

Lewis Acid Mediated, Mild C-H Aminoalkylation of Azoles via Three Component Coupling

Marion H. Emmert,^{*‡a} Cyndi Qixin He,^{*‡b} Akshay A. Shah^{‡c}, and Stephanie Felten^{‡a}

^a*Process Research & Development, MRL, Merck & Co. Inc, 770 Sumneytown Pike, West Point, PA 19486.*

^b*Computational and Structural Chemistry, MRL, Merck & Co. Inc, 126 E Lincoln Ave, Rahway, NJ 07065.*

^c*Discovery Chemistry, MRL, Merck & Co. Inc, 770 Sumneytown Pike, West Point, PA 19486.*

Table of Contents

Materials and Methods.....	5
Reaction Optimization: Ni/Ligand/Solvent Screen.....	6
Reaction Time Course in the Absence of Ni Catalysts.....	8
Reaction Optimization: TBSOTf, Et ₂ N-TMS, and benzoxazole loading	9
Reaction Optimization: Influence of Added Base	11
General Procedure 1: Amine scope.....	13
General Procedure 2: Amine, Aldehyde, and Azole Substrate Scope	14
Modifications for Substrates with Acidic NH or CH bonds	14
Amine Scope 1	15
5-Chloro-2-(morpholino(phenyl)methyl)benzo[d]oxazole.....	15
5-Chloro-2-(phenyl(pyrrolidin-1-yl)methyl)benzo[d]oxazole.....	17
5-Chloro-2-((4-methylpiperazin-1-yl)(phenyl)methyl)benzo[d]oxazole.....	19
2-(Azepan-1-yl(phenyl)methyl)-5-chlorobenzo[d]oxazole	21
2-(Azetidin-1-yl(phenyl)methyl)-5-chlorobenzo[d]oxazole	23
<i>N</i> -(5-Chlorobenzo[d]oxazol-2-yl)(phenyl)methyl)cyclohexanamine	25
<i>N</i> -(5-Chlorobenzo[d]oxazol-2-yl)(phenyl)methyl)-N-phenylaniline	27
Amine with low reactivity (<2 LCAP) under conditions of General Procedure 1	29
Modified Conditions for Amine-HCl Salts as Substrates.....	30
Amine Scope II Via Parallel Medicinal Chemistry.....	31
General Procedure 3.....	31
5-Chloro-2-((4-chlorophenyl)(3-(trifluoromethyl)piperidin-1-yl)methyl)benzo[d]oxazole.....	32
5-Chloro-2-((4-chlorophenyl)(3,3-dimethyl-4-(trifluoromethyl)piperidin-1-yl)methyl)benzo[d]oxazole	35
5-Chloro-2-((4-chlorophenyl)(7,7-difluoro-6-methyl-3-azabicyclo[4.1.0]heptan-3-yl)methyl)benzo[d]oxazole	38
5-Chloro-2-((4-chlorophenyl)(6,6-difluoro-3-azabicyclo[3.1.0]hexan-3-yl)methyl)benzo[d]oxazole	42
5-Chloro-2-((4-chlorophenyl)(3,3-difluoro-2-methylpyrrolidin-1-yl)methyl)benzo[d]oxazole	45
5-Chloro-2-((4-chlorophenyl)(7-(trifluoromethyl)-1,4-oxazepan-4-yl)methyl)benzo[d]oxazole	48
5-Chloro-2-((4-chlorophenyl)(6,6-difluoro-3-azabicyclo[3.1.1]heptan-3-yl)methyl)benzo[d]oxazole...51	51
5-Chloro-2-((4-chlorophenyl)(8,8-difluoro-3-azabicyclo[3.2.1]octan-3-yl)methyl)benzo[d]oxazole	54
5-Chloro-2-((4-chlorophenyl)(4,4-difluoro-5-methylazepan-1-yl)methyl)benzo[d]oxazole	57

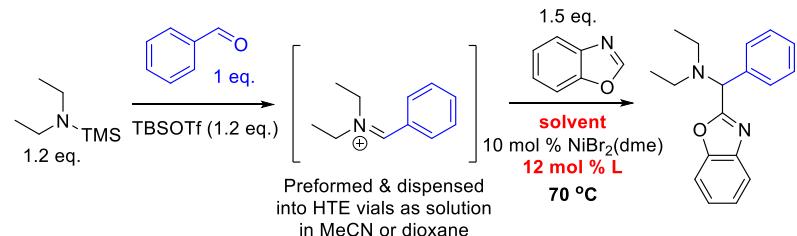
Azole Scope	60
<i>N</i> -((5-Chlorobenzo[d]oxazol-2-yl)(phenyl)methyl)- <i>N</i> -ethylethanamine	60
<i>N</i> -Ethyl- <i>N</i> -((4-fluorobenzo[d]oxazol-2-yl)(phenyl)methyl)ethanamine	62
<i>N</i> -Ethyl- <i>N</i> -((5-nitrobenzo[d]oxazol-2-yl)(phenyl)methyl)ethanamine	65
<i>N</i> -ethyl- <i>N</i> -((5-(4-fluorophenyl)oxazol-2-yl)(phenyl)methyl)ethanamine	67
<i>N</i> -((1 <i>H</i> -imidazol-2-yl)(phenyl)methyl)- <i>N</i> -ethylethanamine	70
2-((diethylamino)(phenyl)methyl)- <i>N,N</i> -diphenyl-1 <i>H</i> -imidazole-1-carboxamide	72
<i>N</i> -ethyl- <i>N</i> -(phenyl(5-((trimethylsilyl)ethynyl)thiazol-2-yl)methyl)ethanamine	75
<i>N</i> -((6-bromopyridin-2-yl)methyl)-2-((diethylamino)(phenyl)methyl)oxazole-5-carboxamide	78
<i>N</i> -((5-(5-bromothiophen-2-yl)oxazol-2-yl)(phenyl)methyl)- <i>N</i> -ethylethanamine	81
(4-chlorophenyl)(2-((diethylamino)(phenyl)methyl)oxazol-5-yl)methanone	83
1-(2-((diethylamino)(phenyl)methyl)oxazol-5-yl)ethan-1-one	85
Synthesis according to General Procedure 2	85
Crude UPLC/MS before hydrolysis	85
Crude UPLC/MS after hydrolysis.....	86
<i>N</i> -((5-(4-bromophenyl)thiazol-2-yl)(phenyl)methyl)- <i>N</i> -ethylethanamine.....	90
<i>N</i> -((6-Bromobenzo[d]thiazol-2-yl)(phenyl)methyl)- <i>N</i> -ethylethanamine.....	92
<i>N</i> -(benzo[d]thiazol-2-yl(phenyl)methyl)- <i>N</i> -ethylethanamine	94
<i>N</i> -((5-Bromooxazolo[4,5-b]pyridin-2-yl)(phenyl)methyl)- <i>N</i> -ethylethanamine.....	96
C-H aminoalkylation of imidazole and benzimidazole via <i>in-situ</i> tosylation.....	100
Imidazole: <i>N</i> -((1 <i>H</i> -imidazol-2-yl)(phenyl)methyl)- <i>N</i> -ethylethanamine	100
Benzimidazole: <i>N</i> -((1 <i>H</i> -benzo[d]imidazol-2-yl)(phenyl)methyl)- <i>N</i> -ethylethanamine	100
Azoles With Low Reactivity (<2 LCAP).....	104
Aldehyde Scope	105
<i>N</i> -((5-Chlorobenzo[d]oxazol-2-yl)(4-fluorophenyl)methyl)- <i>N</i> -ethylethanamine	105
<i>N</i> -((5-Chlorobenzo[d]oxazol-2-yl)(4-methoxyphenyl)methyl)- <i>N</i> -ethylethanamine	110
<i>N</i> -((4-Bromophenyl)(5-chlorobenzo[d]oxazol-2-yl)methyl)- <i>N</i> -ethylethanamine	112
<i>N</i> -((5-Chlorobenzo[d]oxazol-2-yl)(4-(trifluoromethyl)phenyl)methyl)- <i>N</i> -ethylethanamine	114
<i>N</i> -((5-Chlorobenzo[d]oxazol-2-yl)(5-methylthiophen-2-yl)methyl)- <i>N</i> -ethylethanamine	116
1-(5-Chlorobenzo[d]oxazol-2-yl)- <i>N,N</i> -diethyl-2,2-dimethylpropan-1-amine.....	118
Aldehydes showing no product formation under conditions of General Procedure 2	120
Experimental data supporting enamine formation for aliphatic aldehydes with acidic β-C-H bonds.....	121
Experiments in support of proposed mechanism: Observation of azole-TBS adduct and H/D exchange	124

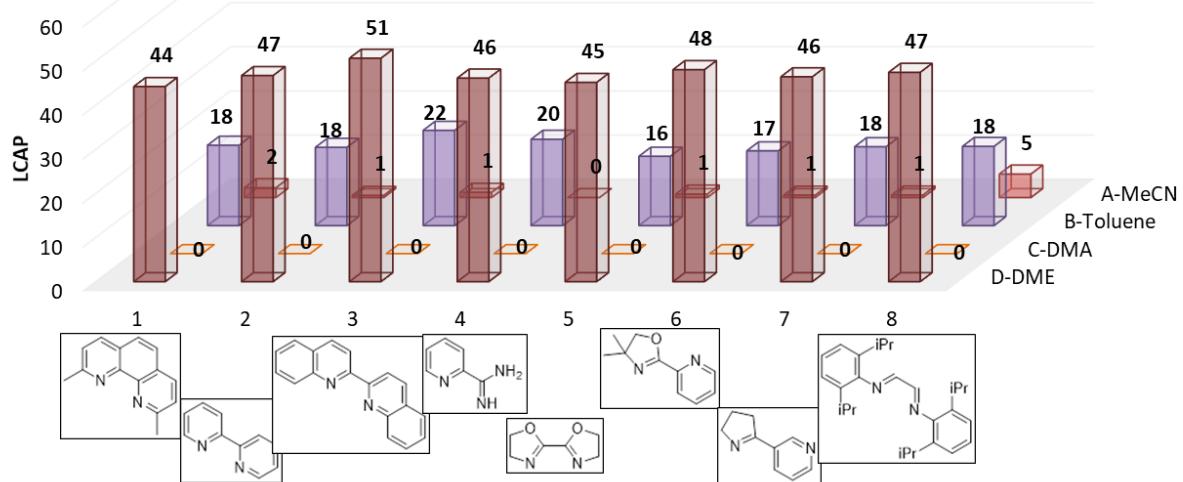
DFT Results.....	128
Proposed Mechanism	128
Computational Methods	129
Calculated Transition States for C-C Bond Formation Step	130
Insights into Azole Reactivity: Calculated Deprotonation Equilibria with Successful and Unsuccessful Substrates.....	132
Cartesian Coordinates for Transition State Structures in the Amine Scope	133

Materials and Methods

Reaction optimization was performed via high-throughput experimentation in 1000 uL glass vials. Analysis of crude reaction mixtures was performed by reverse-phase UPLCMS. Yields in reaction optimizations are provided in LCAP (Liquid Chromatography Area Percent) at 215 nm or are shown as calibrated yields using biphenyl as internal standard. Data obtained from parallel synthesis experiments and optimization were analyzed using Virscidian to quantify and export data.

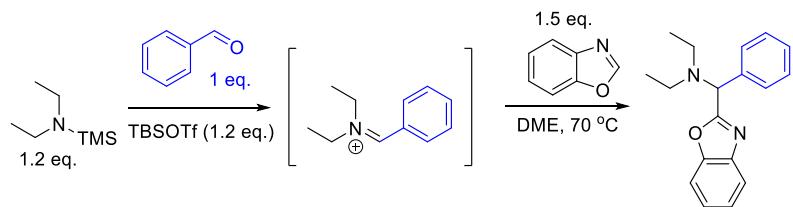
Reaction Optimization: Ni/Ligand/Solvent Screen



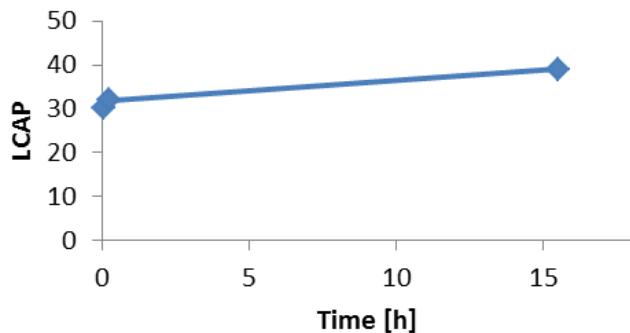


Scheme 1. LC Area Percent (LCAP) of product obtained in different solvent with 12 mol % *N,N* bidentate ligands. Wells in column 7 serve as control, as the base contained in these wells cannot ligate to a metal center in a bidentate fashion.

Reaction Time Course in the Absence of Ni Catalysts

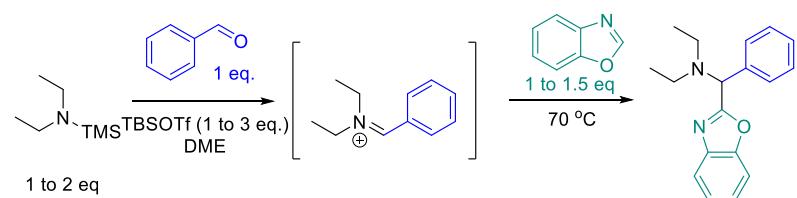


N,N-diethyl-1,1,1-trimethylsilanamine (214 µL, 1.129 mmol), *tert*-butyldimethylsilyl trifluoromethanesulfonate (259 µL, 1.129 mmol), and benzaldehyde (96 µL, 0.941 mmol) were mixed in 1,2-dimethoxyethane (2.5 ml) in the glovebox and stirred at room temperature for 5 minutes. The solution was added to a vial containing benzoxazole (168 mg, 1.411 mmol) and the mixture was sampled after stirring vigorously for 10 sec. Then, the mixture was placed on a hotplate and heated to 70 °C. The mixture was sampled at 15 min and 15 h.



Scheme 2. LC Area Percent vs. Time in the absence of metal catalyst and ligands.

Reaction Optimization: TBSOTf, Et₂N-TMS, and benzoxazole loading



A stock solution of 297.1 mg benzaldehyde and 215.9 mg biphenyl (as internal standard) in 6.499 mL was prepared. 50 uL of this solution (corresponding to 1.00 equiv. benzaldehyde and 0.50 equiv. biphenyl) was added to each well of a 96-well plate.

A stock solution of benzoxazole (595.6 mg in 4.40 mL DME) was prepared.

3.8 uL (1.00 equiv.), 4.7 uL (1.25 equiv.), 5.7 uL (1.50 equiv.), or 7.6 uL (2.00 equiv.) $\text{Et}_2\text{N-SiMe}_3$ were added to the respective vials (see design in Figure 1). Then, 4.6 uL (1.00 equiv.), 5.7 uL (1.25 equiv.), 6.9 uL (1.50 equiv.), 8.0 uL (1.75 equiv.), 9.2 uL (2.00 equiv.), 11.5 uL (2.50 equiv.), or 13.8 uL (3.00 equiv.) TBS-OTf were added to the respective vials (see design in Figure 1). Then, 20 uL (1.00 equiv.), 25 uL (1.25 equiv.), 30 uL (1.50 equiv.), 40 uL (2.00 equiv.), or 50 uL (2.50 equiv.) of the benzoxazole stock solution were added to the respective vials.

The plate was sealed in the glovebox, removed, and placed on a tumblestirrer outside the glovebox. The plate was heated to 70 °C for 18 h. After the reaction time was complete, the plate was taken off the hotplate and allowed to cool to room temperature. 700 uL MeCN was added to each well; 10 uL of the corresponding solution was added to 800 uL of MeCN. The solutions were analyzed by UPLC/MS. Data analysis and quantification was performed using Virscidian.

benzoxazole		1 eq	1.25 eq	1.5 eq	2 eq	2.5 eq	1 eq	1.25 eq	1.5 eq	1.75 eq	2 eq	2.5 eq	3 eq	TBSOTf
Et ₂ NTMS		1	2	3	4	5	6	7	8	9	10	11	12	
1 eq	A													
1.25 eq	B													
1.5 eq	C													
2 eq	D													
1 eq	E													
1.25 eq	F													
1.5 eq	G													
2 eq	H													

Figure 1. Design of high throughput optimization.

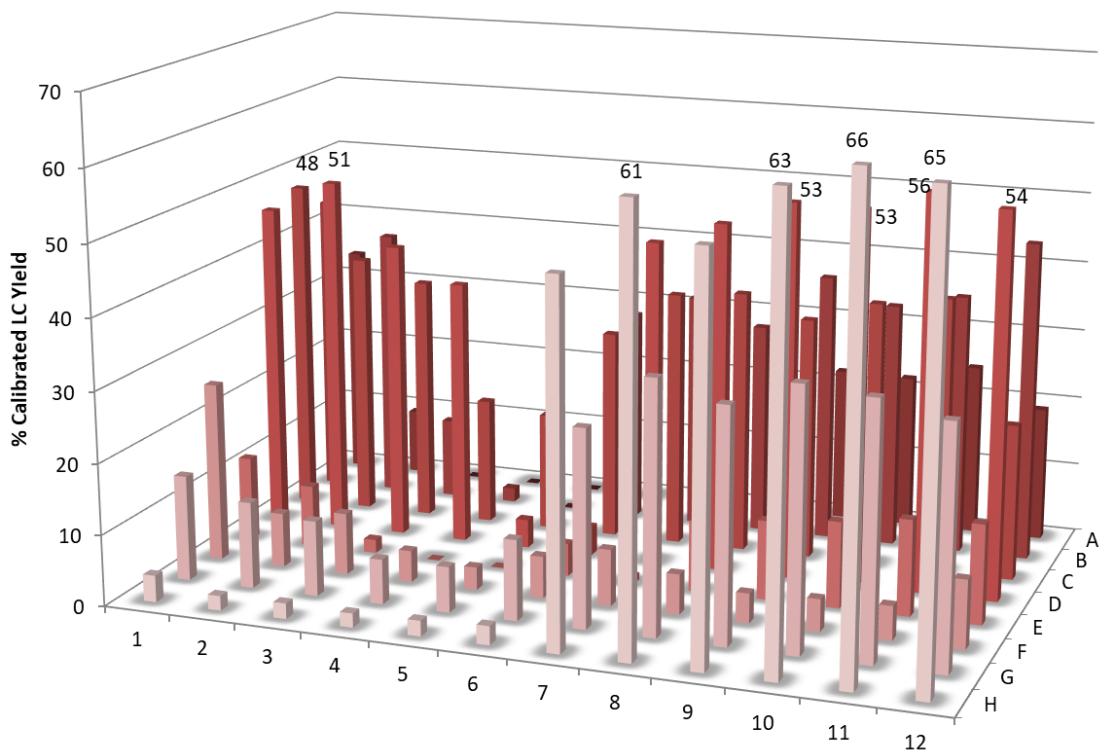
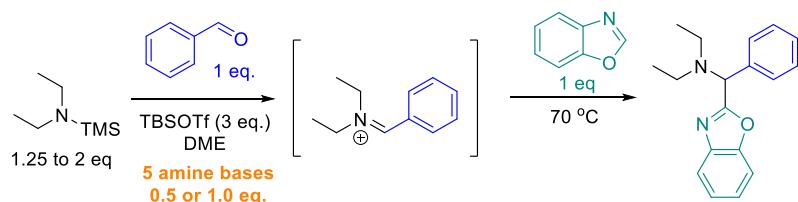


Figure 2. Calibrated LC yields for high-throughput optimization.

Reaction Optimization: Influence of Added Base



A stock solution of benzaldehyde (102.0 μ L), biphenyl (77.1 mg), and TBS-OTf (689 μ L) in DME (1.63 mL) was prepared. 50 μ L of this solution (corresponding to 1.00 equiv. benzaldehyde, 0.50 equiv. biphenyl, and 3.00 equiv. TBSOTf) was added to each of the 24 wells (1000 μ L vials) in a high-throughput plate.

4.8 μ L (1.25 equiv.) or 7.6 μ L (2.00 equiv.) Et₂N-SiMe₃ were added to the respective vials (see design in Figure 3).

A stock solution of benzoxazole (178.7 mg) in DME (1.32 mL) was prepared. 20 μ L of this solution was added to each well (corresponding to 1.00 equiv. benzoxazole).

Then, 0.8 μ L (0.50 equiv.) or 1.6 μ L (1.0 equiv.) pyridine, 1.7 μ L (0.50 equiv.) or 3.5 μ L (1.00 equiv.) iPrNEt₂, 1.5 μ L (0.50 equiv.) or 3.0 μ L (1.00 equiv.) DBU, 1.1 μ L (0.50 equiv.) or 2.2 μ L (1.00 equiv.) N-methyl morpholine, or 1.2 μ L (0.50 equiv.) or 2.3 μ L (1.00 equiv.) 2,6-lutidine were added to the respective vials (see design in Figure 3).

The plate was sealed in the glovebox, removed, and placed on a hotplate outside the glovebox. The plate was heated to 70 °C for 18 h. After the reaction time was complete, the reaction block was taken off the hotplate and allowed to cool to room temperature. 700 μ L MeCN was added to each well; 10 μ L of the corresponding solution was added to 800 μ L of ACN. The solutions were analyzed by UPLC/MS. Data analysis and quantification was performed using Virscidian.

	no base	pyridine	EtNiPr ₂	DBU	N-Me morpholin e	2,6-lutidine	
	1-no base	2-pyr	3-iPr ₂ NEt	4-DBU	5-NMO	6-lutidine	
A-1.25 Et ₂ NTMS, 0.5 base	34	16	57	56	52	52	1.25 eq. Et ₂ NTMS
B-1.25 Et ₂ NTMS, 1.0 base	49	22	96	64	53	17	
C-2.0 Et ₂ NTMS, 0.5 base	0	64	16	53	39	53	2.0 eq. Et ₂ NTMS
D-2.0 Et ₂ NTMS, 1.0 base	52	13	65	66	30	19	

Figure 3. Base Screen Design and Calibrated LC Yields.

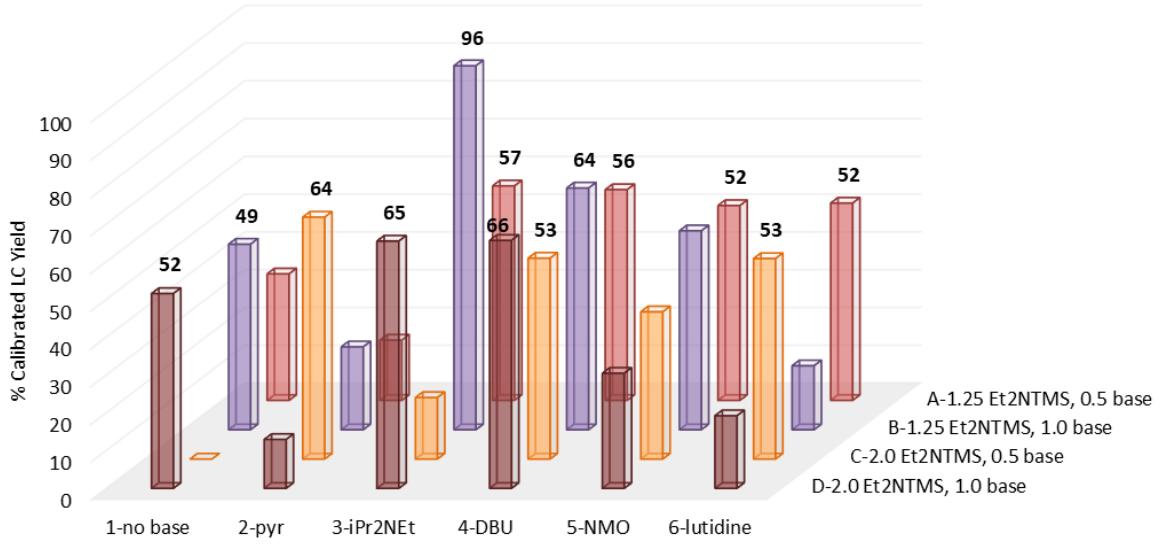
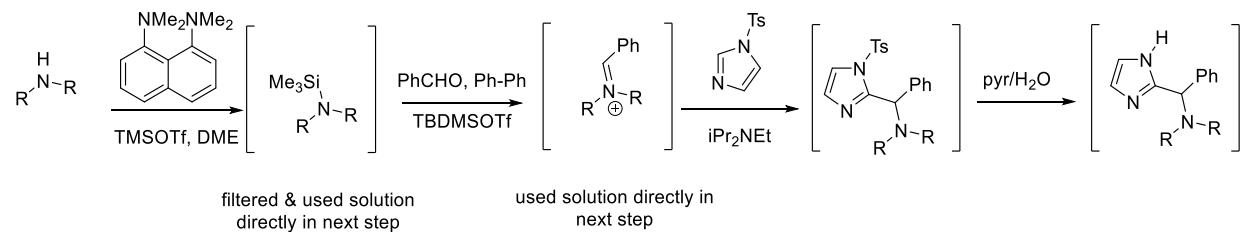


Figure 4. Calibrated LC yields obtained from base screening.

General Procedure 1: Amine scope

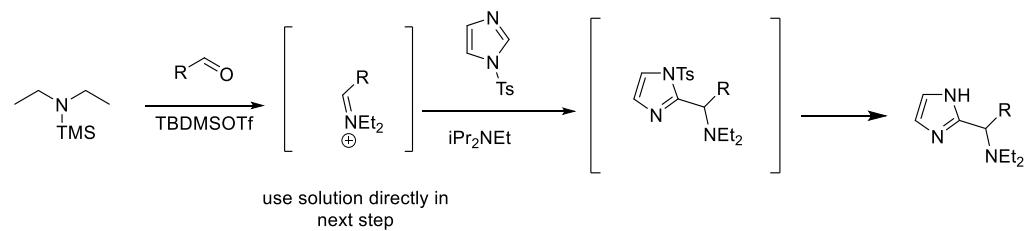


In the glovebox, an oven-dried 1-dram vial equipped with a stir bar was charged with *N*1,*N*1,*N*8,*N*8-tetramethylnaphthalene-1,8-diamine (72.7 mg, 0.339 mmol, 1.20 equiv.) and amine (1.25 equiv.). 1,2-Dimethoxyethane (1000 μ L) was added and the mixture was stirred for 5 min. Trimethylsilyl trifluoromethanesulfonate (0.064 mL, 0.353 mmol, 1.25 equiv.) was added and the vial was capped and allowed to stir vigorously at room temperature for 2h.

The suspension was filtered through a kimwipe-clogged pipette-tip into another 1-dram vial. 1,2-dimethoxyethane (0.50 mL) was used to rinse the original reaction vial and the filtercake. Benzaldehyde (0.029 mL, 0.283 mmol, 1.00 equiv.) and *tert*-Butyldimethylsilyl trifluoromethanesulfonate (0.195 mL, 0.848 mmol) were added to the filtrate and the reaction mixture was stirred for 10 min, before adding *N*-ethyl-*N*-isopropylpropan-2-amine (1.00 or 3.00 equiv.). Then, the mixture was added to a vial containing the azole (1.00 equiv.). The vial was sealed, removed from the glovebox, and heated to 50 °C overnight.

The residue was cooled to room temperature, diluted with 10 mL water, and extracted with 10 mL ethyl acetate. The organic phase was purified by preparative HPLC.

General Procedure 2: Amine, Aldehyde, and Azole Substrate Scope



1-Tosyl-1H-imidazole (1.00 or 1.20 equiv.) was weighed into an oven-dried vial and brought into the glovebox. *tert*-Butyldimethylsilyl trifluoromethanesulfonate (0.416 mL, 1.813 mmol, 3.00 equiv.), *N,N*-diethyl-1,1,1-trimethylsilanamine (1.00 or 1.25 equiv.), and aldehyde (1.00 equiv.) were mixed in a separate oven-dried vial in the glovebox in 1,2-dimethoxyethane (1.0 mL) and stirred for 15 min. Then, this solution was added to the vial containing *N*-tosyl imidazole. *N*-ethyl-*N*-isopropylpropan-2-amine (1.00 equiv.) was added. The resulting solution was removed from the glovebox and heated on a hotplate to 50 °C overnight.

To hydrolyze the tosyl protecting group (only for tosyl-protected imidazole substrate), pyridine (2.0 mL) and water (0.50 mL) were added and the reaction was stirred at 50 °C for 3 h.

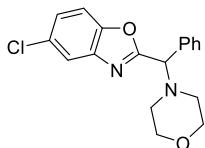
Modifications for Substrates with Acidic NH or CH bonds

Compounds were prepared according to the general procedures, but with several modifications:

- 1) 4.00 equiv. of TBSOTf were used
- 2) 2.00 equiv. or 3.00 equiv. of *i*Pr₂NEt were used
- 3) *i*Pr₂NEt was added to the reaction vial containing the azole before addition of the iminium/TBSOTf mixture
- 4) Workup was performed by pouring the mixture onto 4 to 8 equiv. solid KF, adding 0.5 mL pyridine, and stirring until all silylated products had disappeared (UPLC detection).
- 5) Workup was performed by diluting with 10 mL water, extracting with ethyl acetate, and preparative HPLC purification.

Amine Scope 1

5-Chloro-2-(morpholino(phenyl)methyl)benzo[d]oxazole



Chemical Formula: C₁₈H₁₇ClN₂O₂
Exact Mass: 328.10
Molecular Weight: 328.80

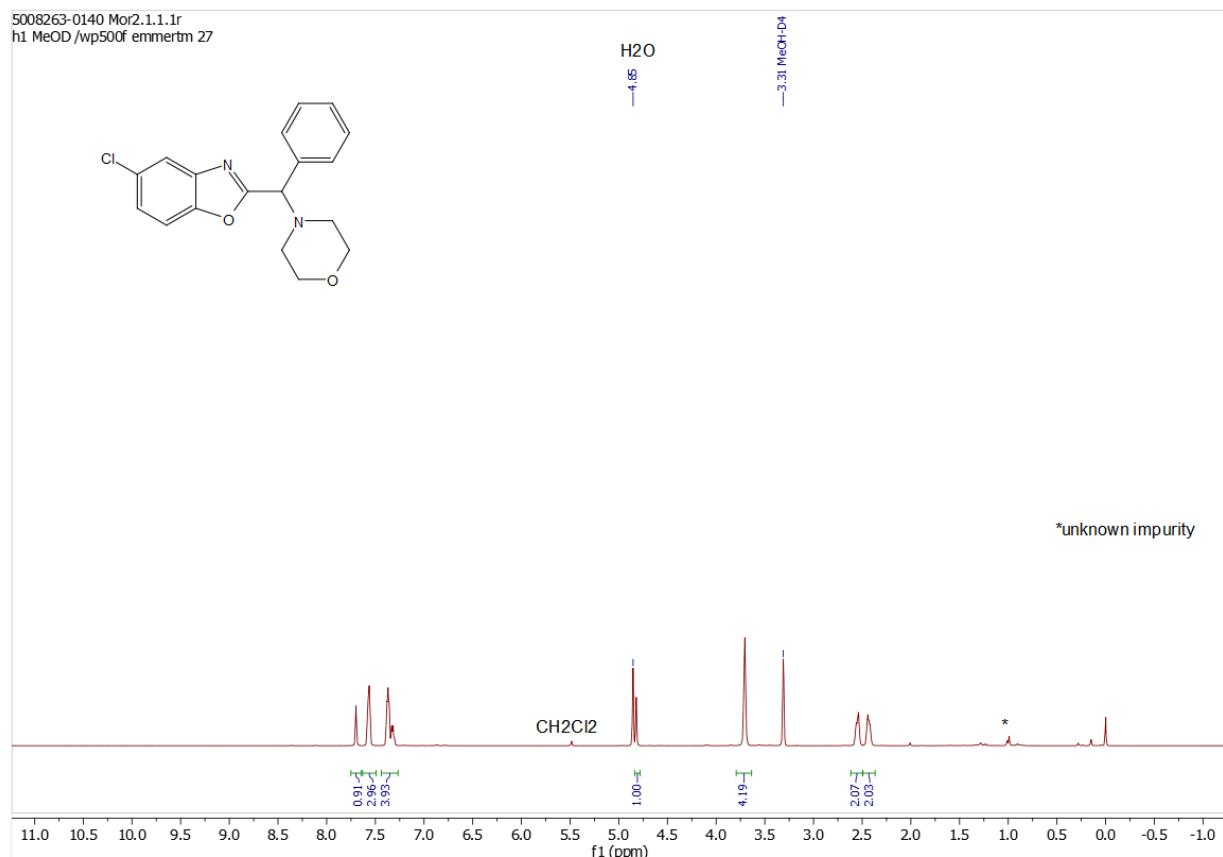
The title compound was prepared according to General Procedure 2 (reaction time 4 h).

Yield: 175 mg (53%); 47 LCAP before workup/column chromatography

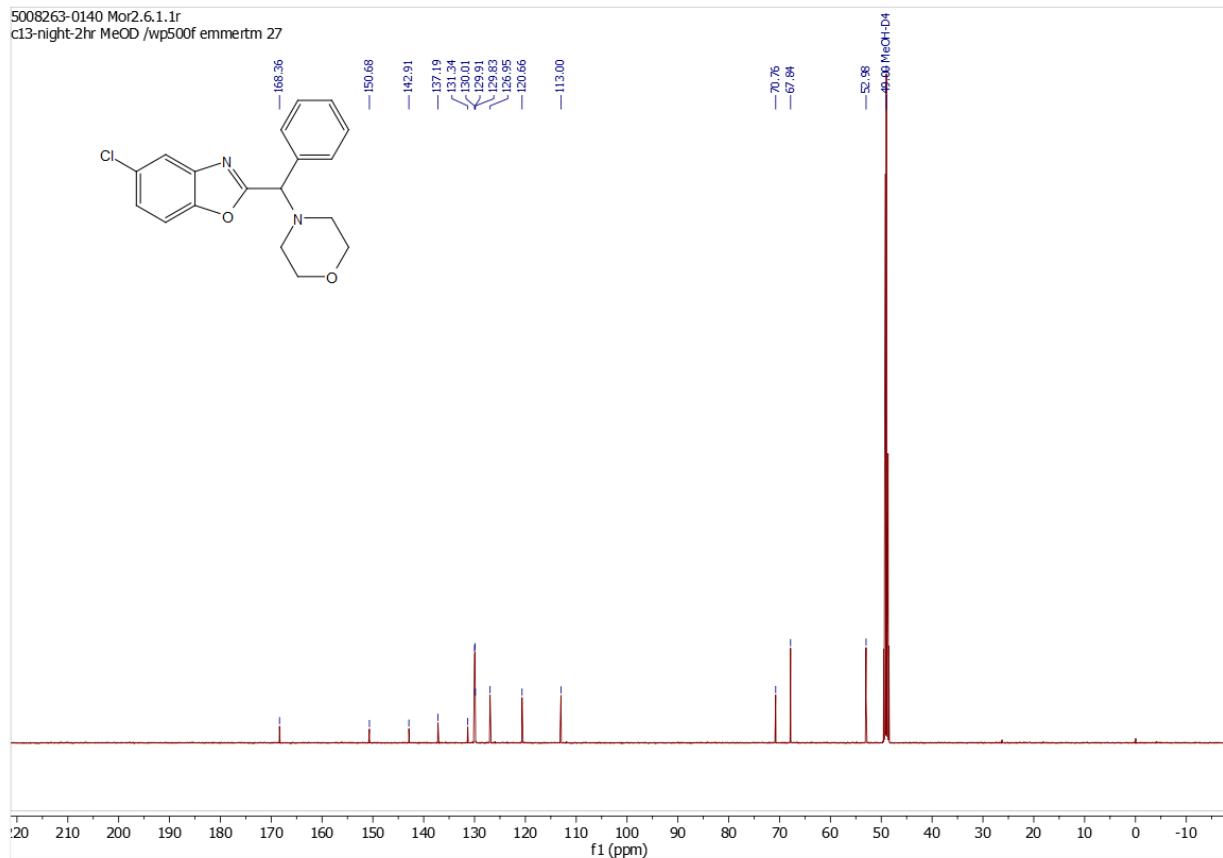
¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.70 (s, 1H), 7.63 – 7.51 (m, 3H), 7.42 – 7.26 (m, 4H), 4.82 (s, 1H), 3.71 (s, 4H), 2.59 – 2.52 (m, 2H), 2.50 – 2.36 (m, 2H).

¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 168.4, 150.7, 142.9, 137.2, 131.3, 130.0, 129.9, 129.8, 126.9, 120.7, 113.0, 70.8, 67.8, 53.0.

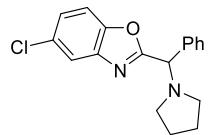
HRMS: Calc. C₁₈H₁₈ClN₂O₂⁺ [M+H⁺] 329.1052; found 329.1046.



5008263-0140 Mor2.6.1.1r
c13-night-2hr MeOD /wp500f emmertm 27



5-Chloro-2-(phenyl(pyrrolidin-1-yl)methyl)benzo[d]oxazole



Chemical Formula: C₁₈H₁₇ClN₂O
Exact Mass: 312.10
Molecular Weight: 312.80

The title compound was prepared according to General Procedure 2 (reaction time 4 h).

Yield: 145 mg (46%); 55 LCAP before workup/column chromatography

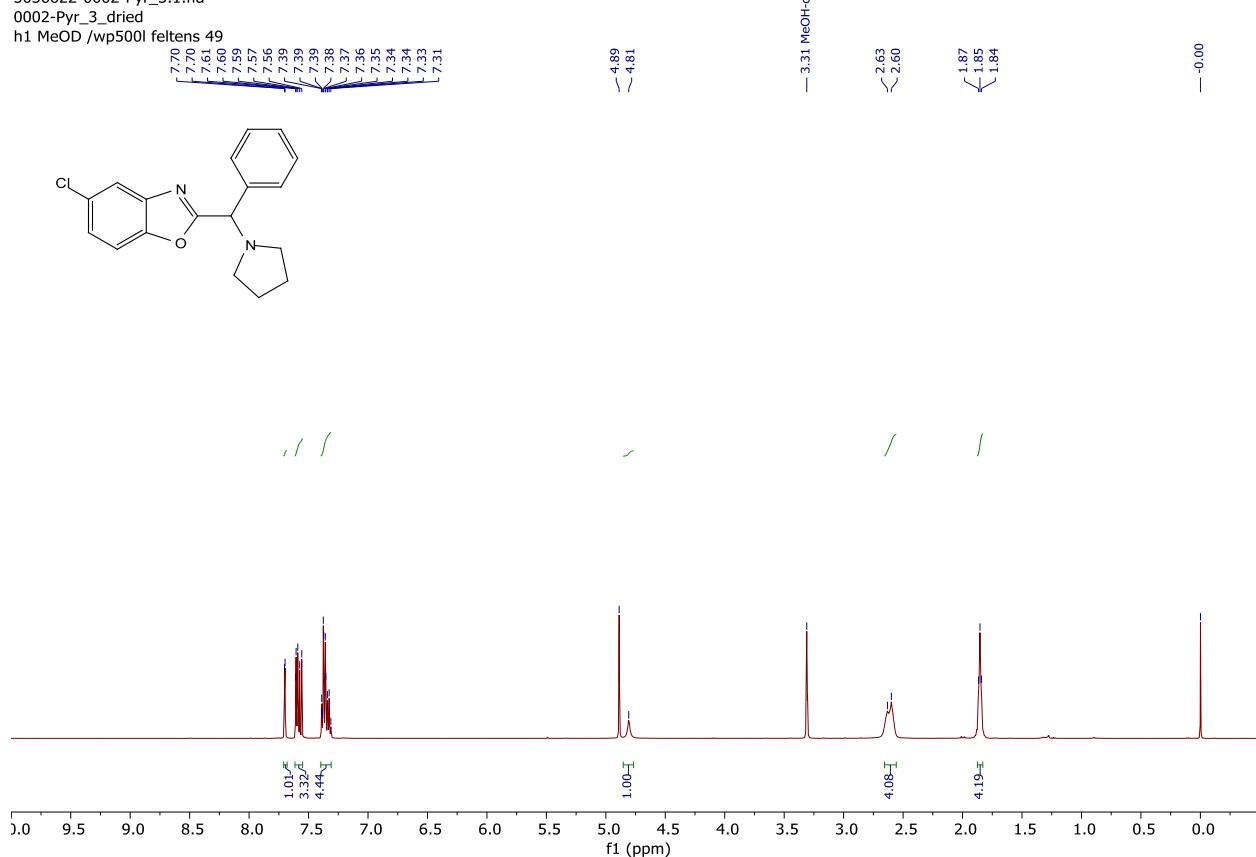
¹H NMR (500 MHz, Methanol-d₄, ppm) δ 7.70 (d, *J* = 2.0 Hz, 1H), 7.61 – 7.55 (m, 3H), 7.36 (m, 4H), 4.81 (s, 1H), 2.62 (d, *J* = 16.4 Hz, 4H), 1.85 (t, *J* = 6.2 Hz, 4H).

¹³C NMR (126 MHz, Methanol-d₄, ppm) δ 168.7, 150.6, 142.9, 138.4, 131.3, 129.9, 129.9, 129.6, 126.9, 120.7, 112.9, 69.8, 54.0, 24.2.

HRMS: Calc. C₁₈H₁₈ClN₂O⁺ [M+H⁺] 313.1102; found 313.1103.

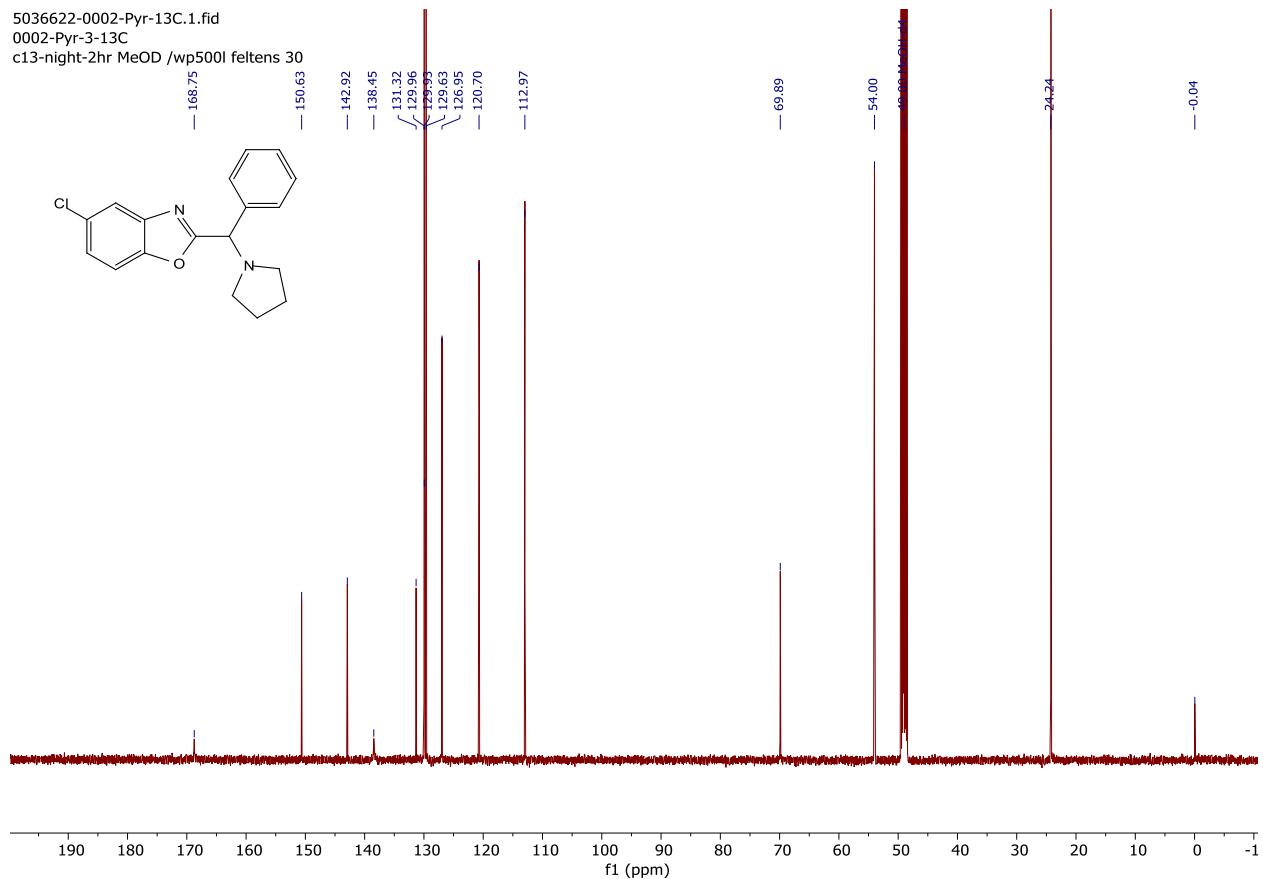
5036622-0002-Pyr_3.1.fid

0002-Pyr_3_dried
h1 MeOD /wp500l feltens 49

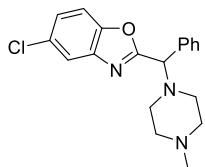


5036622-0002-Pyr-13C.1.fid
0002-Pyr-3-13C

c13-night-2hr MeOD /wp500l feltens 30



5-Chloro-2-((4-methylpiperazin-1-yl)(phenyl)methyl)benzo[d]oxazole



Chemical Formula: C₁₉H₂₀ClN₃O

Exact Mass: 341.1295

Molecular Weight: 341.8390

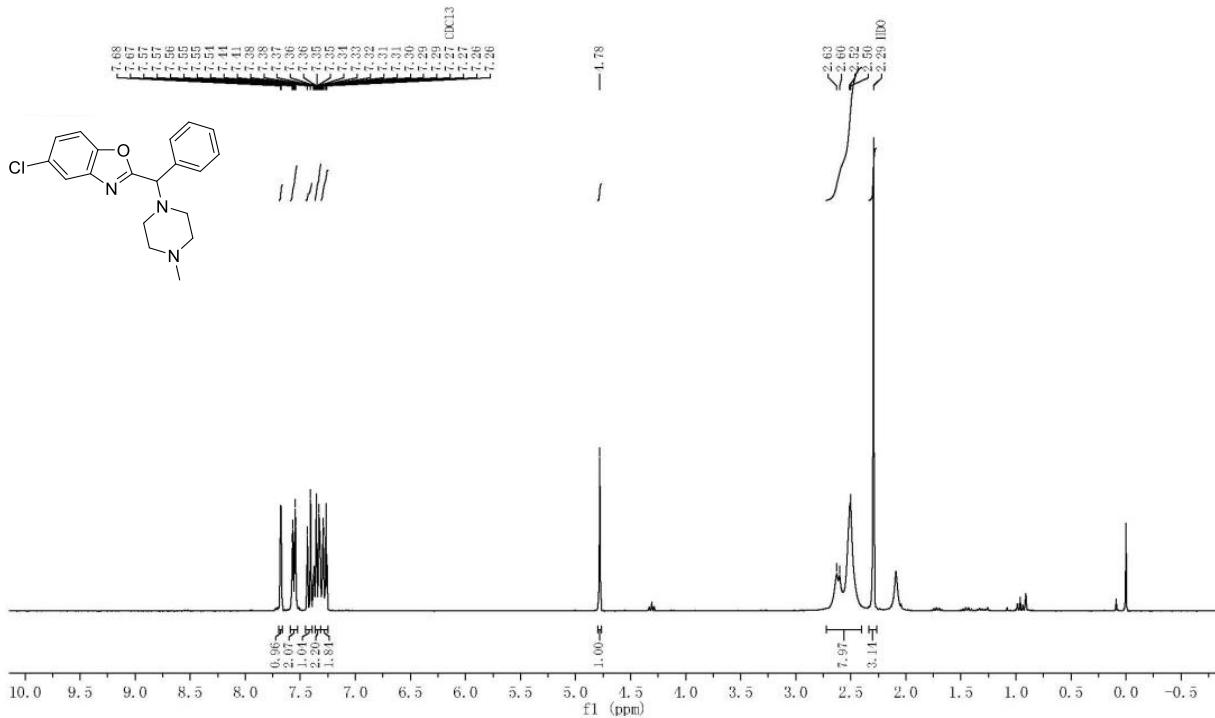
The title compound was prepared according to General Procedure 1 (reaction time 20 h).

