Highly Stereoselective Co(III)-Catalyzed Three-Component C–H Bond Addition Cascade

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I. General Information:

Unless otherwise indicated, all Co(III)-catalyzed reactions were set up in a N_2 filled glovebox, using glassware that was oven-dried (150 °C) and evacuated while hot prior to use. Unless otherwise indicated, all reactions for substrate preparation were carried out on the benchtop under a N_2 atmosphere. Solvents were purified by elution through a column of activated alumina under N_2 before use. Unless otherwise noted, all reagents were purchased from commercial sources and used without further purification. Products and starting materials were visualized on TLC using UV-light or by staining with $KMnO_4$ or p-anisaldehyde. The diastereoselectivity of the reactions was evaluated by NMR analysis of unpurified material. Flash-column chromatography was preformed on SiliaFlash® P60 (230-400 mesh) silica gel, and preparative thin-layer chromatrography plates from Analtech (1 mm SiO_2, 20 x 20 cm) were used. NMR chemical shifts are reported in ppm relative to $CDCl_3$ (7.26 ppm for ^1H and 77.16 ppm for ^{13}C) or C_6D_6 (7.16 ppm for ^1H and 128.06 ppm for ^{13}C). Trifluoroacetic acid (set to -76.55 ppm in $CDCl_3$) was used for standardizing ^{19}F NMR chemical shifts. For IR spectra, only partial data are provided. Melting points are reported uncorrected. High-resolution mass spectra (HRMS) were obtained using electrospray ionization (ESI) on a time of flight (TOF) mass spectrometer.

II. Preparation of Starting Materials:

Catalysts/Additives/Reagents:

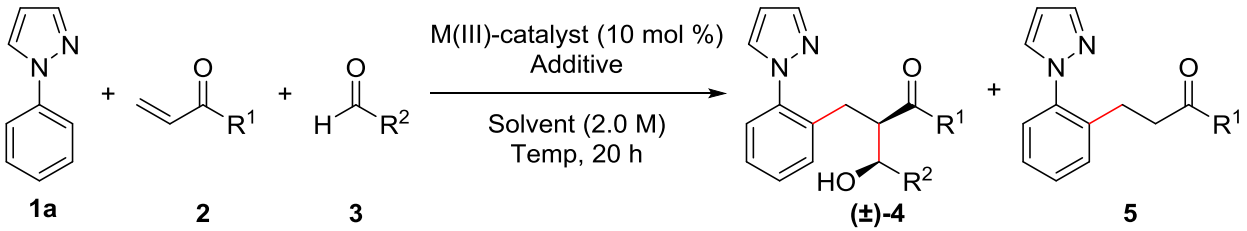
$[Cp^*RhCl_2]_2$,[S1] $AgB(C_6F_5)_4$,[S2] $[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$,[S3] $[Cp^*Co(C_6H_6)][PF_6]_2$,[S4] $[Cp^*Co(CO)I_2]$,[S5] and Fétizon's reagent[S6] were each synthesized according to a published literature procedure. Lithium acetate was dried under high vacuum at 75 °C for 20 h.

Substrates:

1-Phenyl-1*H*-pyrazole was purified by passing over a plug of basic alumina under nitrogen. All liquid aldehydes were freshly distilled prior to use. Phenyl vinyl ketone,[S7] 1-(*m*-tolyl)-1*H*-pyrazole,[S8] 2-(pyridin-2-yl)isoquinolin-1(2*H*)-one,[S9] 1-(1-phenylvinyl)-1*H*-pyrazole,[S10] (*R*,*E*)-2-methyl-*N*-(2,2,2-trifluoroethylidene)propane-2-sulfinamide,[S11] and ethyl (*R*,*E*)-2-((*tert*-butylsulfinyl)imino)acetate[S12] were each synthesized according to literature procedure. 1-Phenyl-3,4-dihydroisoquinoline[S13] was prepared according to a literature procedure and purified by flash

column chromatography eluting with a gradient of 30–60% diethyl ether in pentane prior to use. All other C–H activation substrates were purchased from commercial sources and used without further purification.

III. Supplemental Optimization Table:

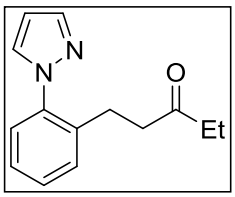


Entry	M(III)-catalyst (mol %)	Additive (mol %)	Solvent	Temp (° C)	R^1	R^2 (equiv)	% Conversion **(±)-4**[b] (dr)	% Conversion **5**[b]
1	$[Cp^*RhCl_2]_2$ (5) / $AgSbF_6$ (20)	None	AcOH	50	Ph	Ph (5)	<5%	87%
2	$[Cp^*RhCl_2]_2$ (5) / $AgSbF_6$ (20)	AcOH (10)	1,4-dioxane	50	Ph	Ph (5)	<5%	82%
3	$[Cp^*Co(C_6H_6)][PF_6]_2$ (10)	AcOH (10)	1,4-dioxane	50	Ph	Ph (5)	47% (90:10 dr)	40%
4	$[Cp^*Co(C_6H_6)][PF_6]_2$ (10)	KOAc (20)	1,4-dioxane	50	Ph	Ph (5)	70% (88:12 dr)	18%
5	$[Cp^*Co(C_6H_6)][PF_6]_2$ (10)	KOAc (20)	1,4-dioxane	50	Et	Ph (5)	65% (95:5 dr)	21%
6	$[Cp^*Co(C_6H_6)][PF_6]_2$ (10)	KOAc (20)	1,4-dioxane	23	Et	Ph (5)	<5%	<5%
7	$[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$ (10)	KOAc (20)	1,4-dioxane	23	Et	Ph (5)	61% (96:4 dr)	33%
8	$[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$ (10)	KOAc (20)	1,4-dioxane	50	Et	Ph (5)	42% (91:1 dr)	16%
9	$[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$ (10)	LiOAc (20)	1,4-dioxane	23	Et	Ph (5)	63% (96:4 dr)	37%
10	$[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$ (10)	CsOAc (20)	1,4-dioxane	23	Et	Ph (5)	57% (96:4 dr)	43%
11	$[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$ (10)	$Cu(OAc)_2$ (10)	1,4-dioxane	23	Et	Ph (5)	41% (97:3 dr)	19%
12	$[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$ (10)	AgOAc (20)	1,4-dioxane	23	Et	Ph (5)	37% (97:3 dr)	19%
13	$[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$ (10)	KOAc (20)	1,4-dioxane	23	Et	Ph (3)	28% (94:6 dr)	16%
14	$[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$ (10)	LiOAc (20)	1,4-dioxane	23	Et	Ph (3)	70% (97:3 dr)	27%
15	$[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$ (2.5)	LiOAc (5)	1,4-dioxane	23	Et	Ph (3)	36% (97:3 dr)	22%
16	$[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$ (10)	LiOAc (20) / H_2O (20)	1,4-dioxane	23	Et	Ph (3)	53% (96:4 dr)	36%
17	$[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$ (10)	LiOAc (20) / H_2O (50)	1,4-dioxane	23	Et	Ph (3)	41% (96:4 dr)	52%
18	$[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$ (10)	LiOAc (20) / H_2O (100)	1,4-dioxane	23	Et	Ph (3)	36% (96:4 dr)	53%
19	$[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$ (10)	None	1,4-dioxane	23	Et	Ph (3)	72% (97:3 dr)	12%
20	$[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$ (10)	LiOAc (20)	1,4-dioxane	23	Ph	Ph (3)	76% (92:8 dr)[c]	17%
21	$[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$ (10)	None	1,4-dioxane	23	Ph	Ph (3)	52% (92:8 dr)	24%
22	$[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$ (10)	LiOAc (20)	1,4-dioxane	23	Et	Cy (3)	81% (>98:2 dr)[c]	15%
23	$[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$ (10)	None	1,4-dioxane	23	Et	Cy (3)	64% (>98:2 dr)	14%
24	$[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$ (10)	LiOAc (20)	THF	23	Et	Ph (3)	55% (94:6 dr)	25%
25	$[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$ (10)	LiOAc (20)	1,2-DCE	23	Et	Ph (3)	54% (96:4 dr)	39%
26	$[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$ (10)	LiOAc (20)	2,2,2-TFE	23	Et	Ph (3)	48% (95:5 dr)	42%
27	$[Cp^*Co(CO)I_2]$ (10) / $AgB(C_6F_5)_4$ (20)	LiOAc (20)	1,4-dioxane	23	Et	Ph (3)	63% (97:3 dr)	32%
28	$[Cp^*Co(CO)I_2]$ (10) / $AgSbF_6$ (20)	LiOAc (20)	1,4-dioxane	23	Et	Ph (3)	57% (96:4 dr)	39%
29	$[Cp^*RhCl_2]_2$ (5) / $AgB(C_6F_5)_4$ (20)	LiOAc (20)	1,4-dioxane	23	Et	Ph (3)	<5%	77%

[a]Conditions: **1a** (1.0 equiv), **2** (1.2 equiv), **3** (3–5 equiv) for 20 h in solvent (2.0 M). [b]Determined by ^1H NMR analysis relative to 1,3,5-trimethoxybenzene as an external standard. [c]Isolated yield on 0.20 mmol scale.

IV. Preparation of Ketone 5a:

Procedure for Synthesis of 1-(2-(1*H*-Pyrazol-1-yl)phenyl)pentan-3-one:



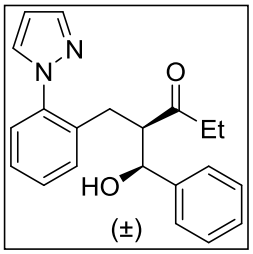
In a N_2-filled glove box, a 0.5–2.0 mL microwave vial was charged with $[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$[S3] (32.6 mg, 0.0200 mmol, 0.10 equiv) and LiOAc (2.7 mg, 0.041 mmol, 0.20 equiv), and 1,4-dioxane (100 μL, ([pyrazole = 2.0 M]) was added to the solid mixture. Following this, 1-phenyl-1*H*-pyrazole (**1a**) (28.8 mg, 0.200 mmol, 1.0 equiv) and ethyl vinyl ketone (**2a**) (20.2 mg, 0.240 mmol, 1.2 equiv) were added successively. The reaction vial was then equipped with a magnetic stir bar, sealed, and taken outside the glove box to stir at 23 °C in a preset water bath for 20 h. The reaction mixture was then uncapped, concentrated, and purified by chromatography eluting with 30% ethyl acetate in hexanes to afford the desired product **5a** as a colorless oil (41.5 mg, 91% yield). IR (film): 2975, 2938, 1710, 1517, 1455, 1394, 1112, 1044, 938, 754 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.70 (d, *J* = 1.5 Hz, 1H), 7.61 (d, *J* = 2.2 Hz, 1H), 7.36-7.32 (m, 2H), 7.31-7.28 (m, 2H), 6.44 (t, *J* = 2.0 Hz, 1H), 2.82 (t, *J* = 7.7 Hz, 2H), 2.56 (t, *J* = 7.7 Hz, 2H), 2.32 (q, *J* = 7.3 Hz, 2H), 0.99 (t, *J* = 7.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 210.68, 140.52, 139.86, 137.53, 130.81, 130.76, 128.92, 127.15, 126.71, 106.59, 43.13, 36.01, 26.16, 7.90; HRMS (ESI/[M+H]+) calcd. for $C_{14}H_{17}N_2O^+$: 229.1335. Found 229.1333.

V. Procedures for Co(III)-Catalyzed Three-Component Synthesis of Alcohols:

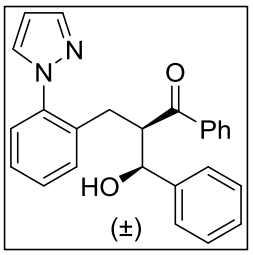
General Procedure:

In a N_2-filled glove box, a 0.5–2.0 mL microwave vial was charged with $[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$[S3] (32.6 mg, 0.0200 mmol, 0.10 equiv) and LiOAc (2.7 mg, 0.041 mmol, 0.20 equiv), and 1,4-dioxane (100 μL, ([pyrazole = 2.0 M]) was added to the solid mixture. Following this, the indicated directing group (**1**) (0.200 mmol, 1.0 equiv), aldehyde (**3**) (0.600 mmol, 3.0 equiv), and vinyl ketone (**2**) (0.240 mmol, 1.2 equiv) were added successively. The reaction vial was then equipped with a magnetic stir bar, sealed, and taken outside the glove

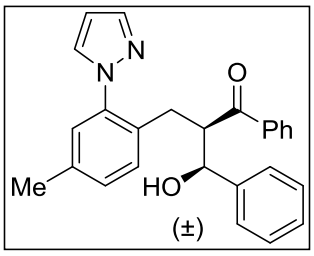
box to stir at 23 °C in a preset water bath for 20 h. The reaction mixture was then uncapped, concentrated, and purified by the corresponding chromatographic method to afford the desired product.



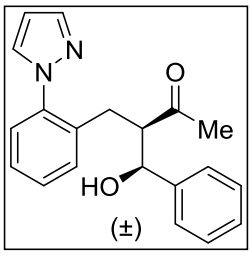
(±)-(1*S*,2*R*)-2-(2-(1*H*-Pyrazol-1-yl)benzyl)-1-hydroxy-1-phenylpentan-3-one (4a): Derived from 1-phenyl-1*H*-pyrazole (**1a**) (28.8 mg, 0.200 mmol, 1.0 equiv), benzaldehyde (**3a**) (63.7 mg, 0.600 mmol, 3.0 equiv), and ethyl vinyl ketone (**2a**) (20.2 mg, 0.240 mmol, 1.2 equiv). Silica gel chromatography eluting with 25% ethyl acetate in hexanes provided the product **4a** as a mixture of diastereomers (45.2 mg, 68% yield, 97:3 dr) as a colorless waxy solid. IR (film): 3240 (br), 2936, 1701, 1396, 1112, 1047, 943, 753, 699, 625, 531 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.69 (d, *J* = 1.8 Hz, 1H), 7.55 (d, *J* = 2.3 Hz, 1H), 7.34–7.25 (m, 6H), 7.21 (t, *J* = 7.2 Hz, 1H), 7.15 (d, *J* = 7.2 Hz, 2H), 6.43 (t, *J* = 2.0 Hz, 1H), 4.65 (t, *J* = 6.0 Hz, 1H), 3.80 (d, *J* = 6.7 Hz, 1H), 3.08–3.04 (m, 1H), 2.89–2.82 (m, 2H), 1.91–1.85 (m, 2H), 0.67 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 216.2, 142.5, 140.6, 139.9, 134.9, 131.7, 130.8, 128.8, 128.4, 127.7, 127.5, 126.7, 125.8, 106.8, 74.4, 58.1, 39.2, 32.1, 6.9; HRMS (ESI/[M+H]+) calcd. for $C_{21}H_{23}N_2O_2^+$: 335.1754. Found 335.1758.



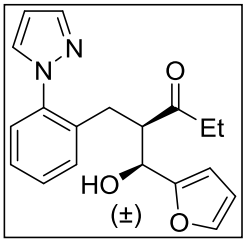
(±)-(2*R*,3*S*)-2-(2-(1*H*-Pyrazol-1-yl)benzyl)-3-hydroxy-1,3-diphenylpropan-1-one (4b): Derived from 1-phenyl-1*H*-pyrazole (**1a**) (28.8 mg, 0.200 mmol, 1.0 equiv), benzaldehyde (**3a**) (63.7 mg, 0.600 mmol, 3.0 equiv), and phenyl vinyl ketone[S7] (**2b**) (31.7 mg, 0.240 mmol, 1.2 equiv). Silica gel chromatography eluting with 25% ethyl acetate in hexanes provided the product **4b** as a mixture of diastereomers (58.4 mg, 76% yield, 92:8 dr) as a colorless oil. IR (film): 3476 (br), 3065, 1674, 1517, 1448, 1394, 1207, 1045, 937, 699 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.56 (d, *J* = 7.6, 2H), 7.52 (d, *J* = 2.2 Hz, 1H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.35–7.34 (m, 1H), 7.25–7.19 (m, 9H), 7.15–7.10 (m, 1H), 6.44 (t, *J* = 1.8 Hz, 1H), 4.84 (dd, *J* = 7.1, 4.8 Hz, 1H), 4.13 (dt, *J* = 7.6, 5.2 Hz, 1H), 3.96 (d, *J* = 7.2 Hz, 1H), 3.04 (d, *J* = 7.7 Hz, 2H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 205.75, 142.56, 140.73, 139.91, 137.84, 134.74, 133.11, 132.26, 130.84, 128.71, 128.45, 128.27, 128.24, 127.59, 127.37, 126.53, 125.98, 106.80, 75.05, 52.74, 32.98; HRMS (ESI/[M+H]+) calcd. for $C_{25}H_{23}N_2O_2^+$: 383.1754. Found 383.1756.



(±)-(2*R*,3*S*)-3-Hydroxy-2-(4-methyl-2-(1*H*-pyrazol-1-yl)benzyl)-1,3-diphenylpropan-1-one (4c): Derived from 1-(*m*-tolyl)-1*H*-pyrazole[S8] (**1e**) (31.6 mg, 0.200 mmol, 1.0 equiv), benzaldehyde (**3a**) (63.7 mg, 0.600 mmol, 3.0 equiv), and phenyl vinyl ketone[S7] (**2b**) (31.7 mg, 0.240 mmol, 1.2 equiv). Silica gel chromatography eluting with 25% ethyl acetate in hexanes provided the product **4c** as a mixture of diastereomers (68.9 mg, 87% yield, 93:7 dr) as a colorless oil. IR (film): 3454 (br), 1674, 1516, 1448, 1392, 1207, 1043, 910, 729, 699 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.55 (d, *J* = 7.6, 2H), 7.52 (d, *J* = 2.0 Hz, 1H), 7.39 (t, *J* = 7.3 Hz, 1H), 7.25–7.22 (m, 3H), 7.19–7.16 (m, 4H), 7.12–7.09 (m, 1H), 7.04–7.03 (m, 2H), 6.43 (t, *J* = 2.1 Hz, 1H), 4.81 (dd, *J* = 7.2, 4.6 Hz, 1H), 4.08 (dt, *J* = 7.6, 5.0 Hz, 1H), 4.01 (d, *J* = 7.3 Hz, 1H), 3.00 (d, *J* = 7.6 Hz, 2H), 2.29 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 205.81, 142.71, 140.63, 139.78, 137.87, 137.61, 133.06, 132.09, 131.51, 130.80, 129.46, 128.50, 128.25, 127.30, 127.20, 125.97, 106.69, 74.90, 52.82, 32.54, 20.83; HRMS (ESI/[M+H]+) calcd. for $C_{26}H_{25}N_2O_2^+$: 397.1911. Found 397.1913.

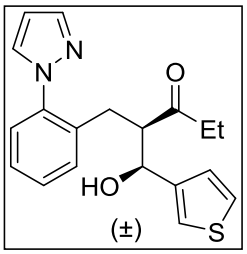


(±)-(3*R*,4*S*)-3-(2-(1*H*-Pyrazol-1-yl)benzyl)-4-hydroxy-4-phenylbutan-2-one (4d): Derived from 1-phenyl-1*H*-pyrazole (**1a**) (28.8 mg, 0.200 mmol, 1.0 equiv), benzaldehyde (**3a**) (63.7 mg, 0.600 mmol, 3.0 equiv), and methyl vinyl ketone (16.8 mg, 0.240 mmol, 1.2 equiv). Silica gel chromatography eluting with 25% ethyl acetate in hexanes provided the product **4d** as a mixture of diastereomers (44.3 mg, 69% yield, 95:5 dr) as a white solid (mp: 100-101 °C). IR (film): 3369 (br), 3270, 1710, 1695, 1517, 1398, 1049, 1024, 764, 746, 702 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.58 (s, 1H), 7.37–7.28 (m, 6H), 7.24–7.20 (m, 3H), 6.46 (s, 1H), 4.69 (t, *J* = 5.7 Hz, 1H), 3.91 (d, *J* = 6.4 Hz, 1H), 3.14 (dt, *J* = 7.8, 5.0 Hz, 1H), 2.93–2.84 (m, 2H), 1.73 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 213.26, 142.49, 140.72, 139.99, 134.94, 131.72, 130.93, 128.97, 128.49, 127.73, 127.57, 126.72, 125.93, 106.94, 74.00, 59.15, 32.84, 31.55; HRMS (ESI/[M+H]+) calcd. for $C_{20}H_{21}N_2O_2^+$: 321.1598. Found 321.1597.

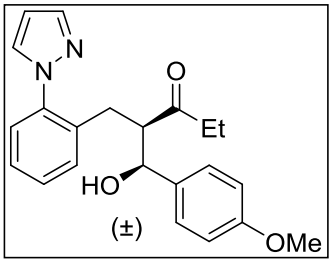


(±)-(1*S*,2*R*)-2-(2-(1*H*-Pyrazol-1-yl)benzyl)-1-(furan-2-yl)-1-hydroxypentan-3-one (4e): Derived from 1-phenyl-1*H*-pyrazole (**1a**) (28.8 mg, 0.200 mmol, 1.0 equiv), furfural (57.7 mg, 0.600 mmol, 3.0 equiv), and

ethyl vinyl ketone (**2a**) (20.2 mg, 0.240 mmol, 1.2 equiv). Silica gel chromatography eluting with a gradient of 10–25% ethyl acetate in hexanes provided the product **4e** as a mixture of diastereomers (48.2 mg, 74% yield, 98:2 dr) as a light yellow waxy solid. IR (film): 3485 (br), 2938, 1710, 1518, 1395, 1149, 1112, 1046, 1009, 939, 746, 623, 598 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.73 (d, *J* = 1.8 Hz, 1H), 7.60 (d, *J* = 2.3 Hz, 1H), 7.36–7.29 (m, 3H), 7.28–7.26 (m, 2H), 6.46 (t, *J* = 2.1 Hz, 1H), 6.26 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.15 (dt, *J* = 3.2, 0.8 Hz, 1H), 4.66 (t, *J* = 5.4 Hz, 1H), 4.18 (d, *J* = 7.2 Hz, 1H), 3.24–3.21 (m, 1H), 2.92–2.85 (m, 2H), 2.17–2.10 (m, 1H), 2.08–2.01 (m, 1H), 0.80 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 215.4, 155.2, 141.8, 140.6, 139.8, 134.6, 131.8, 131.0, 128.9, 127.7, 126.6, 110.4, 106.8, 106.7, 68.3, 55.3, 37.9, 30.9, 7.1; HRMS (ESI/[M+H]+) calcd. for $C_{19}H_{21}N_2O_3^+$: 325.1547. Found 325.1548.

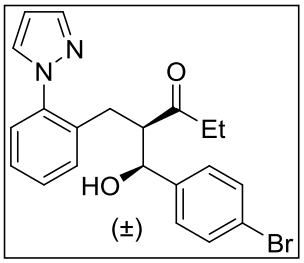


(±)-(1*S*,2*R*)-2-(2-(1*H*-Pyrazol-1-yl)benzyl)-1-hydroxy-1-(thiophen-3-yl)pentan-3-one (4f): Derived from 1-phenyl-1*H*-pyrazole (**1a**) (28.8 mg, 0.200 mmol, 1.0 equiv), 3-thiophenecarboxaldehyde (67.3 mg, 0.600 mmol, 3.0 equiv), and ethyl vinyl ketone (**2a**) (20.2 mg, 0.240 mmol, 1.2 equiv). Silica gel chromatography eluting with a gradient of 10–25% ethyl acetate in hexanes provided the product **4f** as a mixture of diastereomers (49.1 mg, 72% yield, 98:2 dr) as a colorless waxy solid. IR (film): 3464 (br), 2976, 2937, 1708, 1517, 1395, 1112, 1044, 938, 835, 757, 661, 623 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.73 (d, *J* = 1.8 Hz, 1H), 7.58 (d, *J* = 2.3 Hz, 1H), 7.35–7.27 (m, 4H), 7.23 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.05 (dt, *J* = 2.3, 1.0 Hz, 1H), 6.85 (dd, *J* = 5.0, 1.0 Hz, 1H), 6.46 (t, *J* = 2.1 Hz, 1H), 4.72 (t, *J* = 5.8 Hz, 1H), 3.94 (d, *J* = 7.2 Hz, 1H), 3.08–3.05 (m, 1H), 2.92–2.84 (m, 2H), 2.02–1.91 (m, 2H), 0.72 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 216.1, 144.4, 140.6, 139.9, 134.8, 131.8, 130.9, 128.9, 127.7, 126.7, 126.2, 125.5, 121.0, 106.9, 71.1, 57.5, 38.8, 31.8, 7.0; HRMS (ESI/[M+H]+) calcd. for $C_{19}H_{21}N_2O_2S^+$: 341.1318. Found 341.1316.

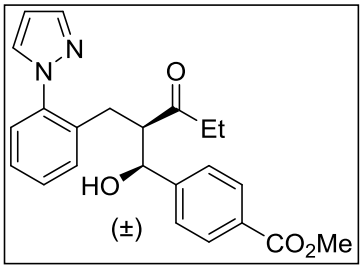


(±)-(1*S*,2*R*)-2-(2-(1*H*-Pyrazol-1-yl)benzyl)-1-hydroxy-1-(4-methoxyphenyl)pentan-3-one (4g): Derived from 1-phenyl-1*H*-pyrazole (**1a**) (28.8 mg, 0.200 mmol, 1.0 equiv), *p*-anisaldehyde (81.7 mg, 0.600 mmol, 3.0 equiv), and ethyl vinyl ketone (**2a**) (20.2 mg, 0.240 mmol, 1.2 equiv). Silica gel chromatography eluting with 40% ethyl acetate in hexanes provided the product **4g** as a mixture of diastereomers (56.0 mg,

77% yield, 95:5 dr) as a colorless waxy solid. IR (film): 3464 (br), 2937, 1709, 1512, 1245, 1032, 833, 758, 624, 543 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.68 (d, *J* = 1.9 Hz, 1H), 7.52 (d, *J* = 2.2 Hz, 1H), 7.31–7.23 (m, 4H), 7.05 (d, *J* = 8.5 Hz, 2H), 6.79 (d, *J* = 8.5 Hz, 2H), 6.42 (t, *J* = 2.1 Hz, 1H), 4.60 (t, *J* = 6.0 Hz, 1H), 3.77 (s, 3H), 3.57 (d, *J* = 6.2 Hz, 1H), 3.00 (q, *J* = 7.5 Hz, 1H), 2.79 (d, *J* = 7.7 Hz, 2H), 2.00–1.92 (m, 1H), 1.91–1.83 (m, 1H), 0.69 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 216.1, 159.0, 140.6, 139.8, 134.9, 134.6, 131.7, 130.8, 128.8, 127.6, 127.1, 126.7, 113.8, 106.8, 74.4, 58.2, 55.3, 39.3, 32.1, 6.9; HRMS (ESI/[M+H]+) calcd. for $C_{22}H_{25}N_2O_3^+$: 365.1860. Found 365.1863.

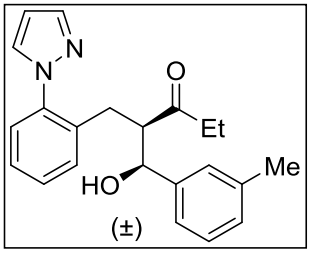


(±)-(1*S*,2*R*)-2-(2-(1*H*-Pyrazol-1-yl)benzyl)-1-(4-bromophenyl)-1-hydroxypentan-3-one (4h): Derived from 1-phenyl-1*H*-pyrazole (**1a**) (28.8 mg, 0.200 mmol, 1.0 equiv), 4-bromobenzaldehyde (111 mg, 0.600 mmol, 3.0 equiv), and ethyl vinyl ketone (**2a**) (20.2 mg, 0.240 mmol, 1.2 equiv). Silica gel chromatography eluting with a gradient of 10–25% ethyl acetate in hexanes provided the product **4h** as a mixture of diastereomers (67.2 mg, 81% yield, 94:6 dr) as a light yellow waxy solid. IR (film): 3483 (br), 2938, 1708, 1518, 1489, 1395, 1045, 1009, 938, 829, 755, 623, 535 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.68 (d, *J* = 1.8 Hz, 1H), 7.54 (d, *J* = 2.3 Hz, 1H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.34–7.29 (m, 2H), 7.28–7.25 (m, 2H), 7.02 (d, *J* = 8.4 Hz, 2H), 6.43 (t, *J* = 2.1 Hz, 1H), 4.58 (t, *J* = 5.8 Hz, 1H), 4.05 (d, *J* = 6.7 Hz, 1H), 3.03–2.99 (m, 1H), 2.87–2.78 (m, 2H), 1.93–1.88 (m, 2H), 0.69 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 215.8, 141.7, 140.6, 139.8, 134.6, 131.7, 131.4, 130.8, 128.9, 127.8, 127.6, 126.7, 121.3, 106.9, 73.7, 58.0, 39.1, 31.9, 6.9; HRMS (ESI/[M+H]+) calcd. for $C_{21}H_{22}BrN_2O_2^+$: 413.0859. Found 413.0860.

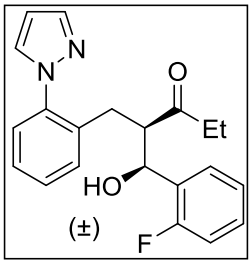


(±)-Methyl 4-((1*S*,2*R*)-2-(2-(1*H*-pyrazol-1-yl)benzyl)-1-hydroxy-3-oxopentyl)benzoate (4i): Derived from 1-phenyl-1*H*-pyrazole (**1a**) (28.8 mg, 0.200 mmol, 1.0 equiv), methyl 4-formylbenzoate (98.5 mg, 0.600 mmol, 3.0 equiv), and ethyl vinyl ketone (**2a**) (20.2 mg, 0.240 mmol, 1.2 equiv). Silica gel chromatography eluting with 40% ethyl acetate in hexanes provided the product **4i** as a mixture of diastereomers (60.9 mg, 78% yield, 89:11 dr) as a colorless waxy solid. IR (film): 3479 (br), 1712, 1518, 1395, 1276, 1103, 1045, 1018, 938, 757, 708, 623 cm^{-1}; ^1H NMR (600 MHz,

$CDCl_3$) δ 7.91 (d, *J* = 8.3 Hz, 2H), 7.66 (d, *J* = 1.8 Hz, 1H), 7.54 (d, *J* = 2.3 Hz, 1H), 7.33–7.23 (m, 4H), 7.21 (d, *J* = 8.3 Hz, 2H), 6.41 (t, *J* = 2.1 Hz, 1H), 4.66 (t, *J* = 5.6 Hz, 1H), 4.30 (d, *J* = 6.7 Hz, 1H), 3.87 (s, 3H), 3.07–3.03 (m, 1H), 2.88–2.81 (m, 2H), 1.89–1.81 (m, 2H), 0.64 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 215.6, 166.9, 147.9, 140.6, 139.8, 134.5, 131.7, 130.8, 129.6, 129.2, 128.9, 127.8, 126.6, 125.8, 106.9, 73.7, 57.9, 52.2, 39.0, 31.8, 6.8; HRMS (ESI/[M+H]+) calcd. for $C_{23}H_{25}N_2O_4^+$: 393.1809. Found 393.1810.

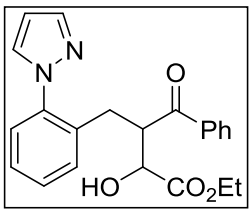


(±)-(1*S*,2*R*)-2-(2-(1*H*-Pyrazol-1-yl)benzyl)-1-hydroxy-1-(*m*-tolyl)pentan-3-one (4j): Derived from 1-phenyl-1*H*-pyrazole (**1a**) (28.8 mg, 0.200 mmol, 1.0 equiv), 3-methylbenzaldehyde (72.1 mg, 0.600 mmol, 3.0 equiv), and ethyl vinyl ketone (**2a**) (20.2 mg, 0.240 mmol, 1.2 equiv). Silica gel chromatography eluting with 25% ethyl acetate in hexanes provided the product **4j** as a mixture of diastereomers (51.1 mg, 73% yield, 95:5 dr) as a light yellow waxy solid. IR (film): 3447 (br), 2974, 2938, 1710, 1518, 1395, 1112, 1043, 938, 754, 705, 623 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 2.0 Hz, 1H), 7.53 (d, *J* = 2.4 Hz, 1H), 7.33–7.24 (m, 4H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 7.6 Hz, 1H), 6.97 (s, 1H), 6.93 (d, *J* = 7.6 Hz, 1H), 6.42 (t, *J* = 2.1 Hz, 1H), 4.62 (d, *J* = 4.7 Hz, 1H), 3.65 (s, 1H), 3.06–3.02 (m, 1H), 2.83 (d, *J* = 7.6 Hz, 2H), 2.32 (s, 3H), 1.98–1.83 (m, 2H), 0.69 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 216.1, 142.4, 140.5, 139.8, 137.9, 134.9, 131.7, 130.8, 128.8, 128.3, 128.2, 127.6, 126.7, 126.5, 123.0, 106.7, 74.7, 58.1, 39.2, 32.1, 21.6, 6.8; HRMS (ESI/[M+H]+) calcd. for $C_{22}H_{25}N_2O_2^+$: 349.1911. Found 349.1909.

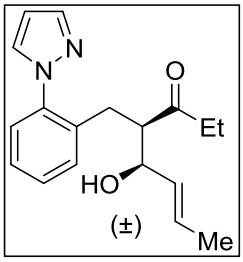


(±)-(1*S*,2*R*)-2-(2-(1*H*-Pyrazol-1-yl)benzyl)-1-(2-fluorophenyl)-1-hydroxypentan-3-one (4k): Derived from 1-phenyl-1*H*-pyrazole (**1a**) (28.8 mg, 0.200 mmol, 1.0 equiv), 2-fluorobenzaldehyde (74.5 mg, 0.600 mmol, 3.0 equiv), and ethyl vinyl ketone (**2a**) (20.2 mg, 0.240 mmol, 1.2 equiv). Silica gel chromatography eluting with 25% ethyl acetate in hexanes provided the product **4k** as a mixture of diastereomers (61.6 mg, 87% yield, 90:10 dr) as a white solid (mp: 91–92 °C). IR (film): 3241 (br), 2987, 2933, 1706, 1485, 1452, 1049, 945, 761, 747 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.59 (s, 1H), 7.34–7.27 (m, 5H), 7.22–7.18 (m, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.96–6.92 (m, 1H), 6.43 (t, *J* = 2.1 Hz, 1H), 4.95 (dd, *J* = 7.3, 4.5 Hz, 1H), 4.34 (d, *J* = 7.3 Hz, 1H), 3.16 (dt, *J* = 7.8, 4.6 Hz, 1H), 2.97 (d, *J* = 7.8

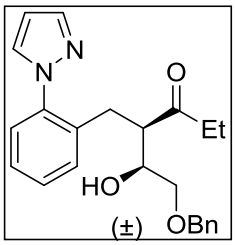
Hz, 2H), 1.99–1.83 (m, 2H), 0.69 (t, J = 7.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 215.62, 159.43 (d, J = 245.5 Hz), 140.70, 139.97, 134.64, 131.83, 130.90, 129.76 (d, J = 13.2 Hz), 128.96 (d, J = 8.2 Hz), 128.81, 127.74, 127.72, 126.56, 124.28 (d, J = 3.4 Hz), 115.13 (d, J = 21.7 Hz), 106.81, 68.25, 56.52, 38.78, 31.44, 6.92; ^{19}F NMR (471 MHz, $CDCl_3$): δ -119.56 (s, 1F); HRMS (ESI/[M+H]+) calcd. for $C_{21}H_{22}FN_2O_2^+$: 353.1660. Found 353.1663.



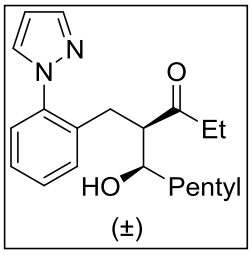
(±)-Ethyl-3-(2-(1*H*-pyrazol-1-yl)benzyl)-2-hydroxy-4-oxo-4-phenylbutanoate (4l): Derived from 1-phenyl-1*H*-pyrazole (**1a**) (28.8 mg, 0.200 mmol, 1.0 equiv), ethyl glyoxylate (61.3 mg, 0.600 mmol, 3.0 equiv), and phenyl vinyl ketone[S7] (**2b**) (31.7 mg, 0.240 mmol, 1.2 equiv). Analysis of unpurified material by ^1H NMR determined the reaction diastereoselectivity to be 75:25 dr. Silica gel chromatography eluting with 30% ethyl acetate in hexanes provided the first step in the purification process. The higher R_f major diastereomer was obtained as a colorless waxy solid (30.0 mg), and the lower R_f minor diastereomer was isolated as a mixture containing the two-component product of direct arene C–H bond addition to ethyl glyoxylate.[S14] The mixture containing the lower R_f minor diastereomer was then loaded onto a C18 reverse phase column as a solution in 1 mL of DMSO. Reverse phase purification was performed with 15.5 g of reverse phase media and a 50 column volume gradient from 5 to 55% CH_3CN:H_2O containing 0.1% TFA. Fractions containing the lower R_f minor diastereomer were combined and diluted with sat. aq. $NaHCO_3$ (50 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were then washed with brine (50 mL), dried over $MgSO_4$, and concentrated to afford the lower R_f minor diastereomer (8.8 mg) as a colorless waxy solid (38.8 mg total for both diasteromers, 51% yield). Fractions containing the two-component product of direct arene C–H bond addition to ethyl glyoxylate were also combined and diluted with sat. aq. $NaHCO_3$ (50 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were then washed with brine (50 mL), dried over $MgSO_4$, and concentrated to afford the two-component product (7.2 mg, 15% yield). The analytical data for the two diastereomeric three-component addition products and the direct addition product to ethyl glyoxylate are consistent with previously reported data.[S14–15] The ^1H and $^{13}C\{^1H\}$ NMR spectra for the three compounds are also provided in the spectra section.



