67.3, 62.4, 61.6, 51.0, 34.7, 32.5, 30.3, 29.5, 28.4, 21.5, 14.2; **IR** (cm^{-1}): 3388, 2973, 2933, 2862, 1727, 1456, 1383, 1368, 1310, 1257, 1218, 1186, 1149, 1111, 1057, 1035, 863, 839, 779, 737, 674; **HRMS**: *m*/*z* calculated for $C_{14}H_{26}NO_4^+$ $[M+H]^+$: 272.1856; found: 272.1854.



Ethyl 7-(2-((*N*-cyclopropyl-4-methylphenyl)sulfonamido)ethyl)-3,3-dimethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (34): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), **S34** (100 mg, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 20 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 2:1 and a regioisomer ratio of >20:1. Purification by flash column chromatography (1-35% EtOAc/CH_2Cl_2) afforded the pure *exo*-diastereomer as pale-yellow oil (64 mg, 58%) and the pure *endo*-diastereomer as pale-yellow oil (32 mg, 29%).

***exo*-Diastereomer (major): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 7.71 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.60 – 3.53 (m, 1H), 3.23 (ddd, *J* = 8.0, 6.5, 2.6 Hz, 2H), 2.85 (d, *J* = 12.9 Hz, 1H), 2.50 (d, *J* = 13.0 Hz, 1H), 2.47 – 2.39 (m, 4H), 2.10 – 2.01 (m, 2H), 1.99 – 1.95 (m, 1H), 1.94 – 1.88 (m, 1H), 1.53 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.21 (s, 3H), 0.94 – 0.89 (m, 1H), 0.89 – 0.85 (m, 1H), 0.72 – 0.64 (m, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.6, 143.5, 135.2, 129.6, 127.7, 87.6, 73.5, 64.9, 61.5, 50.9, 47.8, 34.4, 31.0, 30.1, 29.7, 28.5, 21.6, 14.2, 7.6, 7.2; **IR** (cm^{-1}): 2973, 1726, 1598, 1455, 1367, 1341, 1306, 1256, 1160, 1091, 1053, 1027, 860, 815, 775, 712, 690, 648; **HRMS**: *m*/*z* calculated for $C_{22}H_{33}N_2O_5S^+$ $[M+H]^+$: 437.2105; found: 437.2102.

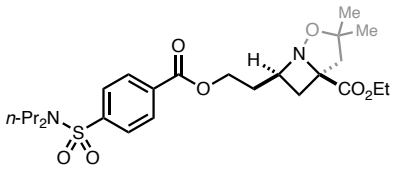
***endo*-Diastereomer (minor): ^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.71 (d, *J* = 7.7 Hz, 2H), 7.29 (d, *J* = 7.8 Hz, 2H), 4.27 (q, *J* = 7.1 Hz, 2H), 3.89 (p, *J* = 7.7 Hz, 1H), 3.25 – 3.10 (m, 2H), 2.83 (dd, *J* = 11.5, 8.3 Hz, 1H), 2.75 (d, *J* = 12.5 Hz, 1H), 2.42 (s, 3H), 2.39 – 2.28 (m, 1H), 2.25 (dd, *J* = 11.6, 7.9 Hz, 1H), 2.20 (d, *J* = 12.5 Hz, 1H), 2.07 – 1.98 (m, 1H), 1.87 – 1.76 (m, 1H), 1.44 (s, 3H), 1.32 (t, *J* = 6.9 Hz, 3H), 1.17 (s, 3H), 0.84 (q, *J* = 9.8, 9.3 Hz, 2H), 0.67 (d, *J* = 6.8 Hz, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.8, 143.47, 135.5, 129.7, 127.8, 83.8, 72.8, 61.8, 58.4, 52.8, 48.6, 36.3, 31.7, 31.0, 27.0, 25.9, 21.6, 14.3, 7.6, 7.3; **IR** (cm^{-1}): 2977, 1727, 1456, 1368, 1342, 1266, 1184, 1161, 1092, 1027, 979, 932, 860, 815, 732, 714, 700, 642; **HRMS**: *m*/*z* calculated for $C_{22}H_{33}N_2O_5S^+$ $[M+H]^+$: 437.2105; found: 437.2101.



Ethyl 3,3-dimethyl-7-(2-(pyridin-3-yloxy)ethyl)-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (35): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), **S35** (56 mg, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 21 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 2:1 and a regioisomer

ratio of >20:1. Purification by flash column chromatography (20-100% EtOAc/hexanes) afforded the pure title compound as yellow oil (54 mg, 67% combined yield; d.r. = 2:1). Characterization data was obtained for the *exo*-diastereomer after purification by flash column chromatography (50-100% EtOAc/hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (s, 1H), 8.19 (t, *J* = 3.1 Hz, 1H), 7.19 (dd, *J* = 3.3, 1.6 Hz, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 4.18 – 4.07 (m, 2H), 3.82 – 3.70 (m, 1H), 2.87 (d, *J* = 13.0 Hz, 1H), 2.51 (d, *J* = 13.0 Hz, 1H), 2.44 (dd, *J* = 11.2, 8.7 Hz, 1H), 2.21 – 2.03 (m, 3H), 1.50 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.20 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.7, 155.2, 142.1, 138.4, 123.9, 121.1, 87.7, 73.5, 64.8, 64.0, 61.7, 50.9, 34.6, 30.1, 29.7, 28.5, 14.2; **IR** (cm^{-1}): 2973, 1725, 1574, 1471, 1426, 1384, 1310, 1260, 1231, 1186, 1148, 1111, 1053, 1014, 925, 861, 800, 707, 678; **HRMS**: *m*/*z* calculated for $C_{17}H_{25}N_2O_4^+$ $[M+H]^+$: 321.1809; found: 321.1812.

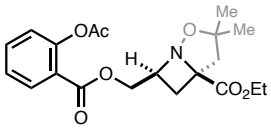


Ethyl 7-(2-((4-(*N*,*N*-dipropylsulfamoyl)benzoyl)oxy)ethyl)-3,3-dimethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (36): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), **S36** (128 mg, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 23 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 2:1 and a regioisomer ratio of >20:1. Purification by flash column chromatography (2-40% EtOAc/CH_2Cl_2) afforded the pure title compound as yellow oil (118 mg, 92% combined yield; d.r. = 2:1). Characterization data for both diastereomers was obtained after separation by flash column chromatography (5-40% EtOAc/CH_2Cl_2).

***exo*-Diastereomer (major): ^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.12 (d, *J* = 8.4 Hz, 2H), 7.84 (d, *J* = 8.4 Hz, 2H), 4.49 – 4.40 (m, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.66 (p, *J* = 8.3 Hz, 1H), 3.11 – 3.04 (m, 4H), 2.86 (d, *J* = 13.0 Hz, 1H), 2.49 (d, *J* = 13.0 Hz, 1H), 2.43 (dd, *J* = 11.2, 8.7 Hz, 1H), 2.21 – 2.01 (m, 3H), 1.56 – 1.49 (m, 4H), 1.49 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.20 (s, 3H), 0.84 (t, *J* = 7.4 Hz, 6H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.6, 165.2, 144.3, 133.6, 130.3, 127.1, 87.7, 73.5, 64.2, 62.4, 61.7, 50.9, 50.0, 34.2, 30.2, 29.7, 28.4, 22.0, 14.2, 11.2; **IR** (cm^{-1}): 2968, 2876, 1721, 1458, 1342, 1271, 1217, 1177, 1157, 1105, 1087, 1052, 991, 863, 778, 740, 693; **HRMS**: *m*/*z* calculated for $C_{25}H_{39}N_2O_7S^+$ $[M+H]^+$: 511.2472; found: 511.2471.

***endo*- Diastereomer (minor): ^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.3 Hz, 2H), 7.86 (d, *J* = 8.3 Hz, 2H), 4.48 – 4.20 (m, 4H), 4.15 (p, *J* = 7.9 Hz, 1H), 3.14 – 3.08 (m, 4H), 2.94 (dd, *J* = 11.8, 7.9 Hz, 1H), 2.75 (d, *J* = 12.4 Hz, 1H), 2.47 (td, *J* = 14.1,

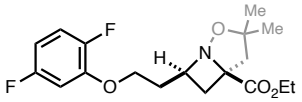
6.0 Hz, 1H), 2.37 (dd, *J* = 11.8, 8.1 Hz, 1H), 2.23 (d, *J* = 12.5 Hz, 1H), 2.05 – 1.96 (m, 1H), 1.57 – 1.50 (m, 4H), 1.47 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.22 (s, 3H), 0.87 (t, *J* = 7.4 Hz, 6H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.7, 165.3, 144.3, 133.7, 130.4, 127.1, 83.9, 72.7, 63.2, 61.9, 57.4, 52.9, 50.0, 36.9, 31.0, 26.9, 26.1, 22.0, 14.3, 11.3; **IR** (cm^{-1}): 2970, 2876, 1722, 1458, 1368, 1271, 1157, 1106, 1087, 992, 862, 734, 695; **HRMS**: *m*/*z* calculated for $C_{25}H_{39}N_2O_7S^+$ $[M+H]^+$: 511.2472; found: 511.2468.



Ethyl 7-(((2-acetoxybenzoyl)oxy)methyl)-3,3-dimethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (37): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), allyl 2-acetoxybenzoate[16] (83 mg, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 23 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 2:1 and a regioisomer ratio of >20:1. Purification by flash column chromatography (1-40% EtOAc/CH_2Cl_2) afforded the pure title compound as pale-yellow oil (92 mg, 94%% combined yield; d.r. = 2:1). Characterization data for both diastereomers was obtained after separation by flash column chromatography (5-40% EtOAc/CH_2Cl_2).

***exo*-Diastereomer (major): ^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.07 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.54 (td, *J* = 7.7, 1.7 Hz, 1H), 7.28 (td, *J* = 7.6, 1.2 Hz, 1H), 7.08 (dd, *J* = 8.1, 1.2 Hz, 1H), 4.45 – 4.35 (m, 2H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.84 (tt, *J* = 8.7, 5.2 Hz, 1H), 2.90 (d, *J* = 13.0 Hz, 1H), 2.48 (d, *J* = 13.0 Hz, 1H), 2.42 (dd, *J* = 11.5, 9.0 Hz, 1H), 2.34 (s, 3H), 2.31 (dd, *J* = 11.5, 8.4 Hz, 1H), 1.53 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.22 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.4, 169.9, 164.2, 151.0, 134.1, 132.1, 126.0, 123.8, 123.0, 87.8, 73.3, 66.1, 64.7, 61.8, 50.8, 29.5, 28.4, 27.5, 21.2, 14.2; **IR** (cm^{-1}): 2974, 2934, 1769, 1720, 1607, 1578, 1452, 1366, 1256, 1186, 1136, 1087, 1012, 917, 866, 817, 784, 755, 701, 671; **HRMS**: *m*/*z* calculated for $C_{20}H_{25}NNaO_7^+$ $[M+Na]^+$: 414.1523; found: 414.1527.

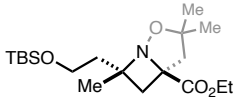
***endo*-Diastereomer (minor): ^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.03 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.55 (td, *J* = 8.0, 1.6 Hz, 1H), 7.29 (td, *J* = 7.7, 1.0 Hz, 1H), 7.09 (dd, *J* = 8.1, 1.2 Hz, 1H), 4.70 (dd, *J* = 11.7, 8.1 Hz, 1H), 4.44 (dd, *J* = 11.8, 5.1 Hz, 1H), 4.34 – 4.24 (m, 3H), 2.89 (dd, *J* = 12.1, 8.3 Hz, 1H), 2.79 (d, *J* = 12.6 Hz, 1H), 2.41 (dd, *J* = 12.2, 8.0 Hz, 1H), 2.36 (s, 3H), 2.24 (d, *J* = 12.6 Hz, 1H), 1.45 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.20 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.4, 169.9, 164.4, 150.9, 134.1, 132.1, 126.1, 123.9, 123.1, 84.3, 72.7, 63.9, 62.0, 57.7, 52.5, 33.5, 26.8, 25.9, 21.2, 14.3; **IR** (cm^{-1}): 2971, 1766, 1722, 1608, 1490, 1448, 1367, 1307, 1263, 1195, 1134, 1083, 1018, 969, 918, 840, 761, 711, 647; **HRMS**: *m*/*z* calculated for $C_{20}H_{26}NO_7^+$ $[M+H]^+$: 392.1704; found: 392.1707.



Ethyl 7-(2-(2,5-difluorophenoxy)ethyl)-3,3-dimethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (38): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), **S38** (69 mg, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 20 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 2:1 and a regioisomer ratio of >20:1. Purification by flash column chromatography (1-20% EtOAc/CH_2Cl_2) afforded the pure title compound as pale-yellow oil (83 mg, 93% combined yield; d.r. = 2:1). Characterization data for both diastereomers was obtained after separation by flash column chromatography (2-25% EtOAc/CH_2Cl_2).

***exo*-Diastereomer (major): ^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.01 – 6.93 (m, 1H), 6.74 – 6.67 (m, 1H), 6.57 – 6.50 (m, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 4.18 – 4.07 (m, 2H), 3.77 (p, *J* = 8.4 Hz, 1H), 2.86 (d, *J* = 12.9 Hz, 1H), 2.51 (d, *J* = 13.0 Hz, 1H), 2.44 (dd, *J* = 11.2, 8.8 Hz, 1H), 2.21 – 2.05 (m, 3H), 1.49 (s, 3H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.20 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 172.7, 158.9 (dd, *J* = 241.9, 2.6 Hz), 149.0 (dd, *J* = 240.9, 3.2 Hz), 147.7 (dd, *J* = 12.4, 10.5 Hz), 116.1 (dd, *J* = 20.8, 10.2 Hz), 106.6 (dd, *J* = 23.9, 7.0 Hz), 103.0 (dd, *J* = 27.6, 1.9 Hz), 87.7, 73.6, 66.1, 64.0, 61.6, 51.0, 34.5, 30.1, 29.7, 28.6, 14.2; **IR** (cm^{-1}): 2974, 1726, 1625, 1512, 1469, 1432, 1368, 1309, 1249, 1186, 1156, 1099, 1053, 1019, 987, 836, 790, 721; **HRMS**: *m*/*z* calculated for $C_{18}H_{24}F_2NO_4^+$ $[M+H]^+$: 356.1668; found: 356.1665.

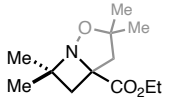
***endo*-Diastereomer (minor): ^{1}H NMR** (500 MHz, $CDCl_3$): δ 6.98 (ddd, *J* = 10.8, 8.9, 5.3 Hz, 1H), 6.71 (ddd, *J* = 9.9, 6.8, 3.0 Hz, 1H), 6.59 – 6.50 (m, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 4.22 – 4.11 (m, 2H), 4.05 – 3.97 (m, 1H), 2.93 (dd, *J* = 11.9, 8.0 Hz, 1H), 2.75 (d, *J* = 12.4 Hz, 1H), 2.56 – 2.45 (m, 1H), 2.40 (dd, *J* = 11.9, 8.2 Hz, 1H), 2.23 (d, *J* = 12.4 Hz, 1H), 2.08 – 1.97 (m, 1H), 1.48 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.22 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 172.7, 158.9 (dd, *J* = 241.9, 2.5 Hz), 149.0 (dd, *J* = 240.9, 3.2 Hz), 147.6 (dd, *J* = 12.7, 10.5 Hz), 116.1 (dd, *J* = 20.6, 10.1 Hz), 106.4 (dd, *J* = 23.9, 6.9 Hz), 102.6 (dd, *J* = 27.7, 2.0 Hz), 83.9, 72.7, 66.8, 61.9, 57.3, 53.0, 37.1, 31.3, 26.9, 26.0, 14.3; **IR** (cm^{-1}): 2975, 1727, 1625, 1512, 1473, 1433, 1368, 1314, 1250, 1187, 1153, 1099, 1025, 988, 836, 790, 721; **HRMS**: *m*/*z* calculated for $C_{18}H_{24}F_2NO_4^+$ $[M+H]^+$: 356.1668; found: 356.1667.



Ethyl 7-(2-((*tert*-butyldimethylsilyl)oxy)ethyl)-3,3,7-trimethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (39): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), *tert*-butyldimethyl((3-methylbut-3-en-1-yl)oxy)silane[8] (76 mg, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 24 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 1.3:1 and a regioisomer ratio of >20:1. Purification by flash column chromatography (2-35% EtOAc/CH_2Cl_2) afforded the pure title compound as pale-yellow oil (82 mg, 88% combined yield; d.r. = 1.3:1). Characterization data for both diastereomers was obtained after separation by flash column chromatography (5-40% EtOAc/hexanes).

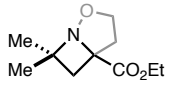
***exo* (C_7-Me)-Diastereomer (major): ^{1}H NMR** (500 MHz, $CDCl_3$): δ 4.33 – 4.21 (m, 2H), 3.77 (ddd, *J* = 10.2, 7.4, 5.4 Hz, 1H), 3.64 (dt, *J* = 10.2, 7.4 Hz, 1H), 2.81 (d, *J* = 12.5 Hz, 1H), 2.44 (d, *J* = 11.9 Hz, 1H), 2.29 (dd, *J* = 12.2, 10.5 Hz, 2H), 2.03 – 1.90 (m, 2H), 1.45 (s, 3H), 1.37 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.17 (s, 3H), 0.88 (s, 9H), 0.04 (d, *J* = 3.1 Hz, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 173.7, 84.2, 69.6, 63.1, 61.7, 59.7, 52.5, 42.1, 39.8, 27.5, 26.8, 26.1, 25.8, 18.4, 14.3, -5.2, -5.3; **IR** (cm^{-1}): 2956, 2929, 2857, 1727, 1462, 1367, 1308, 1253, 1183, 1086, 1031, 1006, 939, 834, 774, 727, 665; **HRMS**: *m*/*z* calculated for $C_{19}H_{38}NO_4Si^+$ $[M+H]^+$: 372.2565; found: 272.2560.

***endo* (C_7-Me)-Diastereomer (minor): ^{1}H NMR** (500 MHz, $CDCl_3$): δ 4.33 – 4.18 (m, 2H), 3.76 (ddd, *J* = 10.5, 6.6, 5.4 Hz, 1H), 3.67 (ddd, *J* = 10.5, 7.6, 6.1 Hz, 1H), 2.86 (d, *J* = 12.7 Hz, 1H), 2.49 (d, *J* = 11.8 Hz, 1H), 2.30 (d, *J* = 12.7 Hz, 1H), 2.13 (d, *J* = 11.8 Hz, 1H), 2.00 (ddd, *J* = 14.0, 7.6, 6.6 Hz, 1H), 1.81 (dt, *J* = 13.9, 5.7 Hz, 1H), 1.45 (s, 3H), 1.35 – 1.28 (m, 6H), 1.15 (s, 3H), 0.86 (s, 9H), 0.02 (d, *J* = 1.7 Hz, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 173.6, 84.5, 70.8, 64.1, 61.6, 59.5, 52.0, 45.1, 40.1, 28.0, 26.0, 25.6, 22.1, 18.3, 14.3, -5.2, -5.3; **IR** (cm^{-1}): 2954, 2929, 2857, 1726, 1463, 1368, 1301, 1253, 1182, 1140, 1089, 1039, 1006, 938, 833, 774, 729, 663; **HRMS**: *m*/*z* calculated for $C_{19}H_{38}NO_4Si^+$ $[M+H]^+$: 372.2565; found: 272.2562.



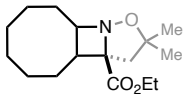
Ethyl 3,3,7,7-tetramethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (40): Prepared according to GP-3 using **14** (200 mg, 1.2 mmol, 1.0 equiv.), *fac*-[Ir(dFppy)$_3$] (1.8 mg, 0.2 mol%) and 1,2-dichloroethane (5 mL) with a reaction time of 24 h under an atmosphere of 2-methylpropene. Purification by flash column chromatography (1-10% EtOAc/CH_2Cl_2) afforded the pure title compound as yellow oil (244 mg, 92%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 4.37 – 4.16 (m, 2H), 2.84 (d, *J* = 12.6 Hz, 1H), 2.40 – 2.16 (m, 3H), 1.45 (s, 3H), 1.36 (s, 3H), 1.34 – 1.28 (m, 6H), 1.17 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 173.5, 84.3, 69.4, 61.9, 61.6, 52.0, 41.6, 30.1, 27.6, 25.7, 24.4, 14.2; **IR** (cm^{-1}): ; **HRMS**: *m*/*z* calculated for $C_{12}H_{22}NO_3^+$ $[M+H]^+$: 228.1594; found: 228.1595.



Ethyl 7,7-dimethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (62): Prepared according to GP-3 using **S19** (250 mg, 1.8 mmol, 1.0 equiv.), *fac*-[Ir(dFppy)$_3$] (2.7 mg, 0.2 mol%) and 1,2-dichloroethane (5 mL) with a reaction time of 24 h under an atmosphere of 2-methylpropene. Purification by flash column chromatography (1-10% EtOAc/CH_2Cl_2) afforded the pure title compound as yellow oil (301 mg, 87%).

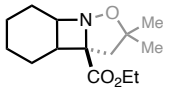
^{1}H NMR (500 MHz, $CDCl_3$): δ 4.30 – 4.06 (m, 4H), 2.63 – 2.49 (m, 2H), 2.33 – 2.26 (m, 1H), 2.11 (d, *J* = 12.0 Hz, 1H), 1.31 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.22 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 173.4, 70.8, 69.4, 62.9, 61.7, 40.1, 39.8, 30.5, 22.7, 14.2; **IR** (cm^{-1}): 2967, 2872, 1727, 1446, 1367, 1318, 1281, 1215, 1175, 1135, 1096, 1027, 938, 877, 860, 782, 748, 703, 658; **HRMS**: *m*/*z* calculated for $C_{10}H_{18}NO_3^+$ $[M+H]^+$: 200.1281; found: 200.1277.



Ethyl 2,2-dimethyldecahydro-3aH-cycloocta[3,4]azeto[1,2-b]isoxazole-3a-carboxylate (41): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), cyclooctene (49 µL, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 20 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 1.3:1. Purification by flash column chromatography (5-30% EtOAc/hexanes) afforded the pure title compound as pale-yellow oil (67 mg, 95% combined yield; d.r. = 1.3:1). Characterization data for the *endo*-diastereomer was obtained after separation by flash column chromatography (5-30% EtOAc/hexanes).

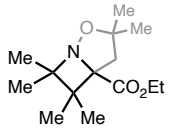
***endo*-Diastereomer (minor): ^{1}H NMR** (400 MHz, $CDCl_3$): δ 4.26 (qd, *J* = 7.1, 3.1 Hz, 2H), 3.19 (ddd, *J* = 11.1, 8.7, 3.8 Hz, 1H), 2.61 – 2.46 (m, 2H), 2.21 – 2.05 (m, 2H), 1.92 – 1.68 (m, 5H), 1.68 – 1.44 (m, 5H), 1.37 – 1.21 (m, 5H), 1.21 – 0.96 (m, 5H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 173.4, 86.1, 77.5, 75.2, 61.4, 44.6, 40.1, 35.8, 30.3, 29.2, 28.6, 28.5, 28.2, 27.7, 26.6, 14.3; **IR** (cm^{-1}): 2972, 2923, 2853, 1745, 1721, 1454,

1366, 1300, 1250, 1210, 1180, 1148, 1123, 1041, 896, 856, 780, 732; **HRMS**: *m*/*z* calculated for $C_{16}H_{28}NO_3^+$ [M+H]$^+$: 282.2064; found: 282.2059.



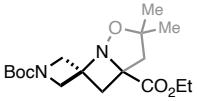
Ethyl 2,2-dimethyloctahydro-3aH-benzo[3,4]azeto[1,2-b]isoxazole-3a-carboxylate (42): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), cyclohexene (38 µL, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 20 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 1.2:1. Purification by flash column chromatography (5-30% EtOAc/CH_2Cl_2) afforded the pure title compound as yellow oil (58 mg, 91% combined yield; d.r. = 1.2:1). Characterization data for the *exo*-diastereomer was obtained after separation by flash column chromatography (5-30% EtOAc/CH_2Cl_2).

***exo*-Diastereomer (major): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.36 – 4.23 (m, 2H), 3.57 (ddd, *J* = 8.4, 5.5, 1.7 Hz, 1H), 2.71 (d, *J* = 13.1 Hz, 1H), 2.63 (d, *J* = 13.1 Hz, 1H), 2.53 (q, *J* = 9.0 Hz, 1H), 2.03 – 1.96 (m, 1H), 1.91 – 1.83 (m, 1H), 1.65 – 1.59 (m, 1H), 1.55 – 1.51 (m, 2H), 1.51 (s, 3H), 1.47 – 1.39 (m, 1H), 1.34 – 1.27 (m, 4H), 1.18 (s, 3H), 1.03 – 0.92 (m, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.6, 87.5, 78.2, 63.4, 61.2, 51.7, 33.8, 30.2, 29.0, 27.0, 25.3, 22.4, 20.9, 14.6; **IR** (cm^{-1}): 2966, 2935, 2861, 1737, 1464, 1366, 1289, 1252, 1178, 1139, 1045, 1015, 947, 861, 777, 728, 716; **HRMS**: *m*/*z* calculated for $C_{14}H_{24}NO_3^+$ [M+H]$^+$: 254.1751; found: 254.1750.



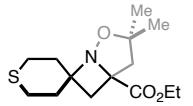
Ethyl 3,3,6,6,7,7-hexamethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (43): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), 2,3-dimethyl-2-butene (45 µL, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 22 h. Purification by flash column chromatography (3-30% EtOAc/CH_2Cl_2) afforded the pure title compound as pale-yellow oil (41 mg, 64%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 4.35 – 4.21 (m, 2H), 2.53 (d, *J* = 13.1 Hz, 1H), 2.45 (d, *J* = 13.1 Hz, 1H), 1.43 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.20 (s, 3H), 1.18 (s, 3H), 1.16 (s, 3H), 1.12 (s, 3H), 1.08 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 173.3, 84.0, 79.7, 68.0, 61.1, 47.6, 39.2, 28.4, 26.0, 25.7, 22.8, 21.7, 20.4, 14.5; **IR** (cm^{-1}): 2974, 2932, 1743, 1717, 1464, 1370, 1294, 1233, 1172, 1124, 1047, 1014, 937, 862, 837, 766, 726, 641; **HRMS**: *m*/*z* calculated for $C_{14}H_{26}NO_3^+$ [M+H]$^+$: 256.1907; found: 256.1908.



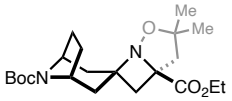
1-(*Tert*-butyl) 1'-ethyl 3',3'-dimethyl-4'-oxa-5'-azaspiro[azetidine-3,6'-bicyclo[3.2.0]heptane]-1,1'-dicarboxylate (44): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), *tert*-butyl 3-methyleneazetidine-1-carboxylate[15] (64 mg, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 24 h. ^{1}H NMR analysis of the crude reaction mixture revealed a regioisomer ratio of >20:1. Purification by flash column chromatography (5-30% EtOAc/CH_2Cl_2) afforded the pure title compound as pale-yellow oil (85 mg, 99%).

^{1}H NMR (700 MHz, $CDCl_3$): δ 4.68 (d, *J* = 9.4 Hz, 1H), 4.26 (qd, *J* = 7.1, 1.4 Hz, 2H), 4.14 (d, *J* = 9.9 Hz, 1H), 3.91 (d, *J* = 9.9 Hz, 1H), 3.74 (d, *J* = 9.4 Hz, 1H), 2.85 (d, *J* = 12.8 Hz, 1H), 2.63 (d, *J* = 12.1 Hz, 1H), 2.57 (d, *J* = 12.0 Hz, 1H), 2.00 (d, *J* = 12.9 Hz, 1H), 1.46 (s, 3H), 1.42 (s, 9H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.20 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 171.9, 156.2, 86.8, 79.8, 71.9, 63.0, 61.8, 61.3, 56.2, 50.3, 37.1, 28.4, 27.9, 26.4, 14.2; **IR** (cm^{-1}): 2977, 2873, 2248, 1733, 1697, 1452, 1394, 1367, 1304, 1252, 1220, 1165, 1142, 1091, 1045, 916, 859, 772, 729, 646; **HRMS**: *m*/*z* calculated for $C_{17}H_{28}N_2NaO_5^+$ $[M+Na]^+$: 363.1890; found: 363.1898.



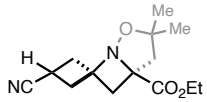
Ethyl 3,3-dimethyltetrahydro-4-oxa-5-azaspiro[bicyclo[3.2.0]heptane-6,4'-thiopyran]-1-carboxylate (45): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), 4-methylenetetrahydro-2*H*-thiopyran[8] (43 mg, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 20 h. ^{1}H NMR analysis of the crude reaction mixture revealed a regioisomer ratio of >20:1. Purification by flash column chromatography (3-50% EtOAc/CH_2Cl_2) afforded the pure title compound as pale-yellow oil (53 mg, 74%).

^{1}H NMR (700 MHz, $CDCl_3$): δ 4.33 – 4.20 (m, 2H), 2.89 (d, *J* = 12.6 Hz, 1H), 2.85 – 2.75 (m, 2H), 2.54 – 2.45 (m, 2H), 2.27 – 2.16 (m, 4H), 2.10 (ddd, *J* = 12.4, 8.9, 3.0 Hz, 1H), 2.02 (ddd, *J* = 13.1, 7.4, 2.7 Hz, 1H), 1.98 (ddd, *J* = 13.8, 7.8, 2.9 Hz, 1H), 1.43 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.17 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 173.2, 84.4, 69.9, 63.1, 61.7, 52.3, 39.9, 39.7, 35.0, 27.4, 25.5, 25.11, 25.06, 14.2; **IR** (cm^{-1}): 2976. 2933, 2212, 1726, 1456, 1429, 1368, 1304, 1232, 1187, 1148, 1098, 1031, 912, 863, 827, 785, 725, 643; **HRMS**: *m*/*z* calculated for $C_{14}H_{24}NO_3S^+$ $[M+H]^+$: 286.1471; found: 286.1470.



8'-(*Tert*-butyl) 1-ethyl 3,3-dimethyl-4-oxa-5,8'-diazaspiro[bicyclo[3.2.0]heptane-6,3'-bicyclo[3.2.1]octane]-1,8'-dicarboxylate (46): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), *tert*-butyl 3-methylene-8-azabicyclo[3.2.1]octane-8-carboxylate (84 mg, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 24 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 5:1 and a regioisomer ratio of >20:1. Purification by flash column chromatography (2-35% EtOAc/CH_2Cl_2) afforded the pure major diastereomer as colorless oil (77 mg, 78%) and the pure minor diastereomer as pale-yellow oil (14 mg, 14%). Characterization is provided for the major (1*S**,1'*R**,5'*S**,6*r**)-diastereomer.

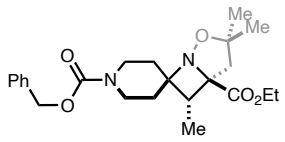
(1*S,1'*R**,5'*S**,6*r**)-Diastereomer (major): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.34 – 4.25 (m, 1H), 4.24 – 4.18 (m, 1H), 4.10 (b, 2H), 2.79 (d, *J* = 12.5 Hz, 1H), 2.53 (b, 1H), 2.27 (m, 2H), 2.20 (b, 2H), 2.12 (d, *J* = 12.3 Hz, 2H), 1.93 – 1.54 (m, 4H), 1.48 (s, 3H) 1.45 (s, 9H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.18 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 173.4, 153.4, 84.6, 79.1, 70.0, 62.0, 61.6, 52.7 (dd, *J* = 144.5, 18.4 Hz, 3C), 43.4 (d, *J* = 148.1 Hz), 43.0, 37.1 (d, *J* = 157.1 Hz), 28.6, 27.6, 27.1 (d, *J* = 103.1 Hz), 26.0, 25.9 (d, *J* = 121.2 Hz), 14.2; **IR** (cm^{-1}): 2974, 1726, 1686, 1452, 1413, 1363, 1329, 1307, 1257, 1169, 1095, 1075, 1010, 971, 879, 846, 735; **HRMS**: *m*/*z* calculated for $C_{21}H_{35}N_2O_5^+$ $[M+H]^+$: 395.2540; found: 395.2535.



Ethyl 3'-cyano-3,3-dimethyl-4-oxa-5-azaspiro[bicyclo[3.2.0]heptane-6,1'-cyclobutane]-1-carboxylate (47): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), 3-methylenecyclobutane-1-carbonitrile (35 mg, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 20 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 1:1 and a regioisomer ratio of >20:1. Purification by flash column chromatography (3-50% EtOAc/CH_2Cl_2) afforded the pure title compound as pale-yellow oil (45 mg, 68% combined yield; d.r. = 1:1). Characterization data was obtained for a 1:1 mixture of diastereomers.

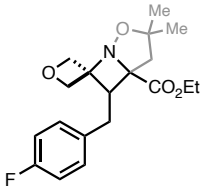
^{1}H NMR (700 MHz, $CDCl_3$): δ 4.26 (q, *J* = 7.1 Hz, 4H), 3.30 – 3.24 (m, 2H), 3.01 (tt, *J* = 9.3, 5.5 Hz, 1H), 2.87 – 2.81 (m, 2H), 2.83 – 2.79 (m, 1H), 2.75 (ddd, *J* = 11.9, 9.4, 1.8 Hz, 1H), 2.68 (dd, *J* = 12.2, 10.1 Hz, 1H), 2.61 – 2.53 (m, 2H), 2.53 – 2.42 (m, 4H), 2.31 – 2.25 (m, 2H), 2.08 (d, *J* = 12.9 Hz, 2H), 1.44 (d, *J* = 4.6 Hz, 6H), 1.31 (td, *J* = 7.1, 2.5 Hz, 6H), 1.19 (d, *J* = 2.2 Hz, 6H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.1, 172.0,

122.5, 121.2, 86.7, 86.6, 71.89, 71.87, 66.7, 65.3, 61.8 (2C), 50.61, 50.55, 39.6, 39.4, 38.4, 37.4, 35.6, 34.7, 28.0, 27.9, 26.4, 26.2, 16.2, 14.4, 14.2 (2C); **IR** (cm^{-1}): 2977, 2237, 1724, 1456, 1369, 1281, 1221, 1185, 1127, 1050, 1022, 957, 856, 779, 718; **HRMS**: *m*/*z* calculated for $C_{14}H_{21}N_2O_3^+$ $[M+H]^+$: 265.1547; found: 265.1551.



1'-Benzyl 1-ethyl 3,3,7-trimethyl-4-oxa-5-azaspiro[bicyclo[3.2.0]heptane-6,4'-piperidine]-1,1'-dicarboxylate (48): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), **S48** (92 mg, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 24 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 3:1 and a regioisomer ratio of 8:1. Purification by flash column chromatography (5-50% EtOAc/CH_2Cl_2) afforded the pure title compound as pale-yellow oil (82 mg, 78% combined yield; d.r. = 2.4:1). Characterization data was obtained for a 2.4:1 mixture of exo/endo diastereomers.

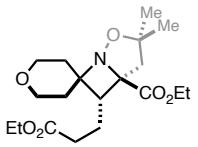
^{1}H NMR (700 MHz, $CDCl_3$): δ 7.37 – 7.29 (m, 17H; major+minor), 5.17 – 5.03 (m, 6.8H), 4.37 – 4.15 (m, 6.8H; major+minor), 3.82 (b, 6.8H; major+minor), 3.35 (b, 6.8H), 2.87 (d, *J* = 12.7 Hz, 1H; minor), 2.54 (d, *J* = 12.8 Hz, 2.4H; major), 2.45 (q, *J* = 7.5 Hz, 1H; minor), 2.30 (b, 5.8H; major+minor), 2.13 (b, 1H; minor), 1.90 (b, 5.8H; major+minor), 1.67 – 1.37 (m, 17H; major+minor), 1.34 – 1.28 (m, 10.2H; major+minor), 1.17 (s, 7.2H; major), 1.13 (s, 3H; minor), 1.03 (d, *J* = 7.3 Hz, 7.2H; major), 1.00 (d, *J* = 7.5 Hz, 3H; minor); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 173.6, 172.0, 155.3 (2C), 136.93, 136.91, 128.5 (2C), 128.0, 127.9, 127.9, 127.8, 84.1, 83.9, 74.8, 74.6, 67.00, 66.98, 66.0, 63.3, 61.5, 61.4, 54.0, 45.3, 44.4, 41.5 (2C), 40.4, 40.04, 40.02, 38.6 (d, *J* = 50.2 Hz), 34.9 (d, *J* = 50.9 Hz), 32.4 (d, *J* =58.5 Hz), 28.8 (d, *J* =56.1 Hz), 27.8, 27.5, 25.6, 25.3, 14.5, 14.2, 10.8, 10.7; **IR** (cm^{-1}): 2976, 2248, 1690, 1432, 1368, 1282, 1235, 1212, 1144, 1090, 1029, 908, 867, 724, 697, 645; **HRMS**: *m*/*z* calculated for $C_{23}H_{33}N_2O_5^+$ $[M+H]^+$: 417.2384; found: 417.2379.



Ethyl 7-(4-fluorobenzyl)-3,3-dimethyl-4-oxa-5-azaspiro[bicyclo[3.2.0]heptane-6,3'-oxetane]-1-carboxylate (49): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), **S49** (67 mg, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 22 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 1:1 and a regioisomer ratio of

8:1. Purification by flash column chromatography (2-40% EtOAc/CH_2Cl_2) afforded the pure title compound as pale-yellow oil (46 mg, 52% combined yield; d.r. = 1:1). Characterization data was obtained for a 1:1 mixture of diastereomers (A/B).

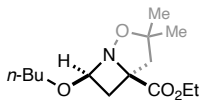
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.19 – 7.09 (m, 4H), 6.97 (t, *J* = 8.2 Hz, 4H), 5.32 (d, *J* = 7.1 Hz, 1H), 5.26 (d, *J* = 7.3 Hz, 1H), 4.84 (d, *J* = 7.7 Hz, 1H), 4.78 (d, *J* = 7.8 Hz, 1H), 4.67 (d, *J* = 7.5 Hz, 2H), 4.44 (d, *J* = 7.1 Hz, 1H), 4.41 (d, *J* = 7.7 Hz, 1H), 4.21 – 4.08 (m, 2H), 4.06 – 3.92 (m, 2H), 3.17 (t, *J* = 8.1 Hz, 1H), 3.09 – 2.93 (m, 2H), 2.89 – 2.78 (m, 4H), 2.68 (d, *J* = 12.9 Hz, 1H), 1.90 (d, *J* = 12.9 Hz, 1H), 1.84 (d, *J* = 12.9 Hz, 1H), 1.41 (d, *J* = 10.8 Hz, 6H), 1.19 (t, *J* = 7.1 Hz, 3H), 1.16 – 1.09 (m, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 171.7, 170.4, 161.8 (d, *J* = 245.0 Hz), 161.7 (d, *J* = 245.2 Hz), 133.7 (d, *J* = 3.4 Hz), 133.3 (d, *J* = 3.5 Hz), 130.2 (d, *J* = 7.7 Hz), 129.7 (d, *J* = 8.0 Hz), 115.7 (d, *J* = 10.8 Hz), 115,5 (d, *J* = 10.9 Hz), 86.6, 85.9, 81.8, 78.3, 77.7, 75.9, 75.6, 72.9, 71.8, 70.2, 61.7, 61.7, 51.7, 48.0, 43.8, 42.7, 33.1, 31.7, 28.1, 27.8, 26.3, 26.1, 14.1, 14.0; **IR** (cm^{-1}): 2975, 2940, 2870, 1727, 1602, 1510, 1456, 1370, 1305, 1221, 1178, 1145, 1117, 1035, 975, 826, 777, 726, 709; **HRMS**: *m*/*z* calculated for $C_{19}H_{25}FNO_4^+$ $[M+H]^+$: 350.1762; found: 350.1760.



Ethyl 7-(3-ethoxy-3-oxopropyl)-3,3-dimethyltetrahydro-4-oxa-5-azaspiro[bicyclo[3.2.0]heptane-6,4'-pyran]-1-carboxylate (50): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), ethyl 4-(tetrahydro-4*H*-pyran-4-ylidene)butanoate[17] (75 mg, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 24 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 4:1 and a regioisomer ratio of 13:1. Purification by flash column chromatography (5-85% EtOAc/CH_2Cl_2) afforded the pure title compound as pale-yellow oil (72 mg, 78% combined yield; d.r. = 4:1). Characterization data was obtained for the *exo*-diastereomer after purification by flash column chromatography (40-60% EtOAc/hexanes).

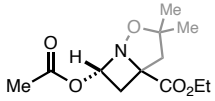
***exo*-Diastereomer (major): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.30 (dq, *J* = 10.8, 7.1 Hz, 1H), 4.20 (dq, *J* = 10.8, 7.1 Hz, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.81 (td, *J* = 11.4, 2.4 Hz, 1H), 3.78 – 3.70 (m, 3H), 2.63 (d, *J* = 12.7 Hz, 1H), 2.32 – 2.22 (m, 2H), 2.21 – 2.13 (m, 2H), 1.91 (dq, *J* = 13.7, 2.7 Hz, 1H), 1.86 – 1.78 (m, 3H), 1.78 – 1.72 (m, 1H), 1.69 – 1.62 (m, 1H), 1.40 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.16 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 173.7, 172.8, 84.1, 74.3, 65.4 (2C), 64.2, 61.8, 60.7, 45.1, 44.5, 39.8, 31.5, 29.7, 27.9, 25.7, 20.8, 14.3, 14.2; **IR** (cm^{-1}): 2972, 2874,

1729, 1463, 1368, 1301, 1231, 1179, 1117, 1101, 1040, 1024, 954, 848, 783, 731; **HRMS**: *m*/*z* calculated for $C_{19}H_{32}NO_6^+$ [M+H]$^+$: 370.2224; found: 370.2223.



Ethyl 7-butoxy-3,3-dimethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (51): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), *n*-butyl vinyl ether (49 µL, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 22 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of >10:1 and a regioisomer ratio of >20:1. Purification by flash column chromatography (2-30% EtOAc/hexanes) afforded the pure title compound as colorless oil (31 mg, 46%).

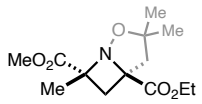
^{1}H NMR (700 MHz, $CDCl_3$): δ 4.57 (t, *J* = 7.1 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.79 (dt, *J* = 9.3, 6.8 Hz, 1H), 3.41 (dt, *J* = 9.3, 6.9 Hz, 1H), 2.85 (d, *J* = 13.0 Hz, 1H), 2.52 (dd, *J* = 11.8, 7.4 Hz, 1H), 2.32 (dd, *J* = 11.8, 6.8 Hz, 1H), 2.25 (d, *J* = 13.0 Hz, 1H), 1.57 (p, *J* = 7.0 Hz, 2H), 1.49 (s, 3H), 1.35 (hd, *J* = 7.3, 2.2 Hz, 2H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.22 (s, 3H), 0.89 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.4, 94.8, 88.9, 68.0, 67.6, 61.8, 50.9, 31.6, 31.3, 29.6, 28.4, 19.3, 14.2, 14.0; **IR** (cm^{-1}): 2962, 2934, 2873, 1727, 1456, 1368, 1298, 1256, 1191, 1157, 1110, 1025, 984, 913, 866, 788, 746, 679; **HRMS**: *m*/*z* calculated for $C_{14}H_{26}NO_4^+$ [M+H]$^+$: 272.1856; found: 272.1851.



Ethyl 7-acetoxy-3,3-dimethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (52): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), vinyl acetate (35 µL, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 22 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 1.4:1 and a regioisomer ratio of >20:1. Purification by flash column chromatography (1-30% EtOAc/CH_2Cl_2) afforded the pure title compound as pale-yellow oil (56 mg, 87% combined yield; d.r. = 1.4:1). Characterization data was obtained for a 1.4:1 mixture of *endo*/*exo* diastereomers.

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.85 (dd, *J* = 5.8, 2.3 Hz, 1.4H; major), 5.71 (t, *J* = 7.1 Hz, 1H; minor), 4.28 – 4.20 (m, 4.8H; major+minor), 2.88 – 2.75 (m, 3.8H; major+minor), 2.67 (dd, *J* = 12.0, 7.5 Hz, 1H; minor), 2.45 (d, *J* = 12.7 Hz, 1.4H; major), 2.35 (dd, *J* = 12.1, 6.7 Hz, 1H; minor), 2.33 – 2.26 (m, 2.4H; major+minor), 2.14 (s, 4.2H; major), 2.05 (s, 3H; minor), 1.51 (s, 3H; minor), 1.44 (s, 4.2H; major), 1.28 (t, *J* = 7.1 Hz, 7.2H; major+minor), 1.20 (s, 3H; minor), 1.16 (s, 4.2H; major);

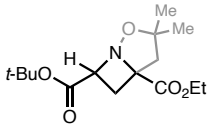
^{13}C NMR (126 MHz, $CDCl_3$): δ 172.3, 171.6, 169.6, 169.1, 89.5, 88.1, 87.7, 84.0, 74.9, 68.9, 62.0, 61.8, 50.4, 50.3, 33.0, 31.4, 29.3, 28.2 (2C), 26.4, 21.01, 20.97, 14.2, 14.1; **IR** (cm^{-1}): 2976, 2931, 1748, 1727, 1455, 1368, 1315, 1217, 1179, 1148, 1118, 1087, 1039, 1016, 913, 865, 828, 777, 692; **HRMS**: *m*/*z* calculated for $C_{12}H_{19}NNaO_5^+$ $[M+Na]^+$: 280.1155; found: 280.1153.



5-Ethyl 7-methyl 3,3,7-trimethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5,7-dicarboxylate (53): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), methyl methacrylate (40 µL, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 24 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 5:1 and a regioisomer ratio of >20:1. Purification by flash column chromatography (5-50% EtOAc/hexanes) afforded the pure major diastereomer as pale-yellow oil (56 mg, 82%) and the pure minor diastereomer as pale-yellow oil (13 mg, 19%).

***exo*(C$_7$-Me)-Diastereomer (major): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.31 – 4.18 (m, 2H), 3.72 (s, 3H), 3.19 (d, *J* = 12.0 Hz, 1H), 2.72 (d, *J* = 12.4 Hz, 1H), 2.54 (d, *J* = 12.4 Hz, 1H), 2.27 (d, *J* = 12.0 Hz, 1H), 1.59 (s, 3H), 1.32 – 1.26 (m, 6H), 1.09 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.8, 171.8, 85.5, 70.2, 68.0, 61.8, 52.4, 50.0, 36.5, 27.0, 26.0, 24.2, 14.2; **IR** (cm^{-1}): 2976, 2361, 2338, 1729, 1451, 1368, 1297, 1255, 1188, 1141, 1094, 1027, 959, 863, 784, 685; **HRMS**: *m*/*z* calculated for $C_{13}H_{22}NO_5^+$ $[M+H]^+$: 272.1492; found: 272.1493.

***endo*(C$_7$-Me)-Diastereomer (minor): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.31 – 4.19 (m, 2H), 3.77 (s, 3H), 3.04 (d, *J* = 12.1 Hz, 1H), 2.88 (d, *J* = 12.8 Hz, 1H), 2.31 (d, *J* = 12.9 Hz, 1H), 2.27 (d, *J* = 12.1 Hz, 1H), 1.54 (s, 3H), 1.48 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.20 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 174.3, 172.5, 86.0, 70.9, 66.4, 61.9, 52.8, 51.2, 37.0, 28.1, 25.6, 20.6, 14.2; **IR** (cm^{-1}): 2977, 2361, 2338, 1733, 1457, 1369, 1295, 1252, 1185, 1138, 1105, 1024, 994, 857, 771, 728, 682; **HRMS**: *m*/*z* calculated for $C_{13}H_{22}NO_5^+$ $[M+H]^+$: 272.1492; found: 272.1493.

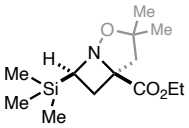


7-(*Tert*-butyl) 5-ethyl 3,3-dimethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5,7-dicarboxylate (54): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), *tert*-butyl acrylate (55 µL, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 42 h. ^{1}H NMR analysis of the

crude reaction mixture revealed a diastereomer ratio of 1:1 and a regioisomer ratio of >20:1. Purification by flash column chromatography (5-35% EtOAc/hexanes) afforded the pure *endo*-diastereomer as colorless oil (34 mg, 45%) and the pure *exo*-diastereomer as white solid (37 mg, 49%).

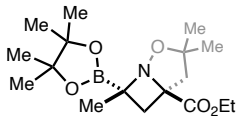
***exo*-Diastereomer: ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.26 (qd, *J* = 7.1, 1.1 Hz, 2H), 3.97 (dd, *J* = 9.6, 8.6 Hz, 1H), 2.88 (d, *J* = 13.0 Hz, 1H), 2.60 (dd, *J* = 11.5, 8.6 Hz, 1H), 2.51 – 2.42 (m, 2H), 1.56 (s, 3H), 1.48 (s, 9H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.26 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.1, 169.6, 88.5, 81.9, 73.3, 66.4, 61.8, 50.8, 29.9, 28.6, 28.1, 27.9, 14.2; **IR** (cm^{-1}): 2977, 1727, 1455, 1365, 1314, 1225, 1144, 1021, 944, 911, 844, 754, 671; **HRMS**: *m*/*z* calculated for $C_{15}H_{25}NNaO_5^+$ $[M+H]^+$: 322.1625; found: 322.1624.