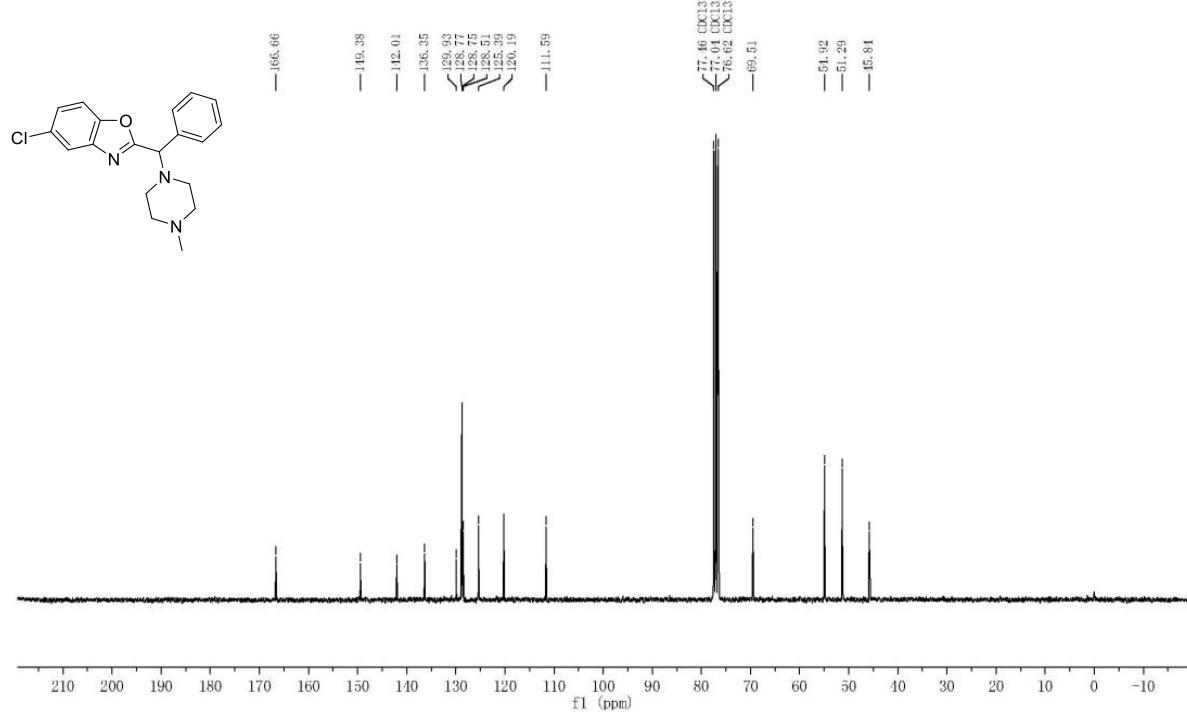
Yield: 150 mg (27%); 55 LCAP before workup/ Prep-HPLC

¹H NMR (300 MHz, Chloroform-d, ppm) δ 7.68 (d, *J* = 2.1 Hz, 1H), 7.59 – 7.53 (m, 2H), 7.42 (d, *J* = 8.6 Hz, 1H), 7.37 – 7.31 (m, 2H), 7.31 – 7.25 (m, 2H), 4.78 (s, 1H), 2.72 – 2.40 (m, 8H), 2.29 (s, 3H).

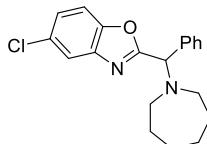
¹³C NMR (75 MHz, Chloroform-d, ppm) δ 166.7, 149.4, 142.0, 136.4, 129.9, 128.8, 128.8, 128.5, 125.4, 120.2, 111.6, 69.5, 54.9, 51.3, 45.8.

HRMS: Calc. C₁₉H₂₀ClN₃O⁺ [M+H⁺] 342.1368; found 342.1360.





2-(Azepan-1-yl(phenyl)methyl)-5-chlorobenzo[d]oxazole



Chemical Formula: C₂₀H₂₁ClN₂O

Exact Mass: 340.1342

Molecular Weight: 340.8510

The title compound was prepared according to General Procedure 1 (reaction time: 20 h).

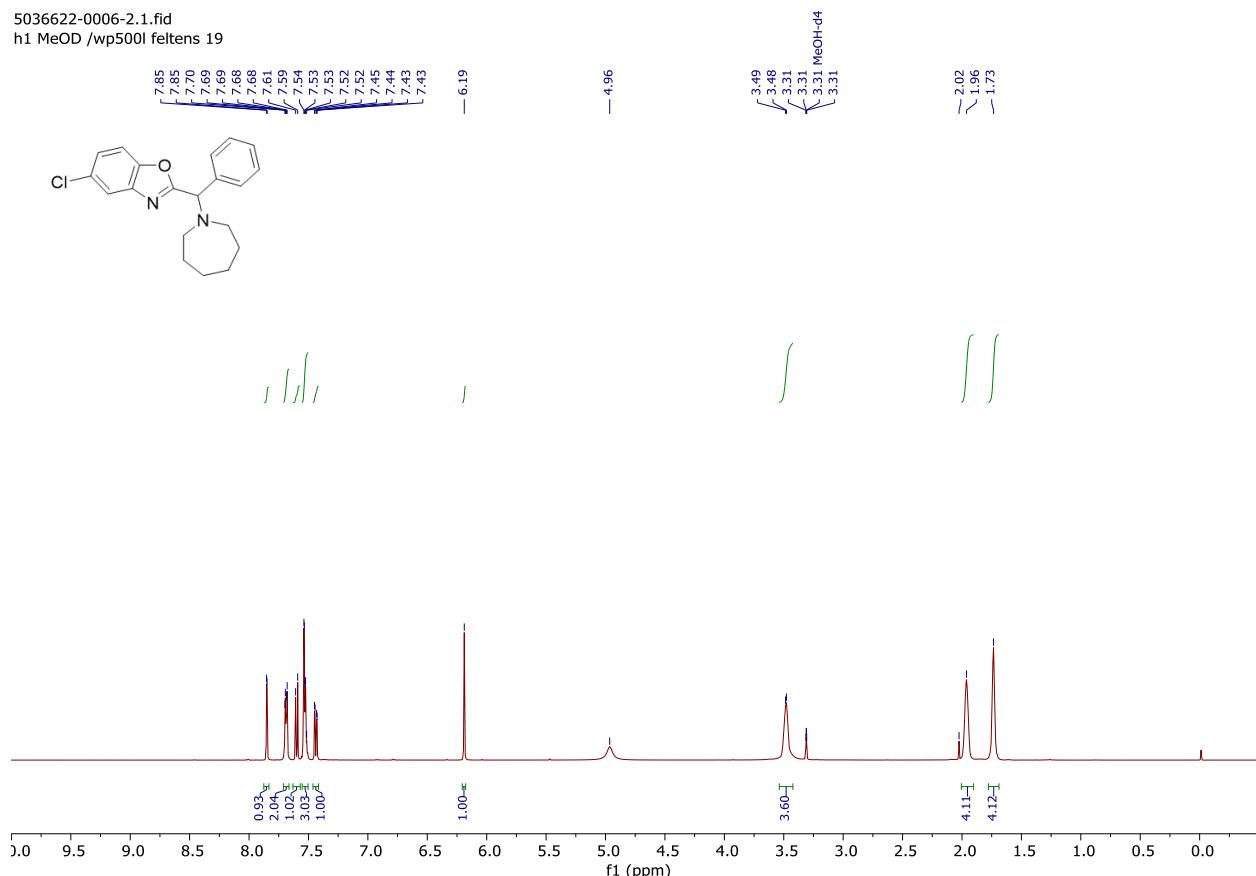
Yield: 147 mg (26%); 48 LCAP before workup/Prep-HPLC

¹H NMR (300 MHz, Methanol-d₄, ppm) δ 7.85 (d, *J* = 1.9 Hz, 1H), 7.71 – 7.66 (m, 2H), 7.60 (d, *J* = 8.8 Hz, 1H), 7.53 (dd, *J* = 5.3, 1.6 Hz, 3H), 7.44 (dd, *J* = 8.8, 2.1 Hz, 1H), 6.19 (s, 1H), 3.54 – 3.42 (m, 4H), 1.96 (s, 4H), 1.73 (s, 4H).

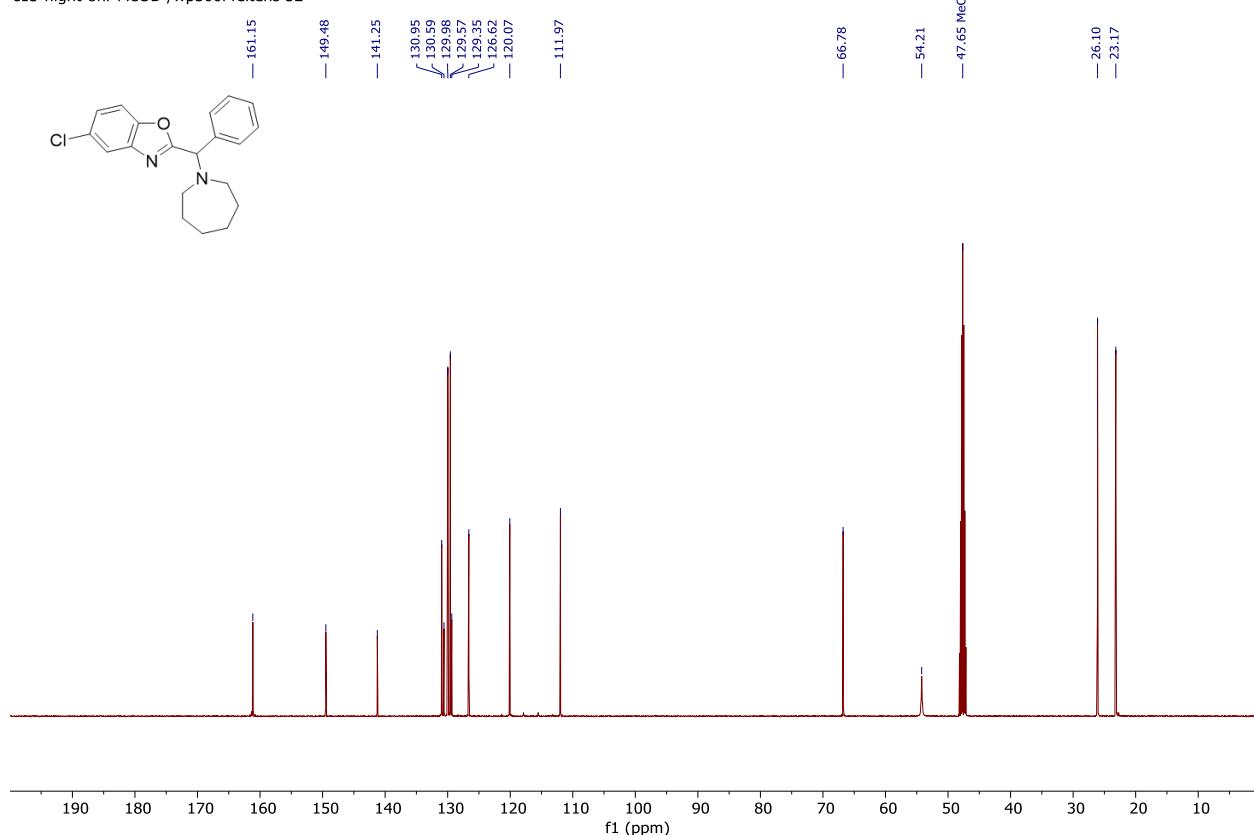
¹³C NMR (126 MHz, Methanol-d₄, ppm) δ 161.1, 149.4, 141.2, 130.9, 130.5, 129.9, 129.5, 129.3, 126.6, 120.0, 111.9, 66.7, 54.2, 26.1, 23.1.

HRMS: Calc. C₂₀H₂₁ClN₂O⁺ [M+H⁺] 341.1415; found 341.1404.

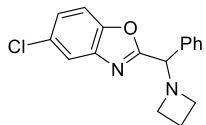
5036622-0006-2.1.fid
h1 MeOD /wp5001 feltens 19



5036622-0006-2-13C.1.fid
c13-night-8hr MeOD /wp500l feltens 52



2-(Azetidin-1-yl(phenyl)methyl)-5-chlorobenzo[d]oxazole



Chemical Formula: C₁₇H₁₅ClN₂O

Exact Mass: 298.0873

Molecular Weight: 298.7700

2-(azetidin-1-yl(phenyl)methyl)-5-chlorobenzo[d]oxazole

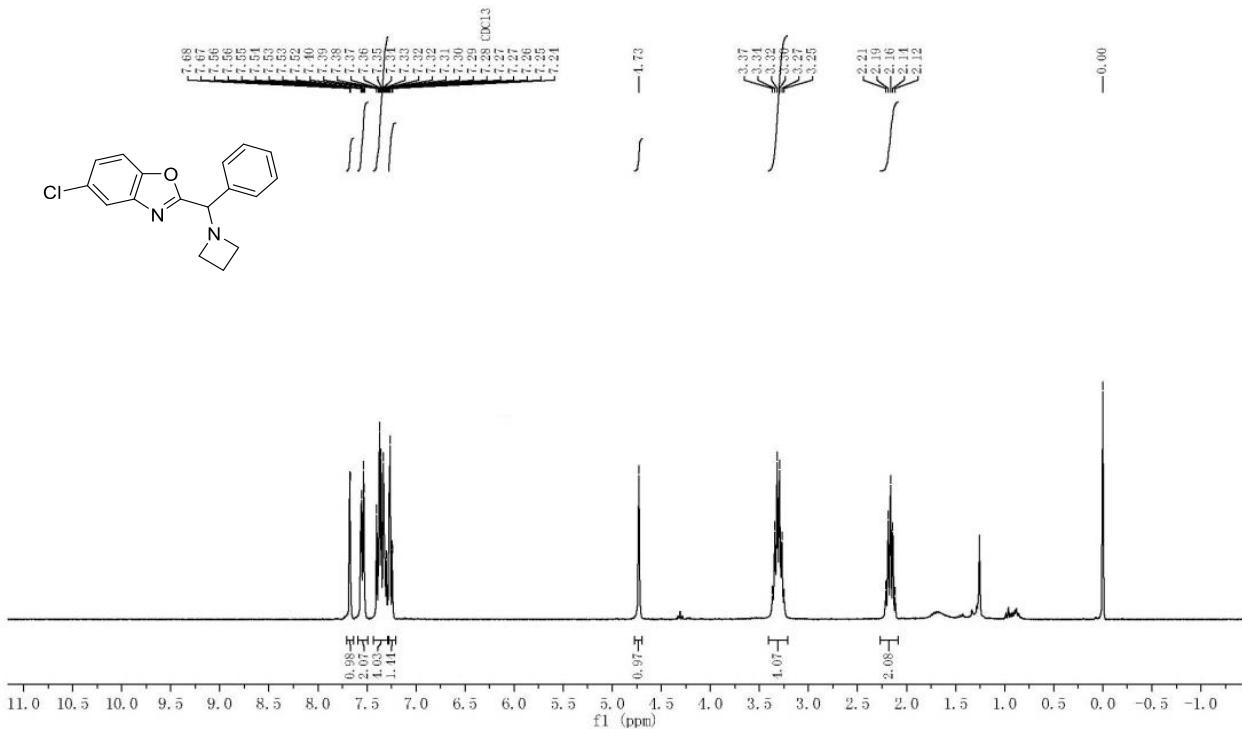
The title compound was prepared according to General Procedure 1 (reaction time: 20 h).

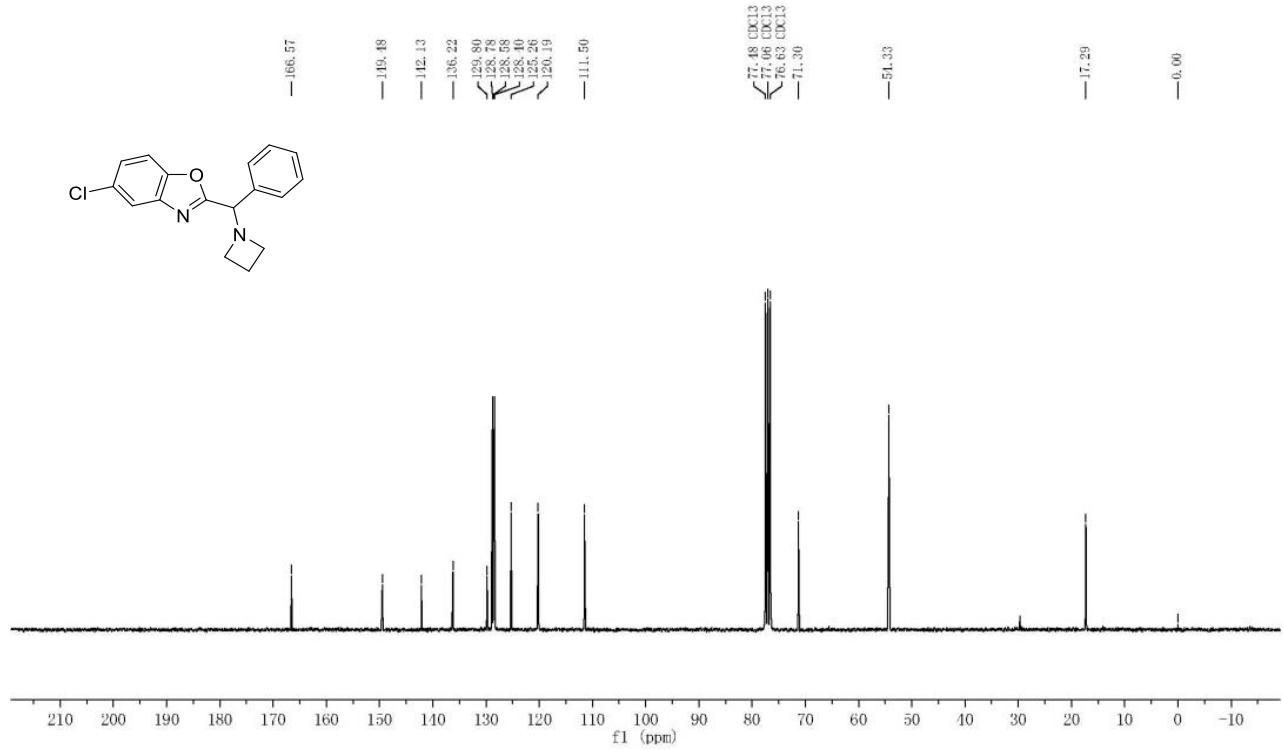
Yield: 71 mg (8%); 22 LCAP before workup/column chromatography

¹H NMR (300 MHz, Chloroform-d, ppm) δ 7.67 (d, *J* = 2.1 Hz, 1H), 7.58 – 7.51 (m, 2H), 7.42 – 7.29 (m, 4H), 7.29 – 7.23 (m, 1H), 4.73 (s, 1H), 3.31 (m, 4H), 2.16 (m, 2H).

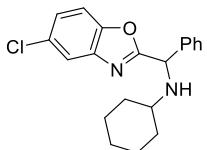
¹³C NMR (75 MHz, Chloroform-d, ppm) δ 166.6, 149.5, 142.1, 136.2, 129.8, 128.8, 128.6, 128.4, 125.3, 120.2, 111.5, 71.3, 54.3, 17.3.

HRMS: Calc. C₁₇H₁₅ClN₂O⁺ [M+H⁺] 299.0946; found 299.0940.





N-(5-Chlorobenzo[d]oxazol-2-yl)(phenyl)methyl)cyclohexanamine



Chemical Formula: C₂₀H₂₁ClN₂O

Exact Mass: 340.1342

Molecular Weight: 340.8510

The title compound was prepared according to General Procedure 1 (reaction time: about 20 h).

Yield: 53 mg (7%); 12 LCAP before workup/column chromatography

¹H NMR (300 MHz, Methanol-*d*₄, ppm) δ 7.85 (d, *J* = 2.0 Hz, 1H), 7.67 – 7.61 (m, 2H), 7.59 (d, *J* = 8.8 Hz, 1H), 7.55 – 7.50 (m, 3H), 7.44 (dd, *J* = 8.8, 2.1 Hz, 1H), 6.16 (s, 1H), 4.92 (br. s, 1H), 3.21 – 3.13 (m, 1H), 2.31 (d, *J* = 12.2 Hz, 1H), 2.24 (d, *J* = 12.0 Hz, 1H), 1.87 (t, *J* = 11.1 Hz, 2H), 1.68 (d, *J* = 10.5 Hz, 1H), 1.49 (dt, *J* = 12.1, 3.9 Hz, 2H), 1.30 – 1.20 (m, 3H).

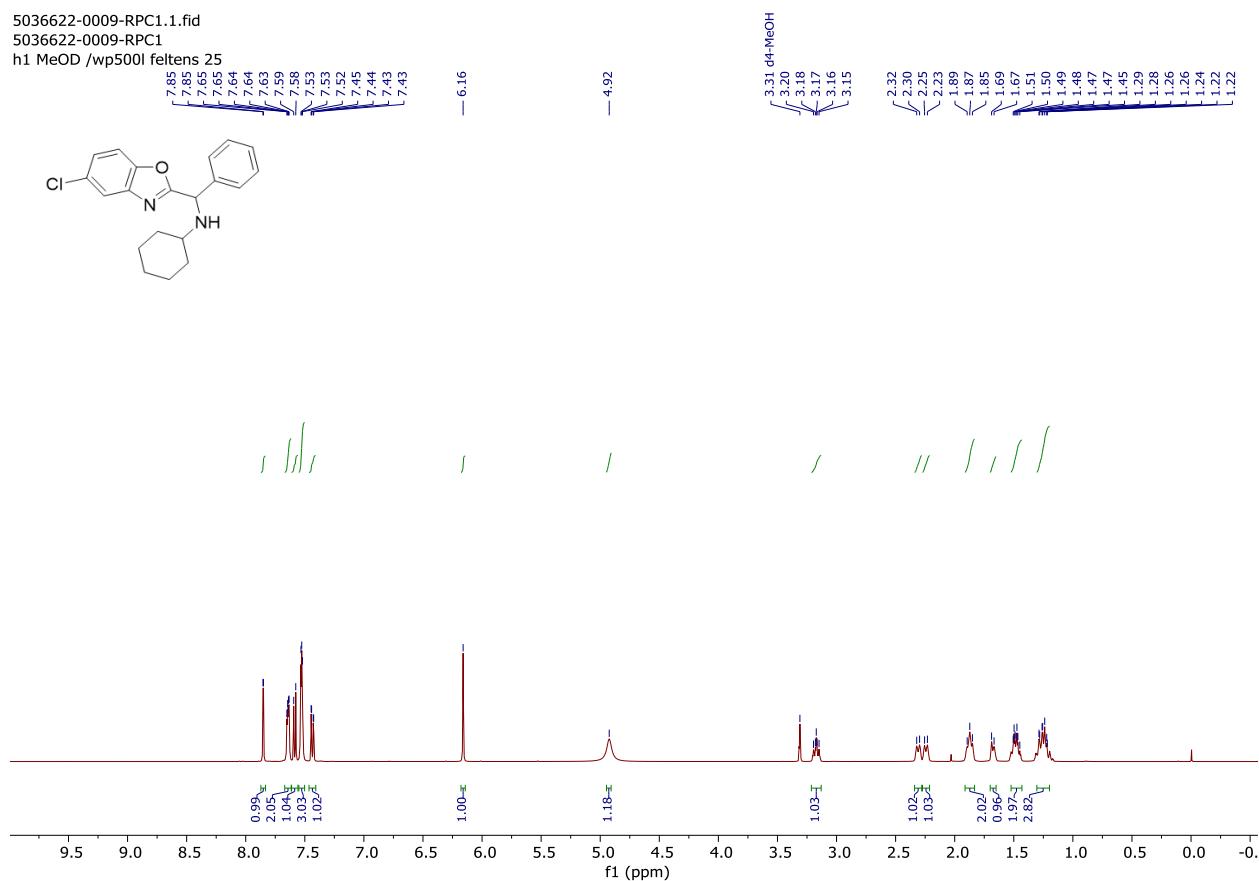
¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 163.4, 151.1, 142.5, 132.3, 131.8, 131.8, 130.9, 130.0, 127.7, 121.3, 113.2, 58.0, 57.3, 30.2, 30.2, 25.9, 25.5, 25.5.

HRMS: Calc. C₂₀H₂₁ClN₂O⁺ [M+H⁺] 341.1415; found 341.1408.

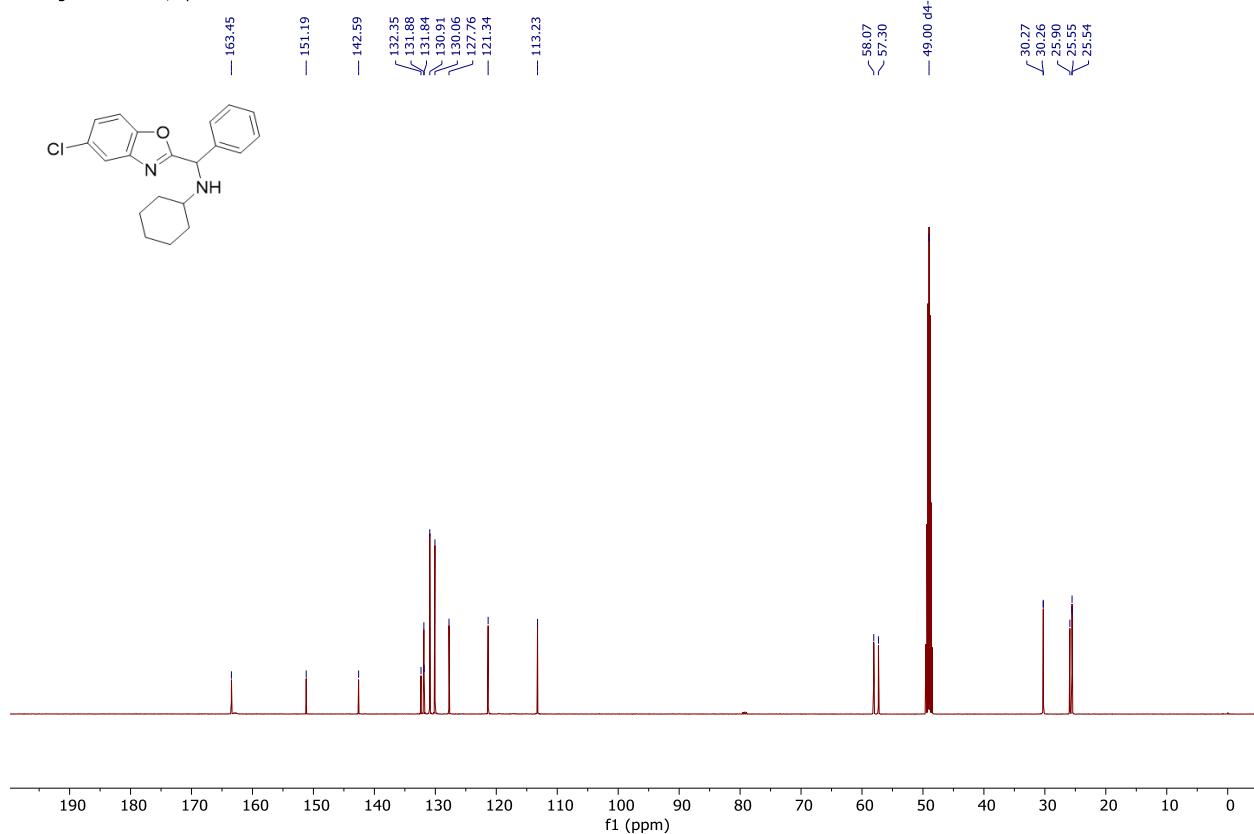
5036622-0009-RPC1.1.fid

5036622-0009-RPC1

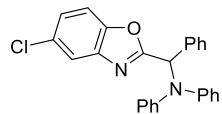
h1 MeOD /wp5001 feltens 25



5036622-0009-RPC1-13C.1.fid
c13-night-8hr MeOD /wp500l feltens 23



N-((5-Chlorobenzo[d]oxazol-2-yl)(phenyl)methyl)-*N*-phenylaniline



Chemical Formula: C₂₆H₁₉ClN₂O

Exact Mass: 410.1186

Molecular Weight: 410.9010

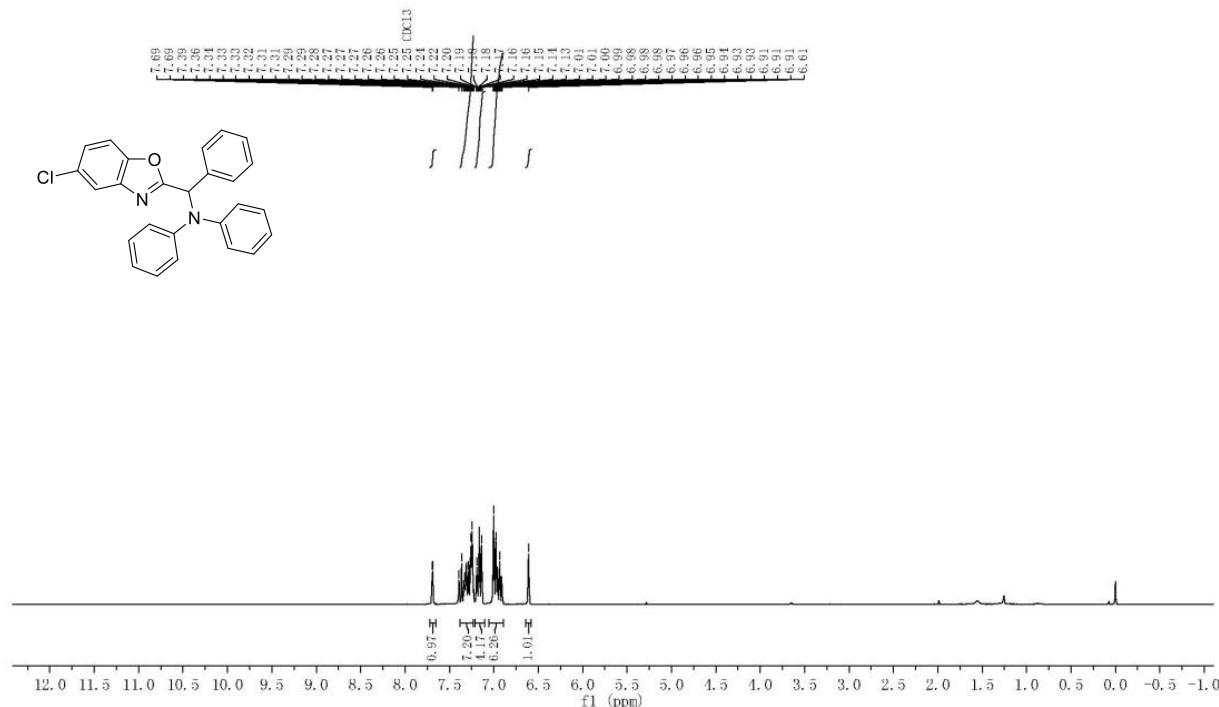
The title compound was prepared according to General Procedure 1 (reaction time: about 20 h).

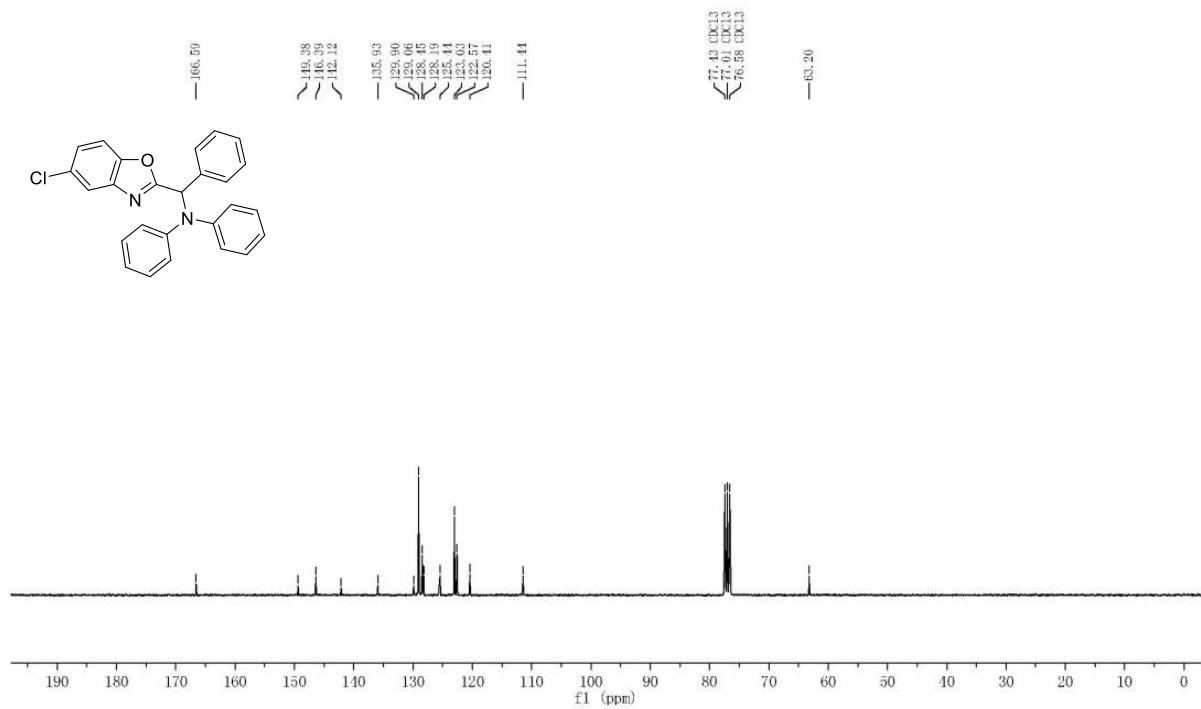
Yield: 30 mg (6%); 19 LCAP before workup/column chromatography

¹H NMR (300 MHz, Chloroform-d, ppm) δ 7.69 (d, *J* = 2.0 Hz, 1H), 7.37 – 7.23 (m, 7H), 7.22 – 7.11 (m, 4H), 7.05 – 6.89 (m, 6H), 6.61 (s, 1H).

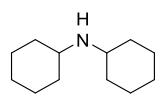
¹³C NMR (75 MHz, Chloroform-d, ppm) δ 166.6, 149.4, 146.4, 142.1, 135.9, 129.9, 129.1, 128.5, 128.2, 125.4, 123.0, 122.6, 120.4, 111.4, 63.2.

HRMS: Calc. C₂₆H₁₉ClN₂O⁺ [M+H⁺] 411.1259; found 411.1255.





Amine with low reactivity (<2 LCAP) under conditions of General Procedure 1



Modified Conditions for Amine-HCl Salts as Substrates



Na_2CO_3 (223 mg, 2.100 mmol) was weighed into a vial containing a stirbar and diethylamine HCl adduct (164 mg, 1.500 mmol). The vial was introduced into the glovebox, where 1,2-dimethoxyethane (1.0 mL) was added. The mixture was stirred vigorously at room temperature in the glovebox for 18 h.

The suspension was filtered through a syringe filter into a vial containing *N*1,*N*1,*N*8,*N*8-tetramethylnaphthalene-1,8-diamine (300 mg, 1.400 mmol; Proton-Sponge®). The filter cake was rinsed with 1,2-dimethoxyethane (0.8 mL). Trimethylsilyl trifluoromethanesulfonate (0.271 mL, 1.500 mmol) was added to the combined filtrates and the resulting suspension was stirred for 3 h in the glovebox. Then, the mixture was filtered through a kimwipe-clogged pipette tip and 1,2-dimethoxyethane (0.50 mL) was used to rinse the reaction vial and the filtercake. To the combined filtrates, benzaldehyde (0.102 mL, 1.0 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.919 mL, 4.00 mmol) were added and the mixture was stirred for 15 min at room temperature in the glovebox.

N-Ethyl-*N*-isopropylpropan-2-amine (0.523 mL, 3.00 mmol) was added to another vial containing 5-chlorobenzo[d]oxazole (154 mg, 1.00 mmol). The contents of both vials were combined, and the reaction mixture was removed from the glovebox and heated to 50 °C for 18 h.

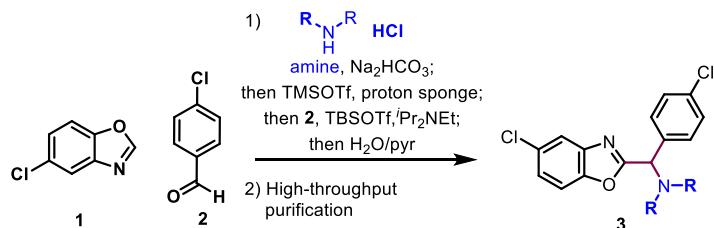
To quench any remaining silyl triflate reagent, the mixture was poured into a mixture of potassium fluoride (465 mg, 8.00 mmol) and pyridine (0.5 mL, 6.21 mmol). The resulting suspension was evaporated to dryness (rotavap). The residue was suspended in 2 mL DCM and 2 mL water and the DCM phase was purified by silica gel chromatography to afford 187 mg (59%) of *N*-((5-chlorobenzo[d]oxazol-2-yl)(phenyl)methyl)-*N*-ethylethanamine as a colorless oil.

^1H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.69 (s, 1H), 7.56 (d, *J* = 8.6 Hz, 1H), 7.50 (d, *J* = 7.4 Hz, 2H), 7.42 – 7.31 (m, 3H), 7.31 – 7.25 (m, 1H), 5.26 (s, 1H), 2.69 (dq, *J* = 13.5, 6.9 Hz, 2H), 2.58 (dq, *J* = 13.5, 6.6 Hz, 2H), 1.03 (t, *J* = 6.9 Hz, 6H).

For full characterization, see page 60.

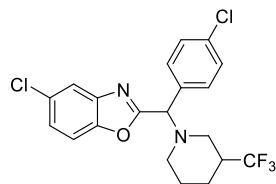
Amine Scope II Via Parallel Medicinal Chemistry

General Procedure 3



Na_2CO_3 (39.6 mg, 0.373 mmol) was weighed into a vial containing amine hydrochloride (0.267 mmol), which was then charged with a stirbar and introduced into the glovebox. Then, 1,2-dimethoxyethane (0.8 mL) was added and the mixture was stirred vigorously at room temperature in the glovebox for 20 h. The mixture was filtered through a syringe filter into a vial containing *N*1,*N*1,*N*8,*N*8-tetramethylnaphthalene-1,8-diamine (53.4 mg, 0.249 mmol). The filter cake was rinsed with 1,2-dimethoxyethane (0.4 mL). Trimethylsilyl trifluoromethanesulfonate (0.048 mL, 0.267 mmol) was added to the combined filtrates and the resulting suspension was stirred for 4 h. The mixture was filtered through a kimwipe-clogged pipette tip directly into a vial containing 4-chlorobenzaldehyde (25 mg, 0.178 mmol); 1,2-dimethoxyethane (0.50 mL) was used to rinse the reaction vial and the filtercake. *tert*-Butyldimethylsilyl trifluoromethanesulfonate (0.163 mL, 0.711 mmol) was added to the combined filtrates and the mixture was stirred for 30 min. *N*-Ethyl-*N*-isopropylpropan-2-amine (0.093 mL, 0.534 mmol) was added into another vial containing 5-chlorobenzo[d]oxazole (27.3 mg, 0.178 mmol); the mixture in both vials were combined and the resulting reaction mixture was removed from the glovebox and heated to 50 °C for 18 h. The mixture was sampled by UPLC/MS. The crude reaction mixture was evaporated and was purified by reverse-phase preparative HPLC. All compounds were isolated as TFA salts.

5-Chloro-2-((4-chlorophenyl)(3-(trifluoromethyl)piperidin-1-yl)methyl)benzo[d]oxazole



Chemical Formula: C₂₀H₁₇Cl₂F₃N₂O

Exact Mass: 428.0670

Molecular Weight: 429.2642

The title compound was prepared according to General Procedure 3 (PMC). Isolated as C₂₀H₁₇Cl₂F₃N₂O(F₃CCO₂H)_{1.5} (M_w 429.2642 + 114.0232 * 1.5 = 600.299).

Yield: 26.3 mg (25%); 36 LCAP before workup/column chromatography; 1:1 mix of 2 diastereomers.

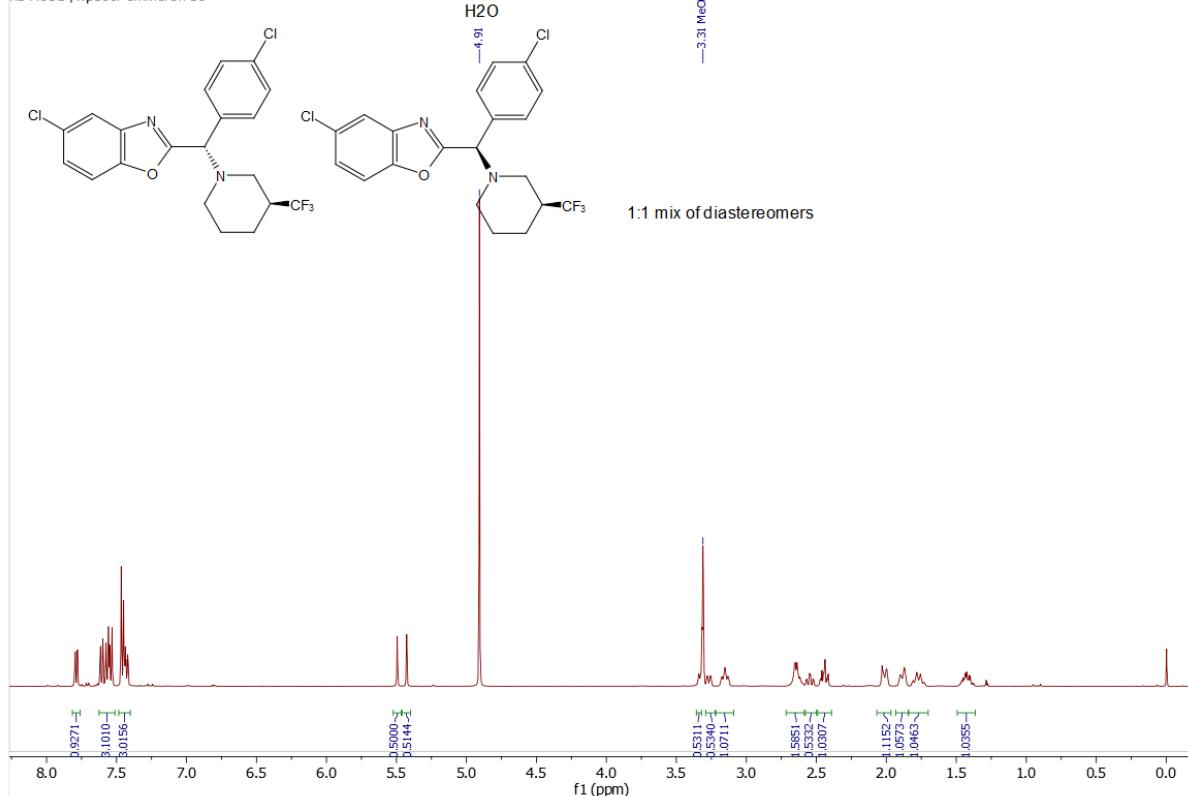
¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.79 (dd, *J* = 8.5, 1.9 Hz, 1H), 7.63 – 7.51 (m, 3H), 7.48 – 7.41 (m, 3H), 5.49 (s, 0.5H; diastereomer 1), 5.43 (s, 0.5H – diastereomer 2), 3.33 (d, *J* = 7.9 Hz, 0.5H – diastereomer 1), 3.27 (d, *J* = 11.2 Hz, 0.5H – diastereomer 2), 3.15 (t, *J* = 11.0 Hz, 1H), 2.69 – 2.50 (m, 2H), 2.48 – 2.40 (m, 1H), 2.01 (d, *J* = 16.2 Hz, 1H), 1.88 (d, *J* = 13.6 Hz, 1H), 1.77 (q, *J* = 12.7 Hz, 1H), 1.42 (qd, *J* = 12.7, 4.6 Hz, 1H).

¹⁹F NMR (470 MHz, Methanol-*d*₄, ppm) δ -73.91 (ds 1), -74.00 (ds 2), -77.58 (TFA).

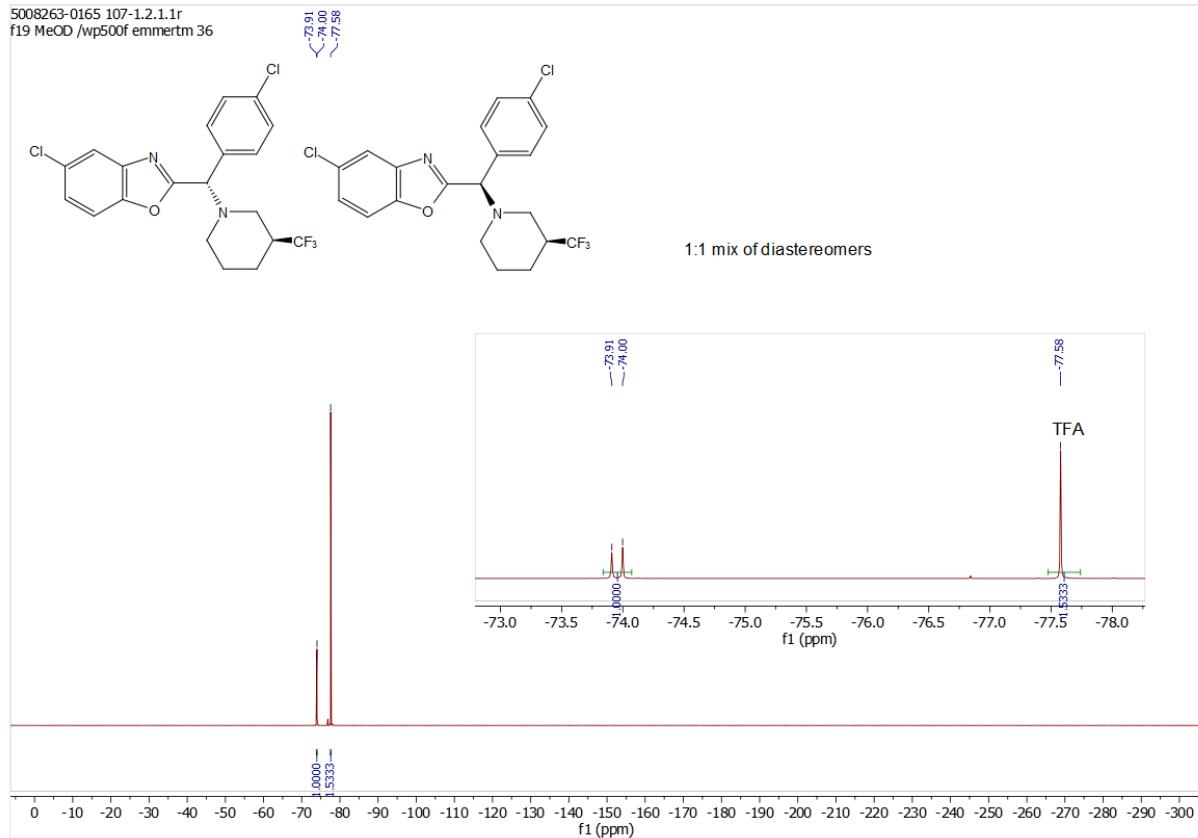
¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 165.9 (ds1), 165.7 (ds 2), 160.7 (q, *J* = 39.0 Hz; TFA), 150.9, 142.9 (ds1), 142.9 (ds2), 136.8 (ds1), 136.8 (ds2), 133.9 (ds1), 133.7 (ds2), 132.1 (ds1), 132.0 (ds2), 131.9 (ds1), 131.8 (ds2), 130.5, 127.9 (q, *J* = 289 Hz; ds1), 127.9 (q, *J* = 289 Hz; ds1), 127.7 (ds1), 127.6 (ds2), 121.2 (ds1), 121.2 (ds2), 117.1 (q, *J* = 290 Hz; TFA), 113.6 (ds1), 113.3 (ds2), 68.7 (ds1), 68.5 (ds2), 52.6 (ds1), 52.6 (ds2), 51.1 (q, *J* = 3.4 Hz; ds1), 50.9 (q, *J* = 3.1 Hz; ds2), 41.7 (q, *J* = 26.7 Hz; ds1), 41.6 (q, *J* = 26.9 Hz; ds2), 24.4 (ds1), 24.2 (ds2), 23.8 (m).