(±)-(4*R*,5*R*,*E*)-4-(2-(1*H*-Pyrazol-1-yl)benzyl)-5-hydroxyoct-6-en-3-one (4m): Derived from 1-phenyl-1*H*-pyrazole (**1a**) (28.8 mg, 0.200 mmol, 1.0 equiv), (*E*)-but-2-enal (42.1 mg, 0.601 mmol, 3.0 equiv), and ethyl vinyl ketone (**2a**) (20.2 mg, 0.240 mmol, 1.2 equiv). Silica gel chromatography eluting with 20% ethyl acetate in hexanes provided the product **4m** as a mixture of diastereomers (39.6 mg, 66% yield, 96:4 dr) as a colorless oil. IR (film): 3385 (br), 2974, 2937, 1708, 1517, 1395, 965, 939, 759, 730 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.61 (s, 1H), 7.31–7.28 (m, 4H), 6.47 (s, 1H), 5.59 (dq, *J* = 12.5, 6.1 Hz, 1H), 5.25 (dd, *J* = 15.1, 6.3 Hz, 1H), 4.01 (q, *J* = 6.1 Hz, 1H), 3.01 (d, *J* = 6.3 Hz, 1H), 2.91–2.85 (m, 1H), 2.79–2.74 (m, 2H), 2.28 (dq, *J* = 14.2, 6.9 Hz, 1H), 2.06 (dq, *J* = 18.3, 7.2 Hz, 1H), 1.63 (d, *J* = 6.6 Hz, 3H), 0.84 (t, *J* = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 215.67, 140.54, 139.92, 135.45, 132.05, 131.76, 130.95, 128.83, 127.94, 127.55, 126.72, 106.73, 73.27, 57.15, 38.77, 31.33, 17.72, 7.10; HRMS (ESI/[M+H]+) calcd. for $C_{18}H_{23}N_2O_2^+$: 299.1754. Found 299.1746.

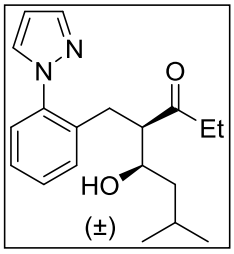


(±)-(4*R*,5*S*)-4-(2-(1*H*-Pyrazol-1-yl)benzyl)-6-(benzyloxy)-5-hydroxyhexan-3-one (4n): Derived from 1-phenyl-1*H*-pyrazole (**1a**) (28.8 mg, 0.200 mmol, 1.0 equiv), 2-(benzyloxy)acetaldehyde (90.1 mg, 0.600 mmol, 3.0 equiv), and ethyl vinyl ketone (**2a**) (20.2 mg, 0.240 mmol, 1.2 equiv). Silica gel chromatography eluting with 10% ethyl acetate in dichloromethane provided the product **4n** as a mixture of diastereomers (49.2 mg, 65% yield, 94:6 dr) as a light yellow oil. IR (film): 3467 (br), 3062, 2937, 1711, 1517, 1454, 1395, 1098, 752, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.60 (s, 1H), 7.32–7.25 (m, 9H), 6.44 (s, 1H), 4.44 (s, 2H), 3.77–3.74 (m, 2H), 3.40 (dd, *J* = 9.7, 4.0 Hz, 1H), 3.34 (dd, *J* = 9.7, 5.0 Hz, 1H), 2.96–2.88 (m, 2H), 2.81–2.77 (m, 1H), 2.30 (dq, *J* = 18.6, 7.2 Hz, 1H), 2.08 (dq, *J* = 18.6, 7.2 Hz, 1H), 0.80 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 215.93, 140.60, 139.84, 137.94, 134.90, 131.94, 130.94, 128.85, 128.47, 127.80, 127.79, 127.68, 126.60, 106.81, 73.54, 73.13, 71.14, 53.17, 38.05, 31.34, 7.03; HRMS (ESI/[M+H]+) calcd. for $C_{23}H_{27}N_2O_3^+$: 379.2016. Found 379.2013.

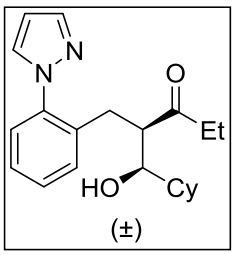


(±)-(4*R*,5*R*)-4-(2-(1*H*-Pyrazol-1-yl)benzyl)-5-hydroxydecan-3-one (4o): Derived from 1-phenyl-1*H*-pyrazole (**1a**) (28.8 mg, 0.200 mmol, 1.0 equiv), hexanal (60.1 mg, 0.600 mmol, 3.0 equiv), and ethyl vinyl ketone

(**2a**) (20.2 mg, 0.240 mmol, 1.2 equiv). Silica gel chromatography eluting with 10% ethyl acetate in dichloromethane provided the product **4o** as a mixture of diastereomers (49.2 mg, 75% yield, >98:2 dr) as a colorless oil. IR (film): 3408 (br), 2933, 2858, 1709, 1518, 1459, 1395, 938, 758, 730 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.62 (s, 1H), 7.35–7.25 (m, 4H), 6.47 (s, 1H), 3.46–3.43 (m, 2H), 2.97 (dd, *J* = 13.3, 8.1 Hz, 1H), 2.84 (dd, *J* = 13.3, 7.2 Hz, 1H), 2.73 (dt, *J* = 7.5, 3.0 Hz, 1H), 2.29–2.13 (m, 2H), 1.41–1.34 (m, 1H), 1.30–1.15 (m, 7H), 0.88–0.82 (m, 6H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 216.80, 140.61, 139.84, 135.22, 131.86, 131.03, 128.90, 127.61, 126.63, 106.89, 71.72, 56.60, 38.22, 35.71, 31.82, 31.27, 25.93, 22.68, 14.14, 7.18; HRMS (ESI/[M+H]+) calcd. for $C_{20}H_{29}N_2O_2^+$: 329.2224. Found 329.2211.

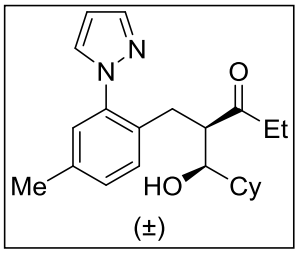


(±)-(4*R*,5*R*)-4-(2-(1*H*-Pyrazol-1-yl)benzyl)-5-hydroxy-7-methyloctan-3-one (4p): Derived from 1-phenyl-1*H*-pyrazole (**1a**) (28.8 mg, 0.200 mmol, 1.0 equiv), isovaleraldehyde (51.7 mg, 0.600 mmol, 3.0 equiv), and ethyl vinyl ketone (**2a**) (20.2 mg, 0.240 mmol, 1.2 equiv). The crude reaction mixture was passed over a pad of silica gel with 30% ethyl acetate in hexanes (4 cm SiO_2 in a Pasteur pipet) to remove colored baseline impurities, and the solvent was removed under reduced pressure. Silica gel chromatography eluting with 10% ethyl acetate in dichloromethane provided the product **4p** as a mixture of diastereomers (41.9 mg, 67% yield, 98:2 dr) as a colorless waxy solid. IR (film): 3448 (br), 2954, 1709, 1517, 1456, 1395, 1110, 1046, 1022, 938, 758, 624 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.75 (d, *J* = 1.8 Hz, 1H), 7.63 (d, *J* = 2.3 Hz, 1H), 7.36–7.28 (m, 4H), 6.49 (t, *J* = 2.1 Hz, 1H), 3.61–3.56 (m, 1H), 3.41 (d, *J* = 8.0 Hz, 1H), 2.98 (dd, *J* = 13.4, 7.8 Hz, 1H), 2.87 (dd, *J* = 13.4, 7.4 Hz, 1H), 2.72 (dt, *J* = 7.4, 3.7 Hz, 1H), 2.30–2.23 (m, 1H), 2.21–2.14 (m, 1H), 1.75–1.67 (m, 1H), 1.29–1.24 (m, 1H), 1.06–1.01 (m, 1H), 0.88 (t, *J* = 7.2 Hz, 3H), 0.82 (d, *J* = 6.6 Hz, 3H), 0.79 (d, *J* = 6.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 217.0, 140.6, 139.8, 135.3, 131.8, 131.1, 128.9, 127.6, 126.6, 106.9, 69.8, 56.9, 44.7, 38.3, 31.3, 24.9, 23.4, 22.0, 7.2; HRMS (ESI/[M+H]+) calcd. for $C_{19}H_{27}N_2O_2^+$: 315.2067. Found 315.2064.

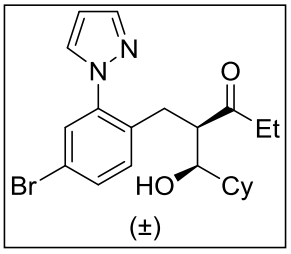


(±)-(1*R*,2*R*)-2-(2-(1*H*-Pyrazol-1-yl)benzyl)-1-cyclohexyl-1-hydroxypentan-3-one (4q): Derived from 1-phenyl-1*H*-pyrazole (**1a**) (28.8 mg, 0.200 mmol, 1.0 equiv), cyclohexanecarbaldehyde (67.3 mg, 0.600 mmol, 3.0 equiv), and ethyl vinyl ketone (**2a**) (20.2 mg, 0.240 mmol, 1.2

equiv). Silica gel chromatography eluting with 10% ethyl acetate in dichloromethane provided the product **4q** as a mixture of diastereomers (55.3 mg, 81% yield, >98:2 dr) as a white solid (mp: 114–115 °C). IR (film): 3300 (br), 2928, 2852, 1710, 1513, 1398, 1051, 946, 768, 748 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.62 (d, *J* = 1.5 Hz, 1H), 7.25 (d, *J* = 7.7 Hz, 1H), 7.07 (d, *J* = 2.3 Hz, 1H), 6.97–6.91 (m, 2H), 6.85 (dt, *J* = 7.7, 1.4 Hz, 1H), 6.12 (t, *J* = 2.1 Hz, 1H), 3.34–3.29 (m, 2H), 3.14–3.04 (m, 2H), 2.91 (dd, *J* = 12.7, 7.3 Hz, 1H), 2.19–2.12 (m, 2H), 2.04 (apparent d, *J* = 12.9 Hz, 1H), 1.69–1.58 (m, 2H), 1.56–1.50 (m, 2H), 1.32–1.25 (m, 1H), 1.14–1.06 (m, 2H), 1.04–0.94 (m, 2H), 0.88 (t, *J* = 7.2 Hz, 3H), 0.86–0.81 (m, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, C_6D_6): δ 216.08, 140.61, 140.42, 135.63, 132.35, 130.71, 128.62, 127.46, 126.69, 106.76, 76.79, 53.48, 42.12, 38.49, 32.39, 30.31, 28.59, 26.77, 26.55, 26.34, 7.33; HRMS (ESI/[M+H]+) calcd. for $C_{21}H_{29}N_2O_2^+$: 341.2224. Found 341.2219.

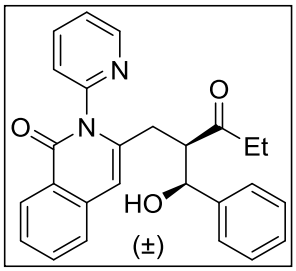


(±)-(1*R*,2*R*)-1-Cyclohexyl-1-hydroxy-2-(4-methyl-2-(1*H*-pyrazol-1-yl)benzyl)pentan-3-one (4r): Derived from 1-(*m*-tolyl)-1*H*-pyrazole[S8] (**1e**) (31.6 mg, 0.200 mmol, 1.0 equiv), cyclohexanecarbaldehyde (67.3 mg, 0.600 mmol, 3.0 equiv), and ethyl vinyl ketone (**2a**) (20.2 mg, 0.240 mmol, 1.2 equiv). Silica gel chromatography eluting with 10% ethyl acetate in dichloromethane provided the product **4r** as a mixture of diastereomers (52.0 mg, 73% yield, >98:2 dr) as a white solid (mp: 101–102 °C). IR (film): 3350 (br), 2927, 2852, 1710, 1517, 1395, 1379, 1115, 1049, 964, 751 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, *J* = 1.5 Hz, 1H), 7.61 (d, *J* = 2.2 Hz, 1H), 7.18 (d, *J* = 7.8 Hz, 1H), 7.13 (d, *J* = 8.2 Hz, 1H), 7.10 (s, 1H), 6.46 (t, *J* = 2.0 Hz, 1H), 3.29 (d, *J* = 8.6 Hz, 1H), 3.11 (dt, *J* = 8.0, 3.2 Hz, 1H), 2.92 (dd, *J* = 12.3, 7.2 Hz, 1H), 2.86–2.79 (m, 2H), 2.35 (s, 3H), 2.23 (dq, *J* = 18.4, 7.2 Hz, 1H), 2.12 (dq, *J* = 18.5, 7.2 Hz, 1H), 1.80 (apparent d, *J* = 13.2 Hz, 1H), 1.71–1.65 (m, 2H), 1.59 (apparent d, *J* = 11.5 Hz, 1H), 1.47 (apparent d, *J* = 12.8 Hz, 1H), 1.19–1.03 (m, 4H), 0.87–0.78 (m, 5H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 217.62, 140.52, 139.74, 137.65, 131.83, 131.77, 130.81, 129.58, 127.34, 106.70, 76.68, 52.85, 41.98, 38.27, 31.89, 30.09, 28.68, 26.49, 26.25, 26.04, 20.90, 7.14; HRMS (ESI/[M+H]+) calcd. for $C_{22}H_{31}N_2O_2^+$: 355.2380. Found 355.2375.

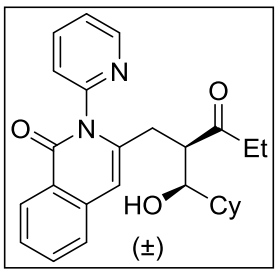


(±)-(1*R*,2*R*)-2-(4-Bromo-2-(1*H*-pyrazol-1-yl)benzyl)-1-cyclohexyl-1-hydroxypentan-3-one (4s): Derived from 1-(3-bromophenyl)-1*H*-pyrazole (44.6 mg, 0.200 mmol, 1.0 equiv), cyclohexanecarbaldehyde

(67.3 mg, 0.600 mmol, 3.0 equiv), and ethyl vinyl ketone (**2a**) (20.2 mg, 0.240 mmol, 1.2 equiv). Silica gel chromatography eluting with 10% ethyl acetate in dichloromethane provided the product **4s** as a mixture of diastereomers (74.9 mg, 89% yield, 92:8 dr) as a white solid (mp: 96–97 °C). IR (film): 3373 (br), 2929, 2853, 1710, 1518, 1405, 1050, 1034, 949, 756 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 1.5 Hz, 1H), 7.63 (d, *J* = 2.2 Hz, 1H), 7.47–7.42 (m, 2H), 7.20 (d, *J* = 8.7 Hz, 1H), 6.49 (t, *J* = 2.1 Hz, 1H), 3.14 (d, *J* = 8.8 Hz, 1H), 3.09 (dt, *J* = 8.0, 3.4 Hz, 1H), 2.95–2.82 (m, 3H), 2.26 (dq, *J* = 18.5, 7.2 Hz, 1H), 2.15 (dq, *J* = 18.5, 7.2 Hz, 1H), 1.80 (apparent d, *J* = 13.1 Hz, 1H), 1.70–1.65 (m, 2H), 1.60 (apparent d, *J* = 11.5 Hz, 1H), 1.45 (apparent d, *J* = 12.7 Hz, 1H), 1.17–1.01 (m, 4H), 0.88 (t, *J* = 7.2 Hz, 3H), 0.86–0.78 (m, 2H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 217.23, 141.11, 140.85, 134.15, 133.52, 131.81, 130.85, 129.62, 120.55, 107.29, 76.68, 52.40, 41.96, 38.38, 31.84, 30.10, 28.67, 26.45, 26.23, 26.00, 7.17; HRMS (ESI/[M+H]+) calcd. for $C_{21}H_{28}BrN_2O_2^+$: 419.1329. Found 419.1331.

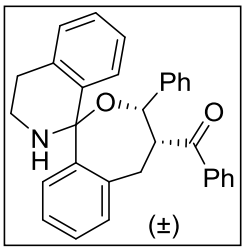


(±)-3-((*R*)-2-((*S*)-Hydroxy(phenyl)methyl)-3-oxopentyl)-2-(pyridin-2-yl)isoquinolin-1(2*H*)-one (4t): Derived from 2-(pyridin-2-yl)isoquinolin-1(2*H*)-one[S9] (**1b**) (44.4 mg, 0.200 mmol, 1.0 equiv), benzaldehyde (**3a**) (63.7 mg, 0.600 mmol, 3.0 equiv), and ethyl vinyl ketone (**2a**) (20.2 mg, 0.240 mmol, 1.2 equiv). Silica gel chromatography eluting with 1:3:6 dichloromethane/acetone/hexanes provided the product **4t** as a mixture of diastereomers (67.8 mg, 82% yield, 95:5 dr) as a white solid (mp: 150–151 °C). IR (film): 3370 (br), 3072, 2978, 2936, 1709, 1647, 1619, 1591, 1434, 1041, 748, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.32 (d, *J* = 7.9, 1H), 7.84 (t, *J* = 7.5 Hz, 1H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 8.3 Hz, 2H), 7.37–7.28 (m, 2H), 7.25–7.19 (m, 3H), 7.01 (d, *J* = 7.0 Hz, 2H), 6.34 (s, 1H), 4.56 (t, *J* = 6.0 Hz, 1H), 3.15 (br s, 1H), 2.85 (d, *J* = 5.8 Hz, 1H), 2.70 (t, *J* = 12.4 Hz, 1H), 2.37 (br s, 1H), 2.14–1.99 (m, 2H), 0.74 (t, *J* = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 215.43, 163.68, 151.82, 149.80, 141.75, 138.76, 138.54, 136.79, 133.14, 128.65, 128.14, 127.93, 126.95, 125.89, 125.86, 125.06, 124.56, 124.16, 107.45, 75.54, 56.08, 39.83, 33.81, 6.89; HRMS (ESI/[M+H]+) calcd. for $C_{26}H_{25}N_2O_3^+$: 413.1860. Found 413.1861.



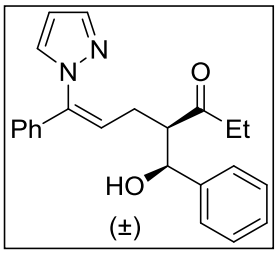
(±)-3-((*R*)-2-((*R*)-Cyclohexyl(hydroxy)methyl)-3-oxopentyl)-2-(pyridin-2-yl)isoquinolin-1(2*H*)-one (4u): Derived from 2-(pyridin-2-yl)isoquinolin-1(2*H*)-one[S9] (**1b**) (44.4 mg, 0.200 mmol, 1.0 equiv),

cyclohexanecarbaldehyde (67.3 mg, 0.600 mmol, 3.0 equiv), and ethyl vinyl ketone (**2a**) (20.2 mg, 0.240 mmol, 1.2 equiv). Silica gel chromatography eluting with 1:3:6 dichloromethane/acetone/hexanes provided the product **4u** as a mixture of diastereomers (55.7 mg, 67% yield, 98:2 dr) as a white solid (mp: 168–169 °C). IR (film): 3391 (br), 2932, 2853, 1715, 1648, 1619, 1587, 1431, 1396, 909, 732 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (d, *J* = 3.7 Hz, 1H), 8.34 (d, *J* = 7.9, 1H), 7.95 (dt, *J* = 7.8, 1.9 Hz, 1H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.48–7.44 (m, 4H), 6.39 (s, 1H), 3.07-3.00 (m, 2H), 2.76–2.65 (m, 3H), 2.24–2.19 (m, 1H), 2.07–2.01 (m, 1H), 1.69–1.59 (m, 3H), 1.50–1.43 (m, 2H), 1.16–0.99 (m, 4H), 0.88–0.76 (m, 5H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 216.88, 163.72, 152.09, 149.85, 138.73, 138.70, 136.80, 133.13, 128.12, 126.93, 125.90, 125.09, 124.90, 124.16, 107.61, 77.31, 50.36, 41.83, 38.96, 34.08, 30.04, 28.07, 26.30, 26.17, 25.96, 7.00; HRMS (ESI/[M+H]+) calcd. for $C_{26}H_{31}N_2O_3^+$: 419.2329. Found 419.2366.



(±)-Phenyl((3*S*,4*R*)-3-phenyl-3',4,4',5-tetrahydro-2'*H*,3*H*-spiro[benzo[c]oxepine-1,1'-isoquinolin]-4-yl)methanone (6): Derived from 1-phenyl-3,4-dihydroisoquinoline[S13] (**1c**) (41.5 mg, 0.200 mmol, 1.0 equiv), benzaldehyde (**3a**) (63.7 mg, 0.600 mmol, 3.0 equiv), and phenyl vinyl ketone[S7] (**2b**) (31.7 mg, 0.240 mmol, 1.2 equiv). The crude reaction mixture was quickly passed over a pad of silica gel with 25–50% acetone in hexanes (2 cm SiO_2 in a Pasteur pipet), and the solvent was removed under reduced pressure. Following this the residue was loaded onto a C18 reverse phase column as a solution in 0.5 mL of DMSO. Reverse phase purification was performed with 15.5 g of reverse phase media and a 50 column volume gradient from 15 to 65% MeOH:H_2O with only the H_2O eluent containing 0.1% TFA. Fractions containing product were combined and diluted with sat. aq. $NaHCO_3$ (50 mL) and extracted with ethyl acetate (3 × 100 mL). The combined organic layers were then washed with sat. aq. $NaHCO_3$ (50 mL) and brine (50 mL), dried over $MgSO_4$, and concentrated to afford the product **6** as a mixture of diastereomers (46.4 mg, 52% yield, 95:5 dr) as an off-white solid (mp: 83–85 °C). IR (film): 3064, 2939, 1734, 1667, 1597, 1447, 1199, 1146, 1002, 748, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.3 Hz, 2H), 7.63 (d, *J* = 7.3 Hz, 2H), 7.45 (t, *J* = 7.4 Hz, 1H), 7.43–7.40 (m, 2H), 7.38 (t, *J* = 7.7 Hz, 2H), 7.32 (t, *J* = 7.7 Hz, 2H), 7.30–7.25 (m, 2H), 7.24–7.19 (m, 2H), 7.19–7.15 (m, 1H), 7.12–7.07 (m, 2H), 7.04–6.99 (m, 1H), 5.52 (d, *J* = 10.0 Hz, 1H), 4.23 (ddd, *J* = 11.7, 10.0, 3.5 Hz, 1H), 3.94–3.87 (m, 1H), 3.53 (dd, *J* = 14.1, 11.7 Hz, 1H),

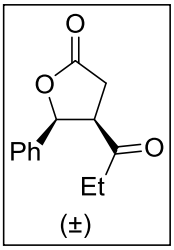
3.28–3.37 (m, 1H), 3.14 (dd, *J* = 14.1, 3.5 Hz, 1H), 3.11–3.06 (m, 1H), 2.91–2.85 (m, 1H); $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): δ 201.1, 142.5, 141.1, 139.3, 137.0, 133.8, 133.1, 130.1, 128.8, 128.7, 128.6, 128.4, 128.3, 128.2, 128.0, 128.0, 127.8, 127.6, 127.2, 127.1, 126.3, 91.3, 76.3, 53.2, 46.1, 44.4, 30.8; HRMS (ESI/[M+H]+) calcd. for $C_{31}H_{28}NO_2^+$: 446.2115. Found 446.2113.



(±)-(*R*,*Z*)-4-((*S*)-Hydroxy(phenyl)methyl)-7-phenyl-7-(1*H*-pyrazol-1-yl)hept-6-en-3-one (4v): Derived from 1-(1-phenylvinyl)-1*H*-pyrazole[S10] (**1d**) (34.0 mg, 0.200 mmol, 1.0 equiv), benzaldehyde (**3a**) (63.7 mg, 0.600 mmol, 3.0 equiv), and ethyl vinyl ketone (**2a**) (20.2 mg, 0.240 mmol, 1.2 equiv). The reaction was run in an oil bath at 40 °C instead of a 23 °C preset water bath. Silica gel chromatography eluting with 10% ethyl acetate in dichloromethane provided the product **4v** as a mixture of diastereomers (55.5 mg, 77% yield, 87:13 dr) as a colorless oil. IR (film): 3342 (br), 2975, 1708, 1448, 1397, 1042, 756, 697 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.33–7.28 (m, 8H), 7.25–7.20 (m, 1H), 7.08–7.06 (m, 2H), 6.37 (t, *J* = 2.1 Hz, 1H), 5.92 (dd, *J* = 8.9, 6.9 Hz, 1H), 4.92 (t, *J* = 5.4 Hz, 1H), 4.10 (d, *J* = 5.1 Hz, 1H), 3.11 (q, *J* = 6.9 Hz, 1H), 2.49 (dt, *J* = 14.4, 8.3 Hz, 1H), 2.36–2.28 (m, 2H), 2.21–2.13 (m, 1H), 0.89 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 214.28, 142.32, 140.91, 140.26, 137.42, 131.26, 128.91, 128.68, 128.55, 127.74, 126.35, 126.12, 123.12, 106.52, 74.14, 58.34, 38.03, 27.72, 7.31; HRMS (ESI/[M+H]+) calcd. for $C_{23}H_{25}N_2O_2^+$: 361.1911. Found 361.1914.

VI. Procedure for Synthesis of Lactone (±)-7:

Procedure for Synthesis of (±)-(4*R*,5*S*)-5-Phenyl-4-propionyldihydrofuran-2(3*H*)-one (7):

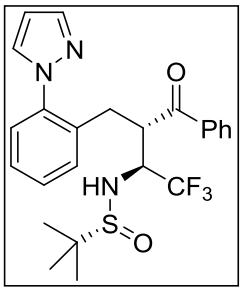


In a 0.5-2.0 mL microwave vial equipped with a magnetic stir bar, **4v** (36.1 mg, 0.100 mmol, 1.00 equiv) was dissolved in 1.5 mL of CH_2Cl_2. The reaction mixture was cooled in a dry ice/acetone bath and ozone was bubbled in until a faint blue color persisted for 5 min. At this point the reaction mixture was flushed with N_2 gas and kept under nitrogen for the duration of the reaction. Once the blue color had dissipated, triphenylphosphine (52.4 mg, 0.200 mol, 2.00 equiv) was added, and the reaction mixture was allowed to warm to ambient temperature and stirred for 1 h. The reaction mixture was concentrated and the crude material was dissolved in a minimal amount of CH_2Cl_2, and purified by silica gel chromatography using 30% ethyl acetate in hexanes to obtain the lactol intermediate as a colorless oil (Stains deep blue on p-anisaldehyde stain, R_f ~0.4). The lactol intermediate was then dissolved in 2.0 mL of benzene, and 570 mg of Fétizons reagent[S6] (~10 equiv) was added. The reaction mixture was then stirred for 1 h at reflux, and the reaction was complete upon a change in color from yellow to black (Note: due to the heterogeneous nature of the reagent, if incomplete color change is observed, simply add more reagent until the mixture becomes dark in color). The mixture was then let to cool to ambient temperature, was diluted with ethyl acetate, and was then filtered over a pad of celite, washing with ethyl acetate. The colorless solution was then concentrated to give the pure product **7** (13.5 mg, 62% yield, >98:2 dr) as a white solid without further purification. (mp: 69–70 °C). IR (film): 2974, 2942, 1775, 1702, 1301, 1194, 1160, 1113, 980, 758, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38–7.32 (m, 3H), 7.23 (d, *J* = 7.5 Hz, 2H), 5.73 (d, *J* = 7.6 Hz, 1H), 3.81 (dt, *J* = 8.0, 4.1 Hz, 1H), 3.04 (dd, *J* = 17.5, 4.1 Hz, 1H), 2.69 (dd, 17.5, 8.4 Hz, 1H), 2.01 (dq, *J* = 18.3, 7.2 Hz, 1H), 1.75 (dq, *J* = 18.3, 7.1 Hz, 1H), 0.61 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 207.76, 175.25, 135.29, 129.30, 128.97, 126.20, 81.73, 51.95, 37.39, 31.68, 7.02.; HRMS (ESI/[M+Na]+) calcd. for $C_{13}H_{14}O_3Na^+$: 241.0835. Found 241.0832.

VII. Procedures for Co(III)-Catalyzed Three-Component Synthesis of Amines

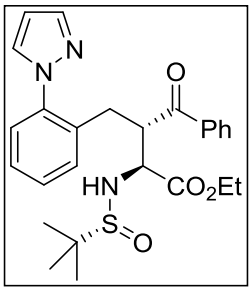
General Procedure:

In a N_2-filled glove box, a 0.5–2.0 mL microwave vial was charged with $[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$[S3] (32.6 mg, 0.0200 mmol, 0.10 equiv) and LiOAc (2.7 mg, 0.041 mmol, 0.20 equiv), and 1,4-dioxane (200 μL, [pyrazole = 1.0 M]) was added to the solid mixture. Following this, 1-phenyl-1*H*-pyrazole (**1a**) (28.8 mg, 0.200 mmol, 1.0 equiv), the indicated *N*-*tert*-butanesulfinyl imine (**11**) (0.600 mmol, 3.0 equiv), and phenyl vinyl ketone[S7] (**2b**) (31.7 mg, 0.240 mmol, 1.2 equiv) were added successively. The reaction vial was then equipped with a magnetic stir bar, sealed, and taken outside the glove box to stir at 65 °C in a preset oil bath for 20 h. Following this, the reaction mixture was then cooled to ambient temperature, uncapped, concentrated, and purified by chromatography to afford the desired product.



(*R*)-*N*-((2*S*,3*S*)-3-(2-(1*H*-Pyrazol-1-yl)benzyl)-1,1,1-trifluoro-4-oxo-4-phenylbutan-2-yl)-2-methylpropane-2-sulfinamide (12a): Derived from 1-phenyl-1*H*-pyrazole (**1a**) (28.8 mg, 0.200 mmol, 1.0 equiv), (*R*,*E*)-2-methyl-*N*-(2,2,2-trifluoroethylidene)propane-2-sulfinamide[S11] (**11a**) (121 mg, 0.600 mmol, 3.0 equiv), and phenyl vinyl ketone[S7] (**2b**) (31.7 mg, 0.240 mmol, 1.2 equiv). Analysis of unpurified material by ^{19}F NMR determined the reaction diastereoselectivity to be at minimum >94:6 dr for all possible stereoisomers. Silica gel chromatography eluting with 30% ethyl acetate in hexanes provided the first step in the purification process. Pure product was then obtained by silica gel chromatography using 75% diethyl ether in pentane to afford the product **12a** (61.8 mg, 65% yield, >98:2 dr) as a white powder (mp: 153–154 °C). IR (film): 1675, 1397, 1264, 1168, 1074, 925, 766, 684, 521 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.96 (d, *J* = 1.9 Hz, 1H), 7.94 (d, *J* = 1.9 Hz, 1H). 7.63 (d, *J* = 2.1 Hz, 1H), 7.08 (d, *J* = 2.4 Hz, 1H), 6.91–6.85 (m, 3H), 6.80 (d, *J* = 7.6 Hz, 1H), 6.76 (d, *J* = 7.6 Hz, 1H), 6.61 (dt, *J* = 7.6, 1.5 Hz, 1H), 6.51 (t, *J* = 7.6 Hz, 1H), 6.14 (t, *J* = 2.1 Hz, 1H), 4.77 (dt, *J* = 11.7, 2.7 Hz, 1H), 4.62–4.54 (m, 1H), 3.74 (dd, *J* = 13.5, 2.7 Hz, 1H), 3.62 (d, *J* = 8.6 Hz, 1H), 3.09 (t, *J* = 12.6 Hz, 1H), 1.04 (s, 9H); $^{13}C\{^1H\}$ NMR (151 MHz, C_6D_6): δ 201.1, 140.6, 140.0, 138.0, 134.1, 133.2, 132.4, 131.8, 128.7, 128.6, 128.5, 127.5, 126.2, 126.0 (q, *J* = 282.1 Hz),

106.8, 62.2 (q, J = 28.7 Hz), 56.7, 46.3, 35.7, 22.5; ^{19}F NMR (376 MHz, C_6D_6): δ -74.6 (d, J = 6.8 Hz, 3F); HRMS (ESI/[M+H]+) calcd. for $C_{24}H_{27}F_3N_3O_2S^+$: 478.1771. Found 478.1773.



Ethyl (2*S*,3*S*)-3-(2-(1*H*-pyrazol-1-yl)benzyl)-2-(((*R*)-*tert*-butylsulfinyl)amino)-4-oxo-4-phenylbutanoate (12b): Derived from 1-phenyl-1*H*-pyrazole (**1a**) (28.8 mg, 0.200 mmol, 1.0 equiv), ethyl (*R*,*E*)-2-((*tert*-butylsulfinyl)imino)acetate[S12] (**11b**) (123 mg, 0.600 mmol, 3.0 equiv), and phenyl vinyl ketone[S7] (**2b**) (31.7 mg, 0.240 mmol, 1.2 equiv). For the first step of the purification process the reaction mixture was loaded onto a C18 reverse phase column as a solution in 1 mL of DMSO. Reverse phase purification was performed with 15.5 g of reverse phase media and a 60 column volume gradient from 10 to 55% CH_3CN:H_2O containing 0.1% TFA. Fractions containing product were combined and diluted with sat. aq. $NaHCO_3$ (50 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were then washed with brine (50 mL), dried over $MgSO_4$, and concentrated. Pure product was then obtained by silica gel chromatography using 1:3:6 dichloromethane/acetone/hexanes as eluent to afford the product **12b** as a mixture of diastereomers (59.7 mg, 62% yield, 96:4 dr) as a colorless waxy solid. IR (film): 1735, 1673, 1394, 1190, 1071, 938, 759, 623, 510 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.74 (d, J = 1.8 Hz, 1H), 7.72–7.69 (m, 2H), 7.66 (d, J = 2.3 Hz, 1H), 7.41 (t, J = 7.4 Hz, 1H), 7.29–7.25 (m, 2H), 7.19–7.17 (m, 1H), 7.16–7.13 (m, 2H), 7.09–7.06 (m, 1H), 6.48 (t, J = 2.1 Hz, 1H), 4.27 (ddd, J = 9.8, 7.4, 5.2 Hz, 1H), 4.19 (t, J = 7.6 Hz, 1H), 4.04–3.99 (m, 1H), 3.98–3.93 (m, 1H), 3.85 (d, J = 7.6 Hz, 1H), 3.37 (dd, J = 13.8, 5.2 Hz, 1H), 3.01 (dd, J = 13.8, 9.8 Hz, 1H), 1.16 (s, 9H), 1.10 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 202.1, 171.2, 140.7, 139.9, 137.1, 134.1, 133.2, 132.2, 131.5, 128.7, 128.5, 128.4, 127.6, 126.5, 106.8, 61.6, 59.7, 56.7, 49.6, 32.7, 22.6, 14.0; HRMS (ESI/[M+H]+) calcd. for $C_{26}H_{32}N_3O_4S^+$: 482.2108. Found 482.2110.

VIII. X-Ray Crystallographic Data:

Single crystals of **4q** were obtained by slow evaporation of a concentrated solution of product **4q** in diethyl ether.