***endo*-Diastereomer: ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.42 (dd, *J* = 8.2, 6.5 Hz, 1H), 4.31 – 4.23 (m, 2H), 2.88 (dd, *J* = 12.2, 6.5 Hz, 1H), 2.73 (d, *J* = 12.3 Hz, 1H), 2.64 – 2.56 (m, 2H), 1.48 (s, 9H), 1.38 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.13 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.7, 168.4, 85.0, 82.0, 73.7, 62.6, 61.8, 50.8, 29.7, 28.2, 26.9, 25.7, 14.2; **IR** (cm^{-1}): 2974, 2933, 1718, 1452, 1367, 1308, 1247, 1186, 1147, 1116, 1055, 1015, 950, 908, 847, 776, 725, 680; **HRMS**: *m*/*z* calculated for $C_{15}H_{25}NNaO_5^+$ $[M+H]^+$: 322.1625; found: 322.1625.



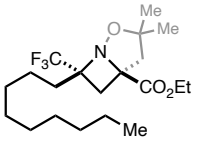
Ethyl 3,3-dimethyl-7-(trimethylsilyl)-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (55): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), vinyltrimethylsilane (55 µL, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 23 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of >10:1 and a regioisomer ratio of >20:1. Purification by flash column chromatography (2-20% EtOAc/hexanes) afforded the pure title compound as pale-yellow oil (36 mg, 53%).

^{1}H NMR (700 MHz, $CDCl_3$): δ 4.27 – 4.15 (m, 2H), 3.27 (t, *J* = 10.2 Hz, 1H), 2.85 (d, *J* = 12.8 Hz, 1H), 2.62 (d, *J* = 12.8 Hz, 1H), 2.26 (dd, *J* = 10.3, 2.0 Hz, 2H), 1.55 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.20 (s, 3H), 0.06 (s, 9H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 173.0, 86.6, 77.9, 61.4, 59.4, 51.5, 30.2, 28.8, 26.2, 14.2, -4.1; **IR** (cm^{-1}): 2973, 1727, 1454, 1367, 1313, 1247, 1215, 1181, 1144, 1040, 988, 915, 835, 728, 693; **HRMS**: *m*/*z* calculated for $C_{13}H_{26}NO_3Si^+$ $[M+H]^+$: 272.1676; found: 272.1673.



Ethyl 3,3,7-trimethyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (56): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), isopropenylboronic acid pinacol ester (71 µL, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 18 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 5:1 and a regioisomer ratio of 17:1. The yield was determined to be 77% by ^{1}H NMR analysis of the crude reaction mixture using mesitylene as internal standard. Characterization data for the *exo*(C_7-Me)-diastereomer was obtained after purification by flash column chromatography (florisil; 0-30% EtOAc/hexanes).

***exo*(C_7-Me)-Diastereomer (major): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.33 – 4.17 (m, 2H), 2.81 (d, *J* = 11.3 Hz, 1H), 2.75 (d, *J* = 12.1 Hz, 1H), 2.54 (d, *J* = 12.1 Hz, 1H), 2.08 (d, *J* = 11.3 Hz, 1H), 1.42 (s, 6H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.28 (s, 6H), 1.24 (s, 6H), 1.08 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 173.7, 84.3, 84.1, 70.4, 61.6, 51.3, 37.2, 26.4, 25.7, 25.5, 24.5, 14.3; **IR** (cm^{-1}): 2978, 1724, 1474, 1453, 1367, 1321, 1270, 1141, 983, 968, 926, 852, 733, 700, 674; **HRMS**: *m*/*z* calculated for $C_{17}H_{31}BNO_5^+$ $[M+H]^+$: 340.2290; found: 340.2295. The boron bearing quaternary carbon was not observed by ^{13}C NMR.

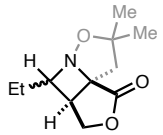


Ethyl 3,3-dimethyl-7-octyl-7-(trifluoromethyl)-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylate (57): Prepared according to GP-3 using **14** (43 mg, 0.25 mmol, 1.0 equiv.), 2-(trifluoromethyl)undec-1-ene[18] (84 mg, 0.38 mmol, 1.5 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 19 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 4:1 and a regioisomer ratio of >20:1. Purification by flash column chromatography (2-15% EtOAc/hexanes) afforded the pure *endo*(C_7-CF_3)-diastereomer as colorless oil (68 mg, 69%) and the pure *exo*(C_7-CF_3)-diastereomer as colorless oil (19 mg, 19%).

***endo*(CF_3)-Diastereomer (major): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.33 – 4.21 (m, 2H), 2.77 (d, *J* = 12.5 Hz, 1H), 2.73 (d, *J* = 12.8 Hz, 1H), 2.49 (dd, *J* = 12.8, 2.9 Hz, 2H), 1.94 – 1.81 (m, 2H), 1.55 – 1.47 (b, 2H), 1.44 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.32 – 1.21 (m, 12H), 1.18 (s, 3H), 0.87 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.6, 125.5 (q, *J* = 283.4 Hz), 85.7, 69.7, 66.4 (q, *J* = 25.6 Hz), 62.0, 50.6, 35.9, 34.3 (d, *J* = 2.5 Hz), 32.0, 30.3, 29.7, 29.6, 29.4, 27.2, 25.5, 23.1, 22.8, 14.2 (2C); **IR** (cm^{-1}): 2925, 2855, 1731, 1459, 1369, 1306, 1252, 1190, 1173, 1141, 1114, 1096,

1055, 943, 882, 784, 722, 678; **HRMS**: *m*/*z* calculated for $C_{20}H_{35}F_3NO_3^+$ $[M+H]^+$: 394.2564; found: 394.2561.

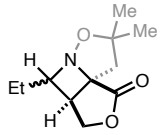
***exo*(CF$_3$)-Diastereomer (minor): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.34 – 4.21 (m, 2H), 2.83 (d, *J* = 12.9 Hz, 1H), 2.75 (d, *J* = 12.6 Hz, 1H), 2.32 (d, *J* = 12.9 Hz, 1H), 2.28 (d, *J* = 12.6 Hz, 1H), 1.96 (t, *J* = 11.0 Hz, 1H), 1.79 (t, *J* = 13.9 Hz, 1H), 1.54 – 1.50 (m, 1H), 1.48 (s, 3H), 1.35 – 1.20 (m, 19H), 0.87 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 172.4, 126.1 (q, *J* = 281 Hz), 85.7, 70.8, 66.6 (q, *J* = 27.9 Hz), 62.0, 52.5, 33.87 (d, *J* = 2.1 Hz), 32.0, 31.5, 30.6, 29.6, 29.4, 29.4, 27.9, 25.9, 23.4, 22.8, 14.3, 14.2; **IR** (cm^{-1}): 2925, 2855, 1729, 1461, 1370, 1305, 1253, 1148, 1122, 1094, 1020, 956, 933, 861, 783, 737; **HRMS**: *m*/*z* calculated for $C_{20}H_{35}F_3NO_3^+$ $[M+H]^+$: 394.2564; found: 394.2560.



4,7,7-Trimethyltetrahydro-1*H*,3*H*-furo[3',4':2,3]azeto[1,2-b]isoxazol-1-one (73): Prepared according to GP-3 using (*E*)-**72** (53 mg, 0.25 mmol, 1.0 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 19 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 1.2:1. Purification by flash column chromatography (2-30% EtOAc/CH_2Cl_2) afforded the pure (3a*S**,4*R**,8a*R**)-diastereomer as white solid (22 mg, 42%) and the pure (3a*S**,4*S**,8a*R**)-diastereomer as pale-yellow oil (18 mg, 34%).

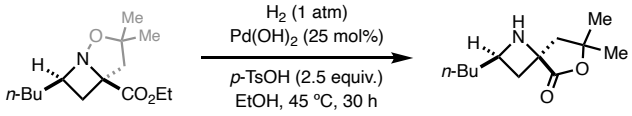
(3a*S,4*R**,8a*R**)-Diastereomer (major): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.51 (d, *J* = 10.3 Hz, 1H), 4.39 (t, *J* = 9.4 Hz, 1H), 3.68 (q, *J* = 7.9 Hz, 1H), 3.30 (t, *J* = 8.6 Hz, 1H), 2.60 (d, *J* = 12.8 Hz, 1H), 2.45 (d, *J* = 12.8 Hz, 1H), 1.78 (dp, *J* = 14.9, 7.4 Hz, 1H), 1.62 – 1.51 (m, 4H), 1.40 (s, 3H), 0.91 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 175.9, 88.5, 72.4, 70.8, 66.0, 46.6, 35.8, 28.3, 27.7, 23.5, 9.7; **IR** (cm^{-1}): 2960, 2939, 2361, 2337, 1770, 1457, 1368, 1264, 1233, 1211, 1155, 1100, 1048, 970, 949, 858, 824, 733, 706; **HRMS**: *m*/*z* calculated for $C_{11}H_{18}NO_3^+$ $[M+H]^+$: 212.1281; found: 212.1286.

(3a*S,4*S**,8a*R**)-Diastereomer (minor): ^{1}H NMR** (700 MHz, $CDCl_3$): δ 4.41 (t, *J* = 8.4 Hz, 1H), 4.35 (d, *J* = 9.8 Hz, 1H), 3.66 (q, *J* = 6.5 Hz, 1H), 3.00 (t, *J* = 6.4 Hz, 1H), 2.49 (d, *J* = 12.4 Hz, 1H), 2.27 (d, *J* = 12.4 Hz, 1H), 2.02 (dp, *J* = 14.2, 7.1 Hz, 1H), 1.66 (dp, *J* = 14.8, 7.4 Hz, 1H), 1.48 (s, 3H), 1.38 (s, 3H), 0.91 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 176.1, 85.3, 71.6, 70.6, 68.9, 48.5, 43.8, 26.8, 26.0, 23.3, 10.1; **IR** (cm^{-1}): 2963, 2932, 2873, 2361, 2338, 1759, 1457, 1366, 1218, 1170, 1133, 1050, 969, 885, 869, 827, 806, 723, 662; **HRMS**: *m*/*z* calculated for $C_{11}H_{18}NO_3^+$ $[M+H]^+$: 212.1281; found: 212.1283.



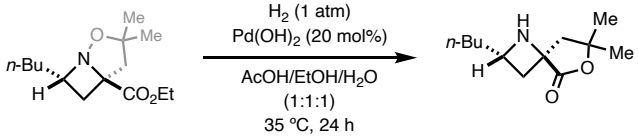
4,7,7-Trimethyltetrahydro-1*H*,3*H*-furo[3',4':2,3]azeto[1,2-b]isoxazol-1-one (73): Prepared according to GP-3 using (Z)-**72** (53 mg, 0.25 mmol, 1.0 equiv.), *fac*-[Ir(dFppy)$_3$] (1.9 mg, 1 mol%) and MeCN (2.5 mL) with a reaction time of 19 h. ^{1}H NMR analysis of the crude reaction mixture revealed a diastereomer ratio of 1.1:1. Purification by flash column chromatography (2-30% EtOAc/CH_2Cl_2) afforded the pure title compounnd as pale-yellow oil (36 mg, 68% combined yield; 1.1:1 d.r.). Spectroscopic data was found consistent with that obtained, when conducting the reaction with (*E*)-**72**.

N–O bond cleavage of Azetidine Products



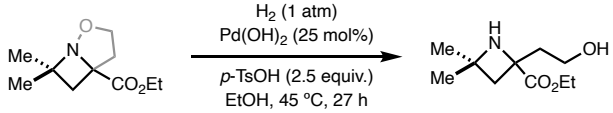
2-Butyl-7,7-dimethyl-6-oxa-1-azaspiro[3.4]octan-5-one (*cis*-59): A 3-dram vial equipped with a magnetic stir bar was charged with *exo*-**15** (50 mg, 0.2 mmol, 1.0 equiv.), $Pd(OH)_2$ (20wt%; 34 mg, 0.05 mmol, 0.25 equiv.) and *p*-TsOH (93 mg, 0.5 mmol, 2.5 equiv.). EtOH (5 mL) was added, the vial subsequently sealed with a septum-equipped cap and the reaction mixture sparged with hydrogen gas for 10 min. Then, the heterogenous reaction mixture was stirred vigorously at 45 °C for 30 h under a hydrogen atmosphere (balloon). After cooling to rt, the reaction mixture was passed through celite, the filter cake washed with CH_2Cl_2 and the filtrate concentrated *in vacuo*. The residue was taken up in CH_2Cl_2 and water and the aqueous layer brought to pH 10-11 with 2 M NaOH (aq.). The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (2x). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (70-100% EtOAc/hexanes) afforded the pure title compound as colorless solid (28 mg, 68%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.70 (p, J = 7.2 Hz, 1H), 2.55 – 2.32 (m, 4H), 2.22 (d, J = 13.2 Hz, 1H), 1.89 – 1.66 (m, 2H), 1.42 (s, 3H), 1.37 – 1.14 (m, 7H), 0.89 (t, J = 7.2 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 179.4, 81.6, 62.9, 54.5, 50.1, 38.4, 37.3, 29.1, 28.0, 27.7, 22.6, 14.2; **IR** (cm^{-1}): 3318, 1957, 2928, 2857, 1761, 1456, 1387, 1374, 1273, 1243, 1204, 1154, 1075, 1027, 946, 923, 876, 810, 730, 677; **HRMS**: *m*/*z* calculated for $C_{12}H_{22}NO_2^+$ $[M+H]^+$: 212.1645; found: 212.1645.



2-Butyl-7,7-dimethyl-6-oxa-1-azaspiro[3.4]octan-5-one (*trans*-59): A 3-dram vial equipped with a magnetic stir bar was charged with *endo*-**15** (100 mg, 0.4 mmol, 1.0 equiv.) and $Pd(OH)_2$ (20wt%; 55 mg, 0.08 mmol, 0.20 equiv.). A 1:1:1 mixture of EtOH, water and acetic acid (10 mL) was added, the vial subsequently sealed with a septum-equipped cap and the reaction mixture sparged with hydrogen gas for 12 min. Then, the heterogenous reaction mixture was stirred vigorously at 35 ºC for 24 h under a hydrogen atmosphere (balloon). After cooling to rt, the reaction mixture was passed through celite, the filter cake washed with MeOH and the filtrate concentrated *in vacuo*. The residue was taken up in CH_2Cl_2 and water and the aqueous layer brought to pH 10-11 with 2 M NaOH (aq.). The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (2x). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (20-100% EtOAc/hexanes) afforded the pure title compound as white solid (53 mg, 64%)

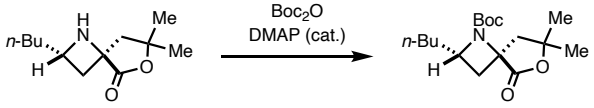
^{1}H NMR (700 MHz, $CDCl_3$): δ 4.09 (p, *J* = 6.8 Hz, 1H), 2.92 (b, 1H), 2.71 (t, *J* = 9.3 Hz, 1H), 2.27 (d, *J* = 13.4 Hz, 1H), 2.12 (d, *J* = 13.4 Hz, 1H), 2.07 (t, *J* = 9.4 Hz, 1H), 1.58 – 1.44 (m, 2H), 1.40 (s, 3H), 1.36 – 1.08 (m, 7H), 0.88 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 180.8, 81.8, 62.8, 54.0, 50.6, 39.1, 38.79, 3.12, 28.1, 27.4, 22.7, 14.2; **IR** (cm^{-1}): 3299, 2920, 2855, 1753, 1466, 1451, 1370, 1289, 1250, 1168, 1148, 1028, 933, 860, 799, 719, 695, 676; **HRMS**: *m*/*z* calculated for $C_{12}H_{22}NO_2^+$ $[M+H]^+$: 212.1645; found: 212.1650.



Ethyl 2-(2-hydroxyethyl)-4,4-dimethylazetidine-2-carboxylate (63): A 3-dram vial equipped with a magnetic stir bar was charged with **62** (40 mg, 0.2 mmol, 1.0 equiv.), $Pd(OH)_2$ (20wt%; 35 mg, 0.05 mmol, 0.25 equiv.) and *p*-TsOH (96 mg, 0.5 mmol, 2.5 equiv.). EtOH (5 mL) was added, the vial subsequently sealed with a septum-equipped cap and the reaction mixture sparged with hydrogen gas for 10 min. Then, the heterogenous reaction mixture was stirred vigorously at 45 ºC for 27 h under a hydrogen atmosphere (balloon). After cooling to rt, the reaction mixture was passed through celite, the filter cake washed with CH_2Cl_2 and the filtrate concentrated *in vacuo*. The residue was taken up in CH_2Cl_2 and water and the aqueous layer brought to pH 10-11 with 2 M NaOH (aq.). The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (2x). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (1-10% MeOH/CH_2Cl_2) afforded the pure title compound as a pale-yellow (18 mg, 45%).

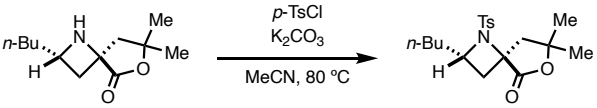
^{1}H NMR (700 MHz, $CDCl_3$): δ 4.24 (q, *J* = 7.1 Hz, 2H), 4.08 (t, *J* = 10.7 Hz, 1H), 3.82 – 3.73 (m, 1H), 2.40 (d, *J* = 12.0 Hz, 1H), 2.25 (d, *J* = 12.1 Hz, 1H), 1.91 (t, *J* = 12.2 Hz, 1H), 1.79 (dd, *J* = 14.6, 4.8 Hz, 1H), 1.30 (t, *J* = 7.9 Hz, 9H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 180.8, 81.8, 62.8, 54.0, 50.6, 39.1, 38.8, 29.1, 28.1, 27.4, 22.7, 14.2; **IR** (cm^{-1}): 3301, 2958, 2868, 1724, 1447, 1376, 1279, 1263, 1208, 1149, 1086, 1054, 1023, 855, 808, 746; **HRMS**: *m*/*z* calculated for $C_{10}H_{20}NO_3^+$ $[M+H]^+$: 202.1438; found: 202.1437.

Synthetic Modifications of Azetidine Products



***Tert*-butyl 2-butyl-7,7-dimethyl-5-oxo-6-oxa-1-azaspiro[3.4]octane-1-carboxylate (60):** A 10-mL round-bottom flask equipped with a magnetic stirbar was charged with *trans*-**59** (21 mg, 0.1 mmol, 1.0 equiv.) and MeCN (2 mL). Boc_2O (50 µL, 0.2 mmol, 2.0 equiv.) and DMAP (2.4 mg, 0.02 mmol, 0.2 equiv.) were added and the solution stirred at rt for 16 h. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (5-40% EtOAc/hexanes) to afford the pure title compound as white solid (24 mg, 78%). Characterization data is provided for a 1.7:1 mixture of rotamers (A/B).

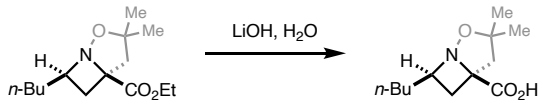
^{1}H NMR (700 MHz, $CDCl_3$): δ 4.55 – 4.49 (m, 2.7H; A+B), 2.79 (d, *J* = 13.5 Hz, 1.7H; A), 2.75 – 2.67 (m, 2.7H; A+B), 2.60 (d, *J* = 13.5 Hz, 1H; B), 2.37 (d, *J* = 13.4 Hz, 1H; B), 2.29 (d, *J* = 13.5 Hz, 1.7H; A), 2.05 – 1.95 (m, 3.7H; A+B), 1.95 – 1.84 (m, 1.7H; A), 1.66 – 1.21 (m, 54H; A+B) 0.94 – 0.85 (m, 8.1H; A+B); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 174.8, 174.7, 148.1 (d, *J* = 356.0 Hz), 147.5 (d, *J* = 371.7 Hz), 85.2, 85.0, 82.1, 81.8, 68.0, 67.1, 60.9, 59.7, 47.0, 45.7, 36.2, 35.8, 35.1, 35.0, 29.2, 29.1, 29.0, 28.9, 27.60, 27.58, 26.6, 26.1, 22.61, 22.57, 14.1 (2C); **IR** (cm^{-1}): 2977, 2934, 2872, 1797, 1762, 1722, 1468, 1398, 1372, 1237, 1134, 1095, 1057, 1026, 944, 923, 890, 826, 762, 694, 666; **HRMS**: *m*/*z* calculated for $C_{17}H_{30}NO_4^+$ $[M+H]^+$: 312.2169; found: 312.2170.



2-Butyl-7,7-dimethyl-1-tosyl-6-oxa-1-azaspiro[3.4]octan-5-one (61): A 10-mL round-bottom flask equipped with a magnetic stirbar was charged with *trans*-**59** (21 mg, 0.1 mmol, 1.0 equiv.) and MeCN (2 mL). *p*-TsCl (57 mg, 0.3 mmol, 3.0 equiv.) and K_2CO_3 (41 mg, 0.3 mmol, 3.0 equiv.) were added and the reaction mixture heated at 80 ºC for 2.5 h. Then, the reaction was concentrated *in vacuo* and purified by flash

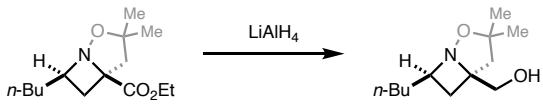
column chromatography (5-40% EtOAc/hexanes) to afford the pure title compound as viscous colorless oil (36 mg, 99%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 4.41 (qd, *J* = 7.9, 3.9 Hz, 1H), 2.84 (d, *J* = 13.7 Hz, 1H), 2.55 (dd, *J* = 10.5, 8.0 Hz, 1H), 2.43 (s, 3H), 2.36 (d, *J* = 13.7 Hz, 1H), 2.02 (dd, *J* = 10.5, 7.4 Hz, 1H), 1.92 – 1.78 (m, 1H), 1.64 – 1.50 (m, 4H), 1.33 (s, 3H), 1.30 – 1.11 (m, 4H), 0.85 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 174.7, 143.7, 136.7, 129.4, 127.7, 81.9, 70.5, 61.7, 48.2, 36.3, 35.2, 29.4, 29.0, 26.0, 22.5, 21.7, 14.0; **IR** (cm^{-1}): 2931, 2861, 1769, 1598, 1453, 1333, 1294, 1152, 1090, 923, 813, 753, 730, 669, 640; **HRMS**: *m*/*z* calculated for $C_{19}H_{27}NNaO_4S^+$ $[M+Na]^+$: 388.1553 found: 388.1548.



7-Butyl-3,3-dimethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carboxylic acid (64): A 10-mL round-bottom flask equipped with a magnetic stir bar was charged with *exo*-**15** (51 mg, 0.2 mmol, 1.0 equiv.) and a 3:1 mixture of MeOH/water (2 mL). Lithium hydroxide monohydrate (13 mg, 0.3 mmol, 1.5 equiv.) was added and the resulting solution stirred at rt for 16 h. The reaction mixture acidified with 1 M HCl (aq.) to pH 1-2 and subsequently extracted with CH_2Cl_2 (5x). The combined organic layers were dried over Na_2SO_4, filtered, concentrated *in vacuo*, then dried using high-vac to afford the pure title compound as colorless oil (44 mg, 97%).

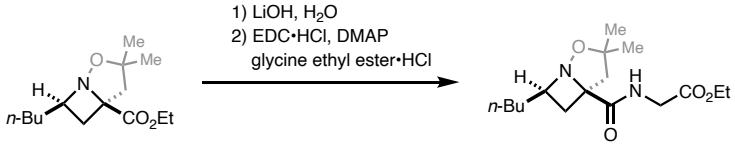
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.12 (b, 1H), 3.72 (p, *J* = 7.9 Hz, 1H), 2.98 (d, *J* = 12.9 Hz, 1H), 2.55 (dd, *J* = 11.7, 8.9 Hz, 1H), 2.49 (d, *J* = 12.9 Hz, 1H), 2.14 (dd, *J* = 11.7, 8.1 Hz), 1.95 – 1.83 (m, 1H), 1.73 – 1.62 (m, 1H), 1.53 (s, 3H), 1.42 – 1.26 (m, 4H), 1.24 (s, 3H), 0.90 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 172.2, 89.9, 74.5, 68.4, 50.2, 33.8, 31.1, 28.3, 27.8, 27.3, 22.5, 14.1; **IR** (cm^{-1}): 2959, 2932, 2873, 1718, 1617, 1457, 1378, 1265, 1194, 1152, 854, 731, 700; **HRMS**: *m*/*z* calculated for $C_{12}H_{22}NO_3^+$ $[M+H]^+$: 228.1594; found: 228.1594.



7-Butyl-3,3-dimethyl-2-oxa-1-azabicyclo[3.2.0]heptan-5-yl)methanol (65): To a 10-mL round-bottom flask equipped with a magnetic stir bar containing a suspension of $LiALH_4$ (10 mg, 0.26 mmol, 1.35 equiv.) in Et_2O (1.25 mL) was added *exo*-**15** (50 mg, 0.2 mmol, 1.0 equiv.) as a solution in Et_2O (0.75 mL) dropwise at 0 ºC. After stirring for 0.5 h at 0 ºC, water was added carefully, the reaction mixture diluted with Et_2O and Rochelle salt solution (aq., sat.) and subsequently stirred for 12 h at rt. The organic layer was separated and the aqueous layer extracted with Et_2O (3x). The

combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*, then dried using high-vac to obtain the pure title compound as clear oil (40 mg, 96%).

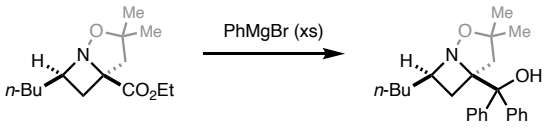
^{1}H NMR (400 MHz, $CDCl_3$): δ 3.62 – 3.48 (m, 2H), 3.43 – 3.33 (m, 1H), 2.86 (d, *J* = 8.6 Hz, 1H), 2.45 (d, *J* = 13.0 Hz, 1H), 2.17 (d, *J* = 13.0 Hz, 1H), 2.08 (dd, *J* = 11.0, 8.9 Hz, 1H), 1.92 (dd, *J* = 11.0, 8.2 Hz, 1H), 1.69 – 1.53 (m, 4H), 1.53 – 1.40 (m, 1H), 1.40 – 1.18 (m, 7H), 0.88 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 87.7, 74.8, 66.2, 66.0, 51.4, 35.1, 31.7, 30.2, 27.8, 27.6, 22.8, 14.2; **IR** (cm^{-1}): 3386, 2955, 2928, 2858, 2361, 2337, 1457, 1380, 1303, 1249, 1226, 1150, 1078, 1043, 971, 864, 773, 686, 668, 640;**HRMS**: *m*/*z* calculated for $C_{12}H_{24}NO_2^+$ $[M+H]^+$: 214.1802; found: 214.1805.



Ethyl 7-butyl-3,3-dimethyl-2-oxa-1-azabicyclo[3.2.0]heptane-5-carbonyl)glycinate (66): A 10-mL round-bottom flask equipped with a magnetic stir bar was charged with *exo*-**15** (51 mg, 0.2 mmol, 1.0 equiv.) and a 3:1 mixture of MeOH/water (2 mL). Lithium hydroxide monohydrate (13 mg, 0.3 mmol, 1.5 equiv.) was added and the resulting solution stirred at rt for 2 h. The reaction mixture acidified with 1 M HCl (aq.) to pH 1-2 and subsequently extracted with CH_2Cl_2 (5x). The combined organic layers were dried over Na_2SO_4, filtered, concentrated *in vacuo*, then dried using high-vac to afford pure **64**.

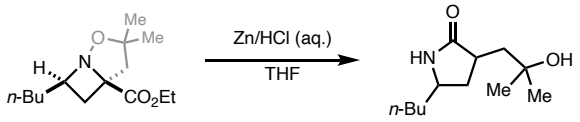
Next, the carboxylic acid was dissolved in CH_2Cl_2 (5 mL) and DMAP (5 mg, 0.04 mmol, 0.2 equiv.), glycine ethyl ester hydrochloride (56 mg, 0.4 mmol, 2.0 equiv.) and EDC•HCl (57 mg, 0.3 mmol, 1.5 equiv.) were added sequentially. After stirring the resulting mixture for 16 h at rt, it was diluted with CH_2Cl_2 and washed with 1 M HCl (aq., 2x) and brine, dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by flash column chromatography (20-40% EtOAc/hexanes) afforded the product as colorless oil (58 mg, 93%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.82 (t, *J* = 6.1 Hz, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 4.14 – 3.95 (m, 2H), 3.50 (p, *J* = 8.0 Hz, 1H), 2.94 (d, *J* = 12.8 Hz, 1H), 2.52 – 2.38 (m, 2H), 1.79 (dd, *J* = 11.1, 8.5 Hz, 1H), 1.74 – 1.65 (m, 1H), 1.58 – 1.46 (m, 4H), 1.42 – 1.21 (m, 7H), 1.17 (s, 3H), 0.90 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 173.6, 169.5, 87.5, 73.2, 67.3, 61.4, 50.0, 41.0, 35.3, 31.5, 29.2, 28.6, 27.5, 22.7, 14.2, 14.1; **IR** (cm^{-1}): 3366, 2957, 2931, 2873, 2361, 2337, 1750, 1671, 1516, 1457, 1369, 1255, 1188, 1098, 1028, 919, 862, 729, 668, 646; **HRMS**: *m*/*z* calculated for $C_{16}H_{29}N_2O_4^+$ $[M+H]^+$: 313.2122; found: 313.2120.



7-Butyl-3,3-dimethyl-2-oxa-1-azabicyclo[3.2.0]heptan-5-yl)diphenylmethanol (67): To a 10-mL round-bottom flask equipped with a magnetic stir bar containing a solution of *exo*-**15** (51 mg, 0.2 mmol, 1.0 equiv.) in THF (2 mL) was added freshly prepared PhMgBr (0.5 M in THF, 4.0 mL, 2.0 mmol, 10.0 equiv.) dropwise at 0 ºC. After stirring for 15 min at 0 ºC, NH_4Cl (aq., sat.) was added and the resulting mixture extracted with Et_2O (3x), the combined organic layers dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (5-10% EtOAc/hexanes) afforded the pure title compound as colorless oil (69 mg, 95%).

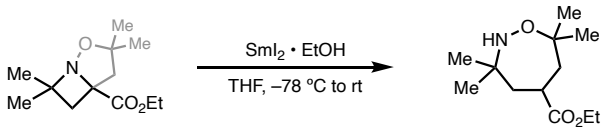
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43 – 7.15 (m, 10H), 4.78 (s, 1H), 3.77 (p, *J* = 7.8 Hz, 1H), 2.59 (q, *J* = 13.1 Hz, 2H), 2.34 (dd, *J* = 11.5, 9.4 Hz, 1H), 1.92 (dd, *J* = 11.5, 7.8 Hz, 1H), 1.59 (s, 3H), 1.56 – 1.44 (m, 1H), 1.39 – 1.14 (m, 5H), 0.87 (t, *J* = 7.1 Hz, 3H), 0.52 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 144.9, 143.1, 128.1, 128.0, 127.8, 127.7, 127.3, 127.2, 89.8, 81.4, 80.6, 65.1, 52.9, 34.7, 33.4, 32.1, 28.2, 27.6, 22.6, 14.2; **IR** (cm^{-1}): 2957, 2858, 2246, 1493, 1447, 1366, 1298, 1229, 1170, 1146, 1024, 907, 759, 728, 698, 668; **HRMS**: *m*/*z* calculated for $C_{24}H_{32}NO_2^+$ $[M+H]^+$: 266.2428; found: 266.2435.



5-Butyl-3-(2-hydroxy-2-methylpropyl)pyrrolidin-2-one (68): A 25-mL round-bottom flask equipped with a magnetic stir bar was charged with *exo*-**15** (50 mg, 0.2 mmol, 1.0 equiv.) and a 9:1 mixture of 1 M HCl (aq.)/THF (5 mL). Zinc powder (128 mg, 2.0 mmol, 10.0 equiv.) was added and the resulting heterogenous mixture heated at 80 ºC for 3 h. After cooling to rt, the reaction mixture was filtered and the filtrate brought to pH 10-11 with 2 M NaOH (aq.). The resulting cloudy mixture was extracted with CH_2Cl_2 (5x) and the combined organic layers dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (50-100% EtOAc/hexanes) afforded the pure title compound as colorless oil as a 2.6:1 mixture of diastereomers (24 mg, 58%). Characterization data was obtained for a 2.6:1 mixture of diastereomers.

^{1}H NMR (700 MHz, $CDCl_3$): δ 6.42 (s, 1H; minor), 6.35 (s, 2.6H; major), 4.92 (s, 2.6H; major), 4.74 (s, 1H; minor), 3.64 – 3.51 (m, 3.6H; major+minor), 2.82 – 2.71 (m, 3.6H; major+minor), 2.46 – 2.39 (m, 2.6H; major), 2.04 (t, *J* = 11.1 Hz, 1H; minor), 1.99 – 1.86 (m, 4.6H; major+minor), 1.60 – 1.20 (m, 49.4H; major+minor), 0.93 – 0.86 (m,

10.8H; major+minor); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 181.2, 180.9, 69.4, 69.2, 53.7, 53.1, 45.2, 45.1, 39.1, 37.0, 36.7, 36.3, 36.1, 35.3, 31.5 (2C), 28.7 (2C), 28.3, 28.1, 22.7, 22.6, 14.11, 14.08; **IR** (cm^{-1}): 3205, 2960, 2927, 2858, 1681, 1662, 1456, 1378, 1362, 1317, 1274, 1186, 1151, 1084, 959, 907, 783, 731, 658; **HRMS**: *m*/*z* calculated for $C_{12}H_{23}NNaO_2^+$ [M+Na]$^+$: 236.1621; found: 236.1621.

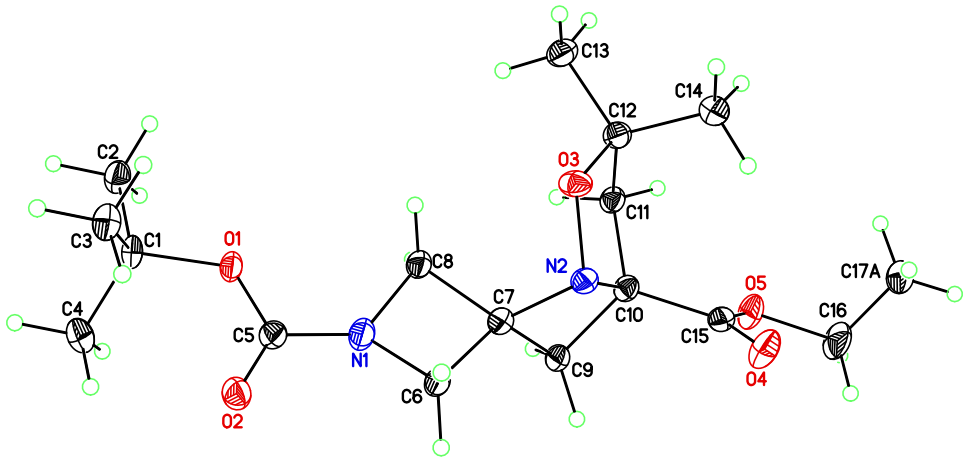


Ethyl 3,3,7,7-tetramethyl-1,2-oxazepane-5-carboxylate (69): A Schlenk flask equipped with a magnetic stirbar was charged with **40** (45 mg, 0.2 mmol 1.0 equiv.) and the flask evacuated and refilled with nitrogen gas. This cycle was repeated twice, before adding a 2:1 mixture (*v*/*v*) of degassed THF/EtOH (2 mL). The resulting solution was cooled to –78 °C and a freshly prepared SmI_2 solution (0.1 M in THF; 12 mL, 1.2 mmol, 6.0 equiv.) was added dropwise. The resulting dark-blue solution was gradually brought to rt over 1 h. Then, the reaction vessel was opened, the reaction mixture diluted with water and sodium thiosulfate solution (aq., sat.) and extracted with EtOAc (3x). The combined organic layers were washed with water and brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (2-10% EtOAc/hexanes) afforded the pure title compound as pale-yellow oil (19 mg, 42%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.43 (s, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 2.69 (t, *J* = 11.0 Hz, 1H), 1.97 (dd, *J* = 14.0, 10.1 Hz, 1H), 1.84 – 1.67 (m, 2H), 1.53 (t, *J* = 12.6 Hz, 1H), 1.29 – 1.19 (m, 9H), 1.10 (s, 3H), 0.98 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 176.9, 77.6, 60.5, 56.1, 45.8, 43.4, 37.9, 27.6, 26.8, 25.9, 24.6, 14.4; **IR** (cm^{-1}): 2971, 1728, 1453, 1362, 1283, 1228, 1155, 1114, 1037, 1020, 911, 840, 787, 733; **HRMS**: *m*/*z* calculated for $C_{12}H_{24}NO_3^+$ [M+H]$^+$: 230.1751; found: 230.1750.

9) X-Ray Crystallographic Data

Diazacyclobutane 44



Supplementary Figure 18: Crystal structure of **44**. X-ray crystallographic coordinates have been deposited at the Cambridge Crystallographic Data Centre (CCDC) with the accession code 1980947.

Colorless plates of **44** were grown from a hexanes solution of the compound at 22 ºC. A crystal of dimensions 0.12 x 0.10 x 0.03 mm was mounted on a Rigaku AFC10K Saturn 944+ CCD-based X-ray diffractometer equipped with a low temperature device and Micromax-007HF Cu-target micro-focus rotating anode (λ = 1.54187 A) operated at 1.2 kW power (40 kV, 30 mA). The X-ray intensities were measured at 85(1) K with the detector placed at a distance 42.34 mm from the crystal. A total of 2028 images were collected with an oscillation width of 1.0° in ω. The exposure times were 1 sec. for the low angle images, 3 sec. for high angle. Rigaku d*trek images were exported to CrysAlisPro for processing and corrected for absorption. The integration of the data yielded a total of 13716 reflections to a maximum 2θ value of 138.76° of which 3286 were independent and 3158 were greater than 2σ(I). The final cell constants (Supplementary Table 9) were based on the xyz centroids of 9574 reflections above 10σ(I). Analysis of the data showed negligible decay during data collection. The structure was solved and refined with the Bruker SHELXTL (version 2018/3) software package, using the space group P1bar with Z = 2 for the formula $C_{17}H_{28}N_2O_5$. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in idealized positions. The terminal methyl group (C17) is disordered over two sites. Full matrix least-squares refinement based on F^2 converged at R1 = 0.0403 and wR2 = 0.1030 [based on I > 2sigma(I)], R1 = 0.0411 and wR2 = 0.1039 for all data. Additional details are presented in Supplementary Table 9 and are given as Supporting Information in a CIF file. Acknowledgement is made for funding from NSF grant CHE-0840456 for X-ray instrumentation.

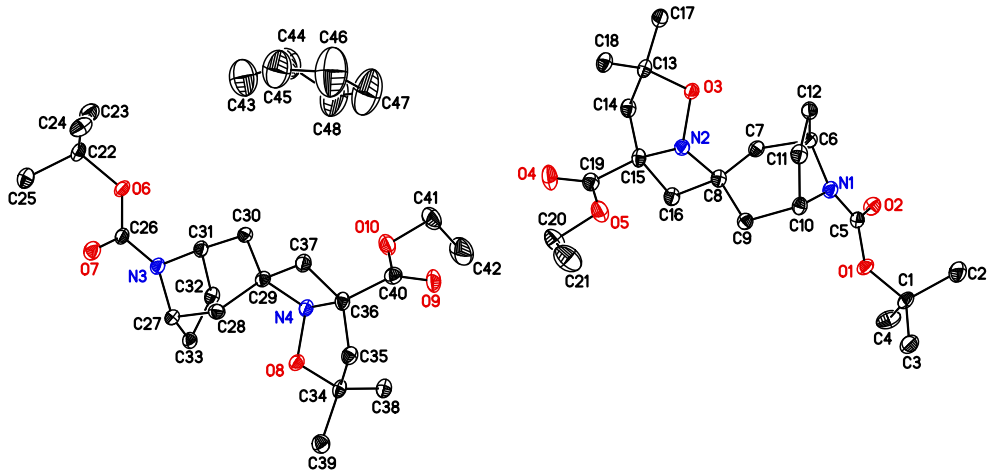
Supplementary Table 9. Crystal data and structure refinement for **44**.

Identification code	1-(*Tert*-butyl) 1'-ethyl 3',3'-dimethyl-4'-oxa-5'-azaspiro[azetidine-3,6'-bicyclo[3.2.0]heptane]-1,1'-dicarboxylate
Empirical formula	C17 H28 N2 O5
Formula weight	340.41
Temperature	85(2) K
Wavelength	1.54184 A
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 5.7853(2) A alpha = 105.136(3) deg. b = 11.3896(3) A beta = 97.310(3) deg. c = 14.8541(4) A gamma = 100.774(3) deg.
Volume	912.02(5) A^3
Z, Calculated density	2, 1.240 Mg/m^3
Absorption coefficient	0.748 mm^-1
F(000)	368
Crystal size	0.120 x 0.100 x 0.030 mm
Theta range for data collection	3.137 to 69.386 deg.
Limiting indices	-7<=h<=6, -13<=k<=13, -16<=l<=17
Reflections collected / unique	13716 / 3286 [R(int) = 0.0427]
Completeness to theta = 67.684	97.90%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.84904
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3286 / 1 / 234
Goodness-of-fit on F^2	1.066
Final R indices [I>2sigma(I)]	R1 = 0.0403, wR2 = 0.1030
R indices (all data)	R1 = 0.0411, wR2 = 0.1039
Extinction coefficient	0.0137(12)
Largest diff. peak and hole	0.356 and -0.279 e.A^-3

G.M. Sheldrick (2015) "Crystal structure refinement with SHELXL", Acta Cryst., C71, 3-8 (Open Access).
CrystalClear Expert 2.0 r16, Rigaku Americas and Rigaku Corporation (2014), Rigaku Americas, 9009, TX, USA 77381-5209, Rigaku Tokyo, 196-8666, Japan.

CrysAlisPro 1.171.38.41 (Rigaku Oxford Diffraction, 2015).

Tropinone-derived azetidine 46



Supplementary Figure 19: Crystal structure of **46**. X-ray crystallographic coordinates have been deposited at the Cambridge Crystallographic Data Centre (CCDC) with the accession code 1980951.

Colorless needles of **46** were grown from a hexanes solution of the compound at 0 ºC. A crystal of dimensions 0.13 x 0.03 x 0.03 mm was mounted on a Rigaku AFC10K Saturn 944+ CCD-based X-ray diffractometer equipped with a low temperature device and Micromax-007HF Cu-target micro-focus rotating anode (λ = 1.54187 A) operated at 1.2 kW power (40 kV, 30 mA). The X-ray intensities were measured at 85(1) K with the detector placed at a distance 42.00 mm from the crystal. A total of 2028 images were collected with an oscillation width of 1.0° in ω. The exposure times were 1 sec. for the low angle images, 4 sec. for high angle. Rigaku d*trek images were exported to CrysAlisPro for processing and corrected for absorption. The integration of the data yielded a total of 35611 reflections to a maximum 2θ value of 138.69° of which 8411 were independent and 8004 were greater than 2σ(I). The final cell constants (Supplementary Table 10) were based on the xyz centroids of 15622 reflections above 10σ(I). Analysis of the data showed negligible decay during data collection. The structure was solved and refined with the Bruker SHELXTL (version 2018/3) software package, using the space group Pn with Z = 2 for the formula $C_{48}H_{80}N_4O_{10}$. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in idealized positions. Full matrix least-squares refinement based on F^2 converged at R1 = 0.0414 and wR2 = 0.1080 [based on I > 2sigma(I)], R1 = 0.0435 and wR2 = 0.1115 for all data. Additional details are presented in Supplementary Table 10 and are given as Supporting Information in a CIF file. Acknowledgement is made for funding from NSF grant CHE-0840456 for X-ray instrumentation.

Supplementary Table 10. Crystal data and structure refinement for **46**.

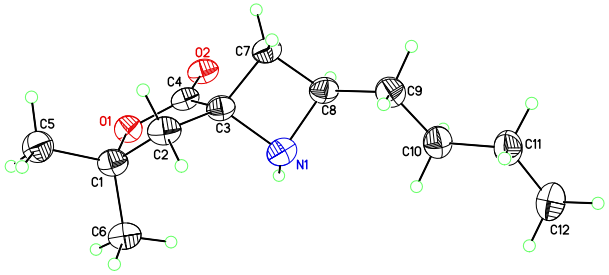
Identification code	8'-(*Tert*-butyl) 1-ethyl-3,3-dimethyl-4-oxa-5,8'-diazaspiro[bicyclo[3.2.0]heptane-6,3'-bicyclo[3.2.1]octane]-1,8'-dicarboxylate
Empirical formula	C48 H80 N4 O10
Formula weight	873.16
Temperature	85(2) K
Wavelength	1.54184 A
Crystal system, space group	Monoclinic, Pn
Unit cell dimensions	a = 17.6585(2) A alpha = 90 deg. b = 6.09660(10) A beta = 98.4520(10) deg. c = 22.7527(3) A gamma = 90 deg.
Volume	2422.88(6) A^3
Z, Calculated density	2, 1.197 Mg/m^3
Absorption coefficient	0.669 mm^-1
F(000)	952
Crystal size	0.130 x 0.030 x 0.030 mm
Theta range for data collection	2.966 to 69.343 deg.
Limiting indices	-21<=h<=20, -7<=k<=7, -25<=l<=27
Reflections collected / unique	35611 / 8411 [R(int) = 0.0621]
Completeness to theta = 67.684	100.00%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.78867
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	8411 / 2 / 573
Goodness-of-fit on F^2	1.043
Final R indices [I>2sigma(I)]	R1 = 0.0414, wR2 = 0.1080
R indices (all data)	R1 = 0.0435, wR2 = 0.1115
Absolute structure parameter	0.4(2)
Extinction coefficient	n/a
Largest diff. peak and hole	0.259 and -0.229 e.A^-3

G.M. Sheldrick (2015) "Crystal structure refinement with SHELXL", Acta Cryst., C71, 3-8 (Open Access).

CrystalClear Expert 2.0 r16, Rigaku Americas and Rigaku Corporation (2014), Rigaku Americas, 9009, TX, USA 77381-5209, Rigaku Tokyo, 196-8666, Japan.

CrysAlisPro 1.171.38.41 (Rigaku Oxford Diffraction, 2015).

Deprotected azetidine *trans*-59



Supplementary Figure 20: Crystal structure of *trans*-**59**. X-ray crystallographic coordinates have been deposited at the Cambridge Crystallographic Data Centre (CCDC) with the accession code 1980952.

Colorless needles of *trans*-**59** were grown from a hexanes solution of the compound at 0 ºC. A crystal of dimensions 0.18 x 0.09 x 0.03 mm was mounted on a Rigaku AFC10K Saturn 944+ CCD-based X-ray diffractometer equipped with a low temperature device and Micromax-007HF Cu-target micro-focus rotating anode (λ = 1.54187 A) operated at 1.2 kW power (40 kV, 30 mA). The X-ray intensities were measured at 85(1) K with the detector placed at a distance 42.00 mm from the crystal. A total of 2028 images were collected with an oscillation width of 1.0° in ω. The exposure times were 1 sec. for the low angle images, 5 sec. for high angle. Rigaku d*trek images were exported to CrysAlisPro for processing and corrected for absorption. The integration of the data yielded a total of 18752 reflections to a maximum 2θ value of 138.92° of which 2257 were independent and 2082 were greater than 2σ(I). The final cell constants (Supplementary Table 11) were based on the xyz centroids of 5417 reflections above 10σ(I). Analysis of the data showed negligible decay during data collection. The structure was solved and refined with the Bruker SHELXTL (version 2018/3) software package, using the space group P2(1)2(1)2(1) with Z = 4 for the formula $C_{12}H_{21}NO_2$. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in a combination of refined and idealized positions. Full matrix least-squares refinement based on F^2 converged at R1 = 0.0467 and wR2 = 0.1131 [based on I > 2sigma(I)], R1 = 0.0512 and wR2 = 0.1195 for all data. Additional details are presented in Supplementary Table 11 and are given as Supporting Information in a CIF file. Acknowledgement is made for funding from NSF grant CHE-0840456 for X-ray instrumentation.

Supplementary Table 11. Crystal data and structure refinement for *trans*-**59**.

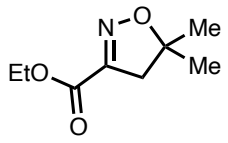
Identification code	2-Butyl-7,7-dimethyl-6-oxa-1-azaspiro[3.4]octan-5-one
Empirical formula	C12 H21 N O2
Formula weight	211.3
Temperature	85(2) K
Wavelength	1.54184 A
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 6.15494(18) A alpha = 90 deg. b = 8.5930(4) A beta = 90 deg. c = 23.1982(8) A gamma = 90 deg.
Volume	1226.94(8) A^3
Z, Calculated density	4, 1.144 Mg/m^3
Absorption coefficient	0.611 mm^-1
F(000)	464
Crystal size	0.180 x 0.090 x 0.030 mm
Theta range for data collection	3.811 to 69.462 deg.
Limiting indices	-7<=h<=7, -9<=k<=8, -27<=l<=28
Reflections collected / unique	18752 / 2257 [R(int) = 0.0771]
Completeness to theta = 67.684	98.60%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.76113
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2257 / 0 / 144
Goodness-of-fit on F^2	1.063
Final R indices [I>2sigma(I)]	R1 = 0.0467, wR2 = 0.1131
R indices (all data)	R1 = 0.0512, wR2 = 0.1195
Absolute structure parameter	0.2(4)
Extinction coefficient	n/a
Largest diff. peak and hole	0.233 and -0.235 e.A^-3

G.M. Sheldrick (2015) "Crystal structure refinement with SHELXL", Acta Cryst., C71, 3-8 (Open Access).