HRMS: Calc. C₂₀H₁₈Cl₂F₃N₂O⁺ [M+H⁺] 429.0743; found 429.0747.

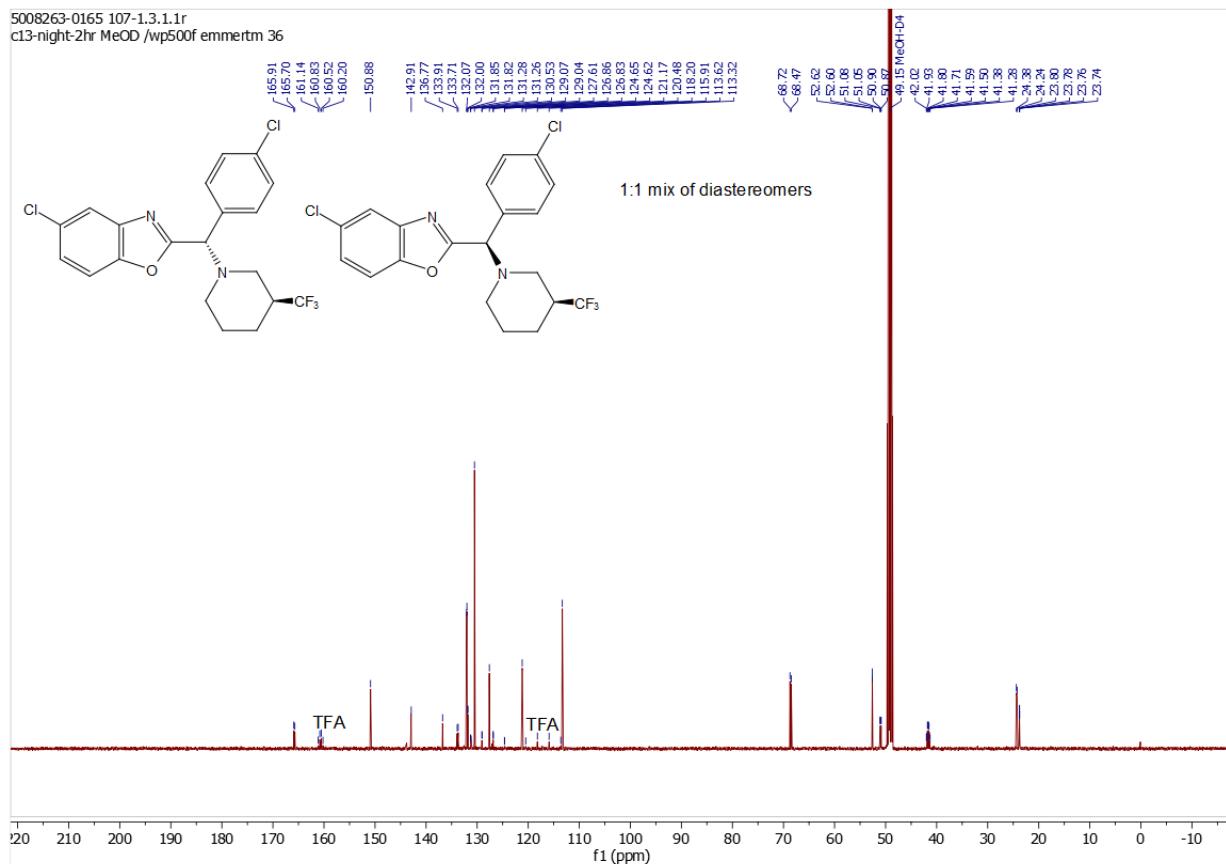
5008263-0165 107-1.1.1.1r
h1 MeOD /wp500f emmertm 36



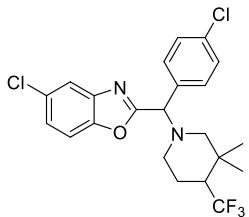
5008263-0165 107-1.2.1.1r
f19 MeOD /wp500f emmertm 36



5008263-0165 107-1.3.1.1r
c13-night-2hr MeOD /wp500f emmertm 36



5-Chloro-2-((4-chlorophenyl)(3,3-dimethyl-4-(trifluoromethyl)piperidin-1-yl)methyl)benzo[d]oxazole



Chemical Formula: C₂₂H₂₁Cl₂F₃N₂O

Exact Mass: 456.0983

Molecular Weight: 457.3182

The title compound was prepared according to General Procedure 3 (PMC). Isolated as C₂₂H₂₁Cl₂F₃N₂O(F₃CCO₂H) (M_w 457.3182 + 114.0232 = 571.3414 g/mol).

Yield: 44 mg (43%); 39 LCAP before workup/column chromatography

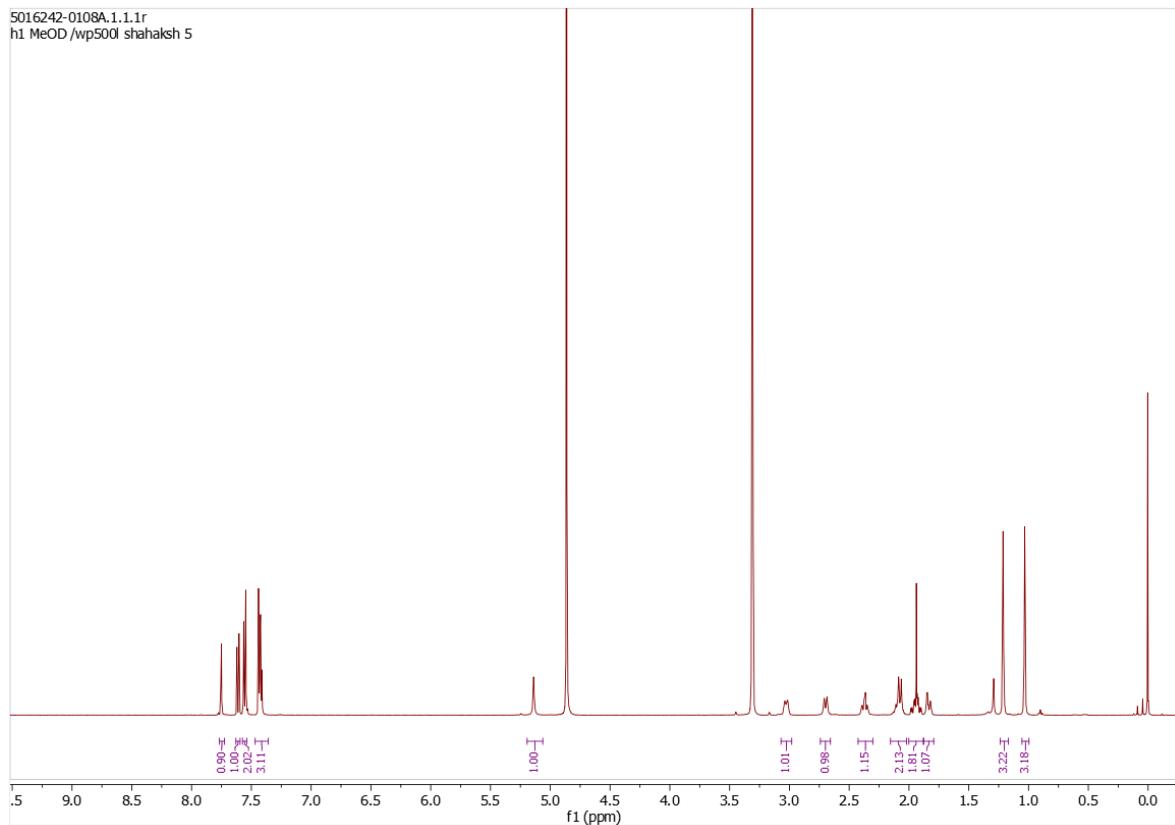
¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.75 (d, *J* = 1.9 Hz, 1H), 7.61 (d, *J* = 8.7 Hz, 1H), 7.56 (d, *J* = 8.5 Hz, 2H), 7.45 – 7.41 (m, 3H), 5.18 (s, 1H), 3.05 (d, *J* = 11.1 Hz, 1H), 2.73 (d, *J* = 11.4 Hz, 1H), 2.40 (t, *J* = 12.6 Hz, 1H), 2.10 (m, 2H), 1.95 (qd, *J* = 12.8, 12.3, 4.2 Hz, 1H), 1.88 – 1.81 (m, 1H), 1.22 (s, 3H), 1.04 (s, 3H).

¹⁹F NMR (470 MHz, Methanol-*d*₄, ppm) δ -66.25, -77.57 (TFA).

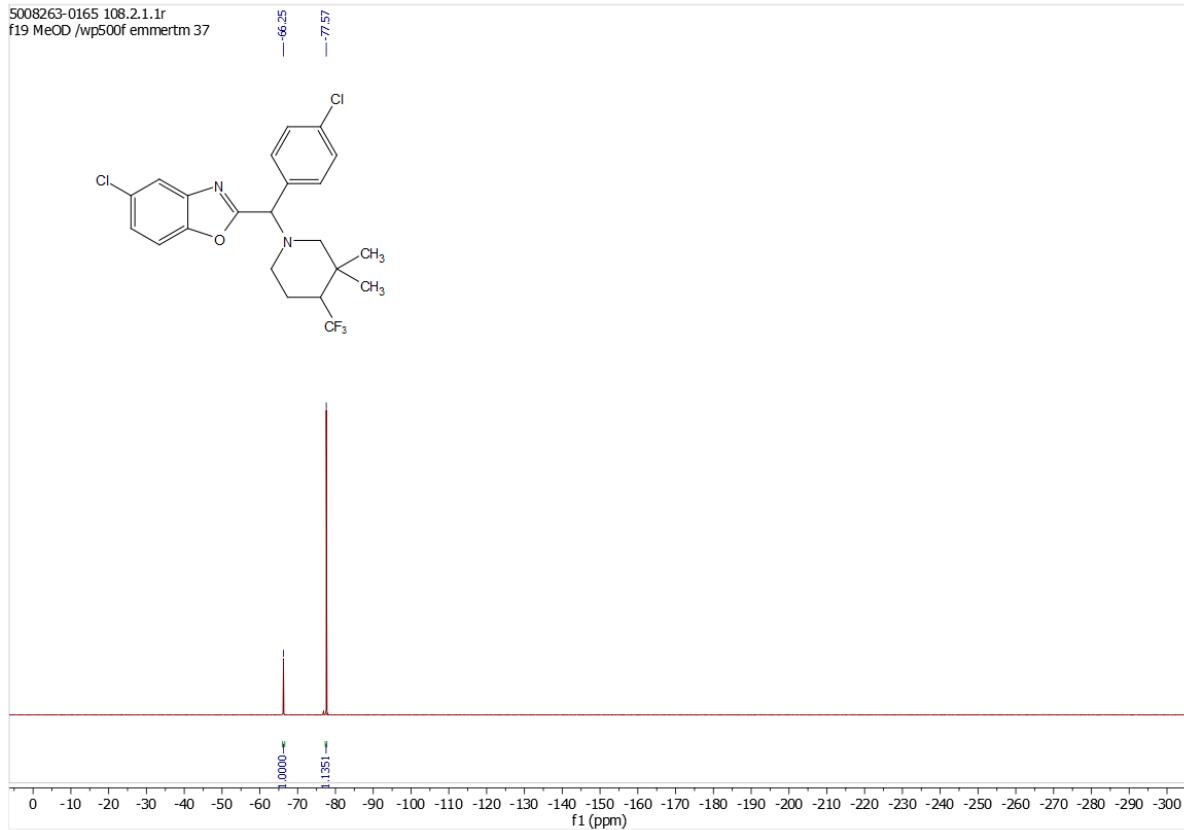
¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 166.6, 160.5 (q, *J* = 39.3 Hz), 150.7, 142.7, 136.1, 130.1, 129.4 (d, *J* = 281.0 Hz), 127.2, 120.8, 116.9 (q, *J* = 289.4 Hz), 113.1, 68.6, 65.8, 51.8, 34.1, 28.2, 23.2, 21.0.

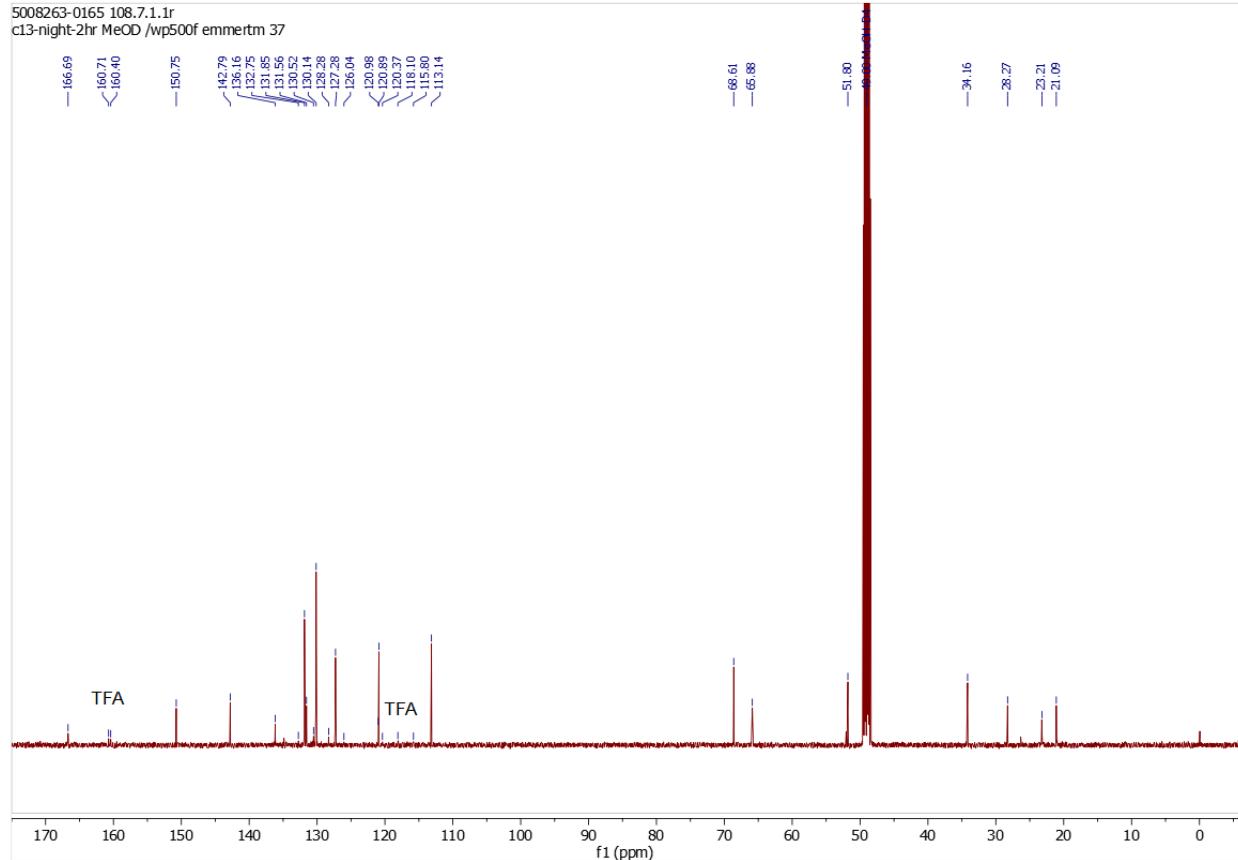
HRMS: Calc. C₂₂H₂₂Cl₂F₃N₂O⁺ [M+H⁺] 457.1056; found 457.1053.

5016242-0108A.1.1.1r
h1 MeOD /wp500f shahaksh 5

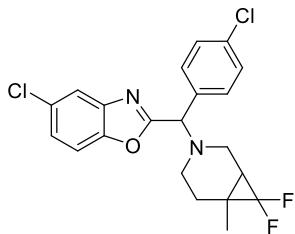


5008263-0165 108.2.1.1r
f19 MeOD /wp500f emmrtrm 37





5-Chloro-2-((4-chlorophenyl)(7,7-difluoro-6-methyl-3-azabicyclo[4.1.0]heptan-3-yl)methyl)benzo[d]oxazole



Chemical Formula: C₂₁H₁₈Cl₂F₂N₂O

Exact Mass: 422.0764

Molecular Weight: 423.2848

The title compound was prepared according to General Procedure 3 (PMC). Isolated as two separated diastereomers of C₂₁H₁₈Cl₂F₂N₂O(F₃CCO₂H)_{2.8} (apparent M_w 423.2848 + 114.0232*2.8 = 742.5498 g/mol).

Yield: 33 mg (both diastereomers combined; 25%); 46 LCAP before workup/column chromatography

Diastereomer 1:

¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.83 (d, *J* = 2.1 Hz, 1H), 7.64 – 7.58 (m, 3H), 7.53 – 7.50 (m, 2H), 7.46 (dd, *J* = 8.8, 2.1 Hz, 1H), 5.65 (s, 1H), 3.39 – 3.33 (m, 1H), 3.28 – 3.15 (m, 2H), 2.98 (dd, *J* = 13.1, 3.7 Hz, 1H), 2.82 – 2.74 (m, 1H), 2.19 (d, *J* = 14.0 Hz, 1H), 2.10 (ddq, *J* = 12.6, 9.2, 5.2, 4.6 Hz, 1H), 1.64 (ddd, *J* = 13.1, 9.6, 3.8 Hz, 1H), 1.32 (s, 3H).

¹⁹F NMR (470 MHz, Methanol-*d*₄, ppm) δ -77.23 (TFA), -137.80 (d, *J* = 157.5 Hz), -146.66 (d, *J* = 157.5 Hz).

¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 164.6, 150.9, 142.6, 137.3, 132.0, 131.8, 130.7, 130.5, 127.7, 121.1, 116.4 (t, *J* = 289 Hz), 113.2, 67.2, 49.2, 46.6 (t, *J* = 172.0 Hz), 45.1, 26.2, 24.8, 23.7 – 23.1 (m), 22.5 – 22.0 (m), 19.2 – 19.0 (m).

Diastereomer 2:

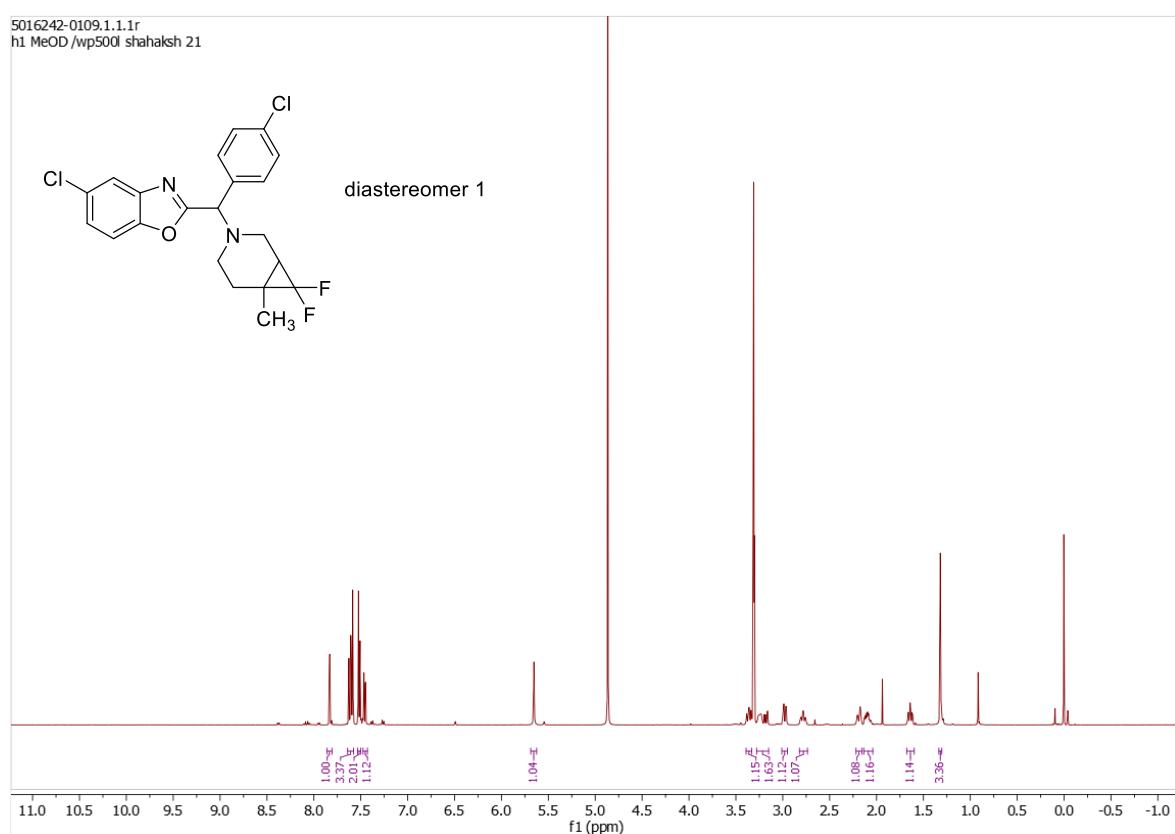
¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.79 (d, *J* = 1.9 Hz, 1H), 7.60 (dd, *J* = 18.7, 8.6 Hz, 3H), 7.49 – 7.40 (m, 3H), 5.44 (s, 1H), 3.41 (t, *J* = 10.9 Hz, 1H), 2.99 (dd, *J* = 12.8, 3.2 Hz, 1H), 2.93 – 2.83 (m, 1H), 2.55 – 2.37 (m, 1H), 2.14 – 2.05 (m, 1H), 1.95 (tdt, *J* = 10.1, 6.0, 3.6 Hz, 1H), 1.60 (ddd, *J* = 12.8, 9.2, 3.4 Hz, 1H), 1.29 (s, 3H).

¹⁹F NMR (470 MHz, Methanol-*d*₄, ppm) δ -77.23, -137.82 (d, *J* = 156.5 Hz), -146.75 (d, *J* = 156.5 Hz).

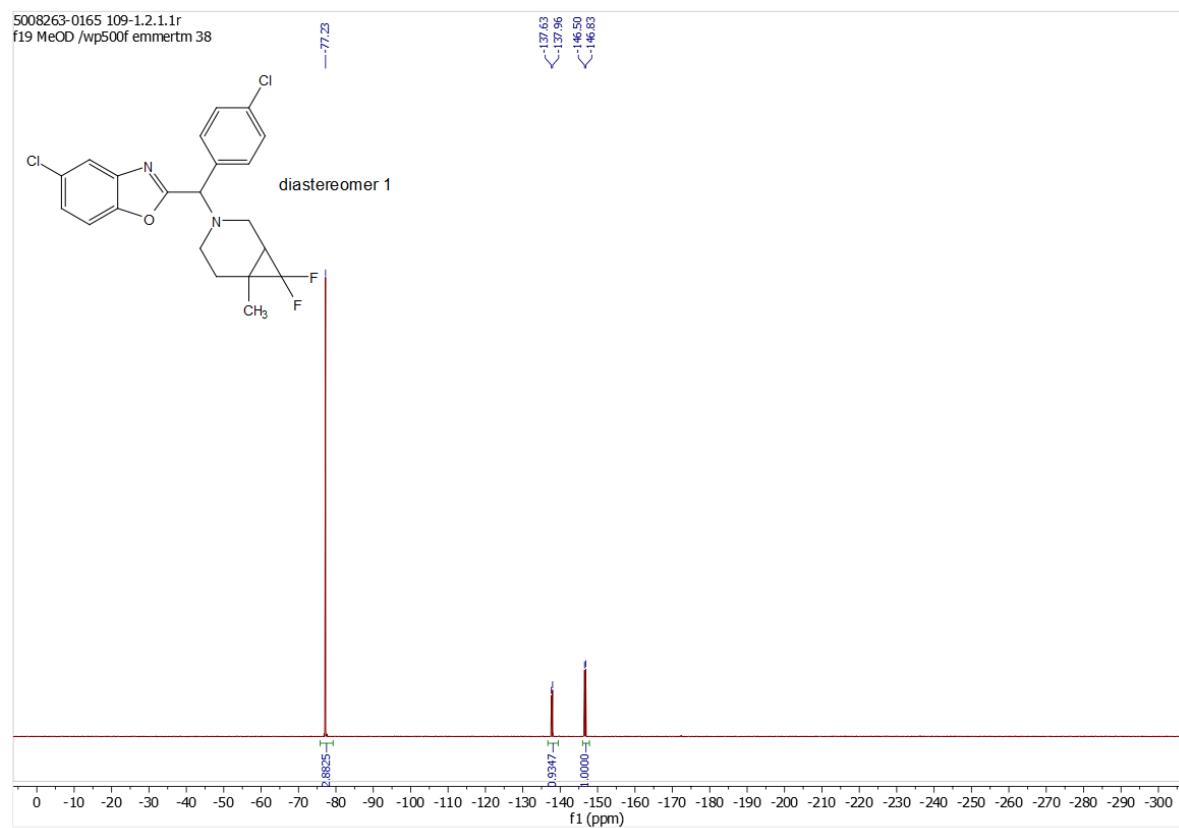
¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 165.1, 150.8, 142.7, 136.9, 133.2, 132.0, 131.7, 130.5, 127.6, 121.1, 116.7 (t, *J* = 289.9 Hz), 113.2, 67.2, 47.7 – 47.3 (m), 45.2, 24.5, 24.0 – 23.2 (m), 22.3 – 21.7 (m), 19.6 – 18.5 (m).

HRMS: Calc. C₂₁H₁₉Cl₂F₂N₂O⁺ [M+H⁺] 423.0837; found 423.0832.

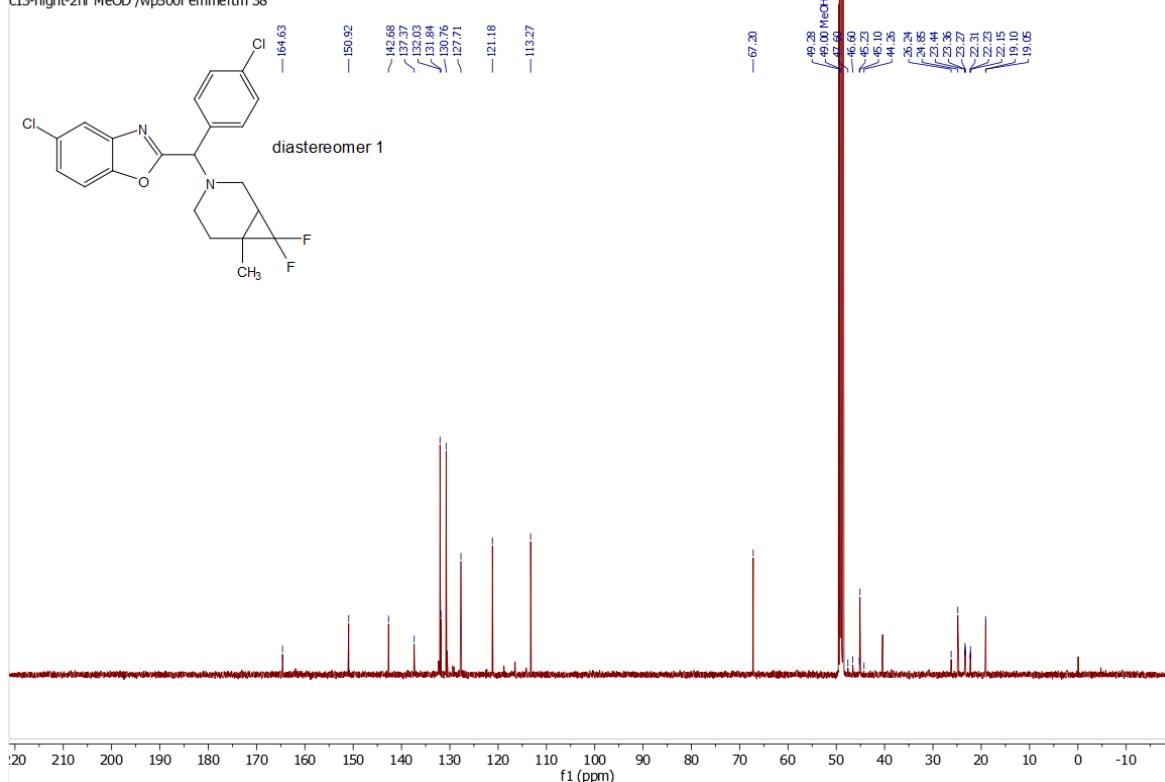
5016242-0109.1.1.1r
h1 MeOD /wp500f shahaksh 21



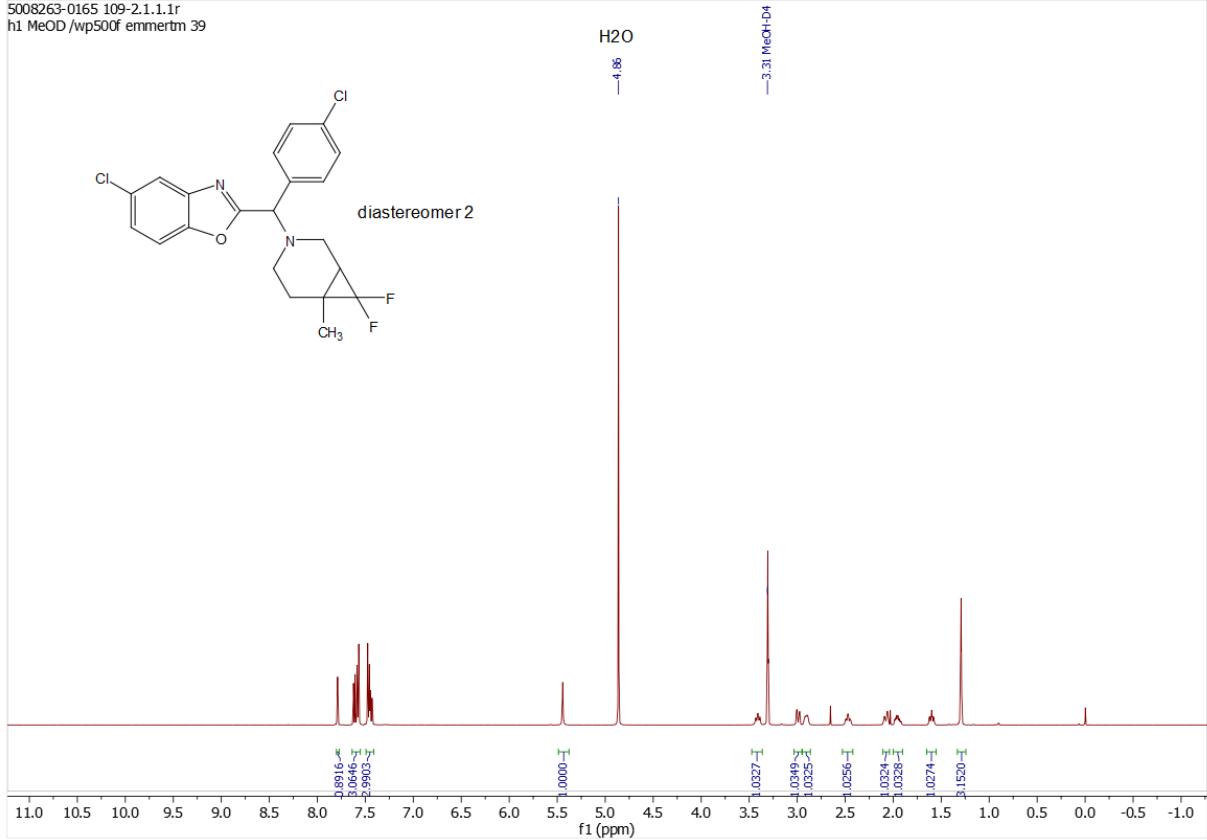
5008263-0165 109-1.2.1.1r
f19 MeOD /wp500f emmrtm 38



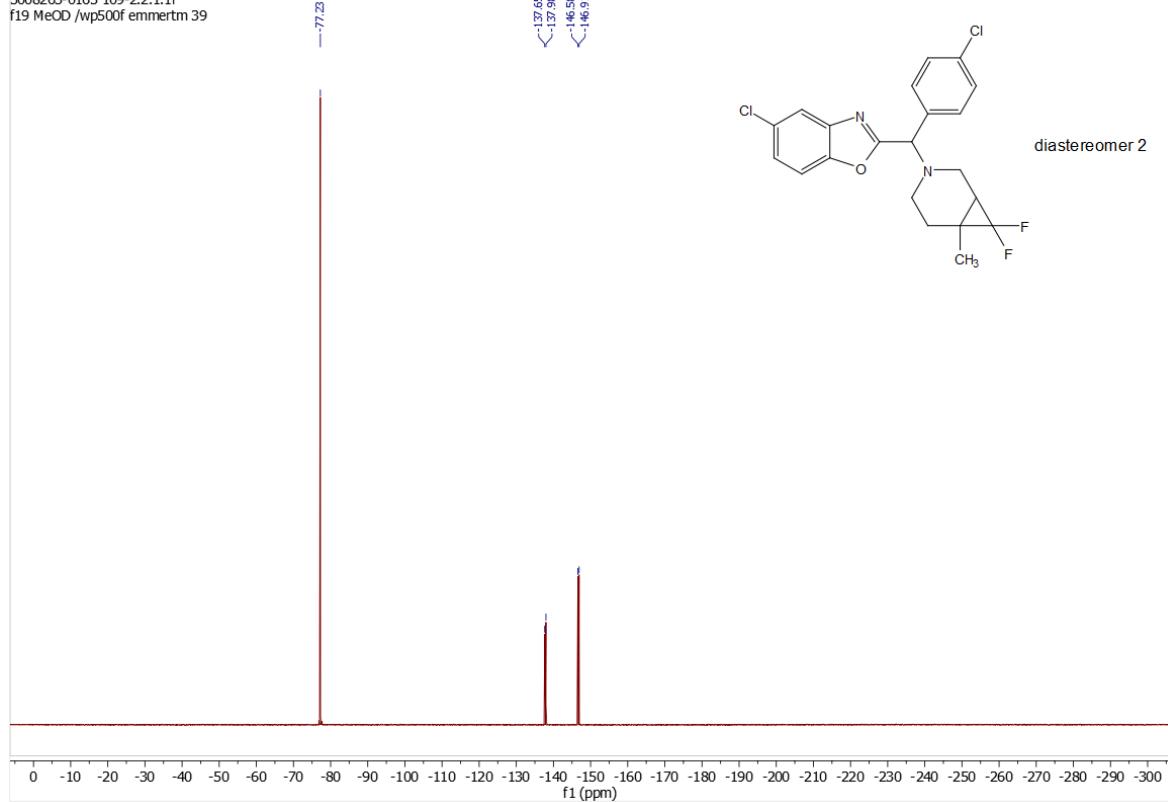
5008263-0165 109-1.3.1.1r
c13-night-2hr MeOD /wp500f emmertm 38



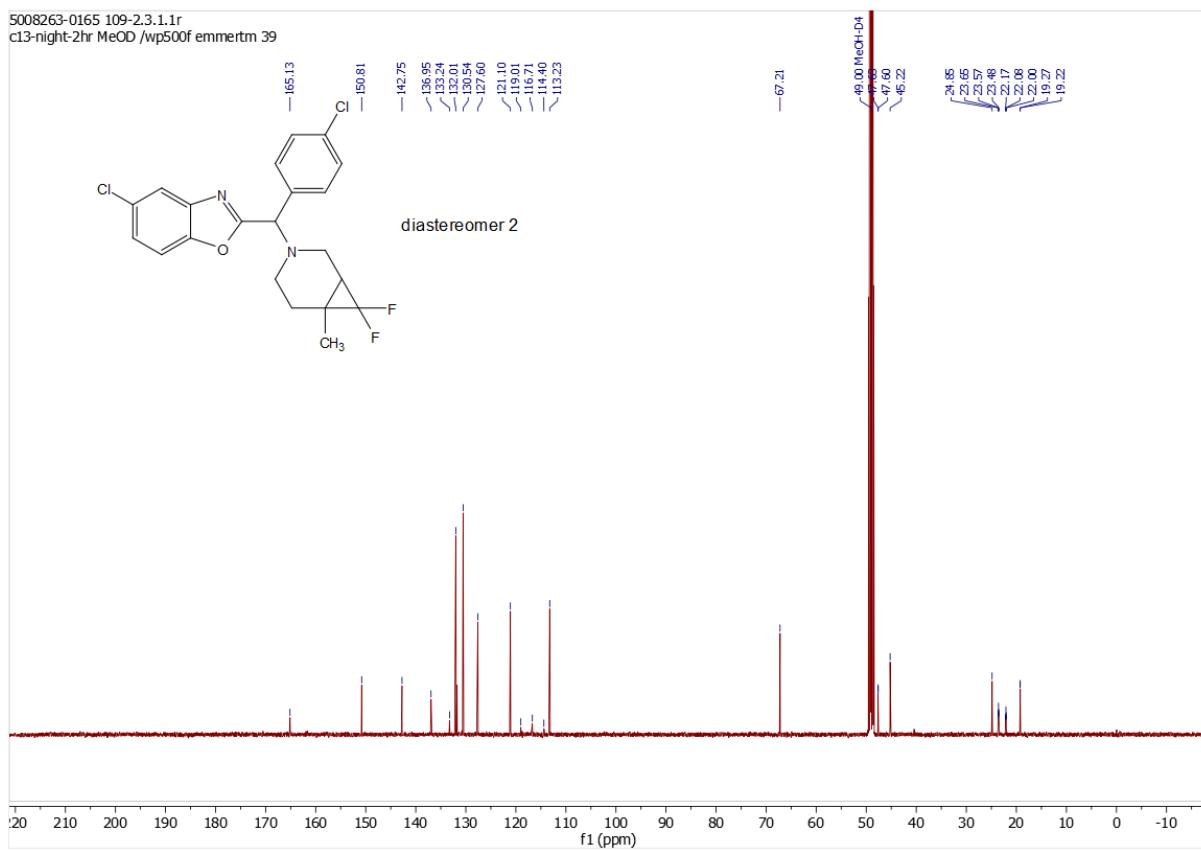
5008263-0165 109-2.1.1.1r
h1 MeOD /wp500f emmertm 39



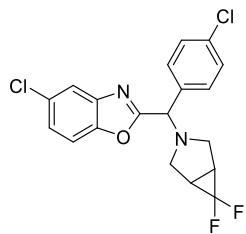
5008263-0165 109-2.2.1.1r
f19 MeOD /wp500f emmertm 39



5008263-0165 109-2.3.1.1r
c13-night-2hr MeOD /wp500f emmertm 39



5-Chloro-2-((4-chlorophenyl)(6,6-difluoro-3-azabicyclo[3.1.0]hexan-3-yl)methyl)benzo[d]oxazole



Chemical Formula: C₁₉H₁₄Cl₂F₂N₂O

Exact Mass: 394.0451

Molecular Weight: 395.2308

The title compound was prepared according to General Procedure 3 (PMC). Isolated as C₁₉H₁₄Cl₂F₂N₂O(F₃CCO₂H)₃ (apparent M_w 395.2308 + 114.0232*3 = 737.3004 g/mol).

Yield: 21 mg (16%); 34 LCAP before workup/column chromatography

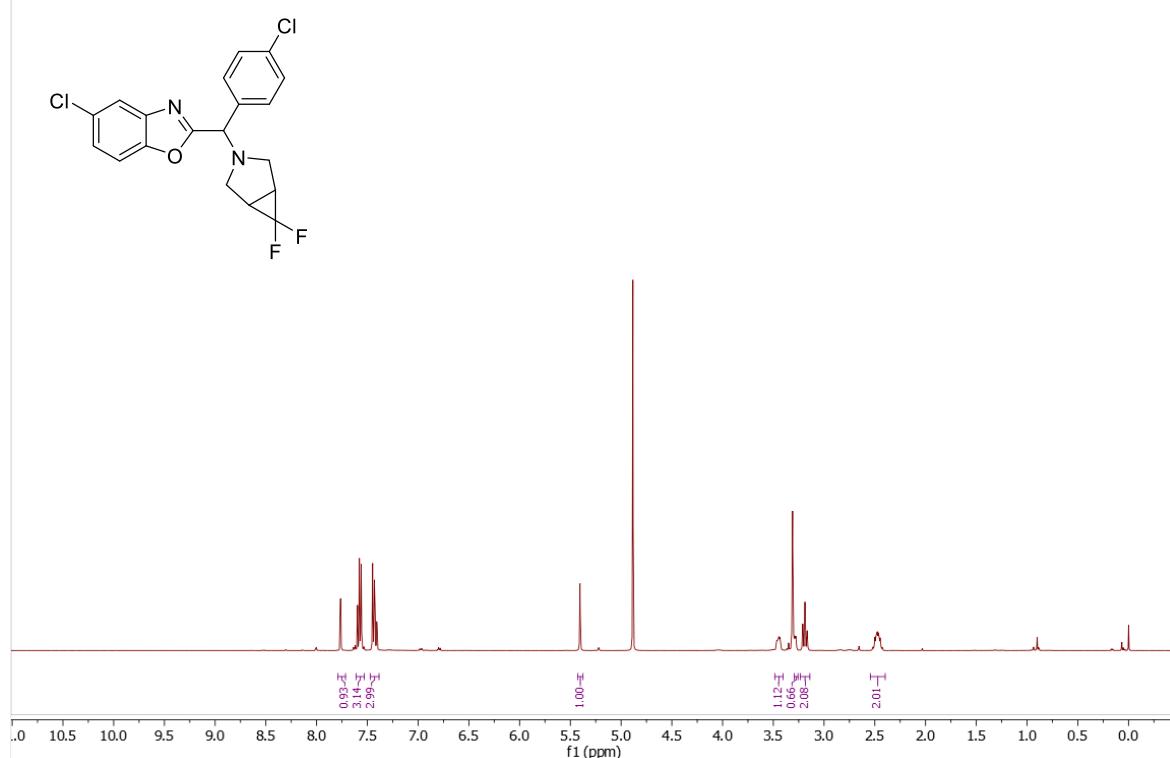
¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.76 (d, *J* = 1.9 Hz, 1H), 7.61 – 7.53 (m, 3H), 7.47 – 7.38 (m, 3H), 5.41 (s, 1H), 3.45 (dd, *J* = 9.6, 5.4 Hz, 1H), 3.28 (d, *J* = 4.9 Hz, 1H), 3.19 (t, *J* = 10.8 Hz, 2H), 2.54 – 2.40 (m, 2H).

¹⁹F NMR (470 MHz, Methanol-*d*₄, ppm) δ -77.42 (TFA), -128.01 (d, *J* = 157.8 Hz), -151.78 (d, *J* = 157.8 Hz).

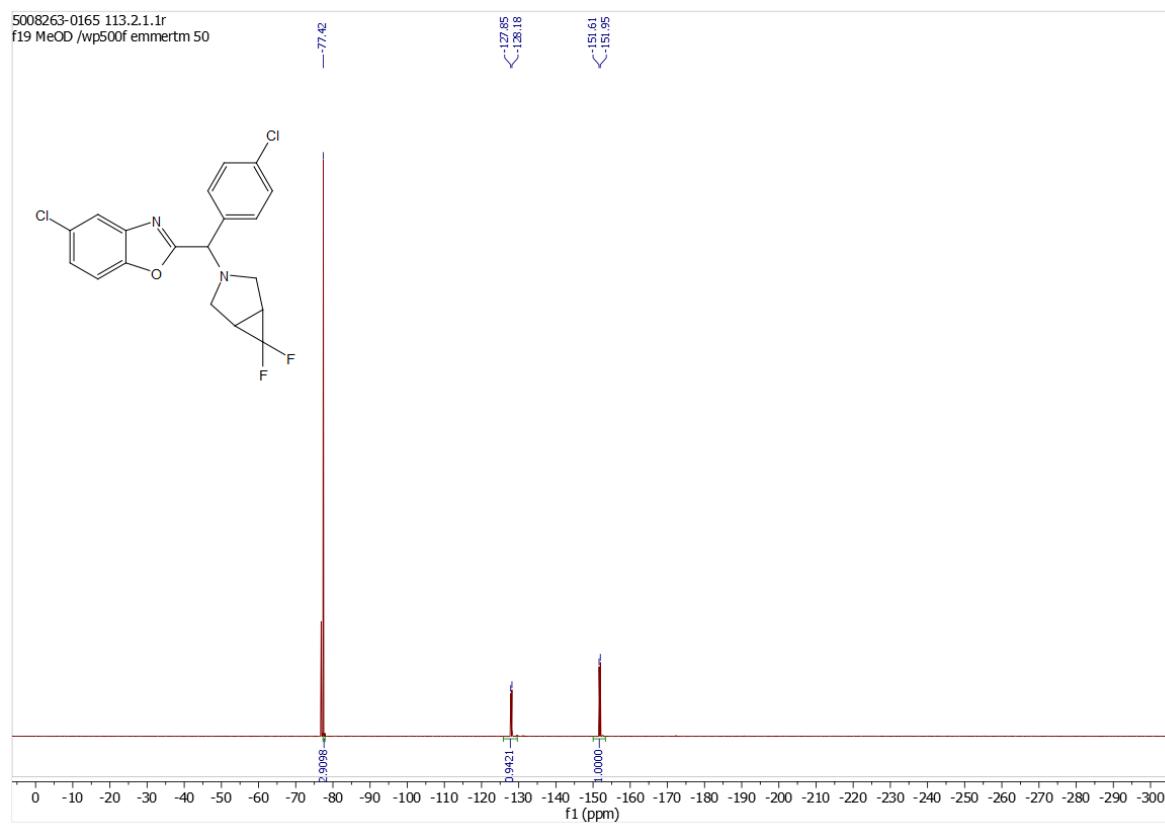
¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 166.3, 161.1 (q, *J* = 37.9 Hz), 150.7, 142.7, 136.4, 135.4, 131.5, 131.3, 130.3, 127.4, 120.9, 117.6 (t, *J* = 189.3 Hz), 114.9 (q, *J* = 297.5 Hz), 113.1, 66.4, 52.6, 52.0, 28.0 (t, *J* = 12.8 Hz), 27.9 (t, *J* = 12.8 Hz).

HRMS: Calc. C₁₉H₁₅Cl₂F₂N₂O⁺ [M+H⁺] 395.0524; found 395.0528.