Experimental

Low-temperature diffraction data (ω-scans) were collected on a Rigaku MicroMax-007HF diffractometer coupled to a Saturn994+ CCD detector with Cu Kα (λ = 1.54178 Å) for the structure of **4q**. The diffraction images were processed and scaled using the Rigaku Oxford Diffraction software (CrysAlisPro; Rigaku OD: The Woodlands, TX, 2015). The structure was solved with SHELXT and was refined against F^2 on all data by full-matrix least squares with SHELXL (G. M. Sheldrick, *Acta Cryst*. **2008**, *A64*, 112). All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included in the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the U value of the atoms to which they are linked (1.5 times for methyl groups). The only exception is H1, which was found in the difference map and freely refined. The D...A distance was also refined as a part of this report (See Table 7). The full numbering scheme of compound **4q** can be found in the full details of the X-ray structure determination (CIF), which is included as Supporting Information. CCDC number 1471274 (**4q**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

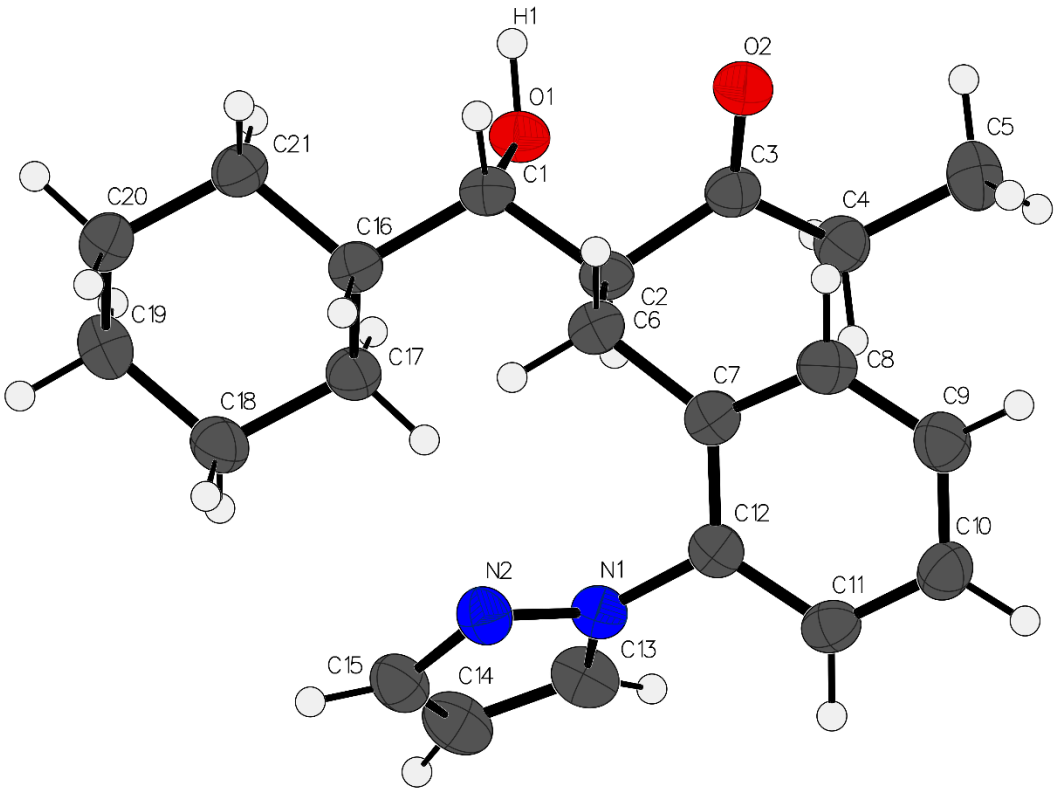


Figure 1. The complete numbering scheme of **4q** with 50% thermal ellipsoid probability levels. The hydrogen atoms are shown as circles for clarity.

Table 1. Crystal data and structure refinement for **4q**.

Identification code	007-16005	
Empirical formula	C21 H28 N2 O2	
Formula weight	340.45	
Temperature	93(2) K	
Wavelength	1.54184 Å	
Crystal system	Monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	a = 6.10754(10) Å	α= 90°.
	b = 15.2412(3) Å	β= 95.0631(16)°.
	c = 20.5393(4) Å	γ = 90°.
Volume	1904.47(6) $Å^3$	
Z	4	
Density (calculated)	1.187 Mg/m^3	
Absorption coefficient	0.601 mm^{-1}	
F(000)	736	
Crystal size	0.200 x 0.200 x 0.120 mm^3	
Theta range for data collection	3.616 to 68.254°.	
Index ranges	-7<=h<=7, -18<=k<=17, -24<=l<=24	
Reflections collected	69423	
Independent reflections	3477 [R(int) = 0.0488]	
Completeness to theta = 67.684°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.55716	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3477 / 0 / 231	
Goodness-of-fit on F^2	1.020	
Final R indices [I>2sigma(I)]	R1 = 0.0343, wR2 = 0.0853	
R indices (all data)	R1 = 0.0361, wR2 = 0.0869	
Largest diff. peak and hole	0.197 and -0.167 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 007-16005. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	6413(1)	7131(1)	2572(1)	31(1)
O(2)	6442(1)	6391(1)	1112(1)	38(1)
N(1)	3879(1)	3697(1)	2627(1)	30(1)
N(2)	5756(2)	3358(1)	2936(1)	33(1)
C(1)	7485(2)	6297(1)	2529(1)	28(1)
C(2)	5882(2)	5698(1)	2124(1)	28(1)
C(3)	5115(2)	6159(1)	1484(1)	30(1)
C(4)	2688(2)	6292(1)	1340(1)	34(1)
C(5)	1981(2)	6550(1)	641(1)	42(1)
C(6)	6886(2)	4804(1)	1955(1)	30(1)
C(7)	5154(2)	4230(1)	1600(1)	30(1)
C(8)	4885(2)	4220(1)	919(1)	35(1)
C(9)	3111(2)	3806(1)	580(1)	38(1)
C(10)	1547(2)	3394(1)	922(1)	36(1)
C(11)	1814(2)	3359(1)	1599(1)	32(1)
C(12)	3616(2)	3766(1)	1929(1)	29(1)
C(13)	2412(2)	3894(1)	3059(1)	39(1)
C(14)	3355(2)	3693(1)	3668(1)	43(1)
C(15)	5415(2)	3360(1)	3566(1)	37(1)
C(16)	8212(2)	5955(1)	3214(1)	28(1)
C(17)	6338(2)	5914(1)	3661(1)	33(1)
C(18)	7137(2)	5592(1)	4345(1)	38(1)
C(19)	9032(2)	6143(1)	4650(1)	37(1)
C(20)	10907(2)	6176(1)	4210(1)	34(1)
C(21)	10105(2)	6507(1)	3531(1)	32(1)

Table 3. Bond lengths [Å] and angles [°] for 007-16005.

O(1)-C(1)	1.4364(12)
O(1)-H(1)	0.942(18)
O(2)-C(3)	1.2144(13)
N(1)-C(13)	1.3486(14)
N(1)-N(2)	1.3622(12)
N(1)-C(12)	1.4325(14)
N(2)-C(15)	1.3276(15)
C(1)-C(2)	1.5297(14)
C(1)-C(16)	1.5304(14)
C(1)-H(1A)	1.0000
C(2)-C(3)	1.5262(14)
C(2)-C(6)	1.5456(14)
C(2)-H(2)	1.0000
C(3)-C(4)	1.4995(15)
C(4)-C(5)	1.5140(16)
C(4)-H(4A)	0.9900
C(4)-H(4B)	0.9900
C(5)-H(5A)	0.9800
C(5)-H(5B)	0.9800
C(5)-H(5C)	0.9800
C(6)-C(7)	1.5104(14)
C(6)-H(6A)	0.9900
C(6)-H(6B)	0.9900
C(7)-C(8)	1.3932(15)
C(7)-C(12)	1.3973(15)
C(8)-C(9)	1.3871(16)
C(8)-H(8)	0.9500
C(9)-C(10)	1.3847(17)
C(9)-H(9)	0.9500
C(10)-C(11)	1.3865(16)
C(10)-H(10)	0.9500
C(11)-C(12)	1.3878(15)
C(11)-H(11)	0.9500
C(13)-C(14)	1.3659(18)

C(13)-H(13)	0.9500
C(14)-C(15)	1.3896(18)
C(14)-H(14)	0.9500
C(15)-H(15)	0.9500
C(16)-C(21)	1.5283(14)
C(16)-C(17)	1.5304(14)
C(16)-H(16)	1.0000
C(17)-C(18)	1.5265(15)
C(17)-H(17A)	0.9900
C(17)-H(17B)	0.9900
C(18)-C(19)	1.5195(17)
C(18)-H(18A)	0.9900
C(18)-H(18B)	0.9900
C(19)-C(20)	1.5204(16)
C(19)-H(19A)	0.9900
C(19)-H(19B)	0.9900
C(20)-C(21)	1.5226(15)
C(20)-H(20A)	0.9900
C(20)-H(20B)	0.9900
C(21)-H(21A)	0.9900
C(21)-H(21B)	0.9900

C(1)-O(1)-H(1)	108.3(10)
C(13)-N(1)-N(2)	111.05(9)
C(13)-N(1)-C(12)	128.23(9)
N(2)-N(1)-C(12)	120.65(8)
C(15)-N(2)-N(1)	104.76(9)
O(1)-C(1)-C(2)	106.75(8)
O(1)-C(1)-C(16)	109.97(8)
C(2)-C(1)-C(16)	114.63(8)
O(1)-C(1)-H(1A)	108.4
C(2)-C(1)-H(1A)	108.4
C(16)-C(1)-H(1A)	108.4
C(3)-C(2)-C(1)	109.05(8)
C(3)-C(2)-C(6)	108.08(8)
C(1)-C(2)-C(6)	113.58(8)

C(3)-C(2)-H(2)	108.7
C(1)-C(2)-H(2)	108.7
C(6)-C(2)-H(2)	108.7
O(2)-C(3)-C(4)	122.57(10)
O(2)-C(3)-C(2)	120.29(9)
C(4)-C(3)-C(2)	117.14(9)
C(3)-C(4)-C(5)	114.69(9)
C(3)-C(4)-H(4A)	108.6
C(5)-C(4)-H(4A)	108.6
C(3)-C(4)-H(4B)	108.6
C(5)-C(4)-H(4B)	108.6
H(4A)-C(4)-H(4B)	107.6
C(4)-C(5)-H(5A)	109.5
C(4)-C(5)-H(5B)	109.5
H(5A)-C(5)-H(5B)	109.5
C(4)-C(5)-H(5C)	109.5
H(5A)-C(5)-H(5C)	109.5
H(5B)-C(5)-H(5C)	109.5
C(7)-C(6)-C(2)	110.14(8)
C(7)-C(6)-H(6A)	109.6
C(2)-C(6)-H(6A)	109.6
C(7)-C(6)-H(6B)	109.6
C(2)-C(6)-H(6B)	109.6
H(6A)-C(6)-H(6B)	108.1
C(8)-C(7)-C(12)	117.07(10)
C(8)-C(7)-C(6)	120.48(10)
C(12)-C(7)-C(6)	122.09(10)
C(9)-C(8)-C(7)	121.82(11)
C(9)-C(8)-H(8)	119.1
C(7)-C(8)-H(8)	119.1
C(10)-C(9)-C(8)	119.63(11)
C(10)-C(9)-H(9)	120.2
C(8)-C(9)-H(9)	120.2
C(9)-C(10)-C(11)	120.05(11)
C(9)-C(10)-H(10)	120.0
C(11)-C(10)-H(10)	120.0

C(10)-C(11)-C(12)	119.42(10)
C(10)-C(11)-H(11)	120.3
C(12)-C(11)-H(11)	120.3
C(11)-C(12)-C(7)	121.85(10)
C(11)-C(12)-N(1)	118.09(10)
C(7)-C(12)-N(1)	120.06(9)
N(1)-C(13)-C(14)	107.53(11)
N(1)-C(13)-H(13)	126.2
C(14)-C(13)-H(13)	126.2
C(13)-C(14)-C(15)	104.91(10)
C(13)-C(14)-H(14)	127.5
C(15)-C(14)-H(14)	127.5
N(2)-C(15)-C(14)	111.75(11)
N(2)-C(15)-H(15)	124.1
C(14)-C(15)-H(15)	124.1
C(21)-C(16)-C(1)	110.56(8)
C(21)-C(16)-C(17)	110.21(9)
C(1)-C(16)-C(17)	113.21(8)
C(21)-C(16)-H(16)	107.5
C(1)-C(16)-H(16)	107.5
C(17)-C(16)-H(16)	107.5
C(18)-C(17)-C(16)	111.69(9)
C(18)-C(17)-H(17A)	109.3
C(16)-C(17)-H(17A)	109.3
C(18)-C(17)-H(17B)	109.3
C(16)-C(17)-H(17B)	109.3
H(17A)-C(17)-H(17B)	107.9
C(19)-C(18)-C(17)	111.78(9)
C(19)-C(18)-H(18A)	109.3
C(17)-C(18)-H(18A)	109.3
C(19)-C(18)-H(18B)	109.3
C(17)-C(18)-H(18B)	109.3
H(18A)-C(18)-H(18B)	107.9
C(18)-C(19)-C(20)	111.13(9)
C(18)-C(19)-H(19A)	109.4
C(20)-C(19)-H(19A)	109.4

C(18)-C(19)-H(19B)	109.4
C(20)-C(19)-H(19B)	109.4
H(19A)-C(19)-H(19B)	108.0
C(19)-C(20)-C(21)	110.88(9)
C(19)-C(20)-H(20A)	109.5
C(21)-C(20)-H(20A)	109.5
C(19)-C(20)-H(20B)	109.5
C(21)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	108.1
C(20)-C(21)-C(16)	112.16(9)
C(20)-C(21)-H(21A)	109.2
C(16)-C(21)-H(21A)	109.2
C(20)-C(21)-H(21B)	109.2
C(16)-C(21)-H(21B)	109.2
H(21A)-C(21)-H(21B)	107.9

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for 007-16005. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	32(1)	25(1)	38(1)	2(1)	7(1)	2(1)
O(2)	35(1)	45(1)	34(1)	5(1)	6(1)	-5(1)
N(1)	31(1)	26(1)	32(1)	0(1)	5(1)	3(1)
N(2)	35(1)	30(1)	34(1)	1(1)	2(1)	5(1)
C(1)	26(1)	25(1)	32(1)	0(1)	6(1)	1(1)
C(2)	26(1)	28(1)	30(1)	1(1)	6(1)	0(1)
C(3)	32(1)	27(1)	31(1)	-2(1)	5(1)	-2(1)
C(4)	31(1)	36(1)	35(1)	2(1)	4(1)	2(1)
C(5)	39(1)	50(1)	36(1)	1(1)	-1(1)	6(1)
C(6)	28(1)	29(1)	34(1)	-2(1)	5(1)	1(1)
C(7)	30(1)	25(1)	34(1)	-2(1)	4(1)	3(1)
C(8)	38(1)	32(1)	34(1)	-1(1)	7(1)	-2(1)
C(9)	45(1)	35(1)	32(1)	-1(1)	1(1)	-2(1)
C(10)	37(1)	32(1)	40(1)	-1(1)	-3(1)	-2(1)
C(11)	31(1)	27(1)	40(1)	0(1)	5(1)	0(1)
C(12)	31(1)	25(1)	32(1)	-1(1)	4(1)	5(1)
C(13)	41(1)	36(1)	41(1)	1(1)	13(1)	9(1)
C(14)	56(1)	39(1)	36(1)	1(1)	15(1)	6(1)
C(15)	49(1)	31(1)	32(1)	2(1)	2(1)	1(1)
C(16)	27(1)	25(1)	33(1)	0(1)	4(1)	2(1)
C(17)	28(1)	39(1)	34(1)	6(1)	4(1)	-1(1)
C(18)	32(1)	48(1)	36(1)	10(1)	6(1)	1(1)
C(19)	39(1)	41(1)	30(1)	1(1)	2(1)	7(1)
C(20)	31(1)	35(1)	36(1)	-2(1)	0(1)	-1(1)
C(21)	29(1)	34(1)	34(1)	-1(1)	4(1)	-3(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for 007-16005.

	x	y	z	U(eq)
H(1)	7320(30)	7565(11)	2412(8)	62(4)
H(1A)	8822	6379	2287	33
H(2)	4576	5590	2374	33
H(4A)	2203	6754	1634	41
H(4B)	1925	5742	1441	41
H(5A)	2266	6063	348	63
H(5B)	2813	7067	522	63
H(5C)	407	6687	599	63
H(6A)	8108	4898	1677	36
H(6B)	7486	4509	2362	36
H(8)	5946	4503	681	42
H(9)	2969	3805	116	45
H(10)	291	3136	692	44
H(11)	772	3058	1834	39
H(13)	983	4130	2957	46
H(14)	2738	3764	4074	52
H(15)	6452	3159	3905	45
H(16)	8774	5344	3167	34
H(17A)	5682	6505	3693	40
H(17B)	5180	5513	3468	40
H(18A)	5905	5615	4628	46
H(18B)	7616	4973	4320	46
H(19A)	9571	5891	5078	44
H(19B)	8508	6747	4724	44
H(20A)	11543	5582	4175	41
H(20B)	12077	6570	4406	41
H(21A)	11340	6495	3250	39
H(21B)	9614	7124	3563	39

Table 6. Torsion angles [°] for 007-16005.

C(13)-N(1)-N(2)-C(15)	-0.62(12)
C(12)-N(1)-N(2)-C(15)	-177.72(9)
O(1)-C(1)-C(2)-C(3)	52.17(10)
C(16)-C(1)-C(2)-C(3)	174.20(8)
O(1)-C(1)-C(2)-C(6)	172.77(8)
C(16)-C(1)-C(2)-C(6)	-65.21(11)
C(1)-C(2)-C(3)-O(2)	58.44(13)
C(6)-C(2)-C(3)-O(2)	-65.47(12)
C(1)-C(2)-C(3)-C(4)	-122.51(10)
C(6)-C(2)-C(3)-C(4)	113.57(10)
O(2)-C(3)-C(4)-C(5)	12.83(16)
C(2)-C(3)-C(4)-C(5)	-166.19(10)
C(3)-C(2)-C(6)-C(7)	-63.02(11)
C(1)-C(2)-C(6)-C(7)	175.84(9)
C(2)-C(6)-C(7)-C(8)	93.27(11)
C(2)-C(6)-C(7)-C(12)	-79.67(12)
C(12)-C(7)-C(8)-C(9)	3.18(16)
C(6)-C(7)-C(8)-C(9)	-170.10(10)
C(7)-C(8)-C(9)-C(10)	0.36(17)
C(8)-C(9)-C(10)-C(11)	-3.16(17)
C(9)-C(10)-C(11)-C(12)	2.28(16)
C(10)-C(11)-C(12)-C(7)	1.43(16)
C(10)-C(11)-C(12)-N(1)	-178.27(9)
C(8)-C(7)-C(12)-C(11)	-4.09(15)
C(6)-C(7)-C(12)-C(11)	169.08(10)
C(8)-C(7)-C(12)-N(1)	175.60(9)
C(6)-C(7)-C(12)-N(1)	-11.23(15)
C(13)-N(1)-C(12)-C(11)	-53.26(15)
N(2)-N(1)-C(12)-C(11)	123.30(10)
C(13)-N(1)-C(12)-C(7)	127.04(12)
N(2)-N(1)-C(12)-C(7)	-56.41(13)
N(2)-N(1)-C(13)-C(14)	0.92(13)
C(12)-N(1)-C(13)-C(14)	177.74(10)
N(1)-C(13)-C(14)-C(15)	-0.82(14)

N(1)-N(2)-C(15)-C(14)	0.08(13)
C(13)-C(14)-C(15)-N(2)	0.46(14)
O(1)-C(1)-C(16)-C(21)	-69.95(10)
C(2)-C(1)-C(16)-C(21)	169.79(8)
O(1)-C(1)-C(16)-C(17)	54.26(11)
C(2)-C(1)-C(16)-C(17)	-66.00(12)
C(21)-C(16)-C(17)-C(18)	-54.16(12)
C(1)-C(16)-C(17)-C(18)	-178.55(9)
C(16)-C(17)-C(18)-C(19)	54.89(13)
C(17)-C(18)-C(19)-C(20)	-55.21(13)
C(18)-C(19)-C(20)-C(21)	55.48(13)
C(19)-C(20)-C(21)-C(16)	-56.21(12)
C(1)-C(16)-C(21)-C(20)	-178.87(9)
C(17)-C(16)-C(21)-C(20)	55.22(12)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for 007-16005 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1)...N(2)#1	0.942(18)	1.869(18)	2.8096(12)	175.6(15)

Symmetry transformations used to generate equivalent atoms:
#1 -x+3/2,y+1/2,-z+1/2

Single crystals of **12a** were obtained by slow evaporation of a concentrated solution of product **12a** in diethyl ether.

Experimental

Low-temperature diffraction data (ω-scans) were collected on a Rigaku MicroMax-007HF diffractometer coupled to a Saturn994+ CCD detector with Cu Kα (λ = 1.54178 Å) for the structure of **12a**. The diffraction images were processed and scaled using the Rigaku Oxford Diffraction software (CrysAlisPro; Rigaku OD: The Woodlands, TX, 2015). The structure was solved with SHELXT and was refined against F^2 on all data by full-matrix least squares with SHELXL (G. M. Sheldrick, *Acta Cryst*. **2008**, *A64*, 112). All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included in the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the U value of the atoms to which they are linked (1.5 times for methyl groups). The full numbering scheme of compound **12a** can be found in the full details of the X-ray structure determination (CIF), which is included as Supporting Information. CCDC number 1471275 (**12a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

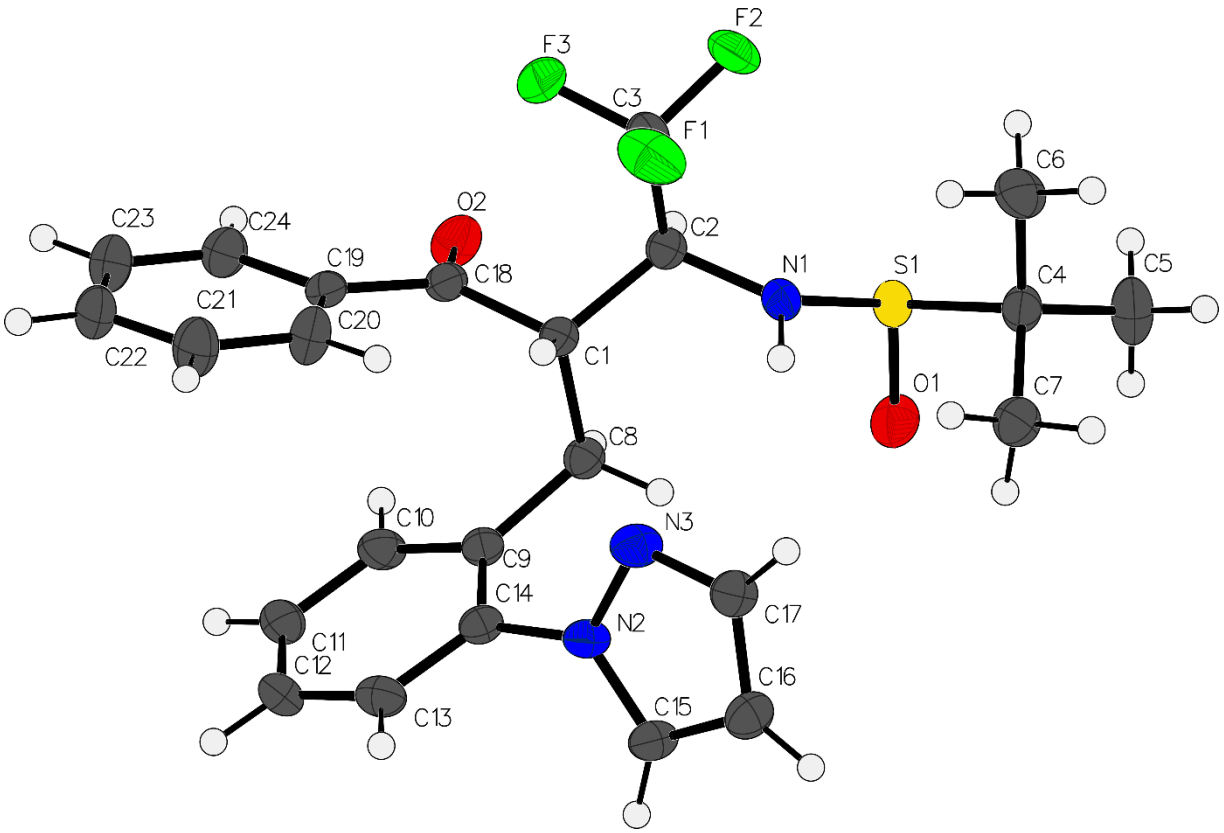


Figure 2. The complete numbering scheme of **12a** with 50% thermal ellipsoid probability levels. The hydrogen atoms are shown as circles for clarity.

Table 8. Crystal data and structure refinement for **12a**.

Identification code	007-16032	
Empirical formula	C24 H26 F3 N3 O2 S	
Formula weight	477.54	
Temperature	93(2) K	
Wavelength	1.54178 Å	
Crystal system	Trigonal	
Space group	$P3_1$	
Unit cell dimensions	a = 18.8083(9) Å	α= 90°.
	b = 18.8083(9) Å	β= 90°.
	c = 5.8941(4) Å	γ = 120°.
Volume	1805.7(2) $Å^3$	
Z	3	
Density (calculated)	1.317 Mg/m^3	
Absorption coefficient	1.622 mm^{-1}	
F(000)	750	
Crystal size	0.200 x 0.190 x 0.120 mm^3	
Theta range for data collection	2.713 to 67.840°.	
Index ranges	-22<=h<=22, -22<=k<=21, -7<=l<=7	
Reflections collected	62695	
Independent reflections	4346 [R(int) = 0.1013]	
Completeness to theta = 67.679°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.000 and 0.741	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4346 / 1 / 305	
Goodness-of-fit on F^2	1.038	
Final R indices [I>2sigma(I)]	R1 = 0.0312, wR2 = 0.0718	
R indices (all data)	R1 = 0.0360, wR2 = 0.0739	
Absolute structure parameter	0.016(9)	
Largest diff. peak and hole	0.199 and -0.143 $e.Å^{-3}$	

Table 9. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 007-16032. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	5180(1)	4142(1)	7106(1)	24(1)
F(1)	4223(1)	2183(1)	4592(3)	37(1)
F(2)	3626(1)	2526(1)	2062(3)	48(1)
F(3)	2909(1)	1619(1)	4564(4)	55(1)
O(1)	5142(1)	4780(1)	8475(4)	34(1)
O(2)	2251(1)	2114(1)	8531(4)	33(1)
N(1)	4433(1)	3746(2)	5202(4)	23(1)
N(2)	2974(2)	4969(1)	3655(4)	24(1)
N(3)	3353(2)	4661(2)	2349(4)	29(1)
C(1)	2913(2)	3108(2)	5664(5)	21(1)
C(2)	3676(2)	3010(2)	5806(5)	23(1)
C(3)	3605(2)	2336(2)	4251(6)	33(1)
C(4)	6057(2)	4702(2)	5175(5)	26(1)
C(5)	6798(2)	5092(2)	6754(6)	42(1)
C(6)	6099(2)	4084(2)	3581(6)	36(1)
C(7)	5977(2)	5356(2)	3865(5)	30(1)
C(8)	3028(2)	3857(2)	7054(5)	22(1)
C(9)	2303(2)	3983(2)	6737(5)	21(1)
C(10)	1616(2)	3584(2)	8135(5)	27(1)
C(11)	914(2)	3630(2)	7759(5)	31(1)
C(12)	876(2)	4079(2)	5959(5)	30(1)
C(13)	1555(2)	4499(2)	4574(5)	28(1)
C(14)	2262(2)	4459(2)	4986(4)	22(1)
C(15)	3379(2)	5795(2)	3627(5)	27(1)
C(16)	4044(2)	6048(2)	2236(5)	30(1)
C(17)	3996(2)	5321(2)	1481(5)	27(1)
C(18)	2171(2)	2351(2)	6677(5)	22(1)
C(19)	1358(2)	1967(2)	5535(5)	22(1)
C(20)	1235(2)	2220(2)	3429(5)	32(1)
C(21)	459(2)	1877(2)	2518(6)	36(1)
C(22)	-207(2)	1275(2)	3681(6)	35(1)

C(23)	-88(2)	1007(2)	5743(6)	39(1)
C(24)	683(2)	1349(2)	6668(5)	31(1)

Table 10. Bond lengths [Å] and angles [°] for 007-16032.

S(1)-O(1)	1.478(2)
S(1)-N(1)	1.656(2)
S(1)-C(4)	1.840(3)
F(1)-C(3)	1.345(3)
F(2)-C(3)	1.333(4)
F(3)-C(3)	1.342(4)
O(2)-C(18)	1.218(3)
N(1)-C(2)	1.449(4)
N(1)-H(1)	0.83(4)
N(2)-C(15)	1.346(4)
N(2)-N(3)	1.360(3)
N(2)-C(14)	1.429(4)
N(3)-C(17)	1.327(4)
C(1)-C(18)	1.531(4)
C(1)-C(2)	1.538(4)
C(1)-C(8)	1.548(4)
C(1)-H(1A)	1.0000
C(2)-C(3)	1.515(4)
C(2)-H(2)	1.0000
C(4)-C(7)	1.521(4)
C(4)-C(5)	1.525(4)
C(4)-C(6)	1.527(4)
C(5)-H(5A)	0.9800
C(5)-H(5B)	0.9800
C(5)-H(5C)	0.9800
C(6)-H(6A)	0.9800
C(6)-H(6B)	0.9800
C(6)-H(6C)	0.9800
C(7)-H(7A)	0.9800
C(7)-H(7B)	0.9800
C(7)-H(7C)	0.9800
C(8)-C(9)	1.508(4)
C(8)-H(8A)	0.9900
C(8)-H(8B)	0.9900

C(9)-C(10)	1.393(4)
C(9)-C(14)	1.393(4)
C(10)-C(11)	1.384(4)
C(10)-H(10)	0.9500
C(11)-C(12)	1.379(5)
C(11)-H(11)	0.9500
C(12)-C(13)	1.384(4)
C(12)-H(12)	0.9500
C(13)-C(14)	1.390(4)
C(13)-H(13)	0.9500
C(15)-C(16)	1.366(4)
C(15)-H(15)	0.9500
C(16)-C(17)	1.396(4)
C(16)-H(16)	0.9500
C(17)-H(17)	0.9500
C(18)-C(19)	1.487(4)
C(19)-C(20)	1.389(4)
C(19)-C(24)	1.390(4)
C(20)-C(21)	1.376(4)
C(20)-H(20)	0.9500
C(21)-C(22)	1.379(5)
C(21)-H(21)	0.9500
C(22)-C(23)	1.377(5)
C(22)-H(22)	0.9500
C(23)-C(24)	1.373(5)
C(23)-H(23)	0.9500
C(24)-H(24)	0.9500

O(1)-S(1)-N(1)	111.07(13)
O(1)-S(1)-C(4)	105.45(13)
N(1)-S(1)-C(4)	98.87(13)
C(2)-N(1)-S(1)	118.1(2)
C(2)-N(1)-H(1)	118(2)
S(1)-N(1)-H(1)	113(2)
C(15)-N(2)-N(3)	111.7(2)
C(15)-N(2)-C(14)	125.5(2)

N(3)-N(2)-C(14)	122.7(2)
C(17)-N(3)-N(2)	104.3(2)
C(18)-C(1)-C(2)	109.7(2)
C(18)-C(1)-C(8)	106.7(2)
C(2)-C(1)-C(8)	111.4(2)
C(18)-C(1)-H(1A)	109.6
C(2)-C(1)-H(1A)	109.6
C(8)-C(1)-H(1A)	109.6
N(1)-C(2)-C(3)	106.5(2)
N(1)-C(2)-C(1)	113.7(2)
C(3)-C(2)-C(1)	111.7(2)
N(1)-C(2)-H(2)	108.2
C(3)-C(2)-H(2)	108.2
C(1)-C(2)-H(2)	108.2
F(2)-C(3)-F(3)	106.6(3)
F(2)-C(3)-F(1)	106.8(3)
F(3)-C(3)-F(1)	106.1(2)
F(2)-C(3)-C(2)	112.6(3)
F(3)-C(3)-C(2)	113.0(3)
F(1)-C(3)-C(2)	111.4(2)
C(7)-C(4)-C(5)	110.9(3)
C(7)-C(4)-C(6)	111.5(3)
C(5)-C(4)-C(6)	111.0(3)
C(7)-C(4)-S(1)	110.8(2)
C(5)-C(4)-S(1)	103.9(2)
C(6)-C(4)-S(1)	108.5(2)
C(4)-C(5)-H(5A)	109.5
C(4)-C(5)-H(5B)	109.5
H(5A)-C(5)-H(5B)	109.5
C(4)-C(5)-H(5C)	109.5
H(5A)-C(5)-H(5C)	109.5
H(5B)-C(5)-H(5C)	109.5
C(4)-C(6)-H(6A)	109.5
C(4)-C(6)-H(6B)	109.5
H(6A)-C(6)-H(6B)	109.5
C(4)-C(6)-H(6C)	109.5

H(6A)-C(6)-H(6C)	109.5
H(6B)-C(6)-H(6C)	109.5
C(4)-C(7)-H(7A)	109.5
C(4)-C(7)-H(7B)	109.5
H(7A)-C(7)-H(7B)	109.5
C(4)-C(7)-H(7C)	109.5
H(7A)-C(7)-H(7C)	109.5
H(7B)-C(7)-H(7C)	109.5
C(9)-C(8)-C(1)	110.6(2)
C(9)-C(8)-H(8A)	109.5
C(1)-C(8)-H(8A)	109.5
C(9)-C(8)-H(8B)	109.5
C(1)-C(8)-H(8B)	109.5
H(8A)-C(8)-H(8B)	108.1
C(10)-C(9)-C(14)	116.7(2)
C(10)-C(9)-C(8)	120.7(2)
C(14)-C(9)-C(8)	122.5(2)
C(11)-C(10)-C(9)	121.9(3)
C(11)-C(10)-H(10)	119.0
C(9)-C(10)-H(10)	119.0
C(12)-C(11)-C(10)	120.3(3)
C(12)-C(11)-H(11)	119.9
C(10)-C(11)-H(11)	119.9
C(11)-C(12)-C(13)	119.2(3)
C(11)-C(12)-H(12)	120.4
C(13)-C(12)-H(12)	120.4
C(12)-C(13)-C(14)	120.1(3)
C(12)-C(13)-H(13)	120.0
C(14)-C(13)-H(13)	120.0
C(13)-C(14)-C(9)	121.7(3)
C(13)-C(14)-N(2)	118.0(2)
C(9)-C(14)-N(2)	120.2(2)
N(2)-C(15)-C(16)	107.5(3)
N(2)-C(15)-H(15)	126.3
C(16)-C(15)-H(15)	126.3
C(15)-C(16)-C(17)	104.5(3)

C(15)-C(16)-H(16)	127.7
C(17)-C(16)-H(16)	127.7
N(3)-C(17)-C(16)	112.1(3)
N(3)-C(17)-H(17)	124.0
C(16)-C(17)-H(17)	124.0
O(2)-C(18)-C(19)	120.9(3)
O(2)-C(18)-C(1)	118.0(3)
C(19)-C(18)-C(1)	120.8(2)
C(20)-C(19)-C(24)	118.5(3)
C(20)-C(19)-C(18)	123.0(3)
C(24)-C(19)-C(18)	118.4(3)
C(21)-C(20)-C(19)	120.5(3)
C(21)-C(20)-H(20)	119.8
C(19)-C(20)-H(20)	119.8
C(20)-C(21)-C(22)	120.4(3)
C(20)-C(21)-H(21)	119.8
C(22)-C(21)-H(21)	119.8
C(23)-C(22)-C(21)	119.5(3)
C(23)-C(22)-H(22)	120.2
C(21)-C(22)-H(22)	120.2
C(24)-C(23)-C(22)	120.4(3)
C(24)-C(23)-H(23)	119.8
C(22)-C(23)-H(23)	119.8
C(23)-C(24)-C(19)	120.7(3)
C(23)-C(24)-H(24)	119.7
C(19)-C(24)-H(24)	119.7

Symmetry transformations used to generate equivalent atoms:

Table 11. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for 007-16032. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	20(1)	26(1)	23(1)	-2(1)	-2(1)	10(1)
F(1)	34(1)	40(1)	49(1)	-10(1)	-6(1)	28(1)
F(2)	60(1)	66(1)	38(1)	-26(1)	-20(1)	46(1)
F(3)	32(1)	28(1)	102(2)	-27(1)	-4(1)	11(1)
O(1)	31(1)	34(1)	34(1)	-10(1)	1(1)	12(1)
O(2)	34(1)	28(1)	32(1)	8(1)	-4(1)	11(1)
N(1)	20(1)	24(1)	26(1)	1(1)	-1(1)	12(1)
N(2)	29(1)	22(1)	23(1)	1(1)	3(1)	15(1)
N(3)	37(2)	27(1)	26(1)	1(1)	8(1)	18(1)
C(1)	20(1)	19(1)	23(1)	-2(1)	-2(1)	10(1)
C(2)	22(1)	22(1)	24(1)	-2(1)	-3(1)	10(1)
C(3)	24(2)	31(2)	46(2)	-9(1)	-8(1)	15(1)
C(4)	20(2)	25(2)	31(2)	3(1)	0(1)	9(1)
C(5)	22(2)	49(2)	44(2)	4(2)	-2(1)	10(2)
C(6)	34(2)	36(2)	42(2)	4(2)	13(2)	20(2)
C(7)	29(2)	30(2)	31(2)	4(1)	4(1)	14(1)
C(8)	22(1)	22(1)	22(1)	-1(1)	0(1)	10(1)
C(9)	23(1)	20(1)	21(1)	-4(1)	-1(1)	11(1)
C(10)	31(2)	25(2)	29(2)	6(1)	6(1)	16(1)
C(11)	27(2)	28(2)	41(2)	2(1)	10(1)	15(1)
C(12)	26(2)	30(2)	41(2)	-2(1)	-1(1)	18(1)
C(13)	33(2)	28(2)	29(2)	-1(1)	-3(1)	19(1)
C(14)	26(2)	19(1)	22(1)	-3(1)	-1(1)	11(1)
C(15)	32(2)	21(2)	29(2)	0(1)	1(1)	14(1)
C(16)	31(2)	24(2)	30(2)	4(1)	3(1)	11(1)
C(17)	29(2)	28(2)	24(1)	4(1)	4(1)	14(1)
C(18)	23(2)	19(1)	24(2)	0(1)	1(1)	10(1)
C(19)	22(1)	17(1)	26(1)	-2(1)	1(1)	10(1)
C(20)	23(2)	32(2)	29(2)	3(1)	-2(1)	6(1)
C(21)	28(2)	40(2)	34(2)	-1(1)	-8(1)	12(2)
C(22)	22(2)	31(2)	45(2)	-6(1)	-4(1)	9(1)

C(23)	24(2)	33(2)	51(2)	4(2)	6(1)	8(1)
C(24)	27(2)	28(2)	33(2)	4(1)	5(1)	11(1)

Table 12. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for 007-16032.

	x	y	z	U(eq)
H(1)	4410(20)	4100(20)	4420(60)	32(9)
H(1A)	2800	3173	4042	25
H(2)	3728	2860	7401	27
H(5A)	6753	5481	7770	62
H(5B)	7301	5384	5852	62
H(5C)	6815	4663	7654	62
H(6A)	6109	3650	4476	54
H(6B)	6598	4364	2659	54
H(6C)	5617	3842	2587	54
H(7A)	5526	5091	2771	46
H(7B)	6490	5709	3055	46
H(7C)	5862	5688	4924	46
H(8A)	3087	3767	8682	26
H(8B)	3536	4355	6557	26
H(10)	1631	3272	9382	32
H(11)	456	3352	8745	38
H(12)	389	4099	5674	36
H(13)	1539	4815	3339	34
H(15)	3231	6140	4428	33
H(16)	4448	6595	1865	36
H(17)	4378	5301	466	32
H(20)	1690	2632	2611	38
H(21)	381	2057	1080	43
H(22)	-744	1048	3063	42
H(23)	-543	582	6531	47
H(24)	757	1161	8097	37

Table 13. Torsion angles [°] for 007-16032.