CrystalClear Expert 2.0 r16, Rigaku Americas and Rigaku Corporation (2014), Rigaku Americas, 9009, TX, USA 77381-5209, Rigaku Tokyo, 196-8666, Japan.

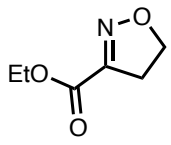
CrysAlisPro 1.171.38.41 (Rigaku Oxford Diffraction, 2015).

10) NMR Spectra


N
O
Me
Me
EtO
O

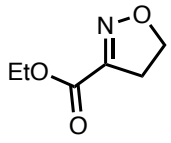
14

4.36
4.34
4.33
4.31
2.96
1.46
1.37
1.36
1.35
1.94
2.00
6.00
2.99
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


N
O
EtO
O

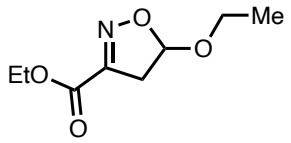
S19

4.56
4.54
4.52
4.37
4.36
4.35
4.34
3.23
3.21
3.19
1.38
1.37
1.36
1.97
1.91
2.00
2.95
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


N
O
EtO
O

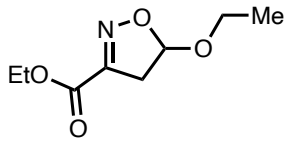
S19

160.76
151.93
71.43
62.17
33.89
14.21
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


N
O
Me
O
EtO
O

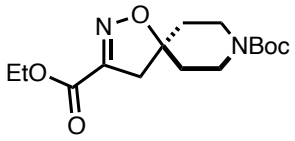
S23

5.71
5.70
4.38
4.36
4.35
4.34
3.93
3.91
3.90
3.88
3.87
3.64
3.63
3.61
3.60
3.58
3.26
3.24
3.22
3.21
3.10
3.06
1.38
1.37
1.35
1.23
1.22
1.20
0.95
1.96
0.99
1.02
1.05
1.02
3.01
3.08
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


N
O
Me
O
EtO
O

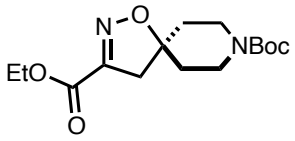
S23

160.39
152.01
104.98
64.47
62.24
40.25
15.05
14.21
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


N
O
NBoc
EtO
O

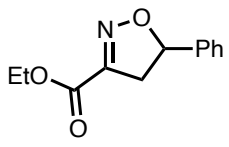
S21

4.36
4.35
4.34
4.33
3.65
3.45
3.44
3.44
3.42
3.42
2.96
1.89
1.87
1.71
1.70
1.69
1.46
1.38
1.37
1.36
2.01
2.00
2.05
2.00
2.00
2.00
9.24
3.11
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


N
O
EtO
O
NBoc

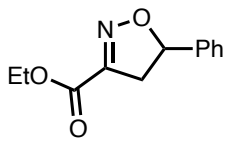
S21

160.92
154.65
151.23
87.95
79.94
62.15
43.80
40.68
35.76
28.49
14.21
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


N
O
Ph
EtO
O

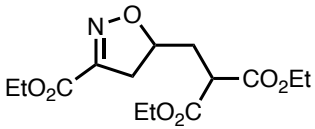
S22

7.41
7.40
7.40
7.39
7.38
7.35
7.35
7.35
7.34
7.34
7.33
7.32
5.80
5.79
5.79
5.77
4.38
4.37
4.36
4.35
3.66
3.65
3.64
3.62
3.24
3.23
3.22
3.21
1.39
1.38
1.37
2.00
3.00
1.00
2.11
1.11
1.08
3.10
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

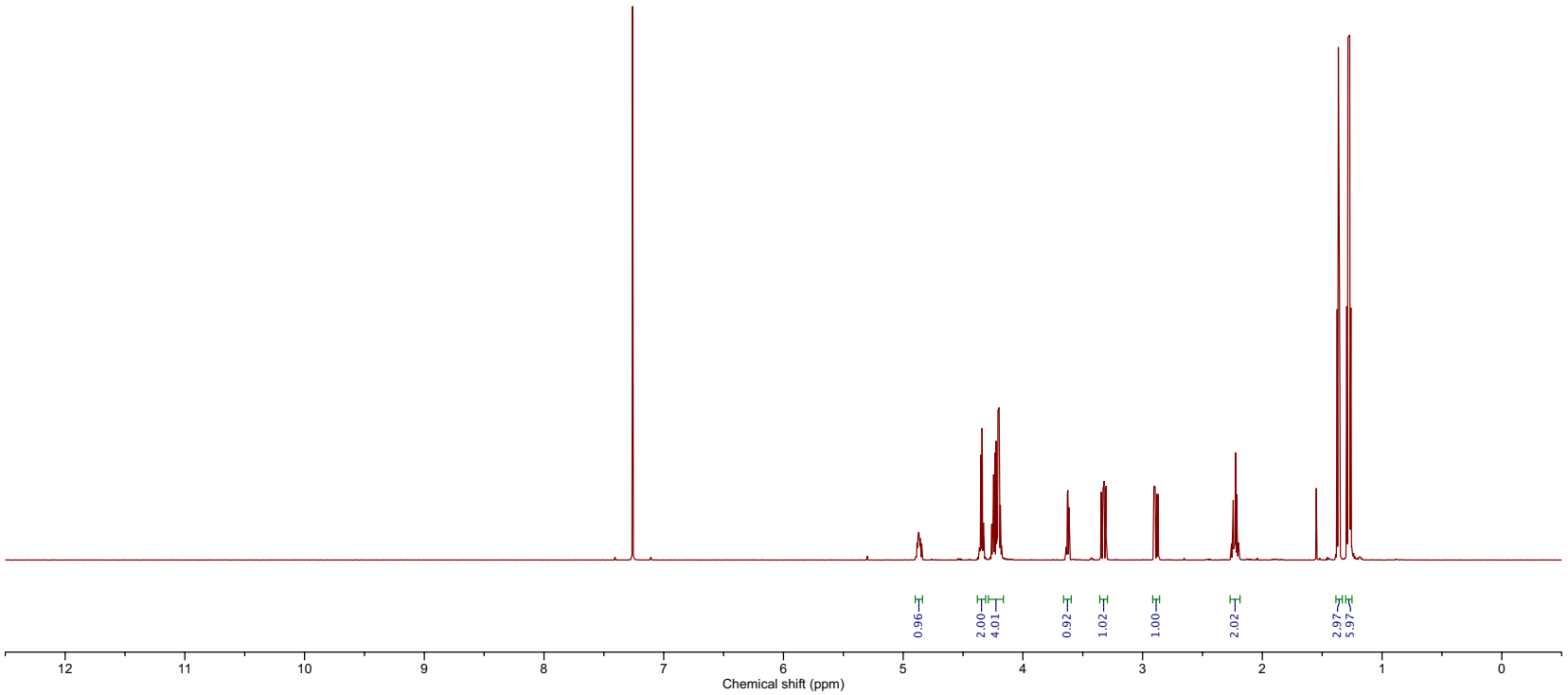

N
O
Ph
EtO
O

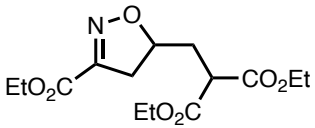
S22

160.69
151.25
139.63
128.99
128.77
125.98
85.07
62.27
41.58
14.24
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


N
O
EtO2C
CO2Et
EtO2C

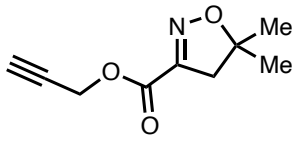
S24


0.96
2.00
4.01
0.92
1.02
1.00
2.02
2.97
5.97
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


N
O
EtO2C
CO2Et
EtO2C

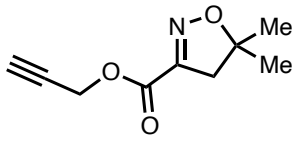
S24

168.90
168.81
160.64
151.63
81.11
62.26
61.91
48.39
39.17
34.28
14.23
14.15
14.12
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


N
O
Me
Me
O
O

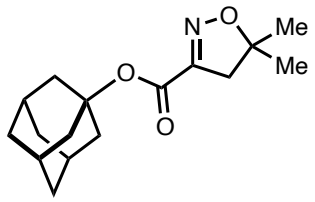
S25

4.87
4.86
2.98
2.52
2.52
2.52
1.47
1.95
2.00
0.78
6.07
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


N
O
Me
Me
O
O

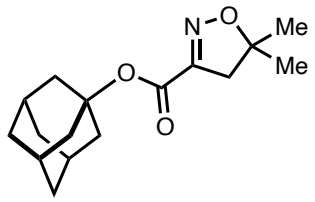
S25

160.39
150.40
89.13
76.87
75.86
53.14
45.07
27.34
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


N
O
Me
Me
O
O

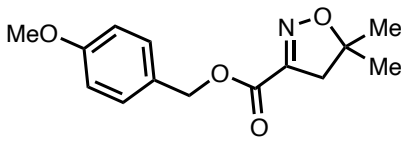
S26

2.92
2.20
1.71
1.69
1.68
1.66
1.54
1.44
1.94
8.96
6.01
6.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


N
O
Me
Me
O
O

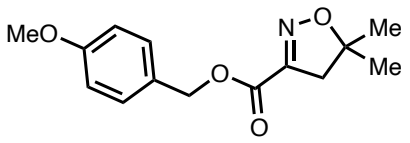
S26

160.04
152.35
88.17
83.36
45.57
41.37
36.21
31.07
27.43
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


MeO
O
N
O
Me
Me
O

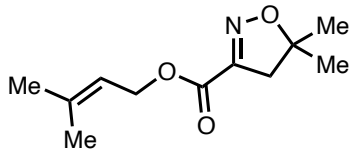
S27

7.37
7.35
6.90
6.88
5.24
3.81
2.95
1.44
1.85
1.88
2.00
3.00
2.00
6.04
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


MeO
O
N
O
Me
Me
O

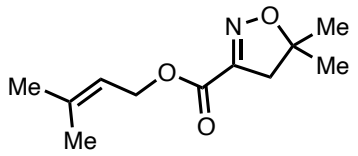
S27

160.98
159.91
150.96
130.60
127.20
114.00
88.59
67.28
55.31
45.18
27.25
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


N
O
Me
Me
O
O
Me
Me

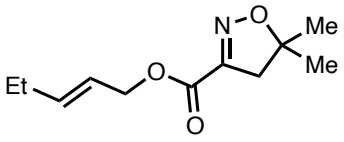
S28

5.40
5.39
5.38
4.76
4.75
2.94
2.94
1.75
1.72
1.44
0.87
1.97
2.00
5.70
6.04
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
O
N
O
Me
Me
O
Me

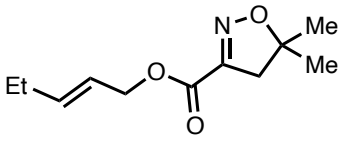
S28

161.19
151.15
140.27
117.89
88.54
62.76
45.30
27.31
25.91
18.19
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


N
O
Me
Me
Et
O
O

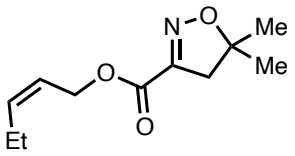
(*E*)-**72**

5.93
5.91
5.90
5.89
5.87
5.86
5.66
5.64
5.62
5.62
5.60
5.58
4.72
4.70
2.96
2.12
2.10
2.08
2.07
2.05
1.46
1.02
1.00
0.99
0.94
0.96
2.02
2.15
2.05
6.44
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


N
O
Me
Me
Et
O
O

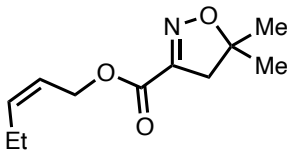
(*E*)-**72**

161.00
151.10
139.47
122.00
88.62
66.74
45.26
27.32
25.36
13.06
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


N
O
Me
Me
O
O
Et

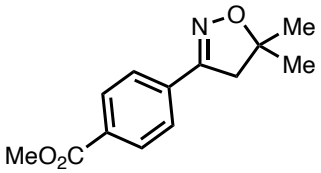
(*Z*)-**72**

5.72
5.70
5.70
5.68
5.66
5.59
5.58
5.56
5.55
5.53
4.83
4.81
2.96
2.19
2.17
2.15
2.13
2.12
1.46
1.02
1.00
0.98
0.94
0.94
2.00
2.00
1.98
6.09
2.92
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


N
O
Me
Me
O
O
Et

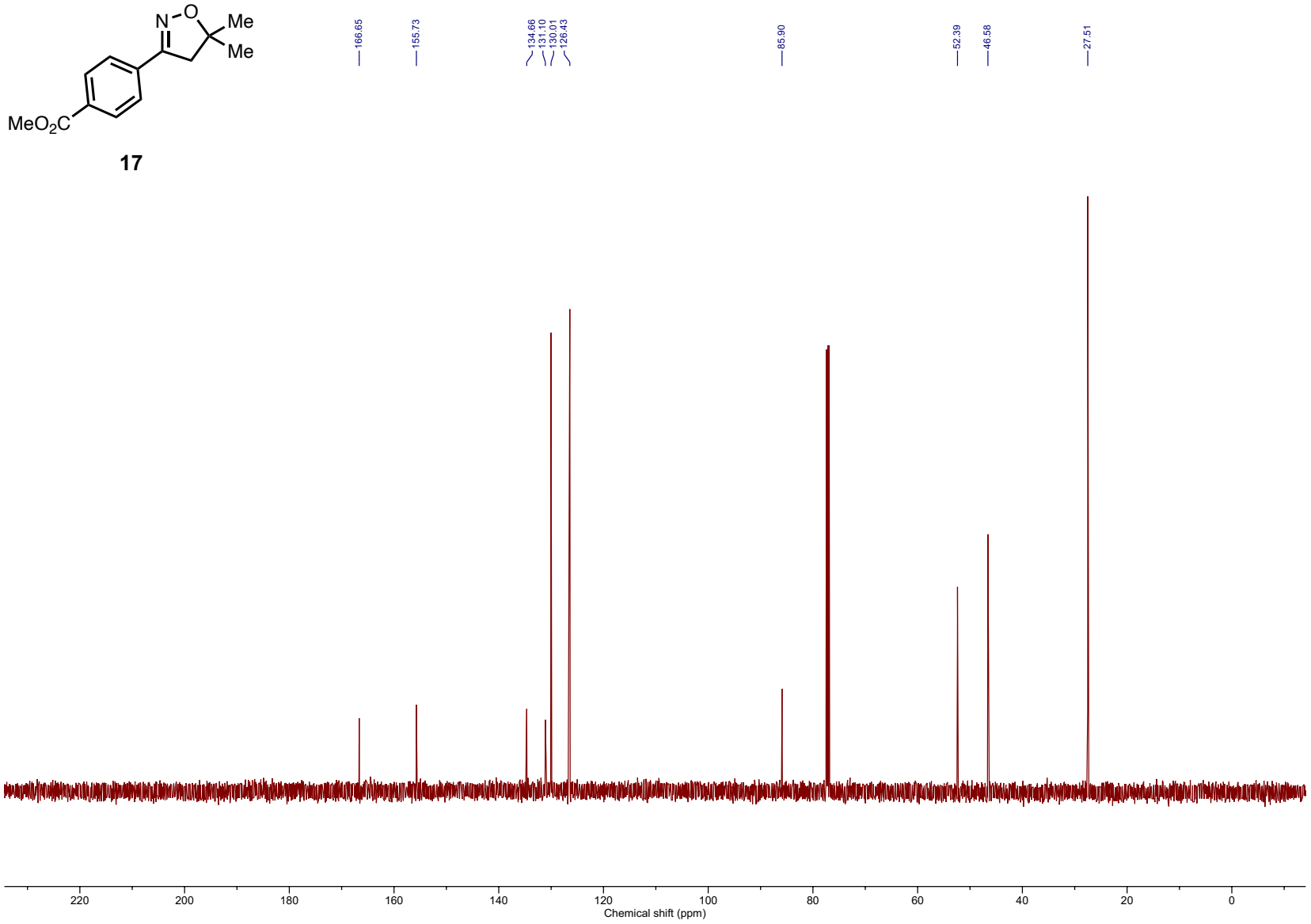
(*Z*)-**72**

161.08
151.03
138.01
121.89
88.63
61.61
45.25
27.31
21.03
14.13
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

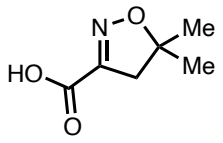

N
O
Me
Me
MeO2C

17

8.07
8.05
7.72
7.70
3.93
3.12
1.51
1.95
2.00
3.00
2.00
6.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

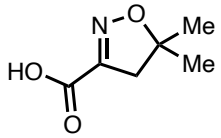

N
O
Me
Me
MeO2C
166.65
155.73
134.66
131.10
130.01
126.43
85.90
52.39
46.58
27.51
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

17


N
O
Me
Me
HO
O

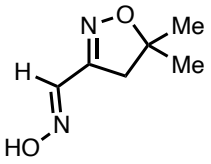
A4

2.98
1.49
2.00
6.02
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


N
O
Me
Me
HO
O

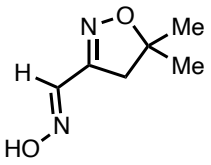
A4

164.19
150.72
90.21
44.53
27.37
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)



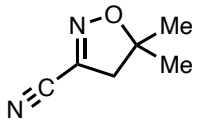
S29a

(4:1 mixture of isomers)



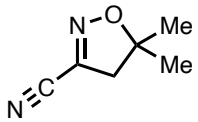
S29a

(4:1 mixture of isomers)


N
O
Me
Me
N
C

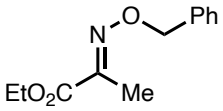
S29

2.93
1.49
2.00
6.25
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


N
O
Me
Me
C
N

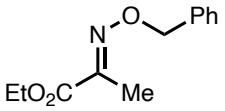
S29

133.85
111.55
89.63
46.87
27.06
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


N
O
Ph
EtO2C
Me

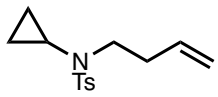
71

7.38
7.37
7.36
7.35
7.33
7.31
5.31
4.35
4.33
4.32
4.30
2.09
1.37
1.35
1.34
4.82
2.00
2.00
2.97
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


N
O
Ph
EtO2C
Me

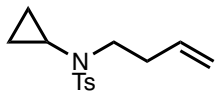
71

163.93
149.62
136.79
128.58
128.38
128.31
77.67
61.91
14.31
11.76
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


N
Ts

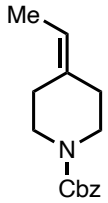
S34

7.75
7.73
7.32
7.30
5.77
5.76
5.76
5.75
5.74
5.73
5.73
5.72
5.72
5.71
5.07
5.06
5.04
5.04
5.03
5.02
3.25
3.24
3.24
3.24
3.23
2.43
2.37
2.36
2.35
2.34
2.05
2.05
2.04
2.04
2.03
2.03
2.03
0.86
0.86
0.85
0.85
0.85
0.84
0.71
0.70
0.70
0.69
0.69
0.68
1.85
1.88
0.88
1.84
2.00
3.02
2.01
0.96
1.98
1.97
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


N
Ts

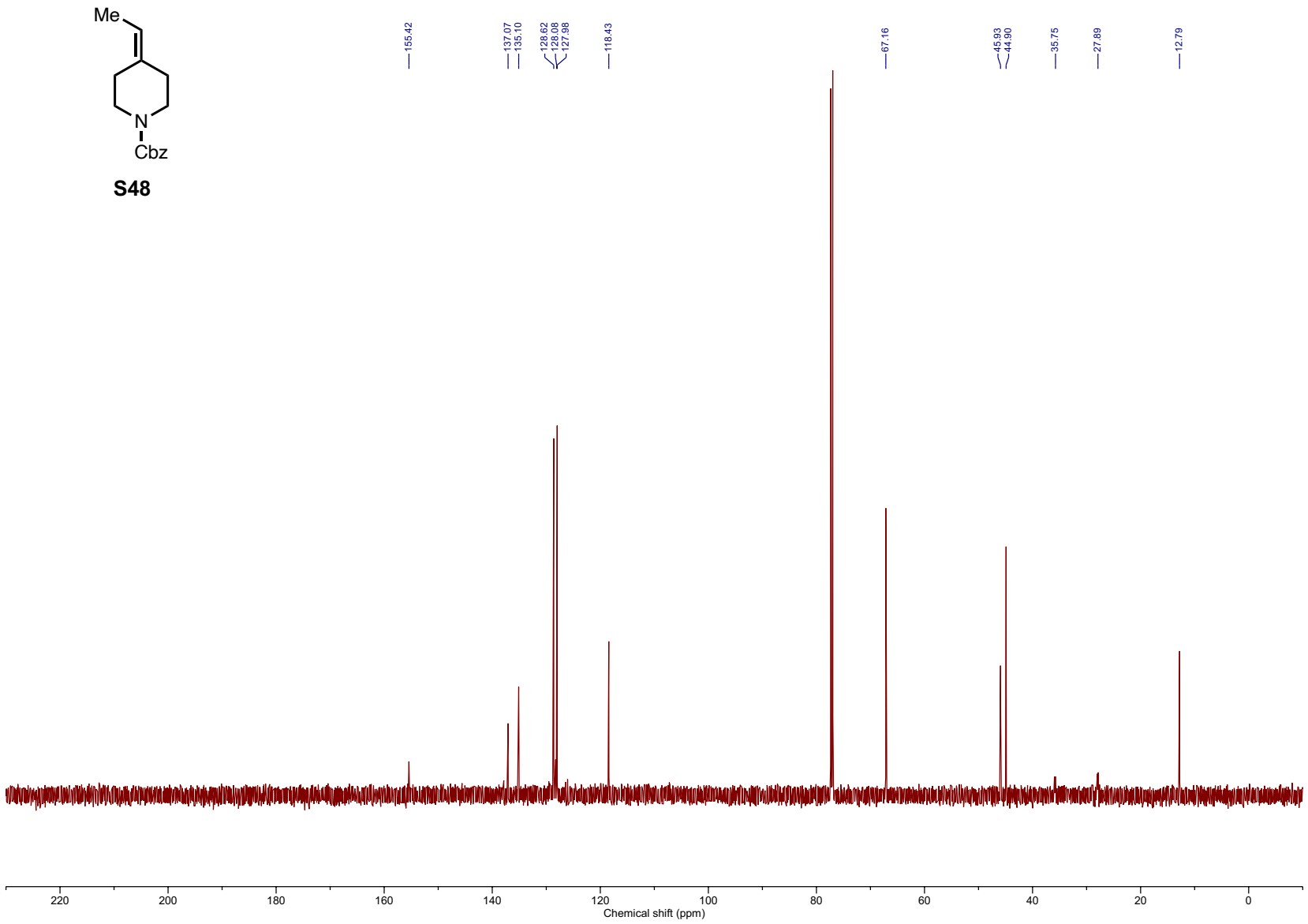
S34

143.43
135.77
135.20
129.61
127.73
116.92
50.70
33.13
30.51
21.62
7.47
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

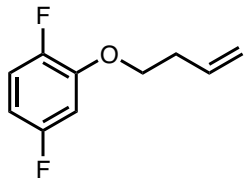

Me
N
Cbz

S48

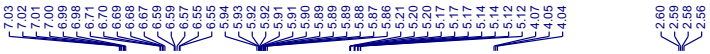
7.37
7.36
7.35
7.33
7.32
7.31
7.31
7.30
5.31
5.30
5.29
5.28
5.14
3.48
3.47
3.46
2.23
2.15
1.60
1.59
4.78
1.11
2.00
4.00
4.00
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

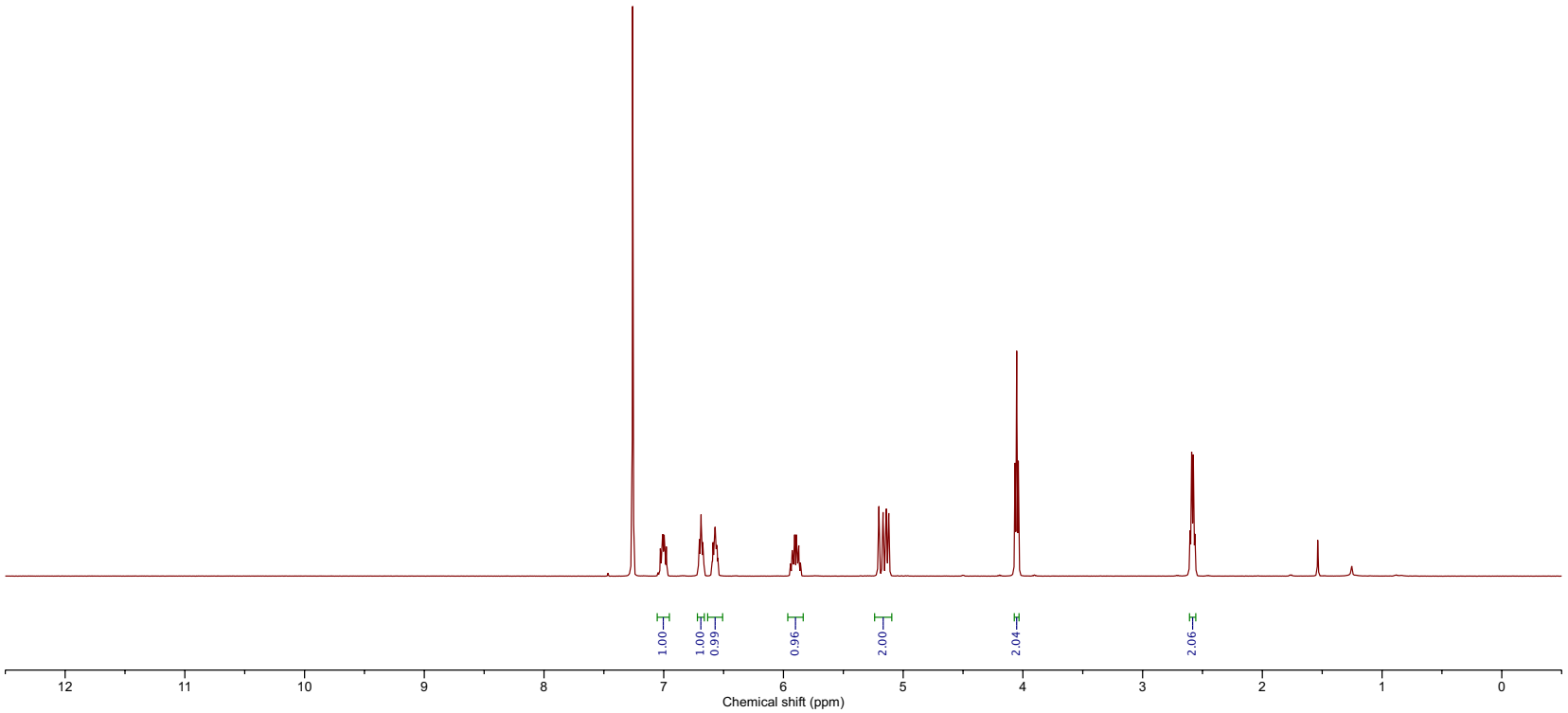

Me
N
Cbz
155.42
137.07
135.10
128.62
128.08
127.98
118.43
67.16
45.93
44.90
35.75
27.89
12.79
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

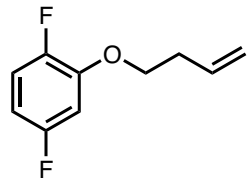
S48


F
O
F

S38

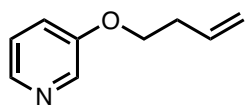

7.03
7.02
7.01
7.00
6.99
6.98
6.71
6.70
6.69
6.68
6.67
6.59
6.59
6.57
6.55
6.55
5.94
5.93
5.92
5.92
5.91
5.91
5.90
5.89
5.89
5.89
5.88
5.87
5.86
5.21
5.20
5.20
5.17
5.17
5.17
5.17
5.14
5.14
5.12
5.12
4.07
4.05
4.04
2.60
2.59
2.58
2.56


1.00
1.00
0.99
0.96
2.00
2.04
2.06
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

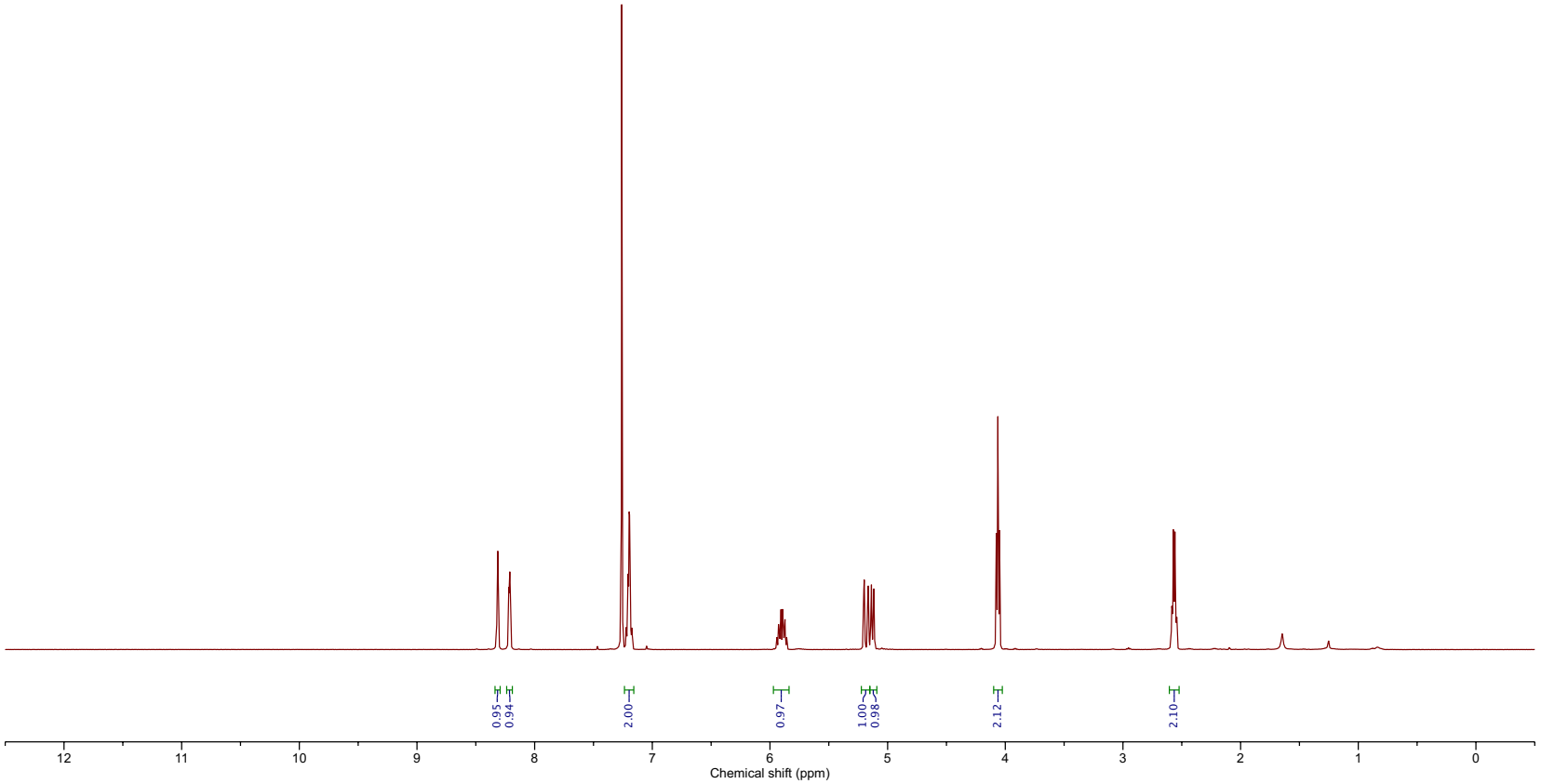

F
O
F

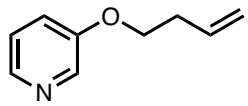
S38

159.55
159.53
158.77
158.16
149.81
149.79
148.44
148.42
147.76
147.70
147.69
147.63
133.85
117.66
116.37
116.32
116.26
116.20
106.75
106.71
106.62
106.58
102.94
102.93
102.79
102.78
68.86
33.52
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


O
N

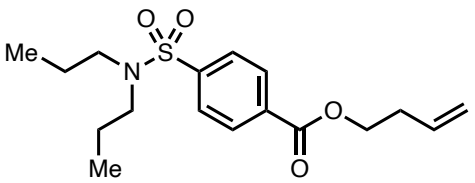
S35


0.95
0.94
2.00
0.97
1.00
0.98
2.12
2.10
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


O
N

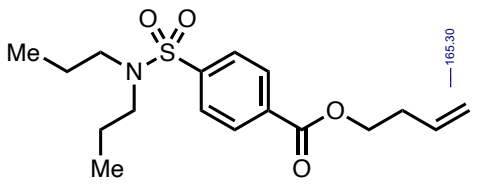
S35

155.15
142.23
138.16
134.09
123.93
121.28
117.53
67.62
33.64
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
N
S
O
O
O
O
Me

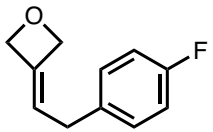
S36

8.15
8.14
7.88
7.86
5.91
5.89
5.89
5.88
5.87
5.86
5.85
5.85
5.84
5.82
5.20
5.17
5.14
5.12
4.42
4.41
4.39
3.11
3.10
3.08
2.56
2.55
2.55
2.55
2.54
2.54
2.53
2.53
2.52
1.58
1.57
1.55
1.54
1.52
1.51
0.88
0.87
0.85
1.90
1.95
0.85
0.90
0.90
2.00
4.04
2.00
4.26
6.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

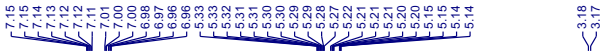

Me
N
S
O
O
Me
O
O

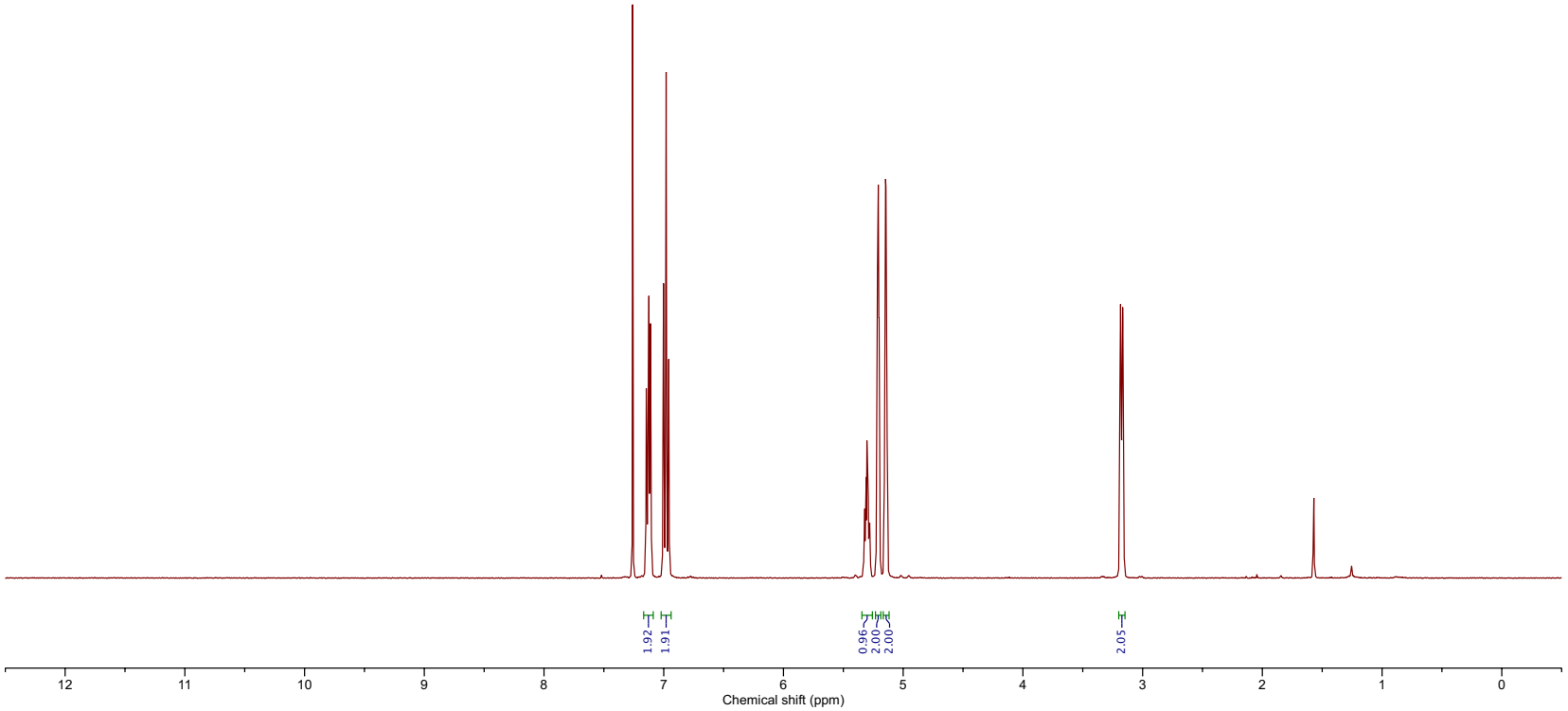
S36

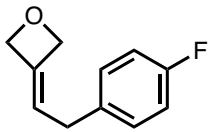
165.30
144.30
133.85
133.71
130.30
127.10
117.72
64.67
50.04
33.17
22.05
11.26
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


O
F

S49

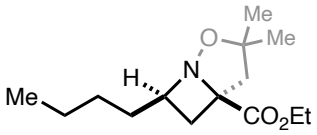

7.15
7.15
7.14
7.13
7.12
7.12
7.11
7.01
7.00
7.00
6.98
6.97
6.96
6.96
5.33
5.33
5.32
5.31
5.31
5.30
5.30
5.29
5.29
5.28
5.27
5.22
5.21
5.21
5.21
5.20
5.20
5.15
5.15
5.14
5.14
3.18
3.17


1.92
1.91
0.96
2.00
2.00
2.05
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


O
F

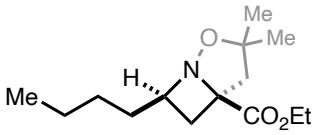
S49

162.60
160.66
135.65
135.43
135.40
129.97
129.91
118.10
115.46
115.30
79.52
78.75
33.84
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
H
N
Me
CO2Et

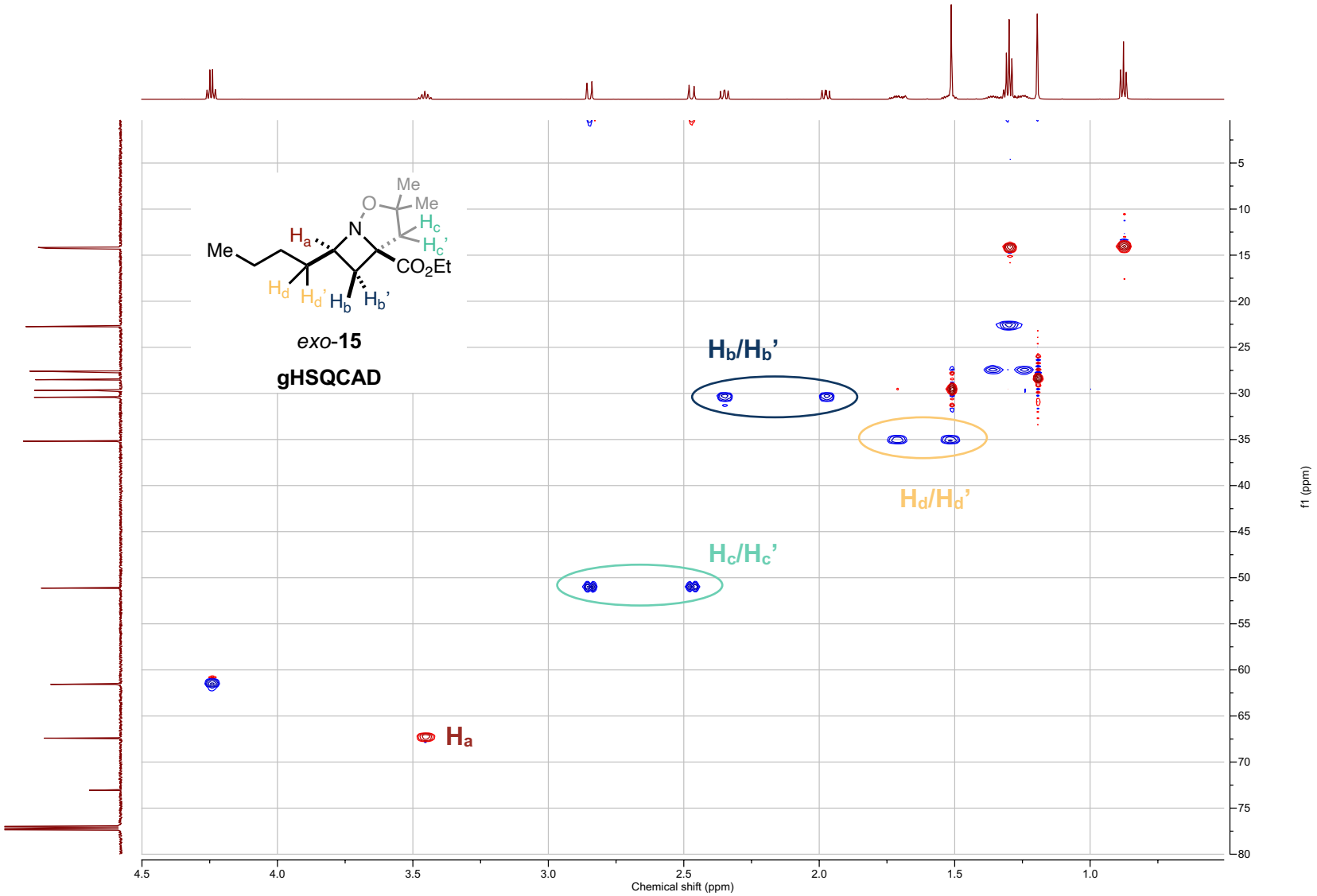
exo-**15**

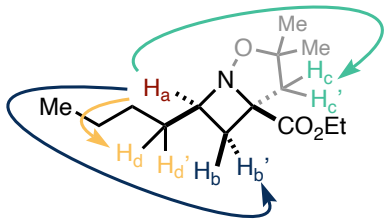
4.26 4.25 4.24 4.23 3.48 3.47 3.46 3.45 3.43 2.86 2.84 2.48 2.46 2.36 2.35 2.35 2.34 1.99 1.98 1.97 1.96 1.74 1.73 1.73 1.73 1.72 1.72 1.72 1.71 1.71 1.71 1.71 1.70 1.70 1.70 1.69 1.68 1.55 1.54 1.54 1.53 1.53 1.52 1.52 1.52 1.52 1.51 1.50 1.38 1.38 1.38 1.38 1.37 1.37 1.37 1.36 1.36 1.36 1.35 1.35 1.35 1.34 1.33 1.33 1.31 1.30 1.29 1.28 1.27 1.27 1.26 1.26 1.26 1.25 1.25 1.25 1.25 1.25 1.24 1.24 1.24 1.23 1.23 1.23 1.22 1.22 1.22 1.21 1.20 0.89 0.88 0.87
1.92
0.98
1.00
1.00
1.00
1.01
1.03
4.04
7.42
3.00
3.00
12 11 10 9 8 7 6 5 4 3 2 1 0
Chemical shift (ppm)


Me
O
Me
H
N
Me
CO2Et

exo-**15**

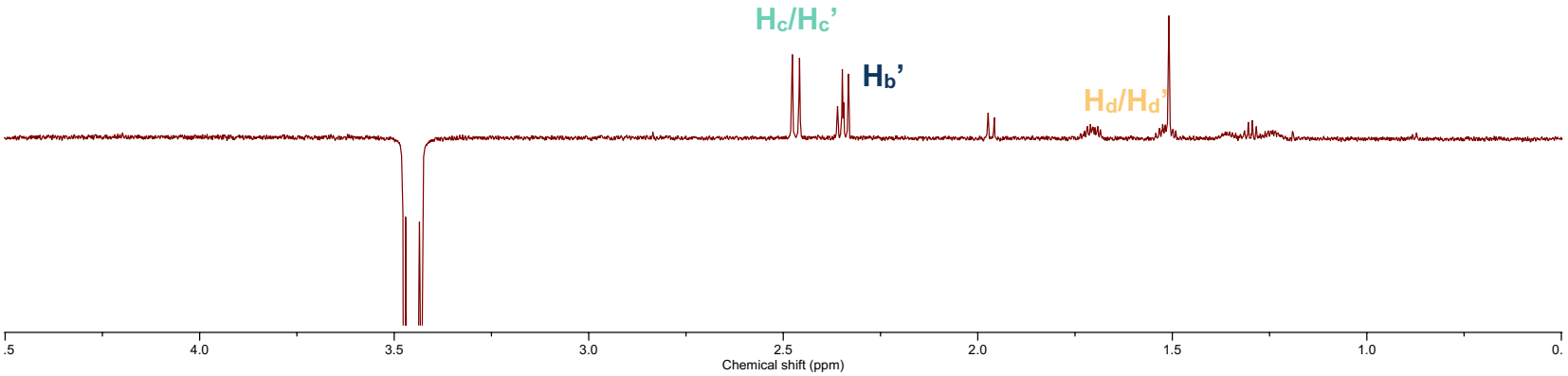
173.03
87.23
73.07
67.41
61.57
51.13
35.18
30.42
29.68
28.51
27.59
22.75
14.26
14.16
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
N
Hc
Hc'
Ha
Me
CO2Et
Hd
Hd'
Hb
Hb'
exo-15
gHSQCAD
Hb/Hb'
Hd/Hd'
Hc/Hc'
Ha
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical shift (ppm)
f1 (ppm)
5
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80

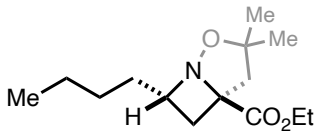


exo-**15**

Saturation of H_a (3.46 ppm)

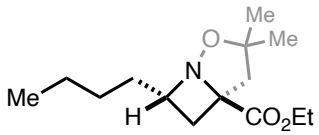


NOE ($CDCl_3$, 700 MHz)