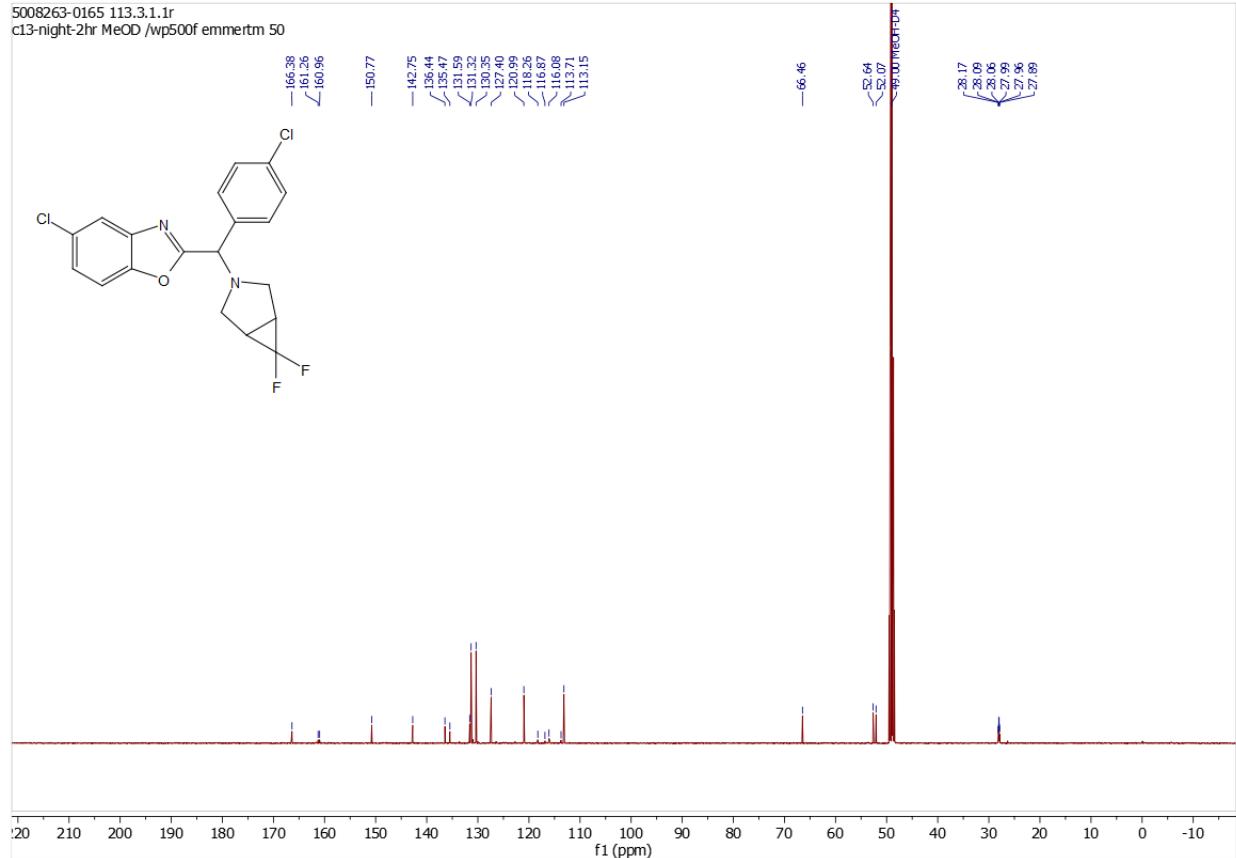
5016242-0113.1.1.1r
h1 MeOD /wp500f shahaksh 7



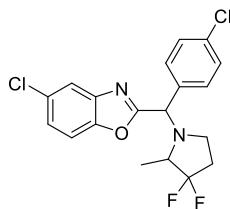
5008263-0165 113.2.1.1r
f19 MeOD /wp500f emmertm 50



5008263-0165 113.3.1.1r
c13-night-2hr MeOD /wp500f emmertm 50



5-Chloro-2-((4-chlorophenyl)(3,3-difluoro-2-methylpyrrolidin-1-yl)methyl)benzo[d]oxazole



Chemical Formula: C₁₉H₁₆Cl₂F₂N₂O
Exact Mass: 396.0608
Molecular Weight: 397.2468

The title compound was prepared according to General Procedure 3 (PMC). Isolated as mixture of two diastereomers (2:1) C₁₉H₁₄Cl₂F₂N₂O(F₃CCO₂H)₃ (apparent M_w 397.2468 + 114.0232*3 = 739.3164 g/mol).

Yield: 31 mg (24%); 20 LCAP before workup/column chromatography

¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.93 – 7.14 (m, 7H), 5.46 (s, 0.66H; major diastereomer), 5.22 (s, 0.33H; minor diastereomer), 3.19 – 2.84 (several overlapping signals, 3H), 2.62 – 2.08 (several overlapping signals, 2H), 1.16 (d, *J* = 6.4 Hz, 2H; major diastereomer), 0.94 (dd, *J* = 6.5, 2.9 Hz, 1H; minor diastereomer).

Minor Diastereomer:

¹⁹F NMR (470 MHz, Methanol-*d*₄, ppm) δ -76.84 (TFA), -96.54 (d, *J* = 228.7 Hz), -105.99 (d, *J* = 228.7 Hz).

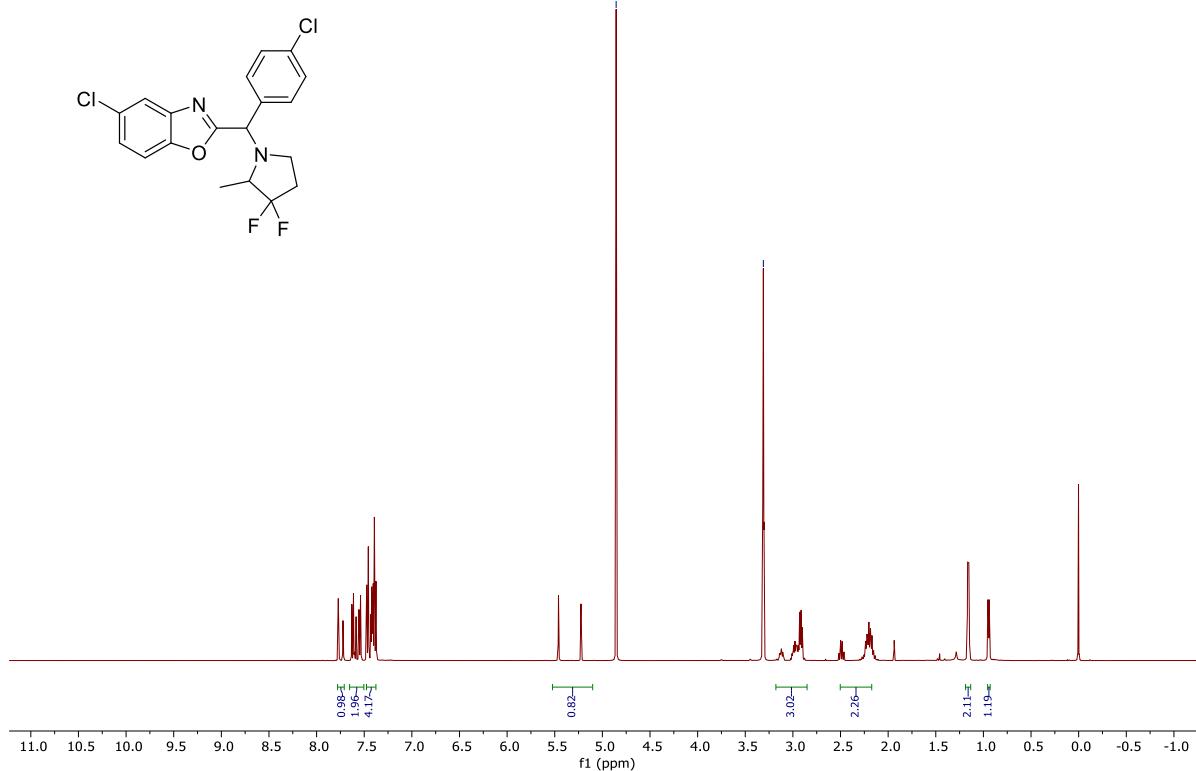
Major Diastereomer:

¹⁹F NMR (470 MHz, Methanol-*d*₄, ppm) δ -77.61 (TFA), -98.45 (d, *J* = 228.3 Hz), -106.37 (d, *J* = 228.3 Hz).

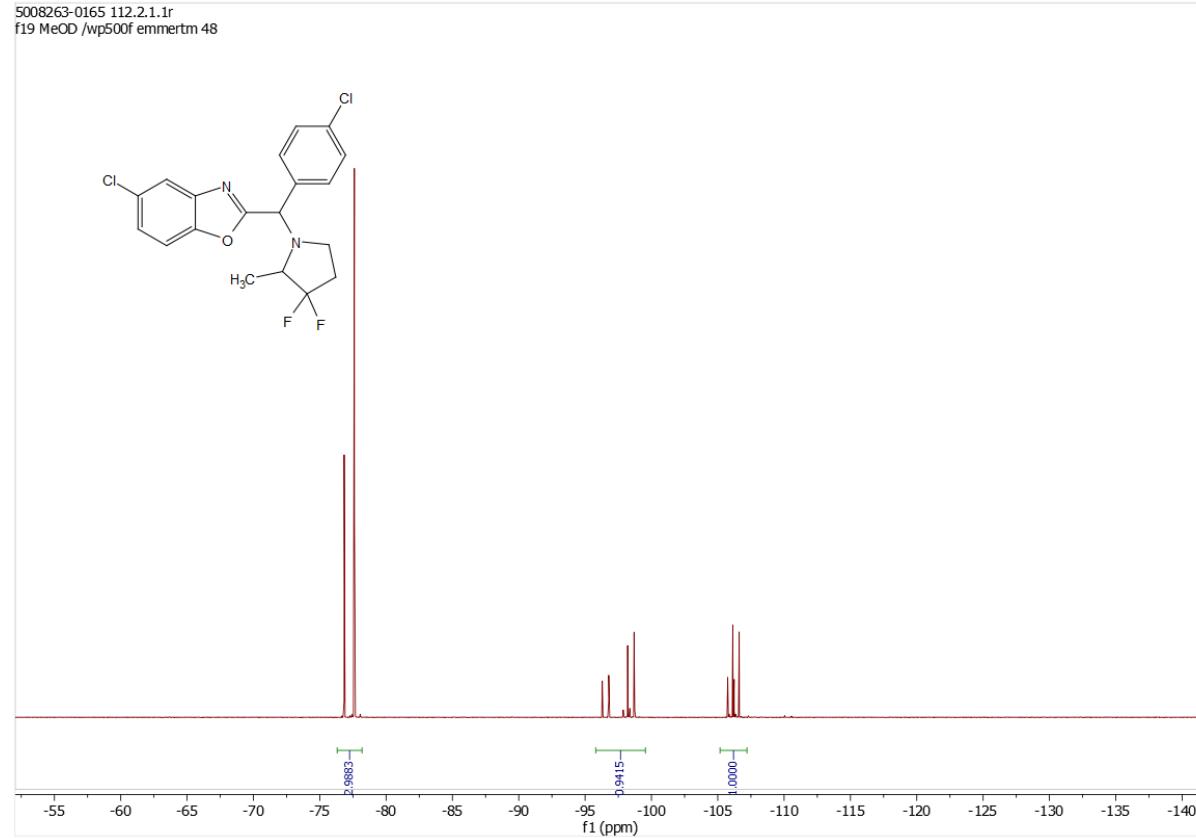
¹³C NMR (126 MHz, Methanol-*d*₄, ppm): Due to many overlapping peaks and fluorine couplings, the ¹³C NMR could not successfully be interpreted.

HRMS: Calc. C₁₉H₁₇Cl₂F₂N₂O⁺ [M+H⁺] 397.0681; found 397.0677.

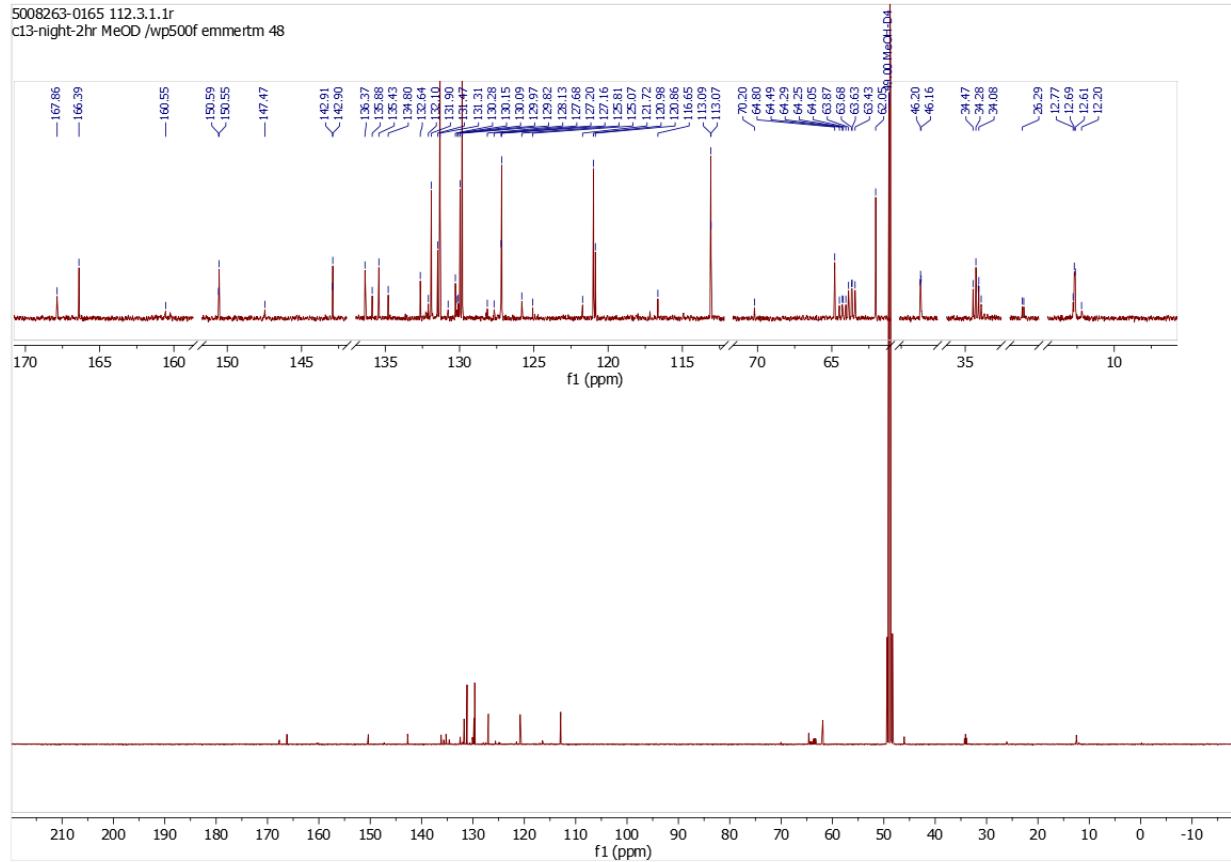
5016242-0112.2.1.1r
h1 MeOD /wp500l shahaksh 18



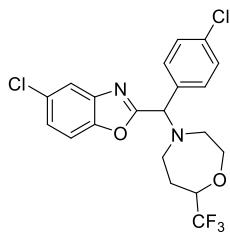
5008263-0165 112.2.1.1r
f19 MeOD /wp500f emmertm 48



5008263-0165 112.3.1.1r
c13-night-2hr MeOD /wp500f emmertm 48



5-Chloro-2-((4-chlorophenyl)(7-(trifluoromethyl)-1,4-oxazepan-4-yl)methyl)benzo[d]oxazole



Chemical Formula: C₂₀H₁₇Cl₂F₃N₂O₂

Exact Mass: 444.0619

Molecular Weight: 445.2632

The title compound was prepared according to General Procedure 3 (PMC). Isolated as ~3:2 mixture of diastereomers C₂₀H₁₇Cl₂F₃N₂O₂(F₃CCO₂H)_{1.3} (apparent M_w 444.0619 + 114.0232*1.3 = 592.2621 g/mol).

Yield: 35.3 mg (34%); 41 LCAP before workup/column chromatography

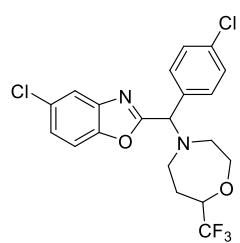
¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.78 (d, *J* = 1.9 Hz, 1H), 7.61 (d, *J* = 8.7 Hz, 1H), 7.55 (dd, *J* = 8.5, 3.1 Hz, 2H), 7.44 (dd, *J* = 10.3, 7.8 Hz, 3H), 5.66 (s, 0.6H; major diastereomer), 5.66 (s, 0.4H; minor diastereomer), 4.29 (hept, *J* = 7.2 Hz, 1H), 4.08 (ddt, *J* = 13.4, 8.7, 4.7 Hz, 1H), 3.80 (dddd, *J* = 16.1, 13.6, 6.7, 2.9 Hz, 1H), 3.30 – 2.97 (m, 4H), 2.25 – 2.14 (m, 2H).

¹⁹F NMR (470 MHz, Methanol-*d*₄, ppm) δ -76.83 (TFA), -77.45 (TFA), -79.95 (minor), -79.99 (major).

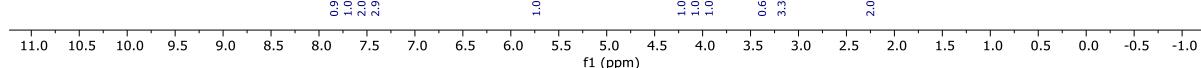
¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 166.1 (minor), 166.0 (major), 161.0 (q, *J* = 37.9 Hz; TFA), 158.9 (q, *J* = 42.7 Hz; TFA), 150.7, 142.8, 136.4, 134.5, 131.8 (major), 131.8 (minor), 131.6, 130.3, 127.4, 126.2 (q, *J* = 281.2 Hz; CF₃), 121.0, 117.1 (q, *J* = 288.3 Hz), 116.0 (q, *J* = 284.4 Hz; TFA), 113.1, 76.7 (q, *J* = 30.3 Hz; major), 76.7 (q, *J* = 30.3 Hz; minor), 68.5 (major), 68.4 (minor), 67.9 (major), 67.8 (minor), 51.5 (major), 51.4 (minor), 28.3.

HRMS: Calc. C₂₀H₁₈Cl₂F₃N₂O₂⁺ [M+H⁺] 445.0692; found 445.0678.

5016242-0114.1.1.ir
h1 MeOD /wp500f shahaksh 8

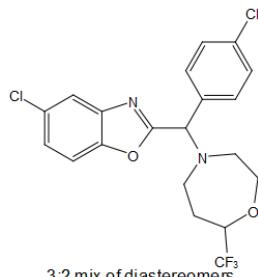


3:2 mixture of diastereomers

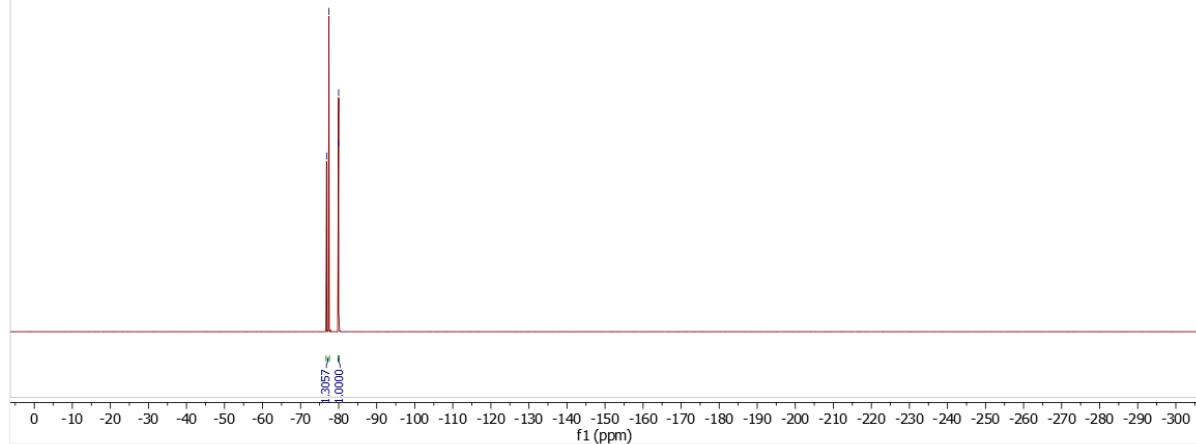


5008263-0165 114.2.1.1r
f19 MeOD /wp500f emmertm 51

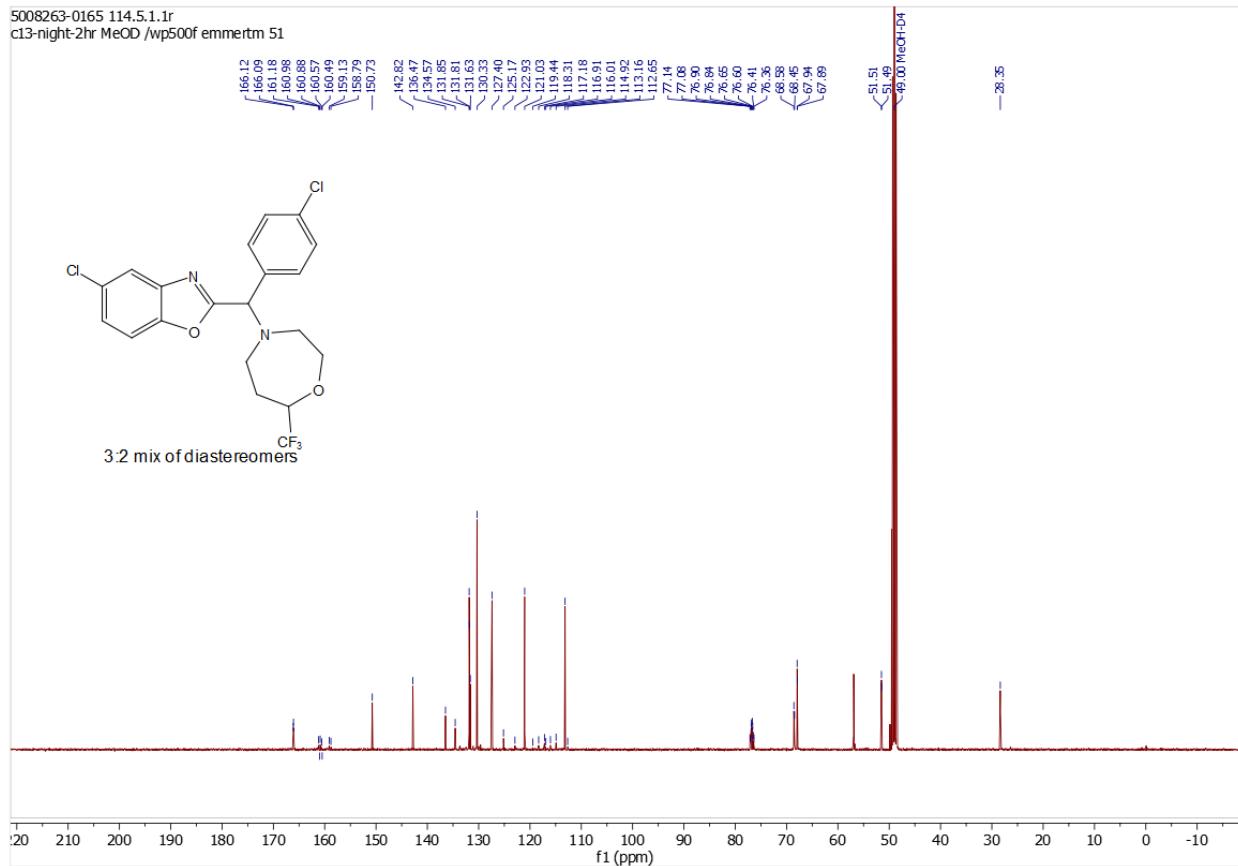
-76.83
-77.45
-79.95
-79.99



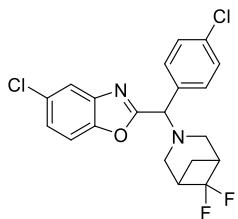
3:2 mix of diastereomers



5008263-0165 114.5.1.1r
c13-night-2hr MeOD /wp500f emmertm 51



5-Chloro-2-((4-chlorophenyl)(6,6-difluoro-3-azabicyclo[3.1.1]heptan-3-yl)methyl)benzo[d]oxazole



Chemical Formula: C₂₀H₁₆Cl₂F₂N₂O

Exact Mass: 408.0608

Molecular Weight: 409.2578

The title compound was prepared according to General Procedure 3 (PMC). Isolated as C₂₀H₁₆Cl₂F₂N₂O(F₃CCO₂H)₃ (apparent M_w 409.2578 + 114.0232*3 = 751.3274 g/mol).

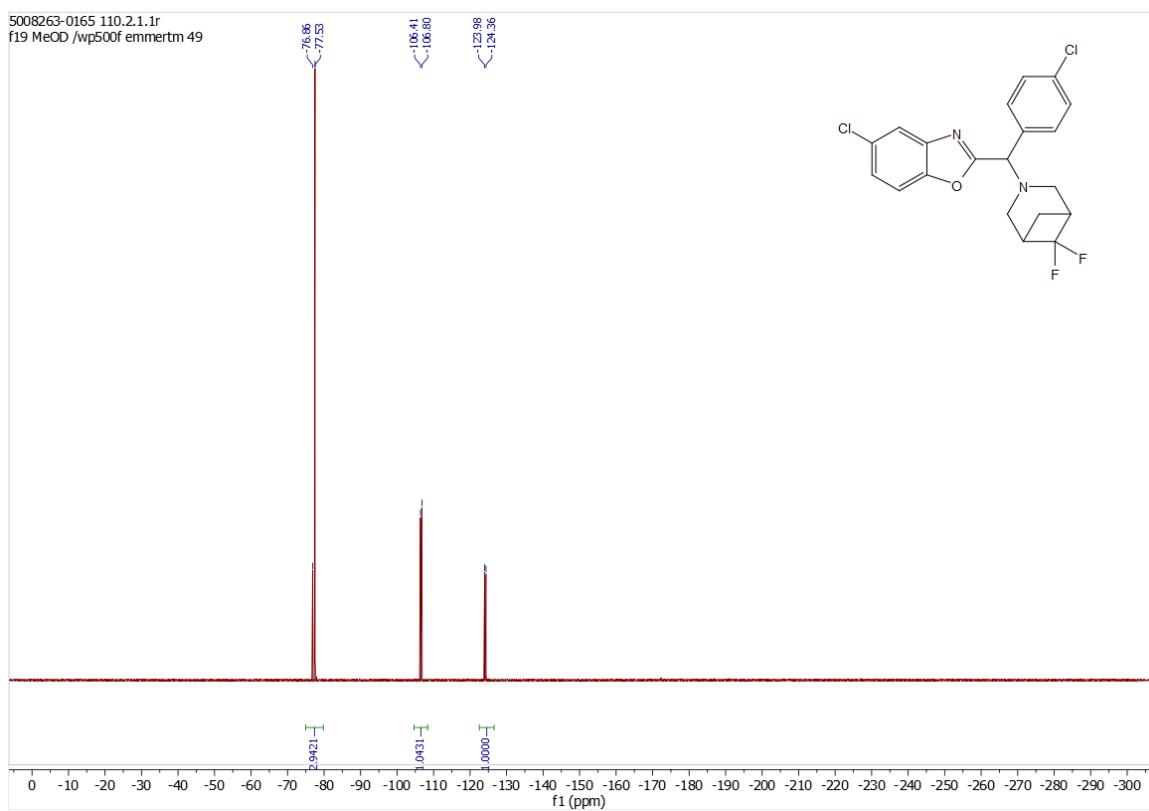
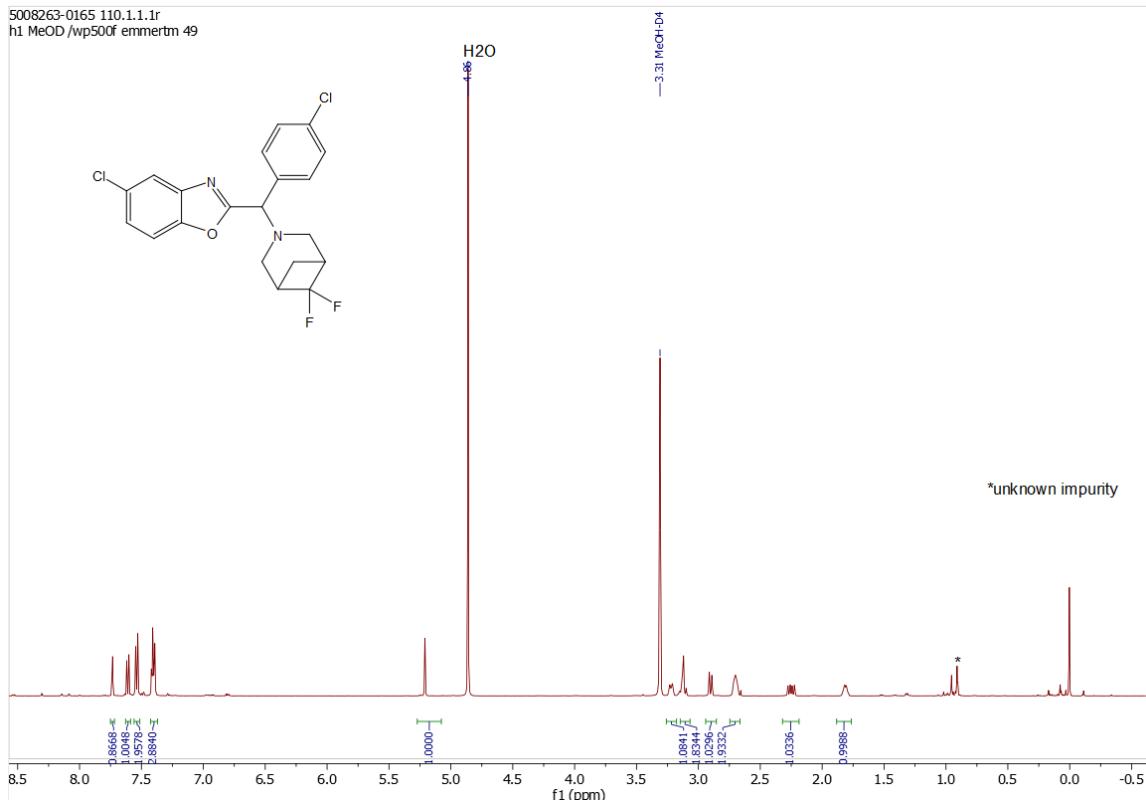
Yield: 7.8 mg (6%); 20 LCAP before workup/column chromatography

¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.73 (d, *J* = 1.9 Hz, 1H), 7.61 (d, *J* = 8.7 Hz, 1H), 7.54 (d, *J* = 8.5 Hz, 2H), 7.43 – 7.37 (m, 3H), 5.21 (s, 1H), 3.22 (d, *J* = 10.4 Hz, 1H), 3.18 – 3.07 (m, 2H), 2.90 (d, *J* = 10.4 Hz, 1H), 2.70 (s, 2H), 2.25 (dd, *J* = 16.9, 9.0 Hz, 1H), 1.86 – 1.77 (m, 1H).

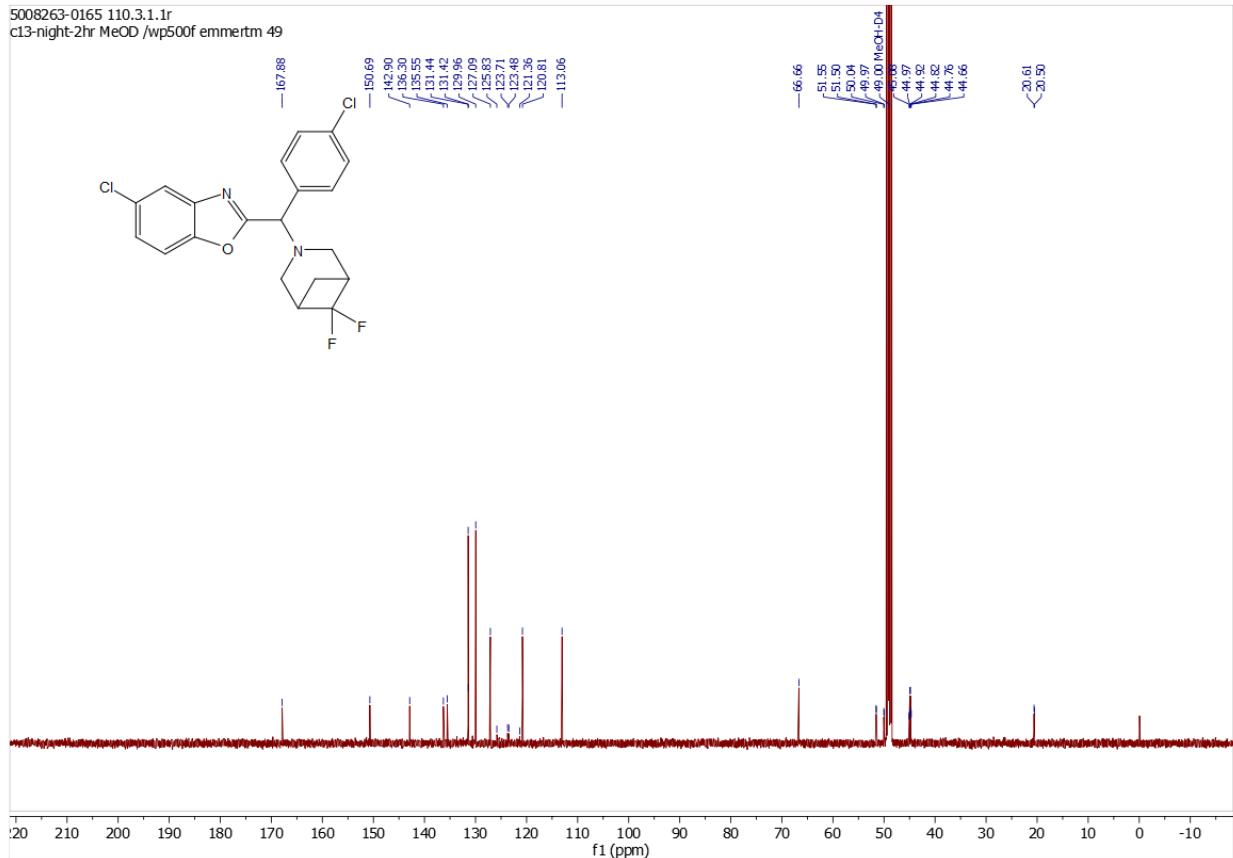
¹⁹F NMR (470 MHz, Methanol-*d*₄, ppm) δ -77.53 (TFA), -106.61 (d, *J* = 181.7 Hz), -124.17 (d, *J* = 181.8 Hz).

¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 167.8, 150.6, 142.9, 136.3, 135.5, 131.4, 131.4, 129.9, 127.0, 123.6 (m), 120.8, 113.0, 66.6, 51.5 (dd, *J* = 6.2, 1.7 Hz), 50.0 (dd, *J* = 6.2, 1.7 Hz), 44.9 (t, *J* = 20.0 Hz), 44.8 (t, *J* = 19.8 Hz), 20.5 (d, *J* = 13.9 Hz).

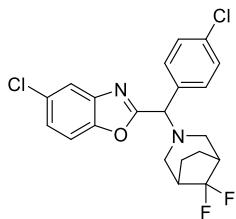
HRMS: Calc. C₂₀H₁₇Cl₂F₂N₂O⁺ [M+H⁺] 409.0681; found 409.0680.



5008263-0165 110.3.1.1r
c13-night-2hr MeOD /wp500f emmertm 49



5-Chloro-2-((4-chlorophenyl)(8,8-difluoro-3-azabicyclo[3.2.1]octan-3-yl)methyl)benzo[d]oxazole



Chemical Formula: C₂₁H₁₈Cl₂F₂N₂O

Exact Mass: 422.0764

Molecular Weight: 423.2848

The title compound was prepared according to General Procedure 3 (PMC). Isolated as C₂₁H₁₈Cl₂F₂N₂O(F₃CCO₂H)_{3.5} (apparent M_w 423.2848 + 114.0232 * 3.5 = 822.3660 g/mol).

Yield: 19.4 mg (13%); 23 LCAP before workup/column chromatography

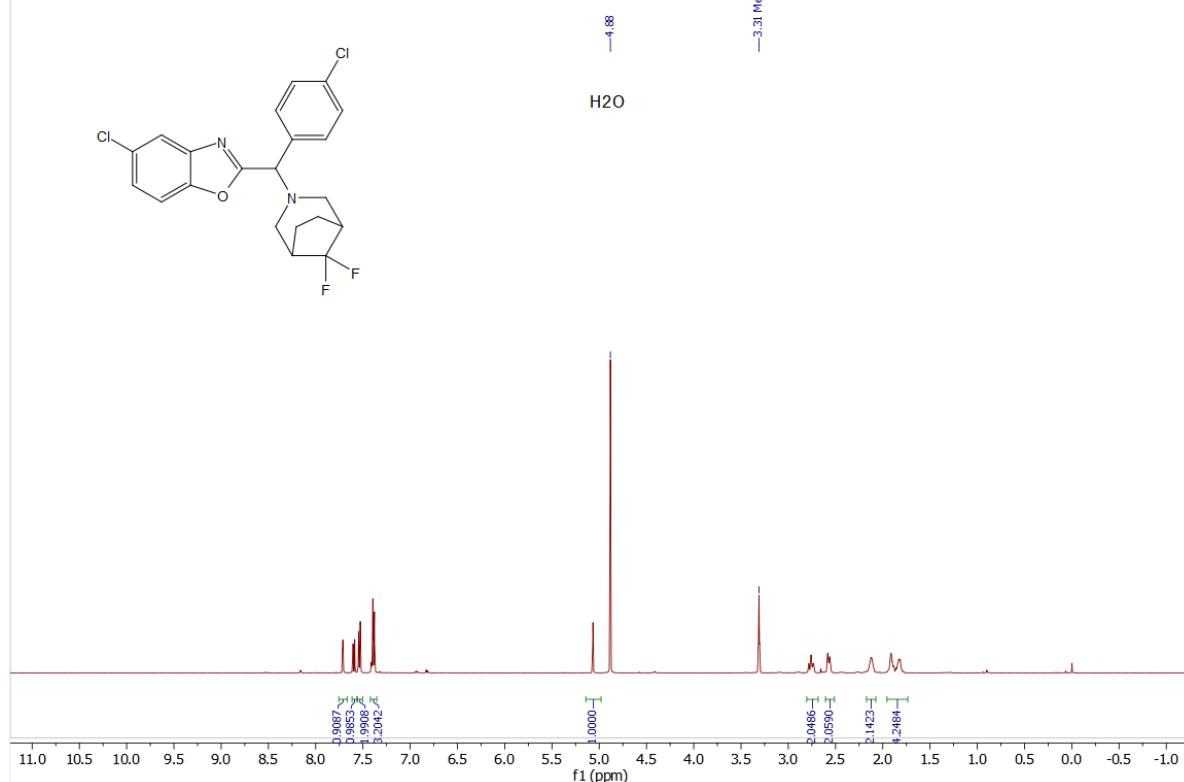
¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.71 (d, *J* = 1.9 Hz, 1H), 7.60 (d, *J* = 8.7 Hz, 1H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.39 (dd, *J* = 8.7, 2.1 Hz, 3H), 5.07 (s, 1H), 2.76 (t, *J* = 11.9 Hz, 2H), 2.57 (d, *J* = 10.8 Hz, 2H), 2.12 (s, 2H), 1.95 – 1.88 (m, 2H), 1.88 – 1.79 (m, 2H).

¹⁹F NMR (470 MHz, Methanol-*d*₄, ppm) δ -77.64 (TFA), -108.80 (d, *J* = 214.9 Hz), -128.04 (d, *J* = 214.9 Hz).

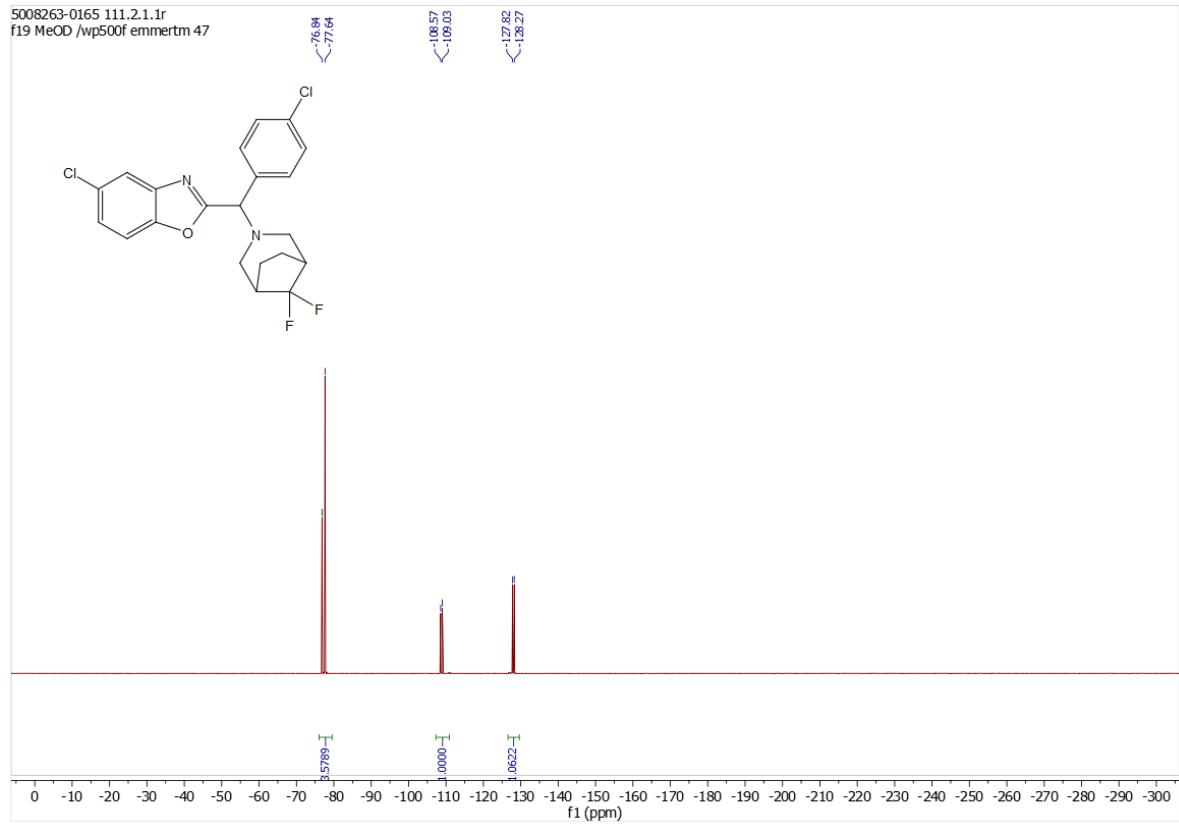
¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 167.8, 150.6, 146.8, 142.9, 136.8, 135.4, 132.3, 131.3, 130.2 (dd, *J* = 257.5, 249.3 Hz), 129.9, 127.0, 120.8, 113.0, 67.6, 53.7 (dd, *J* = 169.9, 9.1 Hz), 41.1 (ddd, *J* = 19.9, 17.9, 14.3 Hz), 24.8 (dd, *J* = 19.5, 6.1 Hz).

HRMS: Calc. C₂₁H₁₉Cl₂F₂N₂O⁺ [M+H⁺] 423.0837; found 423.0821.

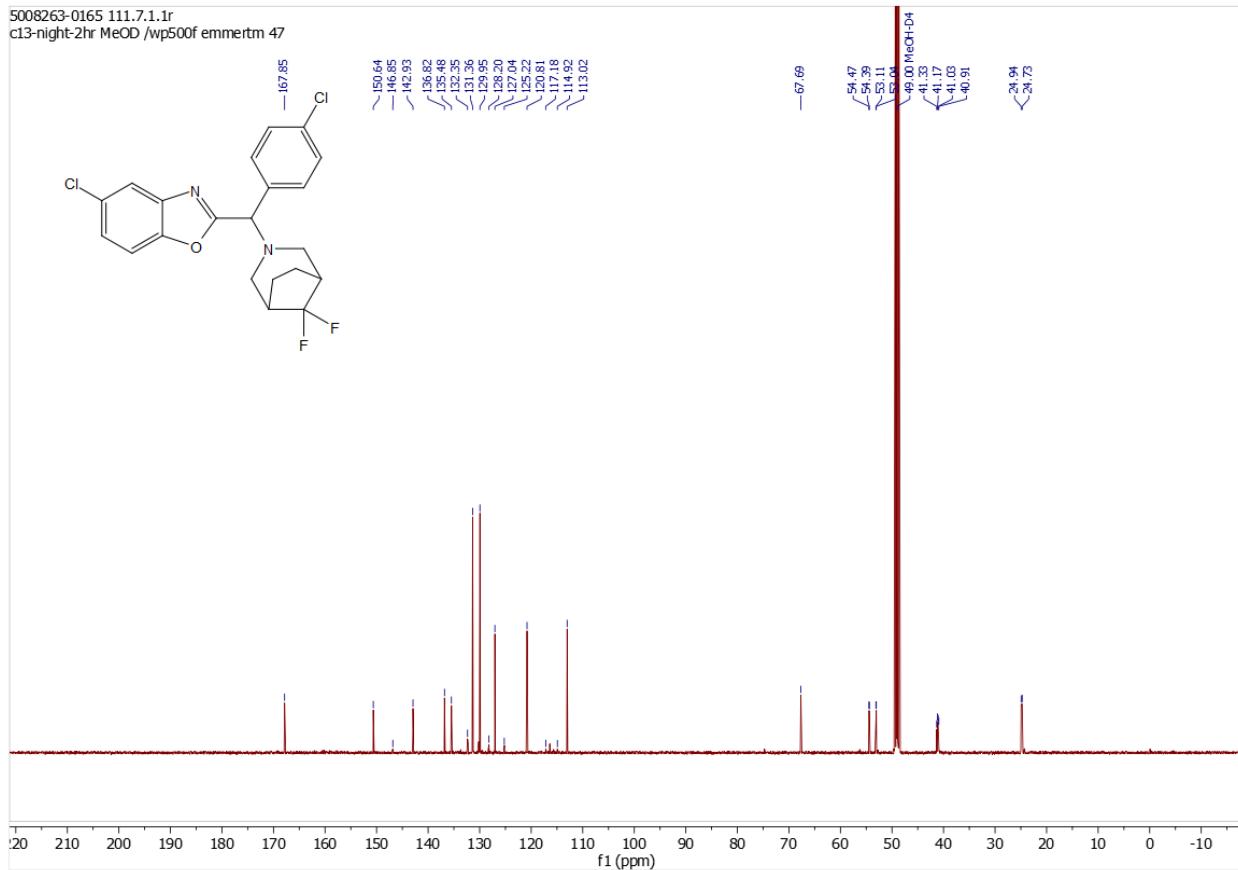
5008263-0165 111.1.1.1r
h1 MeOD /wp500f emmertm 47



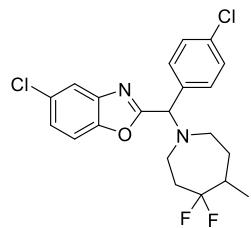
5008263-0165 111.2.1.1r
f19 MeOD /wp500f emmertm 47



5008263-0165 111.7.1.1r
c13-night-2hr MeOD /wp500f emmertm 47



5-Chloro-2-((4-chlorophenyl)(4,4-difluoro-5-methylazepan-1-yl)methyl)benzo[d]oxazole



Chemical Formula: C₂₁H₂₀Cl₂F₂N₂O

Exact Mass: 424.0921

Molecular Weight: 425.3008

The title compound was prepared according to General Procedure 3 (PMC). Isolated as ~3:2 mixture of diastereomers, C₂₁H₂₀Cl₂F₂N₂O(F₃CCO₂H)_{2.7} (apparent M_w 425.3008 + 114.0232 * 2.7 = 733.1634 g/mol).

Yield: 19.3 mg (15%); 32 LCAP before workup/column chromatography

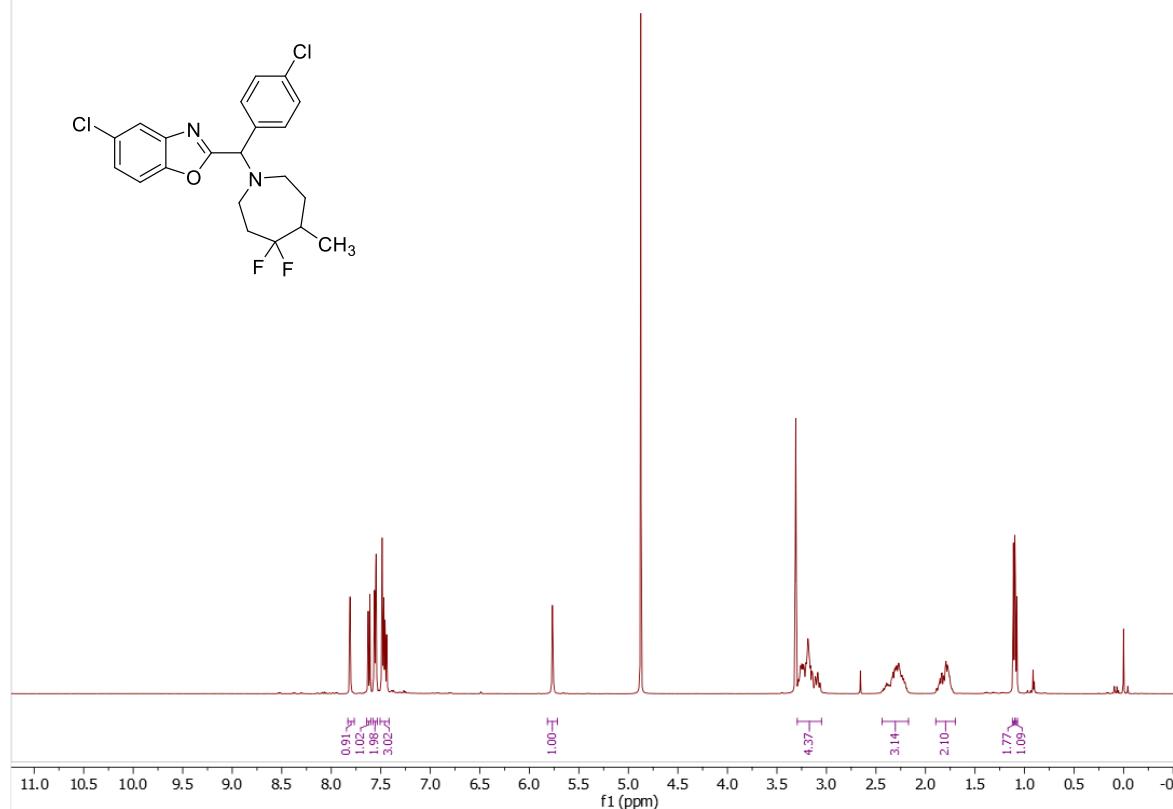
¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.81 (t, *J* = 2.4 Hz, 1H), 7.62 (d, *J* = 8.7 Hz, 1H), 7.58 – 7.54 (m, 2H), 7.51 – 7.42 (m, 3H), 5.77 (s, 0.6H, major diastereomer), 5.76 (s, 0.4H, minor diastereomer), 3.29 – 3.05 (m, 4H), 2.31 (dddt, *J* = 41.2, 33.6, 22.5, 6.3 Hz, 3H), 1.82 (dddt, *J* = 18.0, 15.0, 11.3, 5.1 Hz, 2H), 1.11 (d, *J* = 7.0 Hz, 2H; Me, major diastereomer), 1.09 (d, *J* = 7.1 Hz, 1H; Me, minor diastereomer).