O(1)-S(1)-N(1)-C(2)	-93.4(2)
C(4)-S(1)-N(1)-C(2)	156.2(2)
C(15)-N(2)-N(3)-C(17)	-1.1(3)
C(14)-N(2)-N(3)-C(17)	-177.4(3)
S(1)-N(1)-C(2)-C(3)	-114.6(2)
S(1)-N(1)-C(2)-C(1)	121.9(2)
C(18)-C(1)-C(2)-N(1)	-171.3(2)
C(8)-C(1)-C(2)-N(1)	-53.3(3)
C(18)-C(1)-C(2)-C(3)	68.2(3)
C(8)-C(1)-C(2)-C(3)	-173.8(2)
N(1)-C(2)-C(3)-F(2)	-56.7(3)
C(1)-C(2)-C(3)-F(2)	68.0(3)
N(1)-C(2)-C(3)-F(3)	-177.5(2)
C(1)-C(2)-C(3)-F(3)	-52.8(3)
N(1)-C(2)-C(3)-F(1)	63.1(3)
C(1)-C(2)-C(3)-F(1)	-172.1(2)
O(1)-S(1)-C(4)-C(7)	-53.3(2)
N(1)-S(1)-C(4)-C(7)	61.5(2)
O(1)-S(1)-C(4)-C(5)	65.8(2)
N(1)-S(1)-C(4)-C(5)	-179.3(2)
O(1)-S(1)-C(4)-C(6)	-176.0(2)
N(1)-S(1)-C(4)-C(6)	-61.1(2)
C(18)-C(1)-C(8)-C(9)	-64.8(3)
C(2)-C(1)-C(8)-C(9)	175.4(2)
C(1)-C(8)-C(9)-C(10)	88.1(3)
C(1)-C(8)-C(9)-C(14)	-88.2(3)
C(14)-C(9)-C(10)-C(11)	2.4(4)
C(8)-C(9)-C(10)-C(11)	-174.1(3)
C(9)-C(10)-C(11)-C(12)	0.1(4)
C(10)-C(11)-C(12)-C(13)	-1.7(4)
C(11)-C(12)-C(13)-C(14)	0.7(4)
C(12)-C(13)-C(14)-C(9)	1.9(4)
C(12)-C(13)-C(14)-N(2)	-173.8(3)
C(10)-C(9)-C(14)-C(13)	-3.4(4)

C(8)-C(9)-C(14)-C(13)	173.0(3)
C(10)-C(9)-C(14)-N(2)	172.2(2)
C(8)-C(9)-C(14)-N(2)	-11.3(4)
C(15)-N(2)-C(14)-C(13)	62.5(4)
N(3)-N(2)-C(14)-C(13)	-121.6(3)
C(15)-N(2)-C(14)-C(9)	-113.3(3)
N(3)-N(2)-C(14)-C(9)	62.6(3)
N(3)-N(2)-C(15)-C(16)	0.8(3)
C(14)-N(2)-C(15)-C(16)	177.0(3)
N(2)-C(15)-C(16)-C(17)	-0.2(3)
N(2)-N(3)-C(17)-C(16)	1.0(3)
C(15)-C(16)-C(17)-N(3)	-0.5(4)
C(2)-C(1)-C(18)-O(2)	49.0(3)
C(8)-C(1)-C(18)-O(2)	-71.9(3)
C(2)-C(1)-C(18)-C(19)	-136.8(3)
C(8)-C(1)-C(18)-C(19)	102.3(3)
O(2)-C(18)-C(19)-C(20)	179.6(3)
C(1)-C(18)-C(19)-C(20)	5.6(4)
O(2)-C(18)-C(19)-C(24)	2.2(4)
C(1)-C(18)-C(19)-C(24)	-171.9(3)
C(24)-C(19)-C(20)-C(21)	1.6(5)
C(18)-C(19)-C(20)-C(21)	-175.9(3)
C(19)-C(20)-C(21)-C(22)	-0.4(5)
C(20)-C(21)-C(22)-C(23)	-1.3(5)
C(21)-C(22)-C(23)-C(24)	1.7(5)
C(22)-C(23)-C(24)-C(19)	-0.5(5)
C(20)-C(19)-C(24)-C(23)	-1.2(5)
C(18)-C(19)-C(24)-C(23)	176.4(3)

Symmetry transformations used to generate equivalent atoms:

IX. References:

S1. K.-I. Fujita, Y. Takahashi, M. Owaki, K. Yamamoto, R. Yamaguchi, *Org. Lett*., **2004**, *6*, 2785.

S2. S2. M. Kuprat, M. Lehmann, A. Schulz, A. Villinger, *Organometallics*, **2010**, *29*, 1421.

S3. J. R. Hummel, J. A. Ellman, *J. Am. Chem. Soc.* **2015**, *137*, 490.

S4. T. Yoshino, H. Ikemoto, S. Matsunaga, M. Kanai, *Angew. Chem., Int. Ed*. **2013**, *52*, 2207.

S5. B. Sun, T. Yoshino, S. Matsunaga, M. Kanai, *Adv. Synth. Catal*. **2014**, *356*, 1491.

S6. M. Fetizon, V. Balogh, M. Golfier, *J. Org. Chem*. **1971**, *36*, 1339.

S7. S. Chanthamath, S. Takaki, K. Shibatomi, S. Iwasa, *Angew. Chem. Int. Ed.*, **2013**, *52*, 5818.

S8. P. M. Liu, C. G. Frost, *Org. Lett*. **2013**, *15*, 5862.

S9. D. Das, A. Biswas, U. Karmakar, S. Chand, R. Samanta, *J. Org. Chem*. **2016**, *81*, 842.

S10. T. Tsuchimoto, K. Aoki, T. Wagatsuma, Y. Suzuki, *Eur. J. Org. Chem.* **2008**, 4035.

S11. H. Mimura, K. Kawada, T. Yamashita, T. Sakamoto, Y. Kikugawa, *J. Fluorine Chem.* **2010**, *131*, 477.

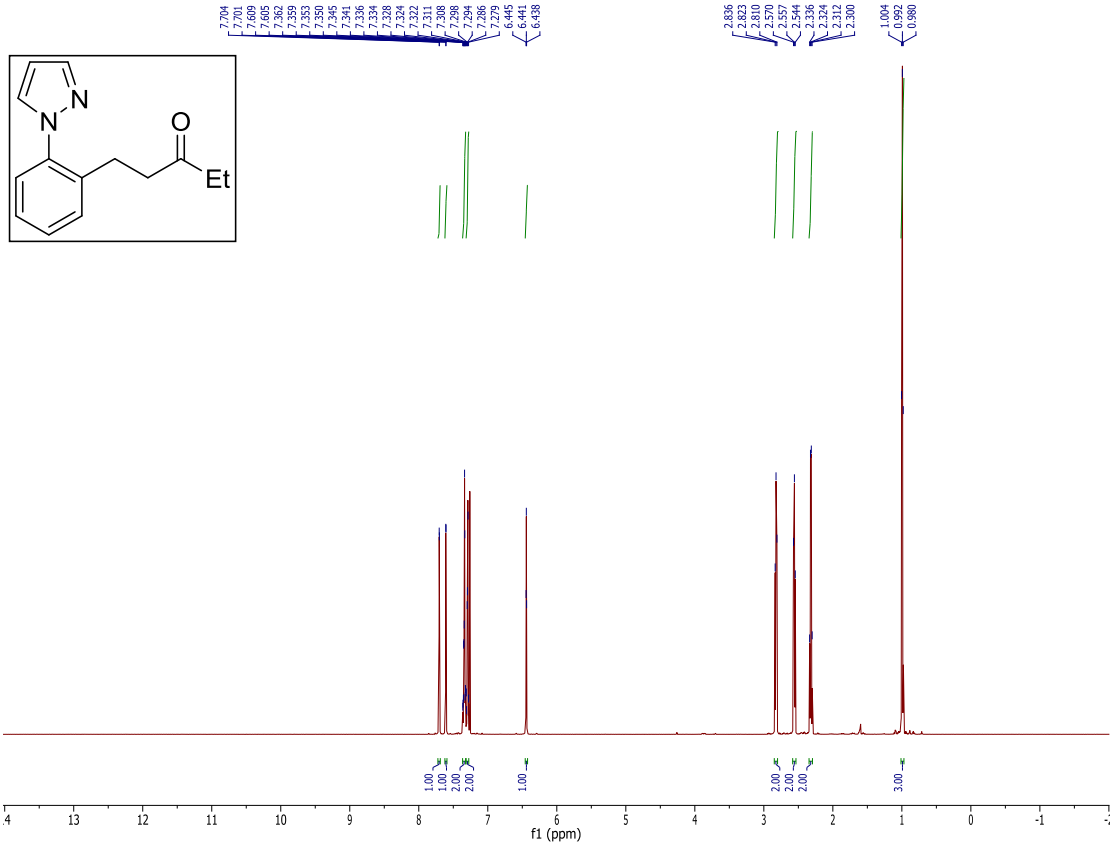
S12. (a) F. A. Davis, W. McCoull, *J. Org. Chem.* **1999**, *64*, 3396. (b) Z. Fei, W. Kong, H. Wang, J. Peng, F. Sun, Y. Yin, J. Bajwa, X. Jiang, *Org. Process Res. Dev.* **2012**, *16*, 1436.

S13. H. Luu, S. Wiesler, G. Frey, J. Streuff, *Org. Lett.* **2015**, *17*, 2478.

S14. L. Yang, C. A. Correia, C.-J. Li. *Adv. Synth. Catal.* **2011**, *353*, 1269.

S15. J. A. Boerth, J. A. Ellman, *Chem. Sci.*, **2016**, *7*, 1474.

X: NMR Data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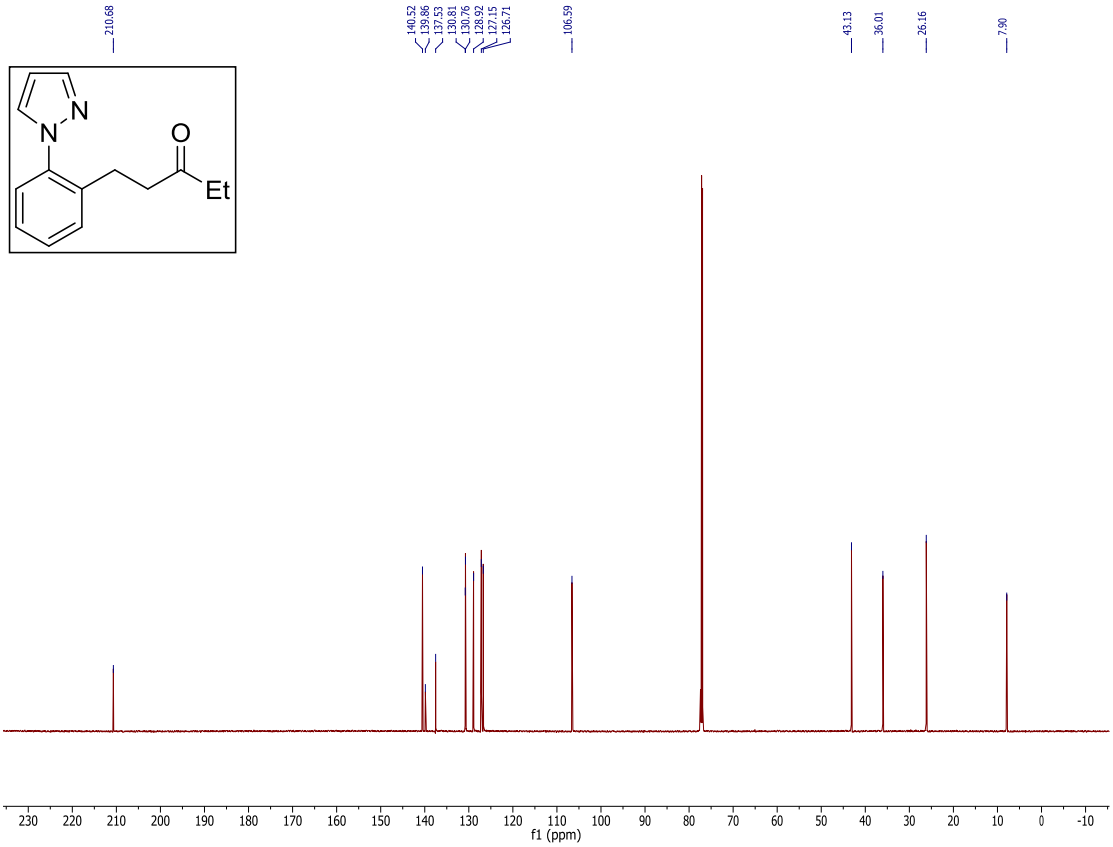
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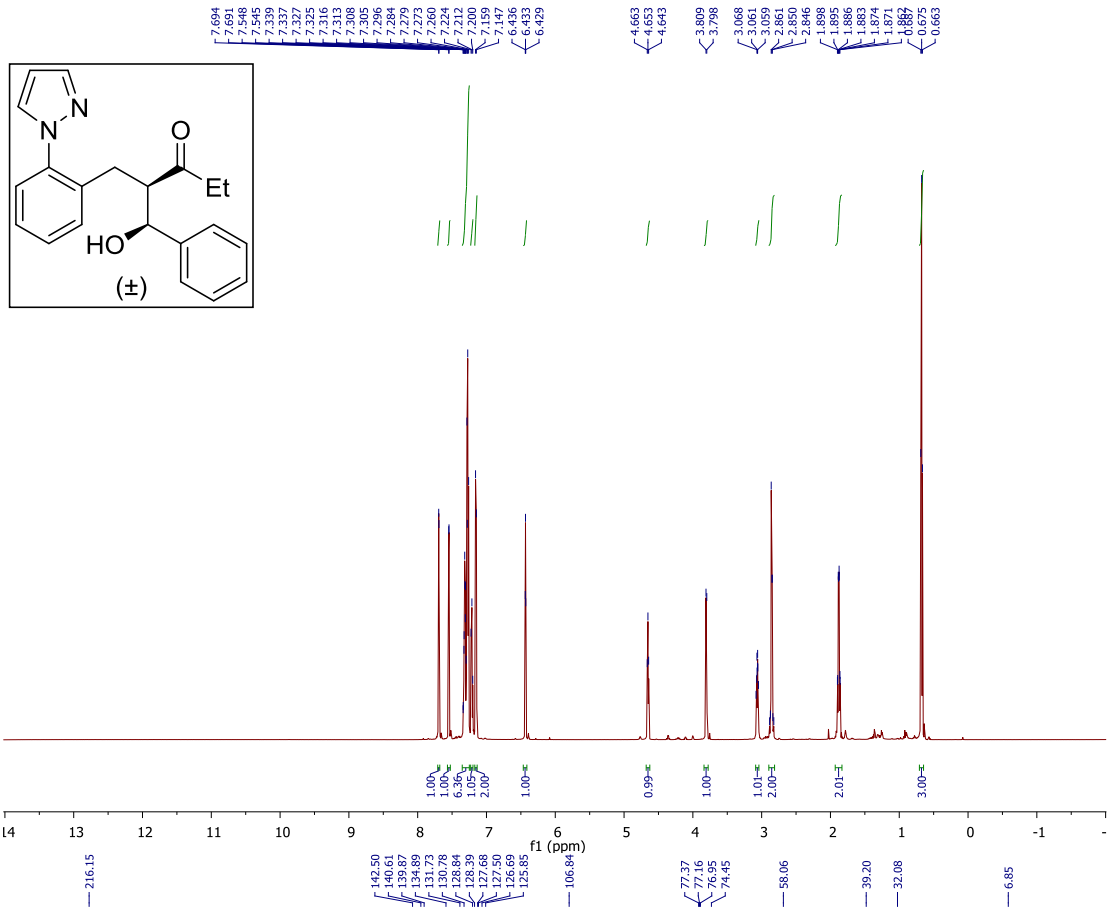
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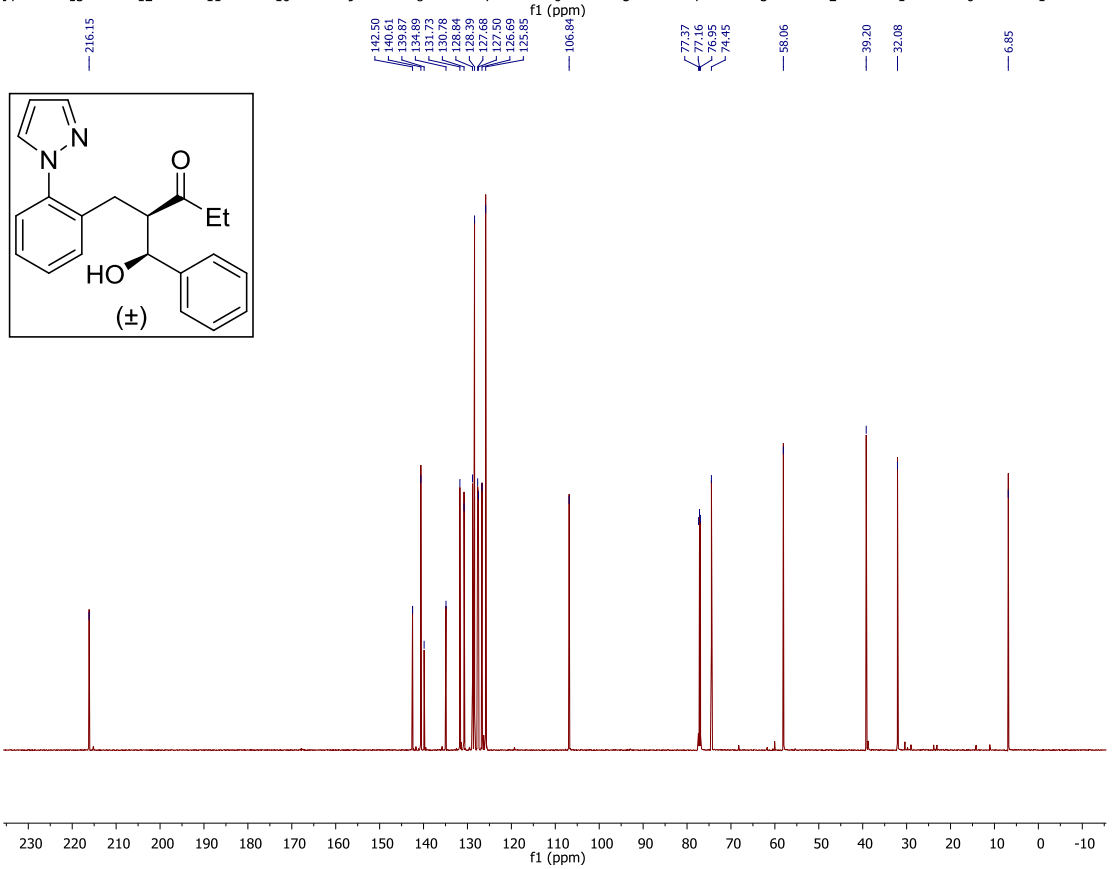
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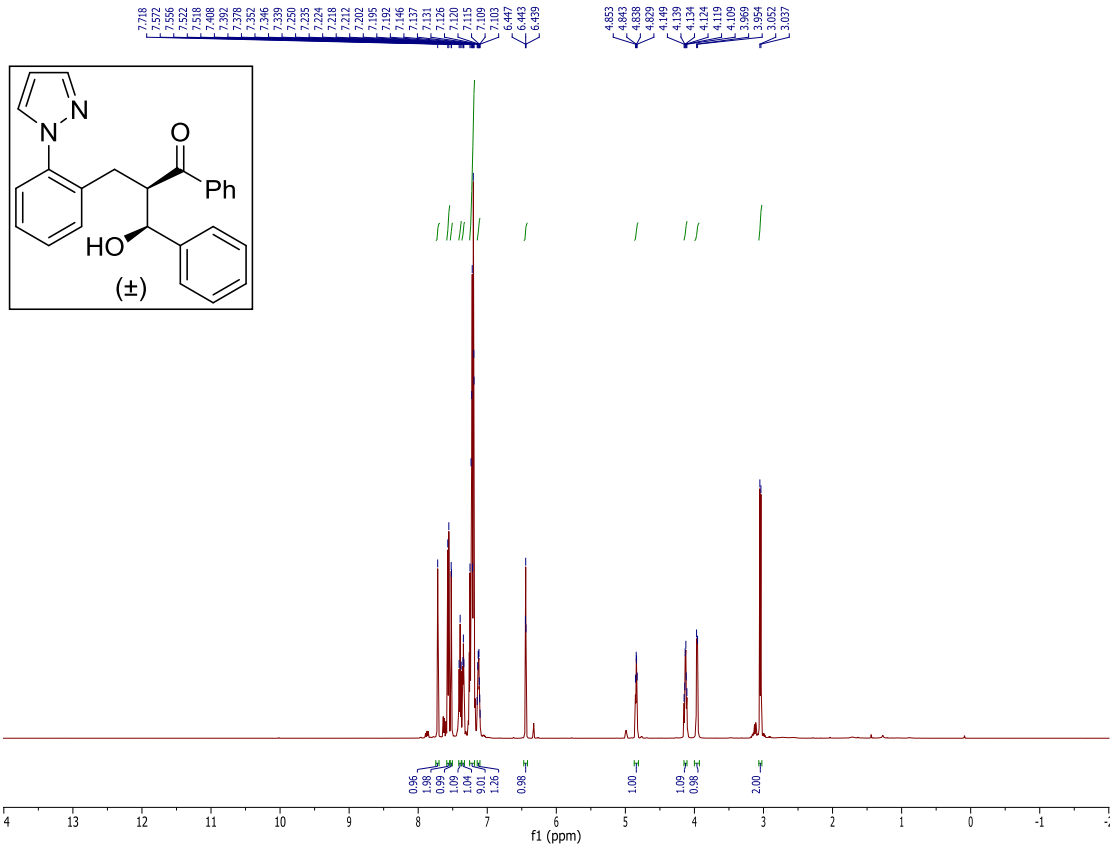
f1 (ppm)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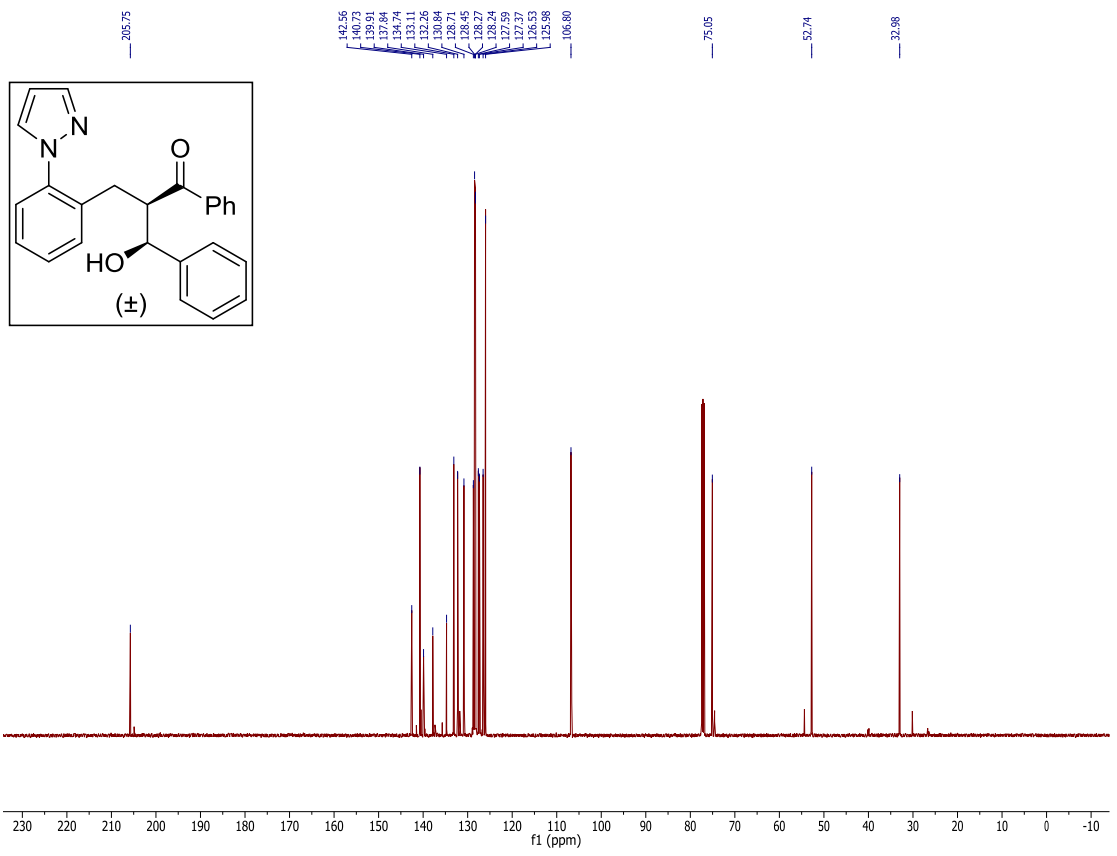
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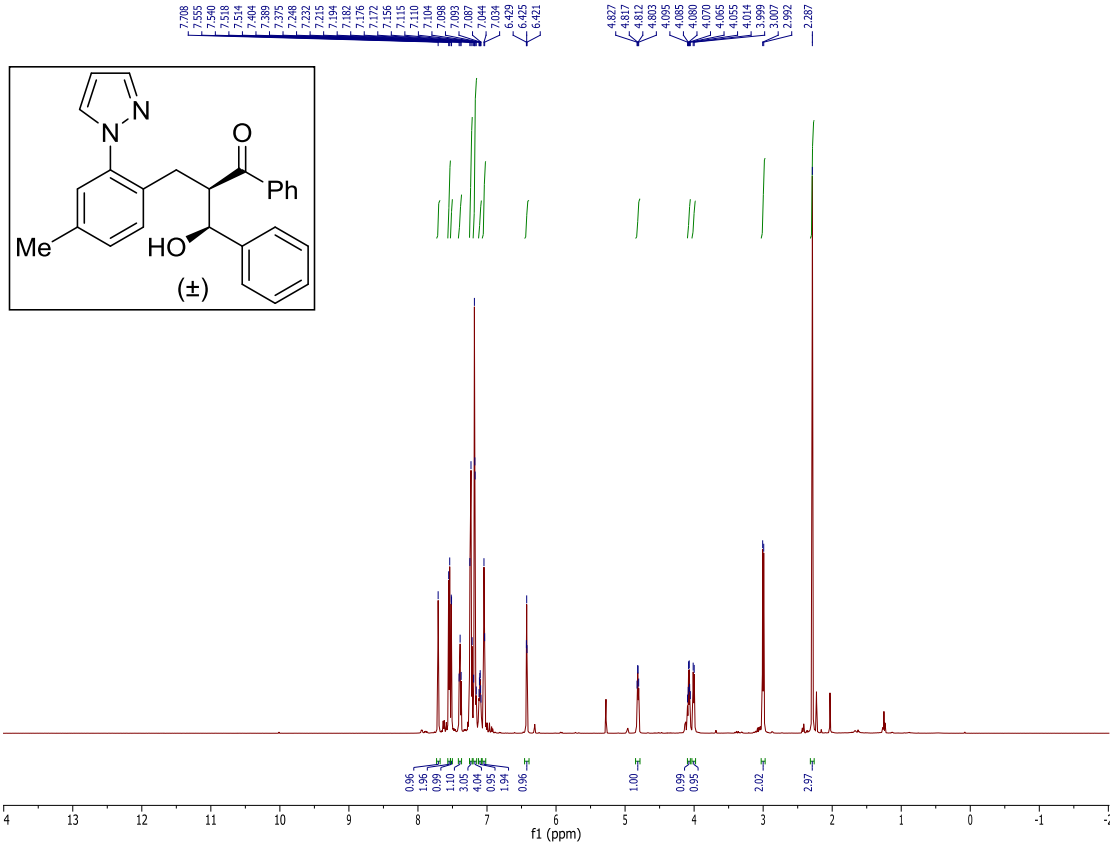
f1 (ppm)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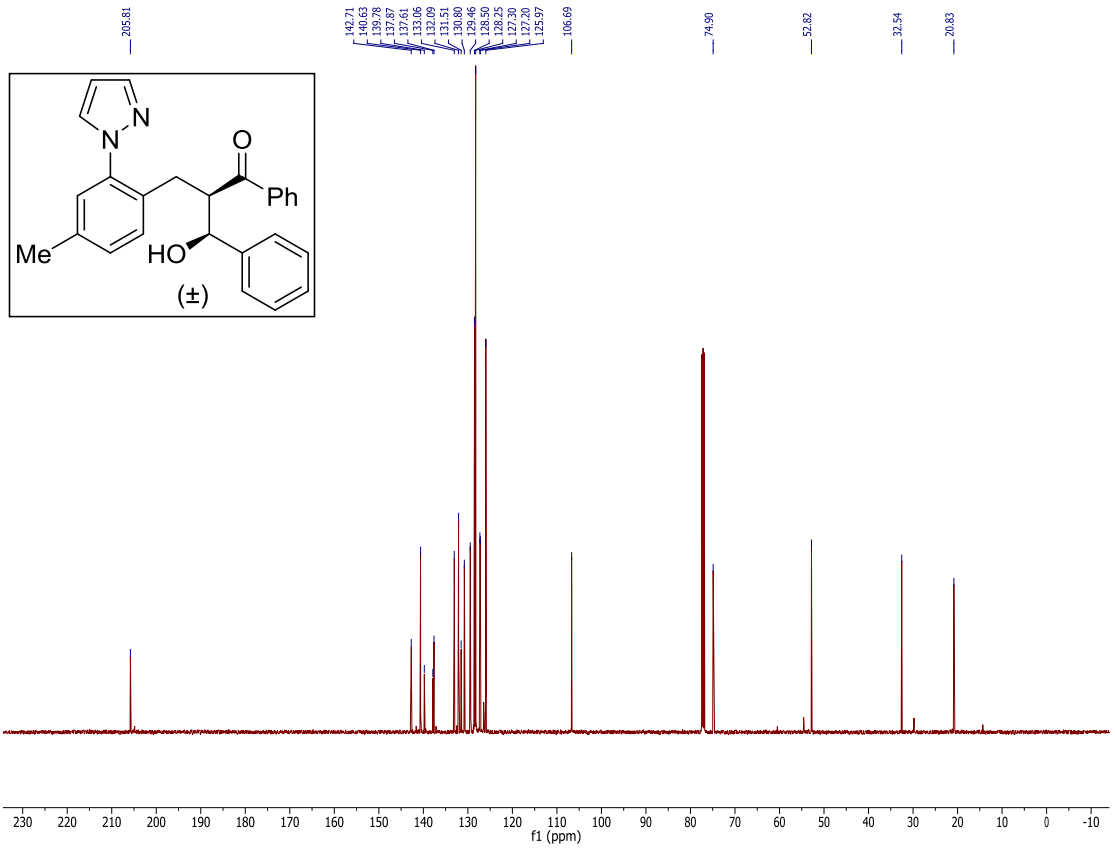
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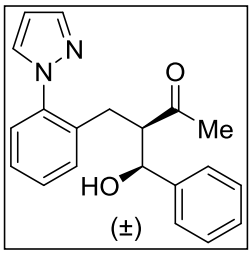
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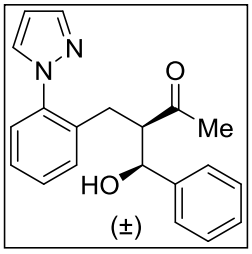
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(±)