Me
O
Me
N
Me
H
CO2Et

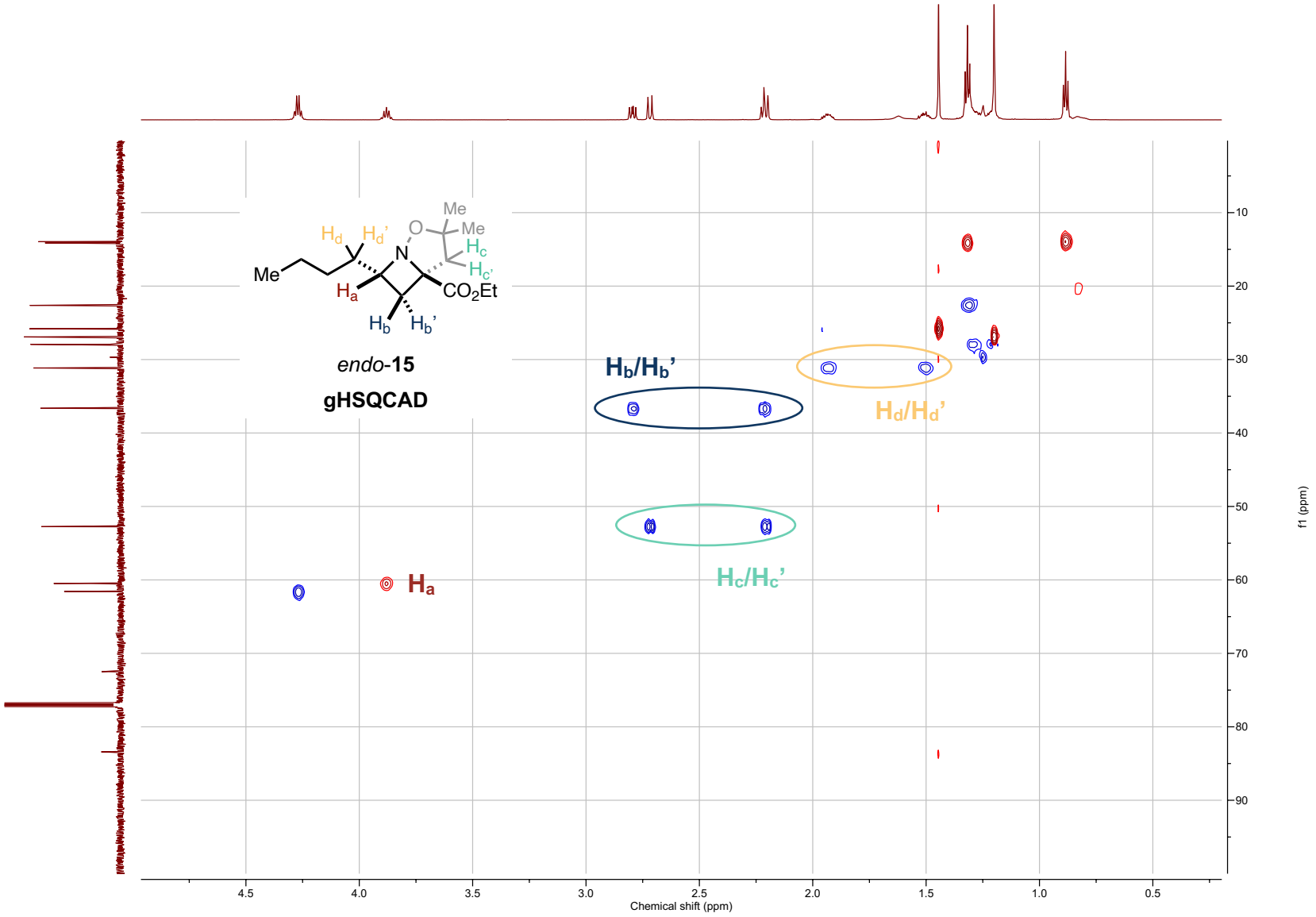
endo-**15**

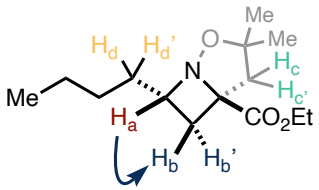
2.02
1.00
1.03
1.03
2.10
1.02
1.22
3.07
7.06
4.00
3.08
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
O
Me
N
Me
H
CO2Et

endo-**15**

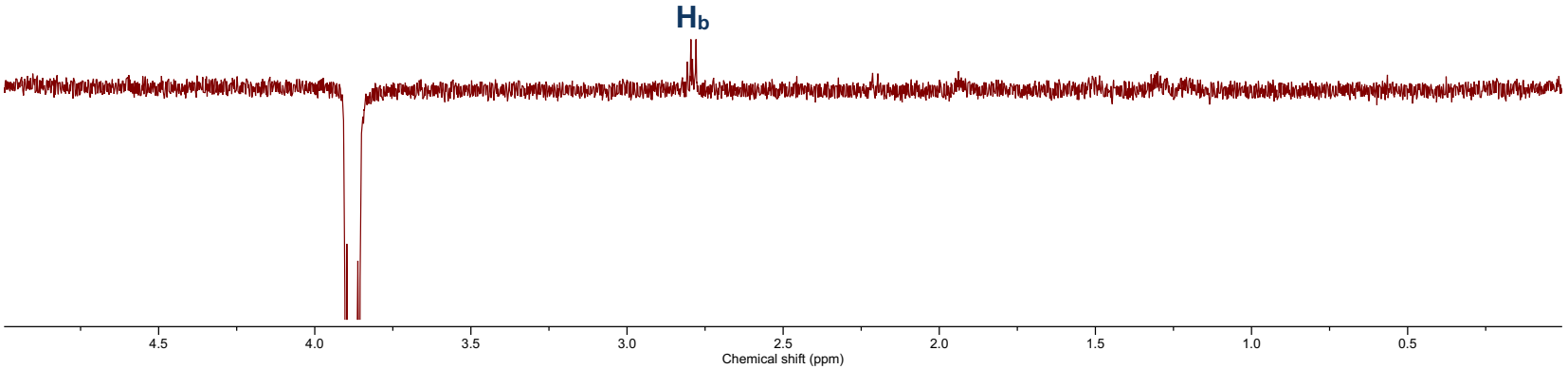
173.14
83.57
72.65
61.73
60.64
52.91
36.80
31.31
29.09
27.08
25.98
22.78
14.28
14.11
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
Hd Hd'
O
Me
N
Hc
Hc'
Me
Ha
CO2Et
Hb Hb'
endo-15
gHSQCAD
Hb/Hb'
Hd/Hd'
Hc/Hc'
Ha
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical shift (ppm)
10
20
30
40
50
60
70
80
90
f1 (ppm)

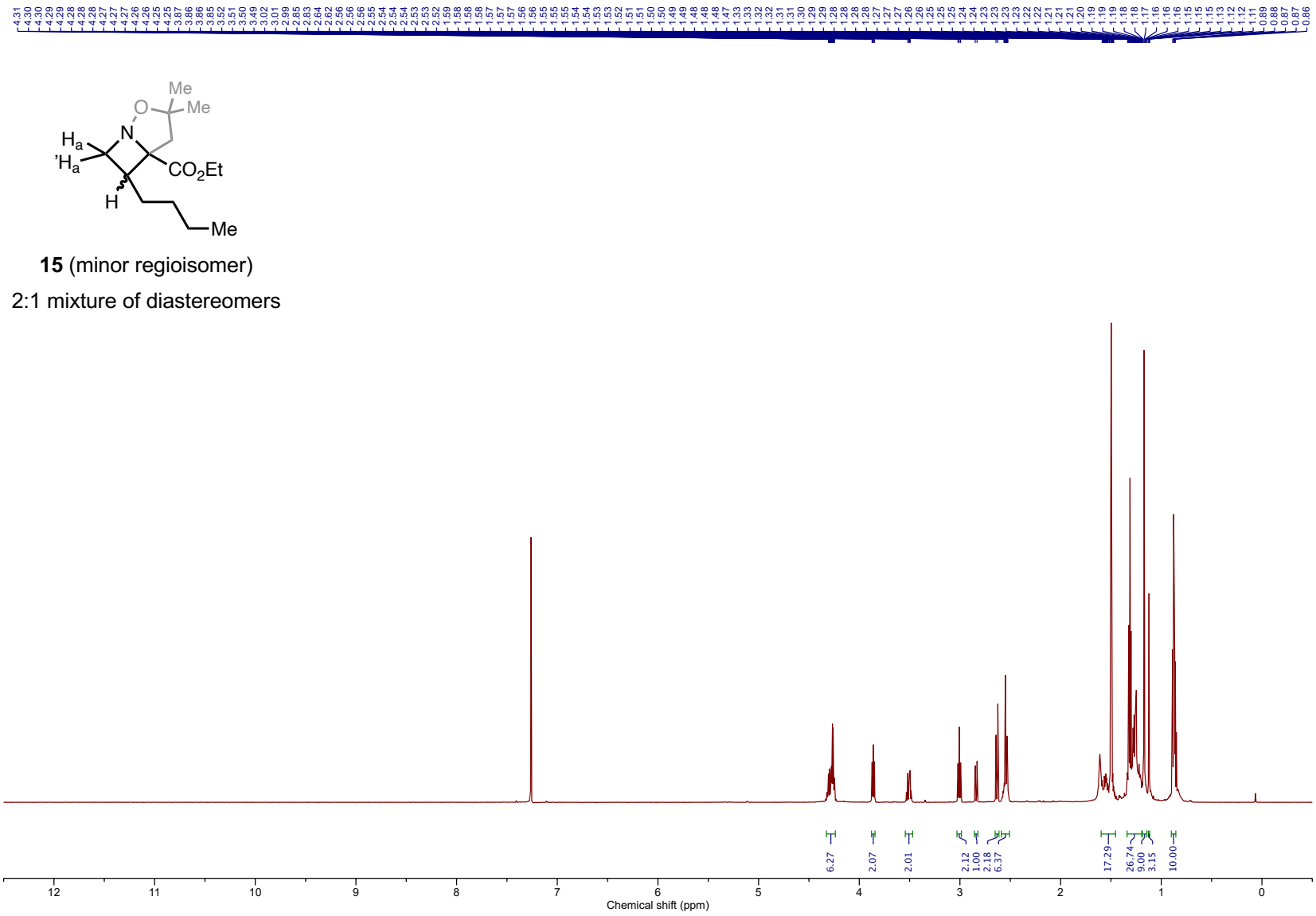


endo-**15**

Saturation of H_a (3.88 ppm)

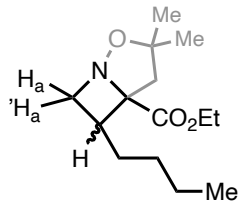


NOE ($CDCl_3$, 700 MHz)



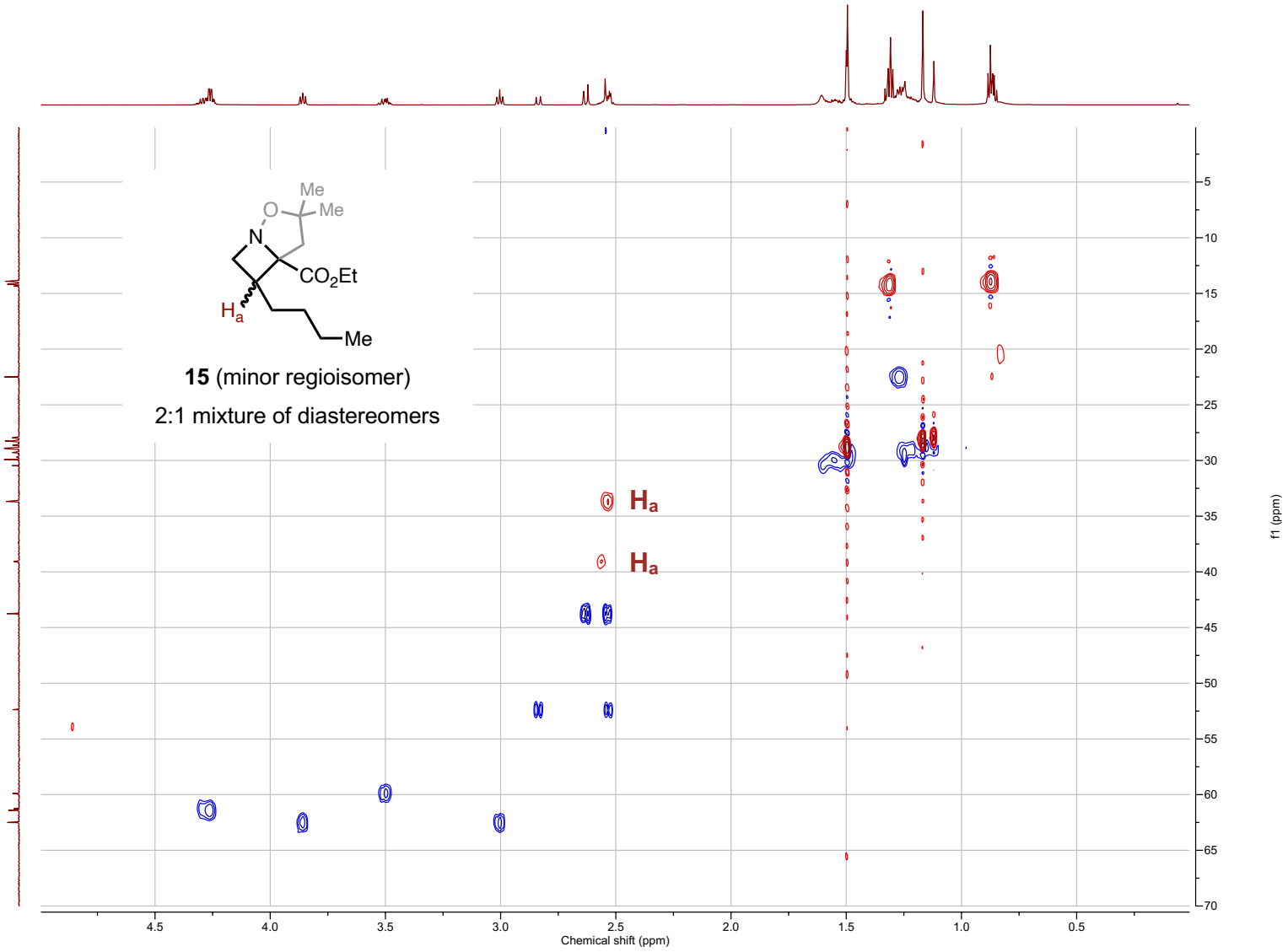
15 (minor regioisomer)

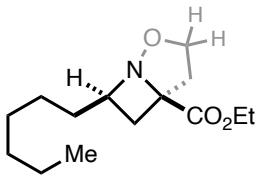
2:1 mixture of diastereomers



15 (minor regioisomer)

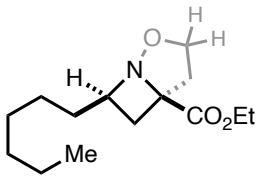
2:1 mixture of diastereomers


Me
O
Me
N
CO2Et
Ha
Me
15 (minor regioisomer)
2:1 mixture of diastereomers
Ha
Ha
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical shift (ppm)
f1 (ppm)
5
10
15
20
25
30
35
40
45
50
55
60
65
70


H
O
H
H
N
CO2Et
Me

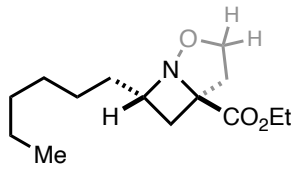
exo-**19**

4.33
4.32
4.31
4.30
4.29
4.28
4.27
4.26
4.25
4.24
4.22
4.21
4.20
4.20
4.19
4.18
3.38
3.37
3.36
2.61
2.60
2.59
2.58
2.58
2.57
2.38
2.38
2.37
2.37
2.37
2.36
2.36
2.35
2.27
2.26
1.72
1.71
1.69
1.56
1.54
1.53
1.38
1.38
1.36
1.31
1.30
1.29
1.28
1.27
1.25
1.24
0.88
0.87
4.01
1.00
1.01
1.02
2.00
1.03
2.83
1.08
10.48
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


H
O
H
H
N
CO2Et
Me

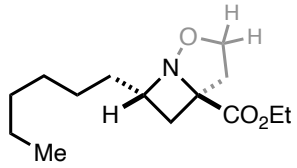
exo-**19**

173.24
71.63
67.79
61.70
61.57
39.06
35.60
31.87
29.55
29.23
25.33
22.66
14.23
14.16
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


H
O
H
N
H
CO2Et
Me

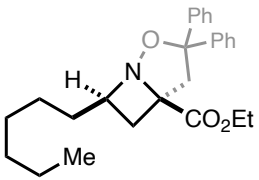
endo-**19**

4.31 4.30 4.29 4.29 4.28 4.28 4.27 4.27 4.27 4.27 4.26 4.26 4.26 4.25 4.25 4.24 4.24 4.23 4.23 4.22 4.22 4.21 4.21 4.20 4.20 4.20 4.19 4.02 4.01 4.00 3.99 3.98 2.95 2.94 2.94 2.92 2.56 2.55 2.55 2.54 2.54 2.53 2.53 2.52 2.28 2.27 2.27 2.26 2.26 2.25 2.25 2.25 2.11 2.00 1.99 1.98 1.87 1.87 1.86 1.86 1.85 1.85 1.84 1.84 1.83 1.83 1.82 1.44 1.43 1.42 1.42 1.41 1.40 1.40 1.39 1.33 1.32 1.31 1.30 1.29 1.28 1.27 1.26 1.25 1.25 1.24 1.23 0.88 0.87 0.86
4.00 0.96 1.00 1.01 1.00 1.00 1.01 1.07 11.71 3.00
12 11 10 9 8 7 6 5 4 3 2 1 0
Chemical shift (ppm)

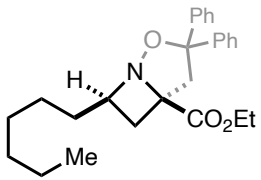

H
O
H
N
H
CO2Et
Me

endo-**19**

172.83
72.98
71.06
62.70
61.78
39.83
34.26
31.82
30.04
29.31
26.00
22.68
14.24
14.18
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

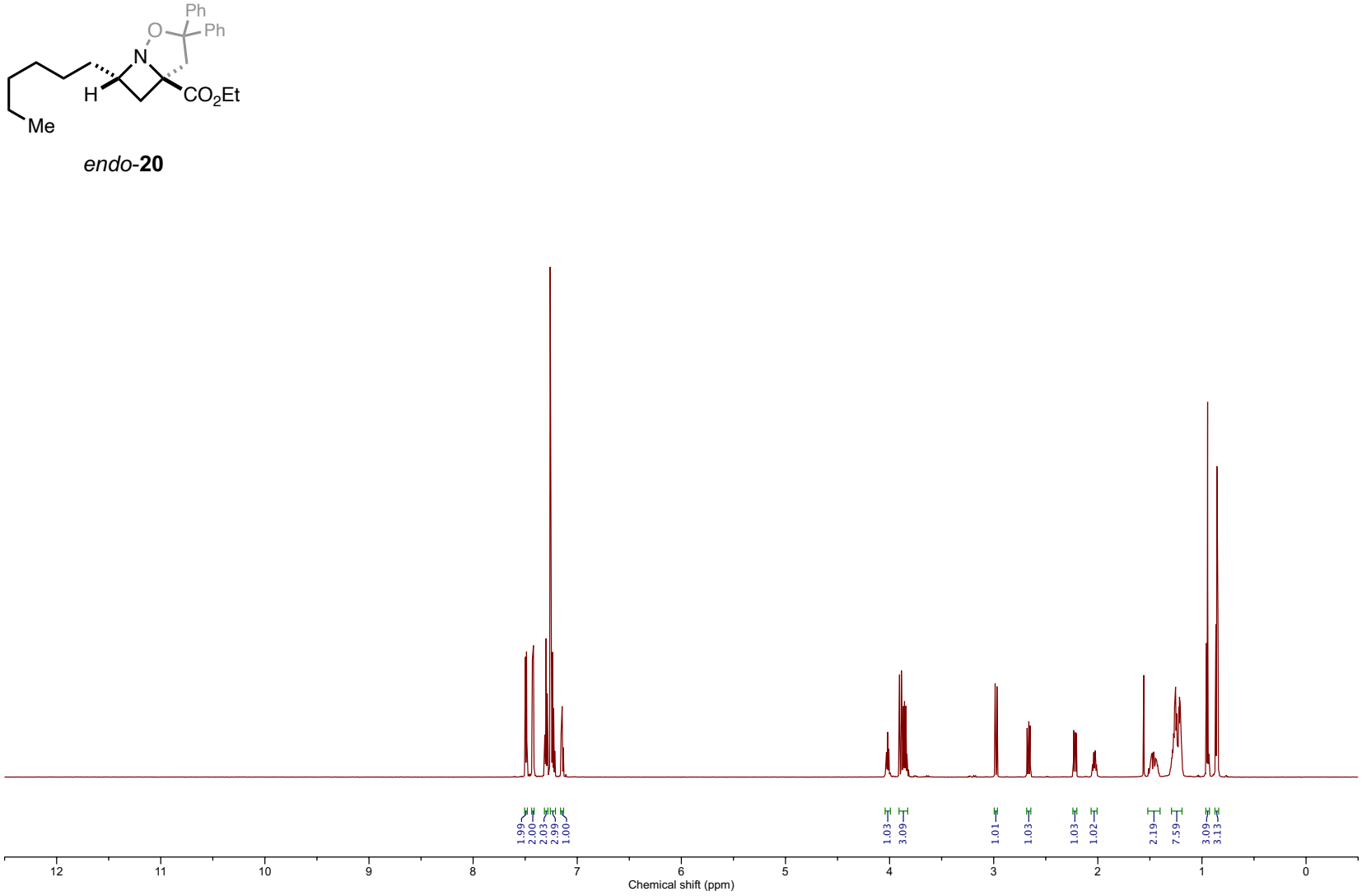


exo-**20**

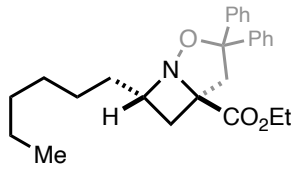

Ph
Ph
O
N
H
CO2Et
Me

exo-**20**

172.03
144.66
144.59
128.39
128.13
127.47
127.12
126.42
126.16
93.39
72.76
66.82
61.39
50.67
35.47
31.90
30.11
29.22
25.41
22.70
14.20
13.95
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

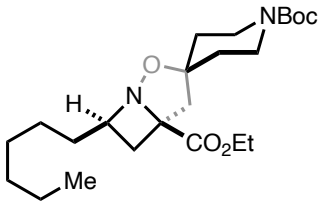


endo-**20**


Ph
O
Ph
N
H
CO2Et
Me

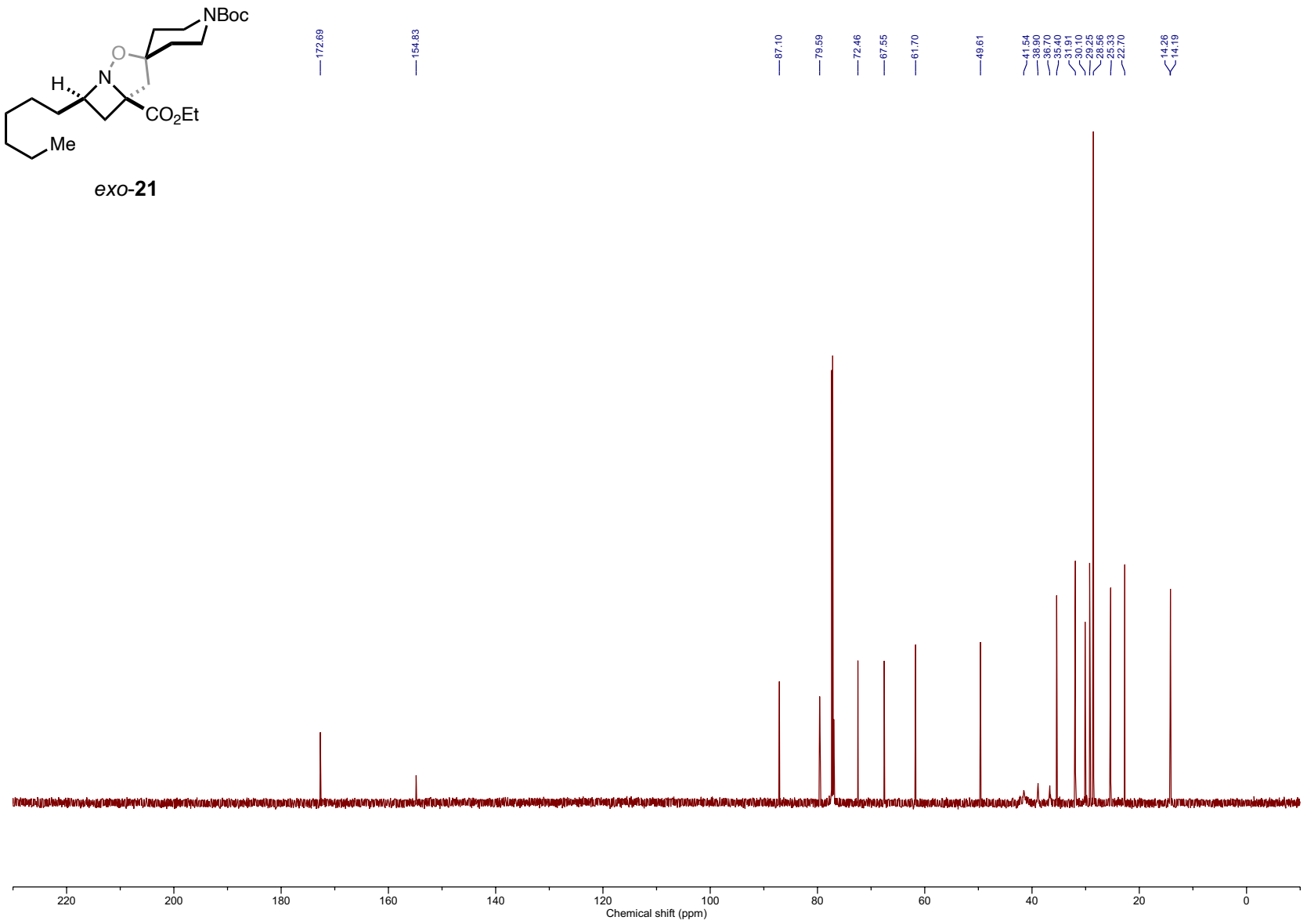
endo-**20**

172.27
144.17
143.32
128.40
128.20
127.39
127.07
125.98
125.97
90.39
72.63
61.70
61.50
52.16
34.73
32.36
31.79
29.31
26.37
22.71
14.22
13.96
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

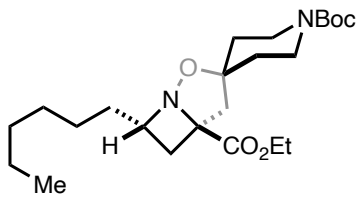

NBoc
O
N
H
CO2Et
Me

exo-**21**

4.27 4.26 4.26 4.25 4.25 4.24 4.22 4.22 4.21 4.21 4.20 3.68 3.47 3.46 3.45 3.44 3.43 3.35 3.33 3.33 3.32 3.31 3.31 3.30 3.29 2.90 2.88 2.44 2.42 2.35 2.34 2.34 2.32 2.04 2.03 2.02 2.01 1.91 1.89 1.88 1.83 1.82 1.75 1.74 1.73 1.73 1.72 1.71 1.70 1.69 1.67 1.54 1.53 1.53 1.52 1.51 1.51 1.50 1.47 1.44 1.39 1.38 1.37 1.37 1.36 1.35 1.34 1.31 1.30 1.29 1.28 1.27 1.27 1.25 0.88 0.87 0.86
1.96 1.00 1.00 1.00 2.00 1.00 1.00 1.01 1.00 1.00 1.00 2.02 1.02 0.97 9.19 1.05 10.37 3.00
12 11 10 9 8 7 6 5 4 3 2 1 0
Chemical shift (ppm)

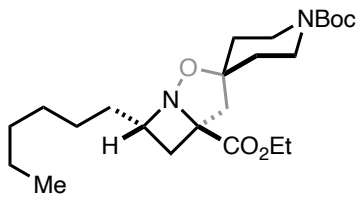

NBoc
O
H
N
CO2Et
Me
172.69
154.83
87.10
79.59
72.46
67.55
61.70
49.61
41.54
38.90
36.70
35.40
31.91
30.10
29.25
28.56
25.33
22.70
14.26
14.19
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

exo-**21**


NBoc
O
N
H
CO2Et
Me

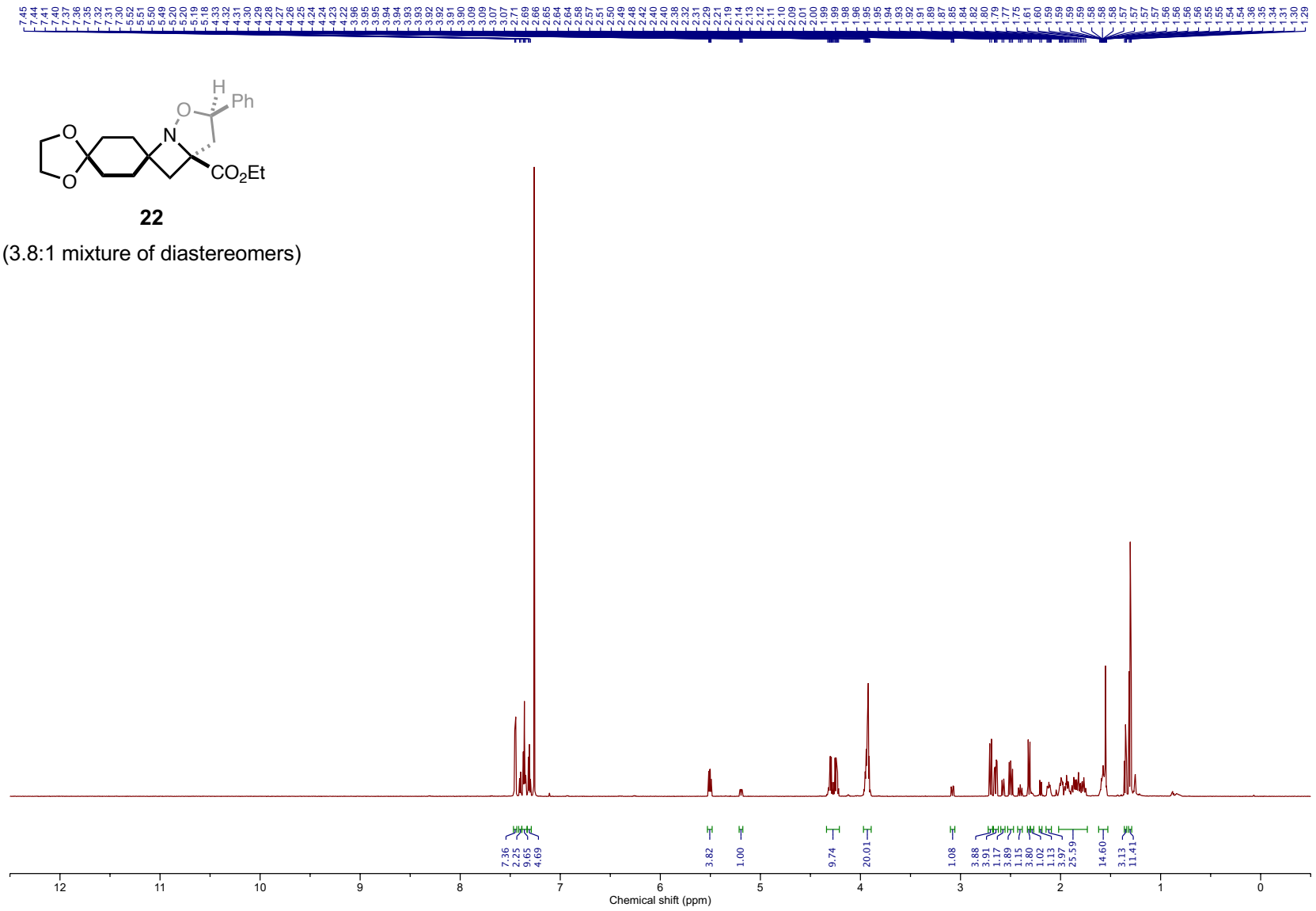
endo-**21**

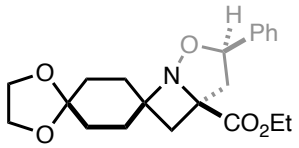
4.28
4.27
4.26
4.25
4.92
3.91
3.90
3.88
3.87
3.73
3.60
3.31
3.31
3.29
3.28
3.28
3.24
2.86
2.85
2.84
2.83
2.75
2.74
2.23
2.22
2.22
2.20
2.16
2.14
1.97
1.96
1.95
1.95
1.94
1.93
1.92
1.92
1.81
1.77
1.76
1.50
1.49
1.48
1.47
1.46
1.46
1.45
1.40
1.38
1.37
1.35
1.33
1.32
1.30
1.30
1.29
1.28
1.27
1.26
1.25
1.23
0.89
0.88
0.87
2.00
1.00
2.06
2.00
1.00
1.00
1.00
1.02
3.00
11.05
13.34
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


NBoc
O
N
H
CO2Et
Me

endo-**21**

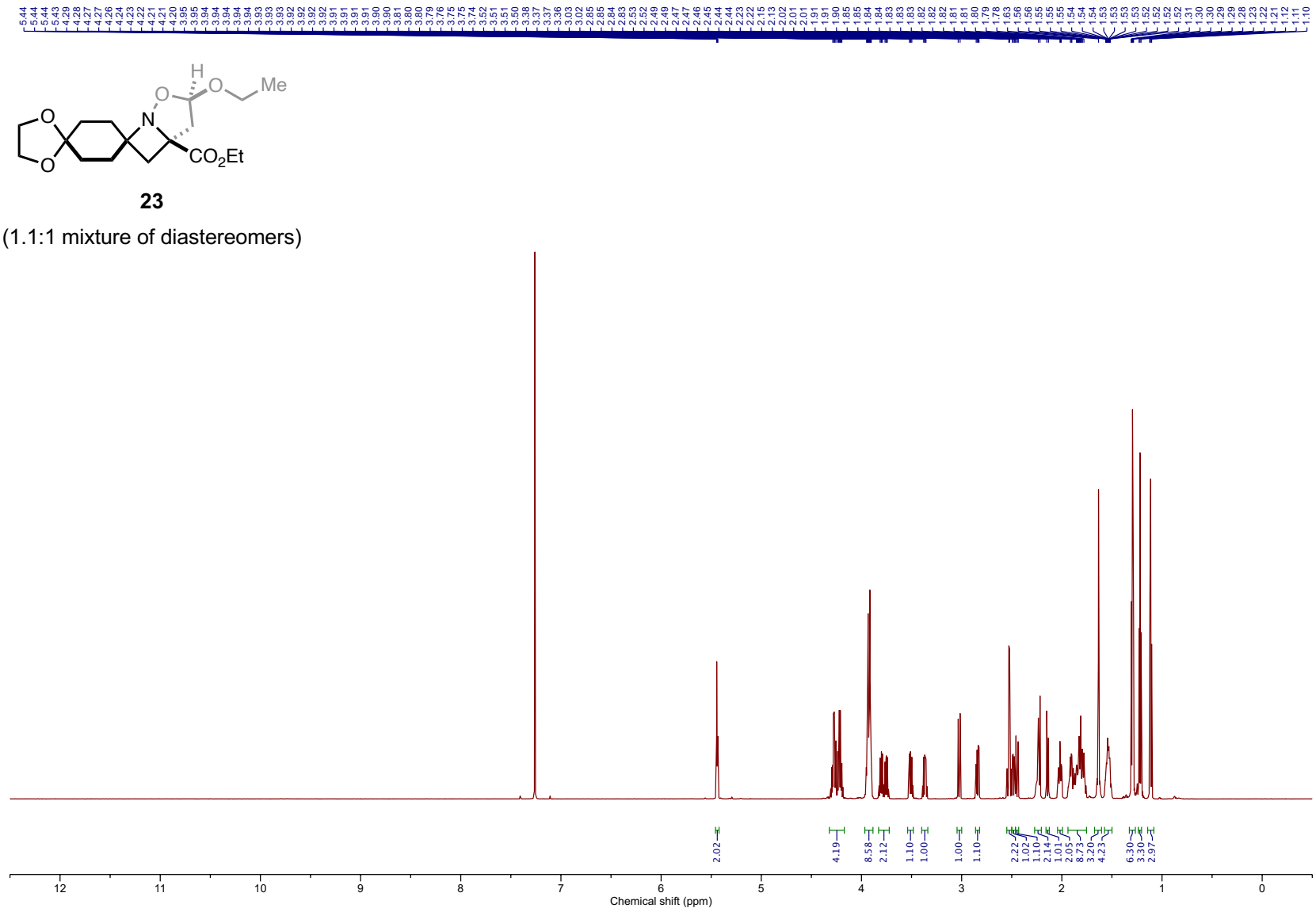
172.79
154.88
83.20
79.55
71.93
61.85
60.77
51.38
41.24
36.74
35.02
34.68
31.82
31.77
29.34
28.56
25.87
22.68
14.25
14.18
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


H
Ph
O
N
O
O
CO2Et
22
(3.8:1 mixture of diastereomers)
Chemical shift (ppm)



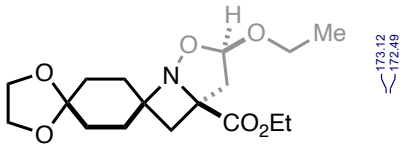
22

(3.8:1 mixture of diastereomers)



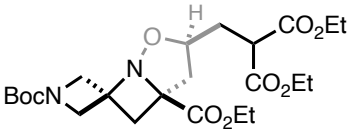
23

(1.1:1 mixture of diastereomers)

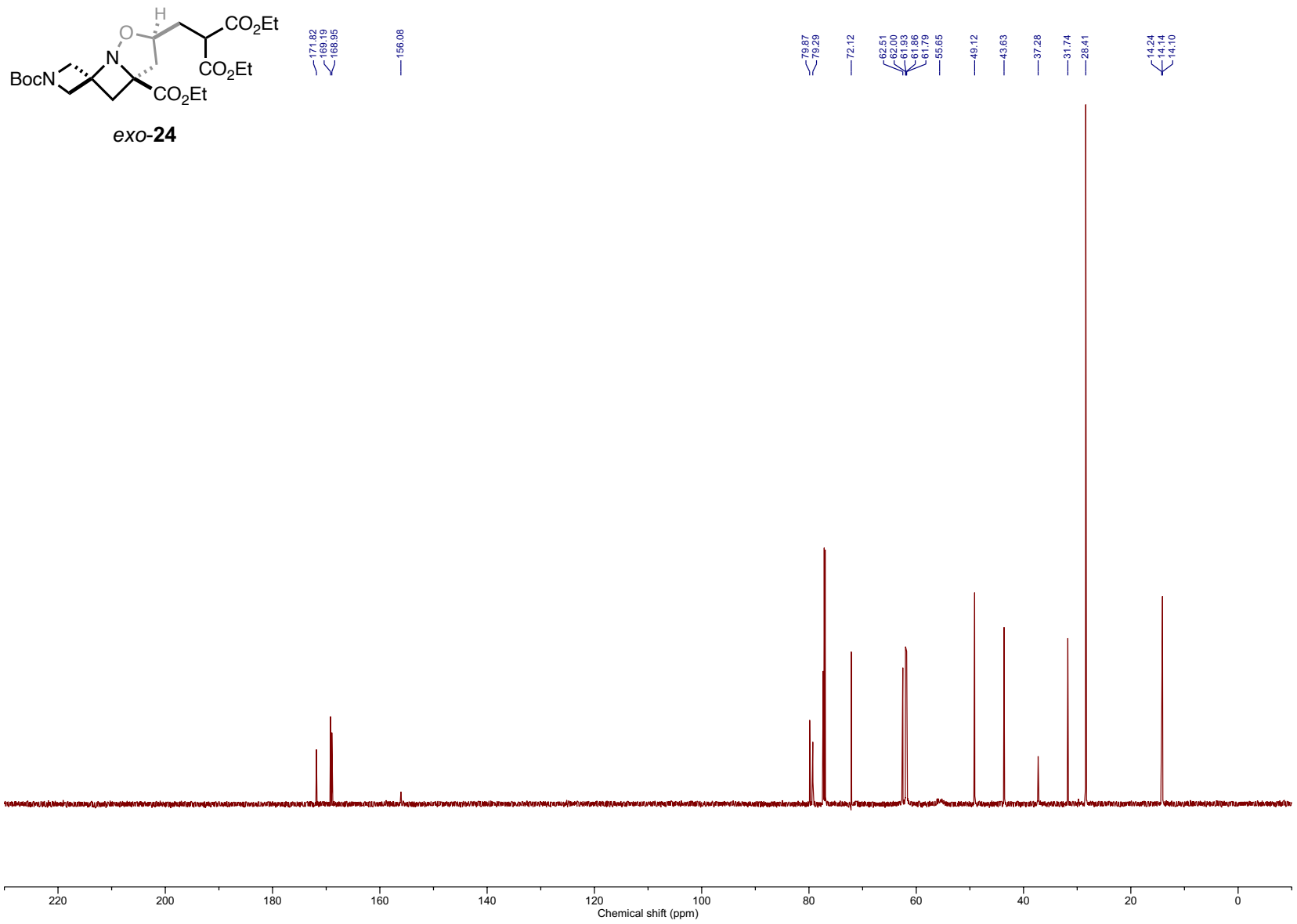


23

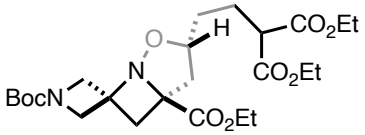
(1.1:1 mixture of diastereomers)



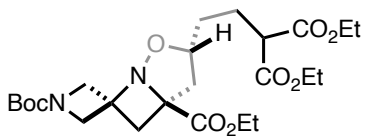
exo-**24**


BocN
N
O
H
CO2Et
CO2Et
CO2Et
171.82
169.19
168.95
156.08
79.87
79.29
72.12
62.51
62.00
61.93
61.86
61.79
55.65
49.12
43.63
37.28
31.74
28.41
14.24
14.14
14.10
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

exo-**24**

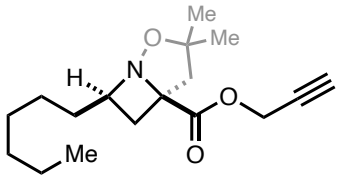


endo-**24**

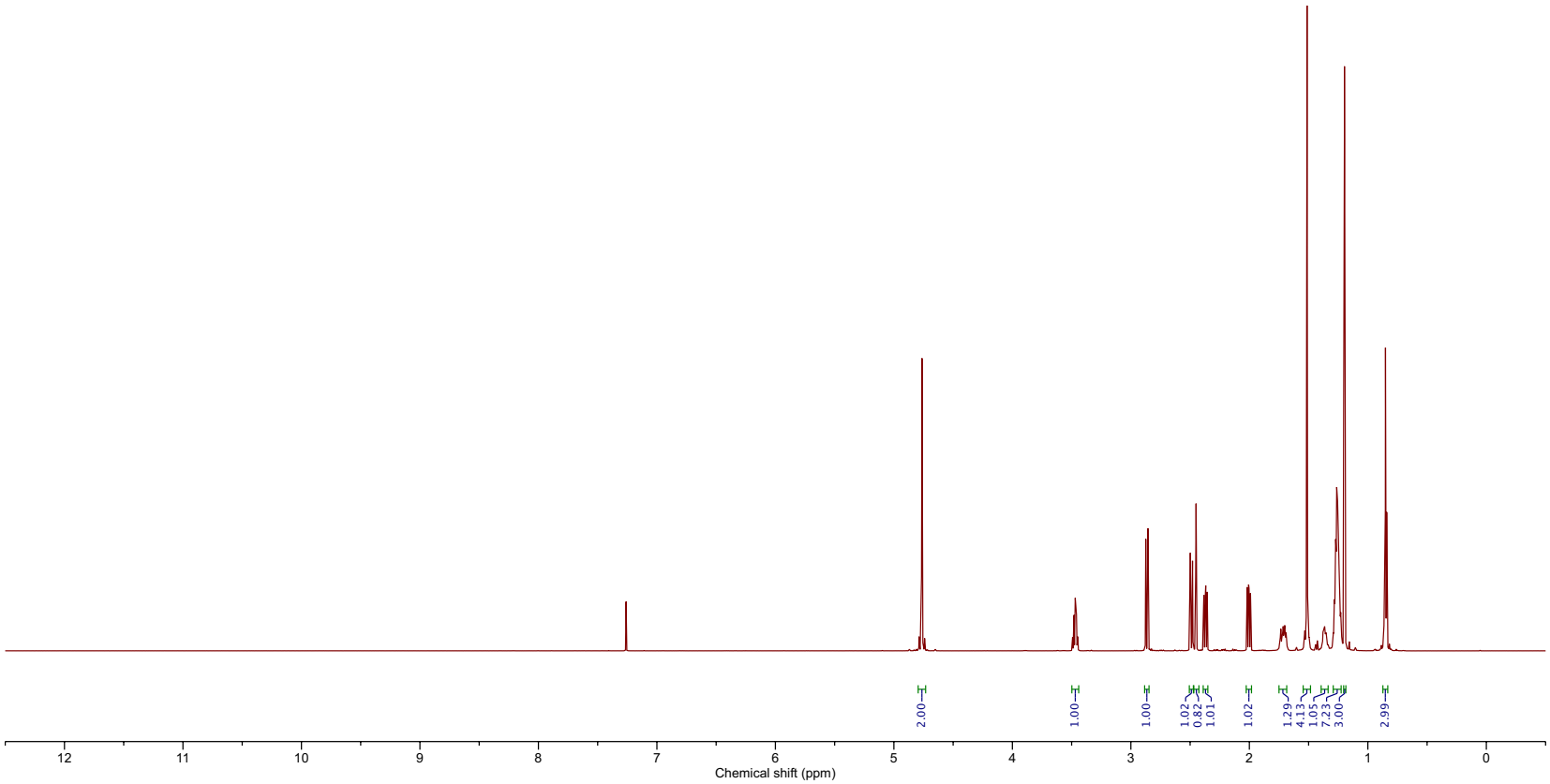

BocN
N
O
H
CO2Et
CO2Et
CO2Et

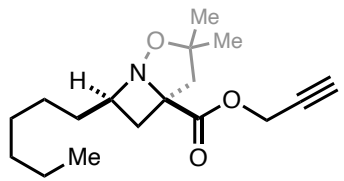
endo-**24**

171.41
168.96
168.93
156.17
81.31
79.96
71.13
63.08
62.00
61.89
61.85
60.96
56.04
49.73
45.26
34.12
31.87
28.48
14.20
14.17
14.15
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
H
N
O
Me
O

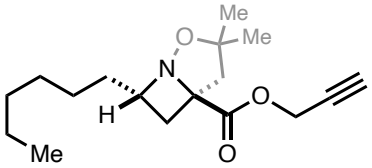
exo-**25**


2.00
1.00
1.00
1.02
0.82
1.01
1.02
1.29
4.13
1.05
7.23
3.00
2.99
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
O
Me
H
N
O
Me
O

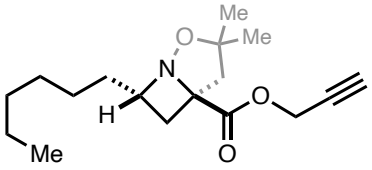
exo-**25**

172.05
87.36
77.36
75.23
72.90
67.53
52.83
50.96
35.47
31.86
30.32
29.65
29.28
28.51
25.36
22.69
14.17
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
N
H
O
Me
O

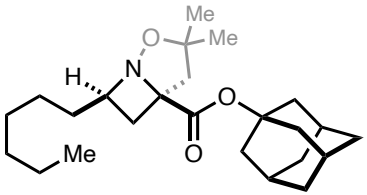
endo-**25**

4.83
4.83
4.81
4.80
4.80
4.78
4.78
3.93
3.92
3.91
3.89
3.88
2.84
2.83
2.82
2.81
2.76
2.74
2.48
2.47
2.25
2.25
2.24
2.23
2.23
2.22
1.97
1.96
1.96
1.95
1.95
1.95
1.94
1.94
1.94
1.94
1.93
1.93
1.93
1.92
1.92
1.53
1.52
1.51
1.51
1.51
1.50
1.50
1.50
1.49
1.49
1.49
1.48
1.48
1.47
1.45
1.31
1.31
1.31
1.30
1.30
1.29
1.28
1.28
1.28
1.27
1.27
1.27
1.27
1.27
1.25
1.25
1.25
1.23
1.23
1.22
1.22
1.22
1.20
0.88
0.87
0.86
2.04
1.00
1.04
1.02
0.86
2.12
1.04
1.08
3.05
12.26
3.06
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
O
Me
N
H
O
Me
O

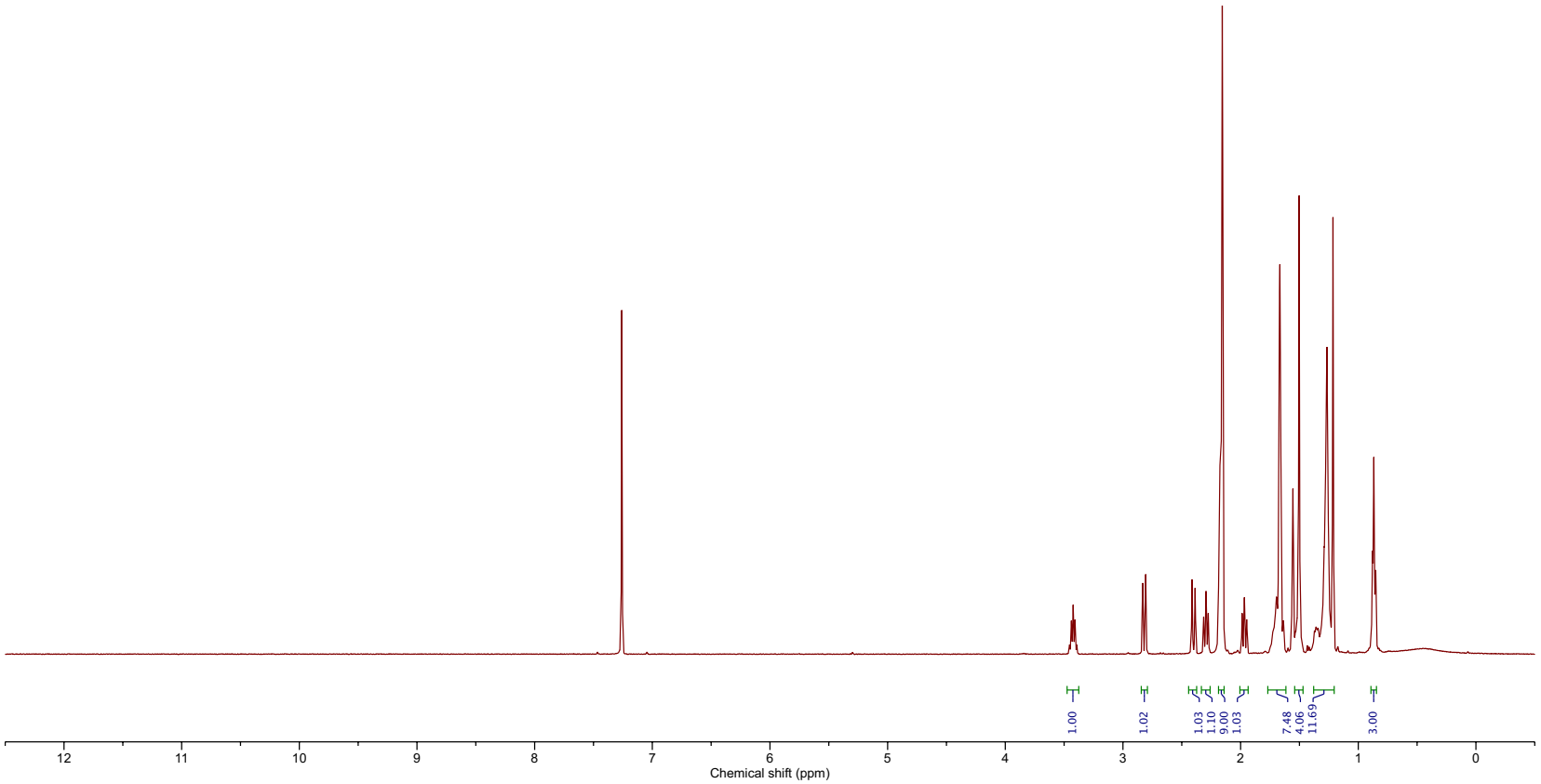
endo-**25**

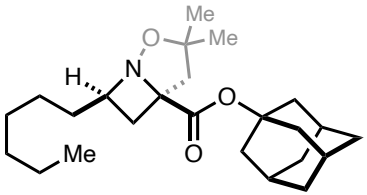
172.28
83.70
77.37
75.32
72.49
60.78
53.04
52.72
36.57
31.84
31.63
29.37
27.10
25.92
25.86
22.73
14.22
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
H
N
O
Me
O

exo-**26**

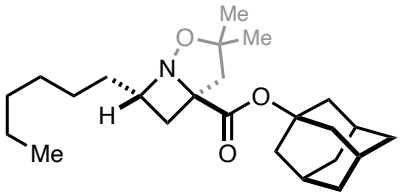

3.45
3.44
3.42
3.41
3.39
2.83
2.81
2.41
2.39
2.31
2.29
2.27
2.17
2.16
1.99
1.97
1.95
1.73
1.70
1.67
1.64
1.53
1.52
1.50
1.48
1.37
1.36
1.34
1.29
1.27
1.21
0.88
0.87
0.85