¹⁹F NMR (470 MHz, Methanol-*d*₄, ppm) δ -77.22, -92.53 (d, *J* = 244.8 Hz), -92.67 (d, *J* = 244.6 Hz).

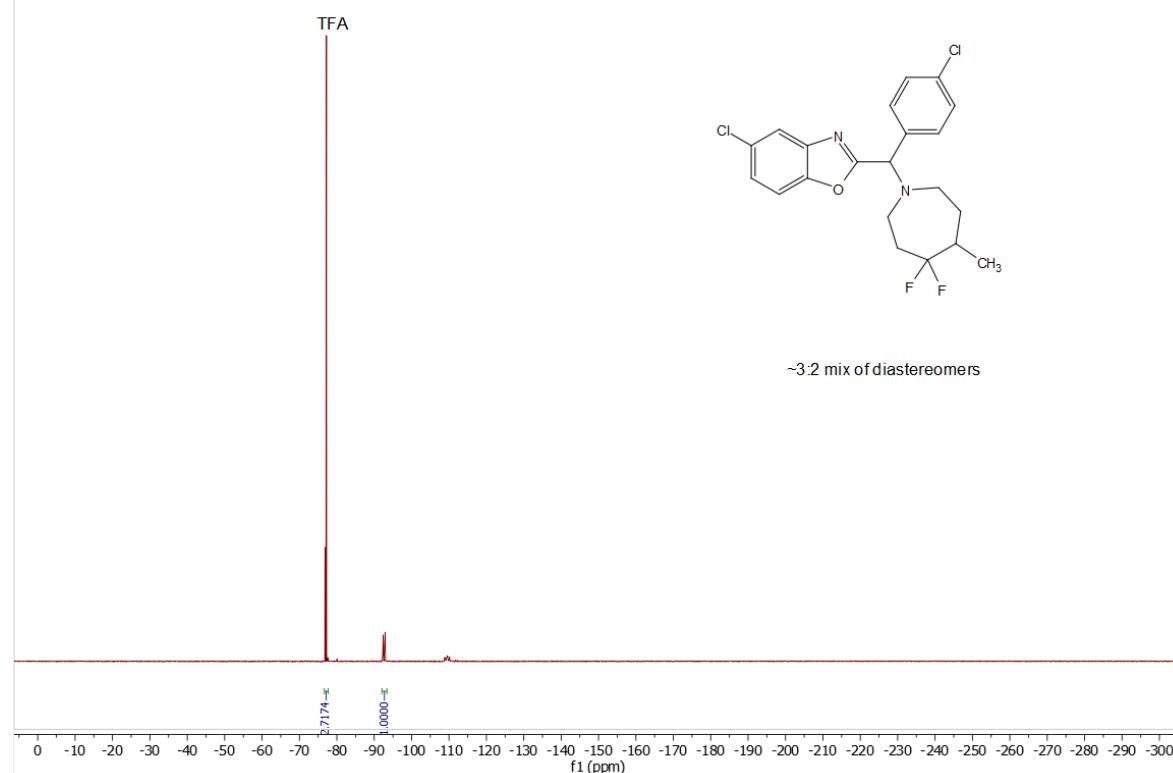
¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 165.4 (minor), 165.3 (major), 161.8 (1, *J* = 35.8 Hz; TFA), 150.8 (major), 150.7 (minor), 142.7, 136.9, 133.7 (minor), 133.6 (major), 132.0 (minor), 131.9 (major), 131.7 (major), 131.7 (minor), 130.5, 127.5, 128.2 – 124.2 (m; CF₂), 121.13, 113.2 (major), 113.2 (minor), 67.89 (minor), 67.7 (major), 53.1 (major), 52.6 (minor), 46.0 (t, *J* = 7.6 Hz; major), 45.9 (dd, *J* = 9.1, 6.2 Hz; minor), 41.3 (t, *J* = 24.4 Hz; major), 41.1 (t, *J* = 24.4 Hz; minor), 36.5 (t, *J* = 28.3; minor), 36.1 (t, *J* = 28.3; major), 28.5 (d, *J* = 8.0 Hz; minor), 28.3 (d, *J* = 8.8 Hz; major), 14.1 (dd, *J* = 6.2, 4.6 Hz; minor), 13.9 (dd, *J* = 6.4, 4.0 Hz; major).

HRMS: Calc. C₂₁H₂₁Cl₂F₂N₂O⁺ [M+H⁺] 425.0994; found 425.0995.

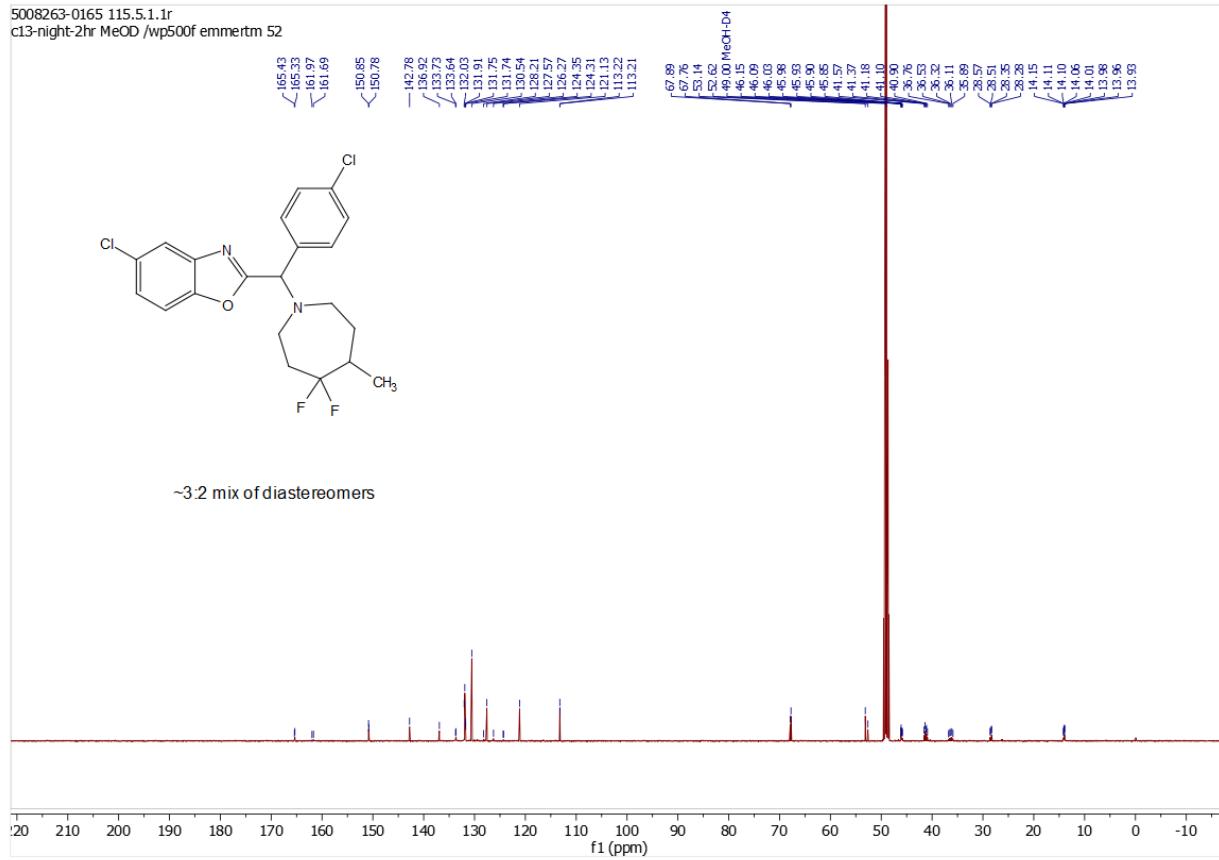
5016242-0115-1.1.1.1r
h1 MeOD /wp500f shahaksh 9



5008263-0165 115.2.1.1r
f19 MeOD /wp500f emmermrtm 52



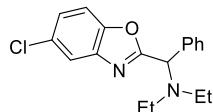
5008263-0165 115.5.1.1r
c13-night-2hr MeOD /wp500f emmertm 52



-3:2 mix of diastereomers

Azole Scope

N-(5-Chlorobenzo[d]oxazol-2-yl)(phenyl)methyl)-*N*-ethylethanamine



Chemical Formula: C₁₈H₁₉ClN₂O

Exact Mass: 314.12

Molecular Weight: 314.81

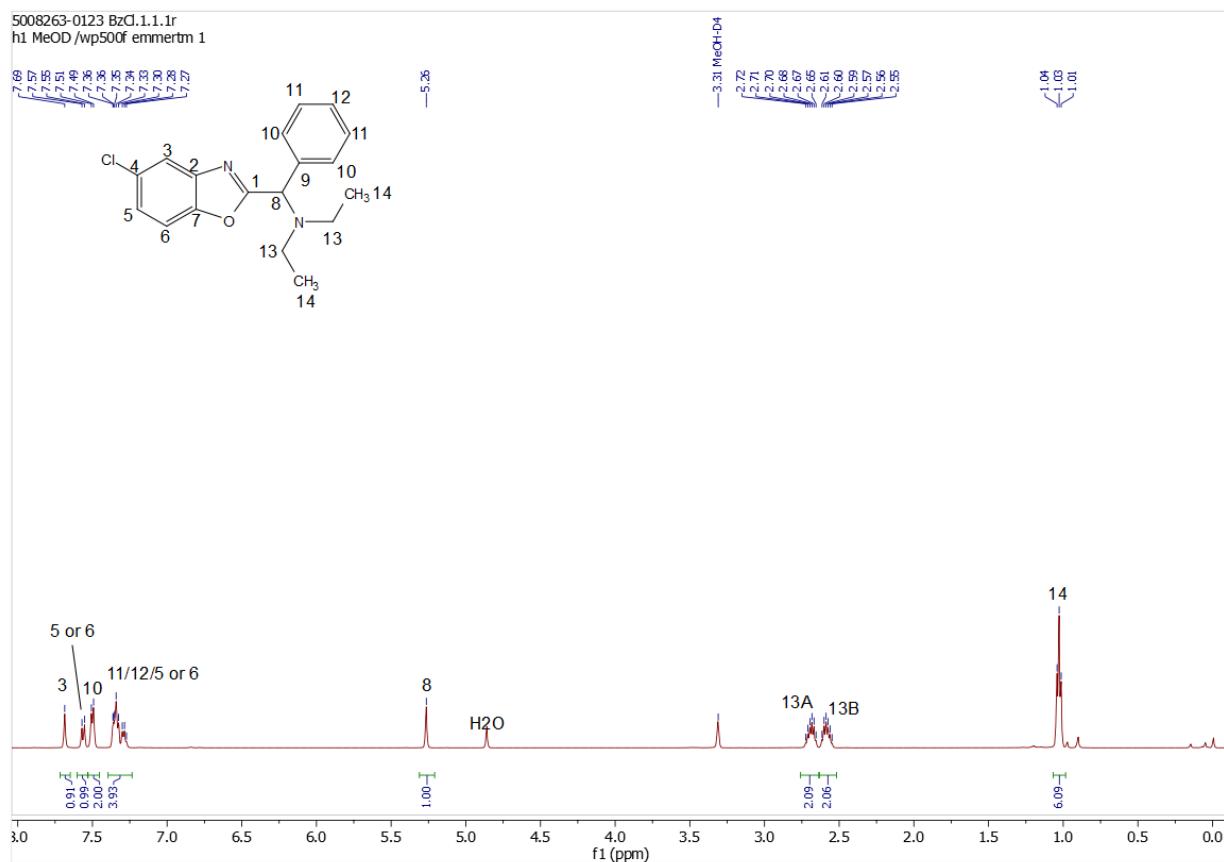
The title compound was prepared according to General Procedure 2 (reaction time 18 h).

Yield: 224 mg (71%); 75 LCAP before workup/column chromatography

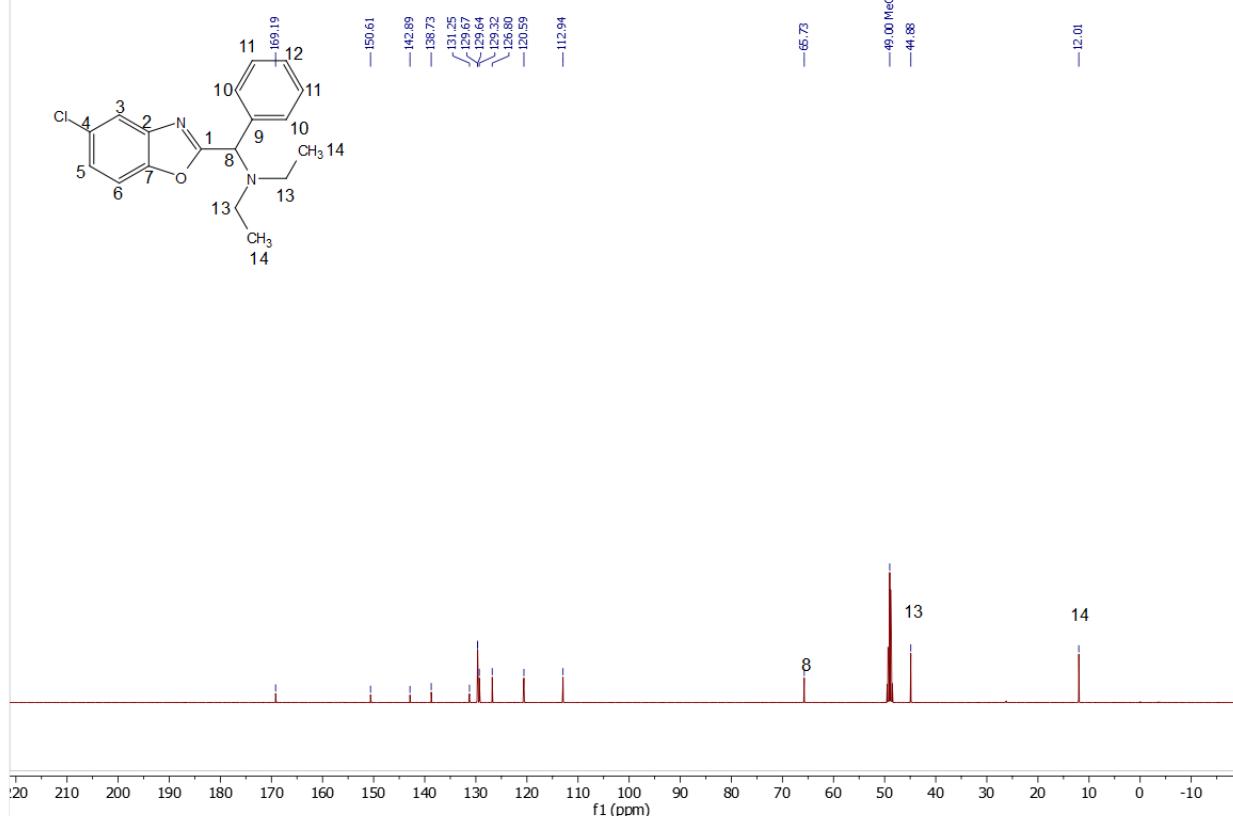
¹H NMR (500 MHz, Methanol-d₄, ppm) δ 7.69 (s, 1H), 7.56 (d, *J* = 8.6 Hz, 1H), 7.50 (d, *J* = 7.4 Hz, 2H), 7.42 – 7.31 (m, 3H), 7.31 – 7.25 (m, 1H), 5.26 (s, 1H), 2.69 (dq, *J* = 13.5, 6.9 Hz, 2H), 2.58 (dq, *J* = 13.5, 6.6 Hz, 2H), 1.03 (t, *J* = 6.9 Hz, 6H).

¹³C NMR (126 MHz, Methanol-d₄, ppm) δ 169.1, 150.6, 142.8, 138.7, 131.2, 129.6, 129.6, 129.3, 126.8, 120.5, 112.9, 65.7, 44.8, 12.0.

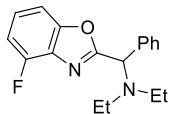
HRMS: Calc. C₁₈H₂₀ClN₂O⁺ [M+H⁺] 315.1259; found 315.1258.



5008263-0123 BzCl.7.1.1r
c13-night-2hr MeOD /wp500f emmertrm 1



N-Ethyl-*N*-(4-fluorobenzo[d]oxazol-2-yl)(phenyl)methylethanamine



Chemical Formula: C₁₈H₁₉FN₂O

Exact Mass: 298.15

Molecular Weight: 298.36

The title compound was prepared according to General Procedure 2 (reaction time 18 h).

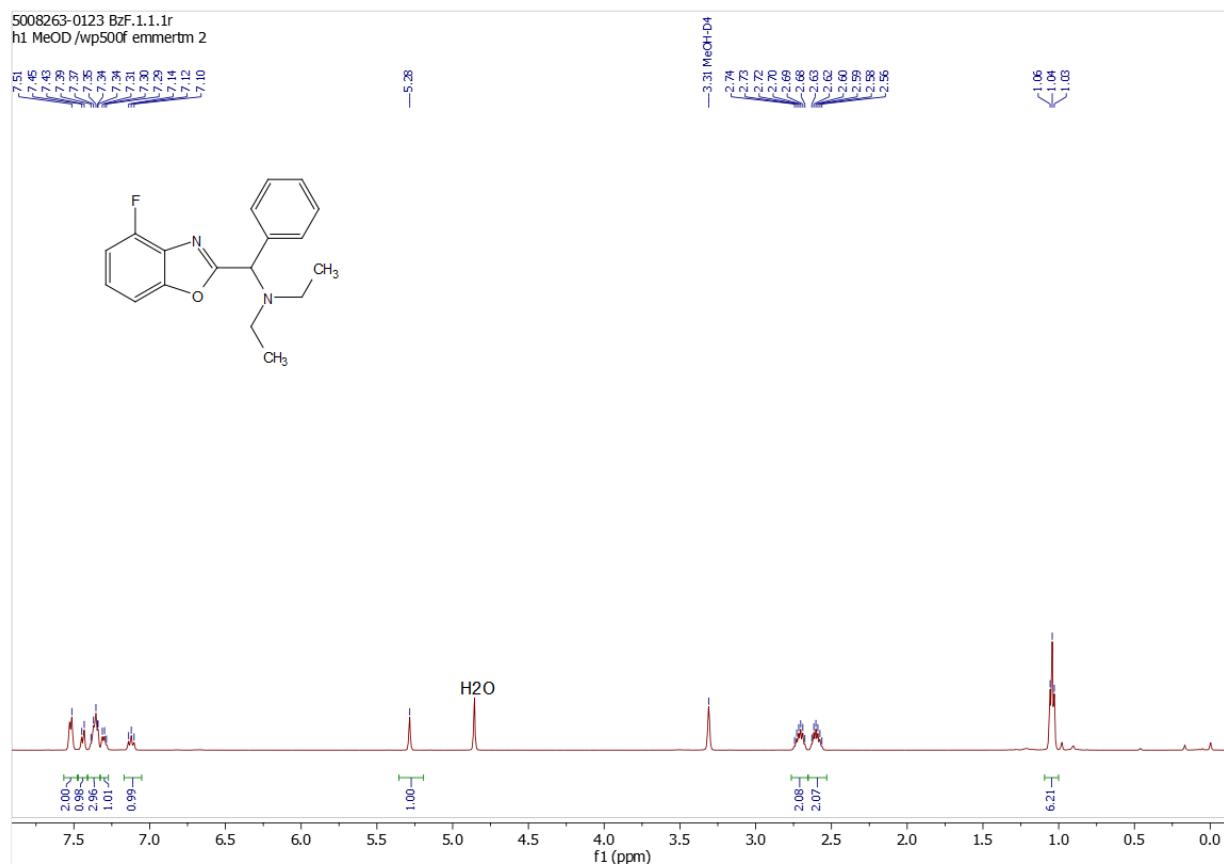
Yield: 188 mg (63%); 67 LCAP before workup/column chromatography

¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.51 (s, 2H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.41 – 7.33 (m, 3H), 7.33 – 7.27 (m, 1H), 7.12 (t, *J* = 9.0 Hz, 1H), 5.28 (s, 1H), 2.71 (dq, *J* = 13.5, 6.9 Hz, 2H), 2.60 (dq, *J* = 13.5, 6.6 Hz, 2H), 1.04 (t, *J* = 6.9 Hz, 6H).

¹⁹F NMR (470 MHz, Methanol-*d*₄, ppm) δ -127.98.

¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 167.9, 154.2 (d, *J* = 7.0 Hz), 153.5, 138.7, 130.1 (d, *J* = 16.9 Hz), 129.6, 129.6, 129.3, 127.2 (d, *J* = 7.2 Hz), 111.8 (d, *J* = 17.8 Hz), 108.2 (d, *J* = 4.5 Hz), 65.7, 44.8, 11.9.

HRMS: Calc. C₁₈H₂₀FN₂O⁺[M+H⁺] 299.1554; found 299.1566.

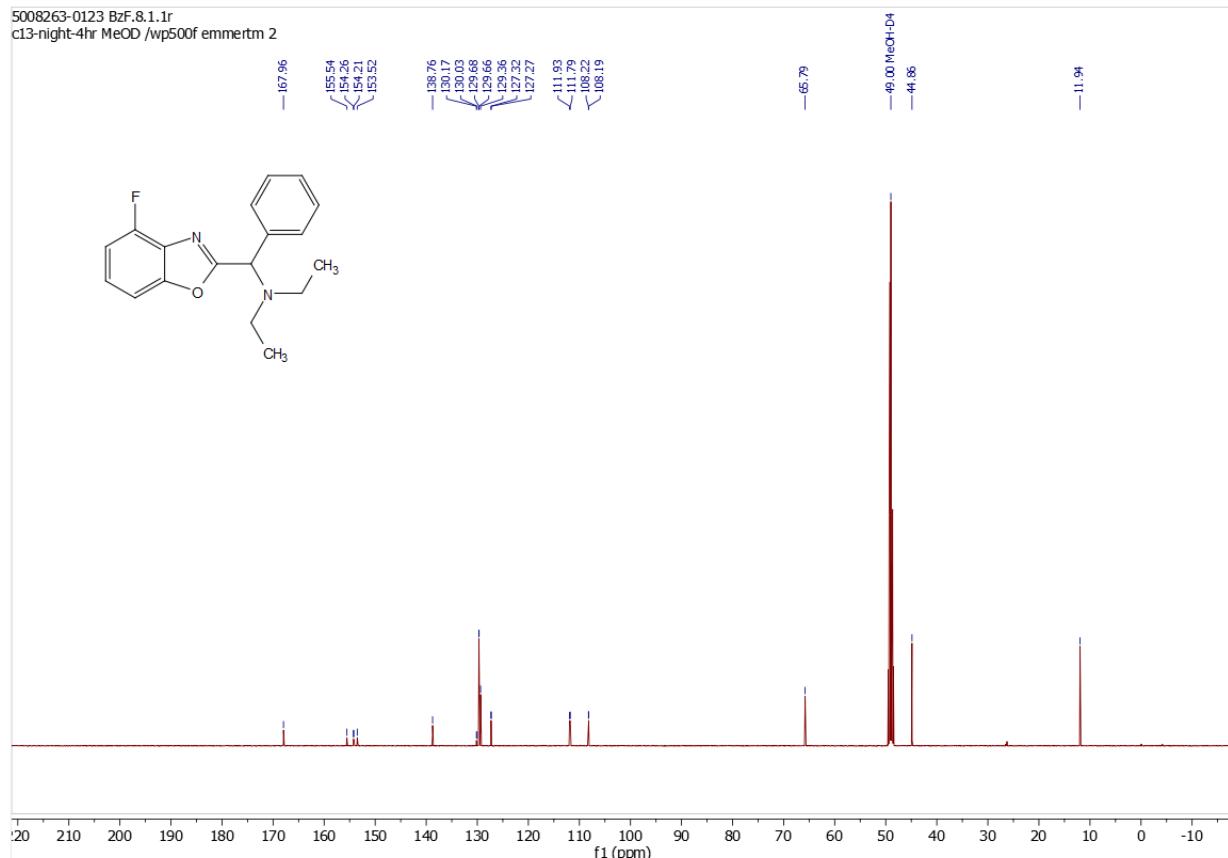


5008263-0123 BzF.2.1.1r
f19 MeOD /wp500f emmertm 2

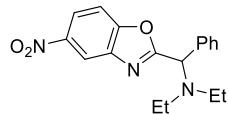
—
86.98
—
-171.98

0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240 -250 -260 -270 -280 -290 -300
f1 (ppm)

5008263-0123 BzF.8.1.1r
c13-night-4hr MeOD /wp500f emmertm 2



N-Ethyl-*N*-(5-nitrobenzo[d]oxazol-2-yl)(phenyl)methyl)ethanamine



Chemical Formula: C₁₈H₁₉N₃O₃

Exact Mass: 325.14

Molecular Weight: 325.37

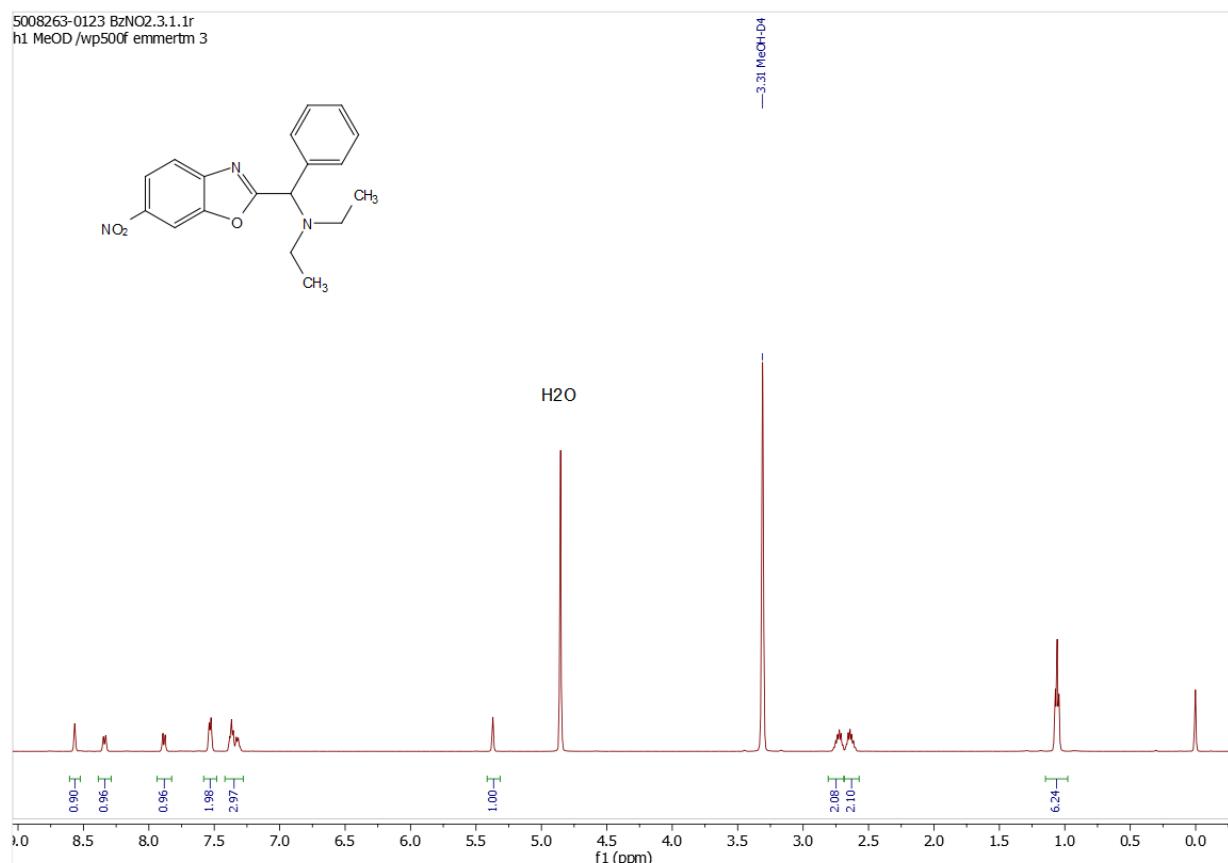
The title compound was prepared according to General Procedure 2 (reaction time 18 h).

Yield: 224 mg (69%); 61 LCAP before workup/column chromatography

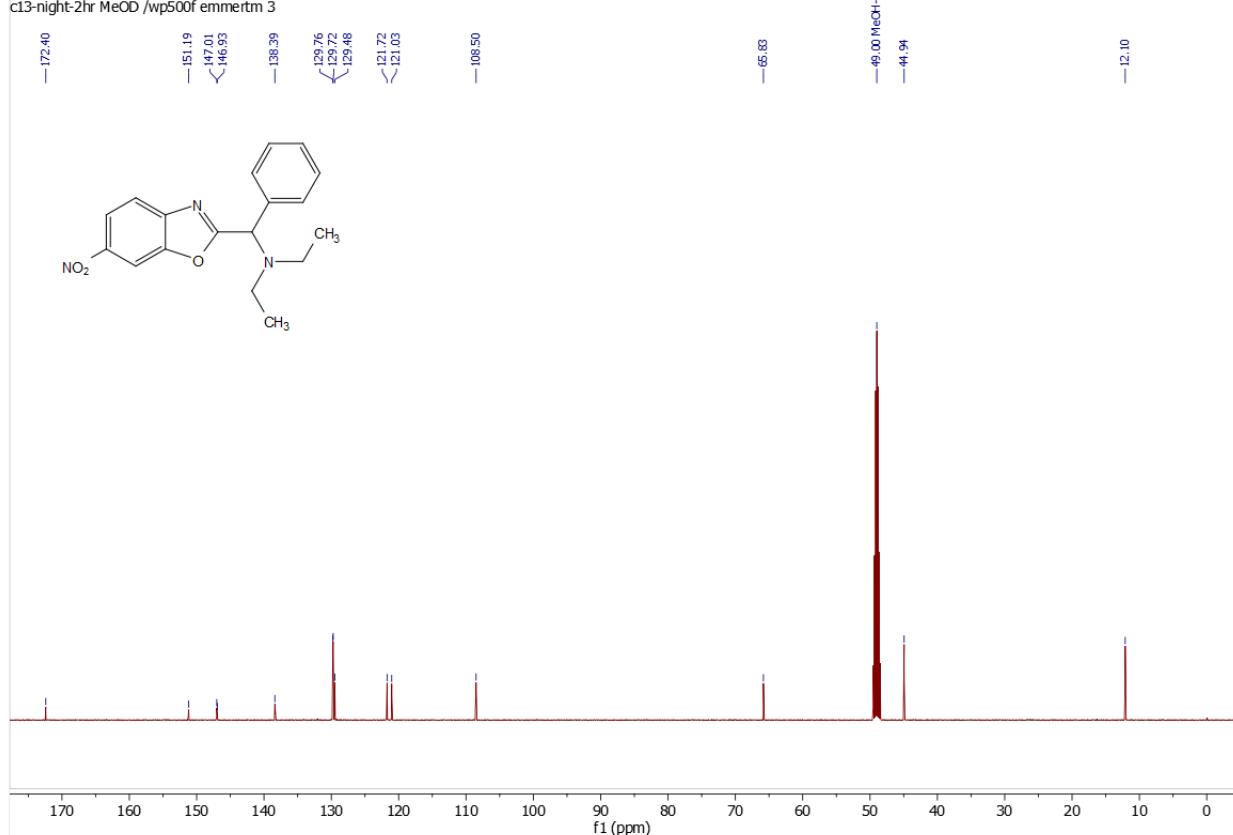
¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 8.57 (s, 1H), 8.34 (d, *J* = 8.7 Hz, 1H), 7.88 (d, *J* = 8.6 Hz, 1H), 7.53 (d, *J* = 7.2 Hz, 2H), 7.42 – 7.28 (m, 3H), 5.37 (s, 1H), 2.73 (dq, *J* = 13.6, 6.8 Hz, 2H), 2.63 (dq, *J* = 13.6, 6.8 Hz, 2H), 1.06 (t, *J* = 6.8 Hz, 6H).

¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 172.4, 151.1, 147.0, 146.9, 138.3, 129.7, 129.7, 129.4, 121.7, 121.0, 108.5, 65.8, 44.9, 12.1.

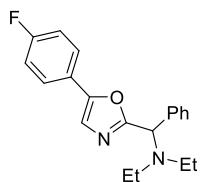
HRMS: Calc. C₁₈H₂₀N₃O₃⁺ [M+H⁺] 326.1499; found 326.1516.



5008263-0123 BzNO2.6.1.1r
c13-night-2hr MeOD /wp500f emmertm 3



N-ethyl-*N*-(5-(4-fluorophenyl)oxazol-2-yl)(phenyl)methylethanamine



Chemical Formula: C₂₀H₂₁FN₂O

Exact Mass: 324.16

Molecular Weight: 324.40

Yield: 175 mg (54%); 89 LCAP before workup/column chromatography

The title compound was prepared according to General Procedure 2 (reaction time 4 h).

¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.73 – 7.64 (m, 2H), 7.50 (d, *J* = 7.4 Hz, 2H), 7.34 (t, *J* = 7.1 Hz, 2H), 7.28 (t, *J* = 7.0 Hz, 1H), 7.20 – 7.12 (m, 2H), 5.15 (s, 1H), 2.69 (dq, *J* = 13.5, 6.8 Hz, 2H), 2.55 (dq, *J* = 13.1, 6.5 Hz, 2H), 1.03 (t, *J* = 6.9 Hz, 6H).

¹⁹F NMR (470 MHz, Methanol-*d*₄, ppm) δ -114.18.

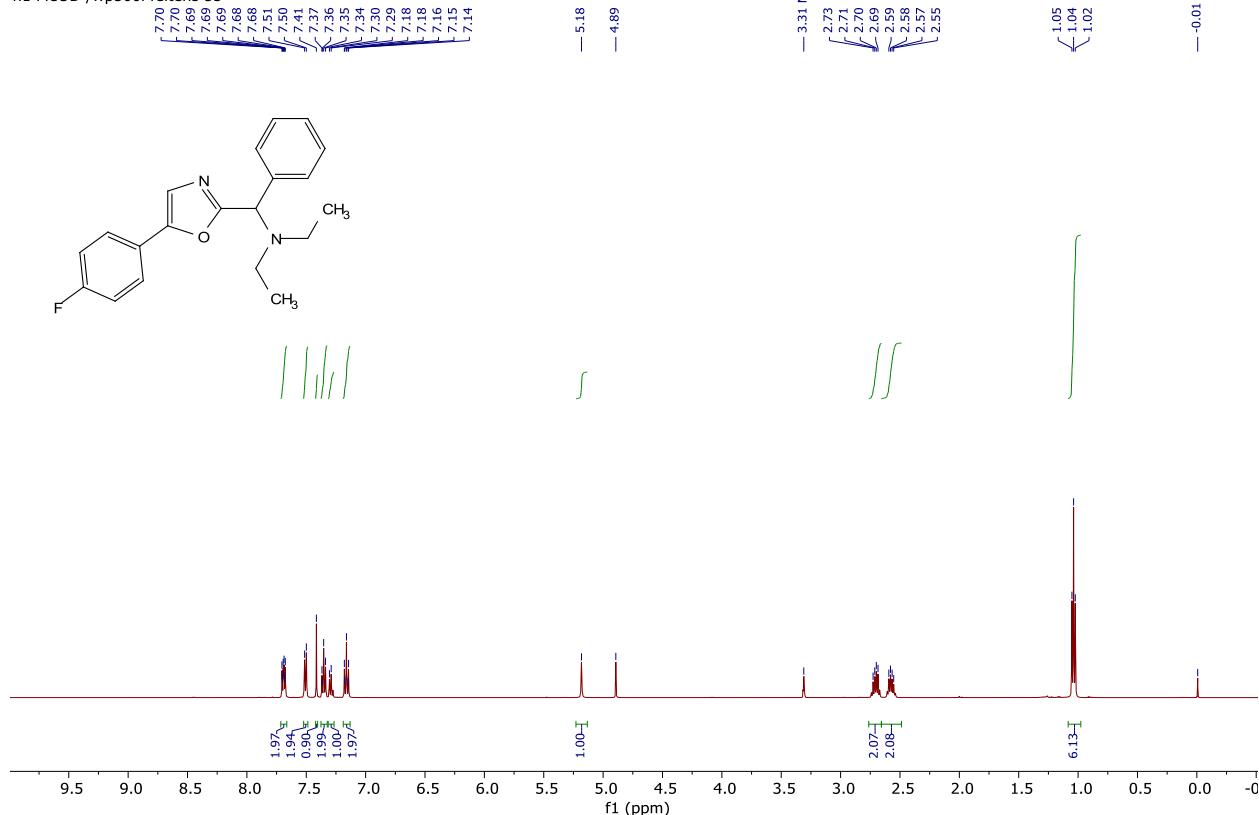
¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 165.1, 164.6, 164.2 (d, *J* = 247.7 Hz), 152.5, 129.6, 129.5, 129.2, 127.4 (d, *J* = 8.4 Hz), 122.0 (d, *J* = 1.2 Hz), 117.1, 116.9, 65.2, 44.9, 11.9.

HRMS: Calc. C₂₀H₂₂FN₂O⁺ [M+H⁺] 325.1711; found 325.1715.

5036622-0002-OxF_3.1.fid

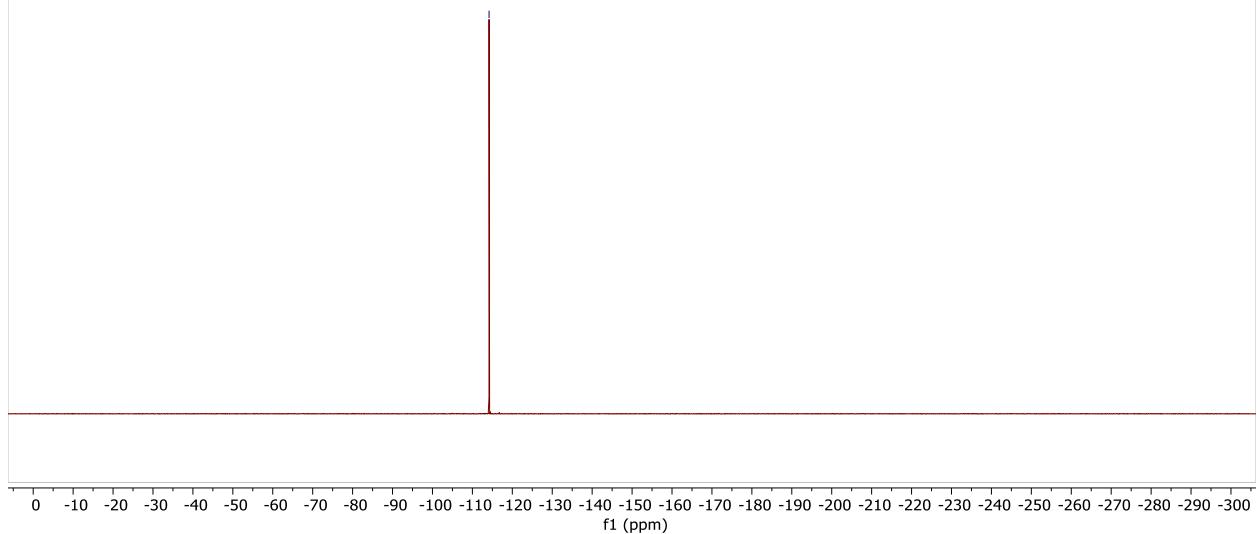
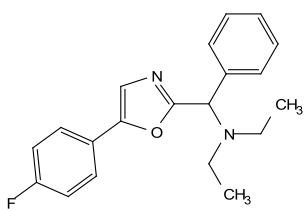
0002-OxF_3_dried

h1 MeOD /wp5001 feltens 53

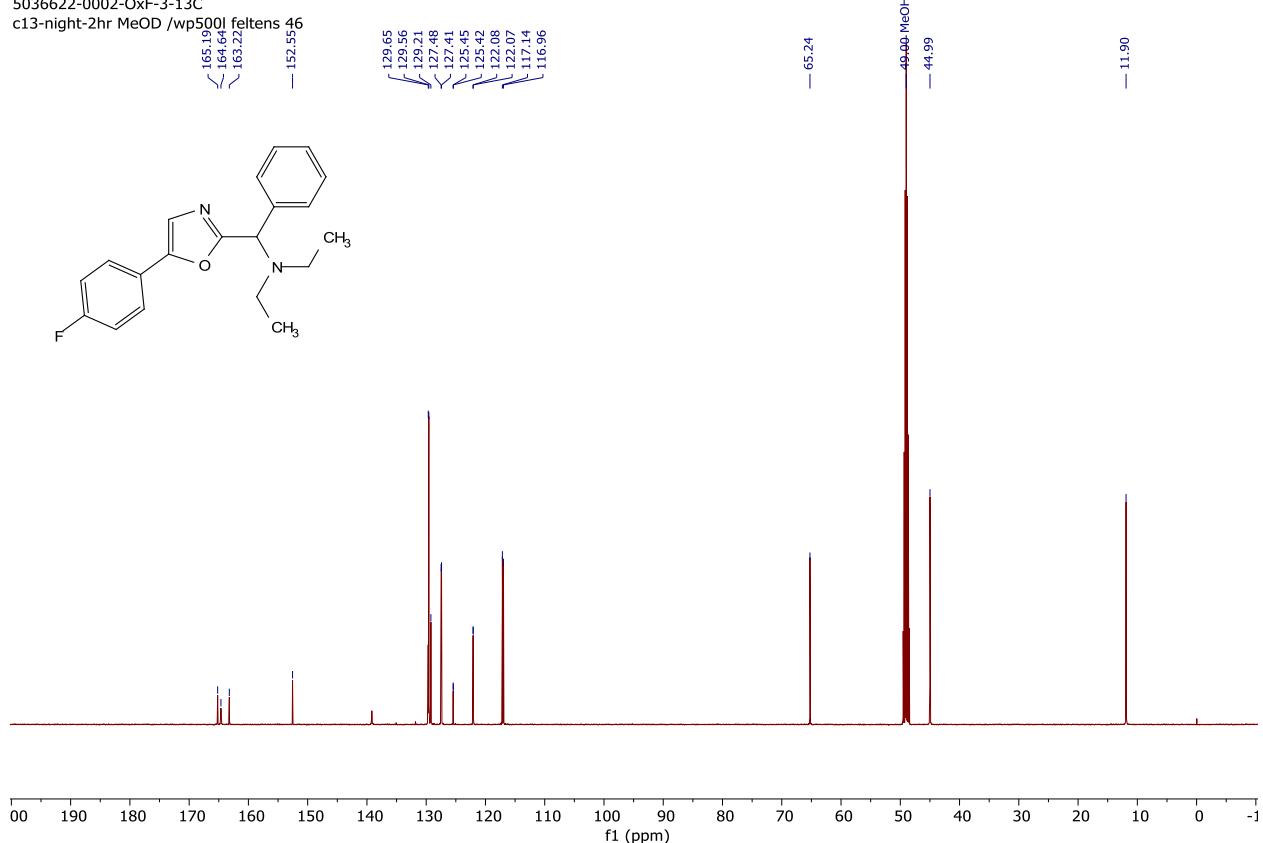


5008263-0134 OxF.5.1.1r
f19 MeOD /wp500f emmertm 4

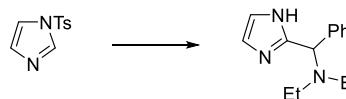
-114.18



5036622-00021-OxF-3_13C.1.fid
5036622-0002-OxF-3-13C
c13-night-2hr MeOD /wp500! feltens 46



N-((1*H*-imidazol-2-yl)(phenyl)methyl)-*N*-ethylethanamine



Chemical Formula: C₁₄H₁₉N₃

Exact Mass: 229.16

Molecular Weight: 229.33

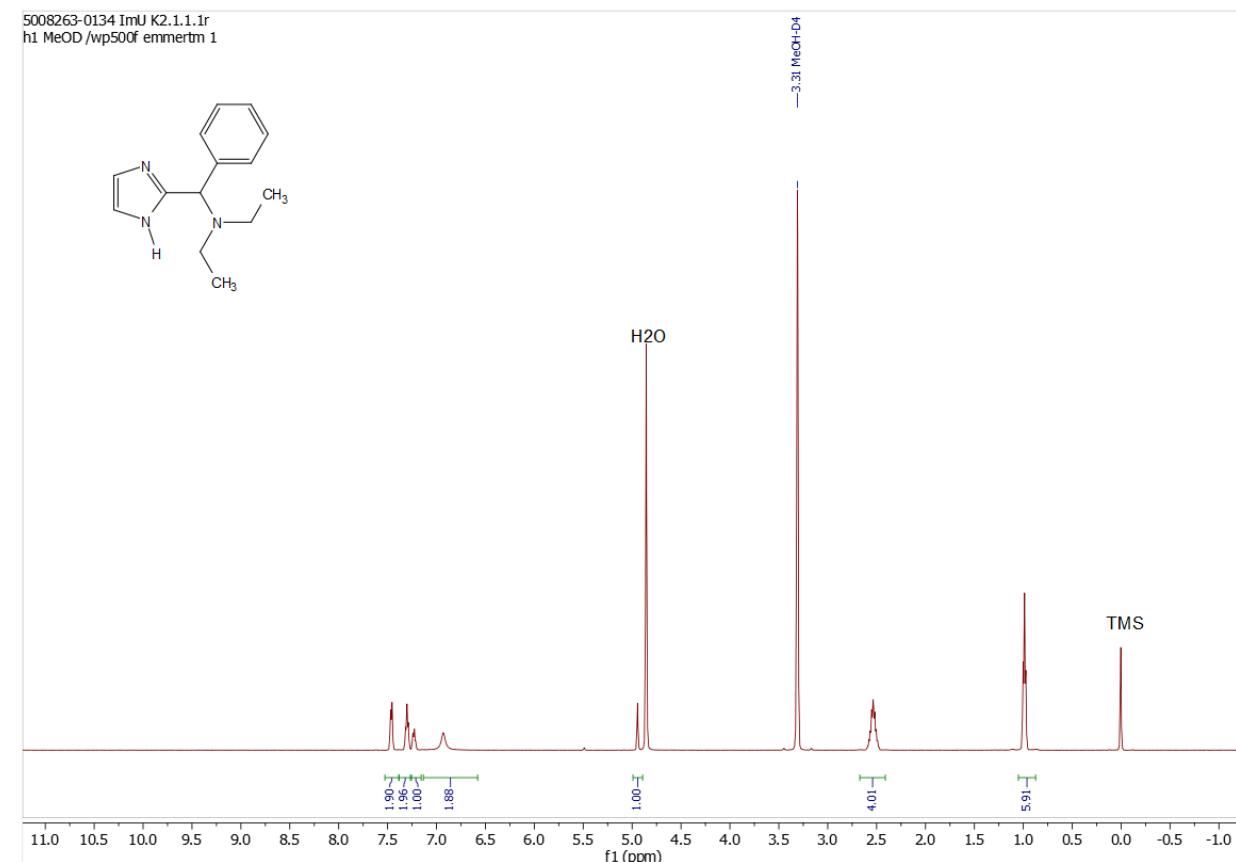
The title compound was prepared according to General Procedure 2 (reaction time 4 h), starting from N-tosylimidazole. After hydrolysis of the tosyl protecting group and silica gel column chromatography, the obtained yellow residue was dissolved in 5 mL dichloromethane and extracted with 3 x 5 mL 1M HCl. 25 mL 1 M NaOH was added to the combined extracts, resulting in precipitation of a crystalline solid, which was collected by filtration.