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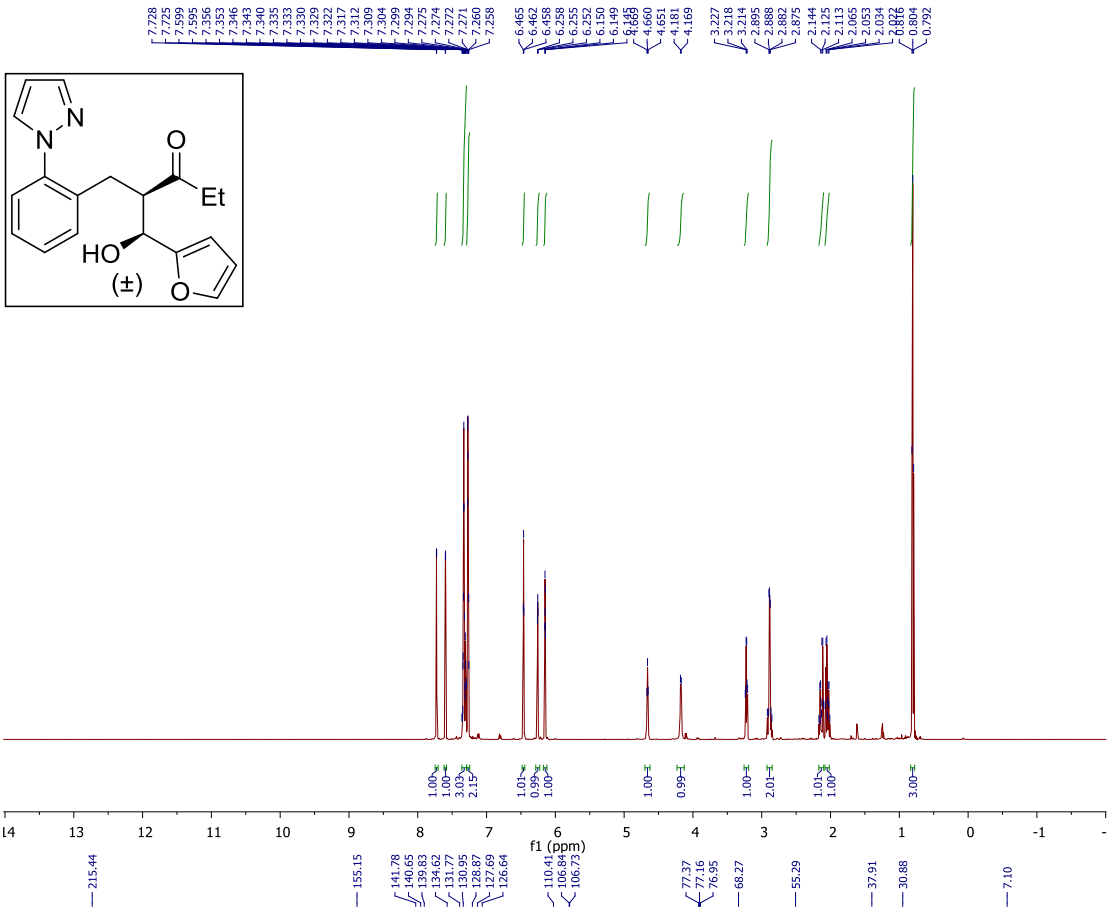
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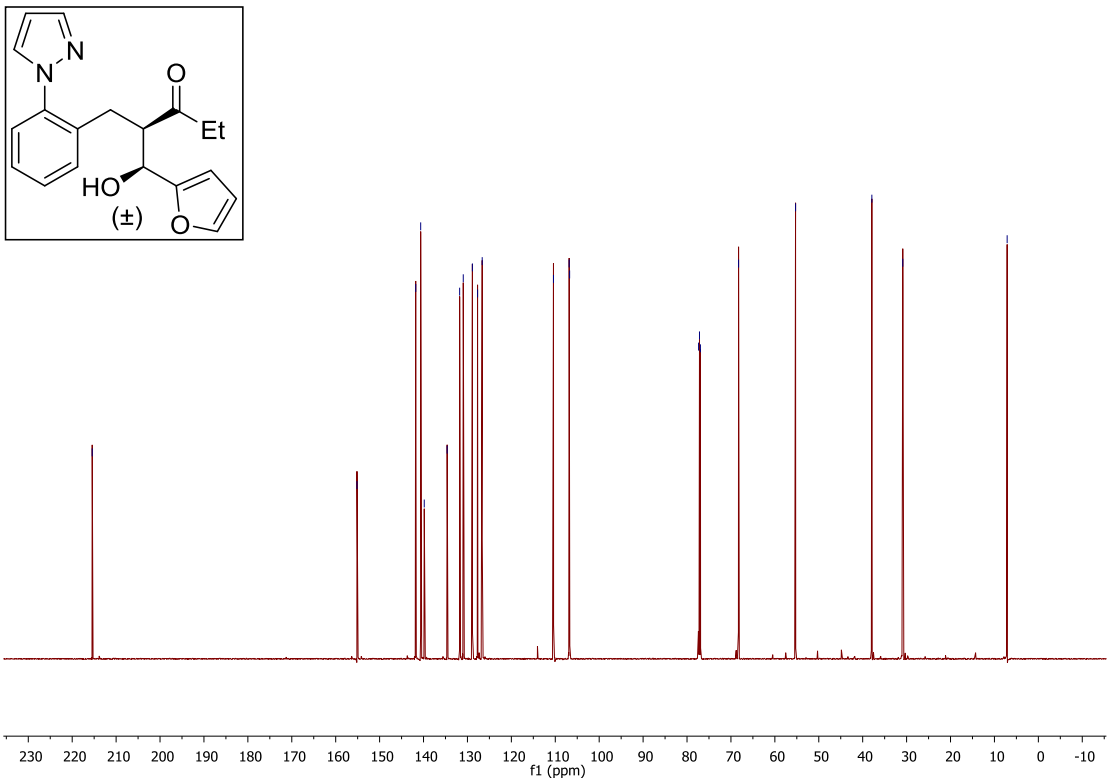
f1 (ppm)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HO
(±)
O
N
N
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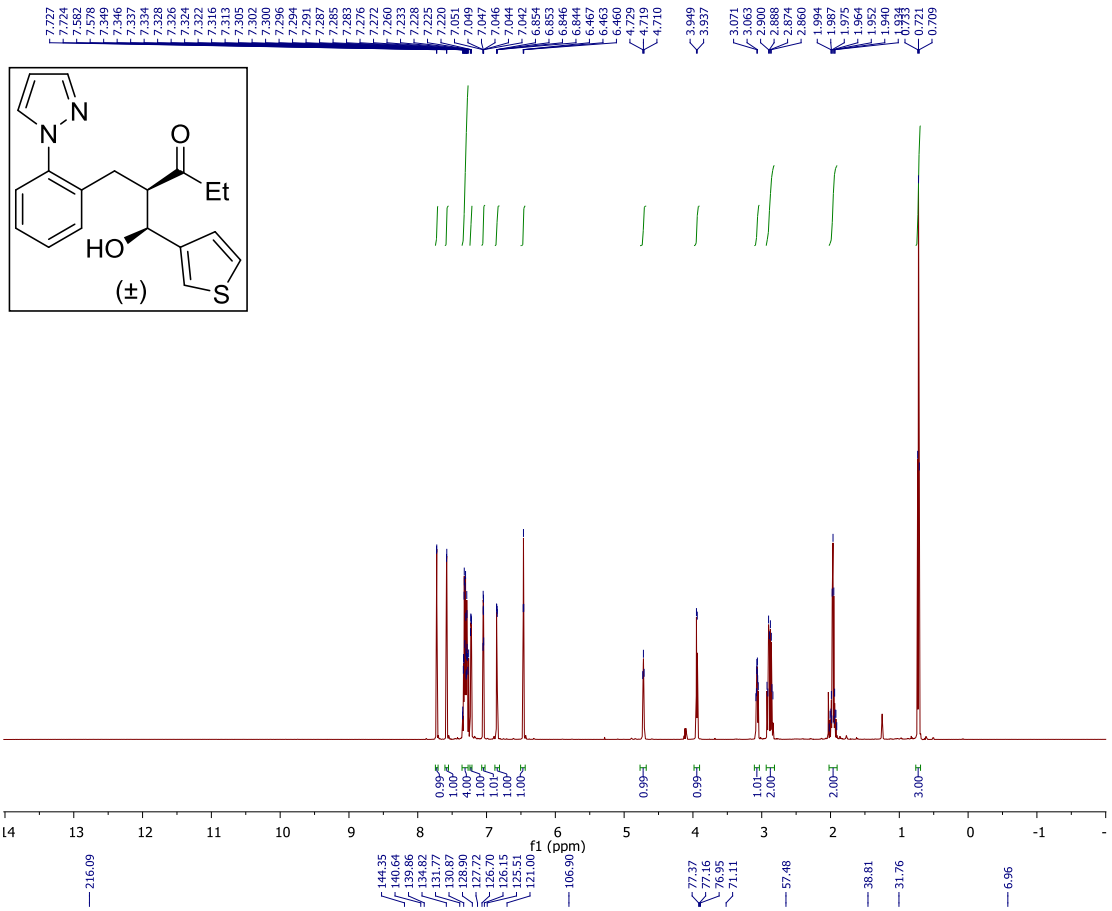
f1 (ppm)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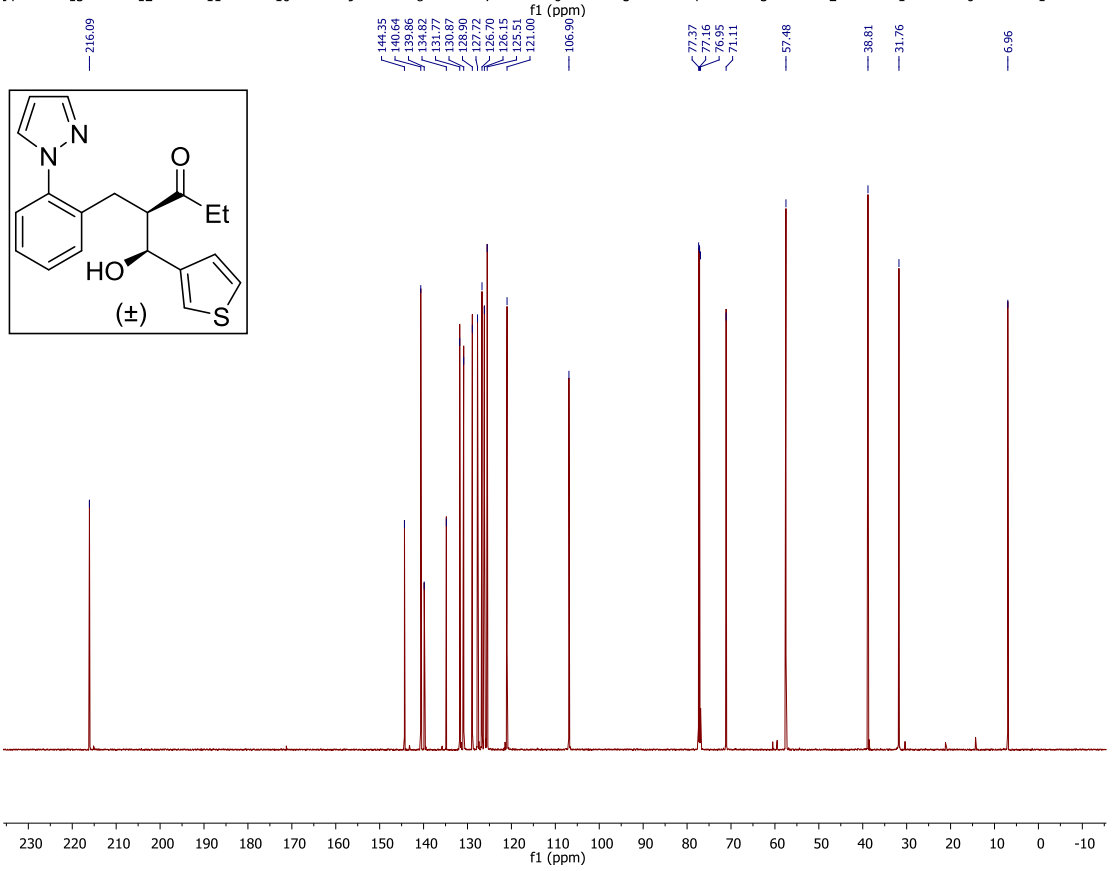
7.334
7.328
7.326
7.324
7.322
7.316
7.313
7.305
7.302
7.300
7.296
7.294
7.291
7.287
7.285
7.283
7.276
7.272
7.260
7.233
7.228
7.225
7.220
7.051
7.049
7.047
7.046
7.044
7.042
6.854
6.853
6.846
6.844
6.467
6.463
6.460
4.729
4.719
4.710
3.949
3.937
3.071
3.063
2.900
2.888
2.874
2.860
1.994
1.987
1.975
1.964
1.952
1.940
1.934
0.733
0.721
0.709
N
N
O
Et
HO
(±)
S
0.99
1.00
4.00
1.00
1.01
1.00
1.00
0.99
0.99
1.01
2.00
2.00
3.00
f1 (ppm)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128.90
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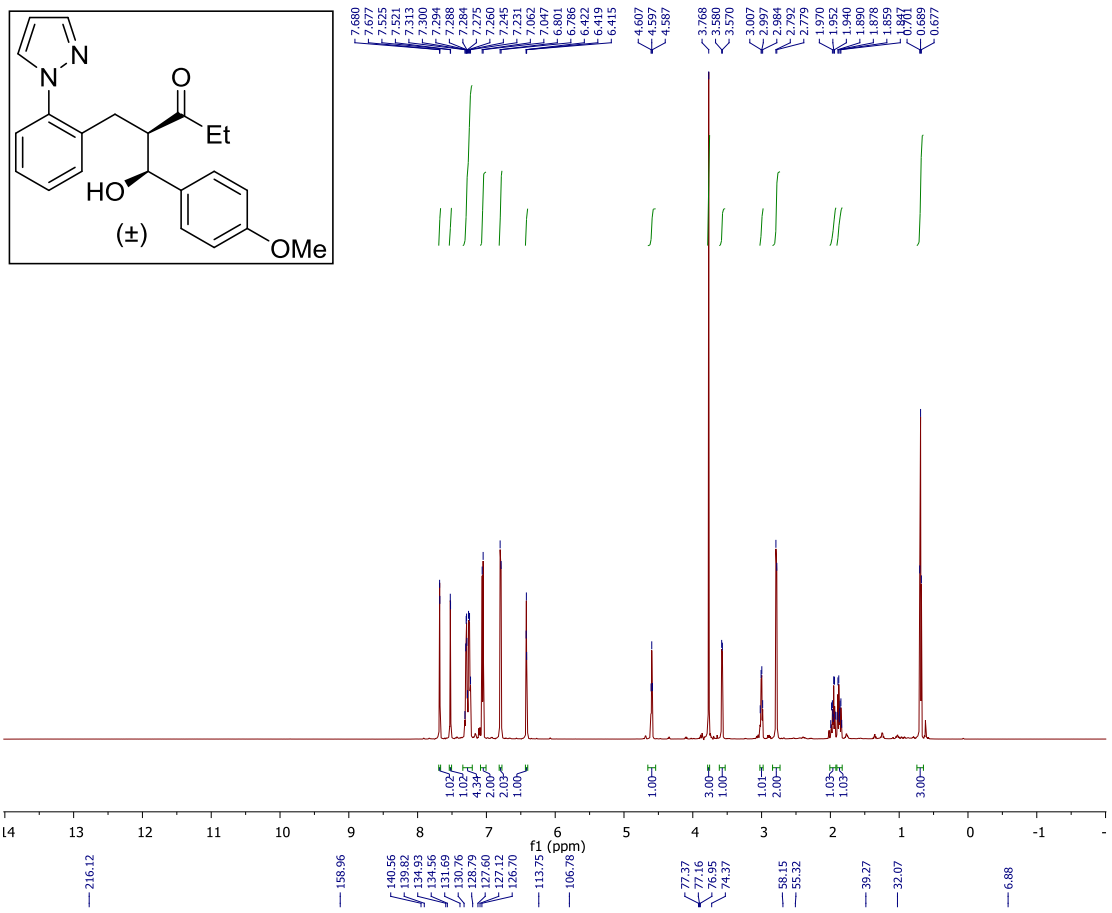
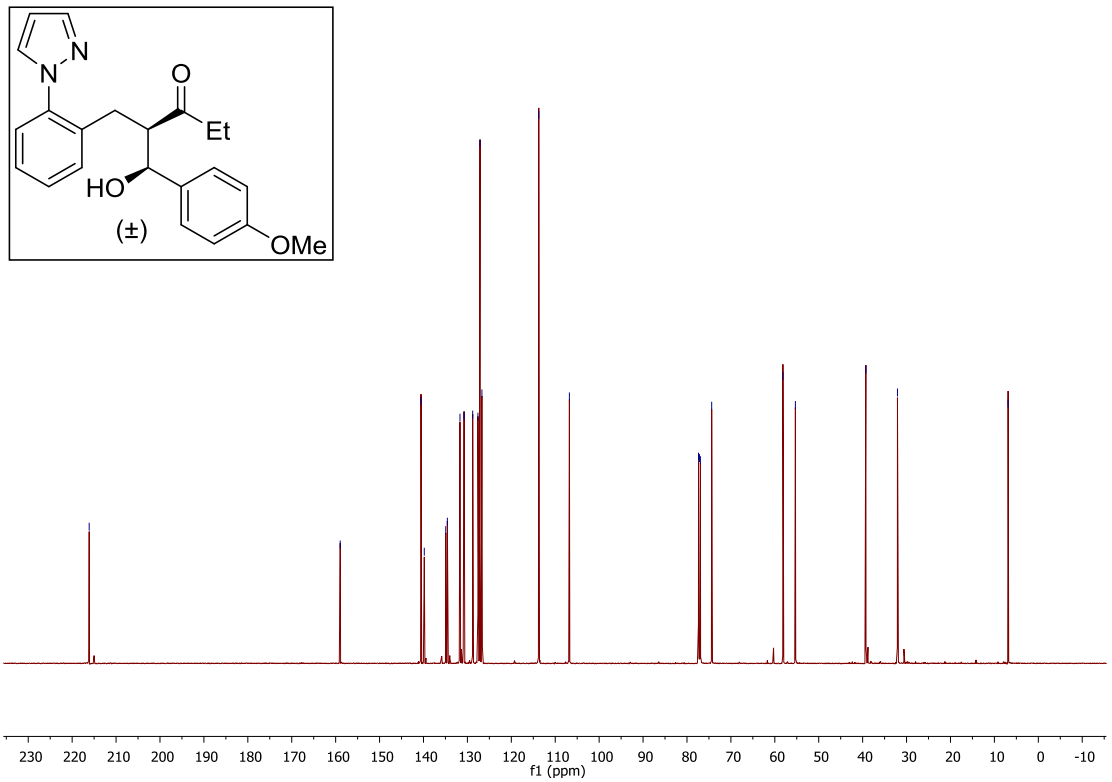
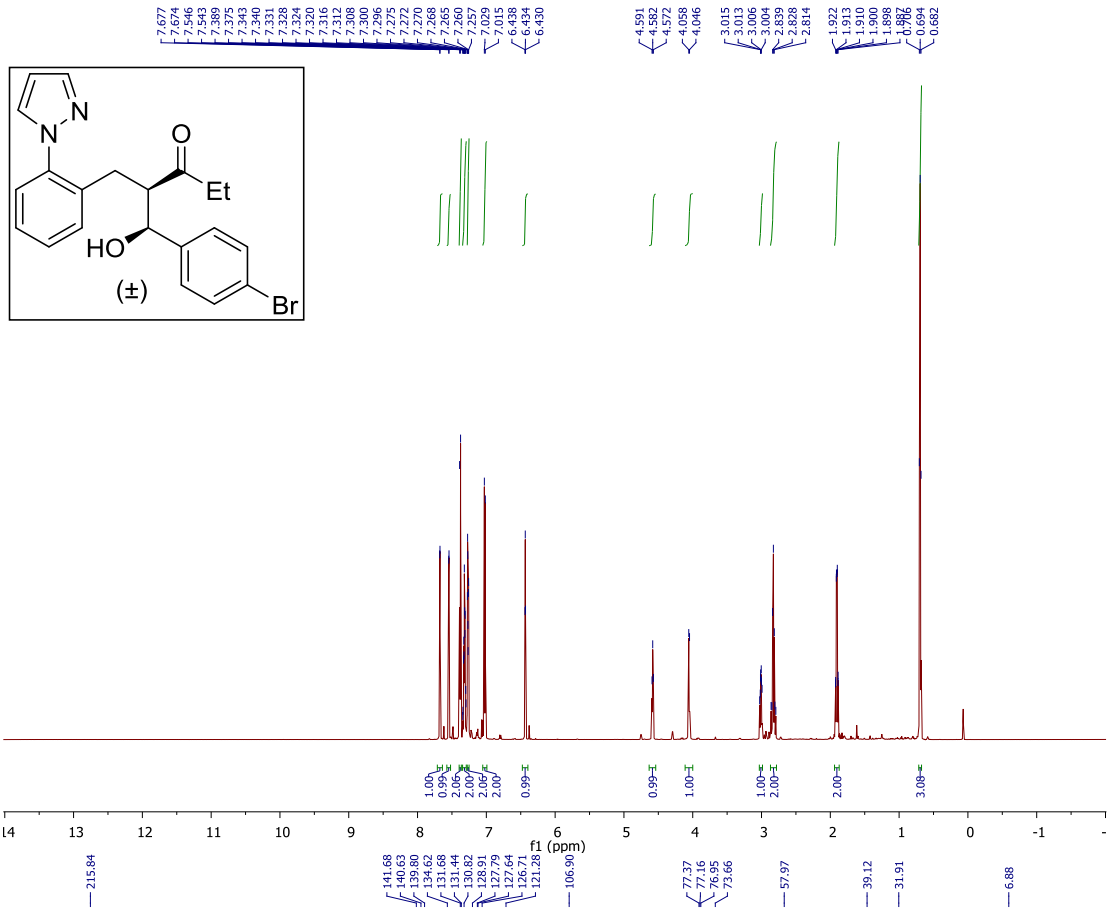
126.70
126.15
125.51
121.00
106.90
77.37
77.16
76.95
71.11
57.48
38.81
31.76
6.96
N
N
O
Et
HO
(±)
S
f1 (ppm)


N
N
O
Et
HO
(±)
OMe
f1 (ppm)


N
N
O
Et
HO
(±)
OMe
f1 (ppm)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7.546
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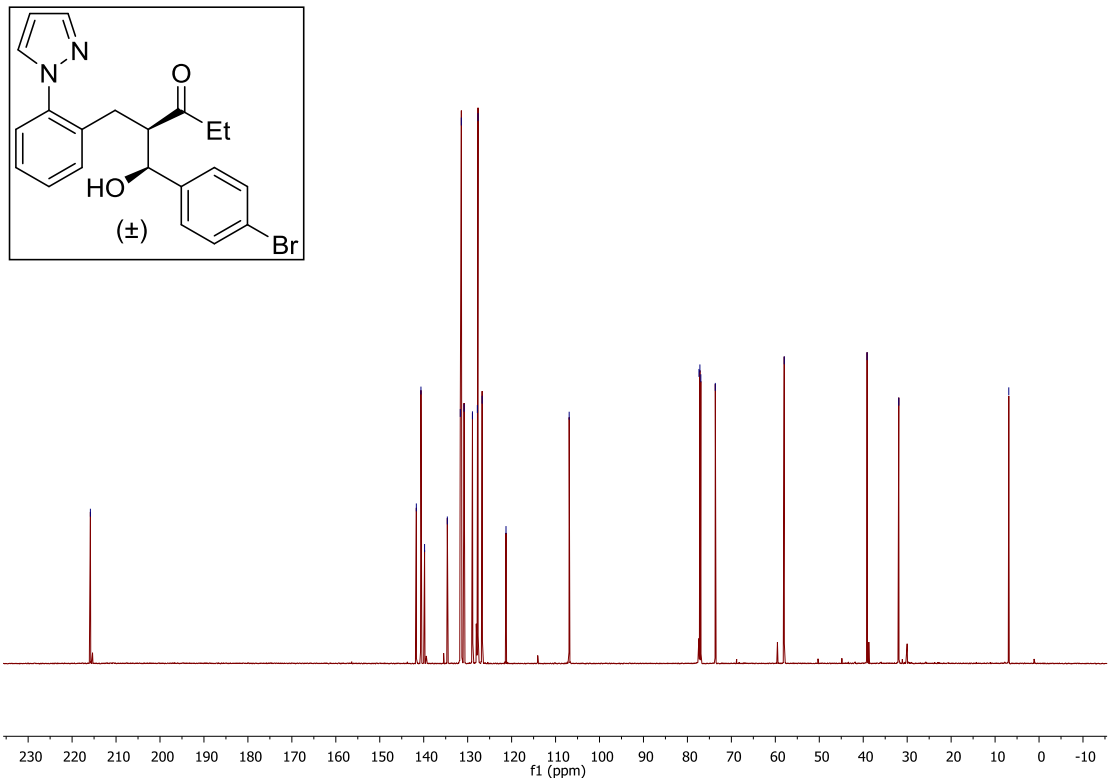
7.375
7.343
7.340
7.331
7.328
7.324
7.320
7.316
7.312
7.308
7.300
7.296
7.275
7.272
7.270
7.268
7.265
7.260
7.257
7.029
7.015
6.438
6.434
6.430
4.591
4.582
4.572
4.058
4.046
3.015
3.013
3.006
3.004
2.839
2.828
2.814
1.922
1.913
1.910
1.900
1.898
1.887
1.706
0.694
0.682
N
N
O
Et
HO
(±)
Br
1.00
0.99
2.06
2.00
2.06
2.00
0.99
0.99
1.00
1.00
2.00
2.00
2.00
3.08
f1 (ppm)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140.63
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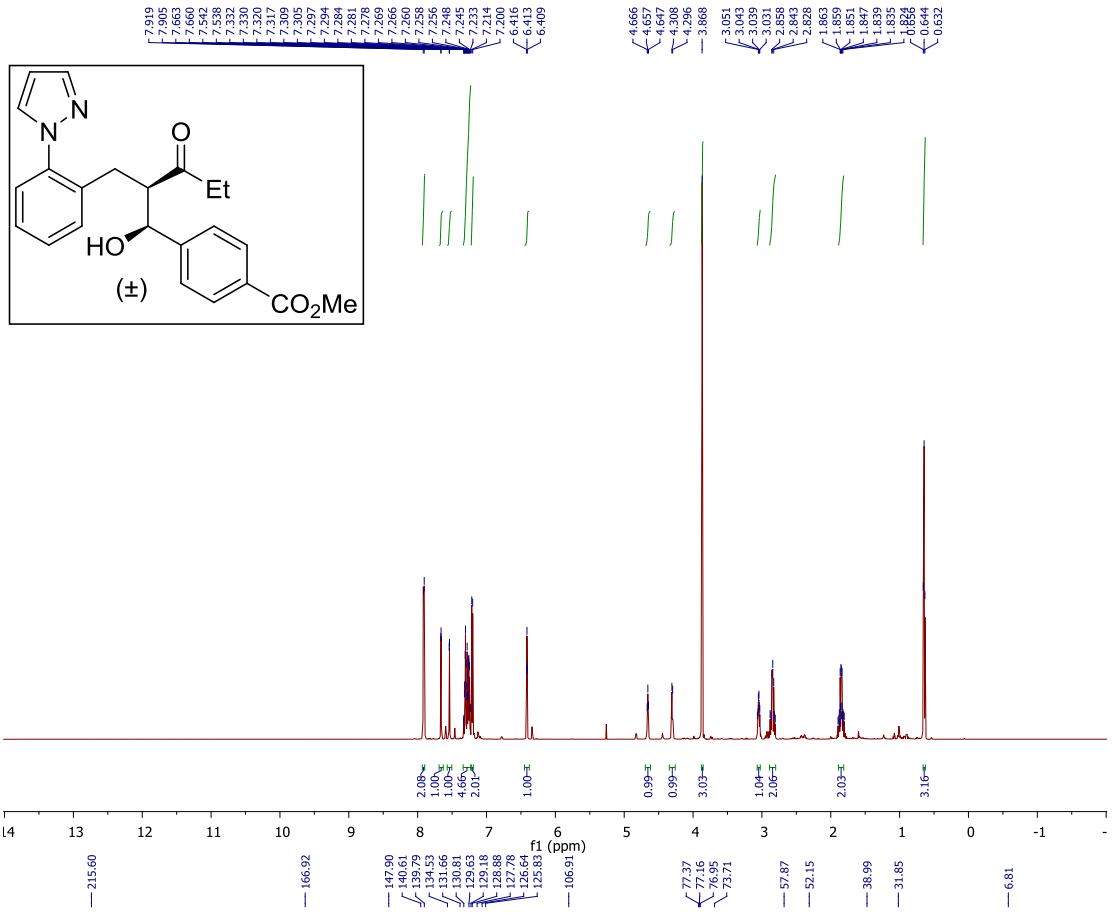
134.62
131.68
131.44
130.82
128.91
127.79
127.64
126.71
121.28
106.90
77.37
77.16
76.95
73.66
57.97
39.12
31.91
6.88
N
N
O
Et
HO
(±)
Br
f1 (ppm)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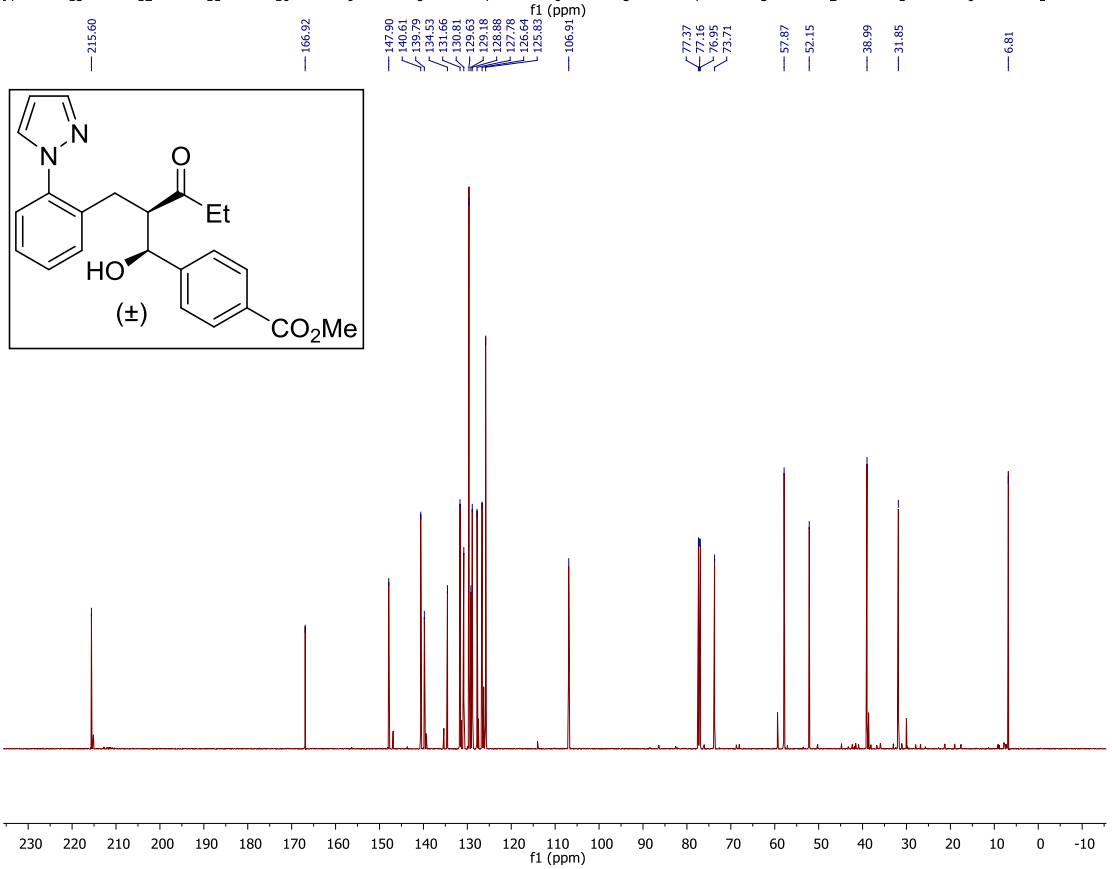
7.660
7.542
7.538
7.332
7.330
7.320
7.317
7.309
7.305
7.297
7.294
7.284
7.281
7.278
7.269
7.266
7.260
7.258
7.256
7.248
7.245
7.233
7.214
7.200
6.416
6.413
6.409
4.666
4.657
4.647
4.308
4.296
3.868
3.051
3.043
3.039
3.031
2.858
2.843
2.828
1.863
1.859
1.851
1.847
1.839
1.835
0.858
0.644
0.632
N
N
O
Et
HO
(±)
CO2Me
2.08
1.00
1.00
4.66
2.01
1.00
0.99
0.99
3.03
1.04
2.06
2.03
3.16
f1 (ppm)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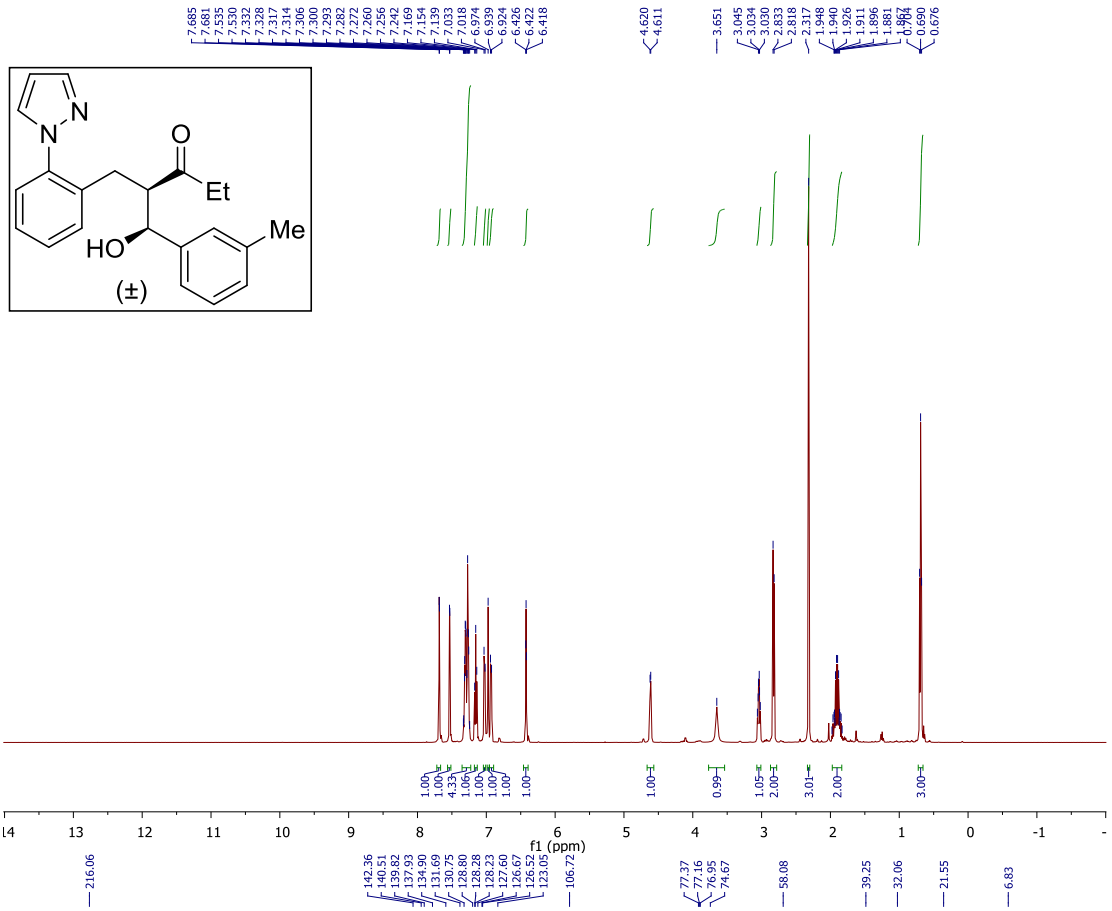
166.92
147.90
140.61
139.79
134.53
131.66
130.81
129.63
129.18
128.88
127.28
126.64
125.83
106.91
77.37
77.16
76.95
73.71
57.87
52.15
38.99
31.85
6.81
N
N
O
Et
HO
(±)
CO2Me
f1 (ppm)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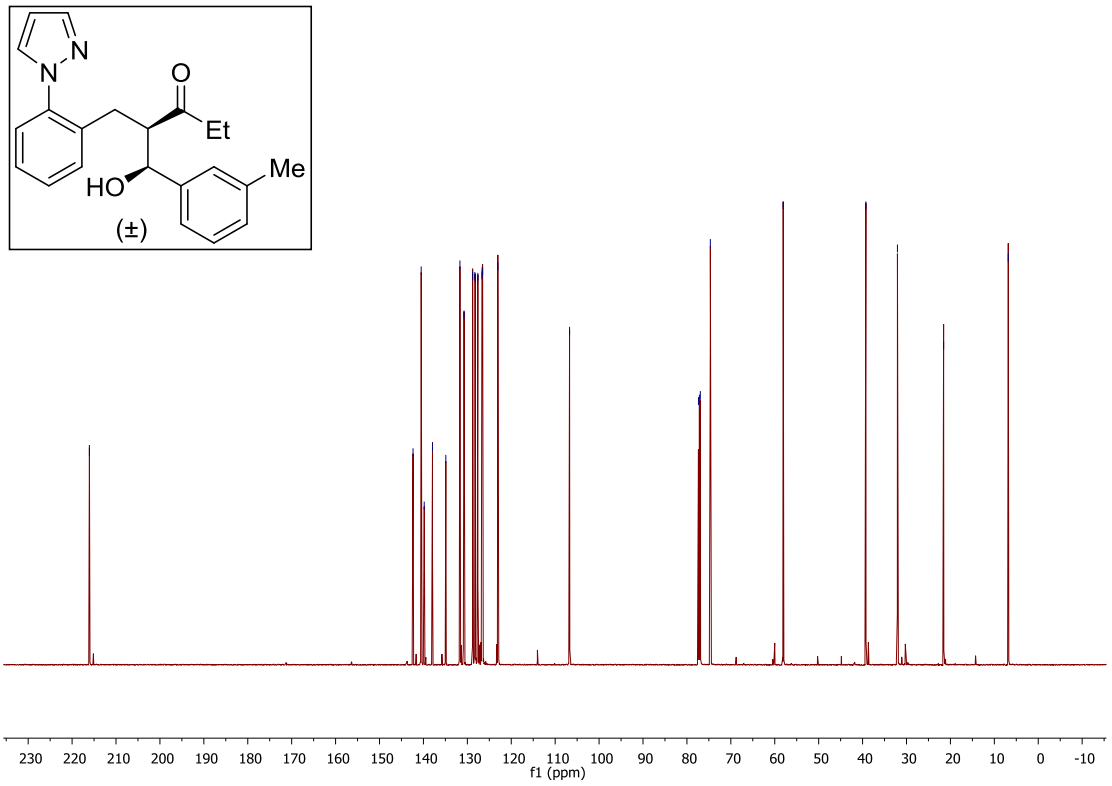
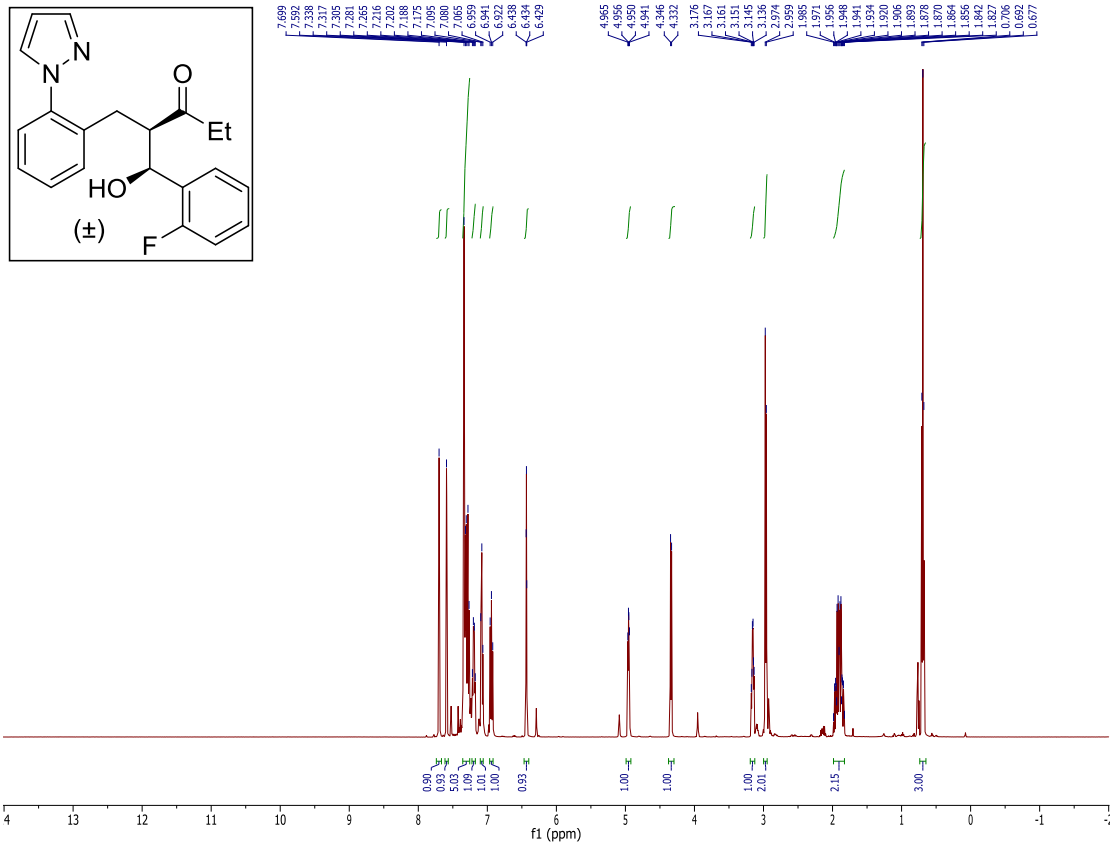
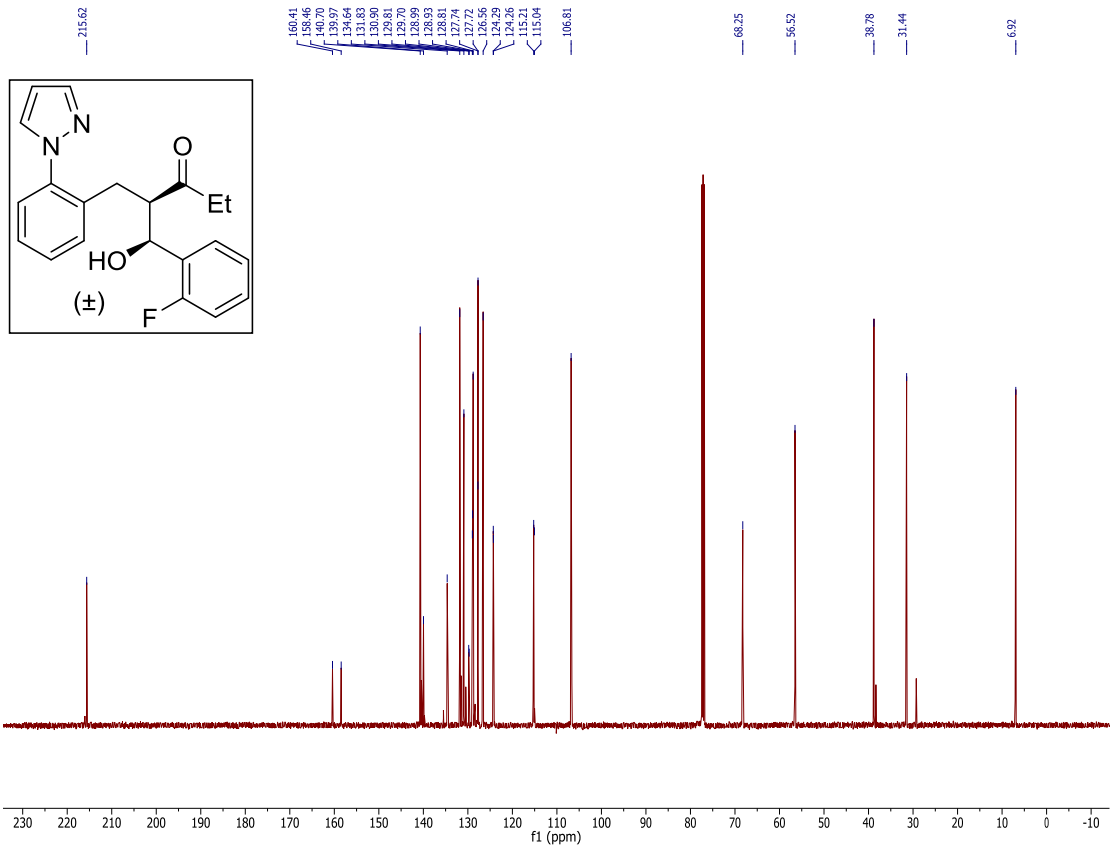
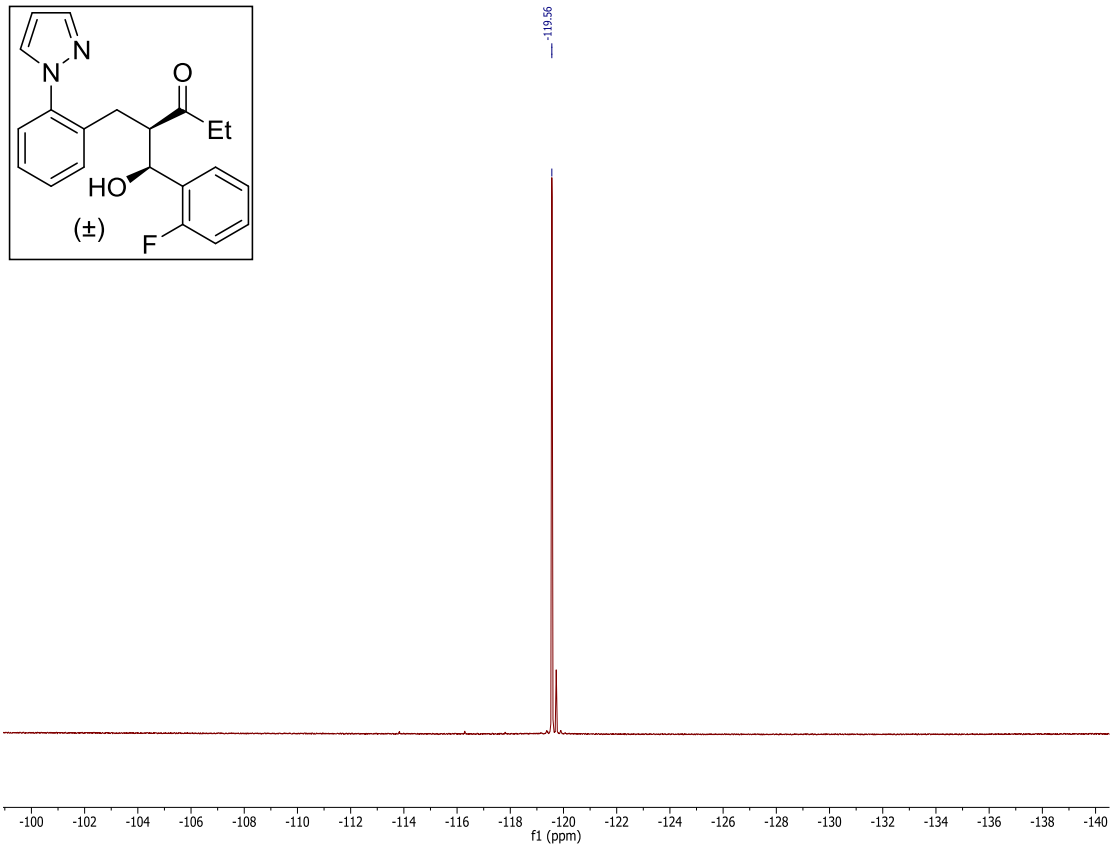
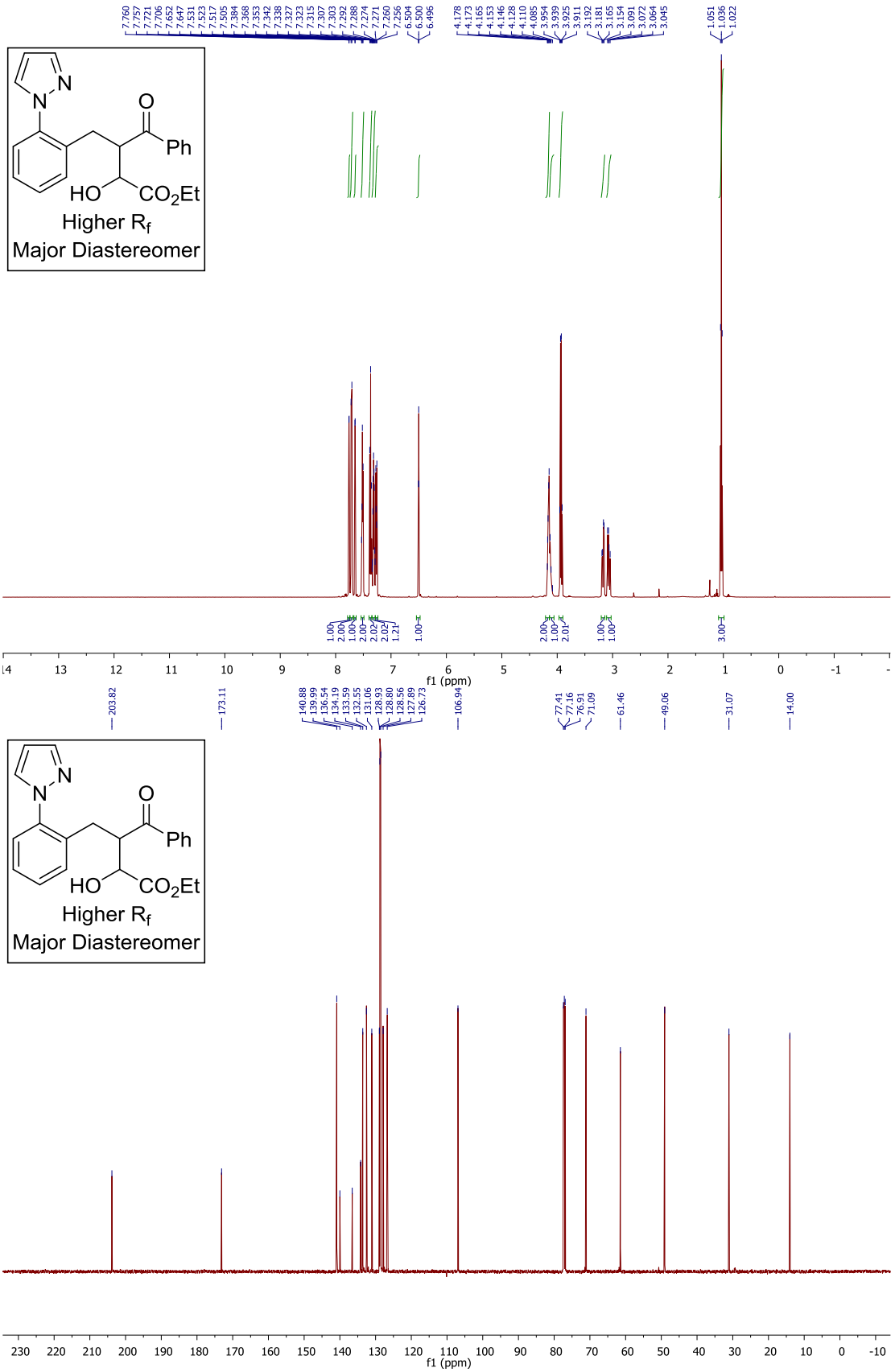
7.535
7.530
7.332
7.328
7.317
7.314
7.306
7.300
7.293
7.282
7.272
7.260
7.256
7.242
7.169
7.154
7.139
7.033
7.018
6.974
6.939
6.924
6.426
6.422
6.418
4.620
4.611
3.651
3.045
3.034
3.030
2.833
2.818
2.317
1.948
1.940
1.926
1.911
1.896
1.881
1.867
1.704
0.690
0.676
N
N
O
Et
HO
Me
(±)
1.00
1.00
4.33
1.06
1.00
1.00
1.00
1.00
0.99
1.05
2.00
3.01
2.00
3.00
f1 (ppm)