1.00
1.02
1.03
1.10
9.00
1.03
7.48
4.06
11.69
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

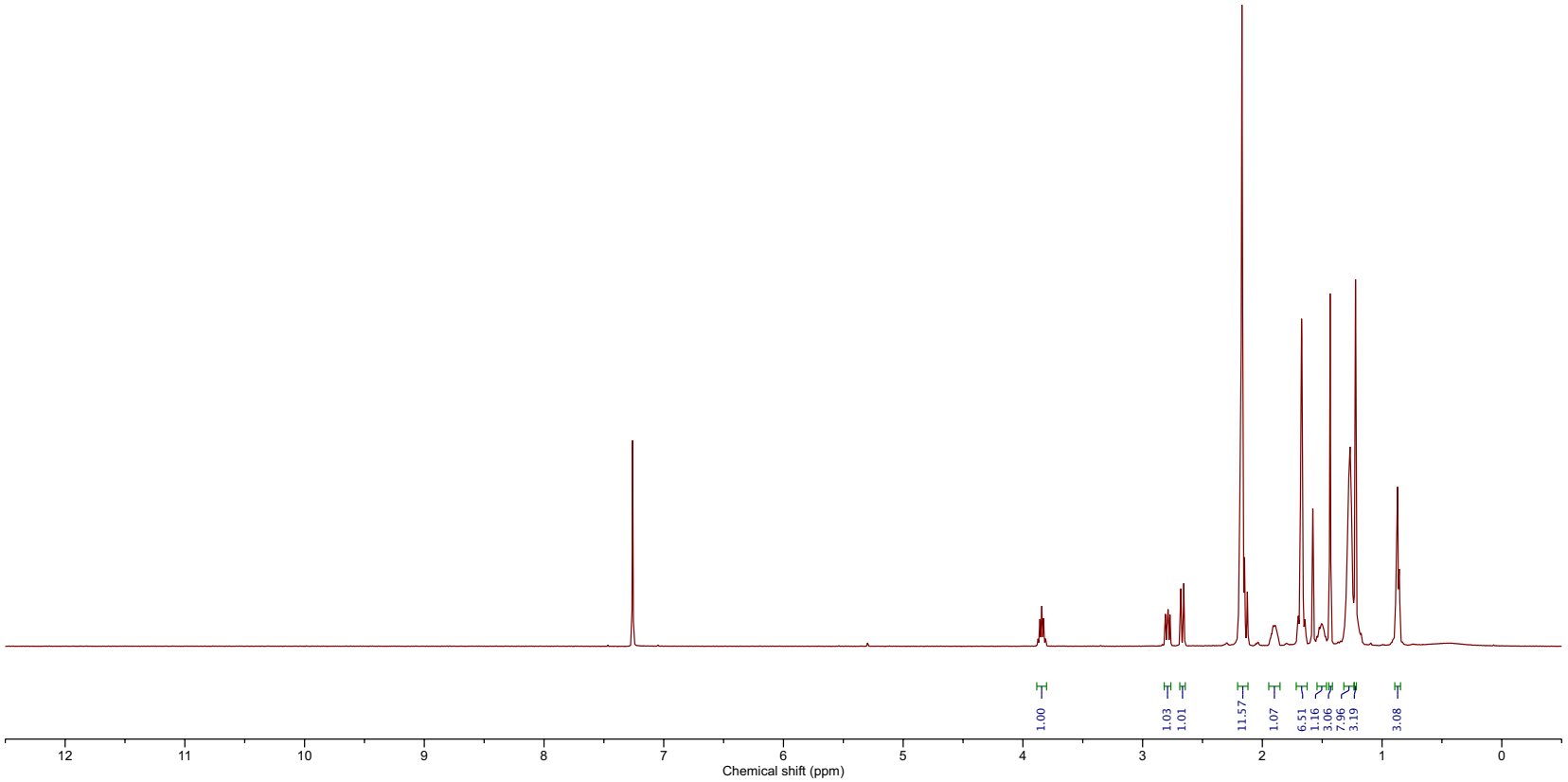

Me
O
Me
H
N
O
O
Me

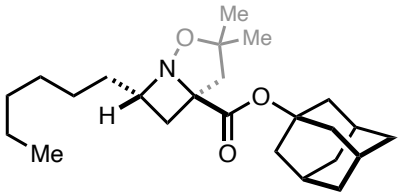
exo-**26**

171.83
86.93
81.62
73.59
67.06
51.04
41.19
36.24
35.36
31.87
30.95
30.44
29.59
29.32
28.38
25.32
22.68
14.16
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
N
H
O
Me
O

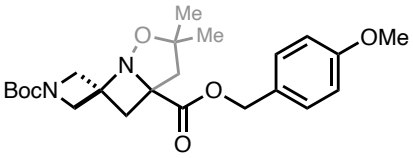
endo-**26**


1.00
1.03
1.01
11.57
1.07
6.51
1.16
3.06
7.96
3.19
3.08
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
O
Me
N
H
O
Me
O

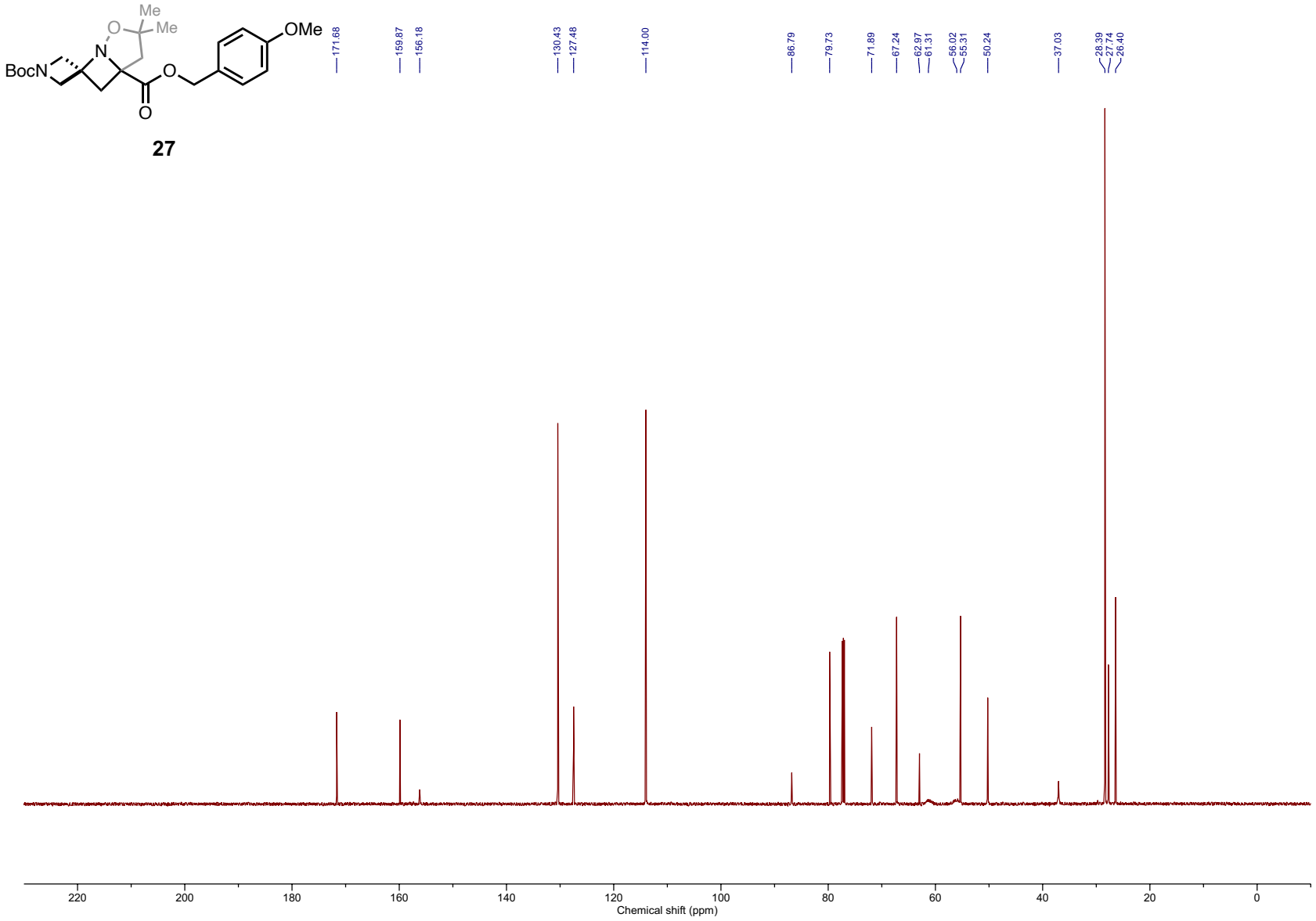
endo-**26**

171.93
83.40
81.82
73.25
60.46
53.01
41.24
37.03
36.28
31.85
31.53
31.01
29.38
26.98
26.12
25.82
22.72
14.21
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

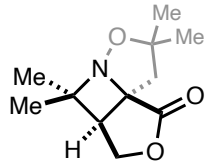

Me
O
Me
N
BocN
O
O
OMe

27

7.31
7.30
6.88
6.87
5.21
5.19
5.13
5.12
4.66
4.65
4.12
4.11
3.88
3.86
3.81
3.72
3.71
2.82
2.80
2.69
2.59
2.54
2.52
1.99
1.97
1.43
1.42
1.12
1.96
1.95
1.00
1.00
1.00
1.00
1.00
3.00
1.00
1.01
1.00
1.03
1.00
12.18
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

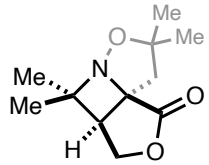

Me
Me
O
N
BocN
O
O
OMe
171.68
159.87
156.18
130.43
127.48
114.00
86.79
79.73
71.89
67.24
62.97
61.31
56.02
55.31
50.24
37.03
28.39
27.74
26.40
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

27


Me
O
Me
Me
N
O
H
O

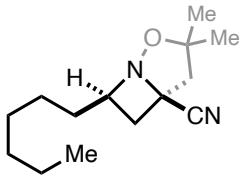
28

4.49
4.47
4.35
4.34
4.34
4.33
2.91
2.90
2.55
2.53
2.35
2.33
1.50
1.42
1.38
1.35
1.00
1.00
0.94
1.00
1.01
3.05
3.00
3.03
3.02
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
O
Me
Me
N
O
H
O

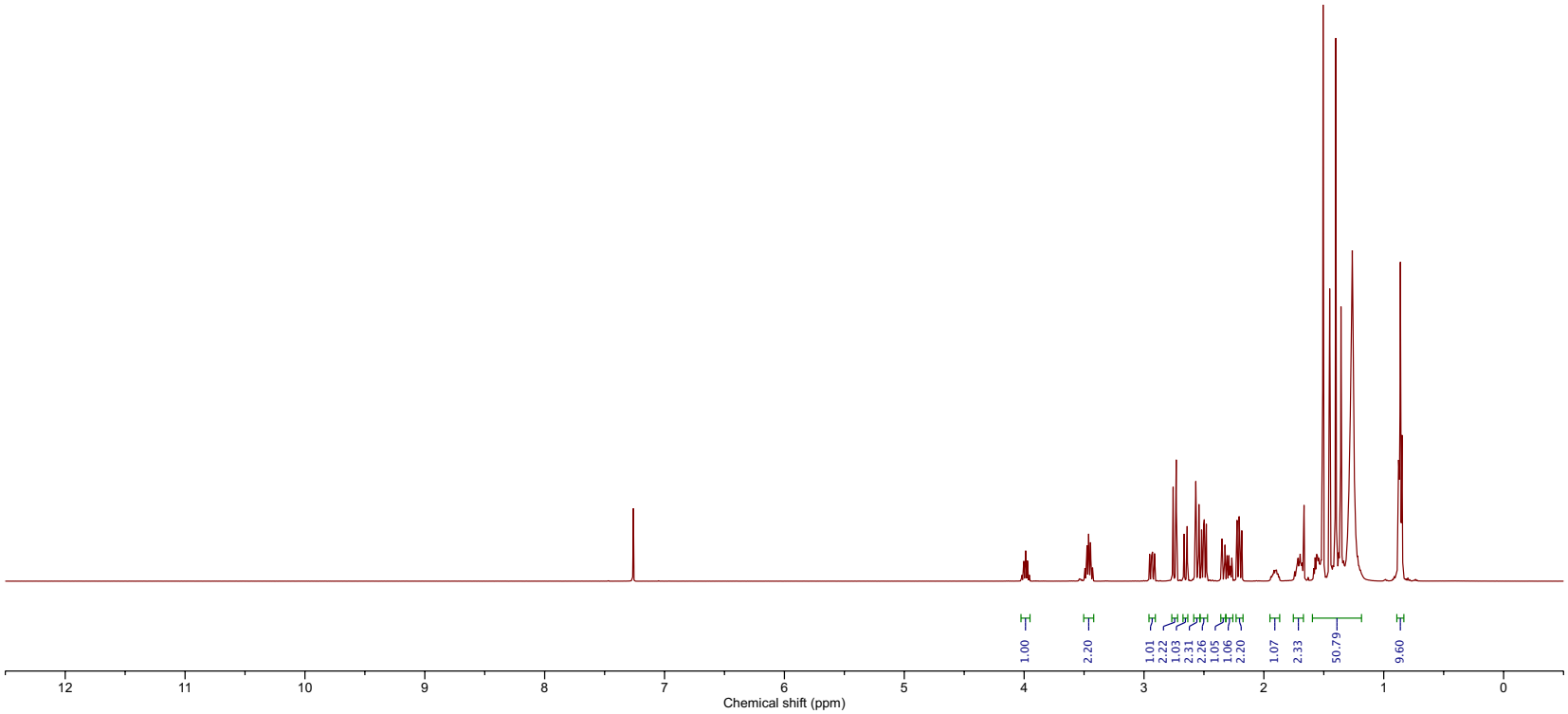
28

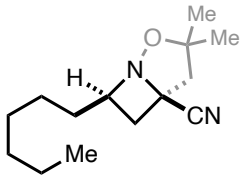
176.73
86.34
69.06
66.75
63.84
48.03
45.34
27.02
25.98
24.58
24.55
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)



29

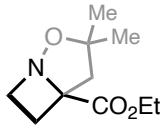
(2.2:1 mixture of diastereomers)





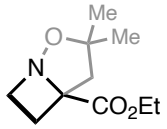
29

(2.2:1 mixture of diastereomers)


Me
O
Me
N
CO2Et

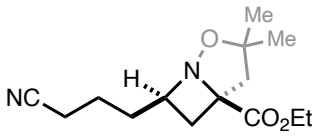
30

4.30
4.29
4.29
4.28
4.28
4.27
4.26
4.25
4.24
4.24
4.23
4.22
3.81
3.80
3.79
3.79
3.78
3.78
3.77
3.76
3.50
3.47
3.45
3.42
2.87
2.83
2.56
2.53
2.51
2.49
2.48
2.46
2.46
2.44
2.32
2.31
2.30
2.29
2.29
2.28
2.27
2.26
2.04
1.55
1.33
1.32
1.30
1.25
1.25
1.20
0.83
1.95
1.00
1.00
1.00
1.00
1.00
1.00
2.99
2.99
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

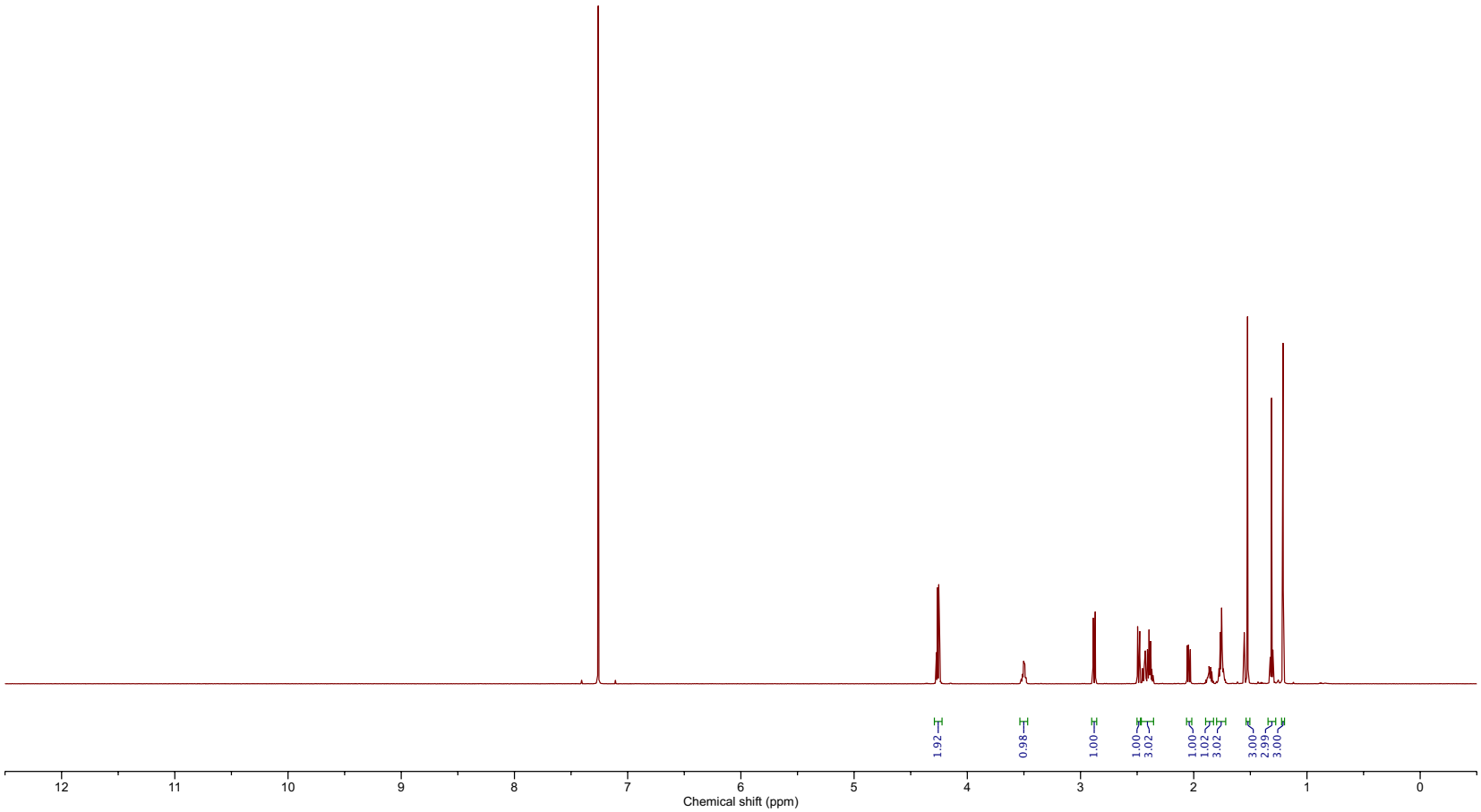

Me
O
Me
N
CO2Et

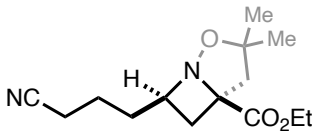
30

172.73
86.99
76.69
61.59
55.23
50.98
29.48
28.29
24.92
14.20
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
H
N
NC
CO2Et

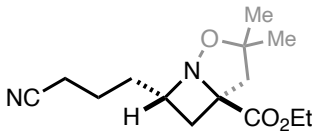
exo-**31**


1.92
0.98
1.00
1.00
3.02
1.00
1.02
3.02
3.00
2.99
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

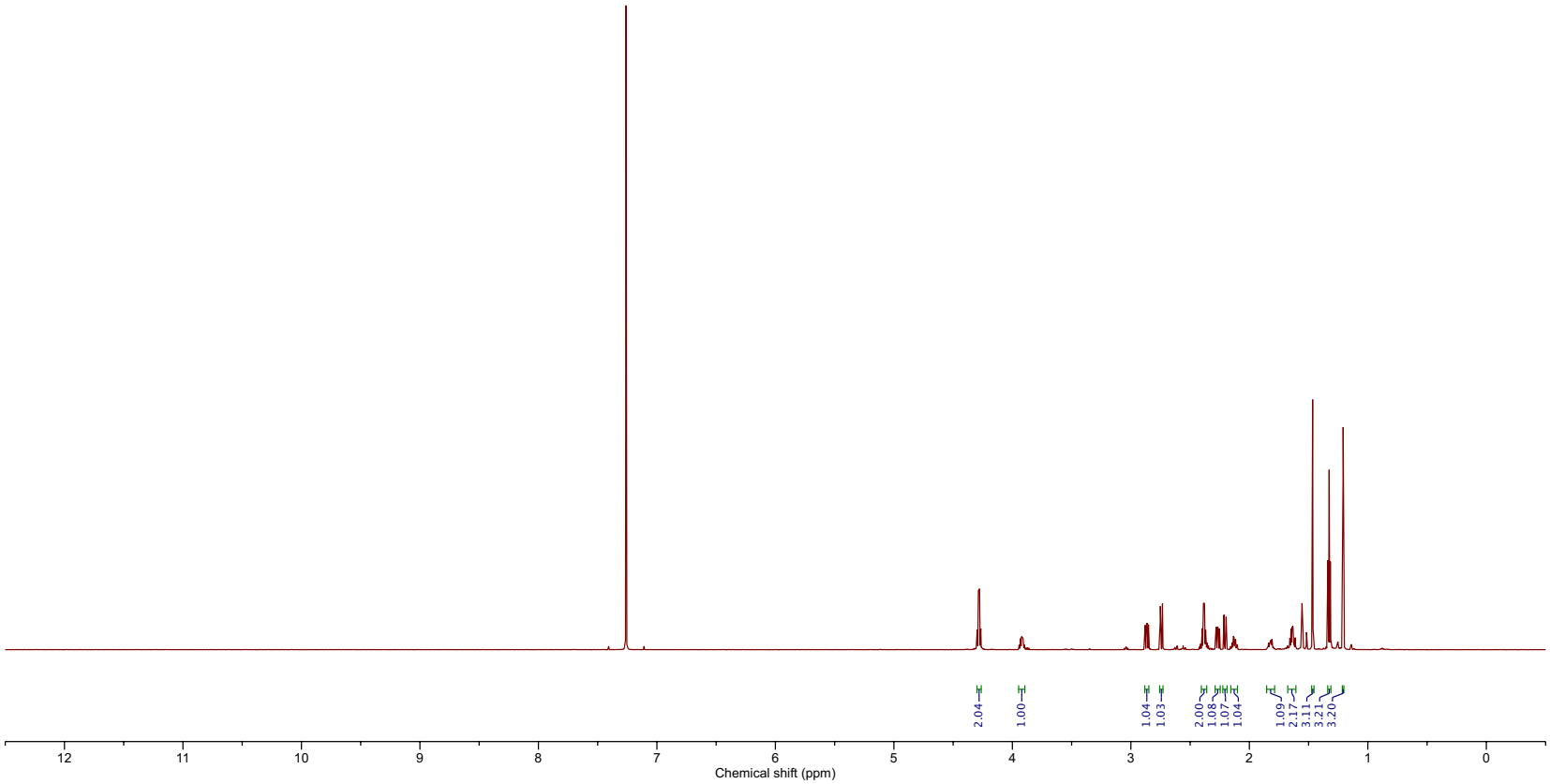

Me
O
Me
H
N
NC
CO2Et

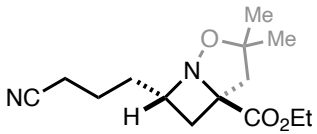
exo-**31**

172.62
119.70
87.69
73.22
66.18
61.72
50.98
33.92
29.95
29.77
28.52
21.57
17.05
14.26
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
N
NC
H
CO2Et

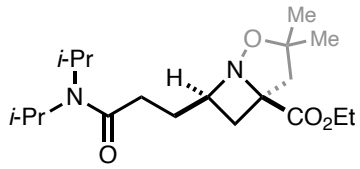
endo-**31**


2.04
1.00
1.04
1.03
2.00
1.08
1.07
1.04
1.09
2.17
3.11
3.21
3.20
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

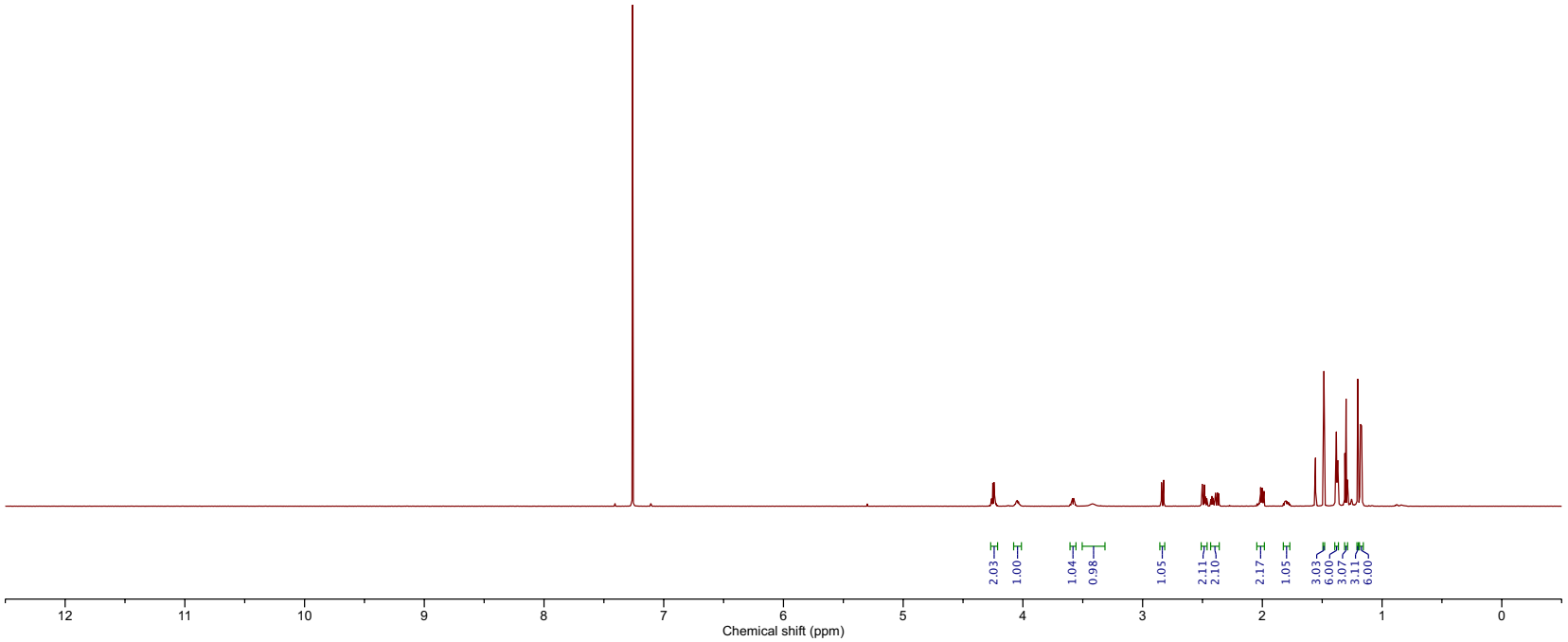

Me
O
Me
N
NC
H
CO2Et

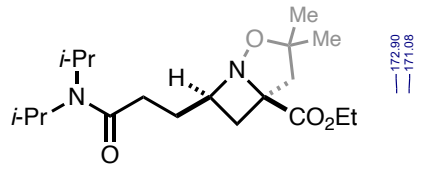
endo-**31**

172.70
119.65
83.84
72.48
61.87
59.51
52.89
36.78
30.82
26.94
25.99
22.61
17.28
14.25
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
Me
O
i-Pr
N
H
N
i-Pr
CO2Et
O

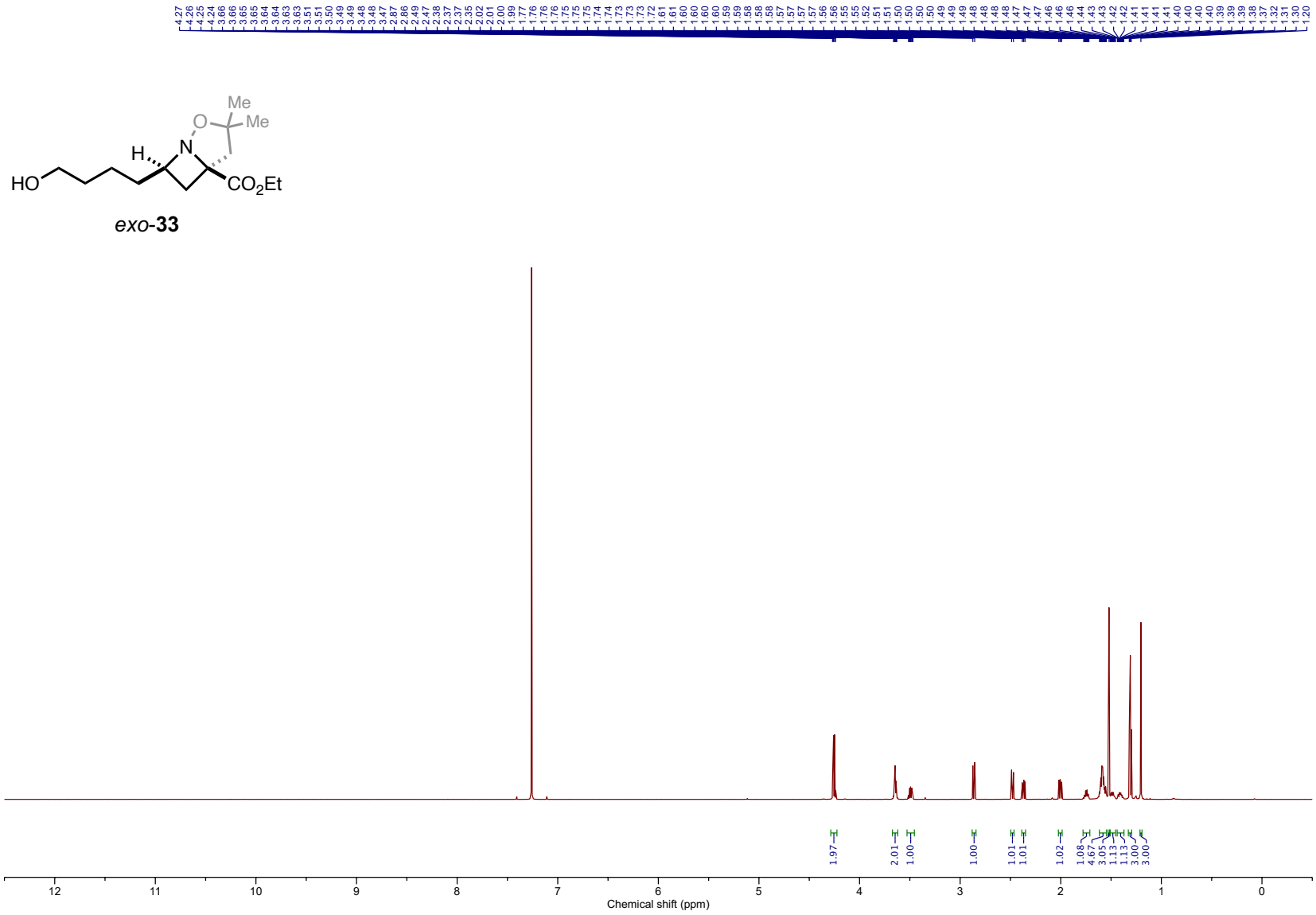
exo-**32**


2.03
1.00
1.04
0.98
1.05
2.11
2.10
2.17
1.05
3.03
6.00
3.07
3.11
6.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

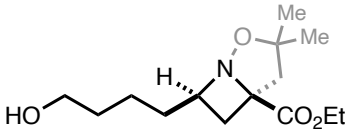

Me
Me
O
i-Pr
N
H
N
i-Pr
CO2Et
O

exo-**32**

172.90
171.08
87.49
73.33
66.55
61.54
51.06
48.37
45.70
30.41
30.13
29.90
28.74
21.01
20.87
20.83
14.26
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

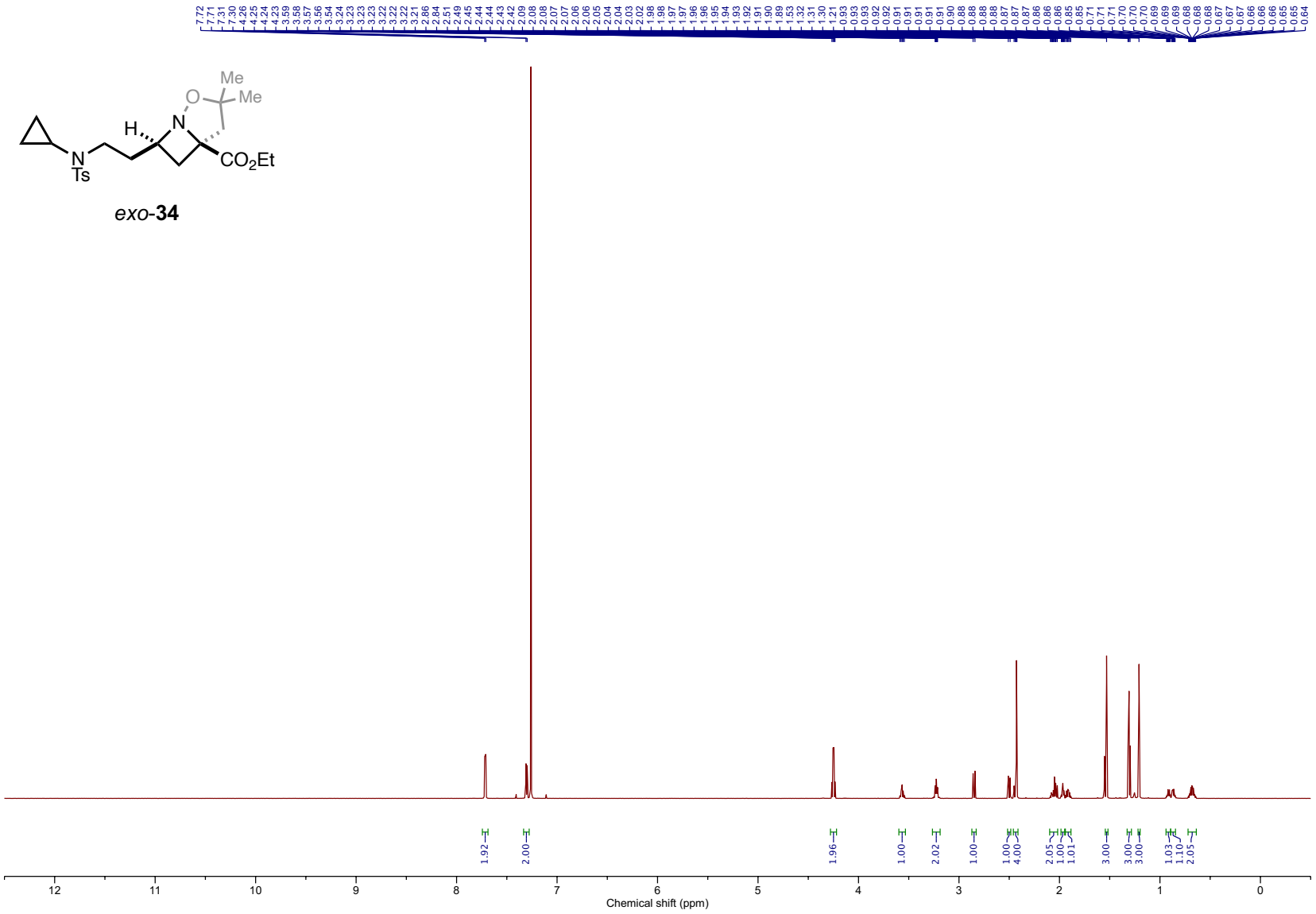

4.27 4.26 4.25 4.24 3.66 3.66 3.65 3.65 3.64 3.64 3.63 3.63 3.51 3.51 3.50 3.49 3.49 3.48 3.48 3.47 2.87 2.86 2.49 2.47 2.38 2.37 2.37 2.35 2.02 2.01 2.00 1.99 1.77 1.76 1.76 1.76 1.75 1.75 1.75 1.74 1.74 1.73 1.73 1.72 1.61 1.61 1.60 1.60 1.60 1.60 1.59 1.59 1.58 1.58 1.57 1.57 1.57 1.57 1.56 1.56 1.55 1.55 1.52 1.51 1.51 1.50 1.50 1.50 1.50 1.49 1.49 1.49 1.48 1.48 1.48 1.48 1.47 1.47 1.47 1.46 1.46 1.46 1.44 1.43 1.42 1.42 1.41 1.41 1.41 1.40 1.40 1.40 1.40 1.39 1.39 1.39 1.38 1.37 1.32 1.31 1.30 1.20
Me
O
Me
H
N
HO
CO2Et
1.97 2.01 1.00 1.00 1.01 1.01 1.02 1.08 4.67 3.05 1.13 3.00 3.00
12 11 10 9 8 7 6 5 4 3 2 1 0
Chemical shift (ppm)

exo-**33**

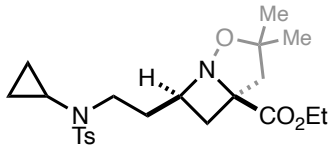

Me
O
Me
H
N
HO
CO2Et

exo-**33**

172.82
87.29
73.00
67.25
62.44
61.58
51.04
34.74
32.46
30.29
29.54
28.40
21.51
14.19
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

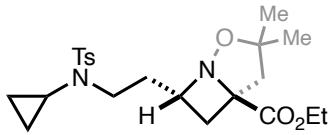


exo-**34**


Me
O
Me
H
N
N
Ts
CO2Et

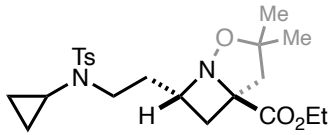
exo-**34**

172.64
143.45
135.24
129.60
127.73
87.58
73.45
64.90
61.53
50.87
47.83
34.42
30.95
30.14
29.71
28.53
21.57
14.19
7.60
7.24
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
Ts
N
N
H
CO2Et

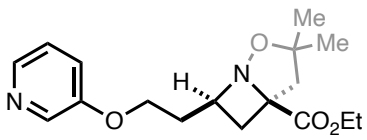
endo-**34**

7.72
7.70
7.30
7.29
4.29
4.27
4.26
4.25
3.93
3.91
3.89
3.88
3.86
3.24
3.22
3.21
3.20
3.19
3.18
3.17
3.16
3.15
3.13
3.12
2.85
2.83
2.82
2.81
2.76
2.73
2.42
2.38
2.36
2.35
2.33
2.32
2.30
2.27
2.25
2.23
2.22
2.19
2.04
2.04
2.03
1.85
1.84
1.82
1.81
1.79
1.78
1.44
1.33
1.32
1.30
1.17
0.87
0.85
0.83
0.81
0.70
0.67
0.66
0.63
1.92
1.99
2.00
1.00
2.04
1.01
1.01
3.01
1.06
1.03
1.02
1.01
1.04
3.00
3.00
3.00
2.11
2.02
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
O
Me
Ts
N
N
H
CO2Et

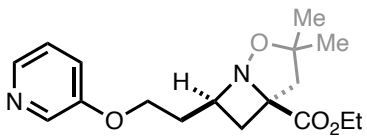
endo-**34**

172.80
143.47
135.54
129.65
127.81
83.81
72.77
61.80
58.41
52.81
48.60
36.27
31.69
30.96
27.00
25.91
21.64
14.26
7.55
7.33
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

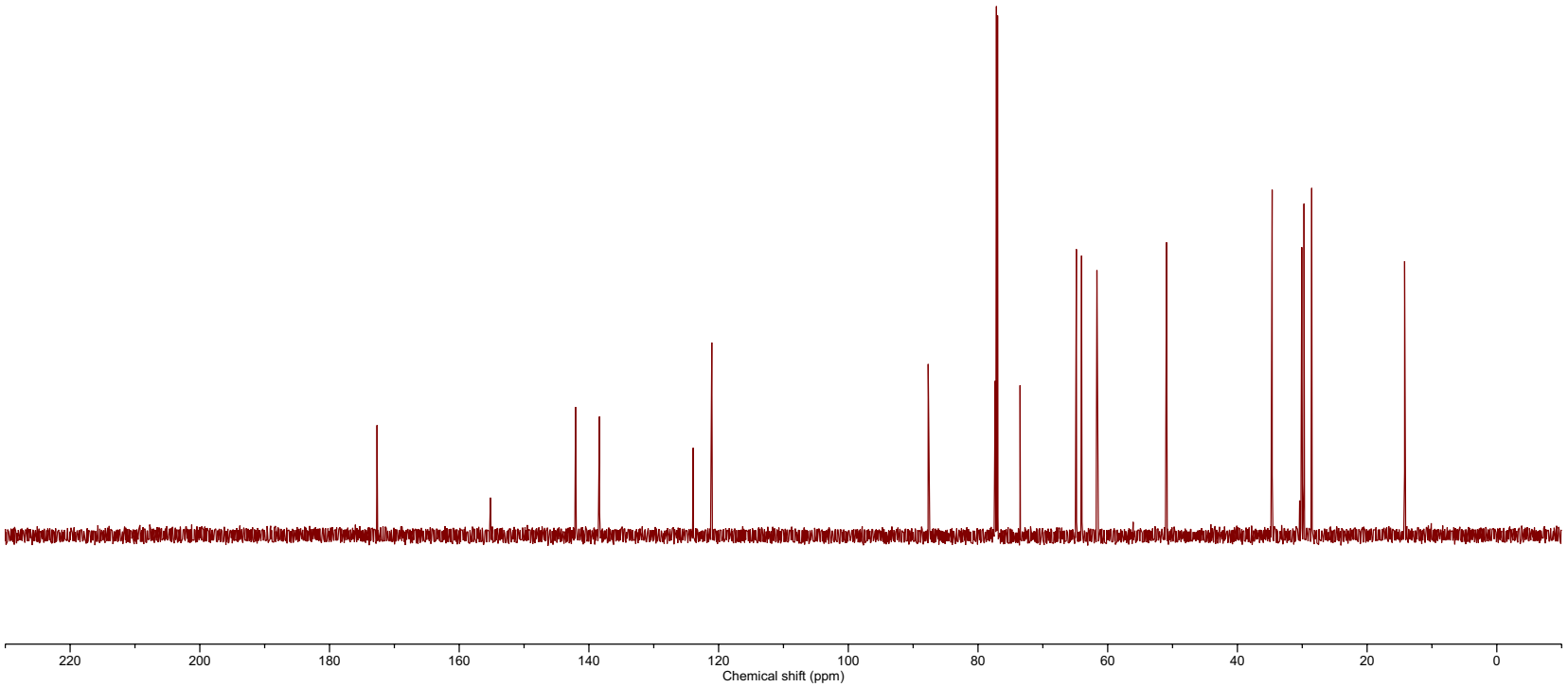

Me
Me
O
N
H
N
O
CO2Et

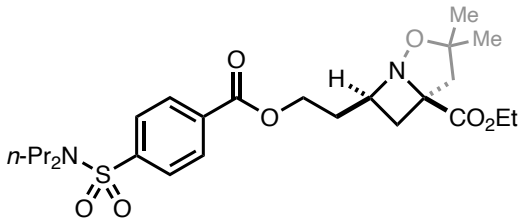
exo-**35**

8.29
8.20
8.19
8.19
7.20
7.19
7.19
7.19
7.19
4.27
4.25
4.23
4.22
4.18
4.16
4.15
4.15
4.14
4.14
4.13
4.12
4.12
4.11
4.11
4.09
3.80
3.79
3.78
3.77
3.76
3.75
3.74
3.74
3.72
2.89
2.85
2.53
2.50
2.47
2.44
2.44
2.42
2.19
2.17
2.17
2.16
2.15
2.15
2.15
2.14
2.14
2.14
2.13
2.13
2.12
2.11
2.11
2.10
2.09
2.08
2.06
1.50
1.31
1.29
1.27
0.96
0.96
1.95
1.99
2.02
1.00
1.01
1.00
1.02
3.03
3.00
3.00
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
O
Me
H
N
N
O
CO2Et

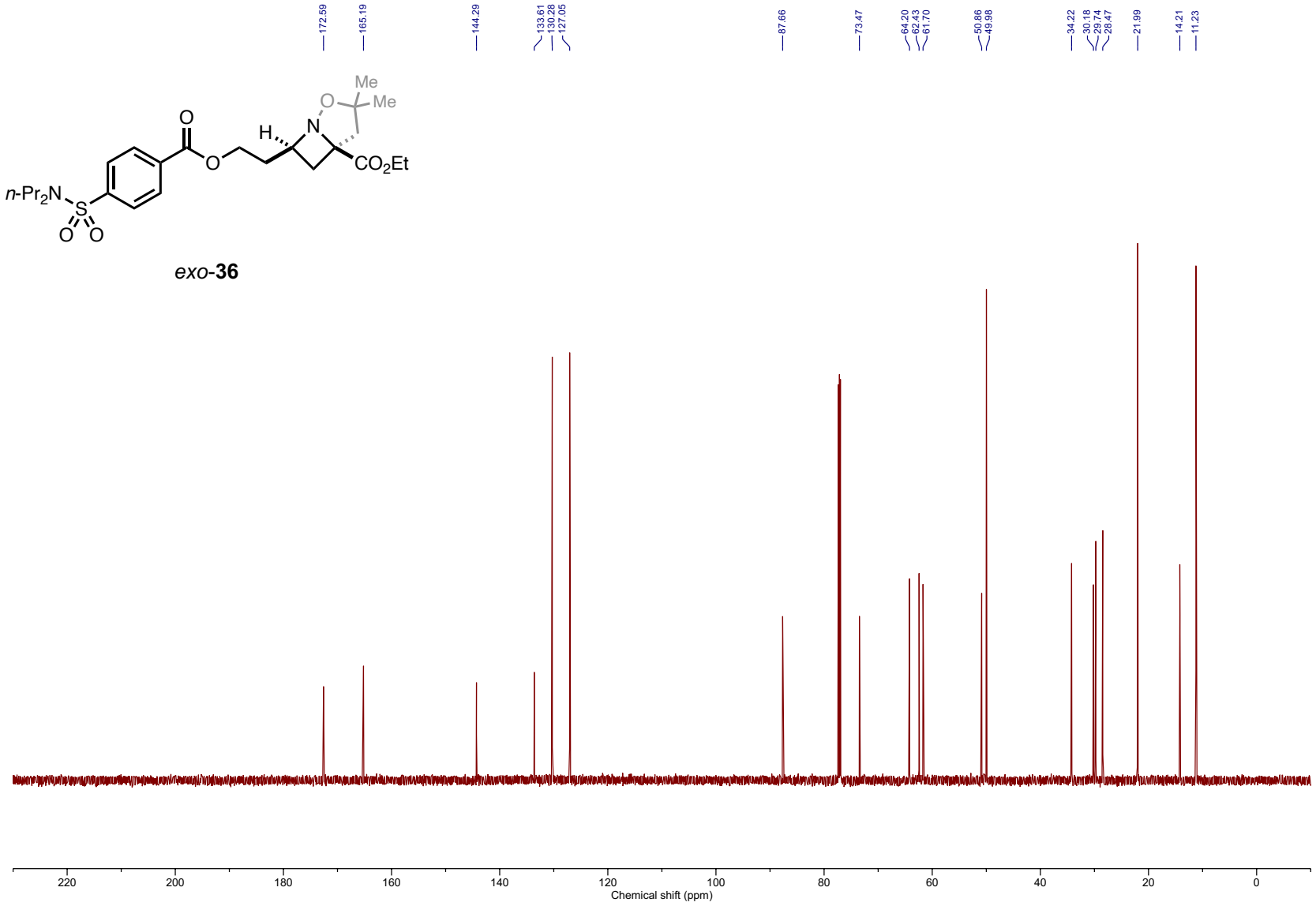
exo-**35**


172.67
155.18
142.06
138.37
123.93
121.05
87.68
73.51
64.83
64.03
61.66
50.93
34.64
30.07
29.73
28.54
14.22
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