Yield: 202 mg (88%); 24 LCAP imidazole-H product (59 LCAP imidazole-tosyl intermediate before hydrolysis)

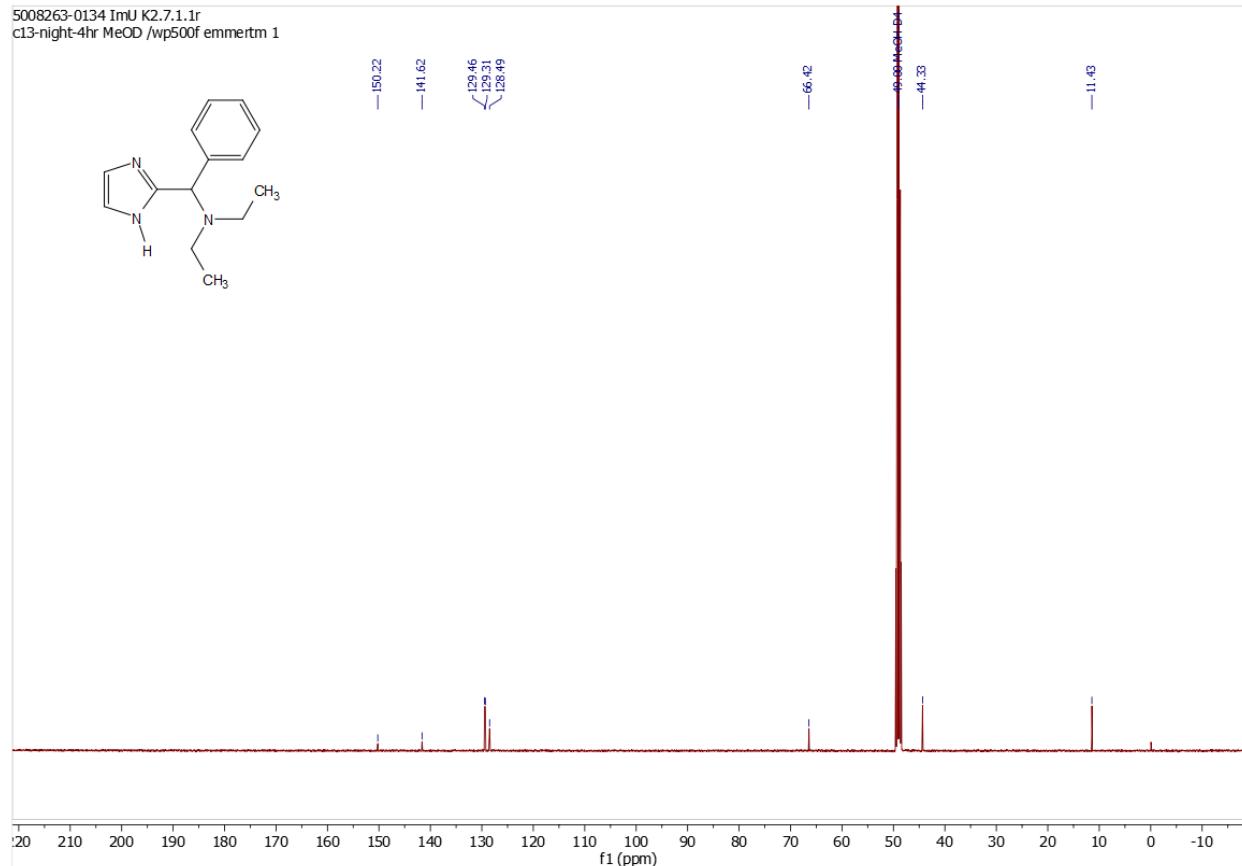
¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.46 (d, *J* = 7.2 Hz, 2H), 7.30 (t, *J* = 7.0 Hz, 2H), 7.23 (t, *J* = 7.1 Hz, 1H), 6.93 (broad s, 2H), 4.94 (s, 1H), 2.54 (m, 4H), 0.99 (t, *J* = 6.7 Hz, 6H).

¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 150.2, 141.6, 129.4, 129.3, 128.4, 66.4, 44.3, 11.4.

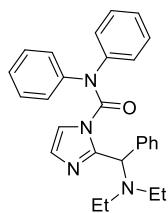
HRMS: Calc. C₁₄H₂₀N₃⁺ [M+H⁺] 230.1652; found 230.1662.



5008263-0134 ImU K2.7.1.1r
c13-night-4hr MeOD /wp500f emmertm 1



2-((diethylamino)(phenyl)methyl)-*N,N*-diphenyl-1*H*-imidazole-1-carboxamide



Chemical Formula: C₂₇H₂₈N₄O

Exact Mass: 424.23

Molecular Weight: 424.55

The title compound was prepared according to General Procedure 2 (reaction time 4 h).

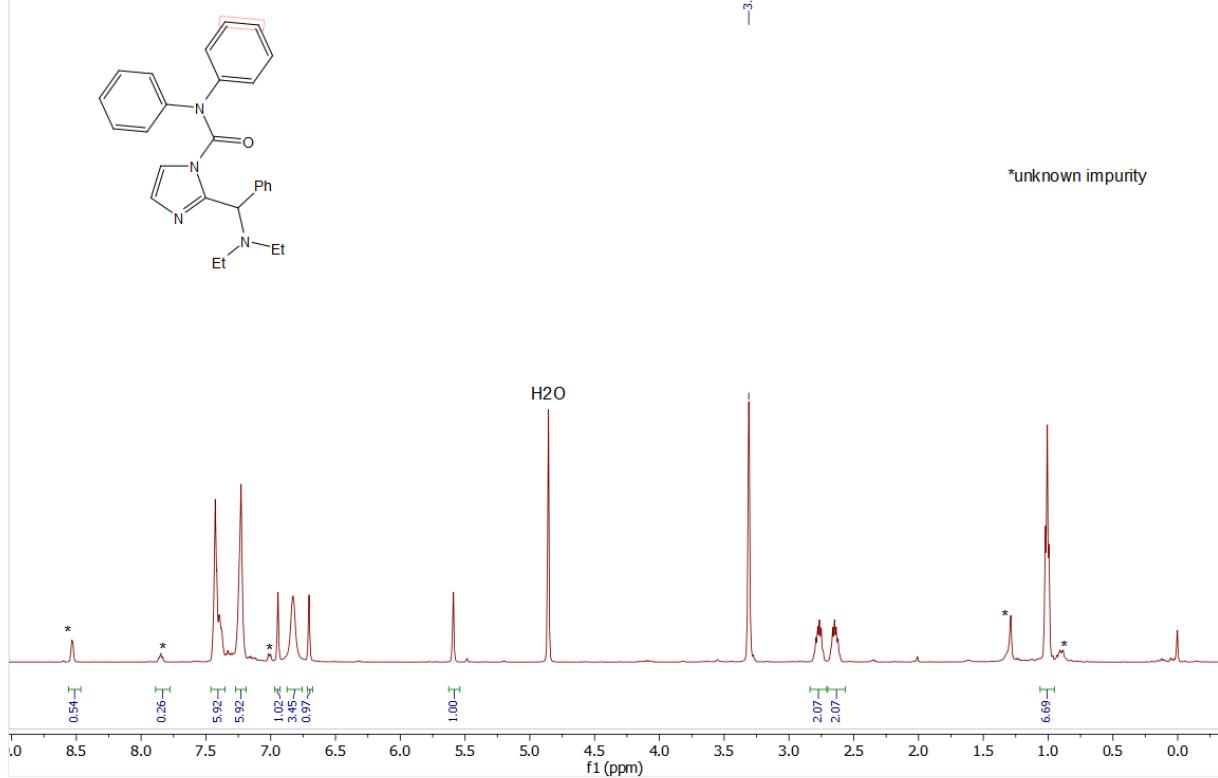
Yield: 14.7 mg (3%); 41 LCAP before workup/column chromatography

¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.45 – 7.35 (m, 6H), 7.23 (m, 6H), 6.94 (s, 1H), 6.83 (broad s, 3H), 6.70 (s, 1H), 5.59 (s, 1H), 2.77 (dq, *J* = 12.9, 6.4 Hz, 2H), 2.65 (dq, *J* = 13.3, 6.7 Hz, 2H), 1.01 (t, *J* = 6.8 Hz, 7H).

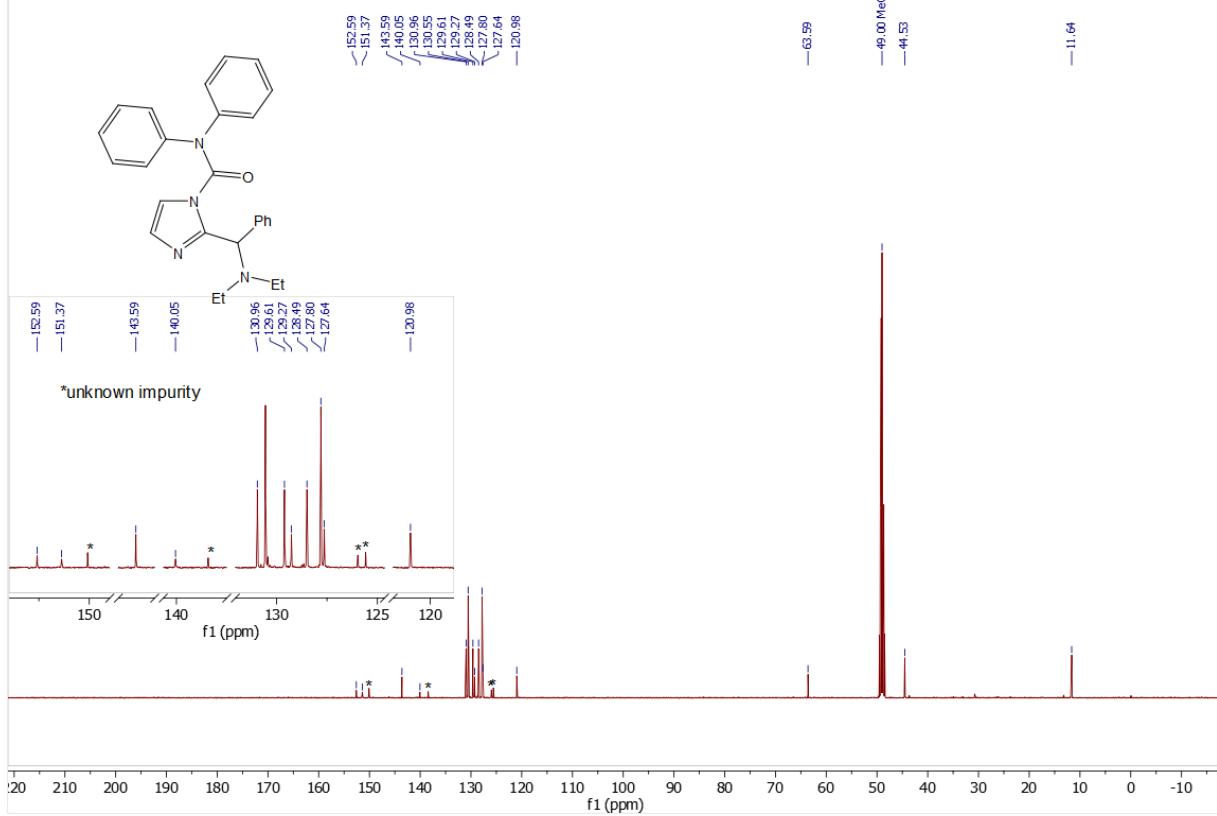
¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 152.5, 151.3, 143.5, 140.0, 130.9, 130.5, 129.6, 129.2, 128.4, 127.8, 127.6, 120.9, 63.5, 44.5, 11.6.

HRMS: Calc. C₂₇H₂₉N₄O⁺ [M+H⁺] 425.2336; found 425.2323.

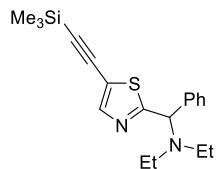
5008263-0134 ImU.1.1.1r
h1 MeOD /wp500f emmertm 1



5008263-0134 ImU.5.1.1r
c13-night-2hr MeOD /wp500f emmertm 1



N-ethyl-*N*-(phenyl(5-((trimethylsilyl)ethynyl)thiazol-2-yl)methyl)ethanamine



Chemical Formula: C₁₉H₂₆N₂SSi

Exact Mass: 342.16

Molecular Weight: 342.58

The title compound was prepared according to General Procedure 2 (reaction time 4 h).

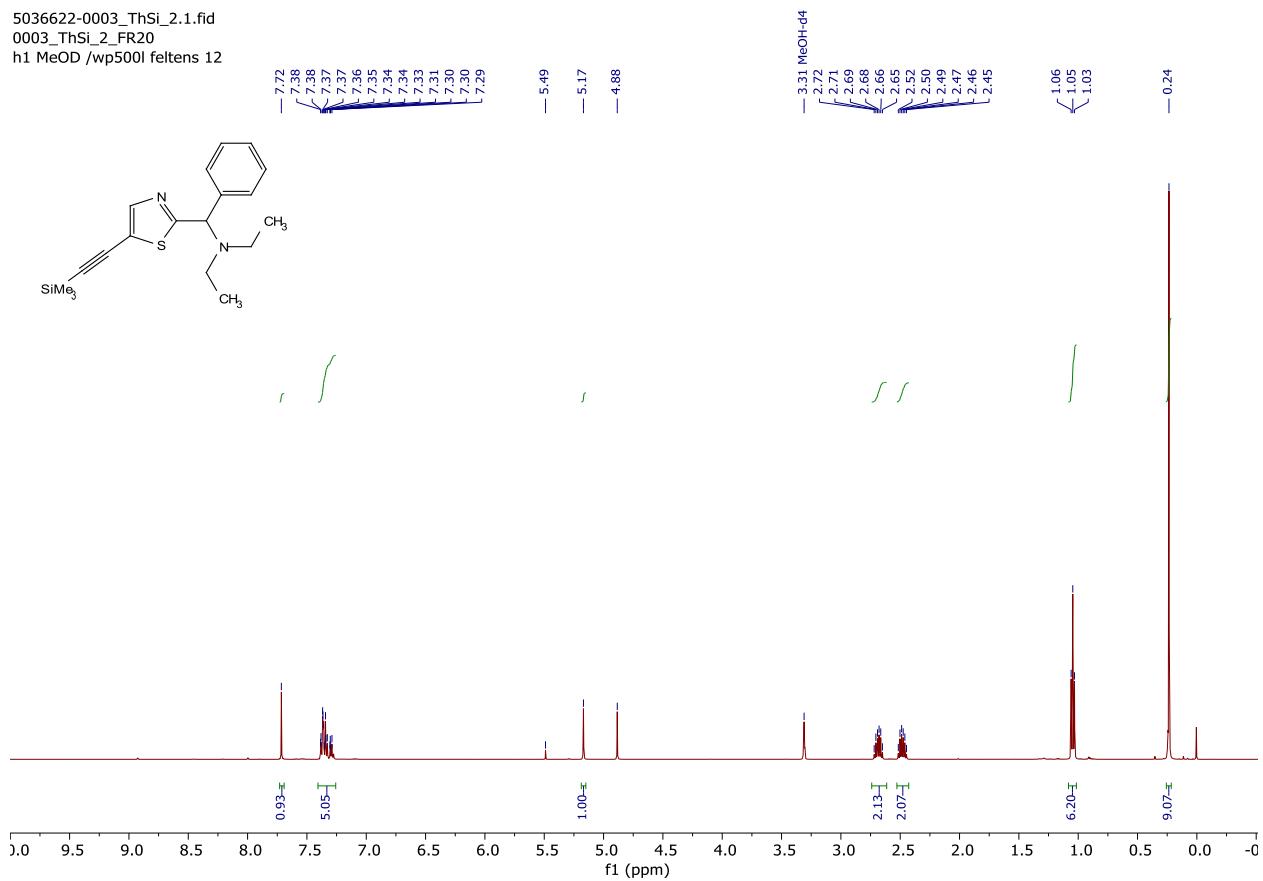
Yield: 170 mg (50%); 74 LCAP before workup/column chromatography

¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.71 (s, 1H), 7.43 – 7.21 (m, 5H), 5.16 (s, 1H), 2.67 (dq, *J* = 13.3, 6.7 Hz, 2H), 2.48 (dq, *J* = 13.1, 6.5 Hz, 2H), 1.04 (t, *J* = 6.8 Hz, 6H), 0.23 (s, 9H).

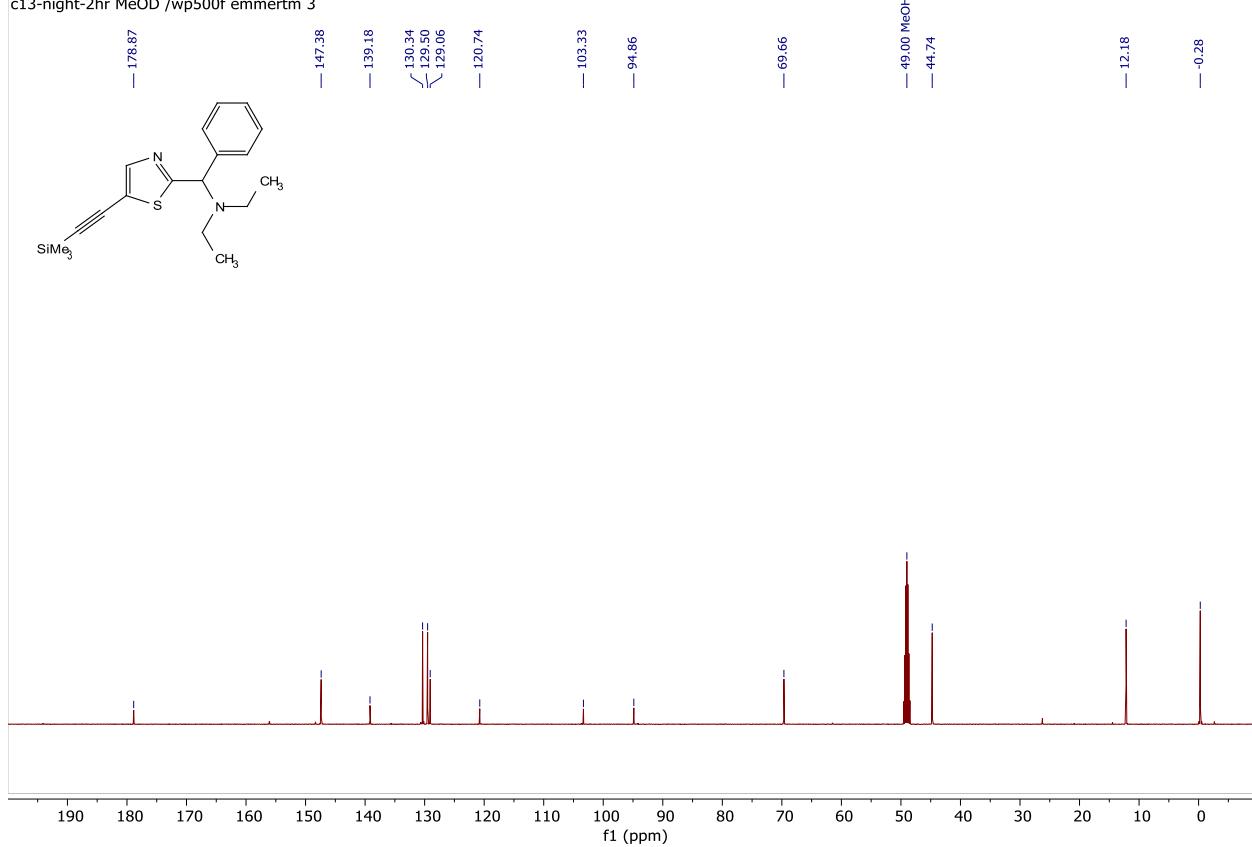
¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 178.8, 147.3, 139.1, 130.3, 129.5, 129.0, 120.7, 103.3, 94.8, 69.6, 44.7, 12.1, -0.2.

HRMS: Calc. C₁₉H₂₇N₂Si⁺ [M+H⁺] 343.1659; found 343.1664.

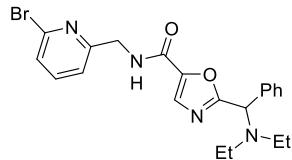
5036622-0003_ThSi_2.1.fid
0003_ThSi_2_FR20
h1 MeOD /wp500l feltens 12



5008263-0134 ThSi.2.1.1r
c13-night-2hr MeOD /wp500f emmertm 3



N-(6-bromopyridin-2-yl)methyl)-2-((diethylamino)(phenyl)methyl)oxazole-5-carboxamide



Chemical Formula: C₂₁H₂₃BrN₄O₂
Exact Mass: 442.10
Molecular Weight: 443.35

The title compound was prepared according to General Procedure 2 (reaction time 4 h).

Yield: 27.3 mg (6%); 29 LCAP before workup/column chromatography

The title compound was prepared according the modified general procedure 2, using 4.0 eq. TBSOTf and 2.0 eq. iPr₂NEt. The quench was performed with 8 eq. KF in pyridine.

Yield: 266 mg (60%); 50 LCAP before workup/column chromatography

¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.72 (s, 1H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 9.9 Hz, 3H), 7.32 (dt, *J* = 27.7, 6.5 Hz, 4H), 5.19 (s, 1H), 4.60 (s, 2H), 2.66 (dq, *J* = 13.4, 6.7 Hz, 2H), 2.55 (dq, *J* = 13.1, 6.5 Hz, 2H), 1.02 (t, *J* = 6.8 Hz, 6H).

¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 167.2, 160.5, 159.2, 146.7, 142.4, 140.9, 138.7, 131.3, 129.6, 129.6, 129.2, 127.9, 121.7, 65.3, 44.8, 12.0.

HRMS: Calc. C₂₁H₂₄BrN₄O₂⁺ [M+H⁺] 443.1077; found 443.1062.

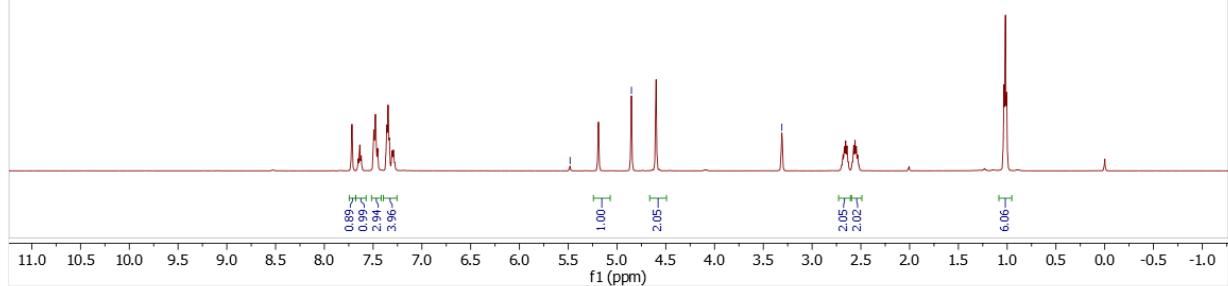
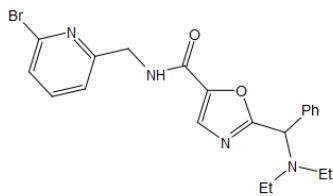
5008263-0141 Oxypr.1.1.1r
h1 MeOD /wp500f emmertm 4

DCM H₂O

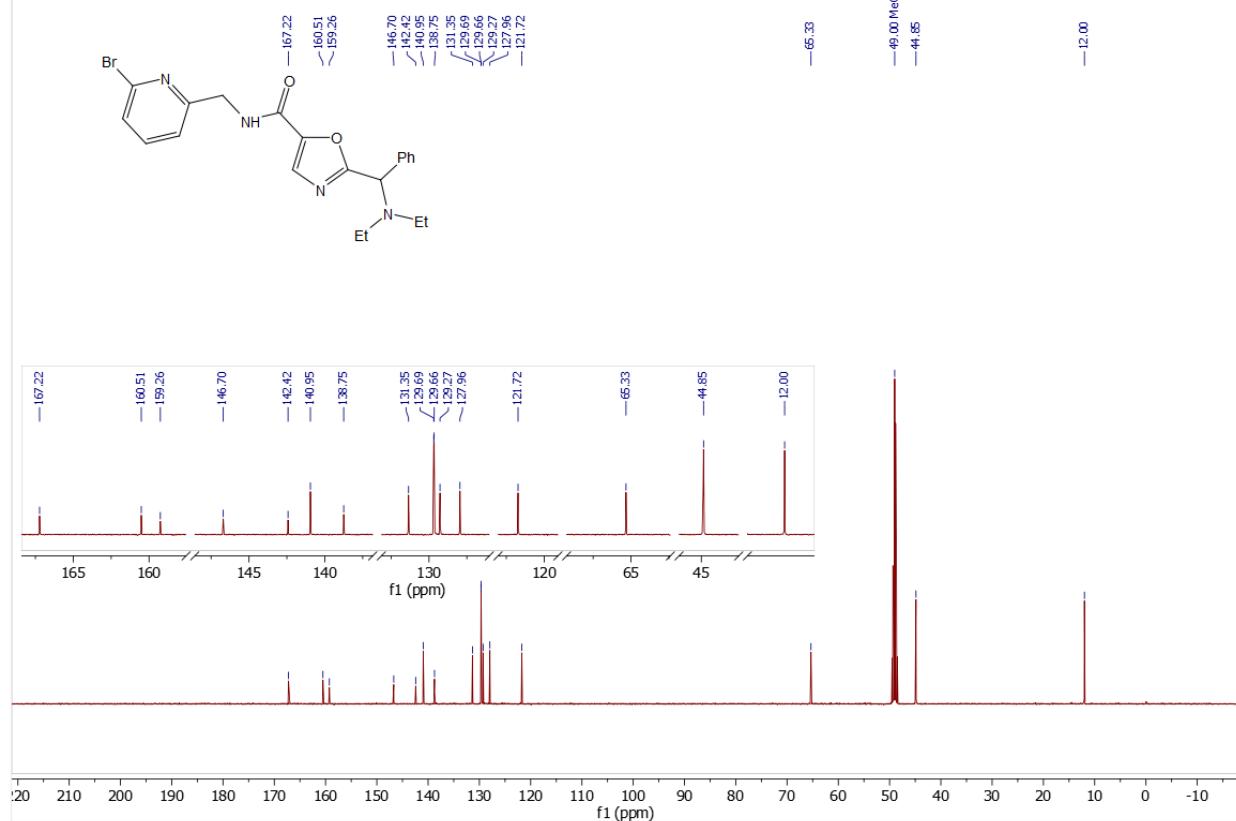
—5.48

—4.85

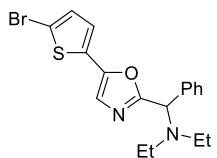
—3.31 MeOH-D4



5008263-0141 Oxpyp.2.1.1r
c13-day MeOD /wp500f emmertm 4



N-(5-(5-bromothiophen-2-yl)oxazol-2-yl)(phenyl)methyl)-*N*-ethylethanamine



Chemical Formula: C₁₈H₁₉BrN₂OS

Exact Mass: 390.04

Molecular Weight: 391.33

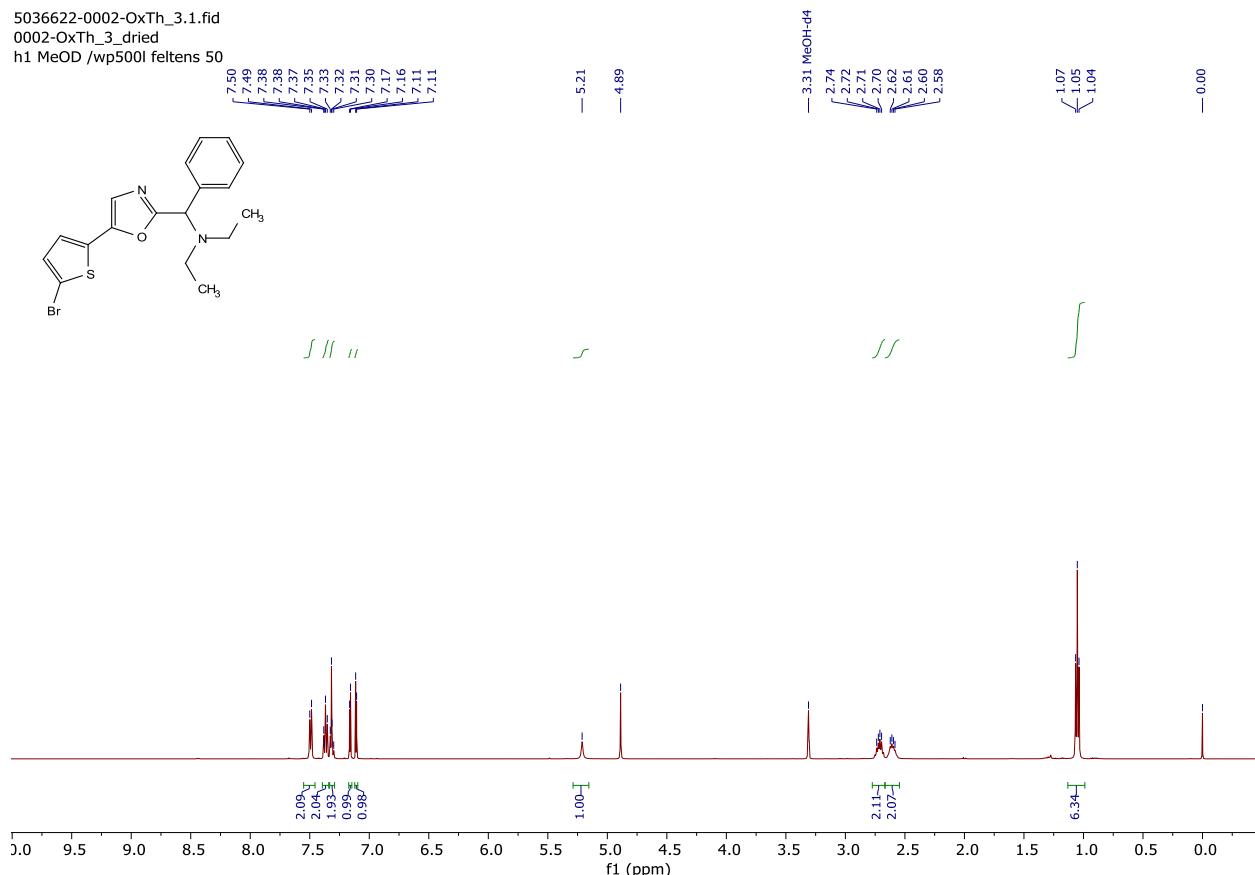
The title compound was prepared according to General Procedure 2 (reaction time 4 h).

Yield: 265.5 mg (68%); 75 LCAP before workup/column chromatography

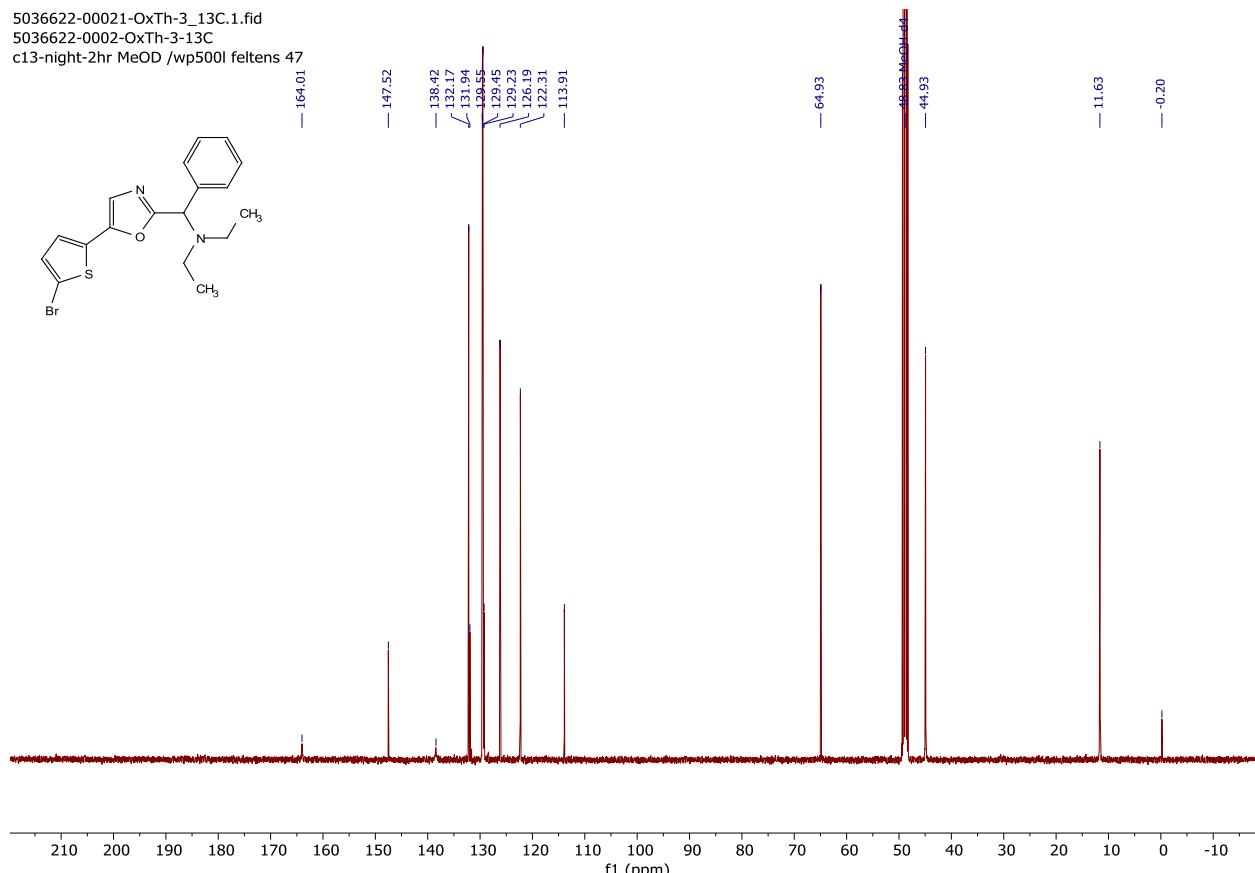
¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.47 (d, *J* = 7.6 Hz, 2H), 7.35 (t, *J* = 7.2 Hz, 2H), 7.29 (m, 2H), 7.15 (d, *J* = 3.5 Hz, 1H), 7.11 (d, *J* = 3.6 Hz, 1H), 5.14 (s, 1H), 2.67 (dq, *J* = 14.0, 7.0 Hz, 2H), 2.54 (dq, *J* = 13.6, 6.8 Hz, 2H), 1.02 (t, *J* = 7.0 Hz, 6H).

¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 164.0, 147.5, 138.4, 132.1, 131.9, 129.5, 129.4, 129.2, 126.1, 122.3, 113.9, 64.9, 44.9, 11.6.

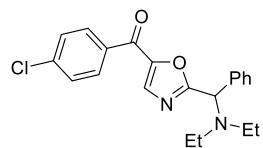
HRMS: Calc. C₁₈H₂₀BrN₂OS⁺ [M+H⁺] 391.0474; found 391.0462.



5036622-00021-OxTh-3_13C.1.fid
5036622-0002-OxTh-3-13C
c13-night-2hr MeOD /wp500l feltens 47



(4-chlorophenyl)(2-((diethylamino)(phenyl)methyl)oxazol-5-yl)methanone



Chemical Formula: C₂₁H₂₁ClN₂O₂
Exact Mass: 368.13
Molecular Weight: 368.86

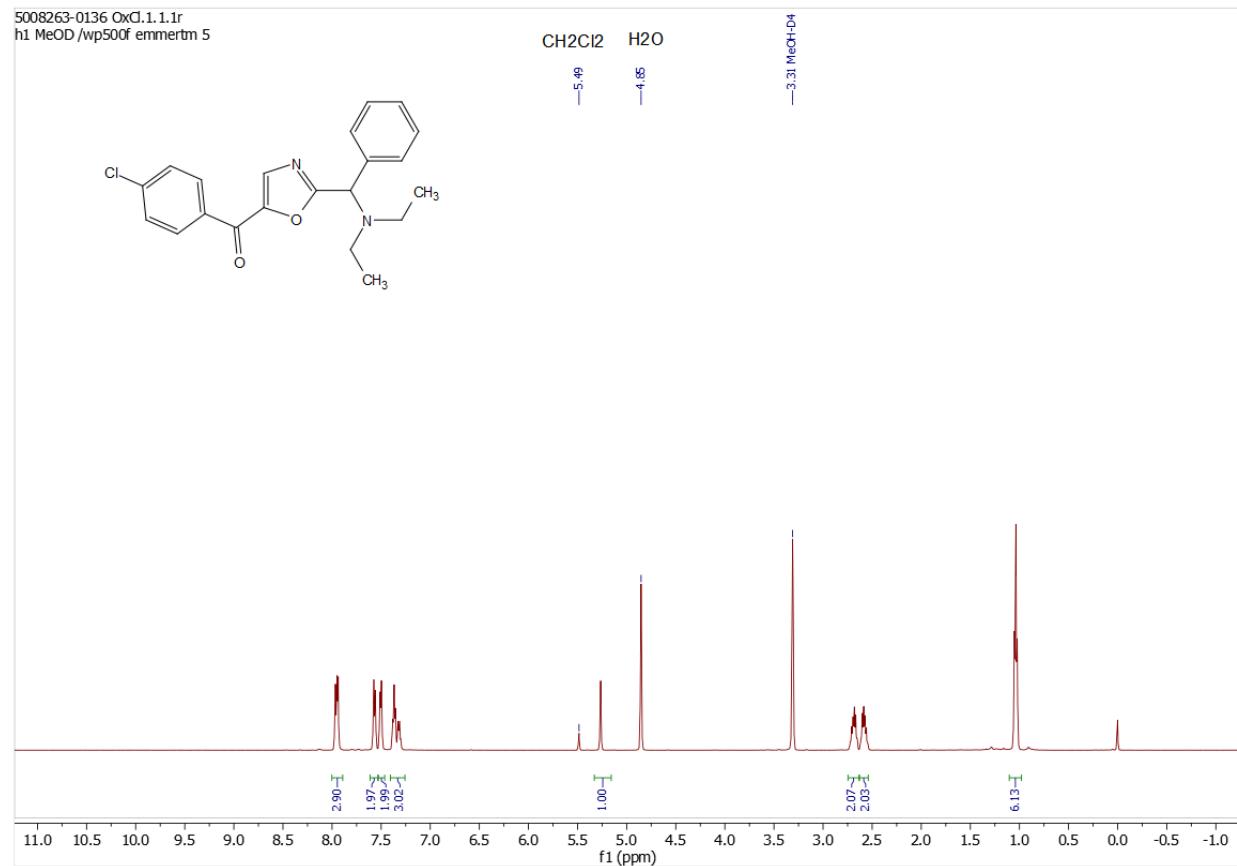
The title compound was prepared according to General Procedure 2 (reaction time 4 h).

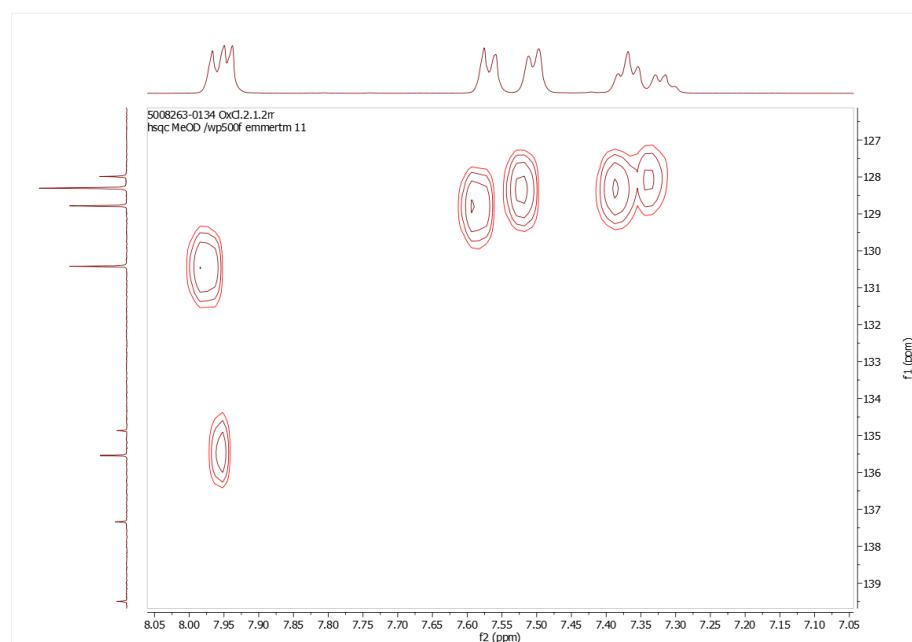
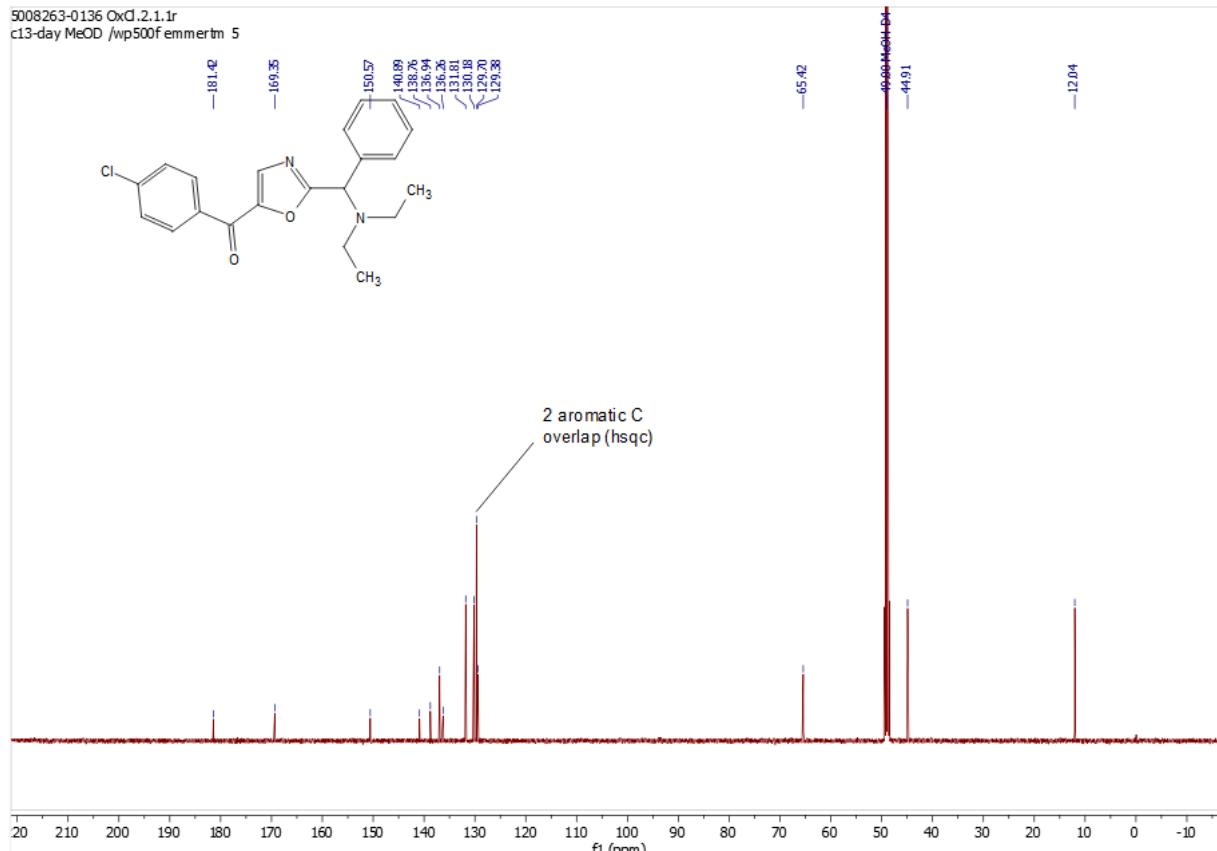
Yield: 81.0 mg (22%); 28 LCAP before workup/column chromatography

¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 8.01 – 7.88 (m, 3H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.51 (d, *J* = 7.4 Hz, 2H), 7.34 (m, 3H), 5.27 (s, 1H), 2.69 (dq, *J* = 13.9, 7.0 Hz, 2H), 2.58 (dq, *J* = 13.5, 6.7 Hz, 2H), 1.04 (t, *J* = 6.9 Hz, 6H).

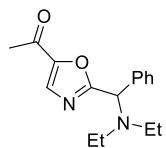
¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 181.4, 169.3, 150.5, 140.8, 138.7, 136.9, 136.2, 131.8, 130.1, 129.7, 129.7, 129.3, 65.4, 44.9, 12.0.

HRMS: Calc. C₂₁H₂₂ClN₂O₂⁺ [M+H⁺] 369.1365; found 369.1358.