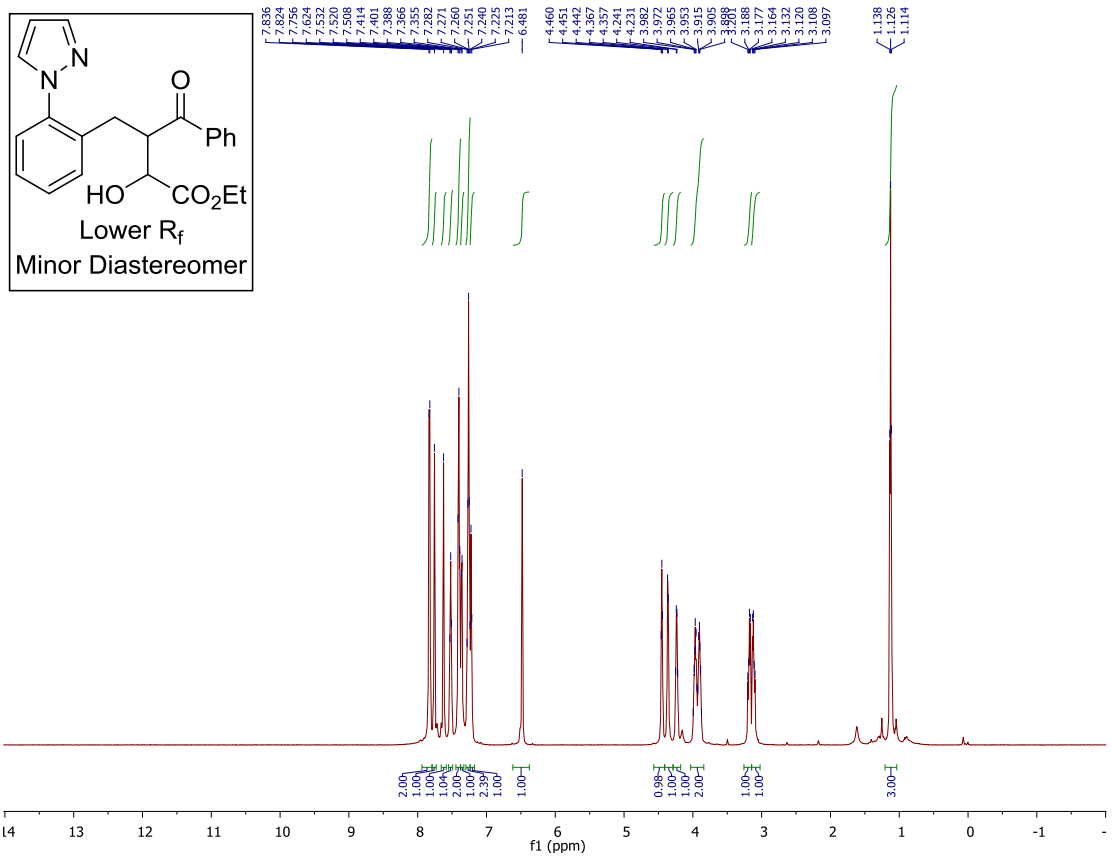

216.06
142.36
140.51
139.82
137.93
134.90
131.69
130.75
128.80
128.28
128.23
127.60
126.67
126.52
123.05
106.72
77.37
77.16
76.95
74.67
58.08
39.25
32.06
21.55
6.83
N
N
O
Et
HO
Me
(±)
f1 (ppm)

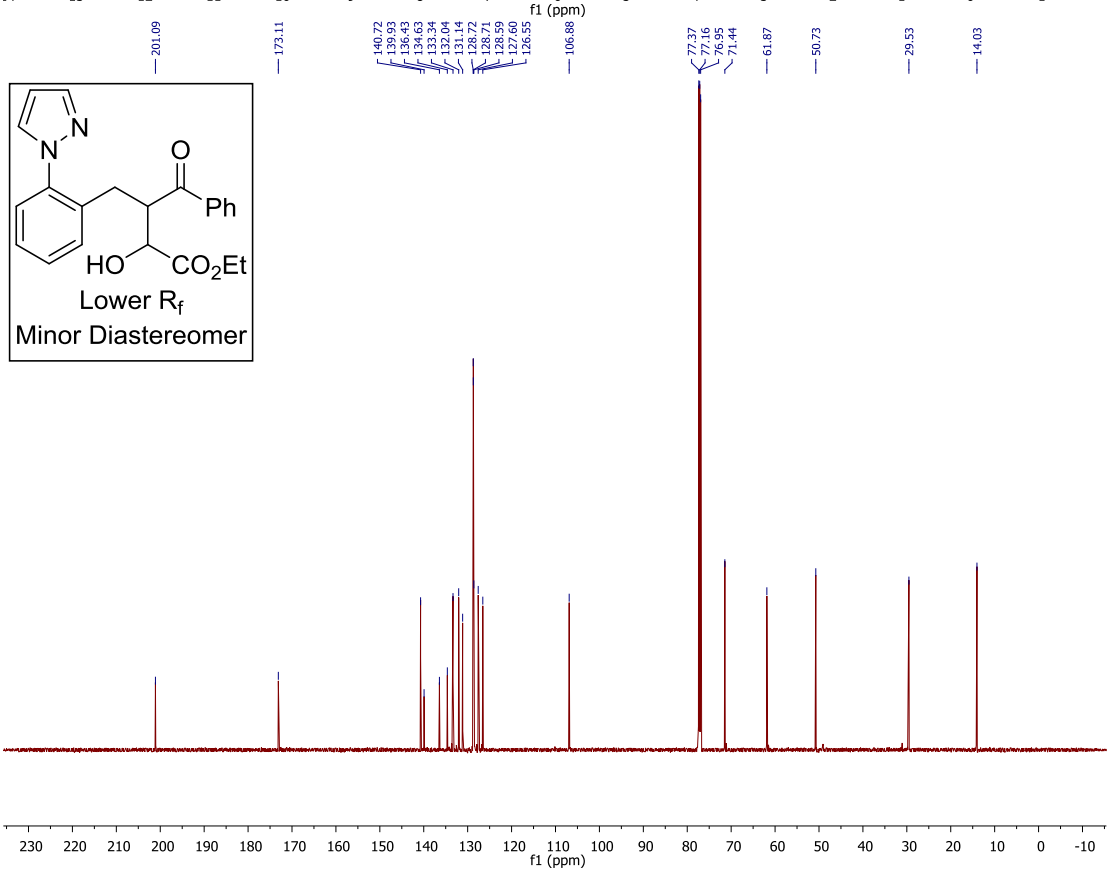

N
N
O
Et
HO
(±)
F
f1 (ppm)

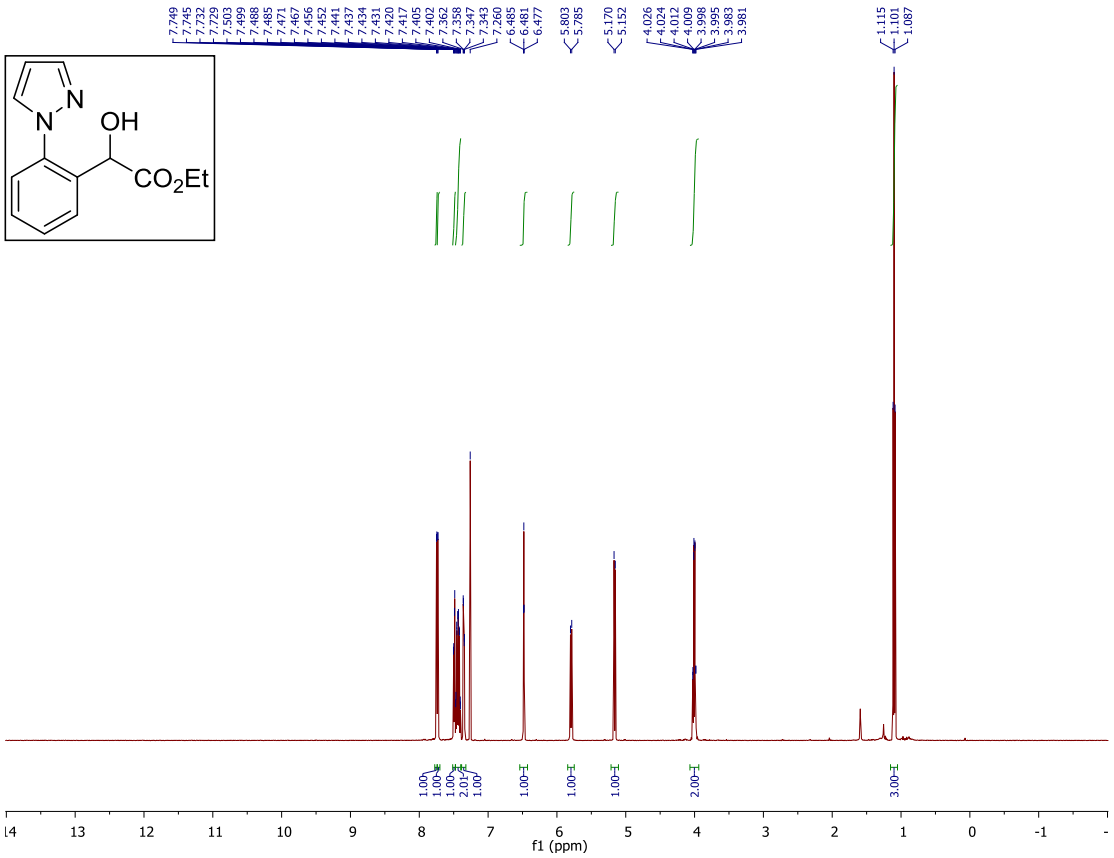

N
N
O
Et
HO
(±)
F
f1 (ppm)


N
N
O
Et
HO
(±)
F
-119.56
-100
-102
-104
-106
-108
-110
-112
-114
-116
-118
-120
-122
-124
-126
-128
-130
-132
-134
-136
-138
-140
f1 (ppm)


Higher R_f
Major Diastereomer
f1 (ppm)
Higher R_f
Major Diastereomer
f1 (ppm)


Ph
HO
CO2Et
Lower Rf
Minor Diastereomer
f1 (ppm)


Ph
HO
CO2Et
Lower Rf
Minor Diastereomer
f1 (ppm)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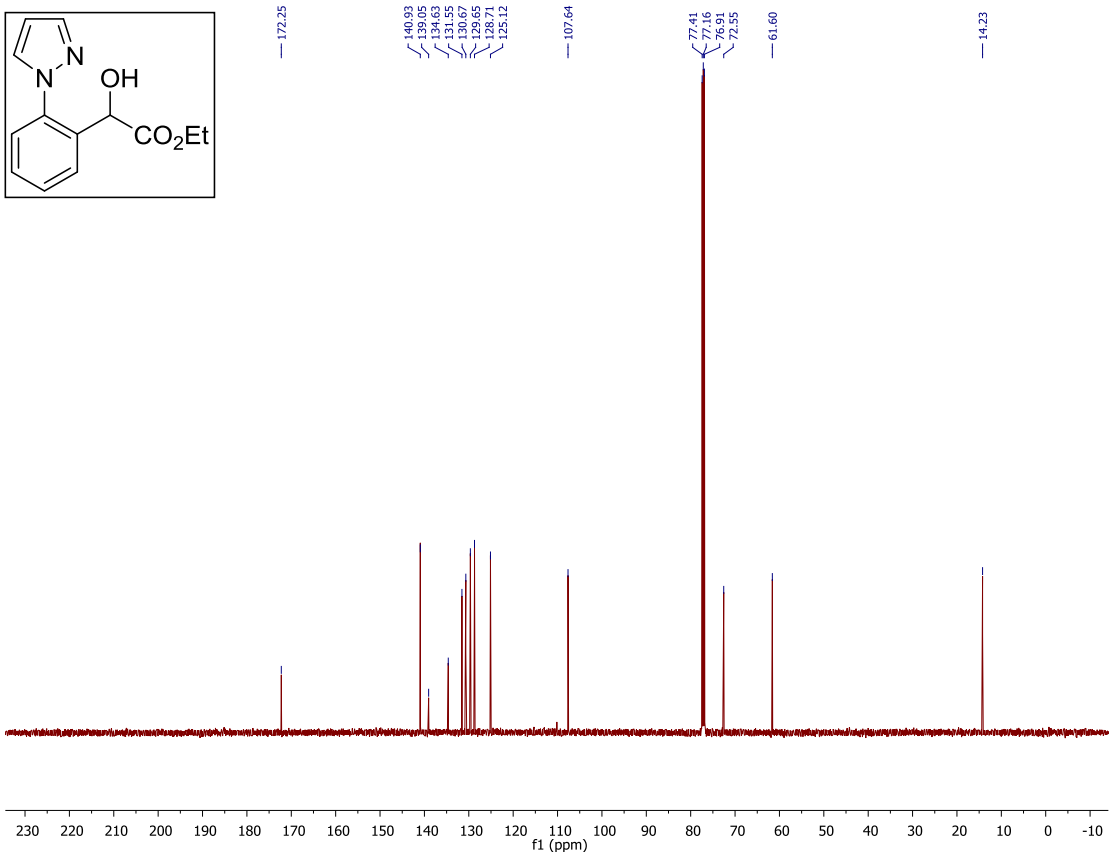
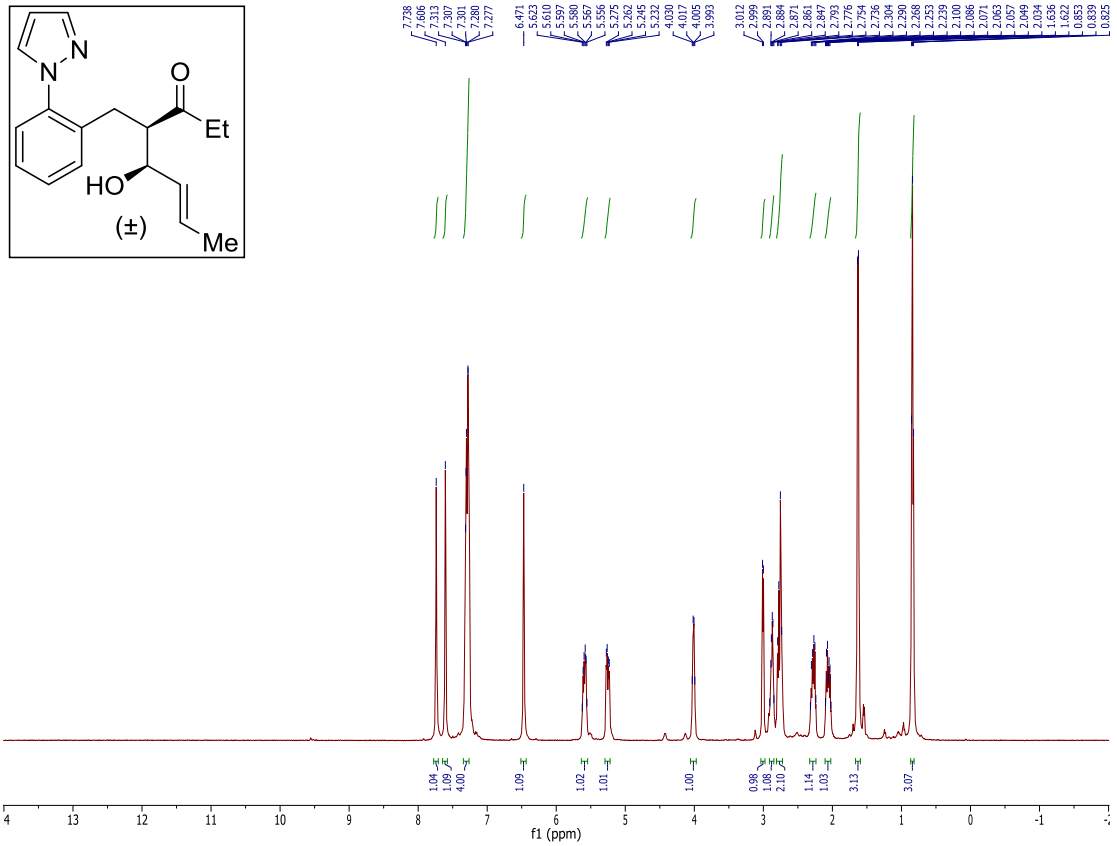
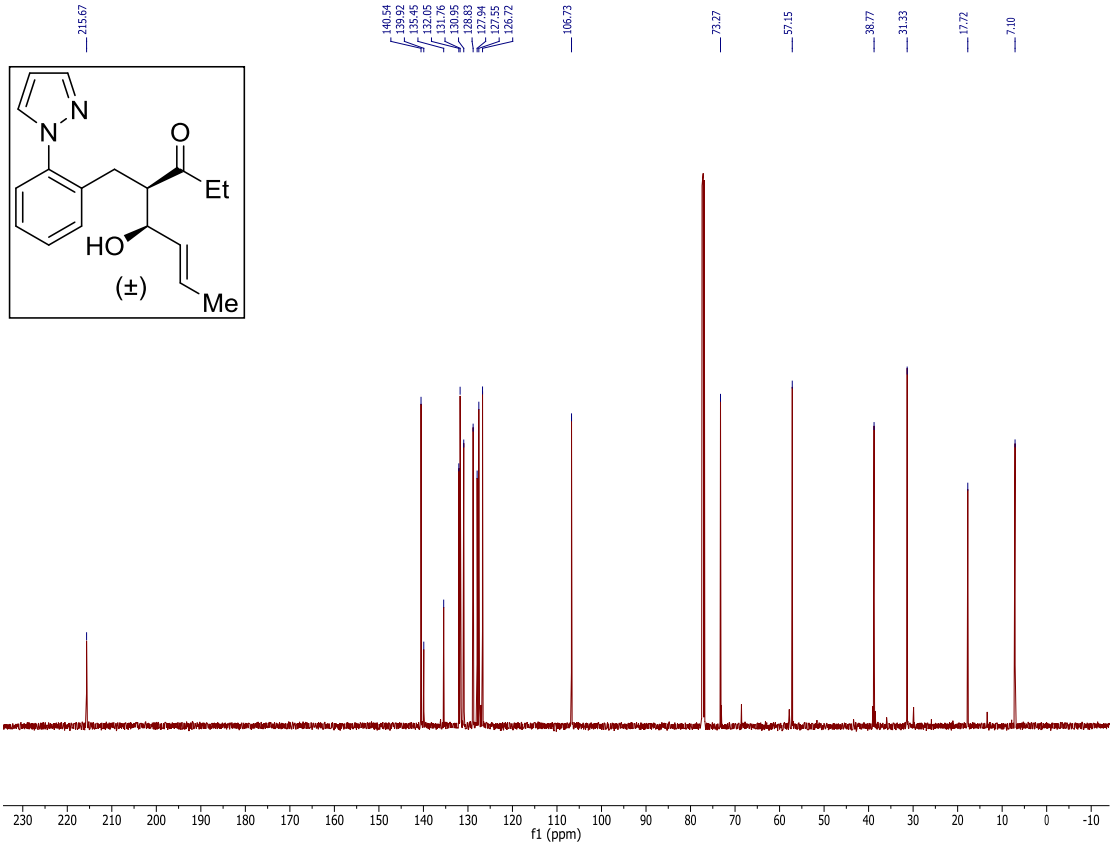
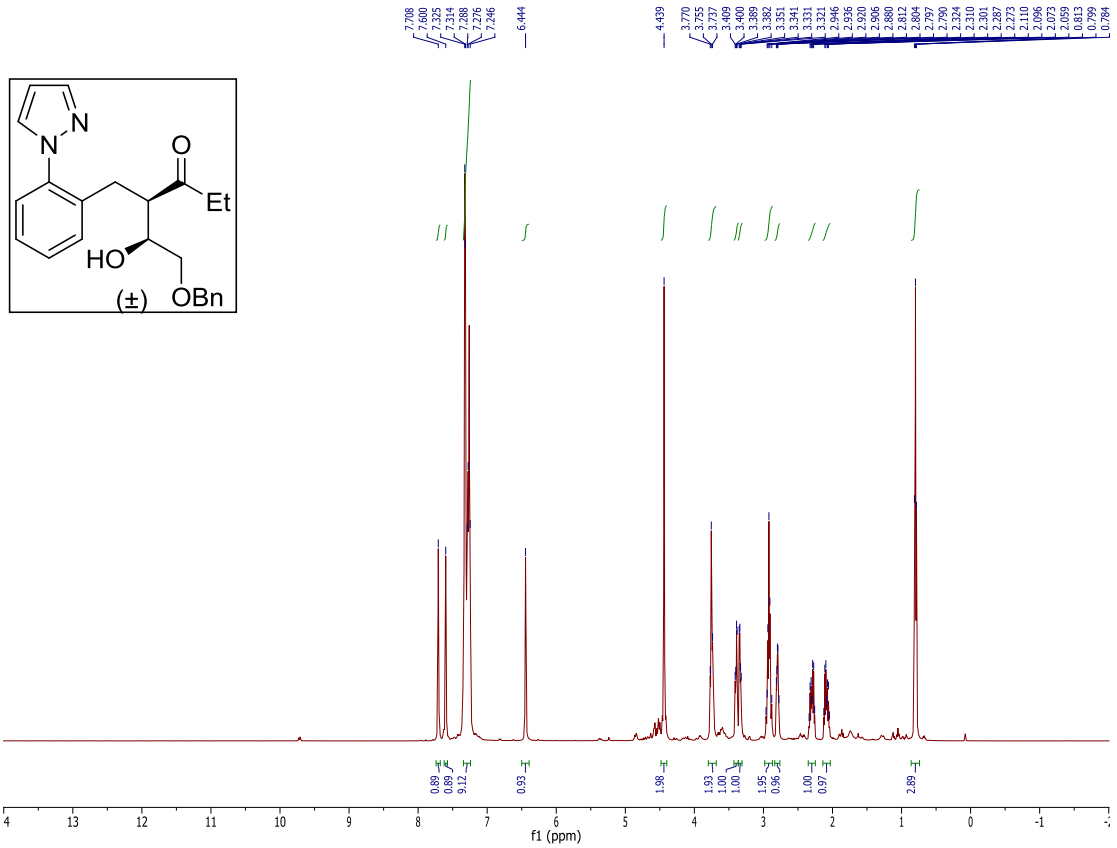
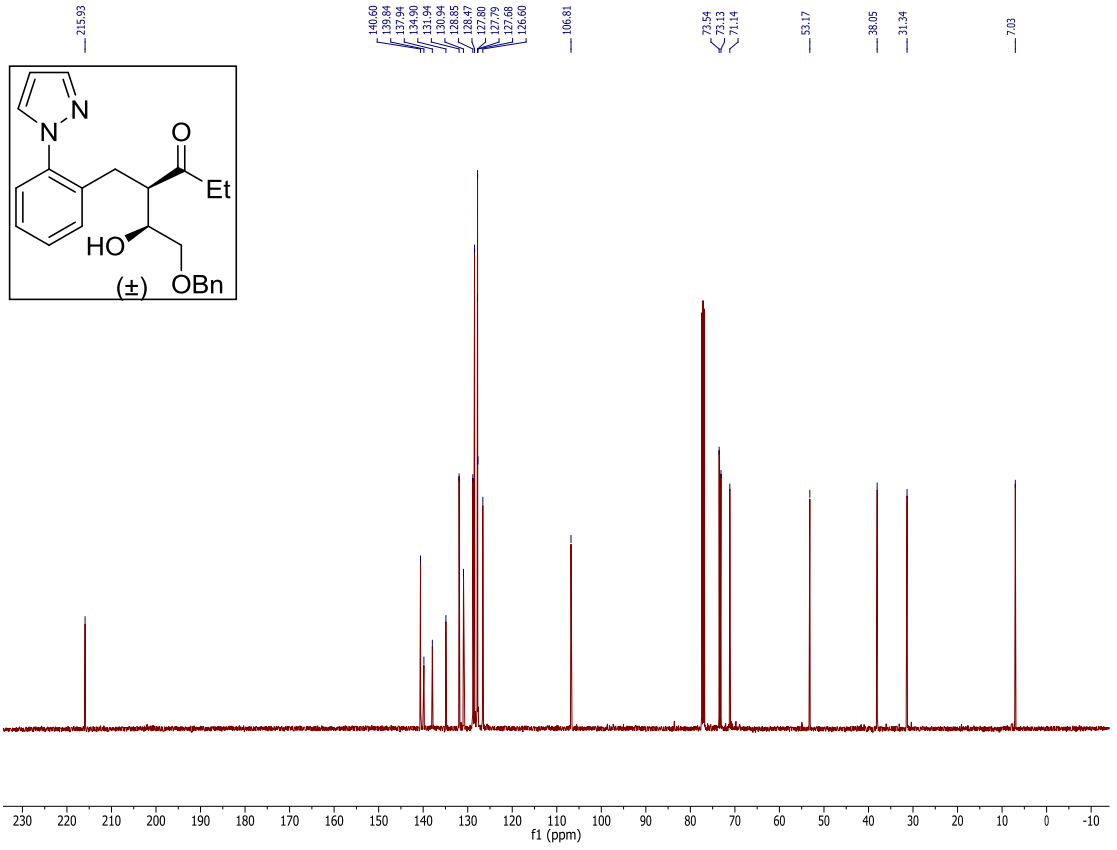
7.729
7.503
7.499
7.488
7.485
7.471
7.467
7.456
7.452
7.441
7.437
7.434
7.431
7.420
7.417
7.405
7.402
7.362
7.358
7.347
7.343
7.260
6.485
6.481
6.477
5.803
5.785
5.170
5.152
4.026
4.024
4.012
4.009
3.998
3.995
3.983
3.981
1.115
1.101
1.087
OH
CO2Et
1.00
1.00
1.00
2.01
1.00
1.00
1.00
1.00
2.00
3.00
f1 (ppm)