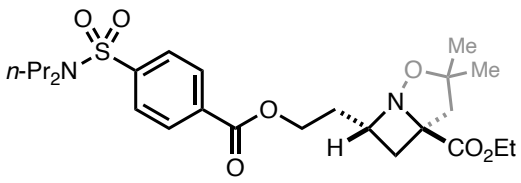

Me
Me
O
O
H
N
O
O
CO2Et
n-Pr2N
S
O
O

exo-**36**

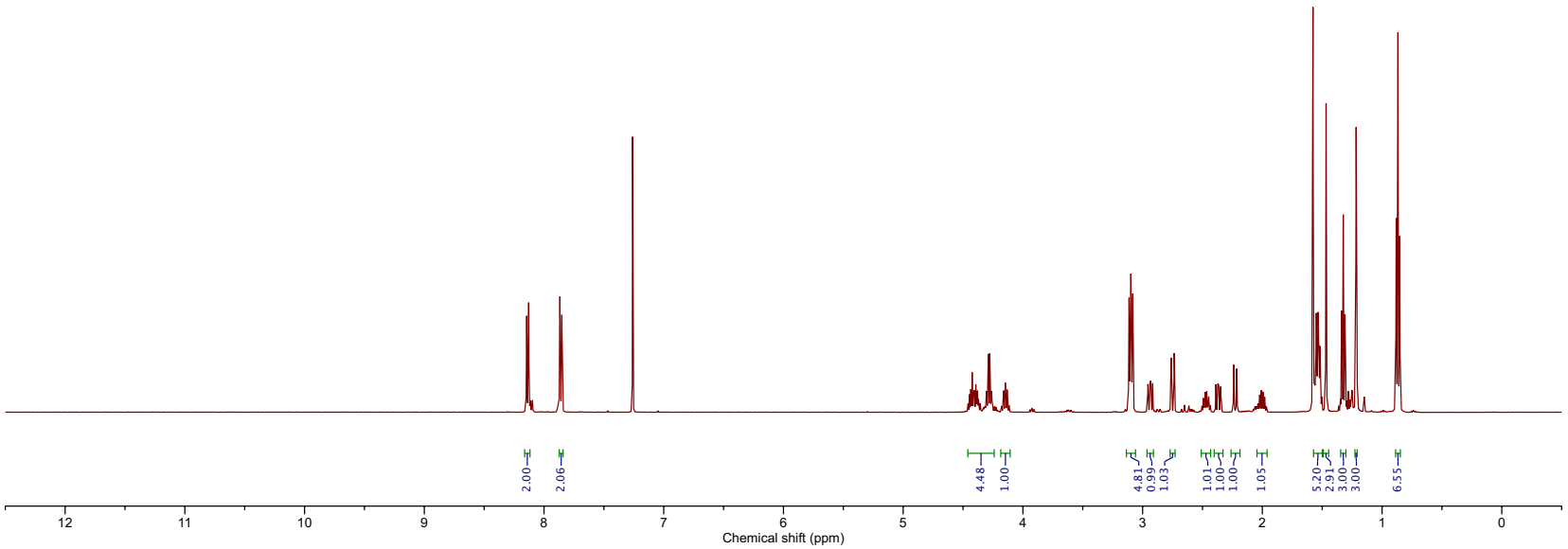
8.13
8.11
7.85
7.83
4.49
4.48
4.47
4.46
4.45
4.44
4.44
4.44
4.43
4.42
4.42
4.41
4.40
4.26
4.24
4.23
4.22
3.69
3.68
3.66
3.65
3.63
3.09
3.08
3.07
3.07
3.06
2.87
2.85
2.50
2.48
2.45
2.43
2.43
2.41
2.19
2.18
2.18
2.17
2.17
2.16
2.15
2.15
2.14
2.14
2.13
2.13
2.11
2.11
2.09
2.08
2.08
2.07
2.06
2.05
2.05
2.04
2.03
1.80
1.56
1.54
1.53
1.52
1.52
1.51
1.51
1.50
1.49
1.44
1.30
1.29
1.28
1.23
1.20
0.86
0.84
2.00
2.00
2.02
2.02
1.00
4.07
1.00
1.00
1.00
3.05
4.18
3.00
3.03
2.99
6.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

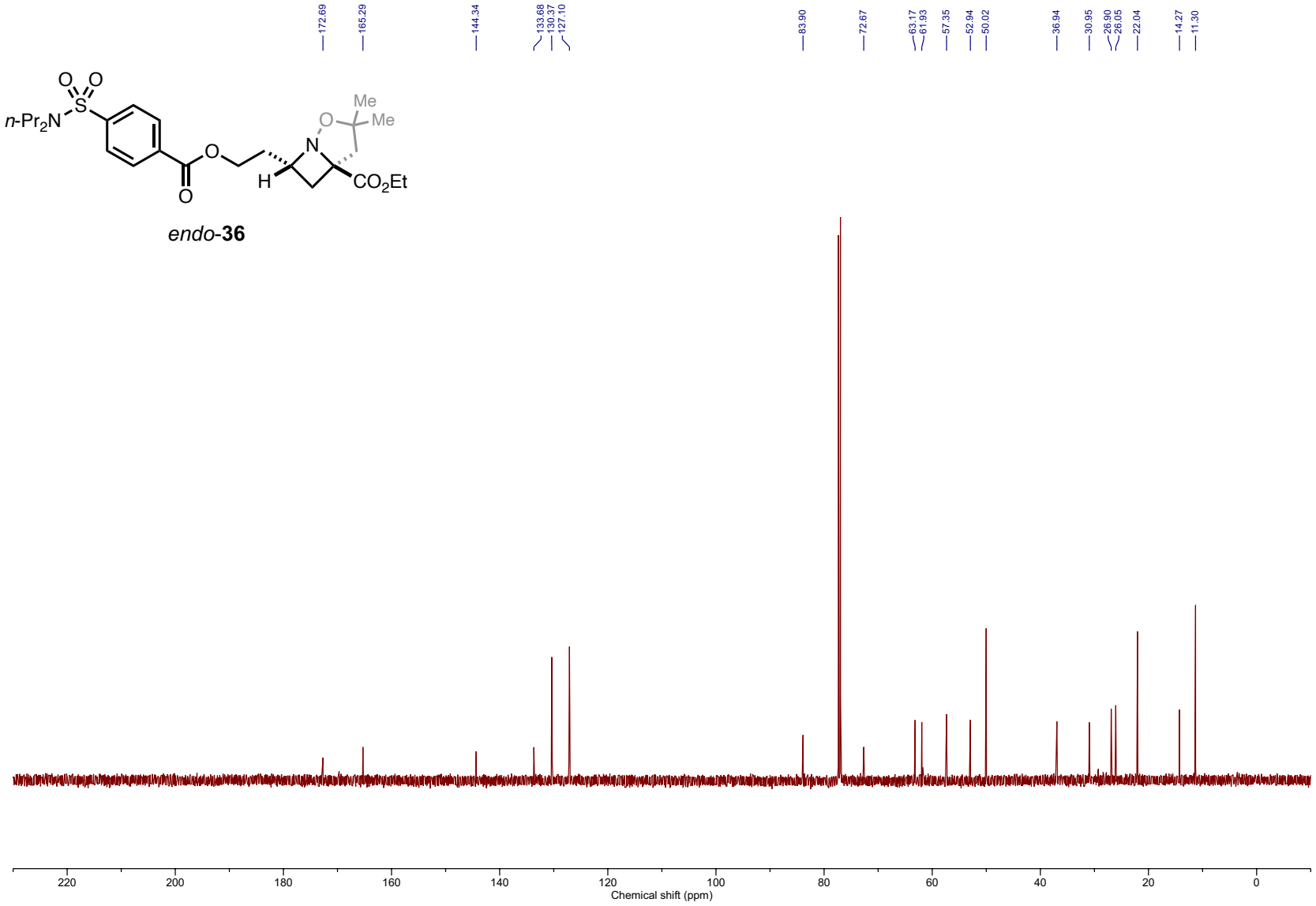

172.59
165.19
144.29
133.61
130.28
127.05
87.66
73.47
64.20
62.43
61.70
50.86
49.98
34.22
30.18
29.74
28.47
21.99
14.21
11.23
Me
Me
O
H
N
O
O
CO2Et
n-Pr2N
S
O
O
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

exo-**36**

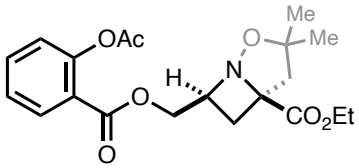

O
O
S
n-Pr2N
O
O
Me
Me
O
N
H
CO2Et

endo-**36**

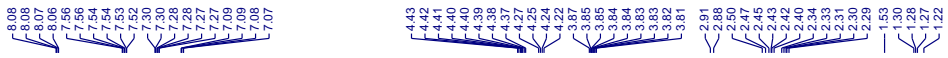

2.00
2.06
4.48
1.00
4.81
0.99
1.03
1.01
1.00
1.00
1.05
5.20
2.91
3.00
3.00
6.55
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

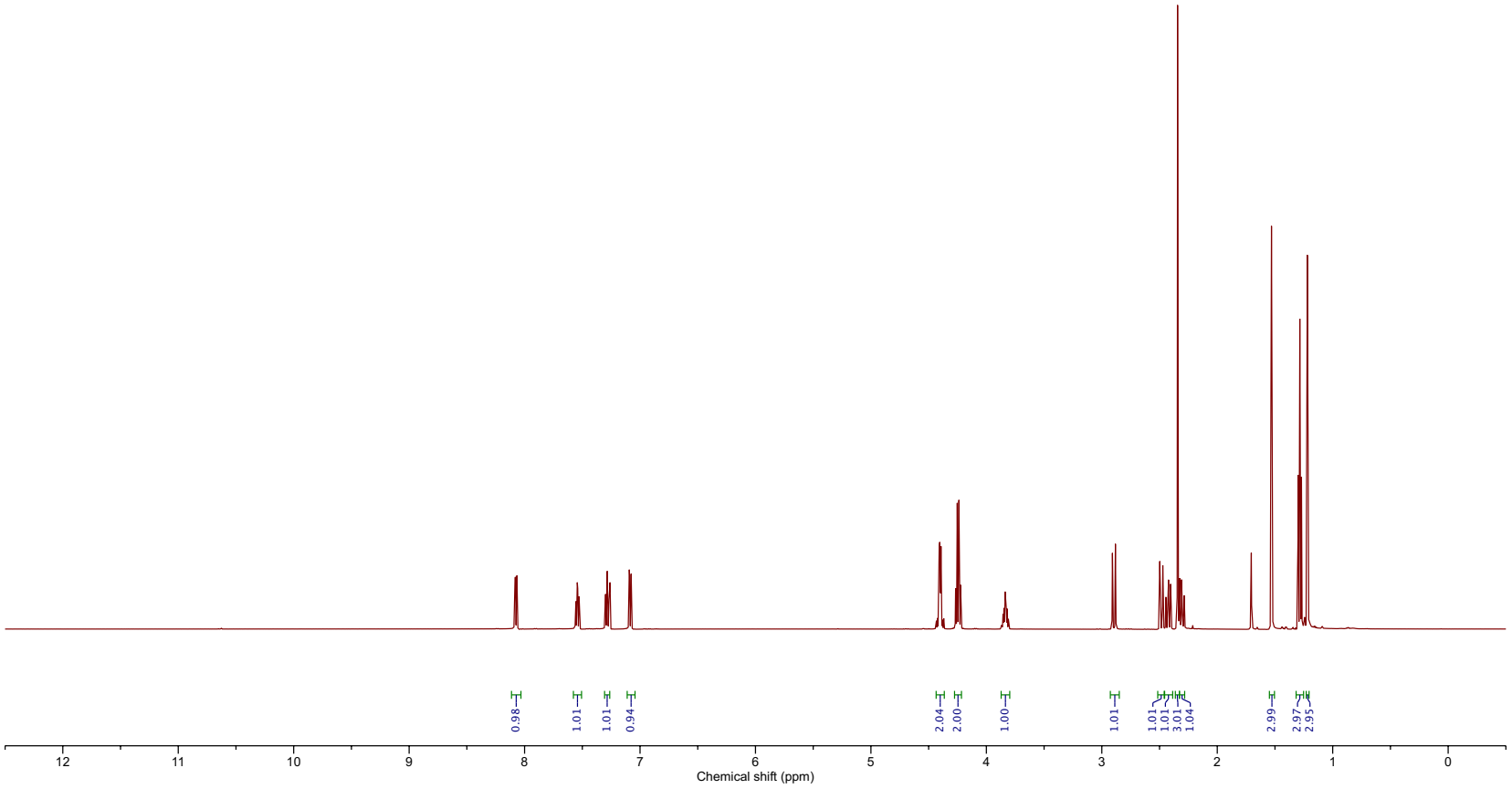

172.69
165.29
144.34
133.68
130.37
127.10
83.90
72.67
63.17
61.93
57.35
52.94
50.02
36.94
30.95
26.90
26.05
22.04
14.27
11.30
n-Pr2N
O
S
O
O
O
O
Me
Me
O
N
H
CO2Et
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

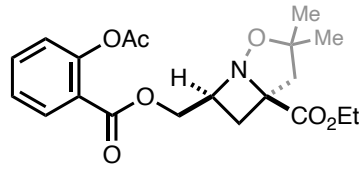
endo-**36**


OAc
O
Me
Me
H
N
O
O
CO2Et

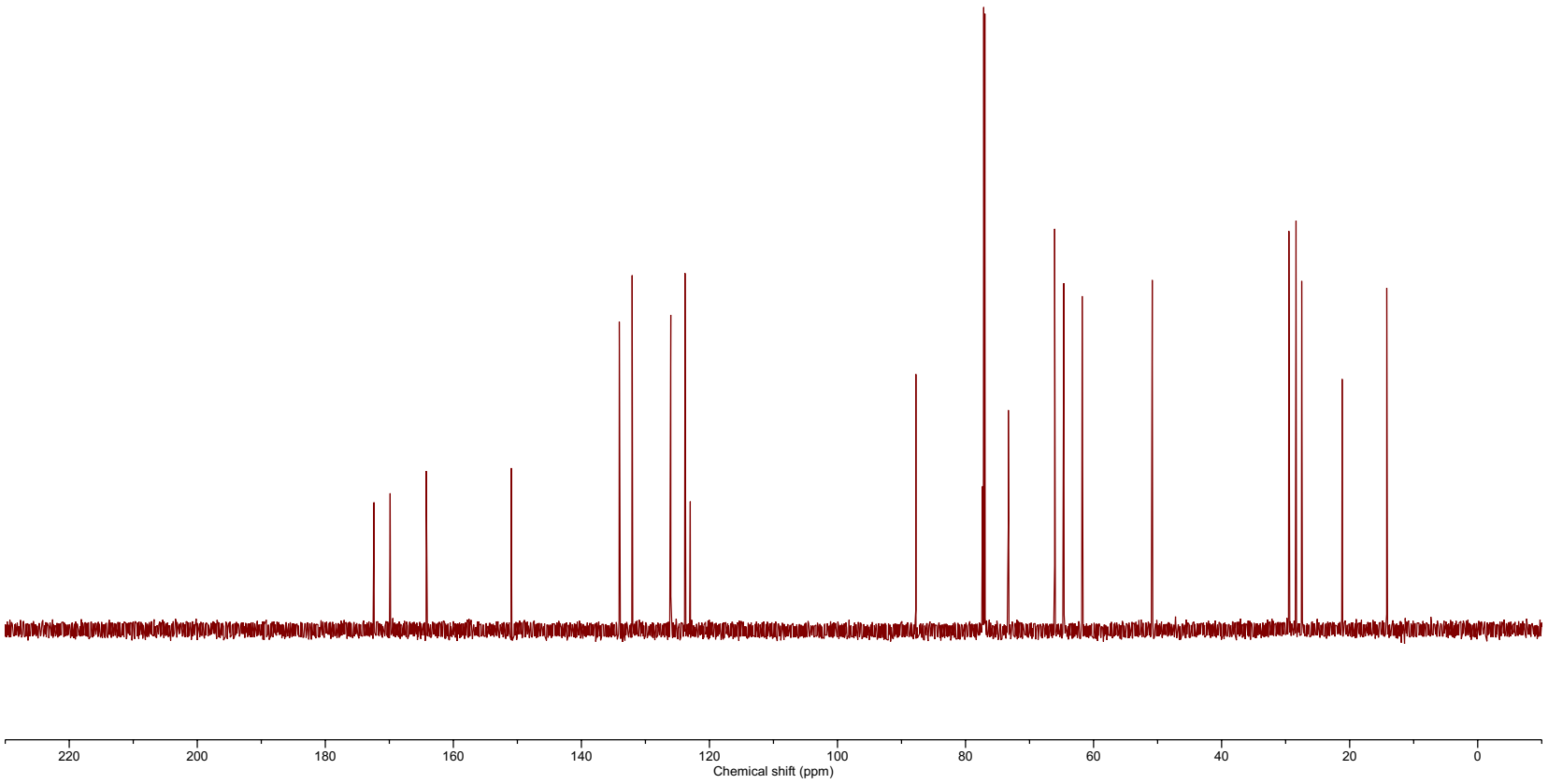
exo-**37**

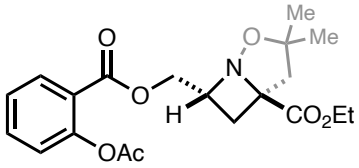

8.08
8.08
8.07
8.06
7.56
7.56
7.54
7.54
7.53
7.52
7.30
7.30
7.28
7.28
7.27
7.27
7.09
7.09
7.08
7.07
4.43
4.42
4.41
4.40
4.40
4.39
4.38
4.37
4.27
4.25
4.24
4.22
3.87
3.85
3.85
3.84
3.84
3.83
3.83
3.82
3.81
2.91
2.88
2.50
2.47
2.45
2.43
2.42
2.40
2.34
2.33
2.31
2.30
2.29
1.53
1.30
1.28
1.27
1.22


0.98
1.01
1.01
0.94
2.04
2.00
1.00
1.01
1.01
1.01
3.01
1.04
2.99
2.97
2.95
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


OAc
Me
Me
O
H
N
O
O
CO2Et

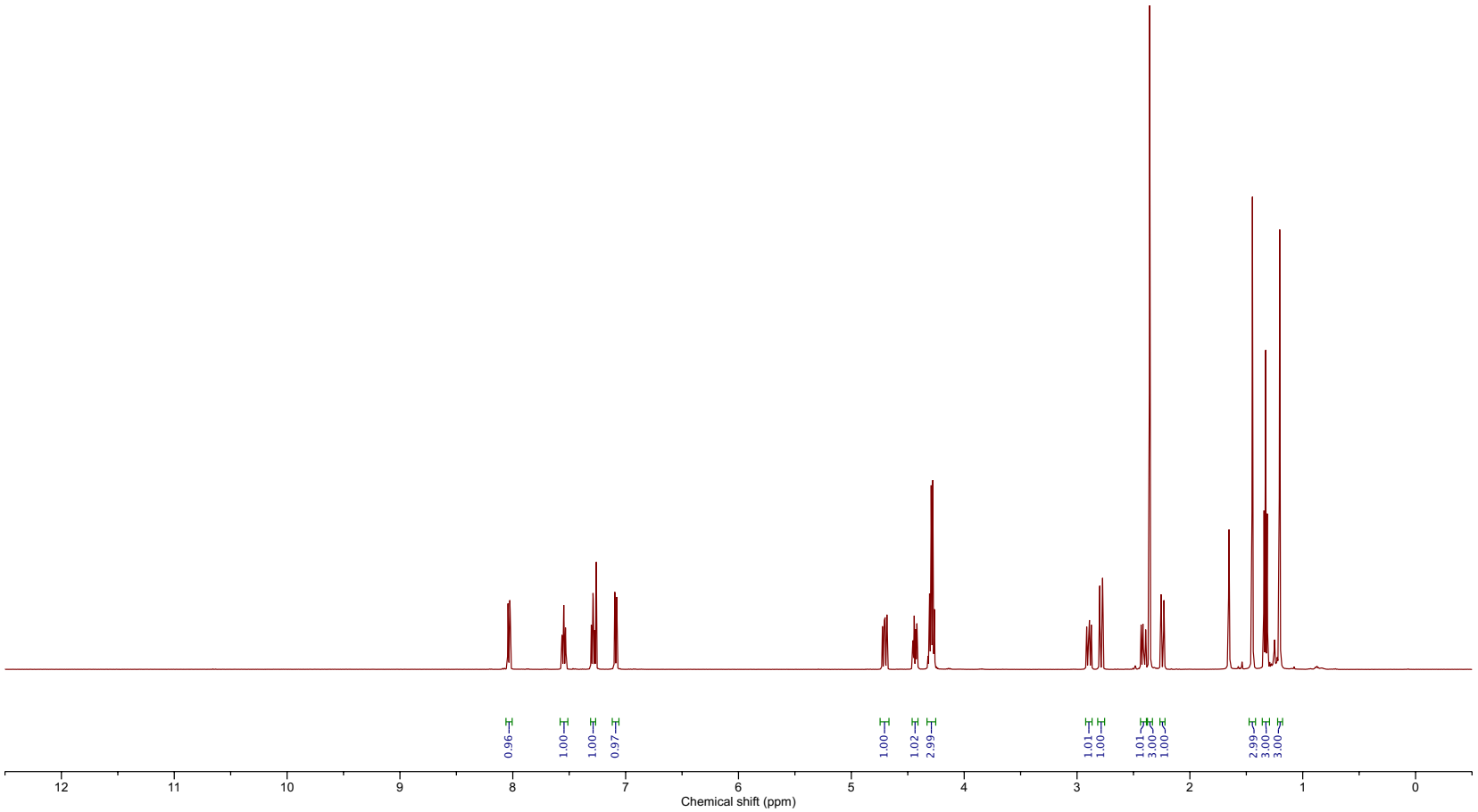
exo-**37**

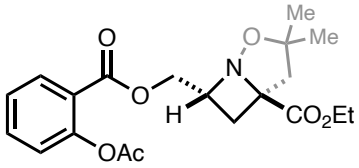

172.40
169.87
164.24
150.95
134.08
132.07
126.04
123.81
123.00
87.75
73.31
66.08
64.65
61.78
50.84
29.49
28.37
27.49
21.17
14.21
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
Me
O
O
N
O
H
CO2Et
OAc

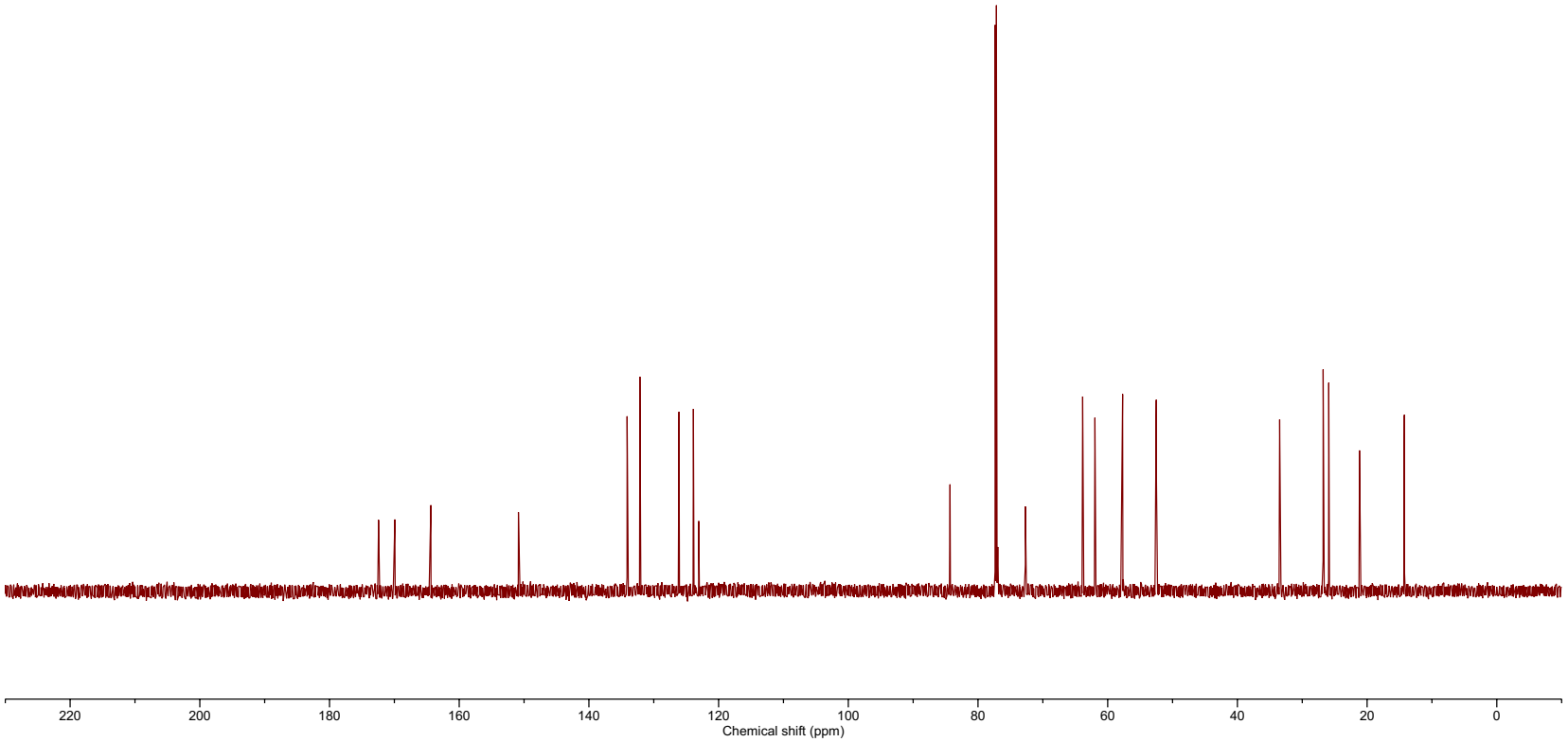
endo-**37**

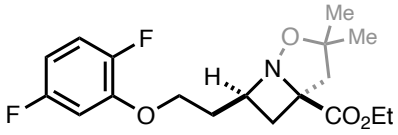

8.04
8.04
8.03
8.02
7.56
7.56
7.55
7.55
7.53
7.53
7.30
7.30
7.29
7.29
7.27
7.27
7.10
7.09
7.08
7.08
4.73
4.72
4.71
4.71
4.70
4.69
4.68
4.45
4.44
4.43
4.42
4.32
4.32
4.31
4.31
4.30
4.29
4.29
4.29
4.28
4.28
4.28
4.27
4.27
4.26
4.26
2.91
2.90
2.89
2.87
2.80
2.77
2.43
2.42
2.41
2.39
2.36
2.25
2.23
1.45
1.35
1.34
1.34
1.33
1.33
1.33
1.32
1.31
1.31
1.29
1.23
1.20
0.83


0.96
1.00
1.00
0.97
1.00
1.02
2.99
1.01
1.00
1.01
3.00
1.00
2.99
3.00
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
Me
O
O
N
O
O
H
CO2Et
OAc

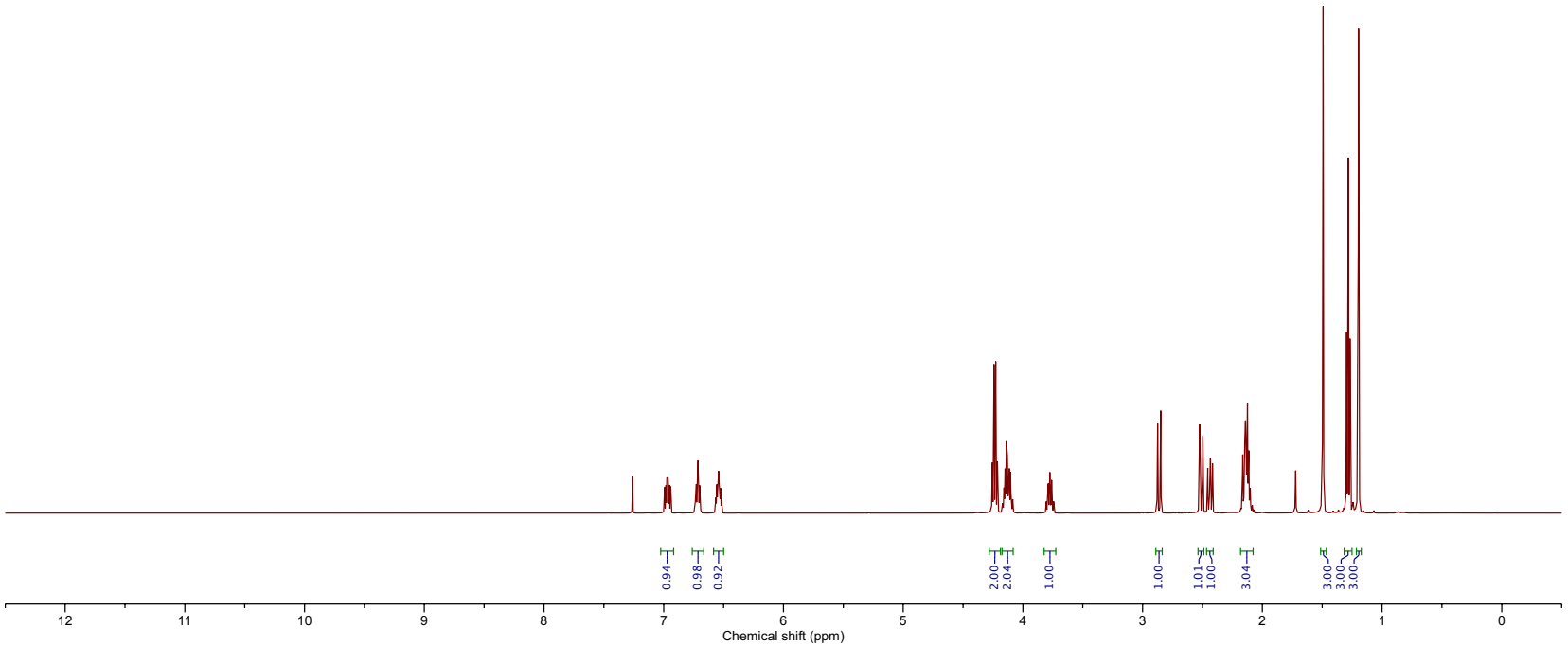
endo-**37**

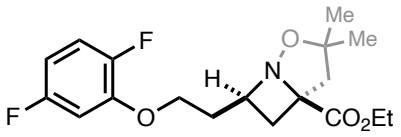

172.44
169.93
164.37
150.87
134.11
132.13
126.11
123.89
123.07
84.32
72.69
63.86
61.97
57.70
52.51
33.49
26.78
25.91
21.17
14.26
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


F
F
O
H
N
O
Me
Me
CO2Et

exo-**38**

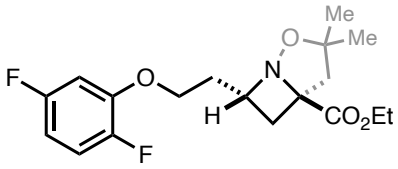

6.99 6.98 6.97 6.97 6.97 6.96 6.96 6.95 6.94 6.73 6.73 6.72 6.71 6.71 6.70 6.69 6.57 6.56 6.56 6.55 6.55 6.55 6.54 6.54 6.54 6.53 6.53 6.52 6.52
4.26 4.24 4.23 4.21 4.17 4.16 4.15 4.15 4.14 4.13 4.13 4.12 4.11 4.11 4.10 4.10 4.10 4.09 3.80 3.79 3.77 3.76 3.74
2.87 2.85 2.52 2.50 2.46 2.44 2.43 2.42 2.17 2.16 2.16 2.15 2.15 2.15 2.14 2.14 2.13 2.13 2.12 2.11 2.10 2.09 2.08 1.49 1.30 1.28 1.27 1.20


0.94
0.98
0.92
2.00
2.04
1.00
1.00
1.01
1.00
3.04
3.00
3.00
3.00
12 11 10 9 8 7 6 5 4 3 2 1 0
Chemical shift (ppm)


Me
Me
O
F
F
H
N
O
CO2Et

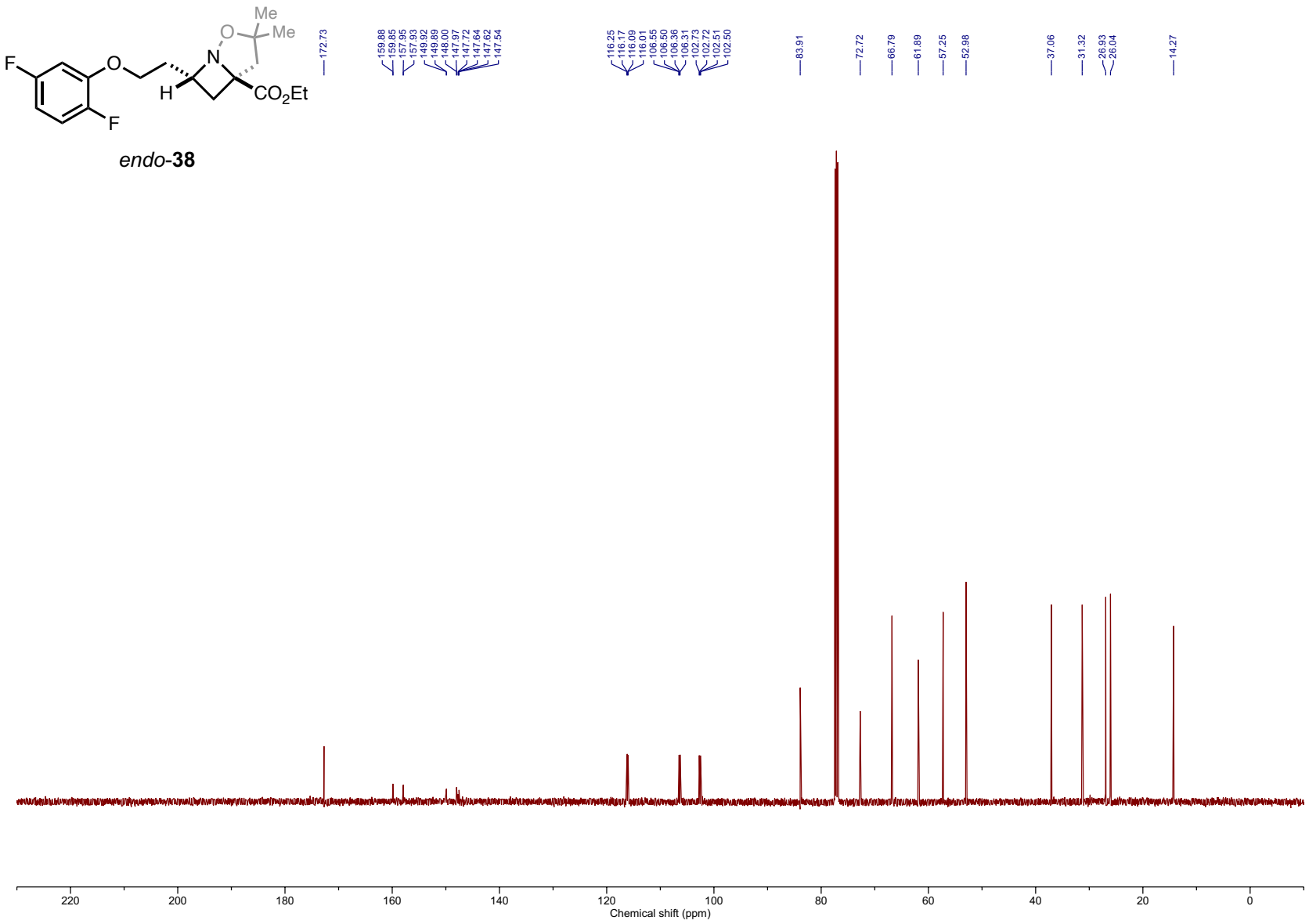
exo-**38**

172.70
159.83
159.61
157.91
157.89
150.00
149.97
148.08
148.06
147.82
147.74
147.72
147.64
116.21
116.13
116.05
115.97
106.70
106.64
106.51
106.45
103.07
103.06
102.86
102.84
87.73
73.61
66.08
64.02
61.64
50.96
34.52
30.10
29.70
28.60
14.21
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

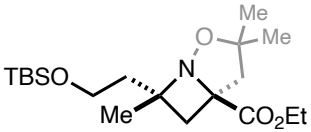

Me
Me
O
N
F
O
H
CO2Et
F

endo-**38**

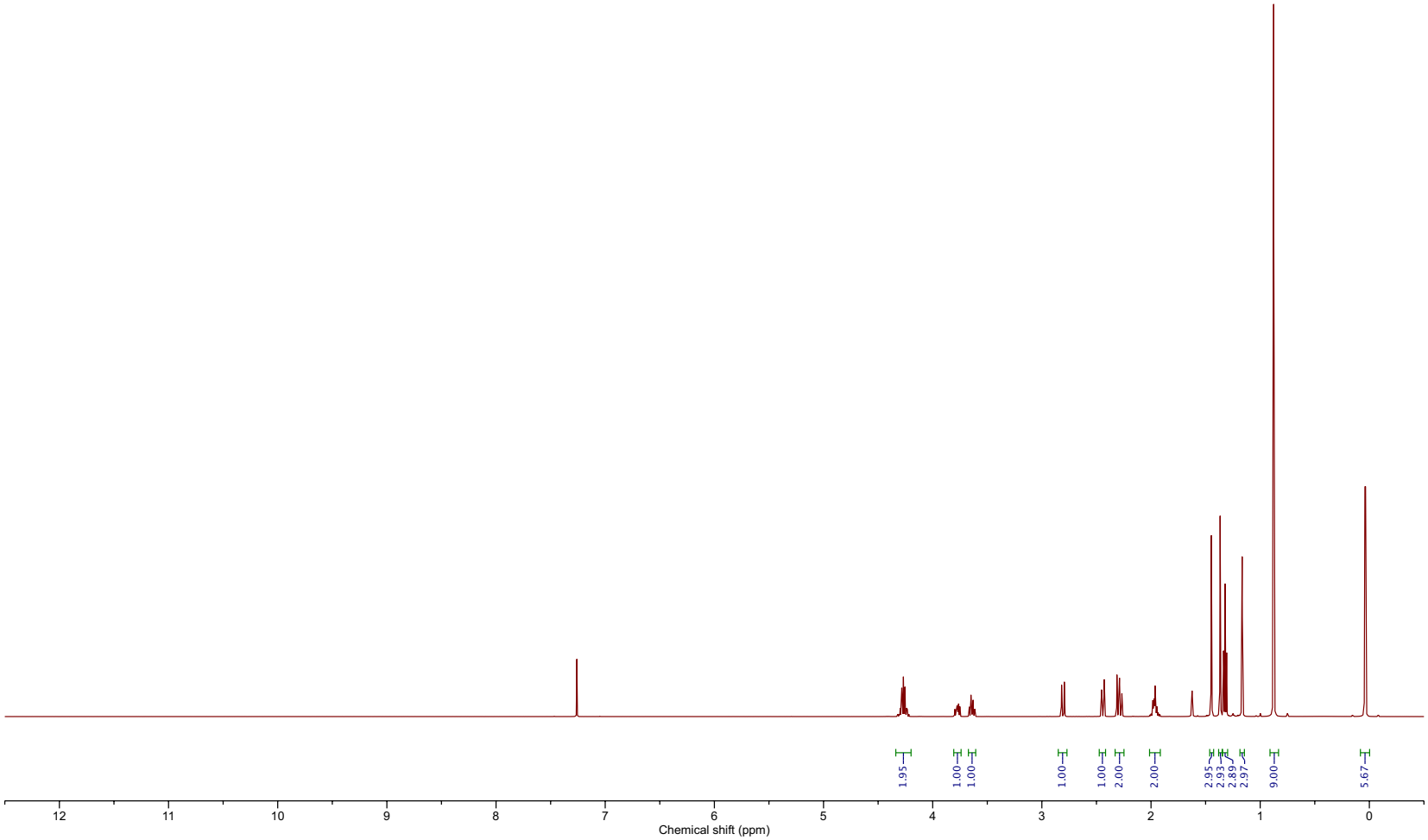
7.00
6.99
6.98
6.98
6.97
6.97
6.96
6.95
6.73
6.73
6.72
6.71
6.71
6.70
6.69
6.56
6.56
6.55
6.55
6.55
6.54
6.54
6.54
6.53
6.53
6.52
6.52
4.30
4.29
4.28
4.26
4.20
4.19
4.19
4.18
4.17
4.17
4.17
4.16
4.15
4.15
4.14
4.14
4.13
4.12
4.04
4.03
4.03
4.02
4.01
4.01
4.01
3.99
2.95
2.94
2.93
2.91
2.77
2.74
2.53
2.52
2.52
2.51
2.51
2.50
2.50
2.49
2.49
2.49
2.48
2.48
2.47
2.46
2.42
2.40
2.39
2.38
2.25
2.22
2.07
2.05
2.05
2.04
2.04
2.02
2.01
2.01
2.00
1.48
1.34
1.33
1.31
1.22
0.93
0.97
0.92
1.98
2.01
1.01
1.00
1.00
1.02
1.00
1.01
1.01
3.00
3.00
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

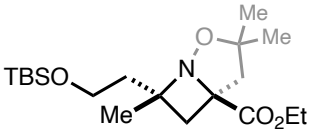

Me
Me
O
N
F
O
F
H
CO2Et
172.73
159.88
159.85
157.95
157.93
149.92
149.89
148.00
147.97
147.72
147.64
147.62
147.54
116.25
116.17
116.09
116.01
106.55
106.50
106.36
106.31
102.73
102.72
102.51
102.50
83.91
72.72
66.79
61.89
57.25
52.98
37.06
31.32
26.93
26.04
14.27
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

endo-**38**


Me
O
Me
TBSO
N
Me
CO2Et

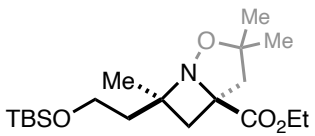
exo(C_7-Me)-**39**


4.32 4.30 4.30 4.29 4.28 4.28 4.27 4.26 4.25 4.25 4.24 4.23 4.22
3.80 3.79 3.78 3.78 3.77 3.77 3.76 3.75 3.66 3.65 3.64 3.63 3.63 3.61 2.02 2.79 2.45 2.43 2.31 2.29 2.29 2.27 2.00 2.00 1.98 1.98 1.97 1.97 1.96 1.96 1.95 1.93 1.92 1.45 1.37 1.34 1.32 1.31 1.17 0.88 0.04
1.95 1.00 1.00 1.00 1.00 2.00 2.00 2.95 2.93 2.89 2.97 9.00 5.67
12 11 10 9 8 7 6 5 4 3 2 1 0
Chemical shift (ppm)

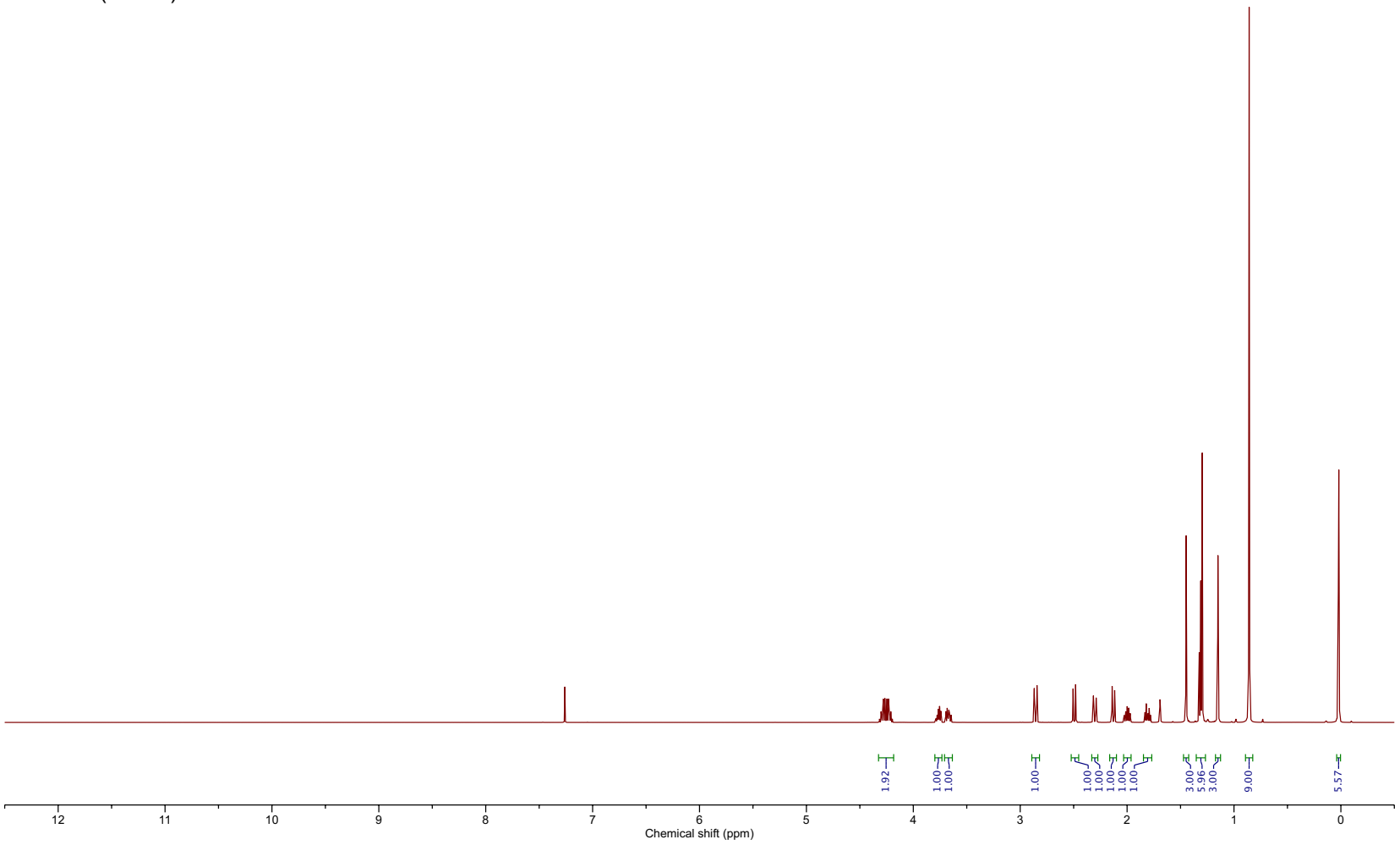

Me
O
Me
TBSO
N
Me
CO2Et

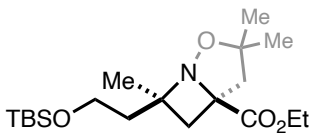
exo(C_7-Me)-**39**

173.68
84.22
69.59
63.14
61.69
59.70
52.53
42.05
39.78
27.45
26.81
26.07
25.83
18.35
14.28
-5.19
-5.26
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
Me
N
TBSO
CO2Et

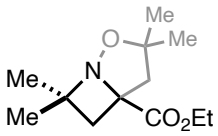
endo(C_7-Me)-**39**


4.32 4.30 4.29 4.29 4.28 4.27 4.27 4.26 4.25 4.25 4.24 4.23 4.22 4.22 4.21 4.20 3.79 3.78 3.77 3.77 3.76 3.76 3.75 3.74 3.70 3.68 3.68 3.67 3.67 3.66 3.66 3.65 2.87 2.84 2.51 2.48 2.31 2.29 2.14 2.12 2.03 2.01 2.01 2.00 1.99 1.98 1.97 1.83 1.82 1.81 1.80 1.79 1.78 1.45 1.33 1.31 1.30 1.15 0.86 0.02 0.02
1.92 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 3.00 5.96 3.00 9.00 5.57
12 11 10 9 8 7 6 5 4 3 2 1 0
Chemical shift (ppm)

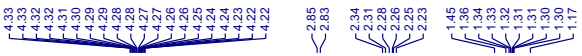

Me
O
Me
Me
N
TBSO
CO2Et

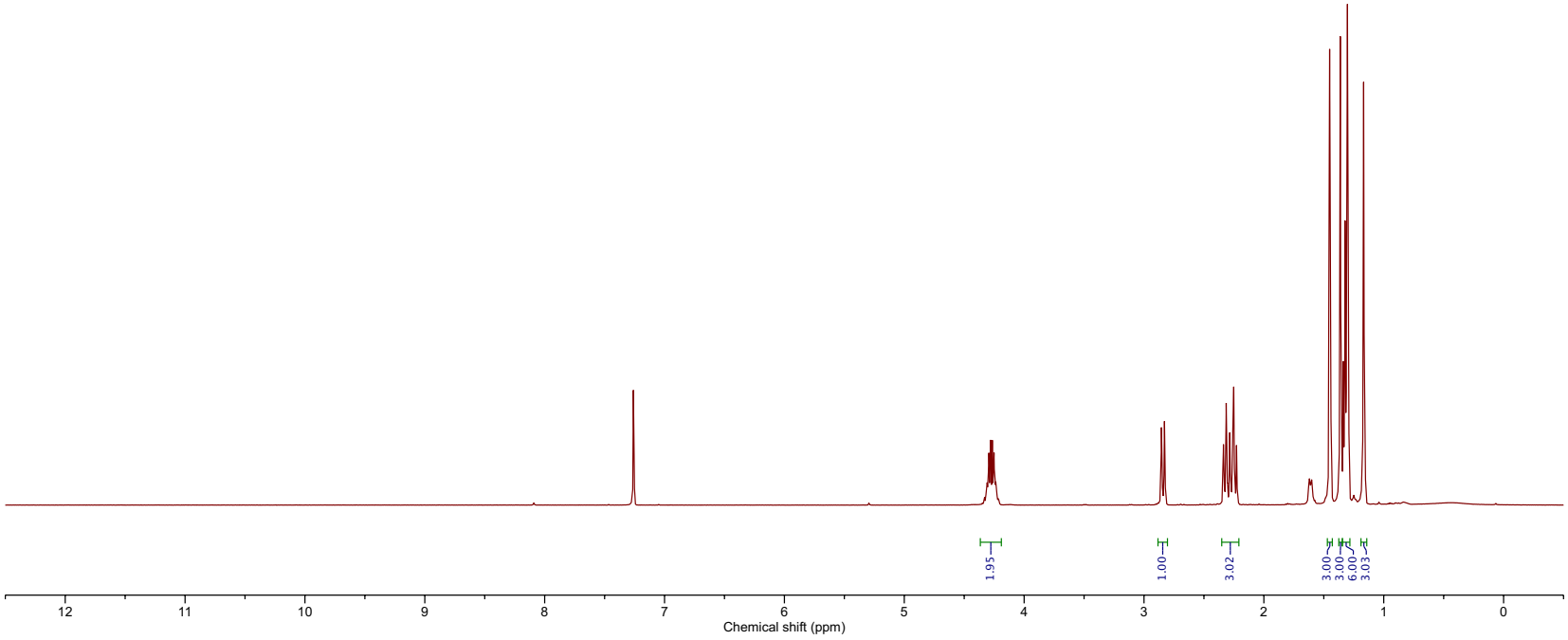
endo(C_7-Me)-**39**

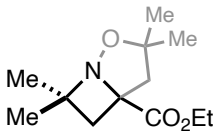
173.56
84.52
70.84
64.12
61.62
59.53
52.01
45.08
40.11
27.97
26.02
25.60
22.11
18.27
14.28
-5.23
-5.26
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
N
Me
Me
CO2Et