172.25
140.93
139.05
134.63
131.55
130.67
129.65
128.71
125.12
107.64
77.41
77.16
76.91
72.55
61.60
14.23
OH
CO2Et
f1 (ppm)


N
N
O
Et
HO
(±)
Me
f1 (ppm)


N
N
O
Et
HO
(±)
Me
f1 (ppm)


N
N
O
Et
HO
(±)
OBn
f1 (ppm)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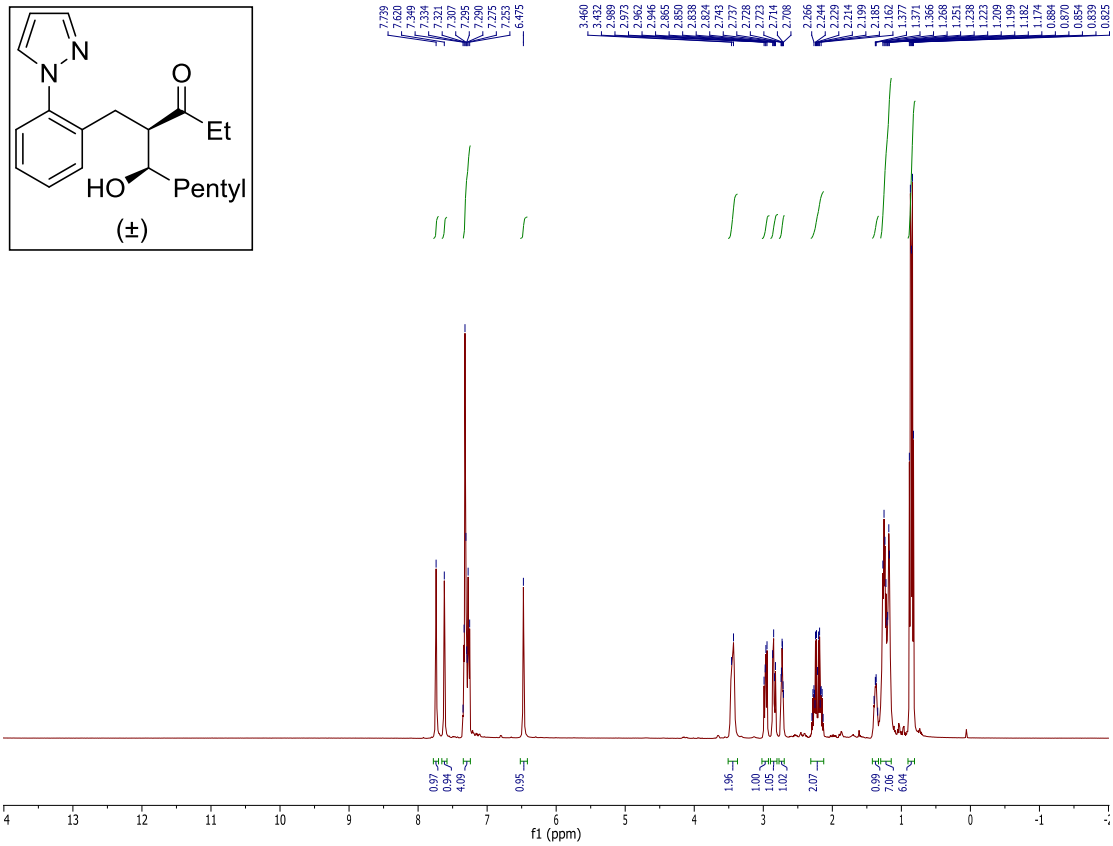
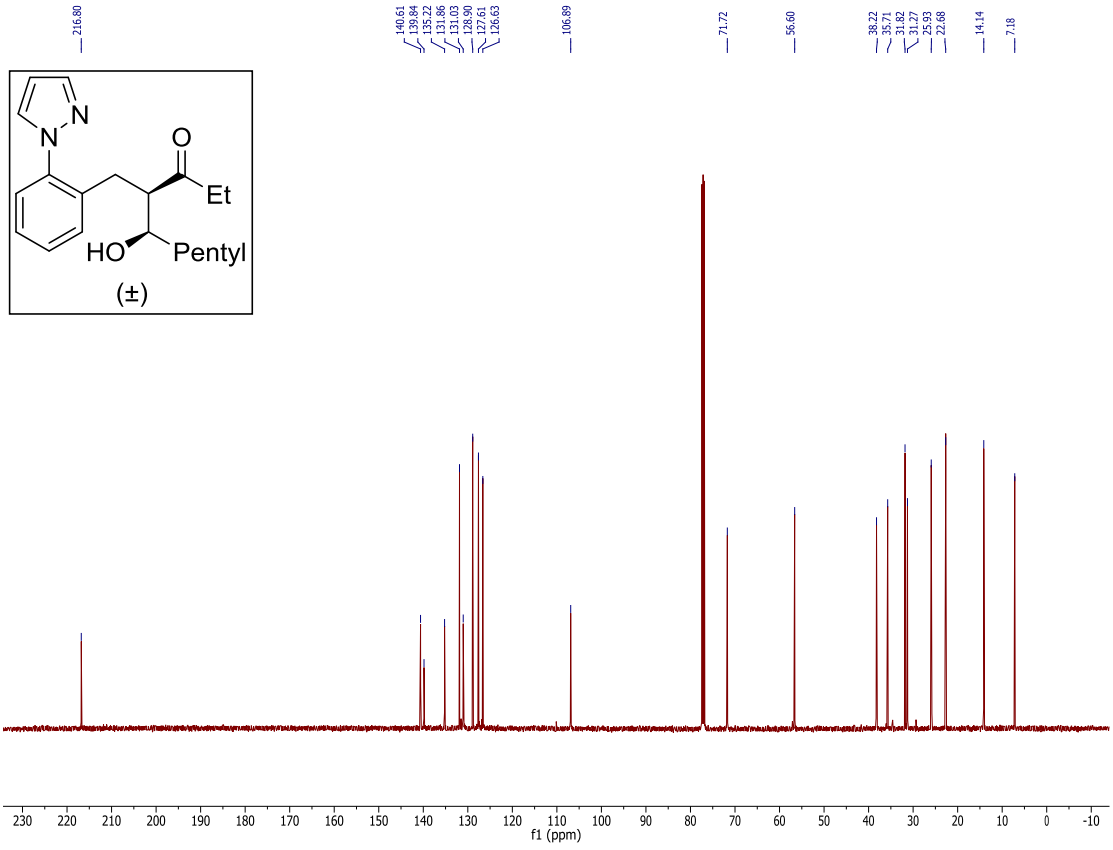
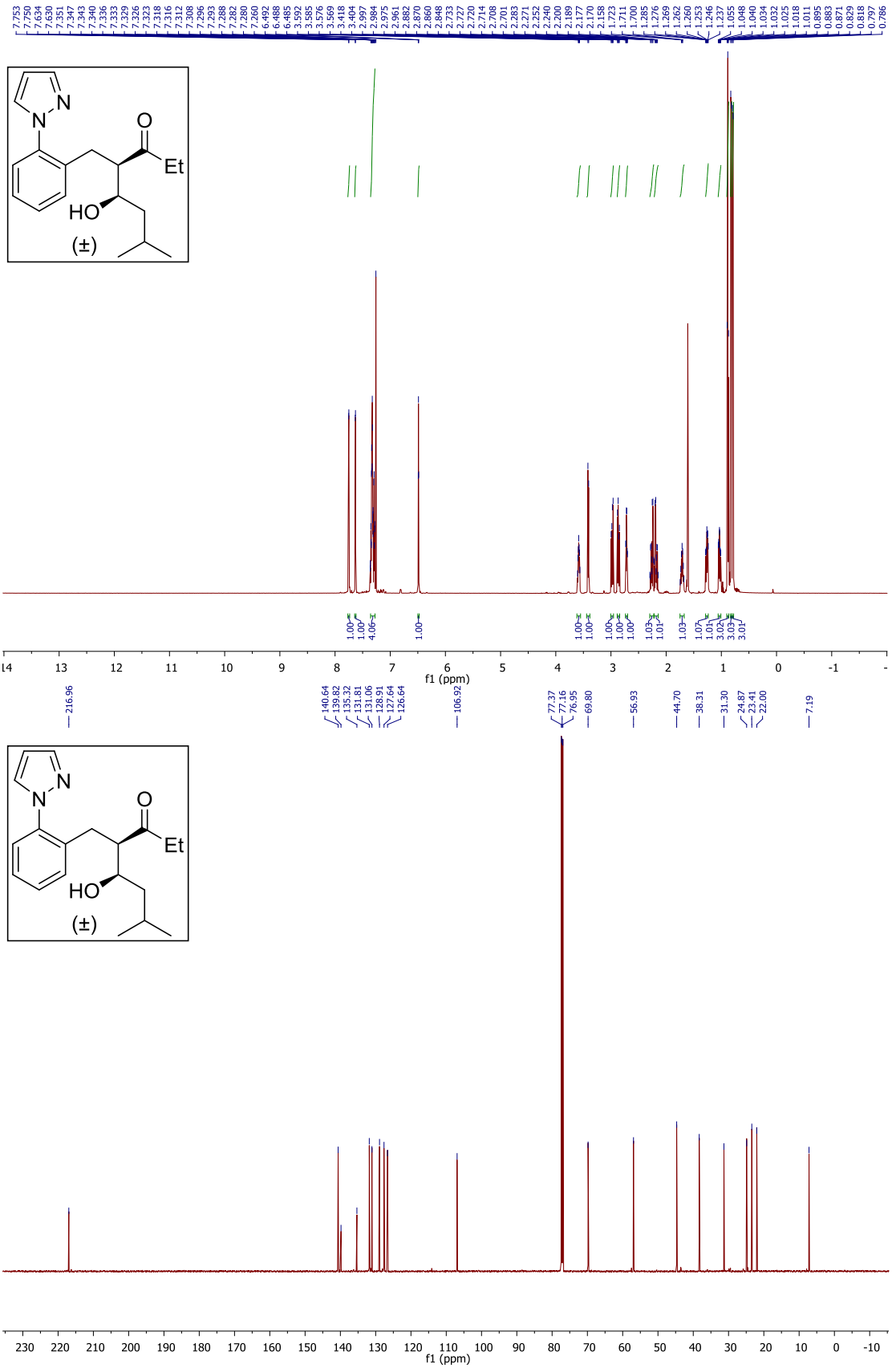
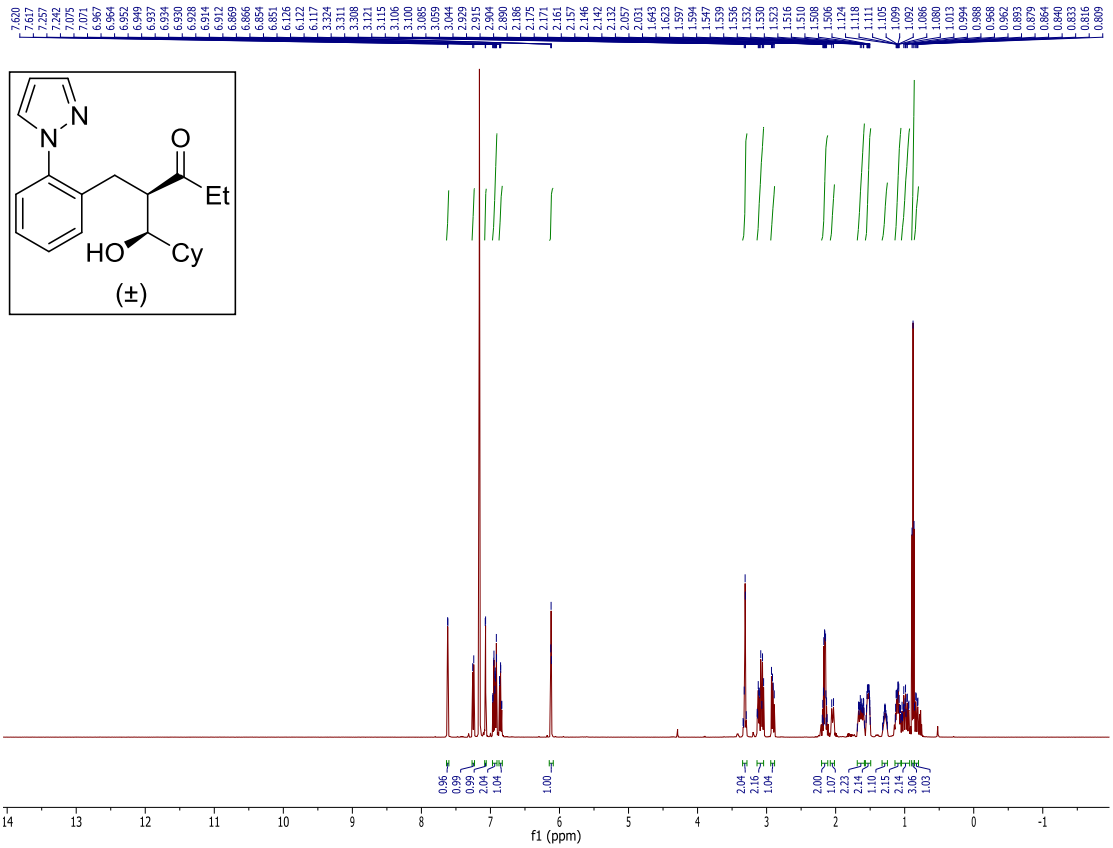
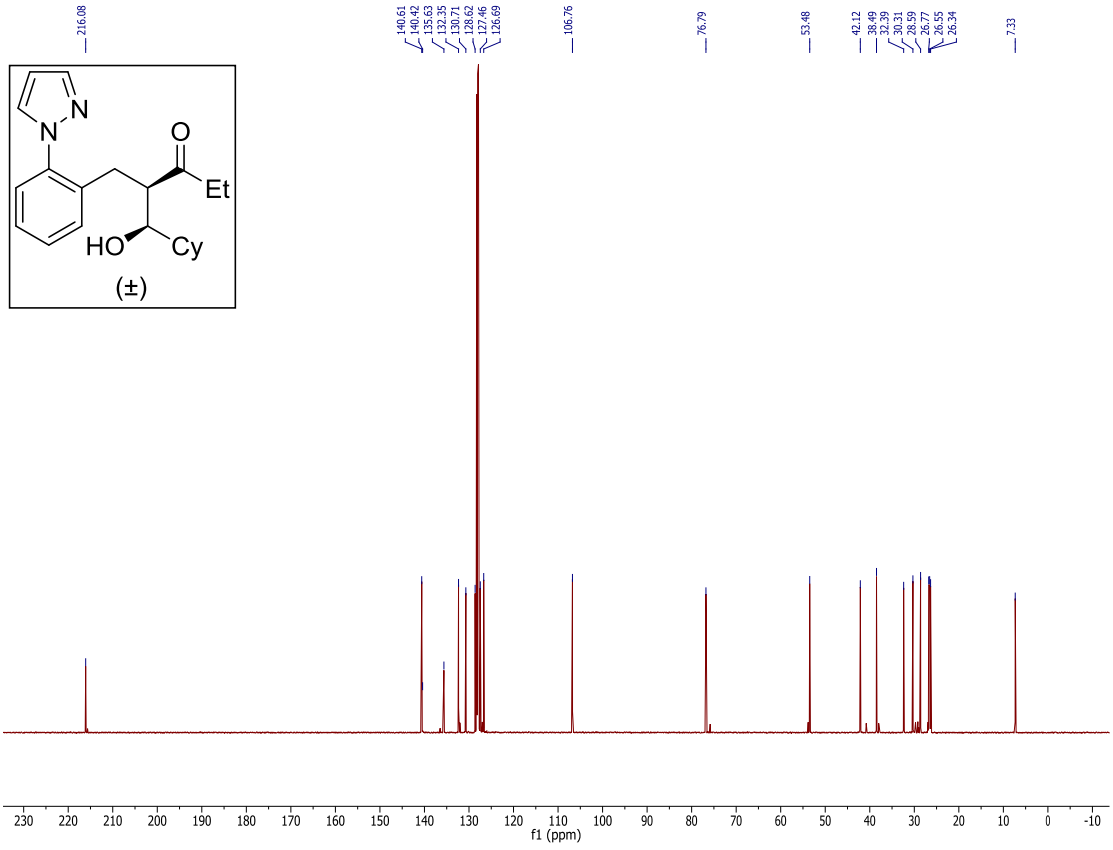
N
O
Et
HO
(±)
OBn
f1 (ppm)

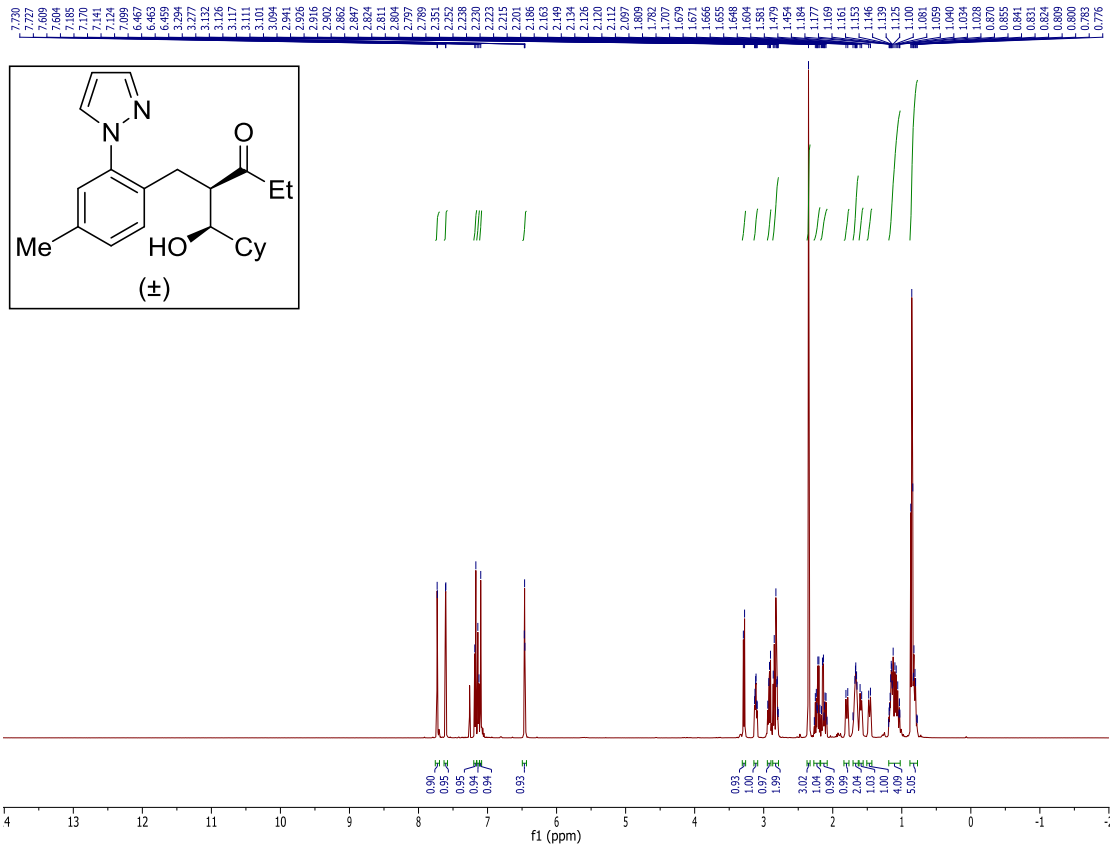

N
N
O
Et
HO
Pentyl
(±)
f1 (ppm)

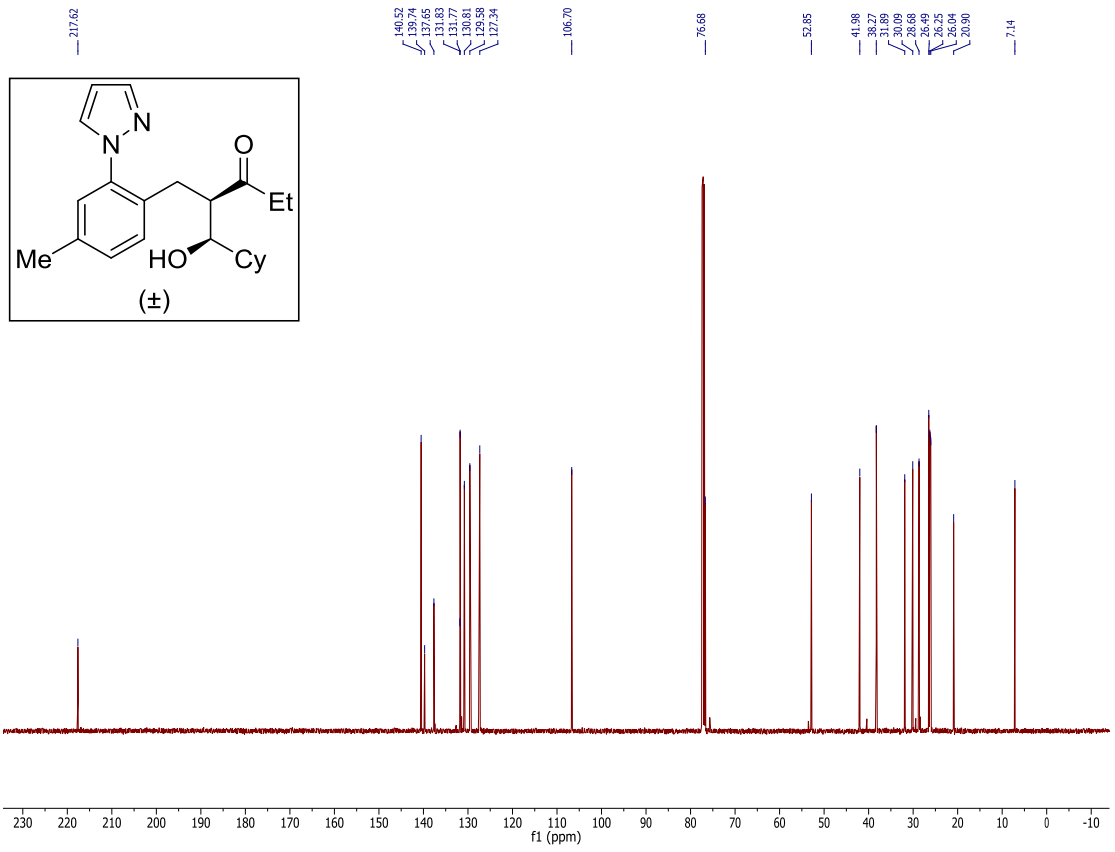

N
N
O
Et
HO
Pentyl
(±)
f1 (ppm)

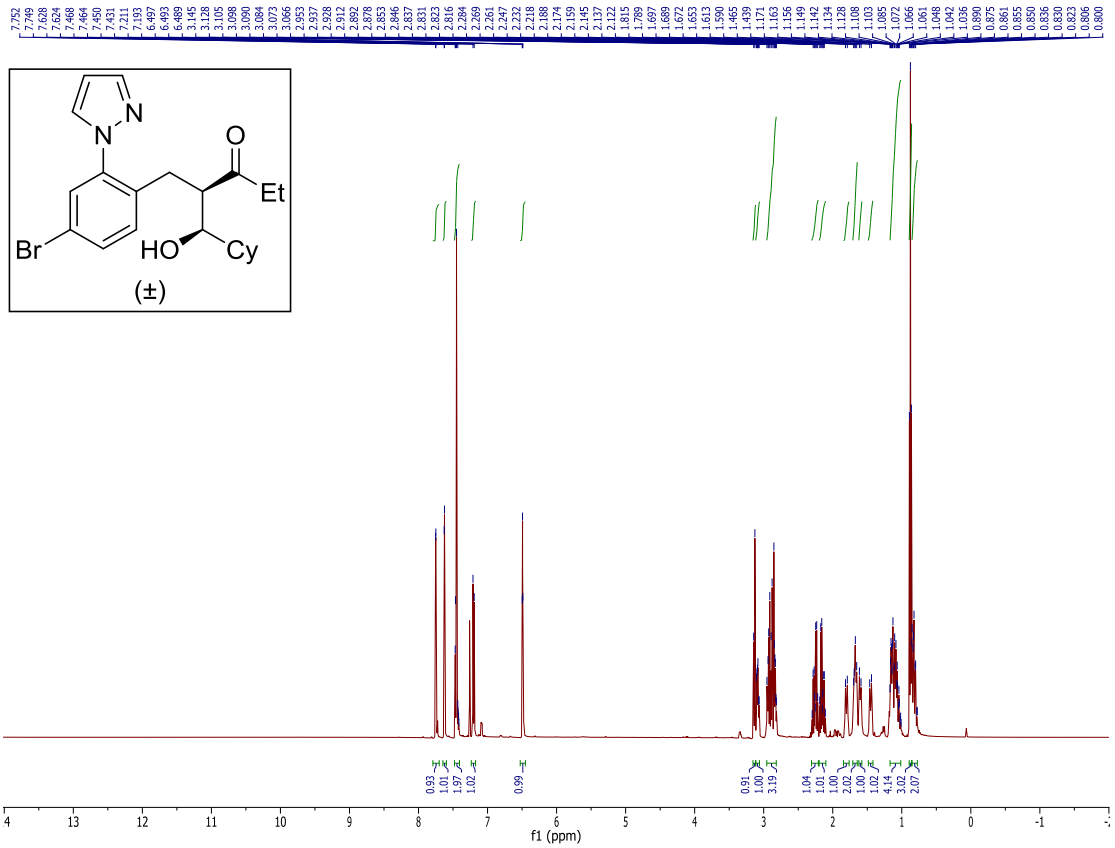

N
N
O
Et
HO
(±)
f1 (ppm)
f1 (ppm)

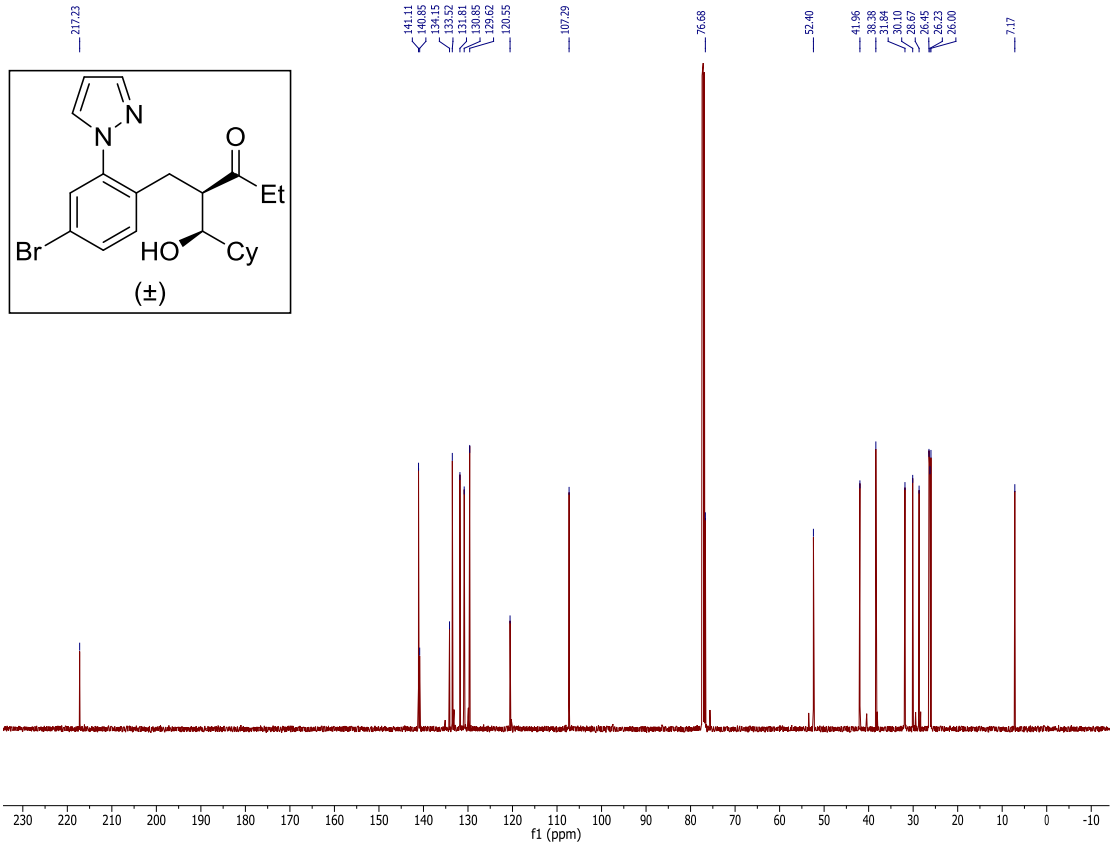

O
Et
HO
Cy
(±)
f1 (ppm)

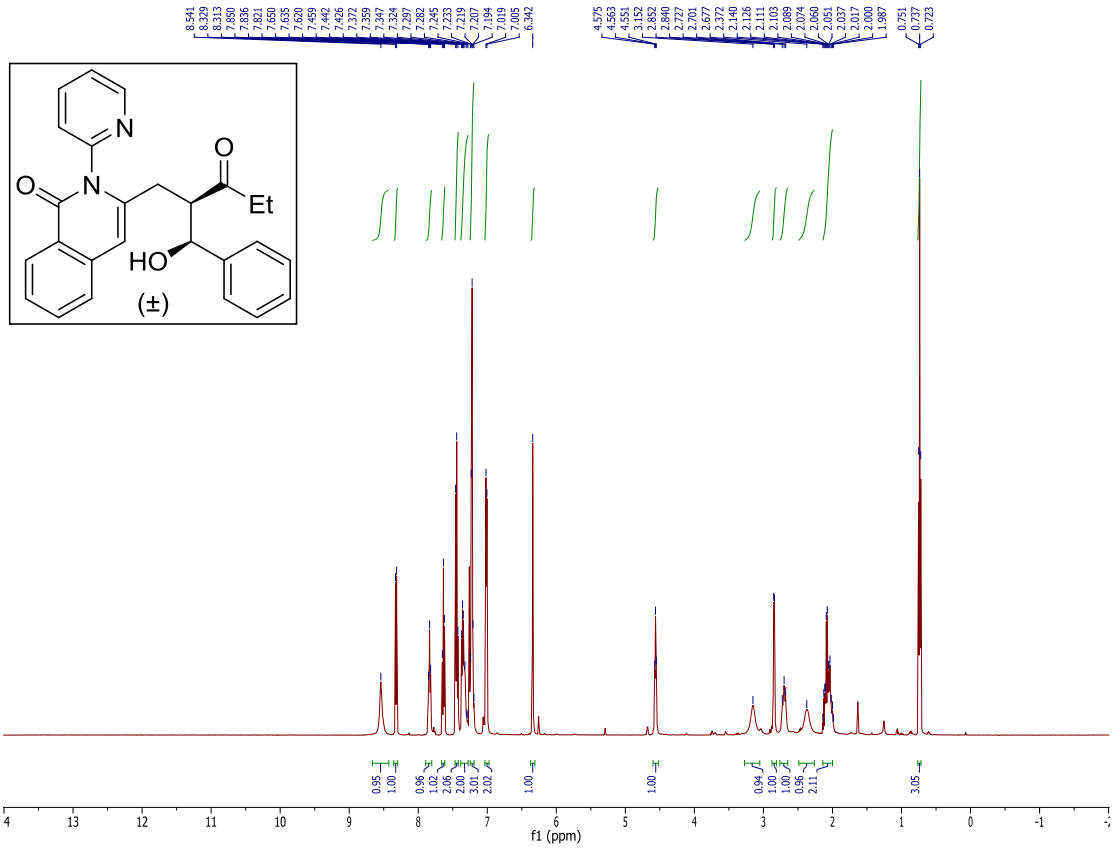

O
Et
HO
Cy
(±)
f1 (ppm)

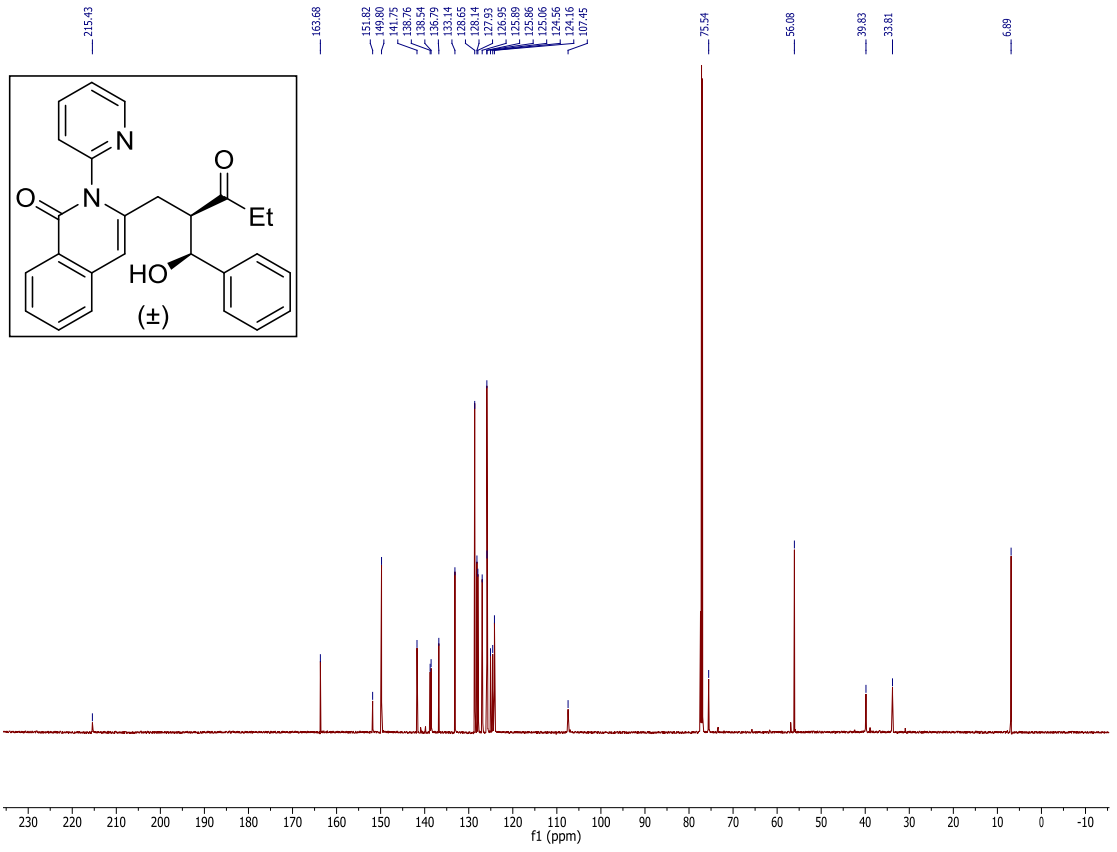

Me
HO
Cy
O
Et
(±)
f1 (ppm)


Me
HO
Cy
O
Et
(±)
f1 (ppm)