40

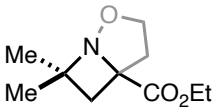

4.33
4.33
4.32
4.32
4.32
4.31
4.30
4.29
4.29
4.28
4.28
4.27
4.27
4.26
4.26
4.25
4.24
4.24
4.23
4.22
4.22
2.85
2.83
2.34
2.31
2.28
2.26
2.25
2.23
1.45
1.36
1.34
1.33
1.32
1.31
1.31
1.30
1.30
1.17


1.95
1.00
3.02
3.00
3.00
6.00
3.03
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
O
Me
N
Me
Me
CO2Et

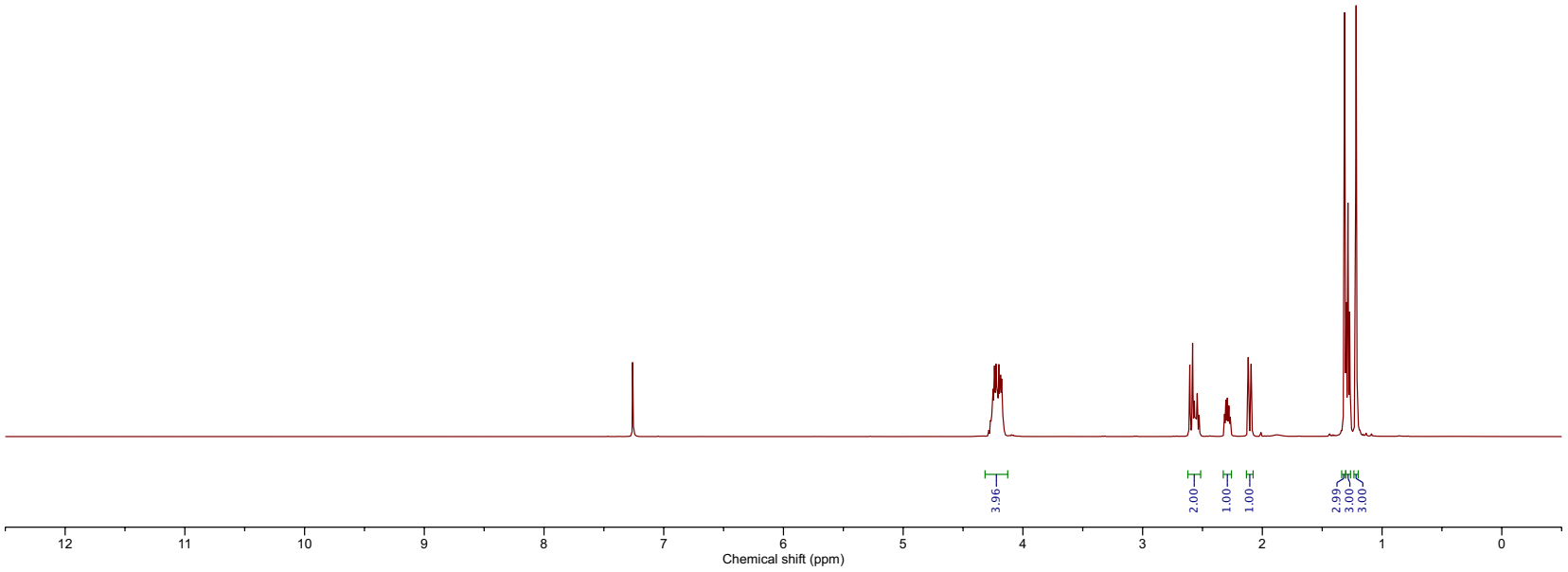
40

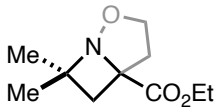
173.51
84.30
69.43
61.93
61.62
51.98
41.56
30.10
27.62
25.71
24.39
14.22
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
Me
N
O
CO2Et

62

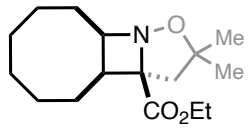

4.28 4.27 4.27 4.26 4.26 4.26 4.25 4.24 4.24 4.23 4.22 4.22 4.21 4.21 4.20 4.20 4.20 4.19 4.19 4.18 4.17 4.16 4.16
2.61 2.61 2.59 2.58 2.57 2.57 2.56 2.56 2.55 2.55 2.54 2.53 2.53 2.32 2.31 2.31 2.31 2.30 2.29 2.28 2.28 2.28 2.27 2.27 2.12 2.09 1.31 1.30 1.28 1.27 1.22


3.96
2.00
1.00
1.00
2.99
3.00
3.00
12 11 10 9 8 7 6 5 4 3 2 1 0
Chemical shift (ppm)

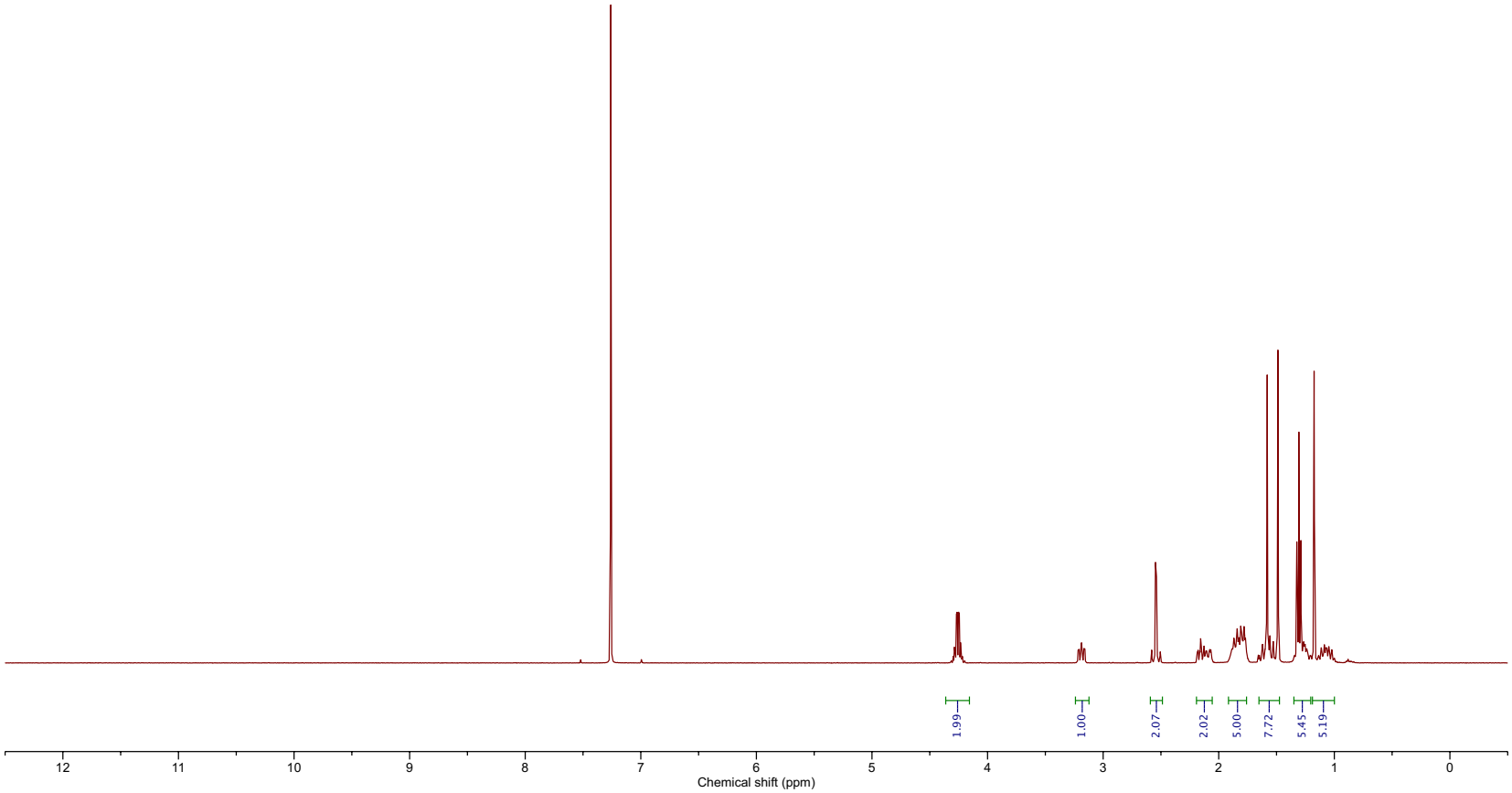

Me
Me
N
O
CO2Et

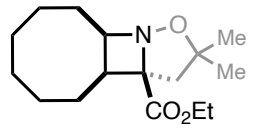
62

173.39
70.80
69.36
62.93
61.66
40.07
39.81
30.48
22.68
14.19
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


N
O
Me
Me
CO2Et

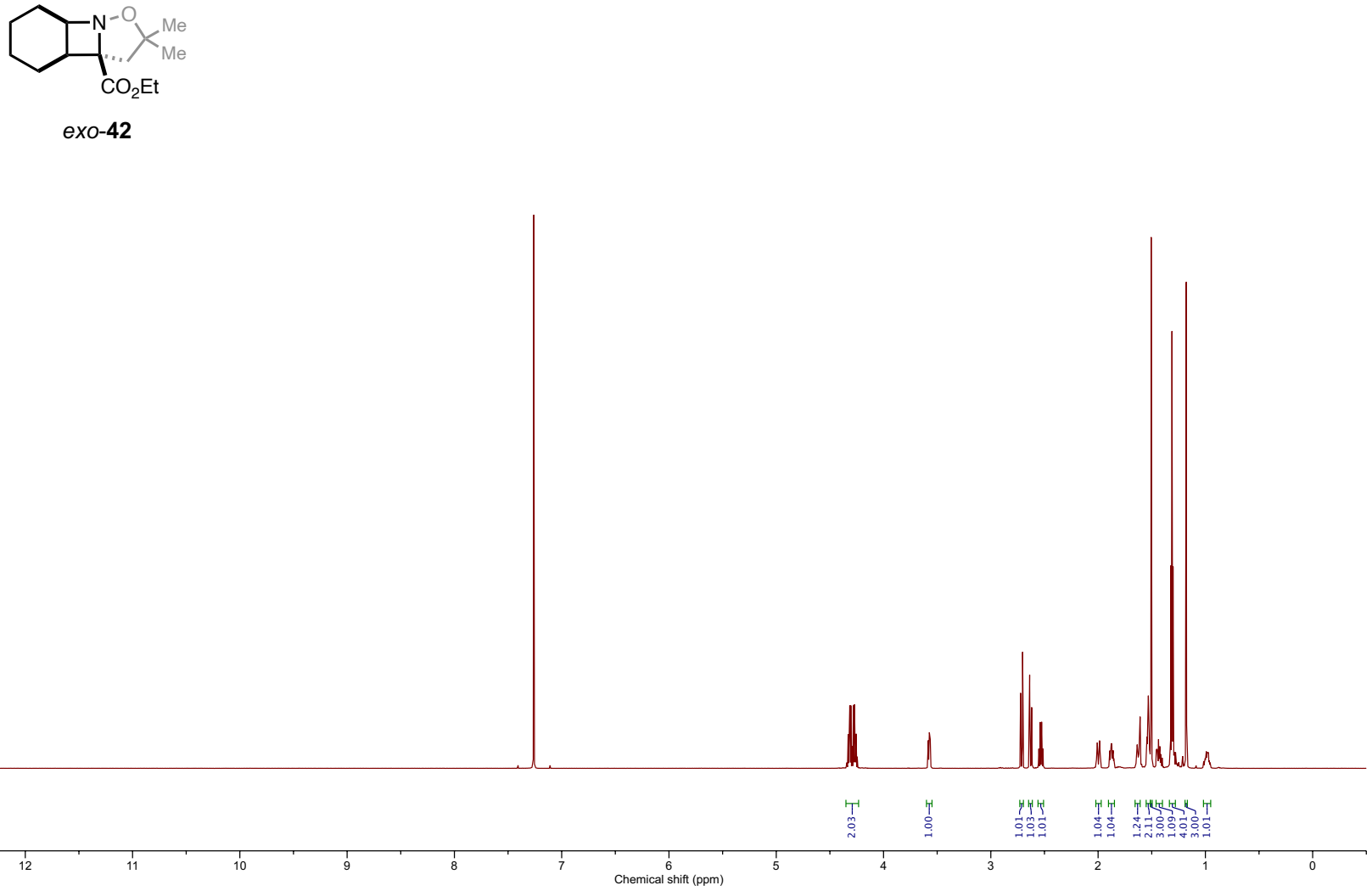
exo-**41**


1.99
1.00
2.07
2.02
5.00
7.72
5.45
5.19
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

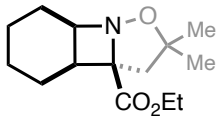

N
O
Me
Me
CO2Et

exo-**41**

173.37
86.10
77.48
75.19
61.42
44.59
40.10
35.81
30.29
29.19
28.62
28.49
28.20
27.67
26.63
14.34
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

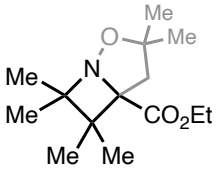


exo-**42**


N
O
Me
Me
CO2Et

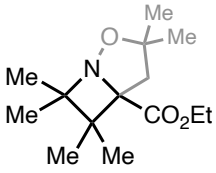
exo-**42**

172.63
87.49
78.19
63.75
61.20
51.70
33.82
30.18
28.97
27.03
25.34
22.38
20.91
14.55
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
N
Me
Me
CO2Et
Me
Me

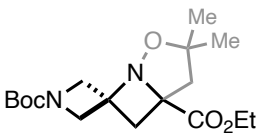
43

4.33
4.32
4.31
4.31
4.31
4.30
4.29
4.29
4.28
4.28
4.27
4.27
4.27
4.26
4.25
4.24
4.23
2.55
2.52
2.46
2.44
1.43
1.33
1.31
1.30
1.20
1.18
1.16
1.12
1.08
1.94
1.00
1.00
3.00
2.99
3.00
3.00
2.94
2.95
2.94
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
O
Me
N
Me
Me
CO2Et
Me
Me

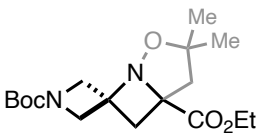
43

173.27
84.00
79.65
68.02
61.05
47.57
39.21
28.39
26.02
25.73
22.84
21.73
20.35
14.51
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
N
BocN
CO2Et

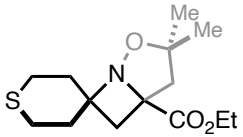
44

4.68
4.67
4.28
4.28
4.27
4.27
4.26
4.26
4.25
4.25
4.15
4.13
3.92
3.90
3.74
3.73
2.86
2.84
2.64
2.62
2.58
2.56
2.01
2.00
1.46
1.42
1.32
1.31
1.30
1.20
0.98
1.97
1.00
1.00
1.00
1.00
0.98
1.00
1.00
3.01
9.01
3.00
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
O
Me
N
BocN
CO2Et

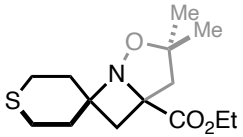
44

171.91
156.22
86.84
79.76
71.92
63.03
61.87
61.27
56.17
50.34
37.10
28.42
27.87
26.44
14.18
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
Me
O
N
S
CO2Et

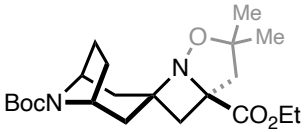
45

4.32 4.30 4.30 4.29 4.29 4.28 4.28 4.28 4.27 4.26 4.25 4.24 4.24 4.23 4.23 4.22 4.21 2.90 2.88 2.83 2.83 2.83 2.83 2.82 2.81 2.80 2.80 2.79 2.78 2.78 2.53 2.53 2.52 2.52 2.52 2.51 2.51 2.50 2.49 2.49 2.48 2.48 2.47 2.47 2.47 2.25 2.23 2.23 2.22 2.21 2.21 2.20 2.19 2.19 2.18 2.17 2.17 2.12 2.12 2.11 2.10 2.10 2.09 2.09 2.04 2.04 2.03 2.02 2.02 2.02 2.01 2.01 2.01 2.00 2.00 1.99 1.98 1.98 1.97 1.97 1.96 1.43 1.33 1.32 1.31 1.17
1.93
1.00
1.99
2.00
4.00
1.01
1.00
0.99
2.99
2.96
3.00
12 11 10 9 8 7 6 5 4 3 2 1 0
Chemical shift (ppm)


Me
Me
O
N
S
CO2Et

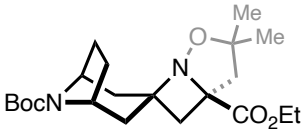
45

173.17
84.42
69.88
63.09
61.73
52.29
39.92
39.68
35.02
27.41
25.53
25.11
25.06
14.18
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
N
BocN
CO2Et

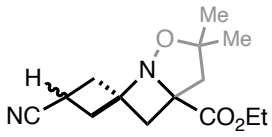
46

4.31
4.30
4.30
4.29
4.29
4.28
4.28
4.28
4.27
4.23
4.22
4.21
4.21
4.20
4.20
4.19
4.18
4.11
4.08
4.02
2.80
2.78
2.53
2.28
2.26
2.20
2.13
2.11
1.89
1.82
1.71
1.70
1.57
1.48
1.45
1.32
1.31
1.30
1.18
1.00
1.25
2.00
1.00
1.00
2.01
2.04
2.01
4.58
3.00
9.02
2.99
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
O
Me
N
BocN
CO2Et

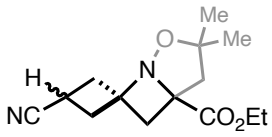
46

173.39
153.40
84.57
79.07
70.02
61.99
61.59
53.16
53.02
52.31
52.24
43.78
43.04
42.93
37.58
36.68
28.59
27.58
27.41
26.82
26.25
25.56
14.18
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)



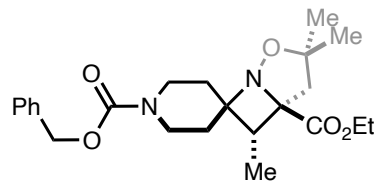
47

(1:1 mixture of diastereomers)



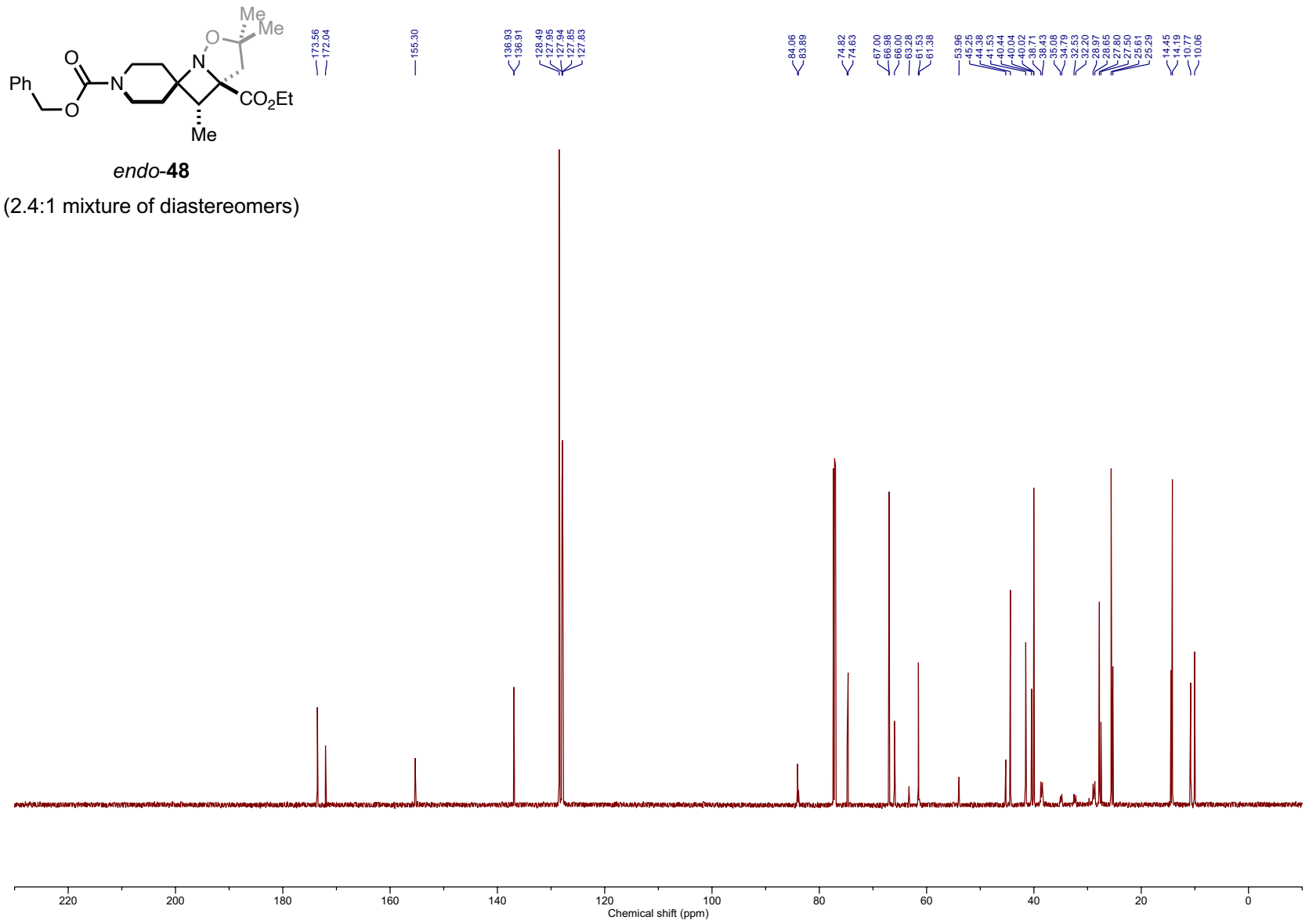
47

(1:1 mixture of diastereomers)



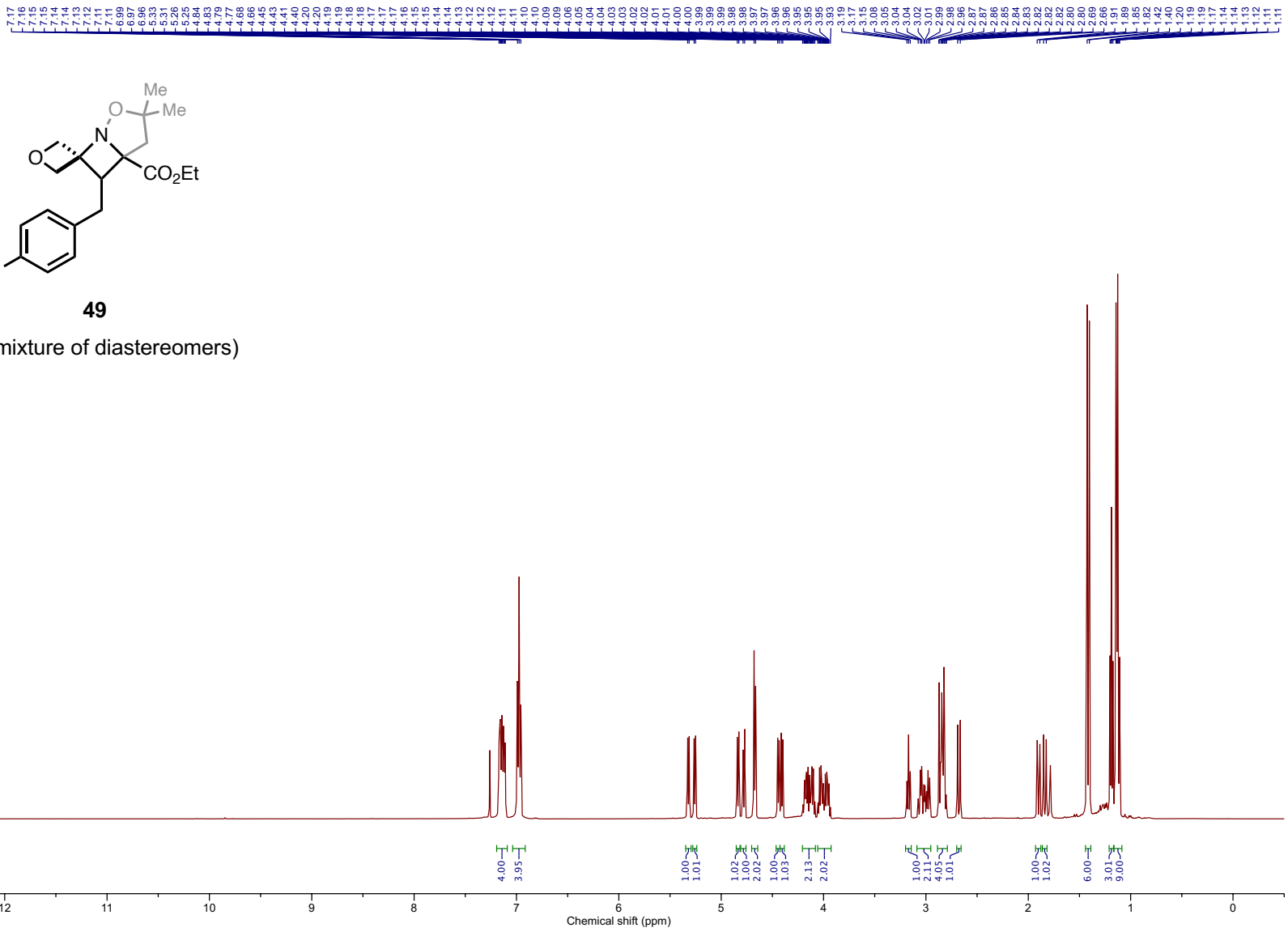
endo-**48**

(2.4:1 mixture of diastereomers)



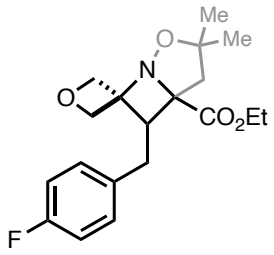
endo-**48**

(2.4:1 mixture of diastereomers)



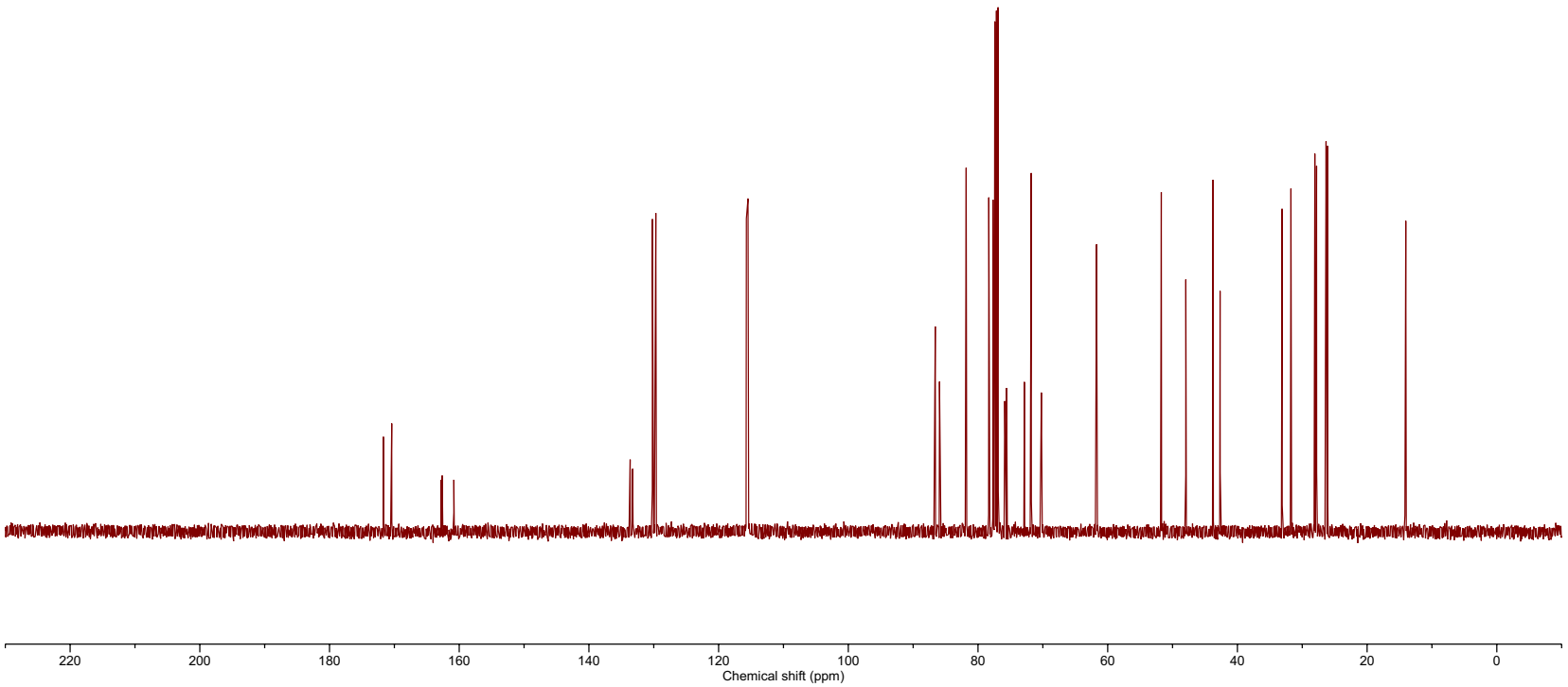
49

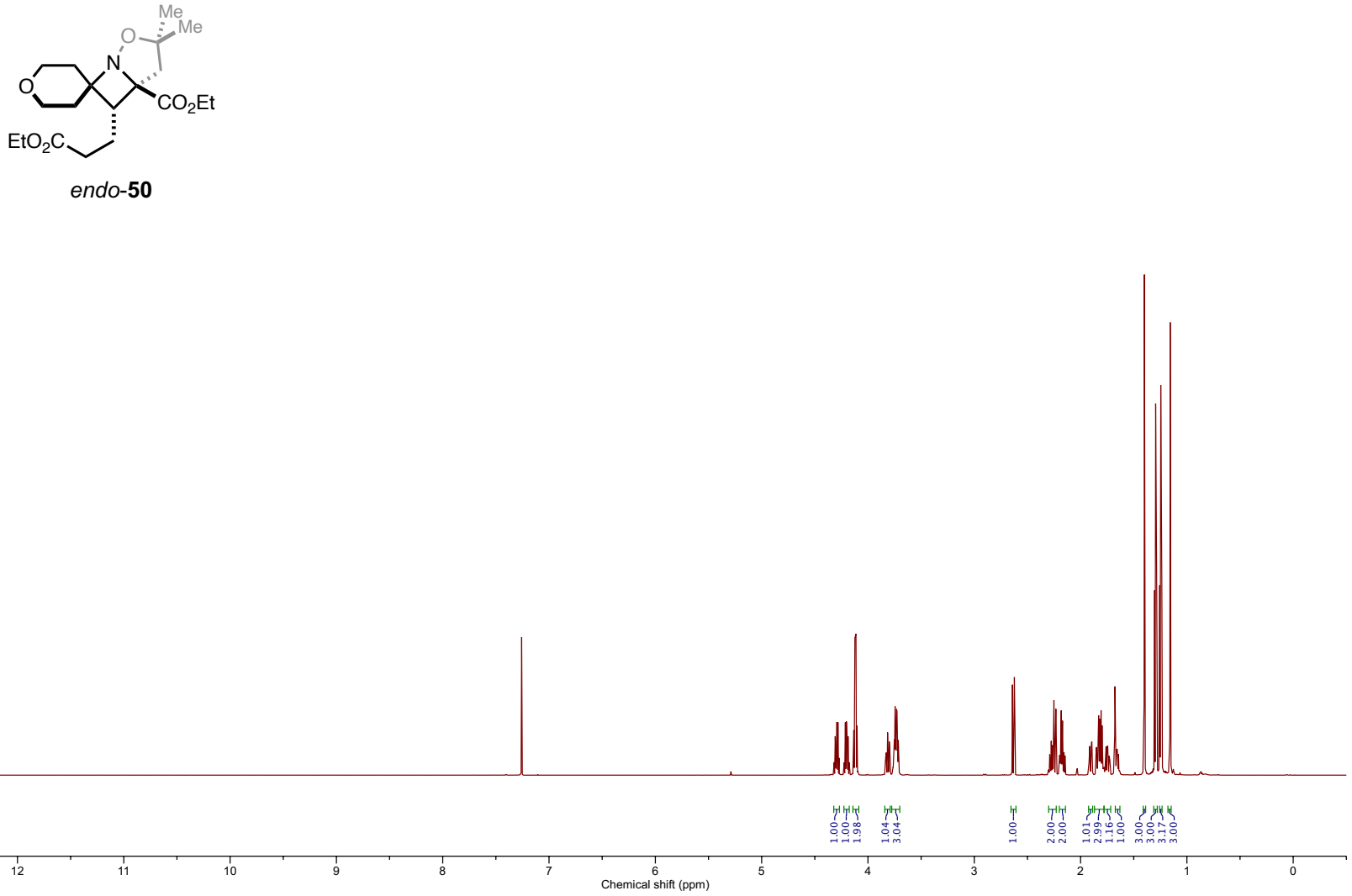
(1:1 mixture of diastereomers)



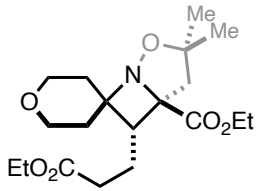
49

(1:1 mixture of diastereomers)



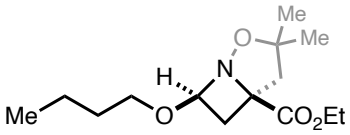


endo-**50**


Me
Me
O
N
O
CO2Et
EtO2C

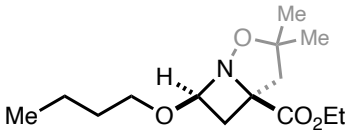
endo-**50**

173.67
172.82
84.14
74.25
65.41
64.24
61.81
60.73
45.11
44.46
39.83
31.52
29.71
27.91
25.69
20.81
14.34
14.24
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
H
N
Me
O
CO2Et

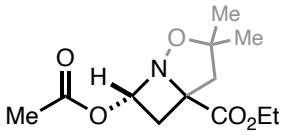
exo-**51**

4.58
4.57
4.56
4.26
4.25
4.24
4.23
3.80
3.79
3.79
3.78
3.43
3.42
3.42
3.41
3.41
2.86
2.84
2.53
2.52
2.52
2.51
2.34
2.33
2.32
2.31
2.26
2.24
1.59
1.57
1.56
1.55
1.49
1.37
1.36
1.36
1.35
1.35
1.34
1.34
1.33
1.30
1.29
1.28
1.22
0.90
0.89
1.00
2.00
1.00
1.02
1.03
1.04
1.02
1.03
2.05
3.02
2.24
2.03
3.00
3.07
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
O
Me
H
N
Me
O
CO2Et

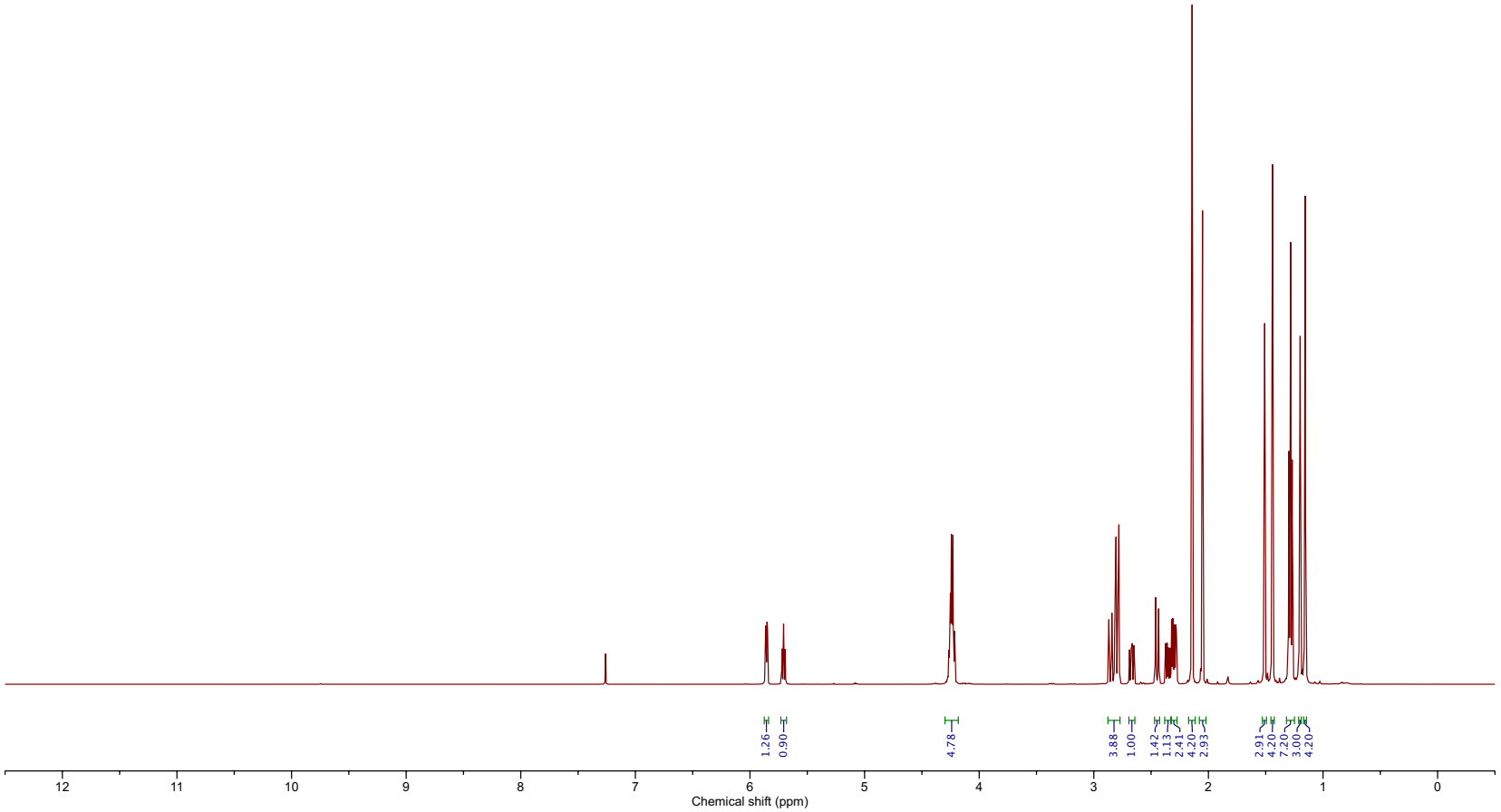
exo-**51**

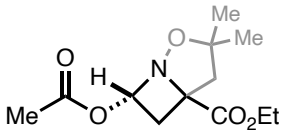
172.38
94.81
88.91
67.99
67.61
61.80
50.92
31.61
31.25
29.57
28.44
19.33
14.22
14.03
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)



endo-**52**

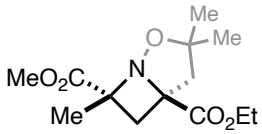
(1.4:1 mixture of diastereomers)





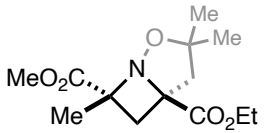
endo-**52**

(1.4:1 mixture of diastereomers)


Me
O
Me
MeO2C
N
Me
CO2Et

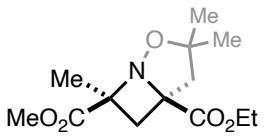
exo(C_7-Me)-**53**

4.28
4.27
4.27
4.26
4.26
4.25
4.24
4.23
4.22
4.22
4.21
4.20
3.72
3.20
3.18
2.72
2.71
2.55
2.53
2.27
2.26
1.59
1.30
1.29
1.28
1.09
1.97
3.00
1.00
1.00
1.01
1.01
3.01
6.00
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
O
Me
N
MeO2C
Me
CO2Et

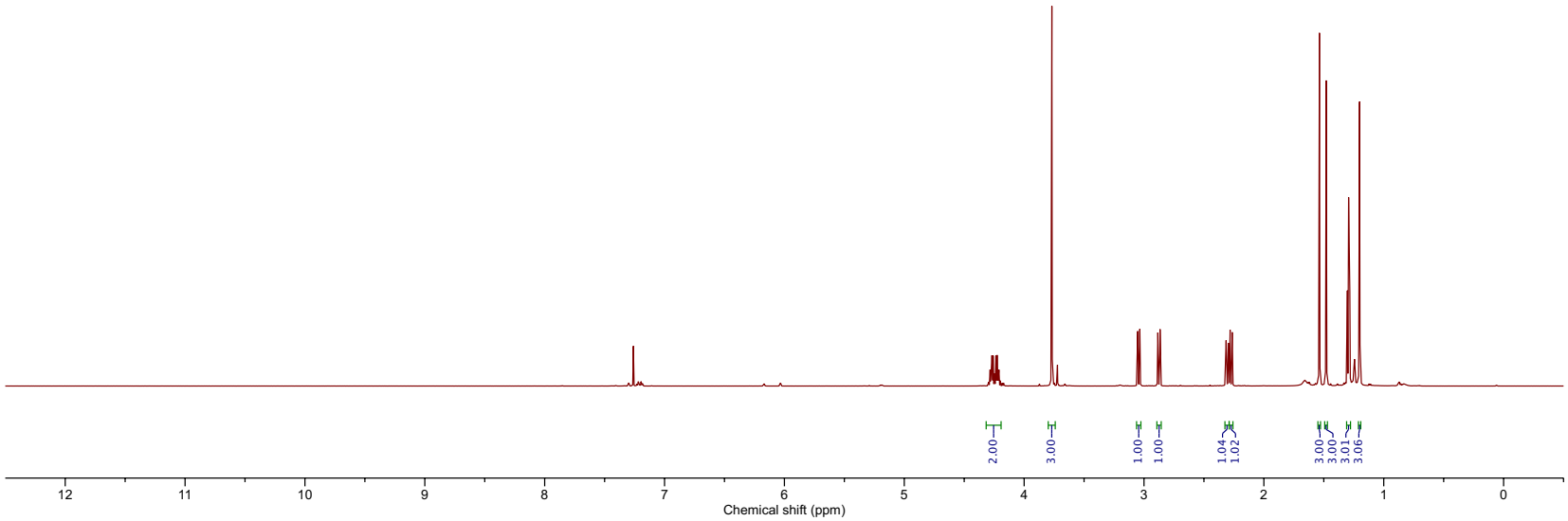
exo(C_7-Me)-**53**

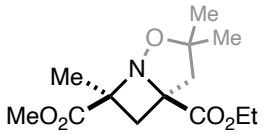
172.81
171.79
85.53
70.18
68.03
61.81
52.37
49.98
36.49
26.98
25.98
24.21
14.17
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
Me
N
MeO2C
CO2Et

endo(C_7-Me)-**53**

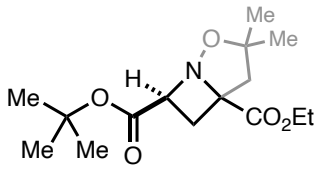

4.29
4.28
4.28
4.27
4.27
4.26
4.26
4.25
4.25
4.24
4.23
4.23
4.22
4.22
4.21
4.20
3.77
3.05
3.03
2.88
2.87
2.31
2.30
2.28
2.26
1.54
1.48
1.30
1.29
1.28
1.20


2.00
3.00
1.00
1.00
1.04
1.02
3.00
3.00
3.01
3.06
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
O
Me
Me
N
MeO2C
CO2Et

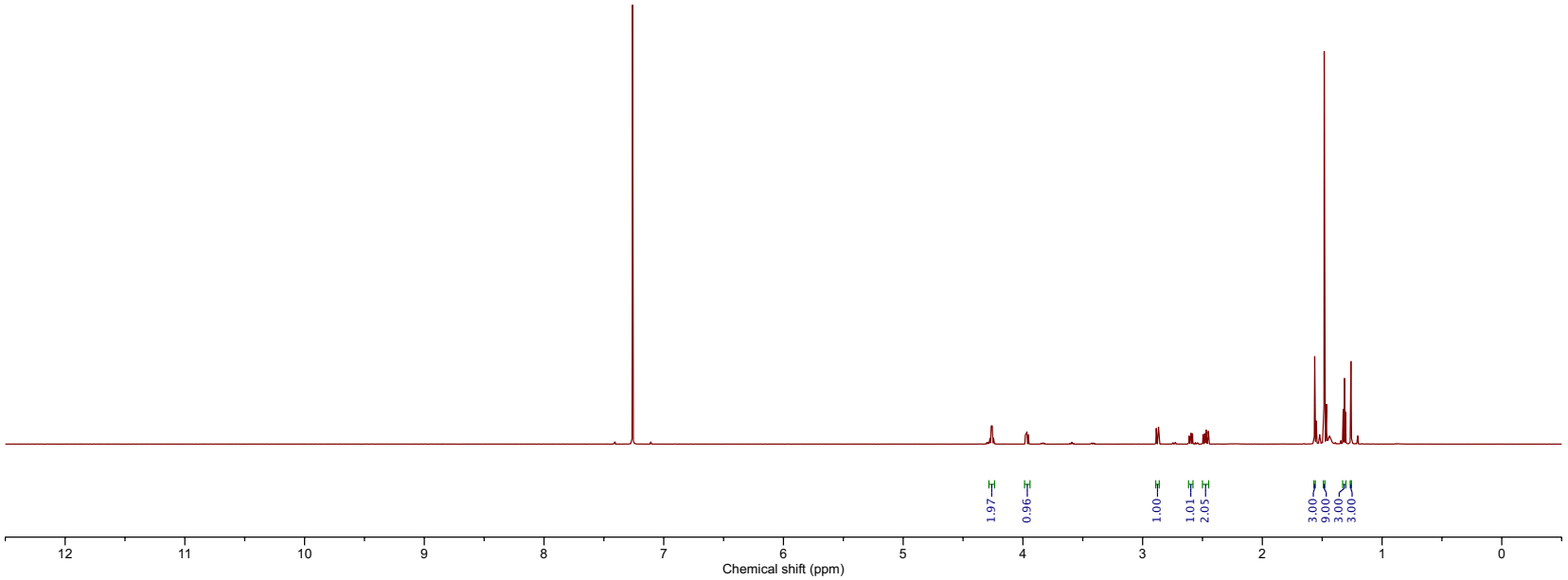
endo(C_7-Me)-**53**

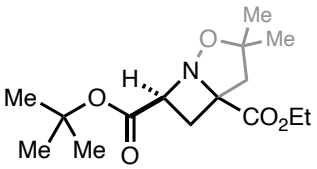
174.27
172.48
85.95
70.85
66.35
61.89
52.84
51.22
36.95
28.07
25.62
20.55
14.19
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
H
N
Me
O
CO2Et
Me
Me
O

exo-**54**

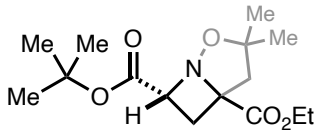

4.28
4.27
4.27
4.26
4.26
4.25
4.25
4.24
3.98
3.97
3.97
3.95
2.89
2.87
2.61
2.60
2.60
2.58
2.50
2.48
2.48
2.47
2.47
2.45
1.56
1.48
1.32
1.31
1.30
1.26


1.97
0.96
1.00
1.01
2.05
3.00
9.00
3.00
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

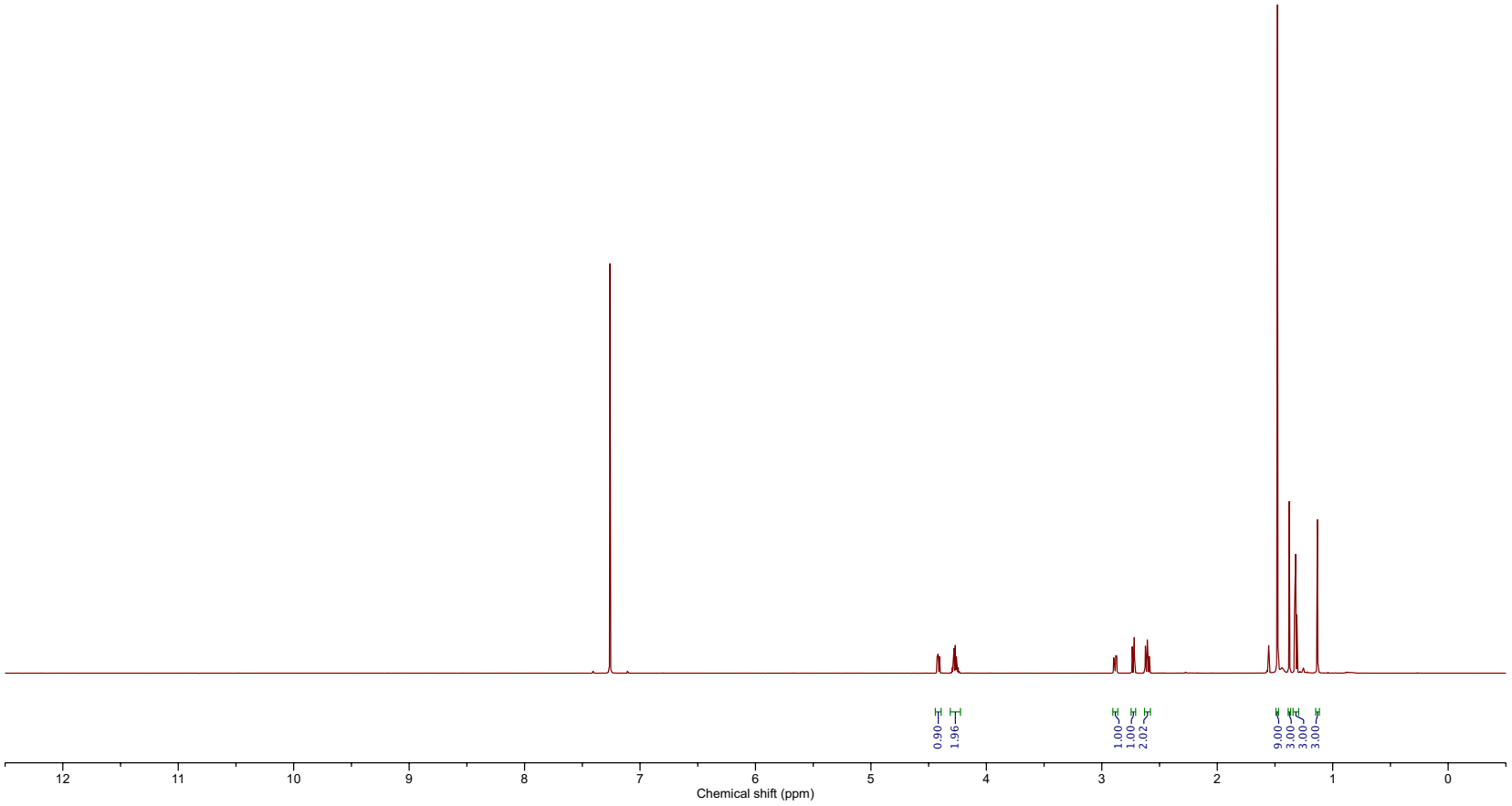

Me
O
Me
H
N
Me
O
CO2Et
Me
Me
O

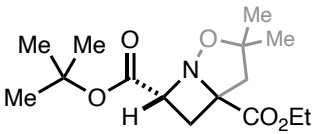
exo-**54**

172.08
169.59
88.47
81.87
73.28
66.43
61.76
50.75
29.89
28.55
28.11
27.85
14.17
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
Me
Me
O
O
N
O
Me
H
CO2Et

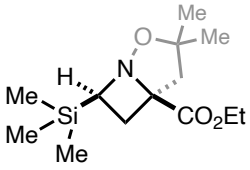
endo-**54**


4.43
4.42
4.42
4.41
4.31
4.29
4.29
4.28
4.28
4.28
4.27
4.27
4.27
4.26
4.26
4.26
4.25
4.25
4.24
2.90
2.89
2.88
2.87
2.74
2.72
2.62
2.62
2.61
2.60
2.60
2.59
1.48
1.38
1.33
1.32
1.31
1.13
0.90
1.96
1.00
1.00
2.02
9.00
3.00
3.00
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
Me
Me
O
O
N
O
Me
H
CO2Et

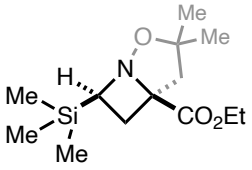
endo-**54**

172.70
168.39
85.01
82.00
73.73
62.59
61.78
50.83
29.69
28.19
26.92
25.66
14.23
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
H
N
Me
Si
Me
Me
CO2Et

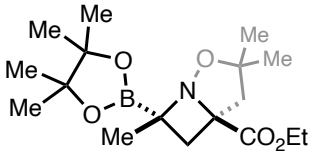
exo-**55**

4.26
4.25
4.25
4.24
4.24
4.23
4.22
4.22
4.22
4.21
4.21
4.20
4.20
4.19
4.19
4.18
4.17
3.29
3.27
3.26
2.86
2.84
2.63
2.61
2.27
2.27
2.25
2.25
1.55
1.30
1.29
1.28
1.20
0.06
1.99
0.98
1.02
1.03
2.07
3.00
3.00
3.02
9.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
O
Me
H
N
Me
Si
Me
Me
CO2Et

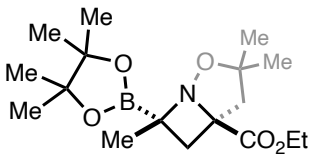
exo-**55**

172.97
86.57
77.86
61.42
59.42
51.51
30.15
28.81
26.20
14.23
-4.05
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
Me
Me
Me
O
B
O
Me
N
O
Me
Me
CO2Et

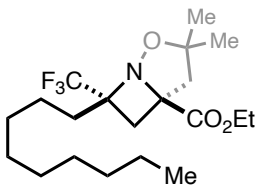
exo(C_7-Me)-**56**

4.31
4.30
4.29
4.29
4.28
4.27
4.26
4.25
4.24
4.23
4.23
4.22
4.21
2.82
2.81
2.76
2.74
2.55
2.53
2.09
2.07
1.42
1.33
1.32
1.31
1.28
1.24
1.08
2.00
1.00
1.00
1.00
1.03
6.00
3.10
6.00
6.13
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
Me
Me
Me
O
B
O
N
O
Me
Me
Me
CO2Et

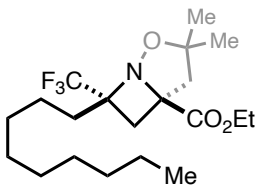
exo(C_7-Me)-**56**

173.72
84.28
84.14
70.40
61.56
51.30
37.21
26.37
25.74
25.51
24.48
14.27
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
F3C
N
CO2Et
Me

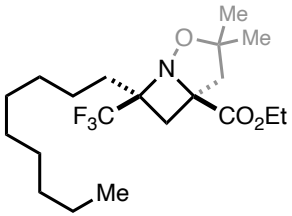
endo(CF_3)-**57**

4.33 4.32 4.31 4.31 4.31 4.31 4.30 4.30 4.30 4.30 4.29 4.29 4.29 4.28 4.28 4.28 4.28 4.27 4.27 4.27 4.26 4.26 4.26 4.26 4.25 4.25 4.25 4.25 4.24 4.24
2.78 2.76 2.74 2.72
2.50 2.50 2.48 2.48 2.48 2.41
1.90 1.89 1.88 1.87 1.87 1.86 1.85 1.54 1.53 1.52 1.52 1.52 1.51 1.44 1.34 1.33 1.32 1.30 1.28 1.25 1.18 0.88 0.87
1.94
1.00 1.00
2.00
2.02
2.05 3.00 3.01 12.19 3.00
2.94
12 11 10 9 8 7 6 5 4 3 2 1 0
Chemical shift (ppm)


Me
O
Me
F3C
N
CO2Et
Me

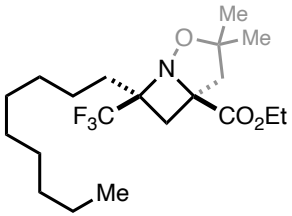
endo(CF_3)-**57**

172.62
127.87
126.26
124.65
123.04
85.66
69.68
66.62
66.47
66.32
66.18
61.95
50.59
35.92
34.33
34.32
31.98
30.30
29.68
29.56
29.41
27.22
25.48
23.08
22.78
14.22
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
N
F3C
CO2Et
Me

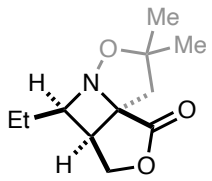
exo(CF_3)-**57**

4.33
4.32
4.31
4.31
4.30
4.30
4.29
4.28
4.27
4.27
4.26
4.26
4.25
4.24
4.23
2.84
2.82
2.76
2.74
2.33
2.31
2.29
2.28
1.96
1.95
1.81
1.79
1.52
1.51
1.51
1.48
1.34
1.33
1.32
1.31
1.30
1.29
1.28
1.27
1.26
1.26
1.26
1.25
1.23
0.88
0.87
2.00
1.00
1.00
1.00
1.00
1.01
1.02
1.00
3.04
20.29
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
O
Me
N
F3C
CO2Et
Me

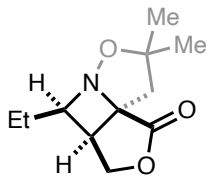
exo(CF_3)-**57**

172.36
128.44
128.84
125.24
123.65
85.67
70.75
66.82
66.67
66.51
66.35
62.00
52.46
33.88
33.86
33.69
31.47
30.59
29.61
29.41
29.40
27.89
25.87
23.43
22.80
14.25
14.16
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
Me
O
H
N
Et
O
H
O

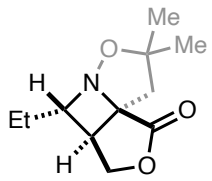
exo-**73**

4.52
4.50
4.40
4.39
4.38
3.70
3.69
3.68
3.67
3.31
3.30
3.29
2.61
2.59
2.45
2.44
1.81
1.80
1.79
1.78
1.77
1.76
1.75
1.60
1.60
1.59
1.59
1.58
1.58
1.57
1.56
1.55
1.55
1.54
1.54
1.40
0.92
0.91
0.90
1.01
1.00
0.97
0.98
1.00
1.00
1.04
4.10
3.00
3.01
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
Me
O
H
N
Et
O
H
O

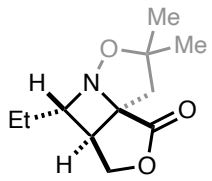
exo-**73**

175.90
88.53
72.37
70.76
66.02
46.55
35.77
28.30
27.73
23.47
9.66
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
Me
O
H
N
Et
O
H
O

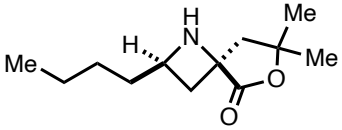
endo-**73**

4.42
4.41
4.40
4.35
4.34
3.68
3.68
3.67
3.66
3.65
3.65
3.64
3.01
3.00
2.99
2.50
2.48
2.28
2.26
2.05
2.04
2.03
2.02
2.01
2.00
1.99
1.69
1.68
1.67
1.66
1.65
1.64
1.63
1.48
1.38
0.93
0.91
0.90
1.00
1.00
0.92
0.93
0.99
1.00
1.00
1.07
3.00
3.00
3.01
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
Me
O
H
N
Et
O
H
O

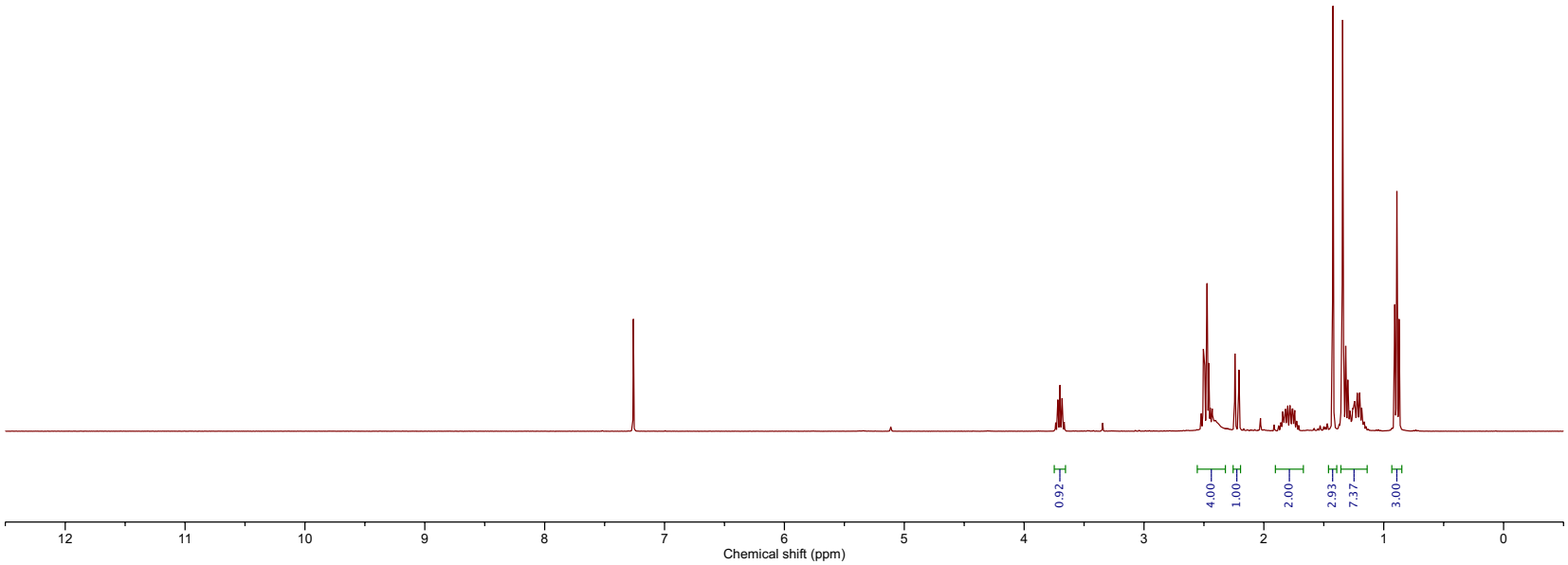
endo-**73**

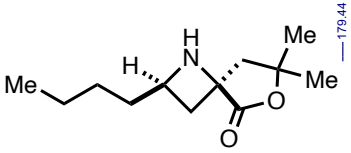
176.07
85.26
71.64
70.63
68.90
48.54
43.82
26.75
26.04
23.31
10.12
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


H
N
Me
Me
H
Me
O
O

cis-**59**

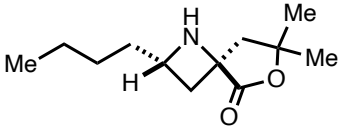

3.74
3.72
3.70
3.68
3.67
3.52
2.50
2.49
2.48
2.47
2.46
2.45
2.43
2.40
2.24
2.21
1.88
1.86
1.86
1.85
1.84
1.84
1.83
1.83
1.82
1.82
1.81
1.80
1.80
1.79
1.78
1.77
1.76
1.75
1.74
1.73
1.73
1.71
1.42
1.37
1.36
1.35
1.34
1.33
1.32
1.30
1.29
1.28
1.28
1.27
1.26
1.25
1.25
1.24
1.24
1.24
1.23
1.22
1.22
1.22
1.21
1.20
1.18
1.18
1.17
1.16
0.91
0.89
0.87


0.92
4.00
1.00
2.00
2.93
7.37
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

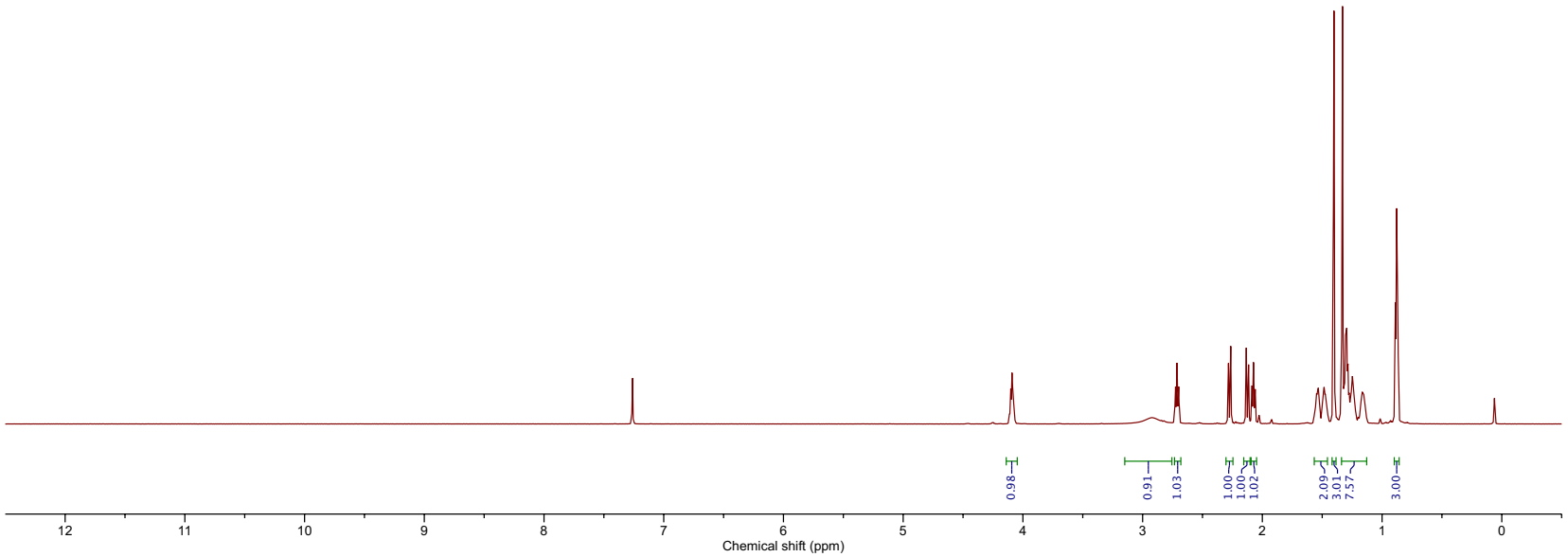

H
N
Me
Me
Me
O
O

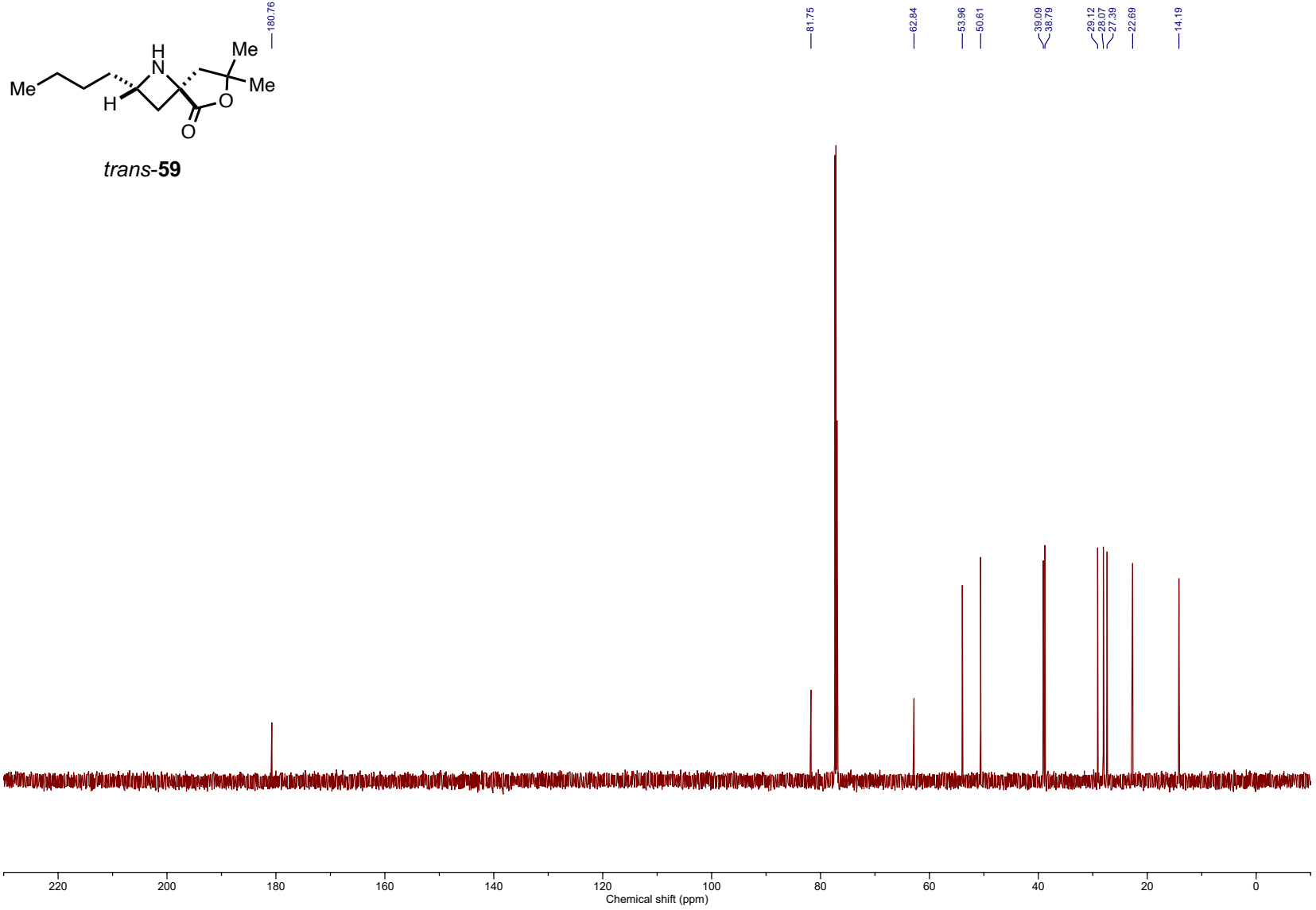
cis-**59**

179.44
81.62
62.90
54.51
50.10
38.41
37.26
29.06
27.97
27.65
22.55
14.15
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

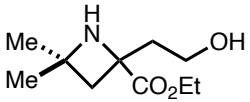

H
N
Me
Me
H
O
O

trans-**59**

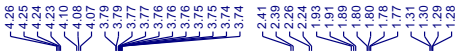

0.98
0.91
1.03
1.00
1.09
1.02
2.09
3.01
7.57
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

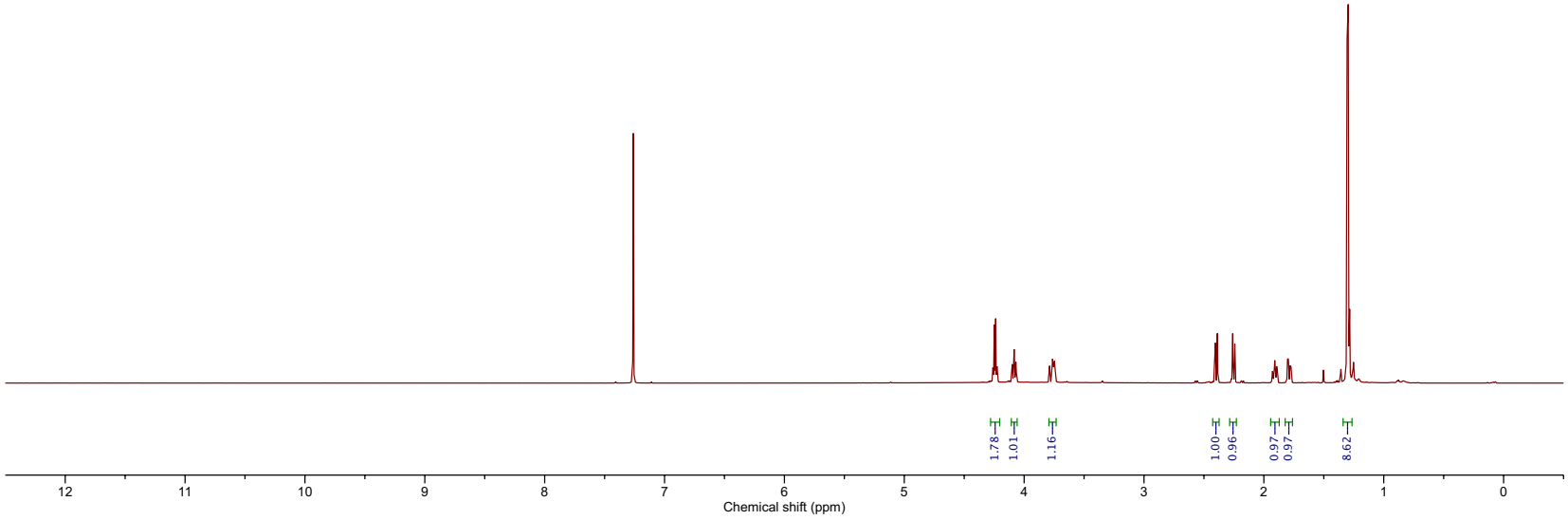

180.76
81.75
62.84
53.96
50.61
39.09
38.79
29.12
28.07
27.39
22.69
14.19
H
N
Me
Me
Me
H
O
O
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

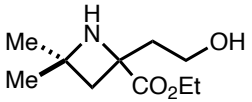
trans-**59**


H
N
Me
Me
OH
CO2Et

63

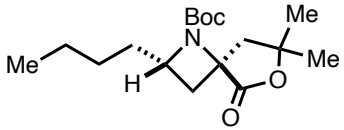

4.26
4.25
4.24
4.23
4.10
4.08
4.07
3.79
3.79
3.77
3.77
3.76
3.76
3.76
3.75
3.75
3.74
3.74
2.41
2.39
2.26
2.24
1.93
1.91
1.89
1.80
1.80
1.78
1.77
1.31
1.30
1.29
1.28


1.78
1.01
1.16
1.00
0.96
0.97
0.97
8.62
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

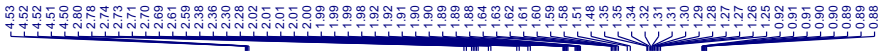

H
N
Me
Me
OH
CO2Et

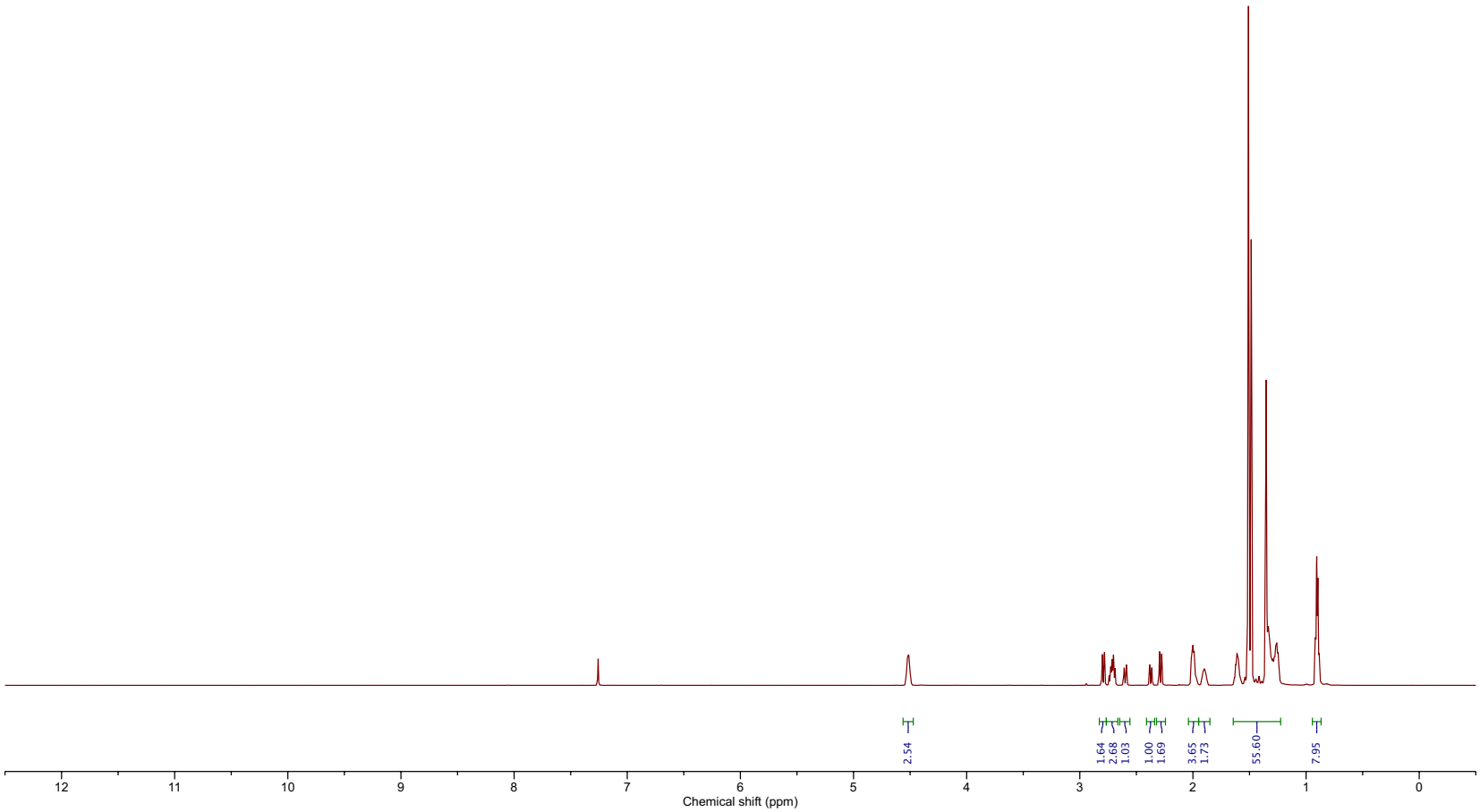
63

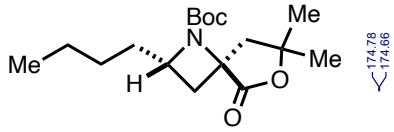
177.26
61.55
60.36
59.63
54.71
40.43
37.67
30.96
29.55
14.17
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Boc
N
Me
Me
H
O
O

60

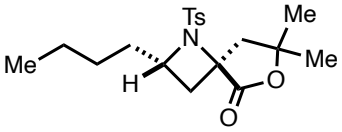



2.54
1.64
2.68
1.03
1.00
1.69
3.65
1.73
55.60
7.95
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Boc
N
Me
Me
Me
H
O
O

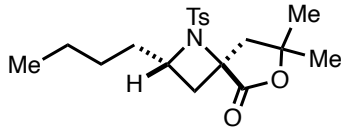
60

174.78
174.66
149.06
148.53
147.04
146.41
85.22
85.03
82.09
81.73
68.00
67.08
60.85
59.70
46.95
45.73
36.21
35.76
35.07
34.97
29.15
29.06
29.03
28.85
27.60
27.58
26.57
26.13
22.61
22.57
14.09
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Ts
N
Me
Me
Me
H
O
O

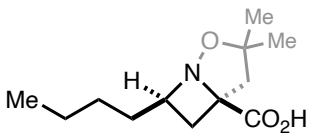
61

7.69
7.67
7.31
7.29
4.45
4.44
4.43
4.42
4.41
4.40
4.39
4.38
2.85
2.82
2.57
2.55
2.54
2.52
2.43
2.38
2.34
2.04
2.03
2.02
2.00
1.88
1.87
1.87
1.86
1.85
1.84
1.84
1.83
1.83
1.82
1.82
1.81
1.80
1.61
1.60
1.59
1.57
1.57
1.56
1.55
1.54
1.52
1.33
1.30
1.28
1.26
1.26
1.25
1.24
1.24
1.23
1.21
1.21
1.20
1.20
1.19
1.18
1.17
1.17
1.16
1.15
1.15
0.87
0.85
0.83
1.93
1.97
1.00
1.00
1.00
3.00
1.04
1.01
1.02
4.07
3.00
4.43
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Ts
N
Me
Me
H
O
O

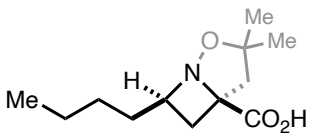
61

174.70
143.68
136.68
129.43
127.72
81.94
70.51
61.73
48.17
36.27
35.21
29.37
28.98
25.99
22.51
21.68
14.04
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
H
N
Me
CO2H

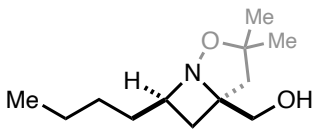
64

7.12
3.75
3.73
3.72
3.70
3.69
2.99
2.97
2.57
2.56
2.55
2.53
2.51
2.48
1.92
1.91
1.91
1.90
1.90
1.89
1.88
1.88
1.87
1.87
1.86
1.85
1.71
1.70
1.69
1.69
1.68
1.68
1.68
1.67
1.66
1.66
1.65
1.65
1.64
1.53
1.41
1.40
1.40
1.39
1.38
1.38
1.38
1.37
1.37
1.36
1.35
1.35
1.34
1.33
1.32
1.31
1.30
1.30
1.30
1.29
1.29
1.28
1.28
1.27
1.27
1.26
1.24
0.92
0.90
0.89
1.74
0.99
1.00
1.00
1.00
1.00
1.02
3.00
4.28
3.00
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
O
Me
H
N
Me
CO2H

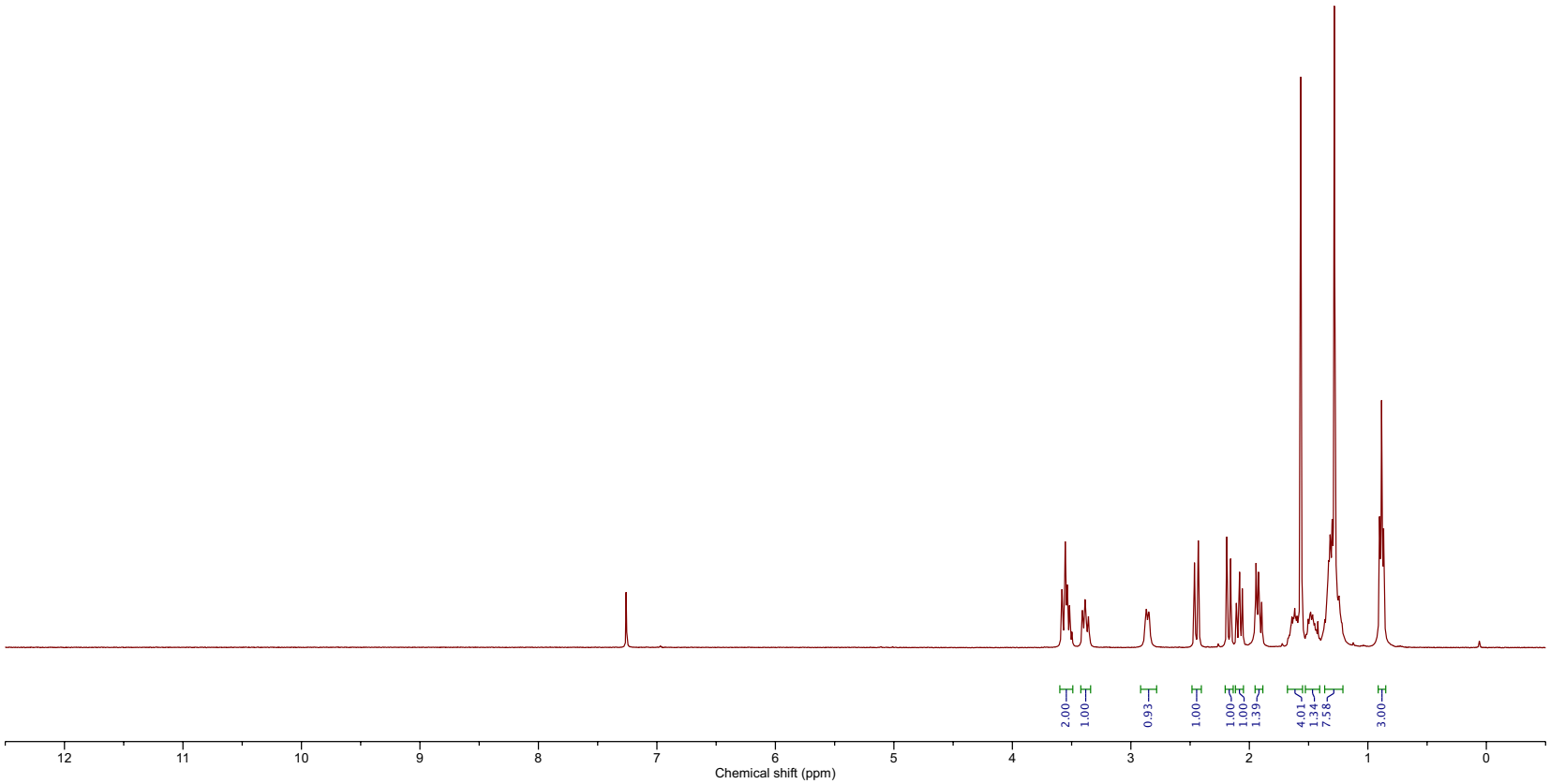
64

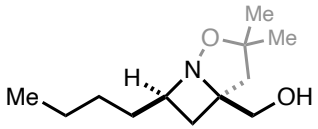
172.17
89.94
74.48
68.41
50.15
33.81
31.05
28.29
27.78
27.31
22.46
14.05
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
H
N
Me
OH

65

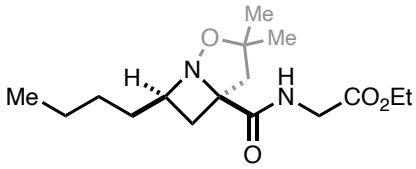

3.58
3.55
3.54
3.52
3.50
3.41
3.39
3.36
2.87
2.85
2.46
2.43
2.19
2.16
2.11
2.09
2.08
2.06
1.94
1.92
1.92
1.90
1.67
1.66
1.66
1.65
1.64
1.63
1.62
1.62
1.61
1.60
1.59
1.57
1.52
1.50
1.50
1.49
1.48
1.47
1.47
1.46
1.45
1.44
1.43
1.42
1.37
1.36
1.35
1.34
1.33
1.32
1.30
1.30
1.28
1.27
1.26
1.25
1.24
1.24
1.23
1.22
1.22
0.90
0.88
0.87


2.00
1.00
0.93
1.00
1.00
1.00
1.39
4.01
1.34
7.58
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

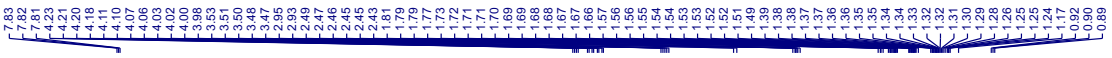

Me
O
Me
H
N
Me
OH

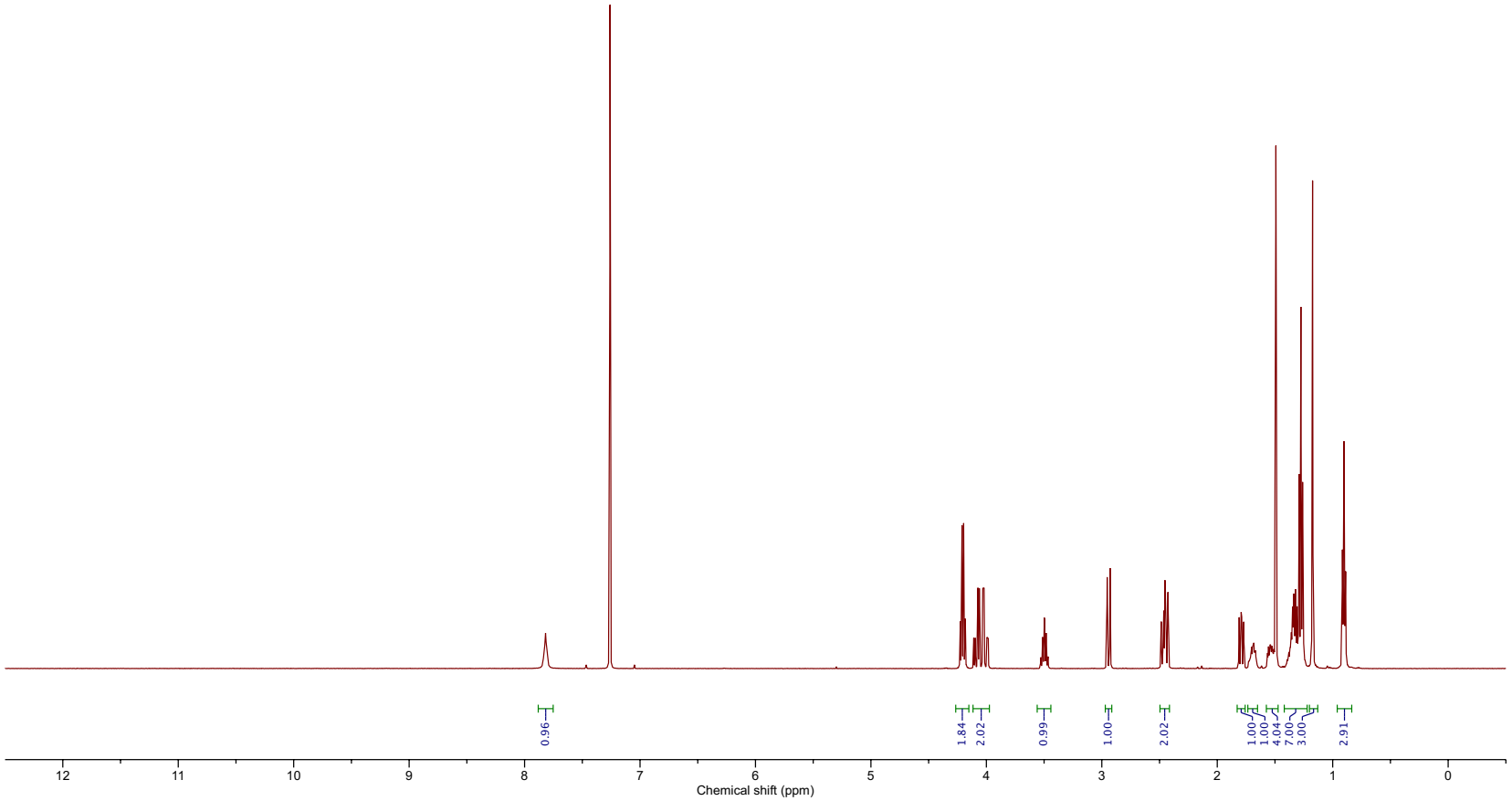
65

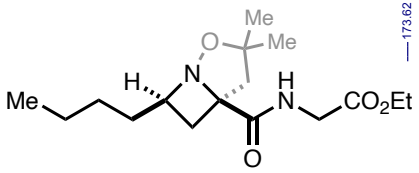
87.73
74.83
66.24
65.95
51.39
35.07
31.70
30.17
27.79
27.64
22.75
14.19
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
H
N
H
N
Me
CO2Et
O

66

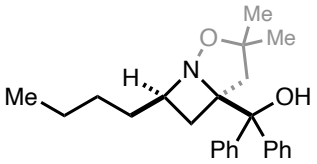



0.96
1.84
2.02
0.99
1.00
2.02
1.00
1.00
4.04
7.00
3.00
2.91
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
O
Me
H
N
H
N
CO2Et
Me
O

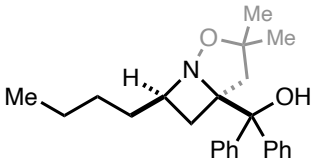
66

173.62
169.45
87.45
73.23
67.34
61.43
49.98
40.98
35.33
31.50
29.17
28.64
27.50
22.66
14.24
14.09
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


Me
O
Me
H
N
Me
OH
Ph
Ph

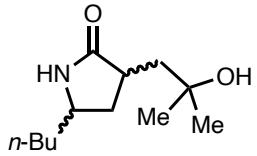
67

7.37 7.37 7.37 7.36 7.35 7.35 7.33 7.33 7.32 7.32 7.30 7.29 7.29 7.29 7.28 7.27 7.26 7.25 7.24 7.23 7.22 7.22 7.21 7.20 7.20
4.78
3.80 3.79 3.77 3.77 3.75 3.74 2.36 2.34 2.34 2.32 1.94 1.92 1.91 1.90 1.59 1.54 1.53 1.52 1.51 1.49 1.38 1.35 1.35 1.35 1.34 1.33 1.32 1.31 1.30 1.28 1.27 1.27 1.26 1.24 1.22 1.22 1.21 1.19 1.19 1.18 1.17 0.88 0.87 0.85 0.52
17.41
0.95
1.00
2.03
1.00
1.00
3.00
1.20
5.38
3.00
2.82
12 11 10 9 8 7 6 5 4 3 2 1 0
Chemical shift (ppm)


Me
O
Me
H
N
Me
OH
Ph
Ph

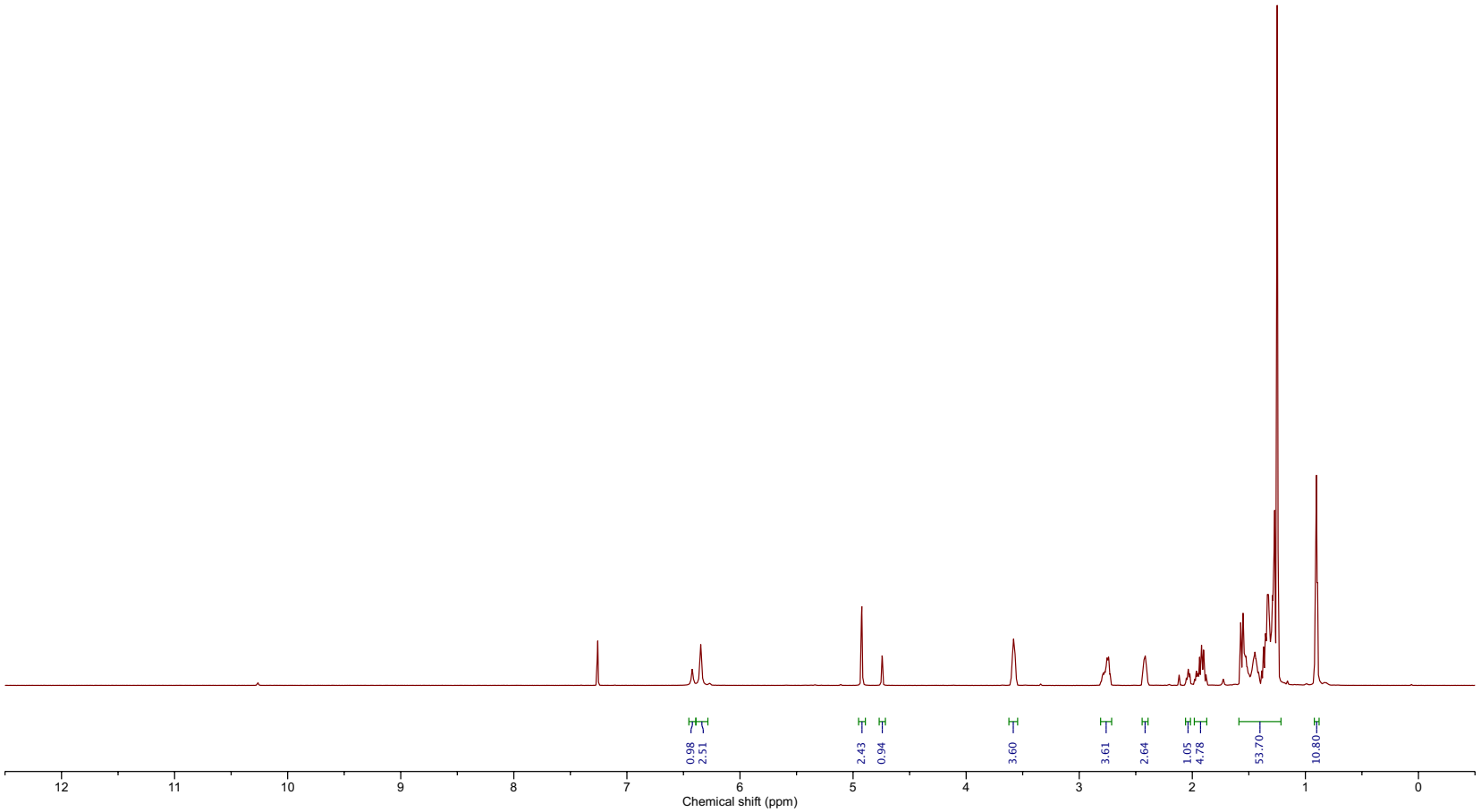
67

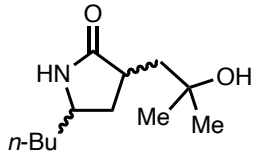
144.88
143.10
128.09
127.95
127.77
127.74
127.31
127.23
89.79
81.35
80.63
65.13
52.86
34.70
33.42
32.11
28.23
27.61
22.64
14.15
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)



68

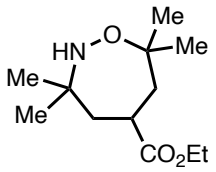
(2.6:1 mixture of diastereomers)





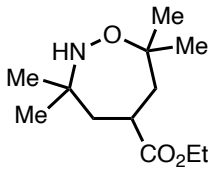
68

(2.6:1 mixture of diastereomers)


Me
HN
O
Me
Me
Me
CO2Et

69

4.43
4.13
4.12
4.10
4.08
2.71
2.69
2.66
2.00
1.97
1.96
1.94
1.79
1.76
1.73
1.69
1.56
1.53
1.50
1.27
1.25
1.24
1.23
1.10
0.98
1.00
2.00
0.91
1.00
2.03
1.00
9.08
3.00
2.95
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)


Me
HN
O
Me
Me
Me
CO_2Et

69

176.85
77.63
60.47
56.14
45.82
43.36
37.91
27.60
26.77
25.91
24.56
14.37
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

11) Supplementary References

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