Br
HO
Cy
O
Et
(±)
f1 (ppm)


Br
HO
Cy
O
Et
(±)
f1 (ppm)


N
O
N
O
Et
HO
(±)
f1 (ppm)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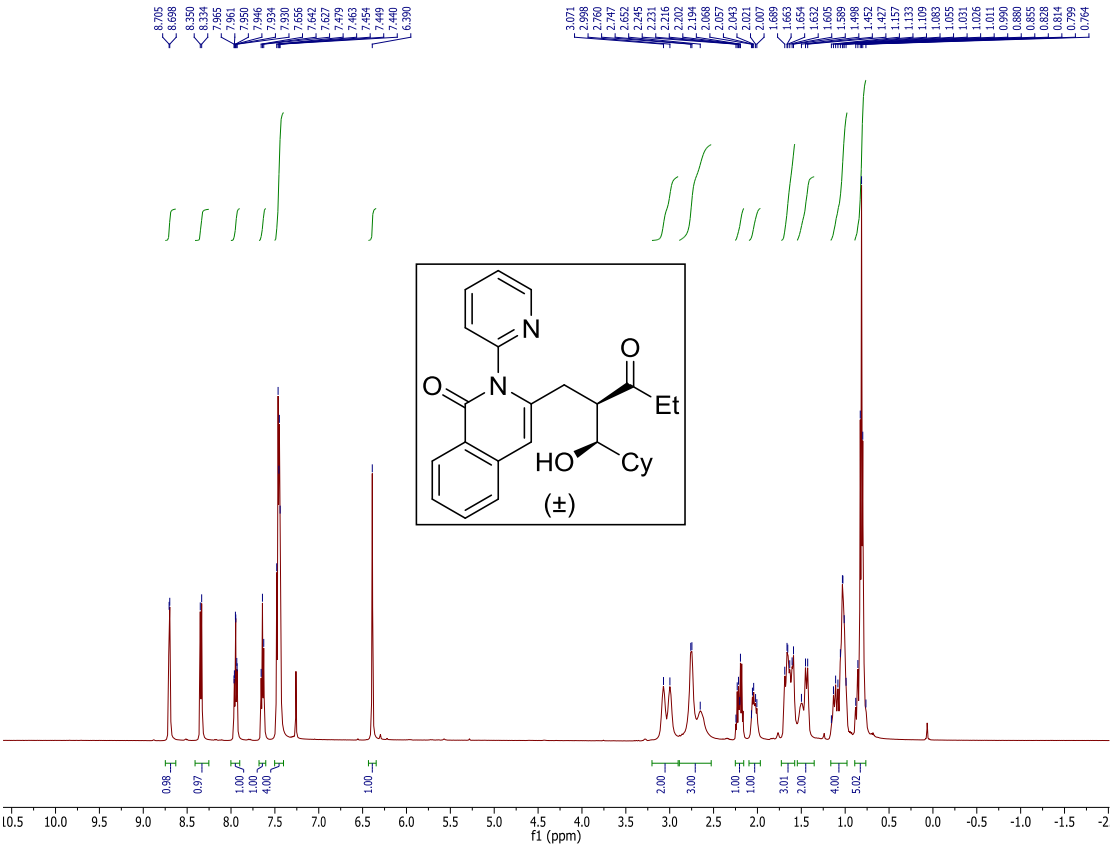
O
N
O
Et
HO
(±)
f1 (ppm)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8.350
8.334
7.965
7.961
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7.946
7.930
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7.627
7.479
7.463
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7.449
7.440
6.390
3.071
2.998
2.760
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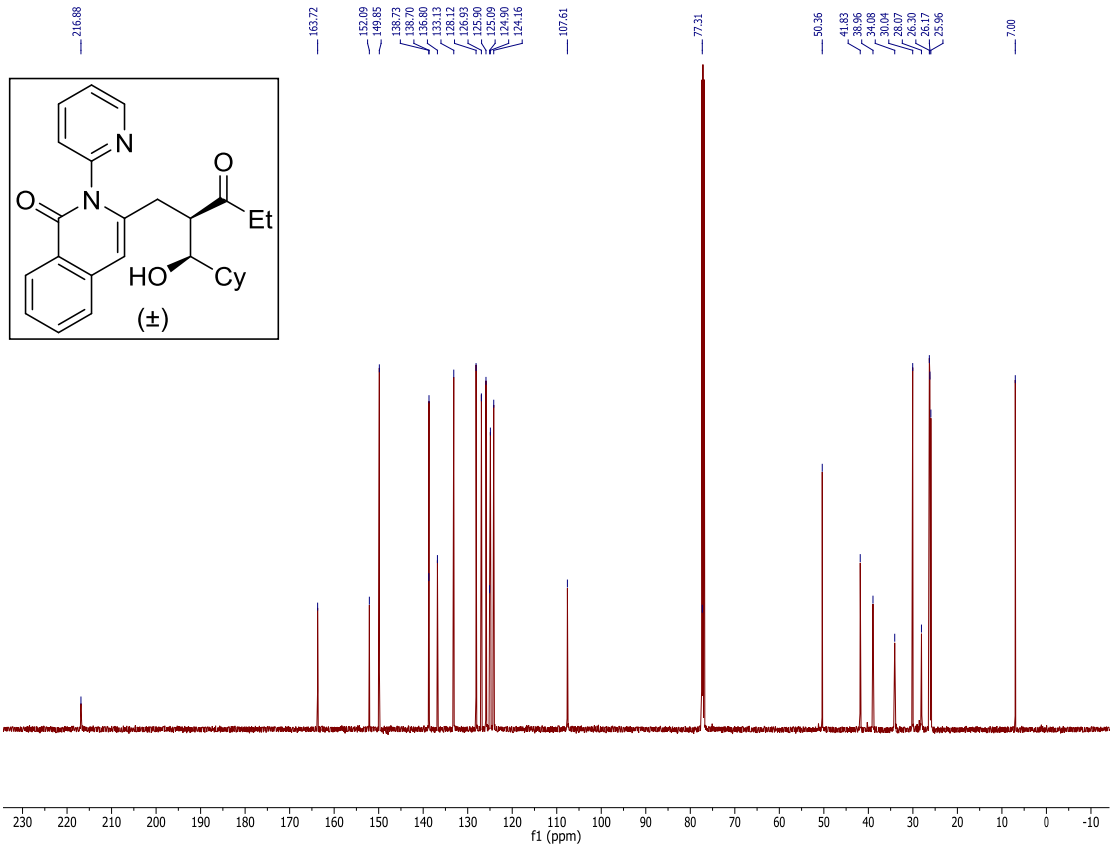
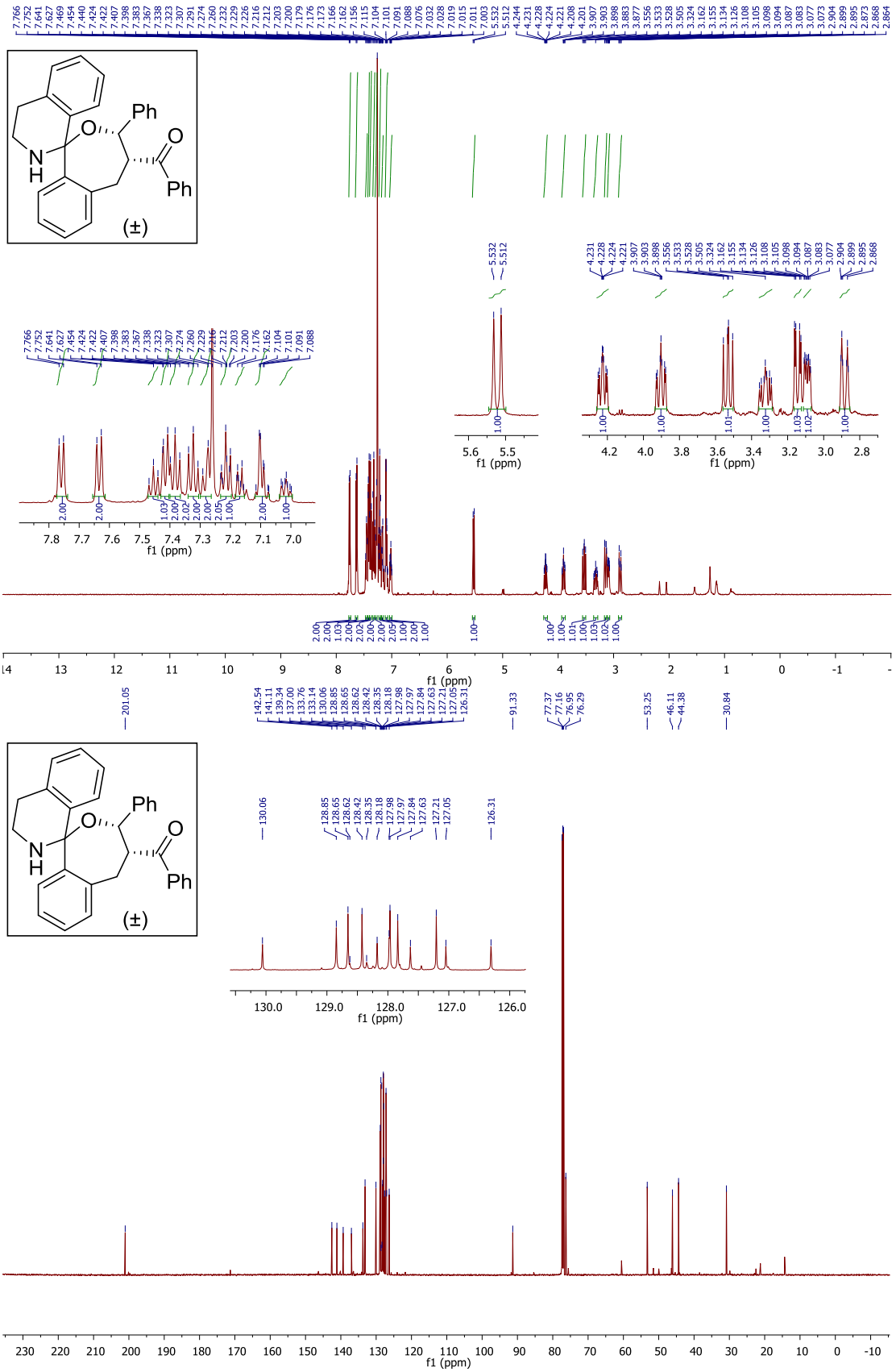
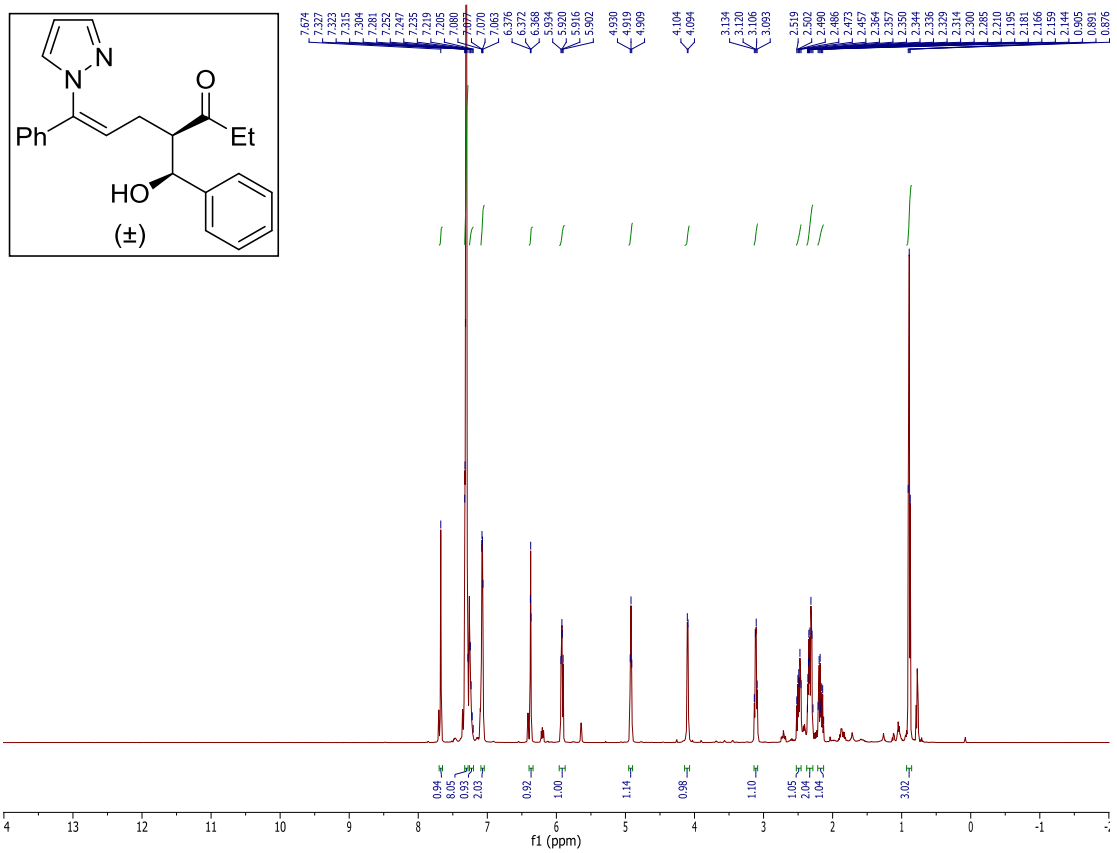
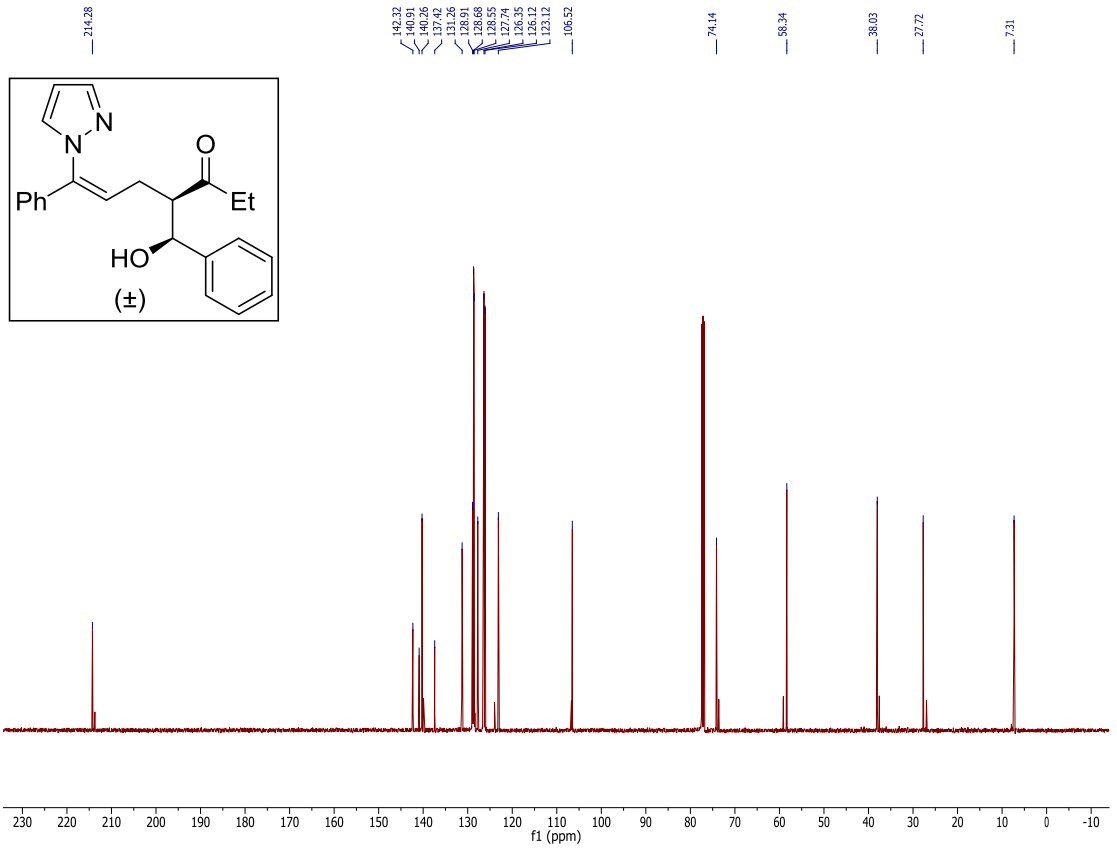
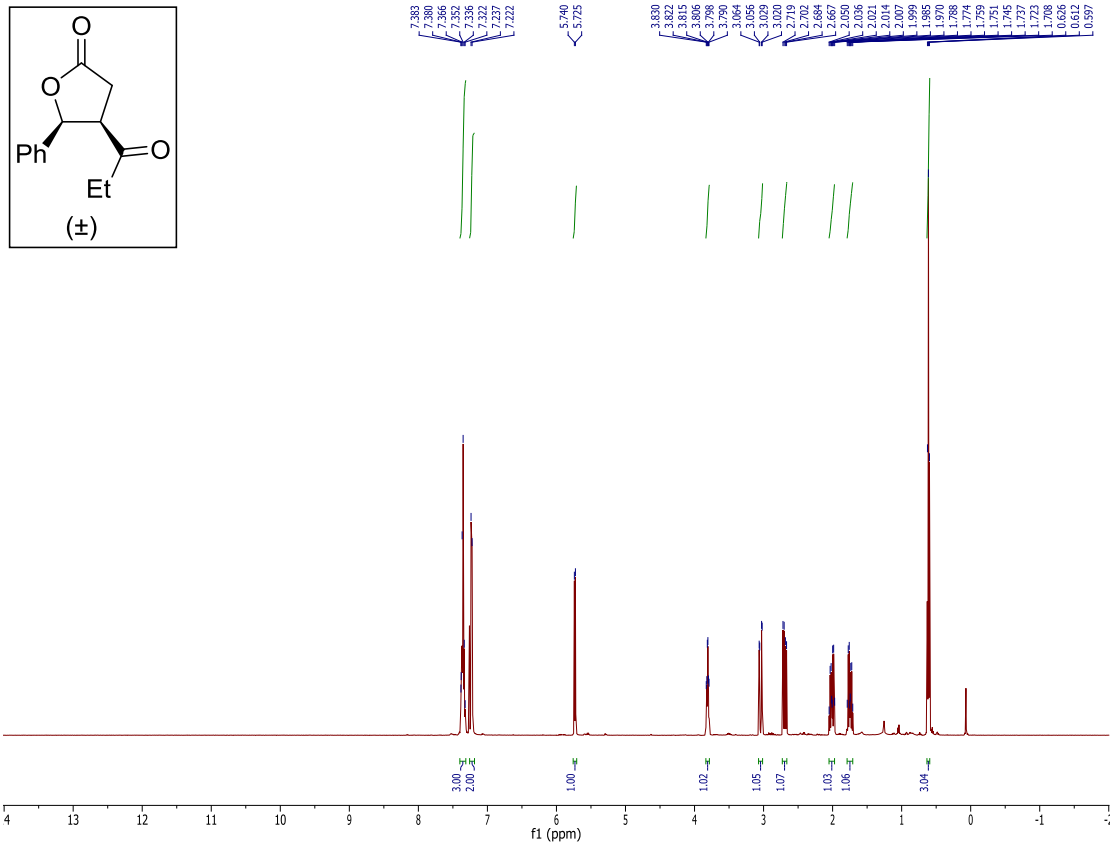
1.00
4.00
1.00
2.00
3.00
1.00
1.00
3.01
2.00
4.00
5.02
f1 (ppm)
N
O
N
O
Et
HO
Cy
(±)

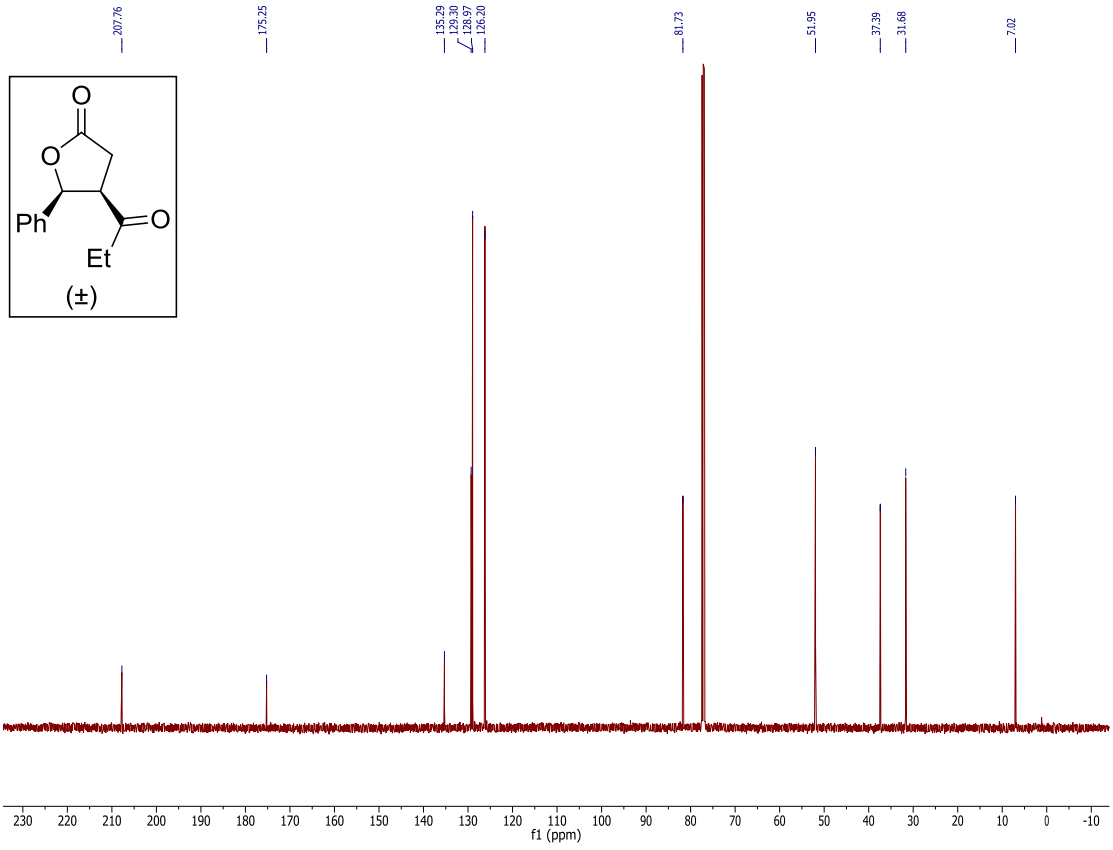

216.68
163.72
152.09
149.85
138.73
138.70
136.80
133.13
128.12
126.93
125.90
125.09
124.90
124.16
107.61
77.31
50.36
41.83
38.96
34.08
30.04
28.07
26.30
26.17
25.96
7.00
f1 (ppm)
N
O
N
O
Et
HO
Cy
(±)

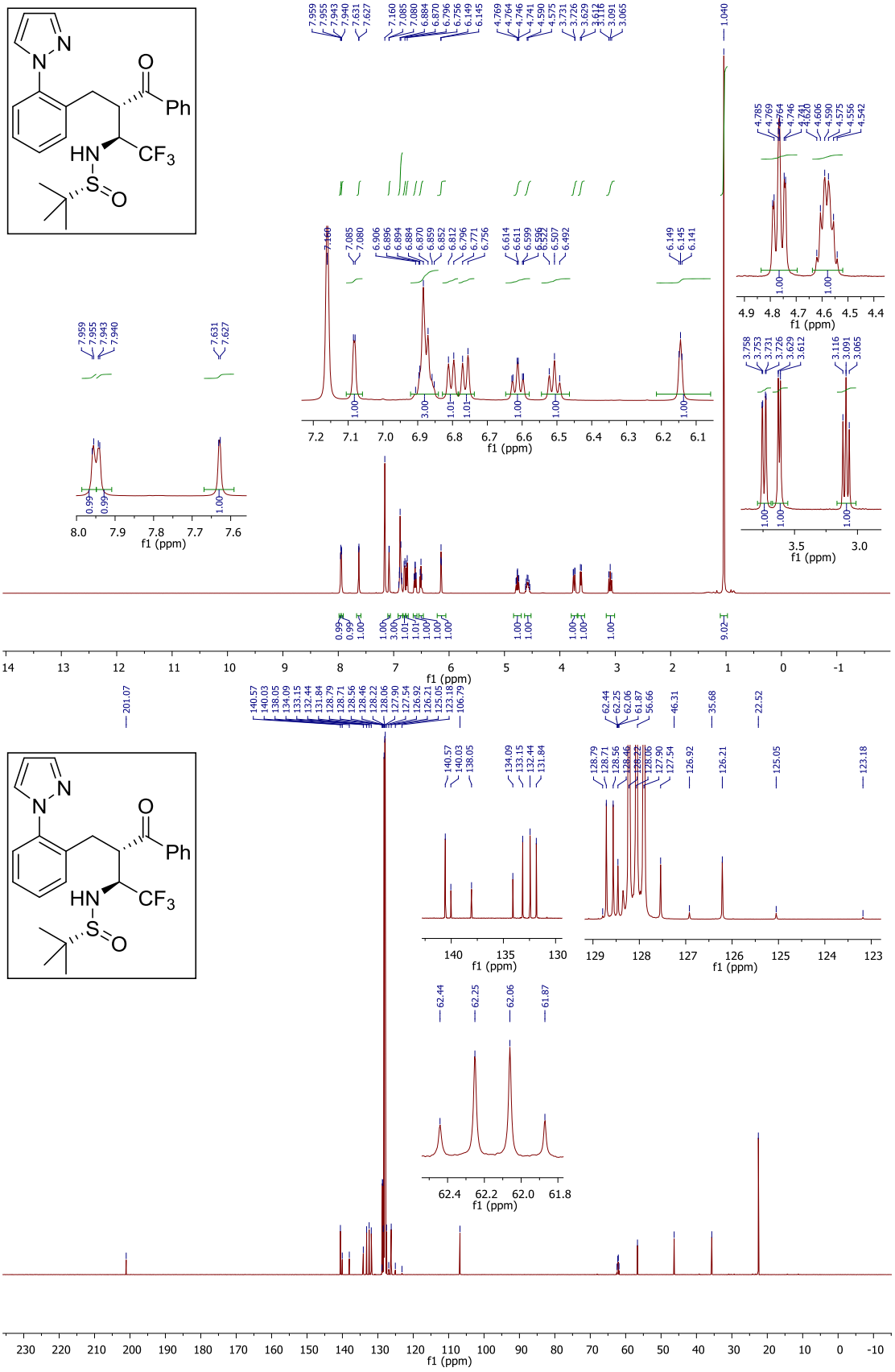

Ph
O
N
H
O
Ph
(±)
f1 (ppm)

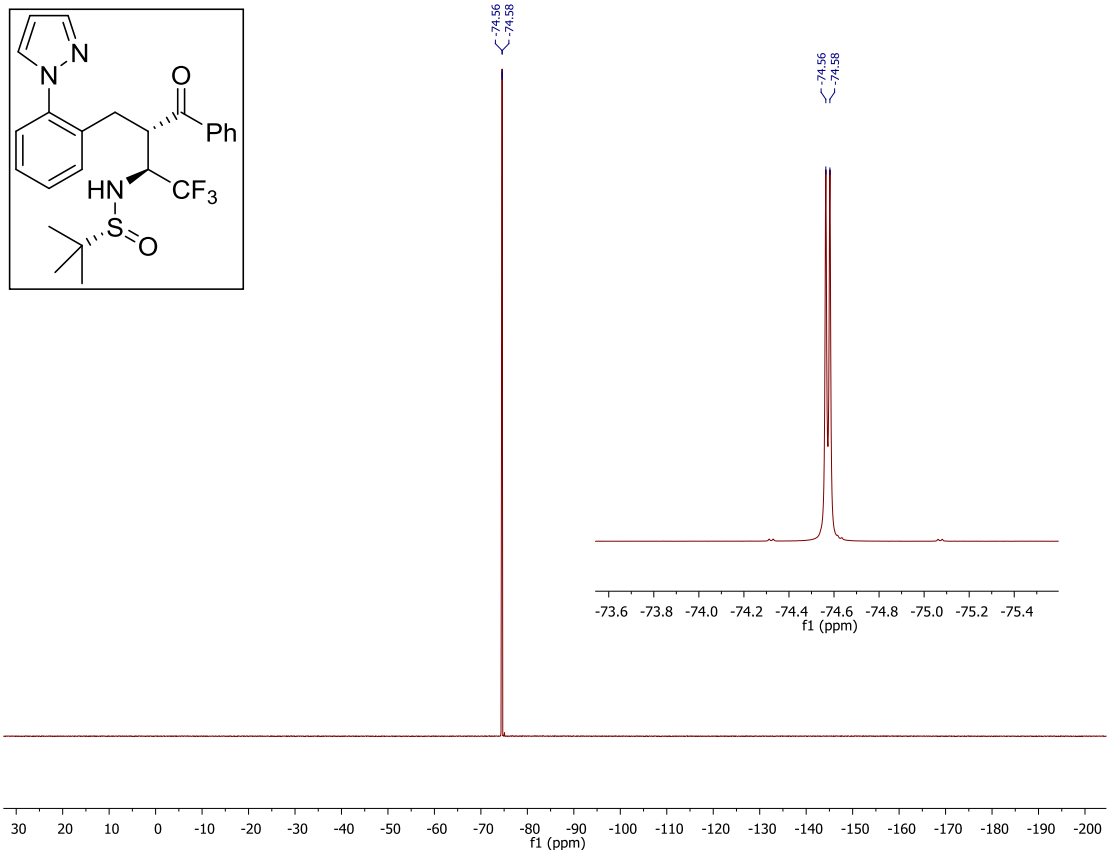

Ph
N
N
O
Et
HO
(±)
f1 (ppm)

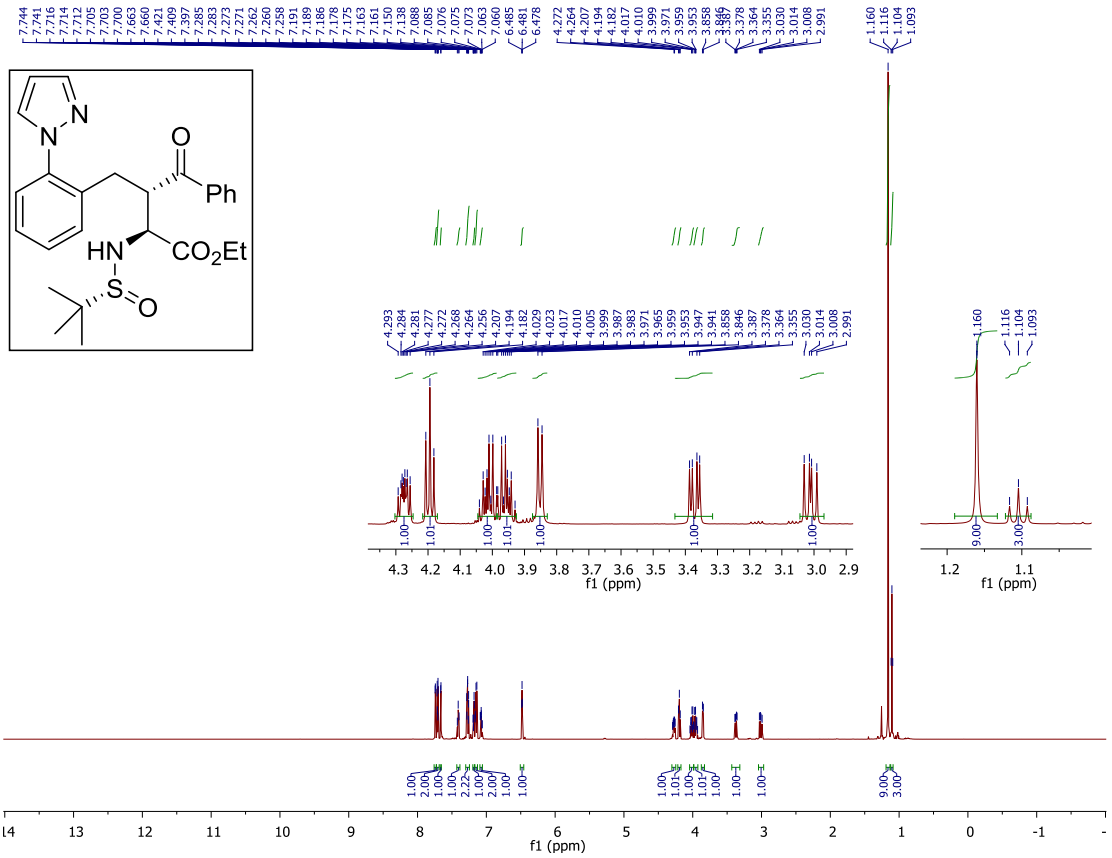

Ph
N
N
O
Et
HO
(±)
f1 (ppm)

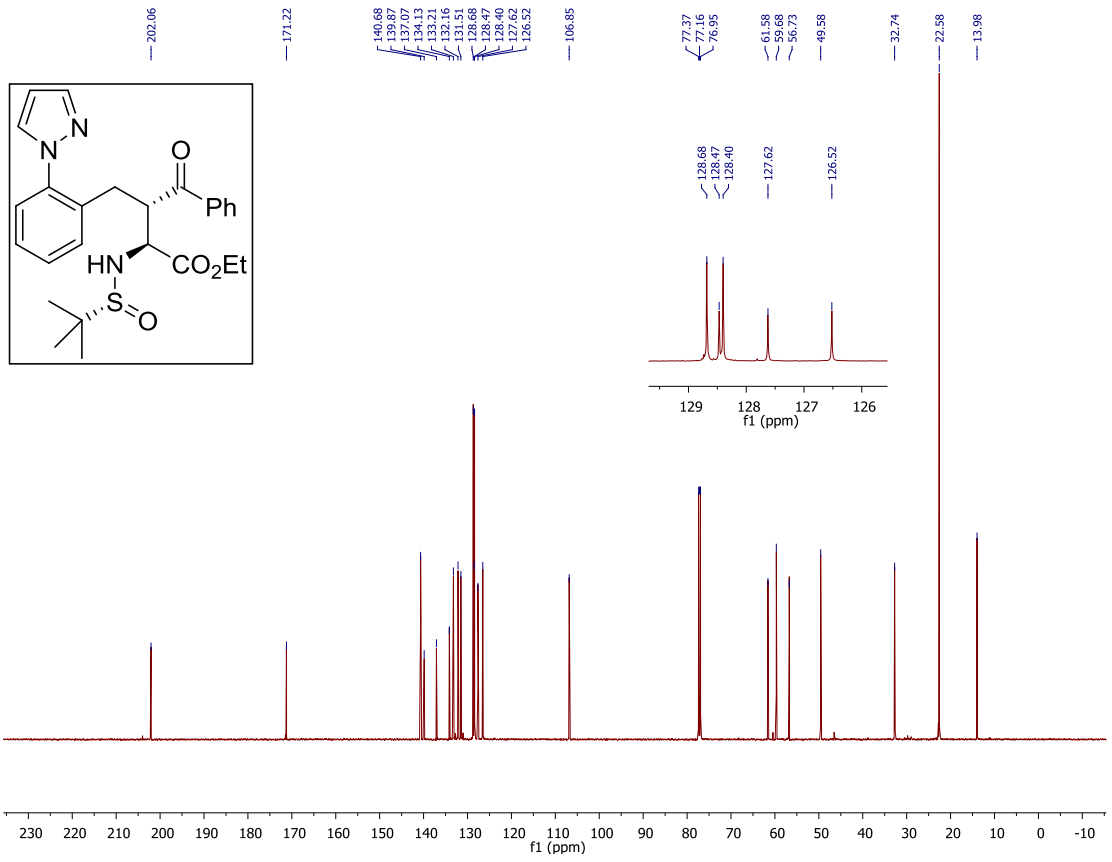

O
O
Ph
O
Et
(±)
7.383
7.380
7.366
7.352
7.336
7.332
7.237
7.222
5.740
5.725
3.830
3.822
3.815
3.806
3.798
3.790
3.064
3.056
3.029
3.020
2.719
2.702
2.684
2.667
2.050
2.036
2.021
2.014
2.007
1.999
1.985
1.970
1.788
1.774
1.759
1.751
1.745
1.737
1.723
1.708
0.626
0.612
0.597
3.00
2.00
1.00
1.02
1.05
1.07
1.03
1.06
3.04
f1 (ppm)


O
O
Ph
O
Et
(±)
207.76
175.25
135.29
129.30
128.97
126.20
81.73
51.95
37.39
31.68
7.02
f1 (ppm)


O
Ph
HN
CF3
S
O
f1 (ppm)


-74.56
-74.58
-74.56
-74.58
-73.6 -73.8 -74.0 -74.2 -74.4 -74.6 -74.8 -75.0 -75.2 -75.4
f1 (ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)


Ph
CO2Et
HN
S
O
f1 (ppm)


Ph
CO2Et
HN
S
O
f1 (ppm)