1-(2-((diethylamino)(phenyl)methyl)oxazol-5-yl)ethan-1-one



Chemical Formula: C₁₆H₂₀N₂O₂

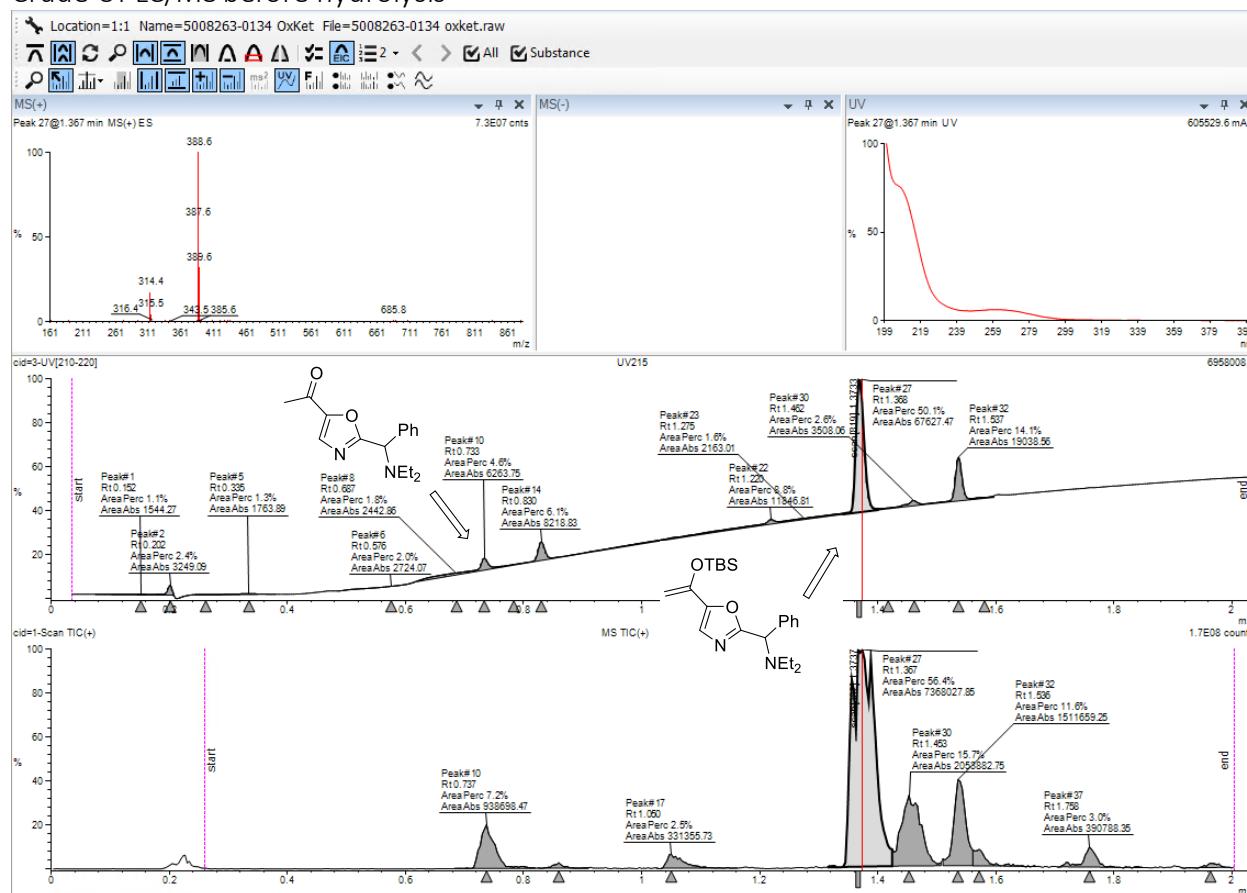
Exact Mass: 272.15

Molecular Weight: 272.35

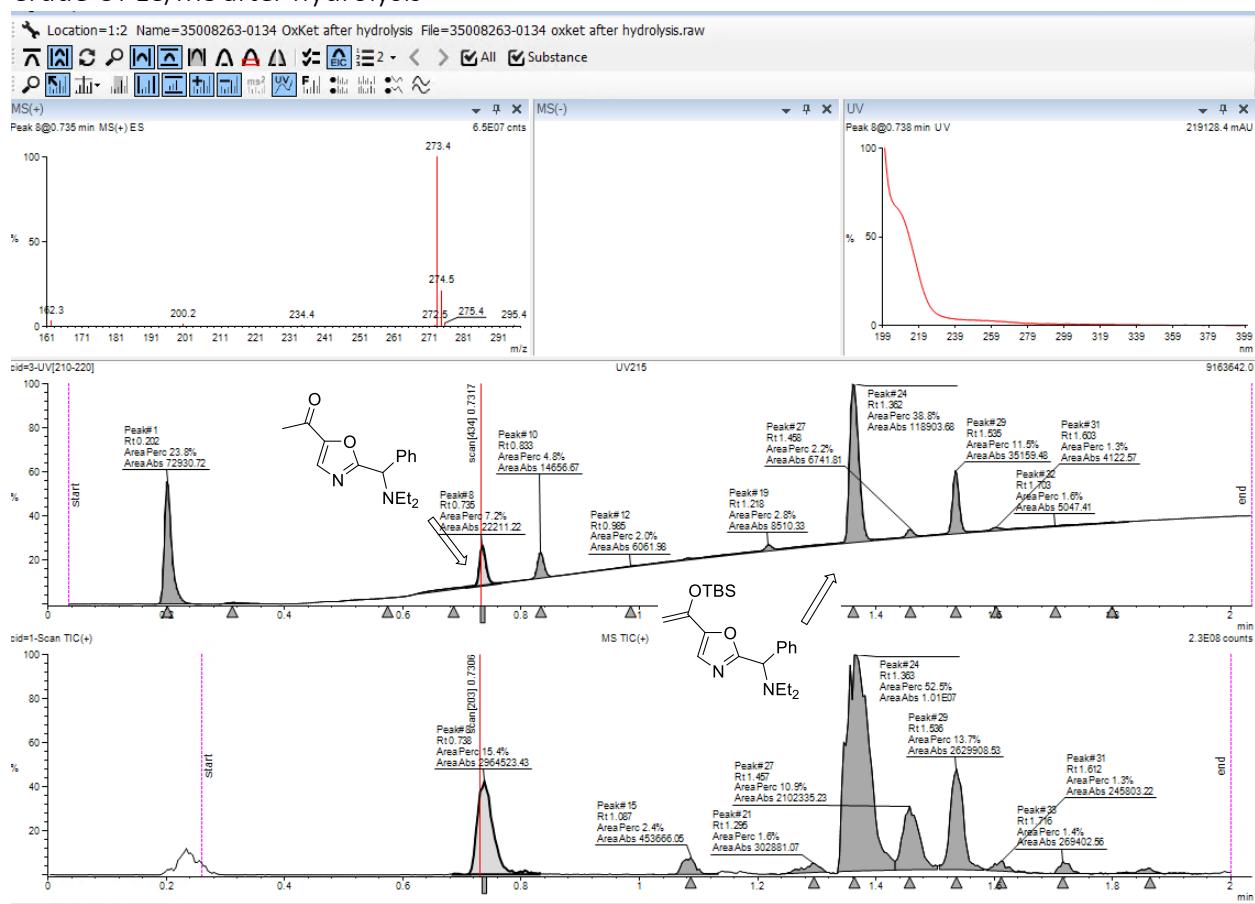
Synthesis according to General Procedure 2

The title compound was prepared according to General Procedure 2 (reaction time 4 h). After the reaction, UPLC analysis (see below) revealed the presence of a TBS-adduct ([M+H]⁺ m/z 388, UPLC retention time 1.37 min). 1.0 mL pyridine and 500 μ L H₂O. Subsequent column chromatography of the mixture on silica only achieved isolation of the TBS adduct with impurities (1H NMR data suggest that the impurity is the TBS-adduct of the starting material, m/z 227, UPLC retention time 1.53 min); the title compound (hydrolysis product, m/z 273, UPLC retention time 0.73 min) was isolated in pure form.

Crude UPLC/MS before hydrolysis



Crude UPLC/MS after hydrolysis



Title compound: 1-(2-((diethylamino)(phenyl)methyl)oxazol-5-yl)ethan-1-one

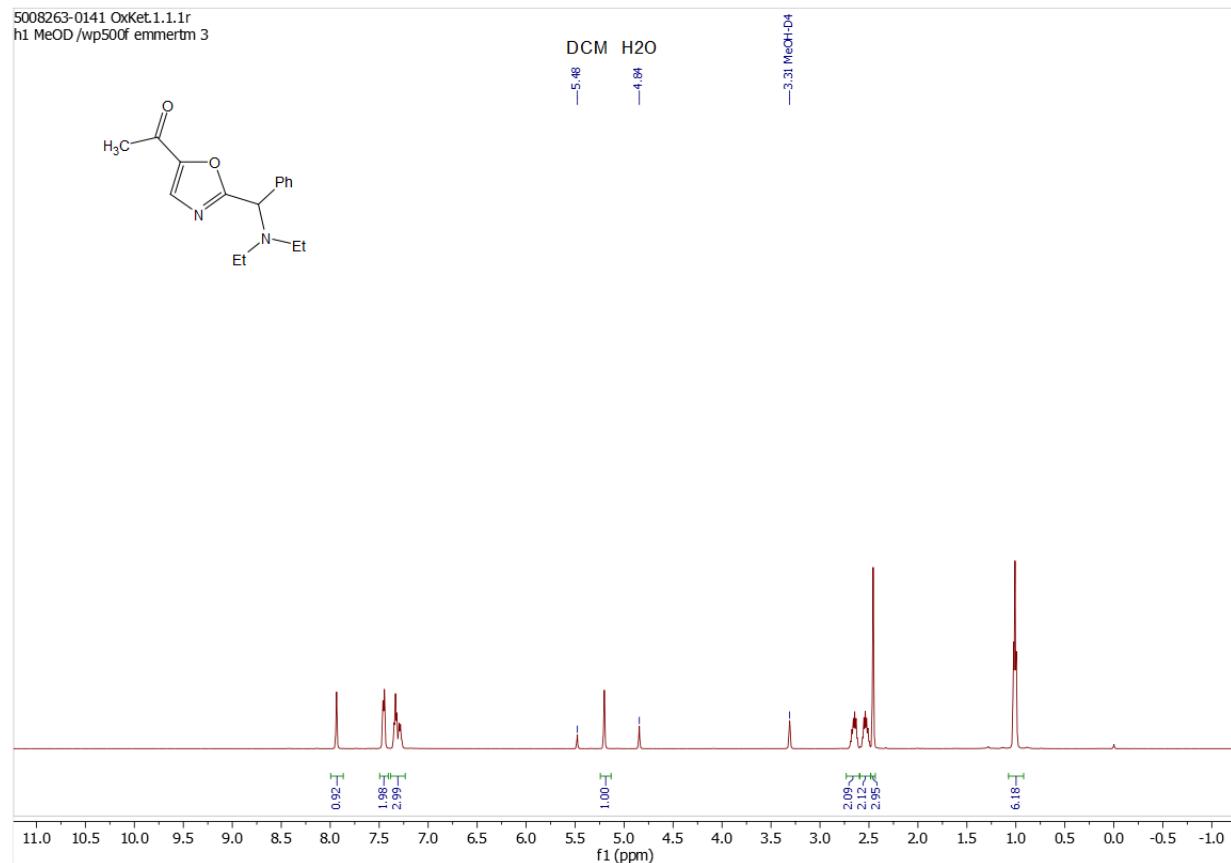
Synthesis according to General Procedure 2: Yield: 80 mg (29%); 5 LCAP before hydrolysis, 7 LCAP after hydrolysis (before column chromatography)

Synthesis according to General Procedure 2 with modifications for substrates with acidic NH or CH bonds:
Yield: 224.3 mg (82%); 39 LCAP before workup (43 LCAP silylated side product), 55 LCAP after workup
(before column chromatography; no silylated side product was detected)

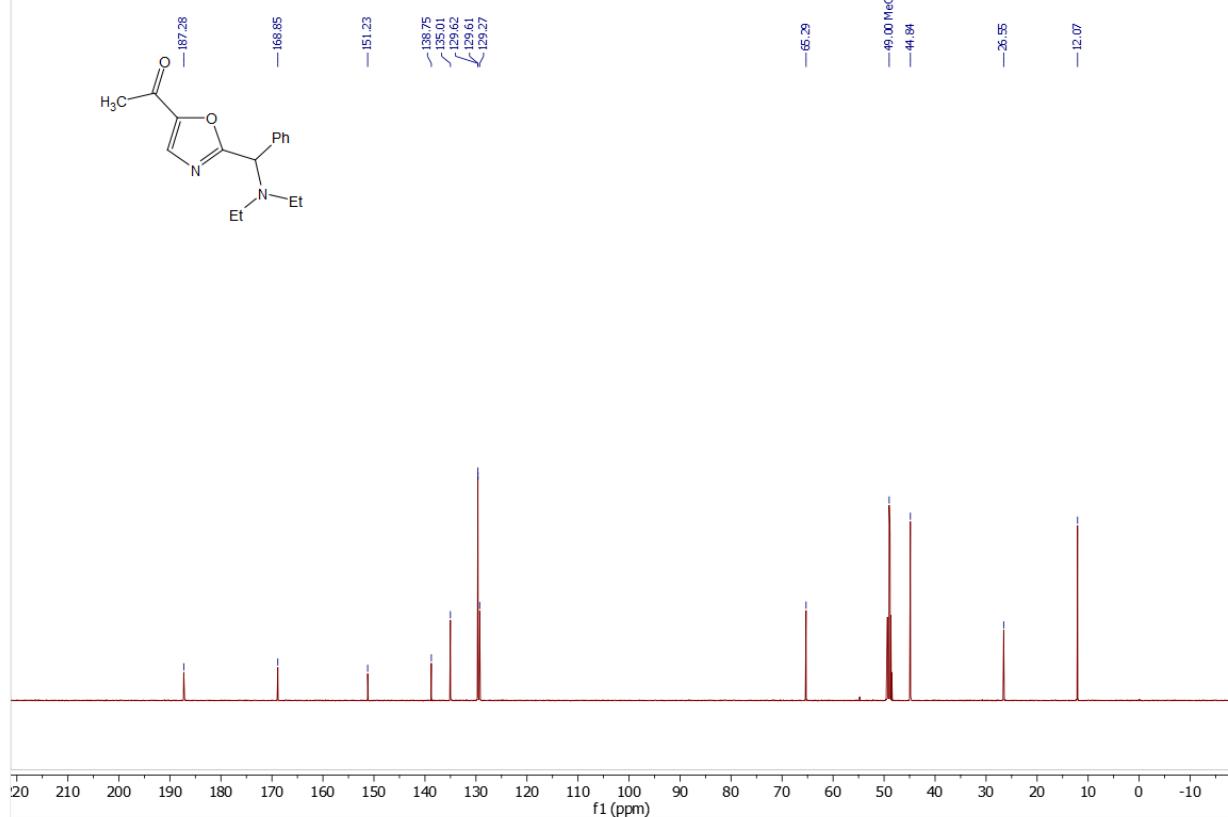
¹H NMR (500 MHz, Methanol-d₄, ppm) δ 7.94 (s, 1H), 7.46 (m, 2H), 7.32 (m, 3H), 5.21 (s, 1H), 2.66 (dq, *J* = 14.0, 6.9 Hz, 2H), 2.54 (dq, *J* = 13.6, 6.9 Hz, 2H), 2.47 (s, 3H), 1.02 (t, *J* = 6.9 Hz, 6H).

¹³C NMR (126 MHz, Methanol-d₄, ppm) δ 187.2, 168.8, 151.2, 138.7, 135.0, 129.6, 129.6, 129.2, 65.2, 44.8, 26.5, 12.0.

HRMS: Calc. C₁₆H₂₁N₂O₂⁺ [M+H⁺] 273.1598; found 273.1606.



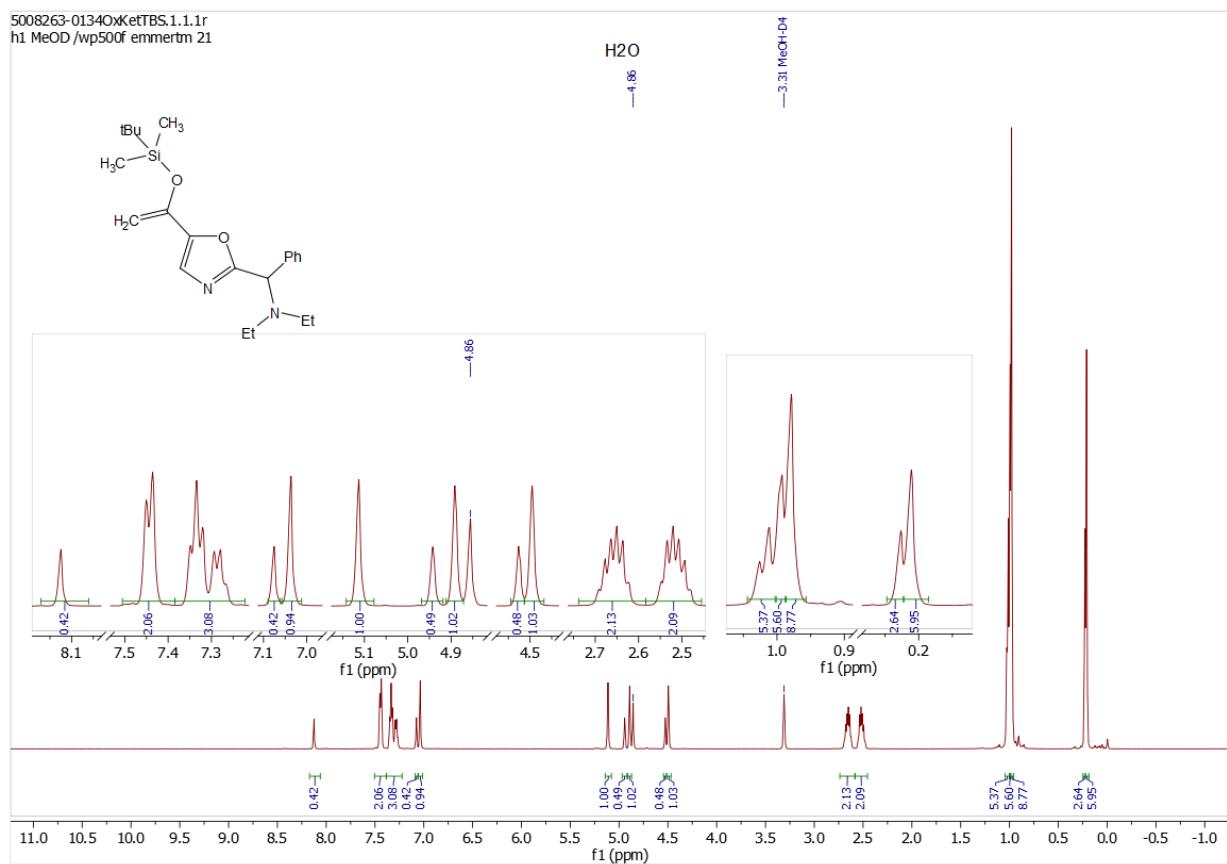
5008263-0141 OxKet2.1.1r
c13-day MeOD /wp500f emmertm 3



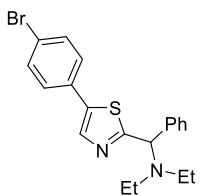
Silyl enol ether of 1-(2-((diethylamino)(phenyl)methyl)oxazol-5-yl)ethan-1-one

Yield: 80 mg (29%); 50 LCAP before hydrolysis, 39 LCAP after hydrolysis (before column chromatography)

^1H NMR (500 MHz, Methanol- d_4 , ppm) δ 7.44 (d, J = 7.3 Hz, 2H), 7.31 (dt, J = 26.8, 6.7 Hz, 3H), 7.04 (s, 1H), 5.11 (s, 1H), 4.89 (s, 1H), 4.50 (s, 1H), 2.66 (dq, J = 13.8, 6.9 Hz, 2H), 2.51 (dq, J = 13.3, 6.6 Hz, 2H), 1.02 (t, J = 6.9 Hz, 6H), 0.98 (s, 9H), 0.21 (s, 6H).



N-((5-(4-bromophenyl)thiazol-2-yl)(phenyl)methyl)-*N*-ethylethanamine



Chemical Formula: C₂₀H₂₁BrN₂S

Exact Mass: 400.06

Molecular Weight: 401.37

The title compound was prepared according to General Procedure 2 (reaction time 4 h).

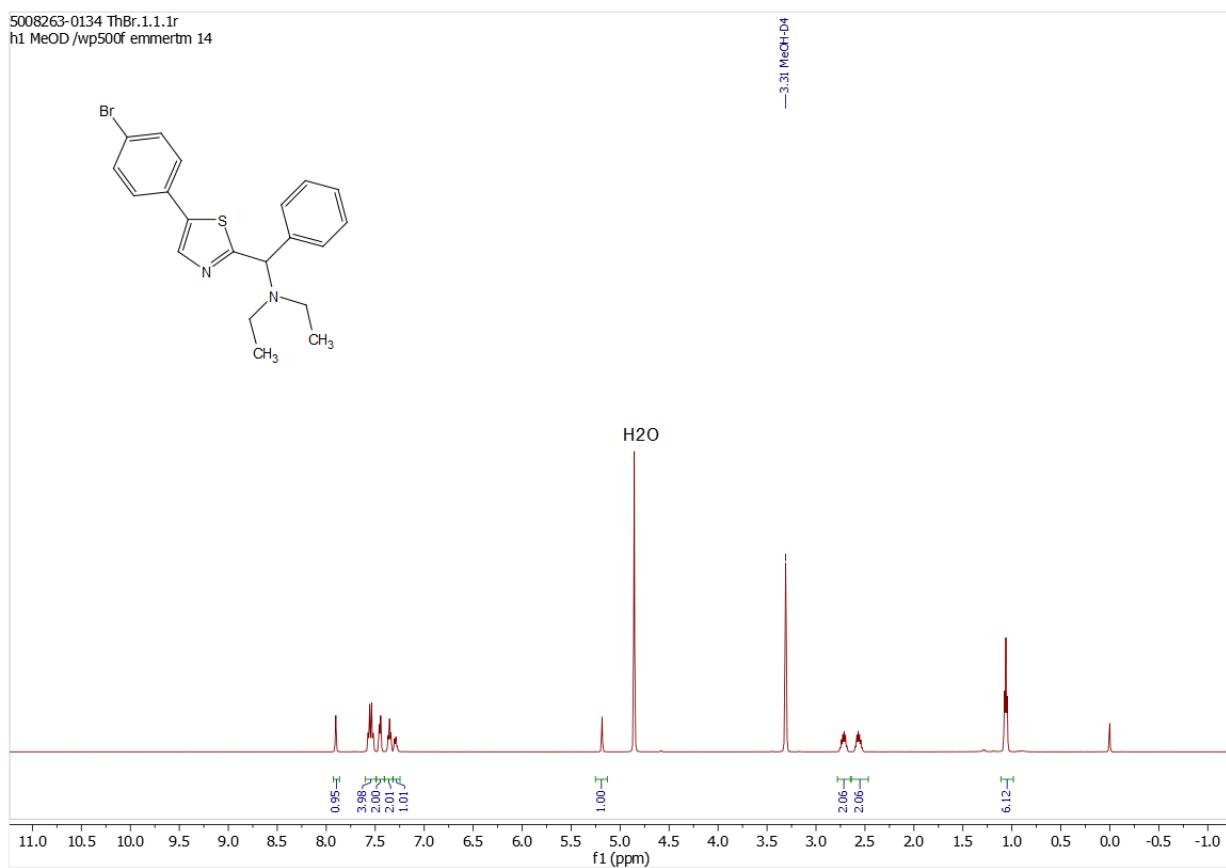
Yield: 229 mg (57%); 79 LCAP before workup/column chromatography

¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.90 (s, 1H), 7.55 (m, 4H), 7.45 (d, *J* = 7.5 Hz, 2H), 7.35 (t, *J* = 7.2 Hz, 2H), 7.29 (t, *J* = 7.1 Hz, 1H), 5.18 (s, 1H), 2.72 (dq, *J* = 13.6, 6.8 Hz, 2H), 2.56 (dq, *J* = 13.6, 6.8 Hz, 2H), 1.06 (t, *J* = 6.9 Hz, 6H).

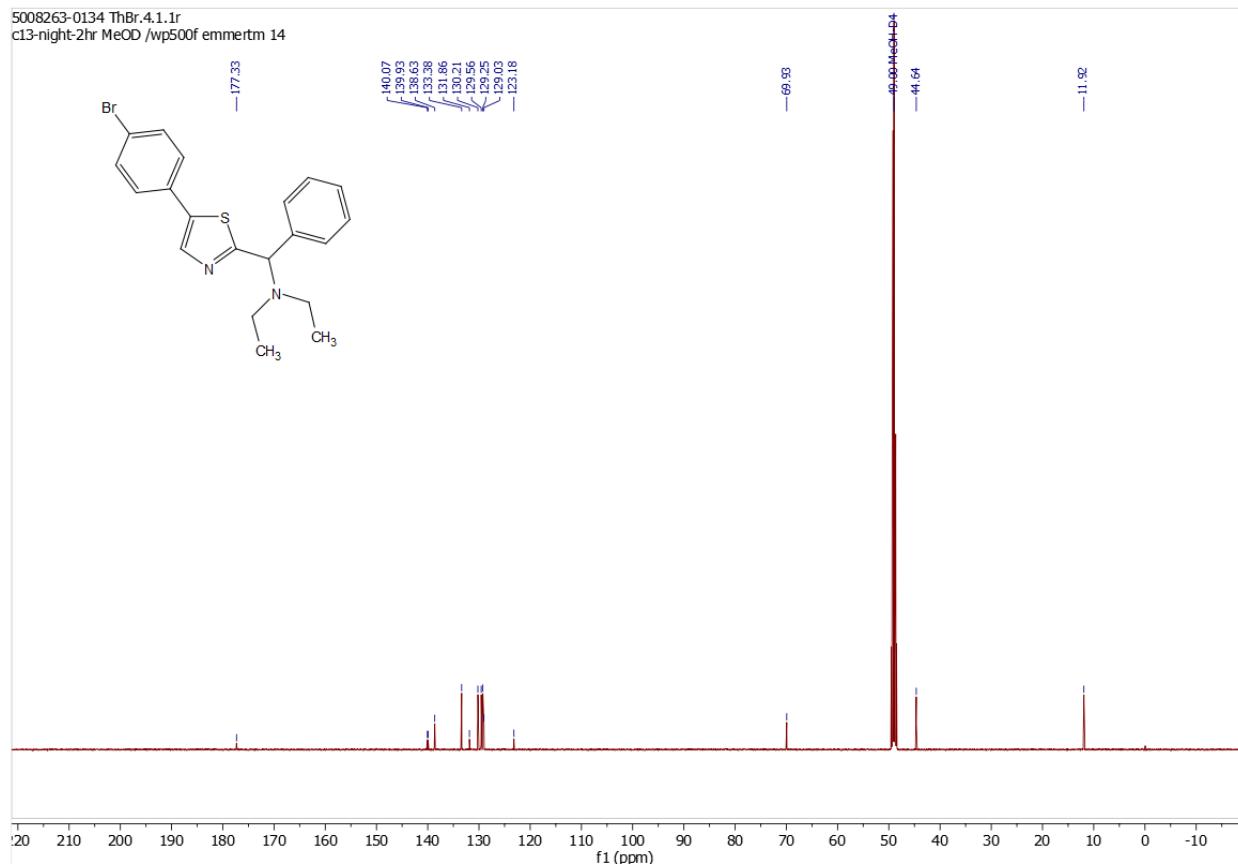
¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 177.3, 140.0, 139.9, 138.6, 133.3, 131.8, 130.2, 129.5, 129.2, 129.0, 123.1, 69.9, 44.6, 11.9.

HRMS: Calc. C₂₀H₂₂BrN₂S⁺ [M+H⁺] 401.0682; found 401.0689.

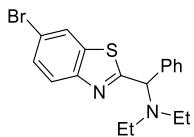
5008263-0134 ThBr.1.1.1r
h1 MeOD /wp500f emnerntm 14



5008263-0134 ThBr.4.1.1r
c13-night-2hr MeOD /wp500f emmer tm 14



N-(6-Bromobenzo[d]thiazol-2-yl)(phenyl)methyl)-*N*-ethylethanamine



Chemical Formula: C₁₈H₁₉BrN₂S

Exact Mass: 374.05

Molecular Weight: 375.33

The title compound was prepared according to General Procedure 2 (reaction time 4 h).

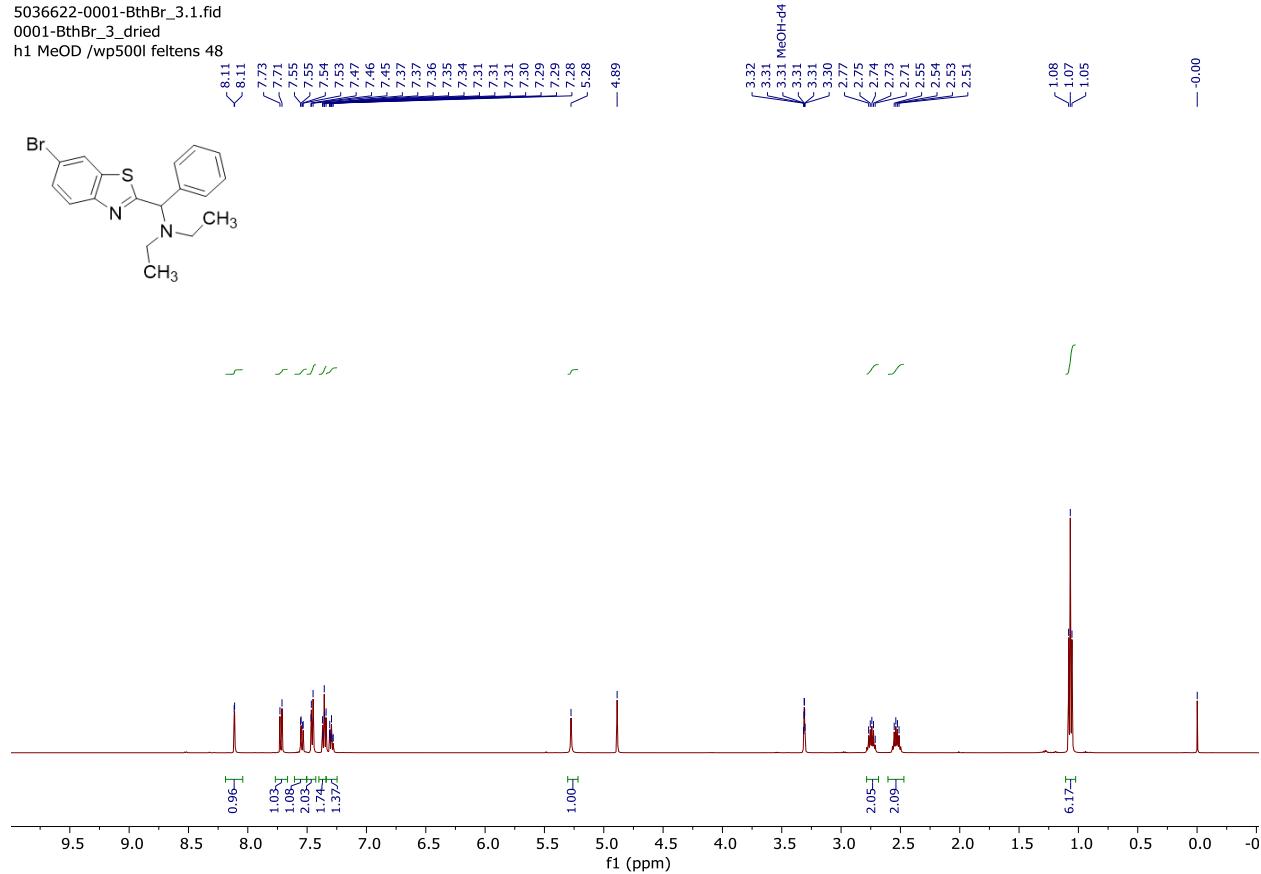
Yield: 272 mg (73%); 71 LCAP before workup/column chromatography

¹H NMR (500 MHz, Methanol-d₄, ppm) δ 8.10 (s, 1H), 7.71 (d, *J* = 8.6 Hz, 1H), 7.53 (d, *J* = 8.6 Hz, 1H), 7.45 (d, *J* = 7.4 Hz, 2H), 7.35 (t, *J* = 7.1 Hz, 2H), 7.29 (t, *J* = 6.7 Hz, 1H), 5.26 (s, 1H), 2.74 (dq, *J* = 13.7, 6.9 Hz, 2H), 2.53 (dq, *J* = 13.3, 6.6 Hz, 2H), 1.06 (t, *J* = 6.9 Hz, 6H).

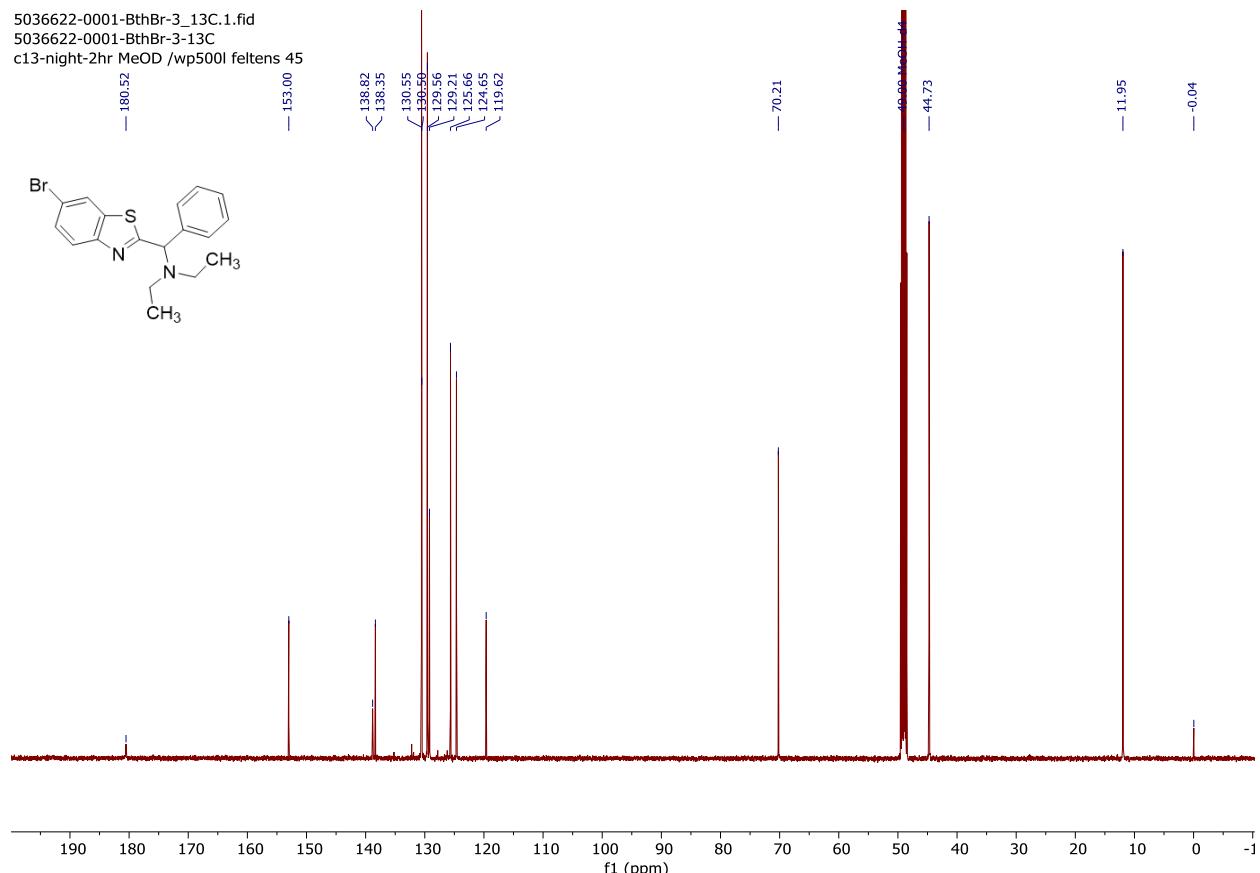
¹³C NMR (126 MHz, Methanol-d₄, ppm) δ 180.5, 153.0, 138.8, 138.3, 130.5, 130.4, 129.5, 129.1, 125.6, 124.6, 119.6, 70.2, 44.7, 11.9.

HRMS: Calc. C₁₈H₂₀BrN₂S⁺ [M+H⁺] 375.0525; found 375.0513.

5036622-0001-BthBr_3.1.fid
0001-BthBr_3_dried
h1 MeOD /wp5001 feltens 48



5036622-0001-BthBr-3_13C.1.fid
5036622-0001-BthBr-3-13C
c13-night-2hr MeOD /wp500l feltens 45



N-(benzo[d]thiazol-2-yl(phenyl)methyl)-*N*-ethylethanamine



Chemical Formula: C₁₈H₂₀N₂S

Exact Mass: 296.13

Molecular Weight: 296.43

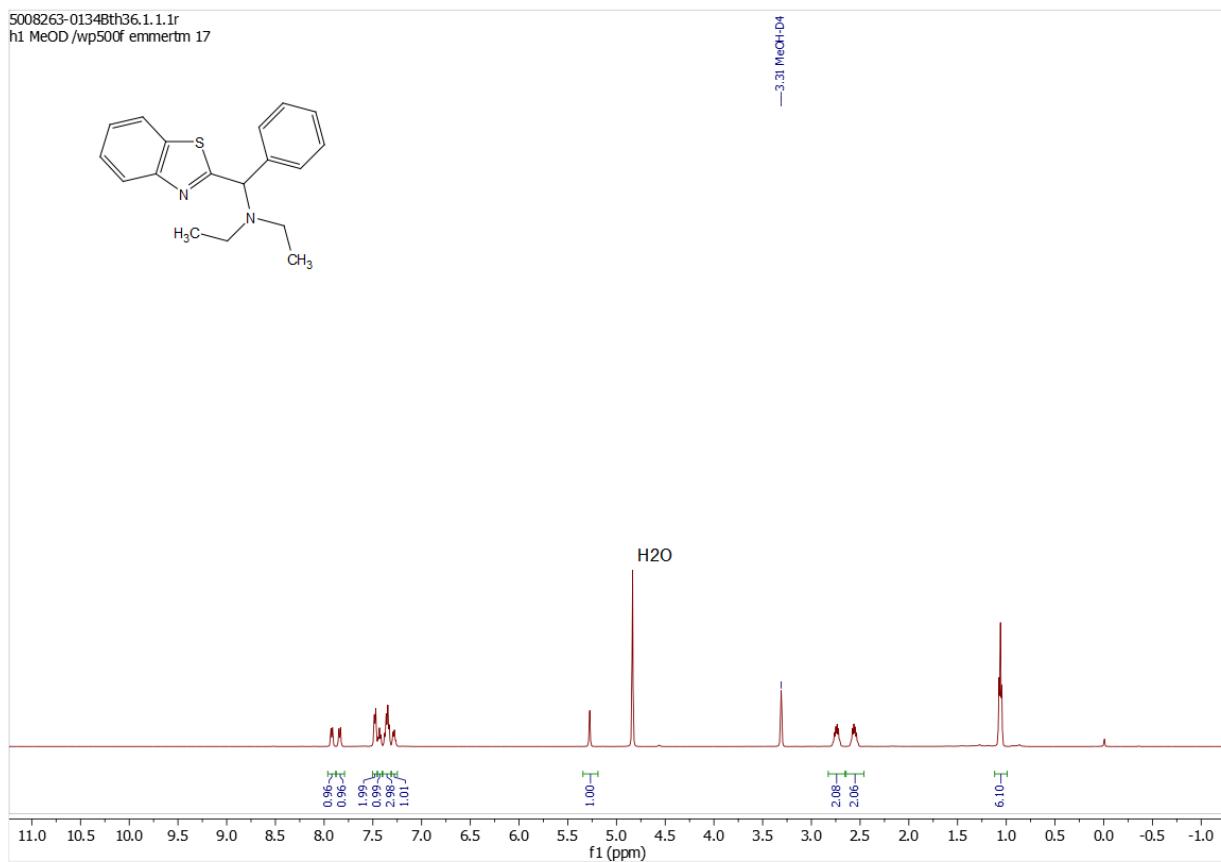
The title compound was prepared according to General Procedure 2 (reaction time 4 h).

Yield: 275 mg (93%); 81 LCAP before workup/column chromatography

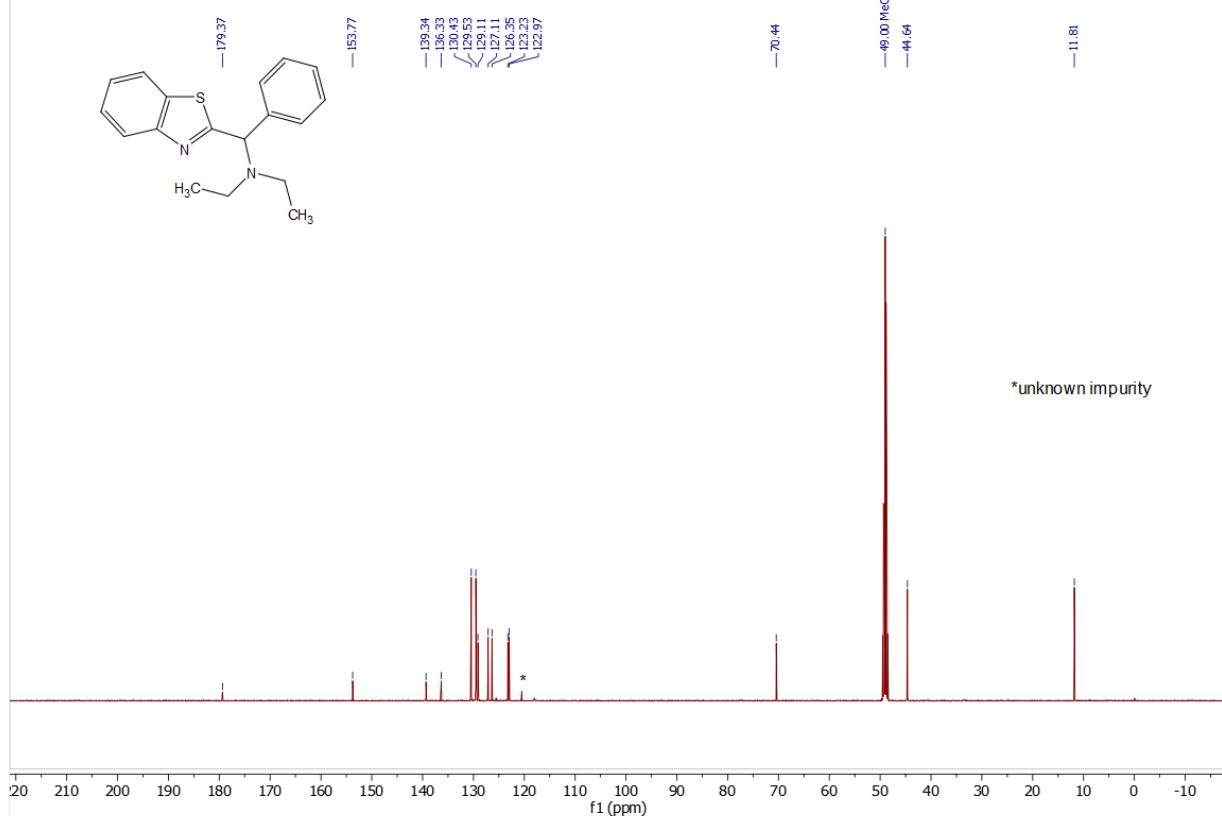
¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.92 (d, *J* = 7.9 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 7.4 Hz, 2H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.35 (q, *J* = 7.7 Hz, 3H), 7.28 (t, *J* = 6.9 Hz, 1H), 5.27 (s, 1H), 2.74 (dq, *J* = 13.6, 6.8 Hz, 2H), 2.56 (dq, *J* = 13.3, 6.6 Hz, 2H), 1.06 (t, *J* = 6.9 Hz, 6H).

¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 179.3, 153.7, 139.3, 136.3, 130.4, 129.5, 129.1, 127.1, 126.3, 123.2, 122.9, 70.4, 44.6, 11.8.

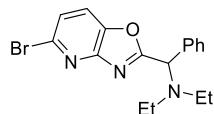
HRMS: Calc. C₁₈H₂₁N₂S⁺ [M+H⁺] 297.1420; found 297.1411.



5008263-0134Bth36.4.1.1r
c13-night-2hr MeOD /wp500f emmertm 17



N-(5-Bromooxazolo[4,5-*b*]pyridin-2-yl)(phenyl)methyl)-*N*-ethylethanamine



Chemical Formula: C₁₇H₁₈BrN₃O

Exact Mass: 359.06

Molecular Weight: 360.26

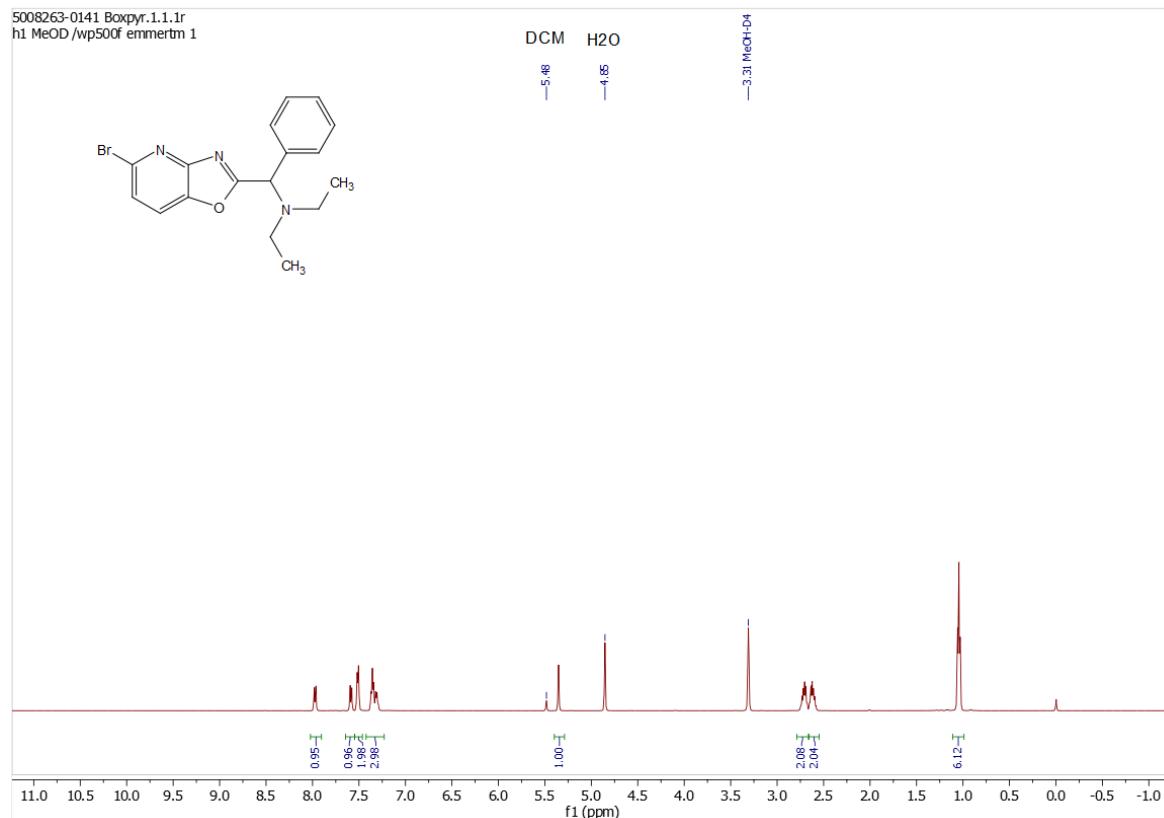
The title compound was prepared according to General Procedure 2 (reaction time 3 h) using 4 equiv. TBSOTf instead of 3 equiv. TBSOTf and 2 equiv. *i*Pr₂NEt instead of 1 equiv. *i*Pr₂NEt. Workup was performed in analogy to the modified procedure for compounds with acidic CH or NH bonds, using 4 equiv. KF/pyridine as a quenching reagent.

Yield: 192 mg (76%); 76 LCAP before workup/column chromatography

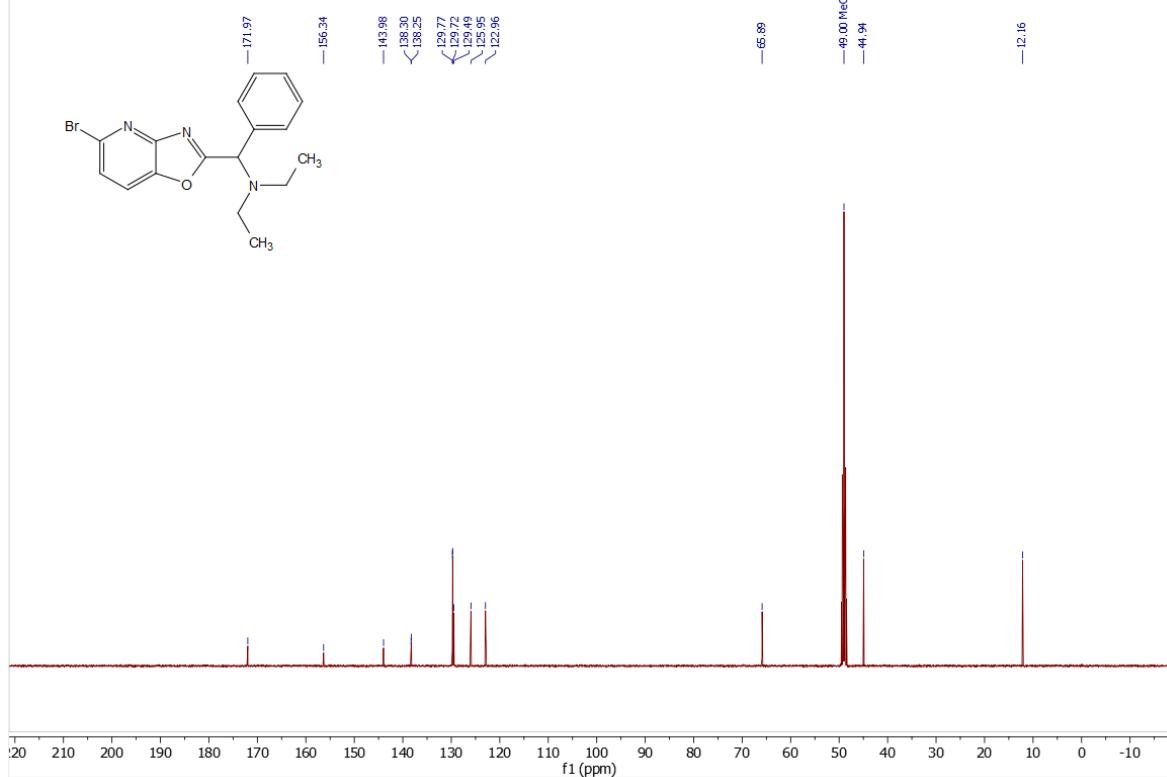
¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.97 (d, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 8.5 Hz, 1H), 7.51 (d, *J* = 7.3 Hz, 2H), 7.33 (m, 3H), 5.35 (s, 1H), 2.71 (dq, *J* = 13.6, 6.9 Hz, 2H), 2.62 (dq, *J* = 13.2, 6.6 Hz, 2H), 1.04 (t, *J* = 6.8 Hz, 6H).

¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 171.9, 156.3, 143.9, 138.3, 138.2, 129.7, 129.7, 129.4, 125.9, 122.9, 65.8, 44.9, 12.1.

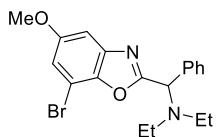
HRMS: Calc. C₁₇H₁₉BrN₃O⁺ [M+H⁺] 360.0706; found 360.0705.



5008263-0141 Boxpyr.2.1.1.r
c13-day MeOD /wp500f emmertm 1



N-(7-Bromo-5-methoxybenzo[d]oxazol-2-yl)(phenyl)methyl)-*N*-ethyletha namine



Chemical Formula: C₁₉H₂₁BrN₂O₂

Exact Mass: 388.0786

Molecular Weight: 389.2930

The title compound was prepared according to General Procedure 2 (reaction time 3 h).

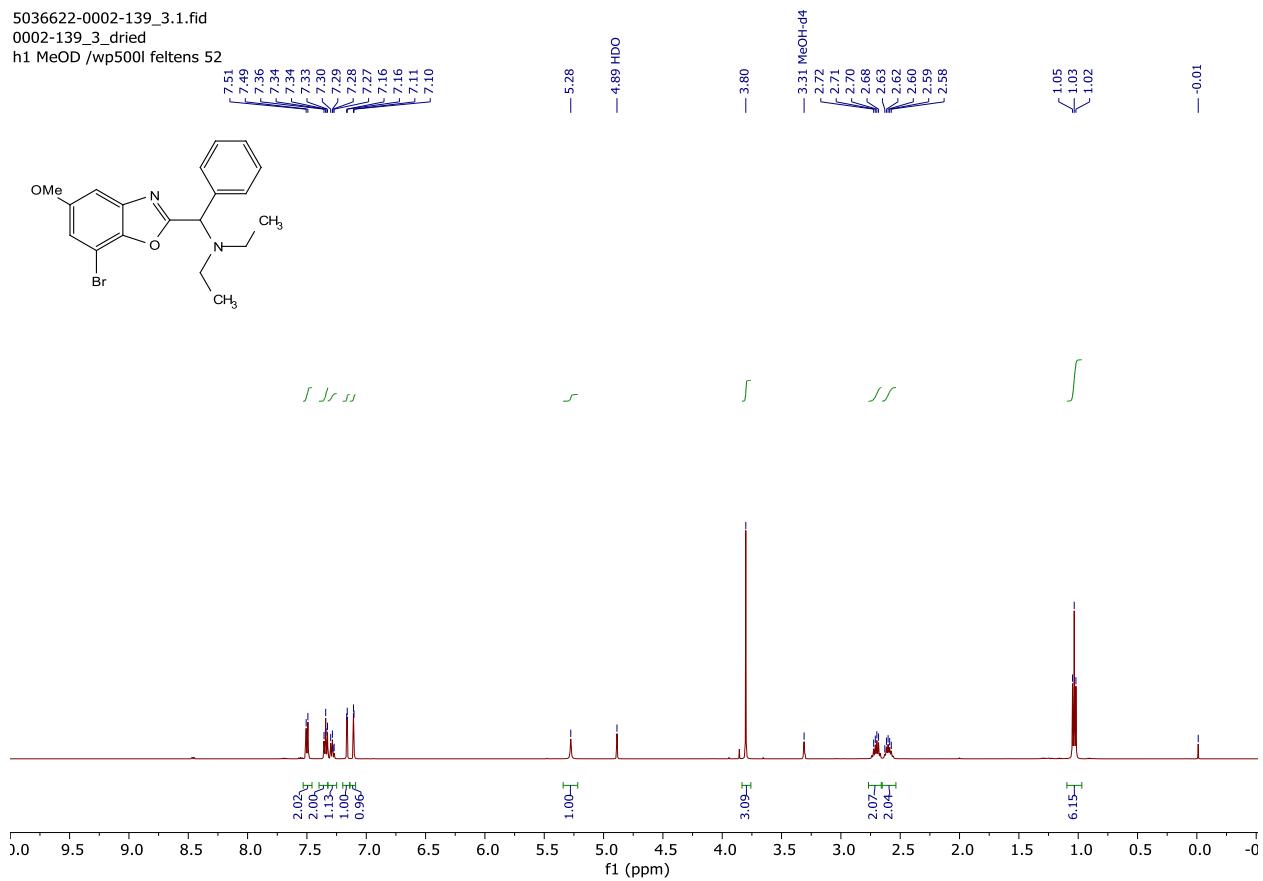
Yield: 307 mg (79%); 76 LCAP before workup/column chromatography

¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.50 (d, *J* = 7.3 Hz, 2H), 7.31 (m, 3H), 7.17 (s, 1H), 7.12 (s, 1H), 5.26 (s, 1H), 3.81 (s, 3H), 2.70 (dq, *J* = 13.6, 6.8 Hz, 2H), 2.58 (dq, *J* = 13.0, 6.5 Hz, 2H), 1.03 (t, *J* = 6.9 Hz, 6H).

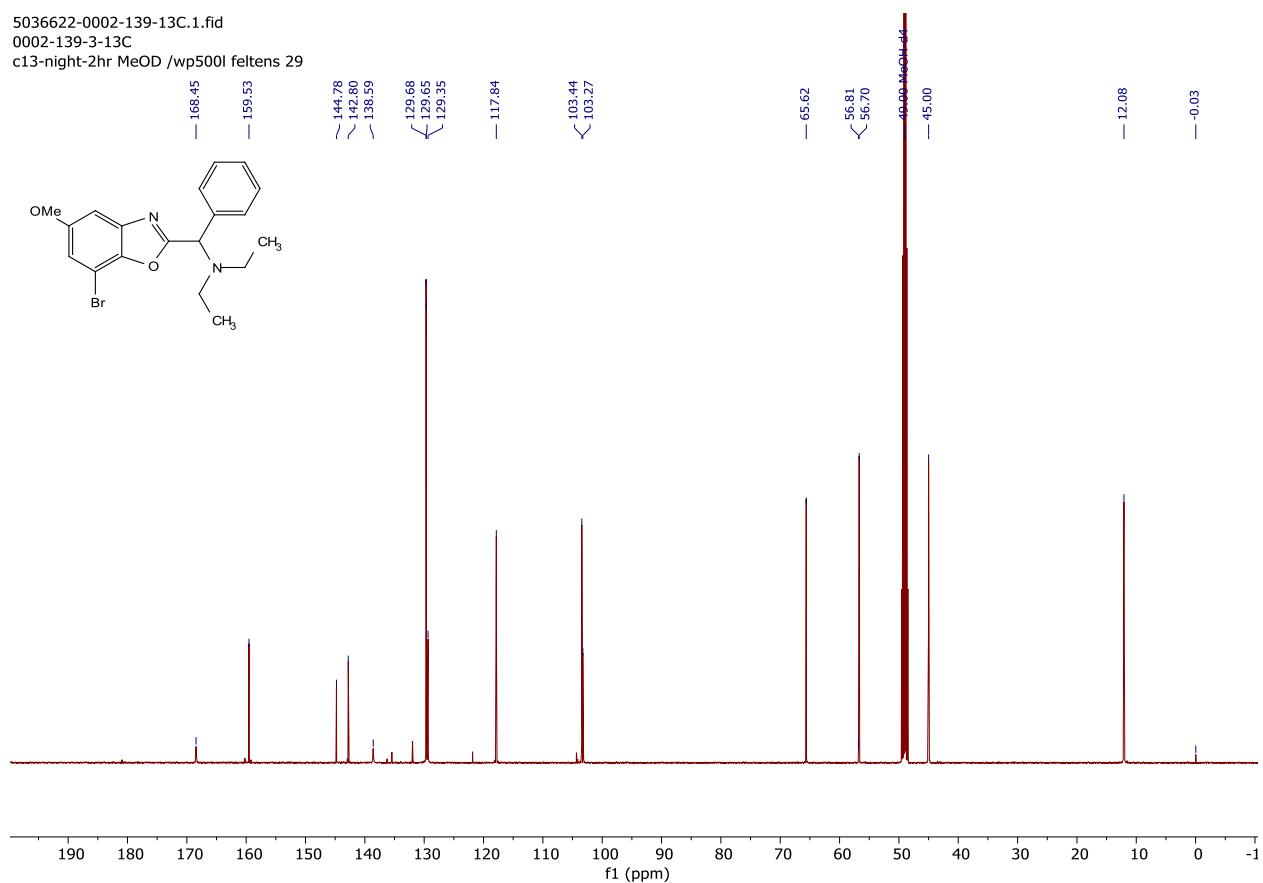
¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 168.6, 159.5, 144.8, 142.8, 138.8, 129.6, 129.6, 129.2, 118.5, 117.8, 103.4, 65.6, 56.7, 44.9, 12.1.

HRMS: Calc. C₁₉H₂₂BrN₂O₂⁺ [M+H⁺] 389.0859; found 389.0856.

5036622-0002-139_3.1.fid
0002-139_3_dried
h1 MeOD /wp500I fultens 52

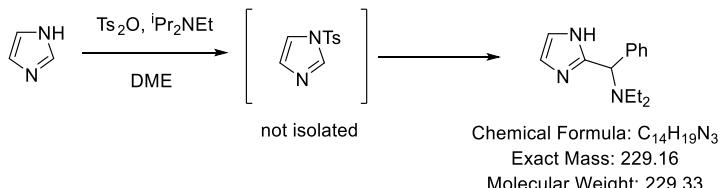


5036622-0002-139-13C.1.fid
0002-139-3-13C
c13-night-2hr MeOD /wp500l feltens 29



C-H aminoalkylation of imidazole and benzimidazole via *in-situ* tosylation

Imidazole: *N*-((1*H*-imidazol-2-yl)(phenyl)methyl)-*N*-ethylethanamine



Imidazole (0.068 g, 1.00 mmol, 1.00 eq.) and tosyl anhydride (0.938 g, 1.20 mmol, 1.20 equiv.) were weighed into a 2-dram vial and brought into the glovebox together with an empty 2-dram vial. 1,2-Dimethoxyethane (1.5 ml) was added to the vial containing imidazole, followed by addition of *N,N*-diethylpropan-2-amine (0.388 ml, 0.288 g, 2.50 mmol, 2.50 equiv.). This resulted at first in a solution, with subsequent precipitate formation after ~1 min. The vial was stirred in the glovebox for 30 min at room temperature.

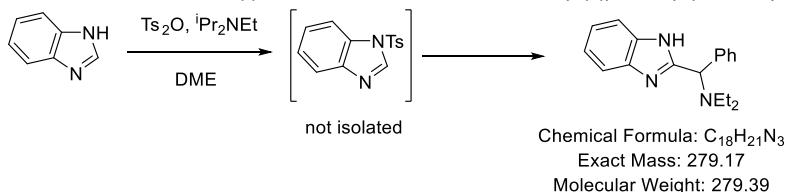
tert-Butyldimethylsilyl trifluoromethanesulfonate (0.689 ml, 0.793 g, 3.00 mmol, 3.0 equiv.), *N,N*-diethyl-1,1,1-trimethylsilanamine (0.237 ml, 0.182 g, 1.25 mmol, 1.25 equiv.), and benzaldehyde (0.102 ml, 0.106 g, 1.00 mmol, 1.00 equiv.) were mixed in 1,2-dimethoxyethane (1.0 ml) in the empty vial and stirred for 10 min at room temperature. Then, the second solution was added to the first mixture and the combined reaction mixture was removed from the glovebox and stirred at 50 °C for 18 h.

To hydrolyze the tosyl protecting group, pyridine (2.0 mL) and water (0.20 mL) were added and the reaction was stirred at 50 °C for 2 h. The resulting mixture was concentrated in vacuum and purified by column chromatography.

Yield: 103 mg (45%); 39 LCAP before tosyl hydrolysis, 22 LCAP after hydrolysis & before column chromatography

For spectroscopic (NMR/HRMS) characterization, see page 70

Benzimidazole: *N*-((1*H*-benzo[d]imidazol-2-yl)(phenyl)methyl)-*N*-ethylethanamine



Benzimidazole (0.118 g, 1.00 mmol, 1.00 equiv.) and tosyl anhydride (0.938 g, 1.20 mmol, 1.20 equiv.) were weighed into a 2-dram vial and brought into the glovebox together with an empty 2-dram vial. 1,2-Dimethoxyethane (1.5 ml) was added to the vial containing benzimidazole, followed by addition of *N,N*-diethylpropan-2-amine (0.388 ml, 0.288 g, 2.50 mmol, 2.50 equiv.). This resulted at first in a solution, with

subsequent precipitate formation after ~1 min. The vial was stirred in the glovebox for 30 min at room temperature.

tert-Butyldimethylsilyl trifluoromethanesulfonate (0.689 ml, 0.793 g, 3.00 mmol, 3.0 equiv.), *N,N*-diethyl-1,1,1-trimethylsilanamine (0.237 ml, 0.182 g, 1.25 mmol, 1.25 equiv.), and benzaldehyde (0.102 ml, 0.106 g, 1.00 mmol, 1.00 equiv.) were mixed in 1,2-dimethoxyethane (1.0 ml) in the empty vial and stirred for 10 min at room temperature. Then, the second solution was added to the first mixture and the combined reaction mixture was removed from the glovebox and stirred at 50 °C for 18 h.

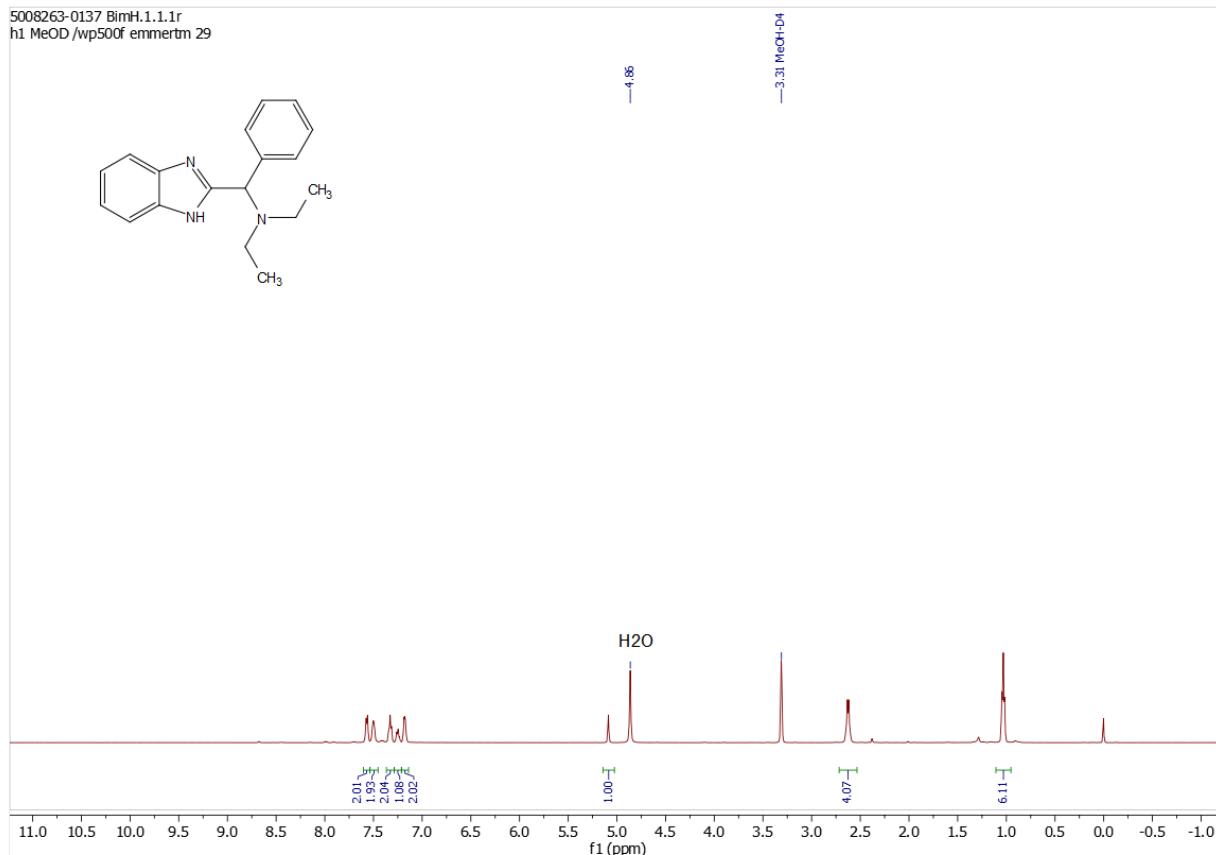
To hydrolyze the tosyl protecting group, pyridine (2.0 mL) and water (0.20 mL) were added and the reaction was stirred at 50 °C for 2 h. The resulting mixture was concentrated in vacuum and purified by column chromatography.

Yield: 207 mg (74%); 22 LCAP before tosyl hydrolysis, 16 LCAP after hydrolysis & before column chromatography

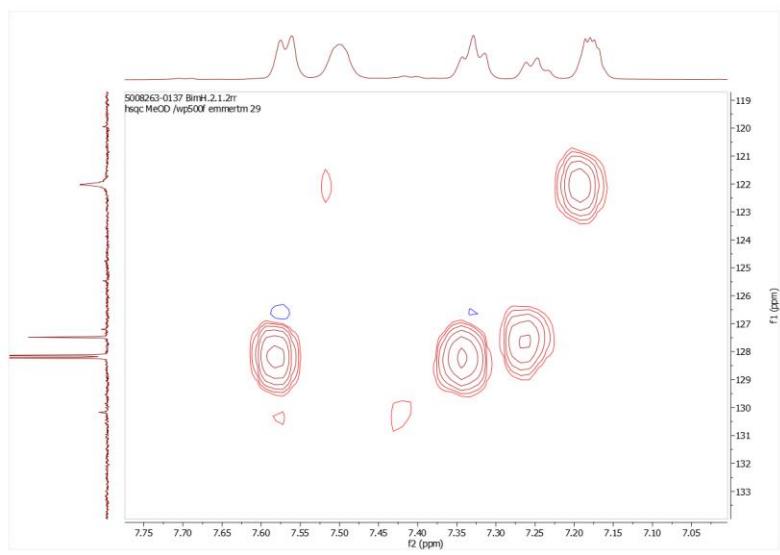
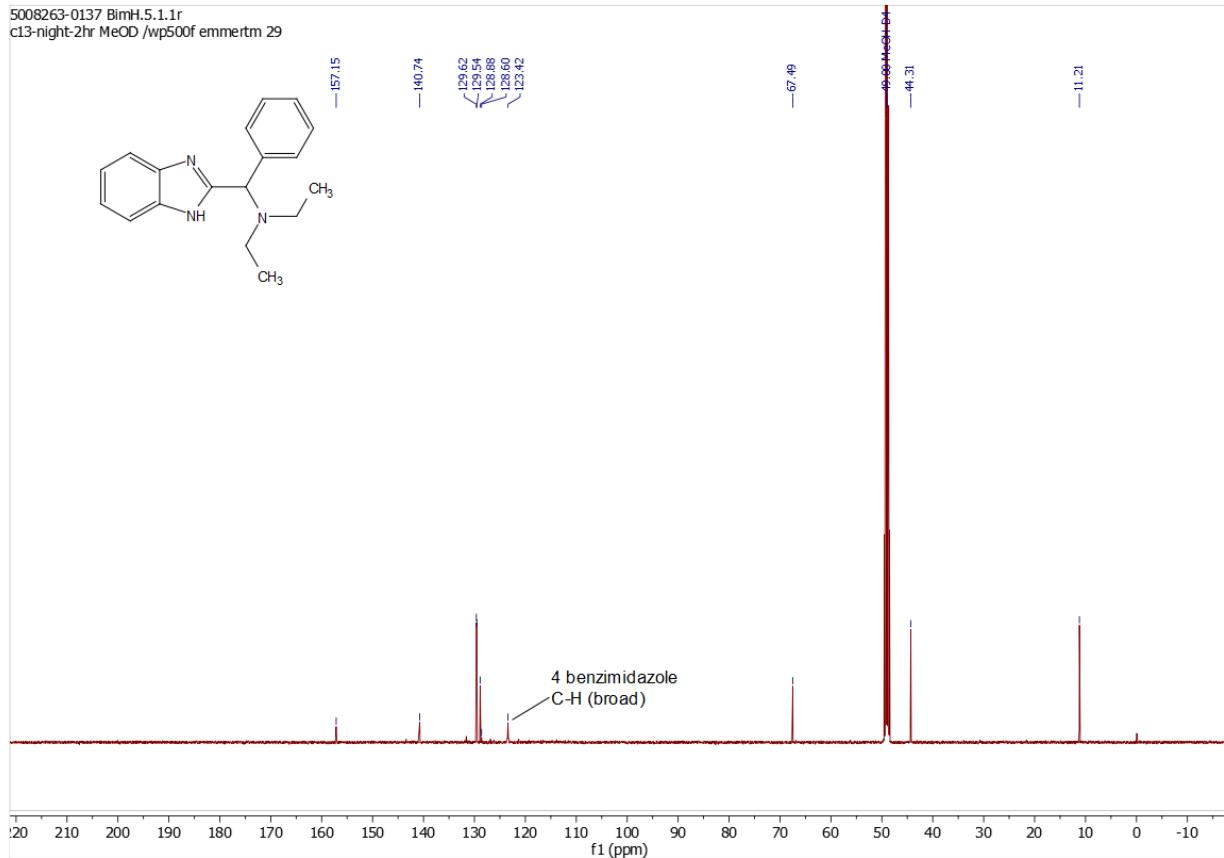
¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.57 (d, *J* = 7.2 Hz, 2H), 7.50 (broad s, 2H), 7.33 (t, *J* = 7.1 Hz, 2H), 7.25 (t, *J* = 6.9 Hz, 1H), 7.21 – 7.15 (m, 2H), 5.09 (s, 1H), 2.63 (q, *J* = 6.2 Hz, 4H), 1.03 (t, *J* = 6.8 Hz, 6H).

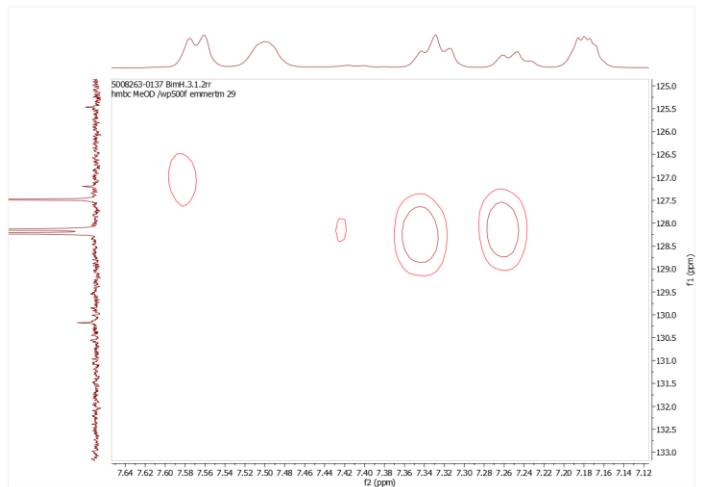
¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 157.1, 140.7, 129.6, 129.5, 128.8, 128.6, 123.4 (broad, 4 C), 67.4, 44.3, 11.2.

HRMS: Calc. C₁₈H₂₂N₃⁺ [M+H⁺] 280.1808; found 280.1812.



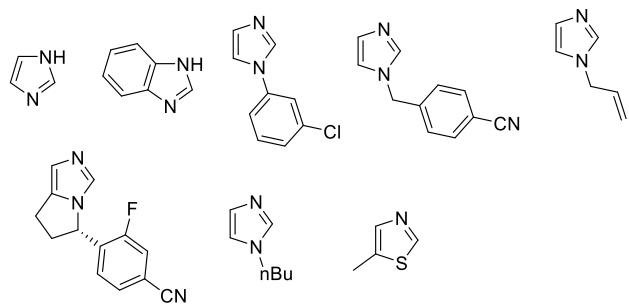
5008263-0137 BimH.5.1.1r
c13-night-2hr MeOD /wp500f emmertm 29





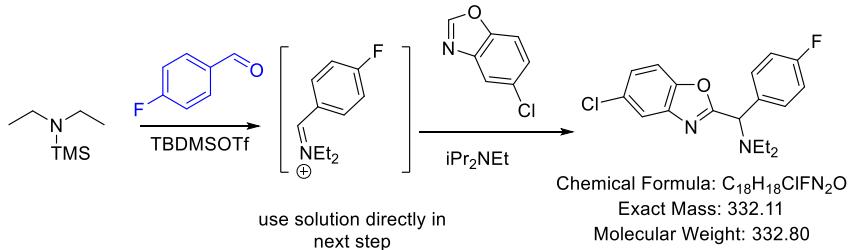
Azoles With Low Reactivity (<2 LCAP)

The following azole structures provided only low or no reactivity, as determined by <2 LCAP of the desired 3-component coupling products.



Aldehyde Scope

N-(5-Chlorobenzo[d]oxazol-2-yl)(4-fluorophenyl)methyl)-*N*-ethylethanamine



The title compound was prepared according to General Procedure 2 (reaction time 18 h).

Yield: 203 mg (61%); 62 LCAP before workup/column chromatography

¹H NMR (500 MHz, Methanol-*d*₄, ppm) δ 7.69 (s, 1H), 7.61 – 7.49 (m, 3H), 7.37 (d, *J* = 8.7 Hz, 1H), 7.15 – 7.02 (m, 2H), 5.27 (s, 1H), 2.68 (dq, *J* = 13.6, 6.8 Hz, 2H), 2.56 (dq, *J* = 13.2, 6.6 Hz, 2H), 1.03 (t, *J* = 6.9 Hz, 6H).

¹⁹F NMR (470 MHz, Methanol-*d*₄, ppm) δ -115.95.

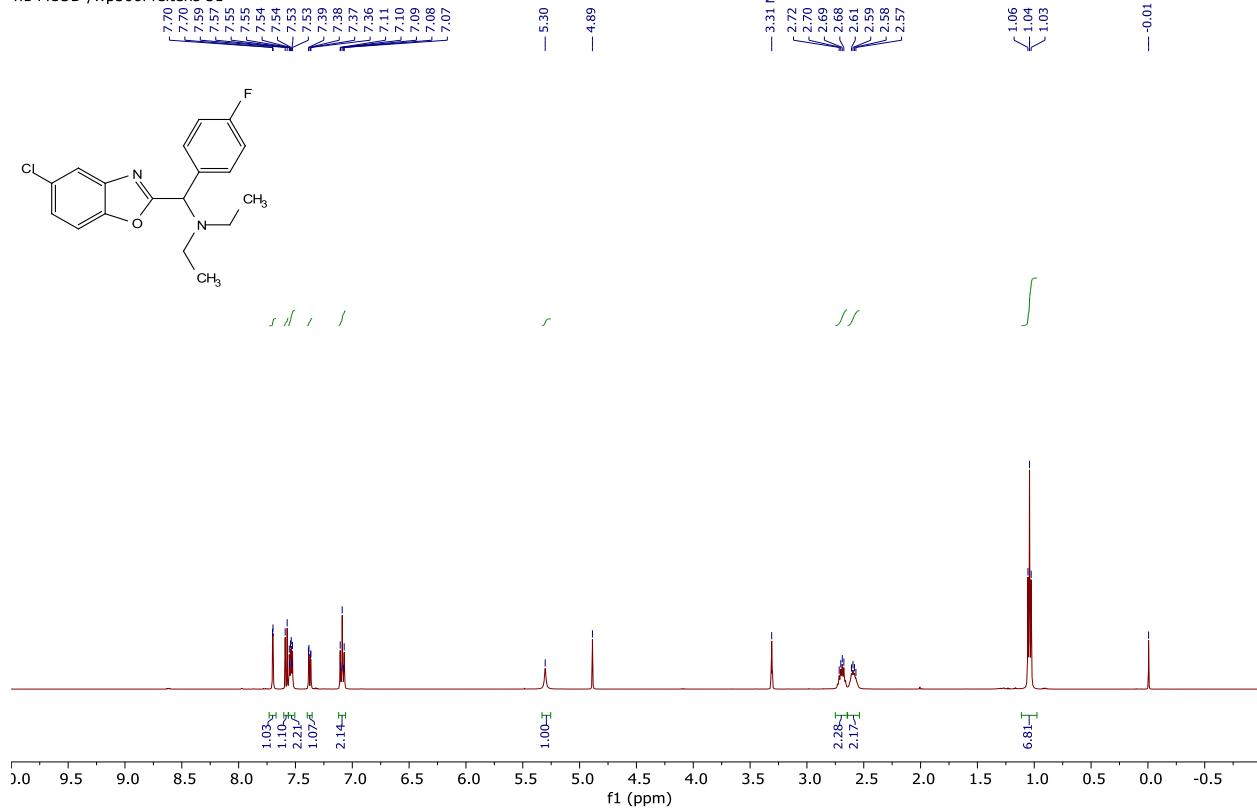
¹³C NMR (126 MHz, Methanol-*d*₄, ppm) δ 167.4, 162.5 (d, *J* = 245.9 Hz), 149.2, 141.5, 133.4 (d, *J* = 3.2 Hz), 130.1 (d, *J* = 8.2 Hz), 129.9, 125.4, 119.2, 114.9 (d, *J* = 21.8 Hz), 111.5, 63.4, 43.4, 10.7.

HRMS: Calc. C₁₈H₁₉ClFN₂O⁺ [M+H⁺] 333.1165; found 333.1170.

5036622-0002-138_3.1.fid

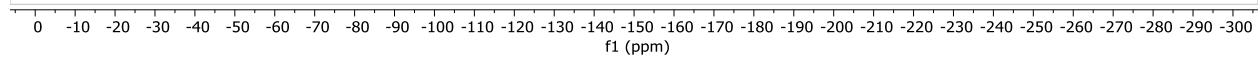
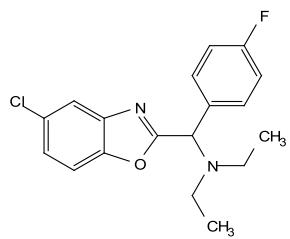
0002-138_3_dried

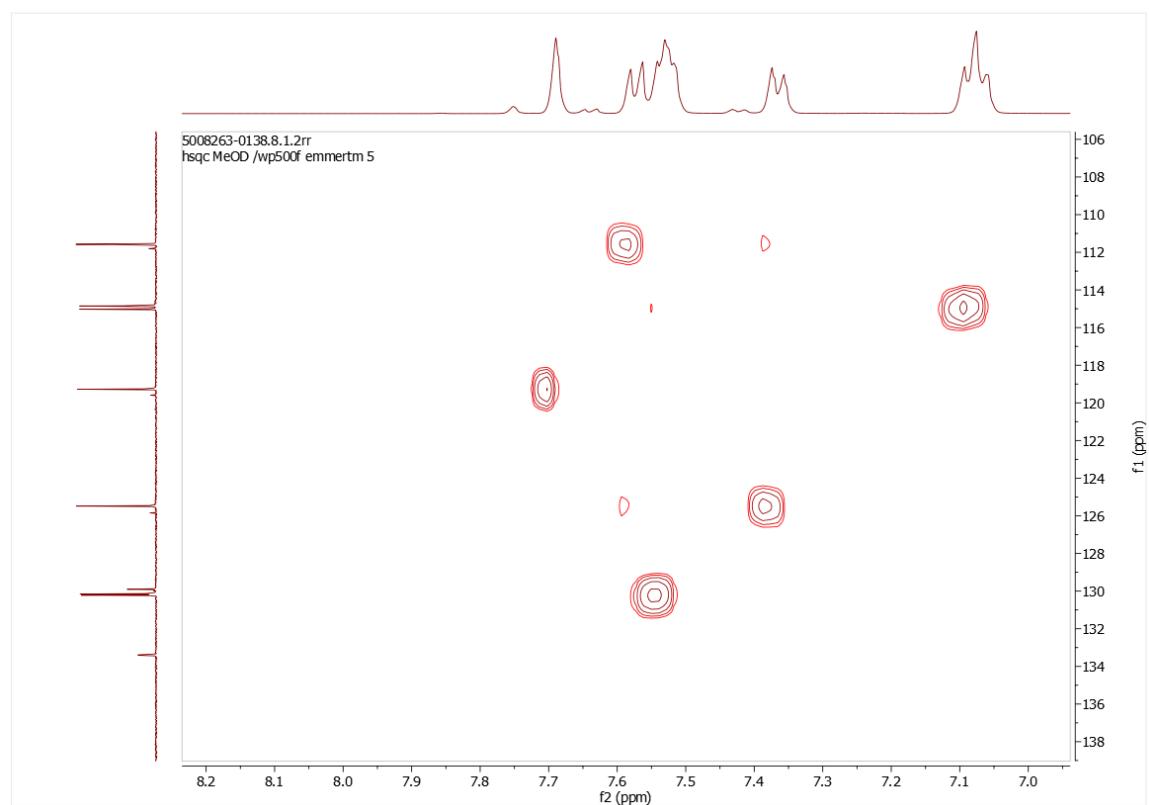
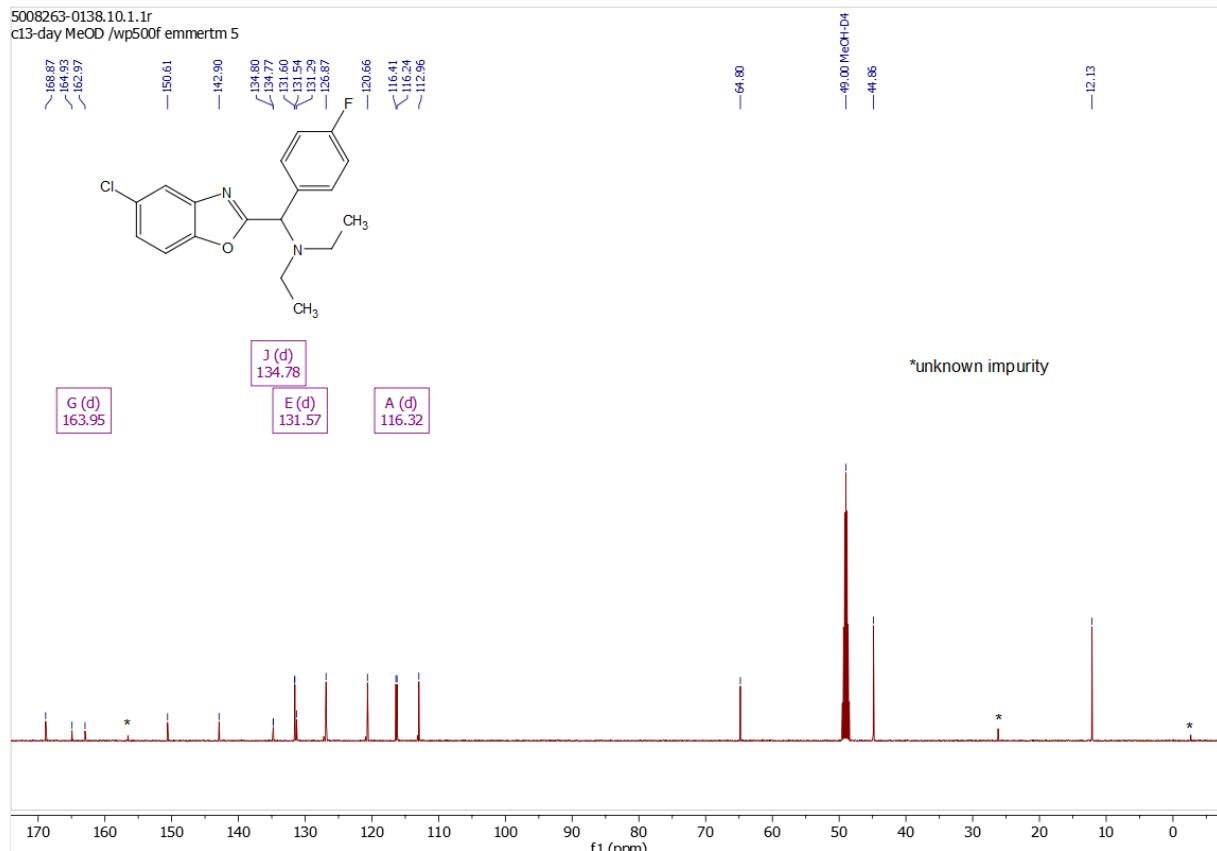
h1 MeOD /wp5001 feltens 51

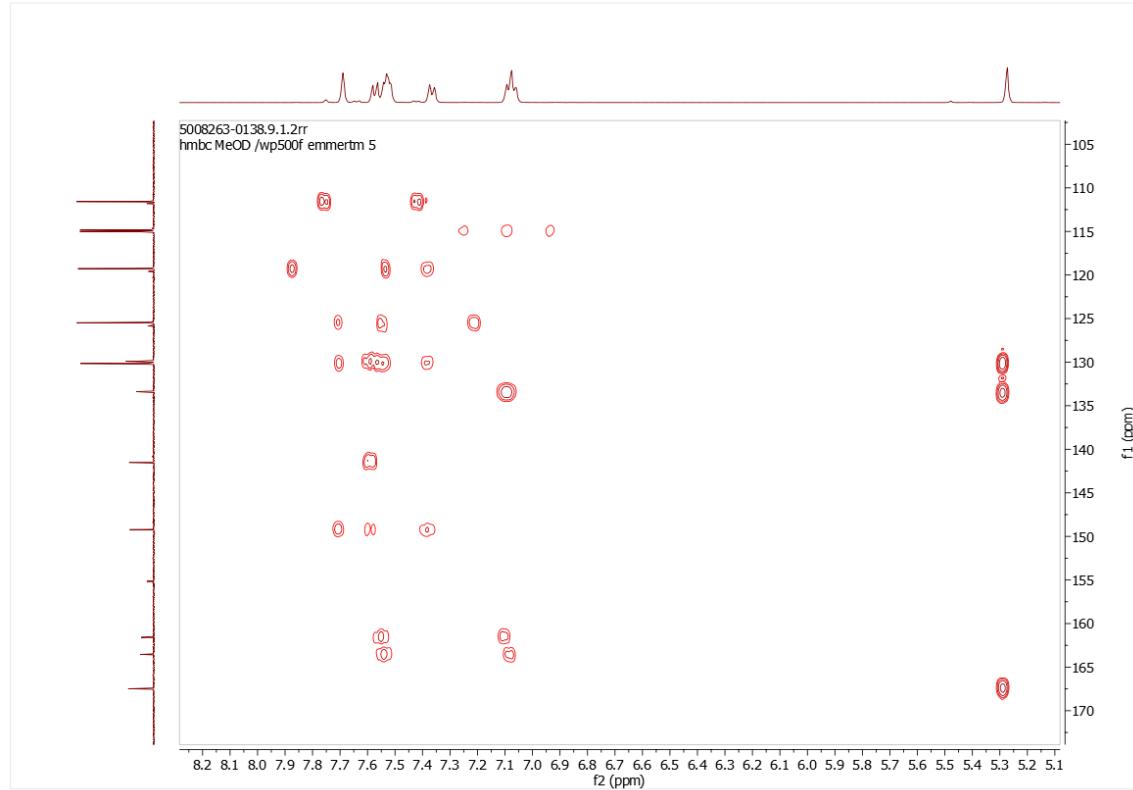


5008263-0138.11.1.r
f19 MeOD /wp500f emmertm 5

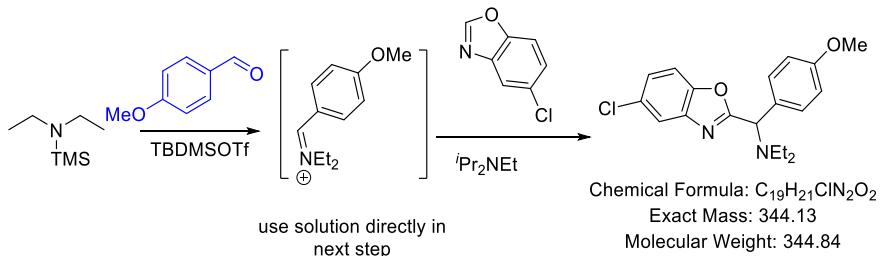
-115.95







N-(5-Chlorobenzo[d]oxazol-2-yl)(4-methoxyphenyl)methyl)-*N*-ethylethanamine



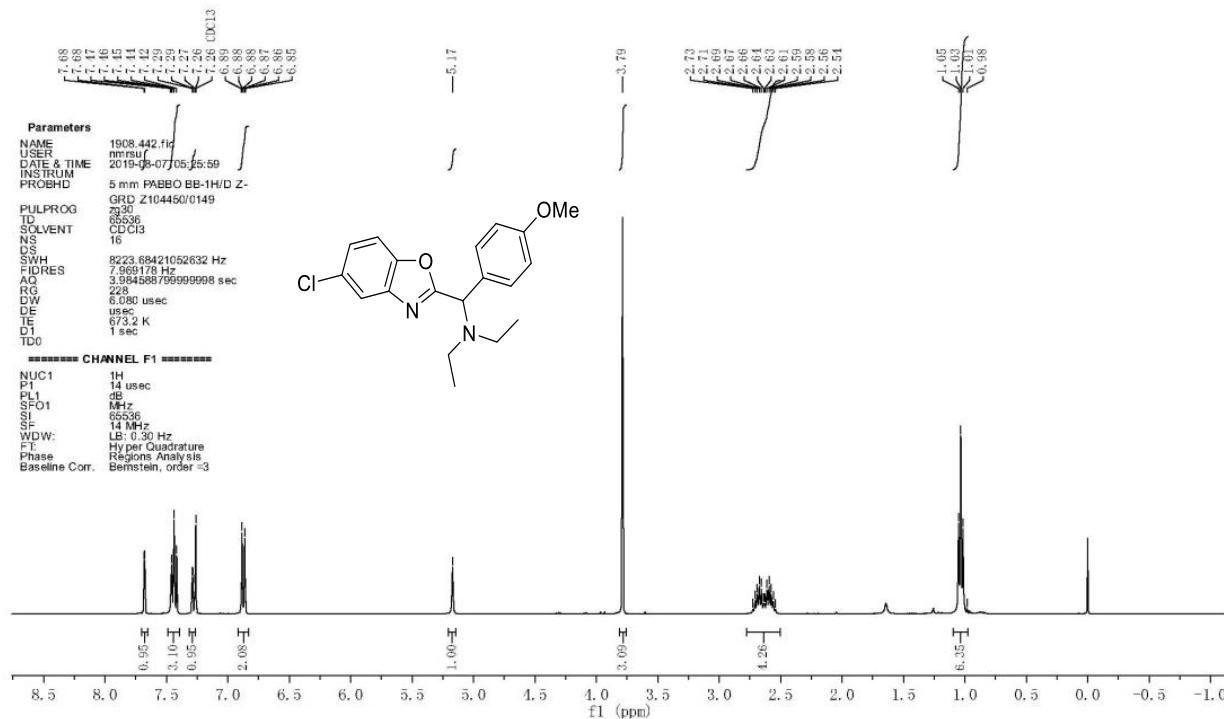
The title compound was prepared according to General Procedure 2 (reaction time: 18 h).

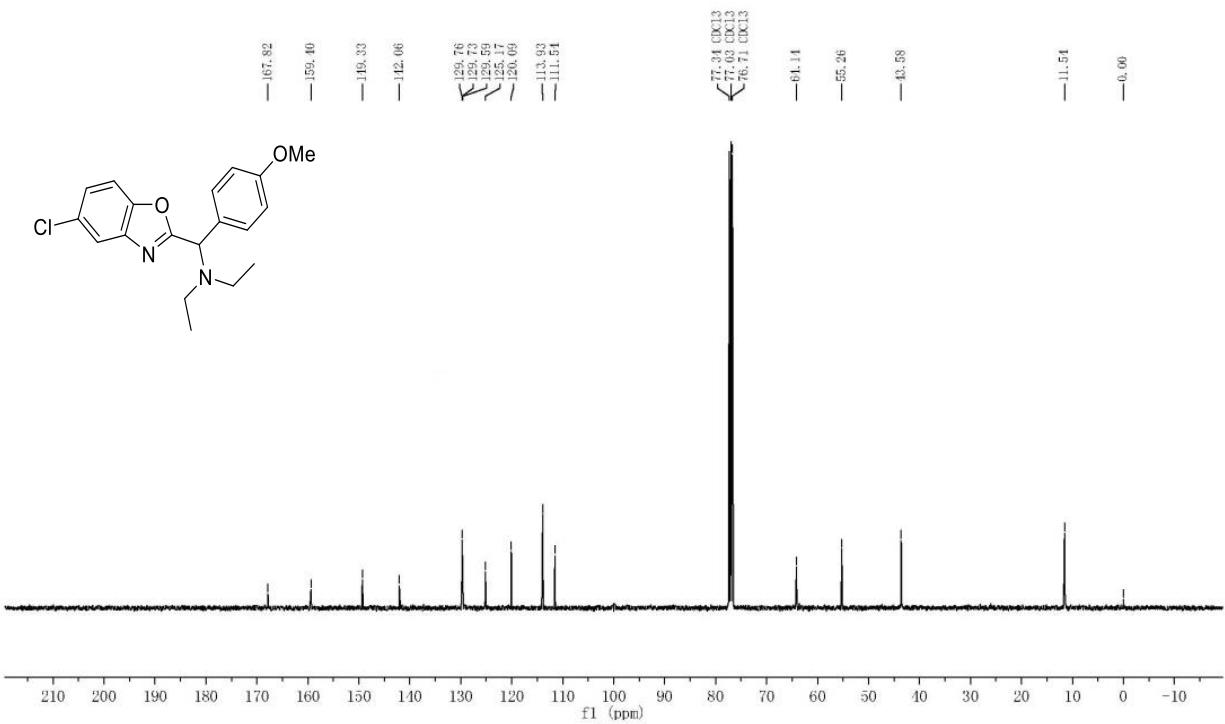
Yield: 122 mg (25%); 74 LCAP before workup/ Prep-HPLC

1H NMR (400 MHz, Chloroform-d, ppm) δ 7.68 (d, J = 2.1 Hz, 1H), 7.44 (m, 3H), 7.31 – 7.27 (m, 1H), 6.91 – 6.85 (m, 2H), 5.17 (s, 1H), 3.79 (s, 3H), 2.63 (m, 4H), 1.03 (t, J = 7.1 Hz, 6H).

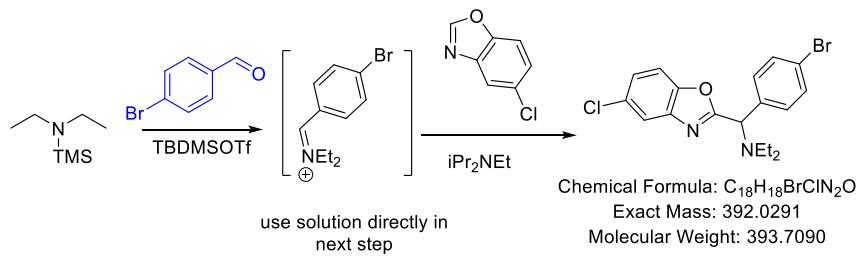
^{13}C NMR (101 MHz, Chloroform-d, ppm) δ 167.8, 159.4, 149.3, 142.0, 129.7, 129.7, 129.5, 125.1, 120.0, 113.9, 111.5, 64.1, 55.2, 43.5, 11.5.

HRMS: Calc. $C_{19}H_{21}ClN_2O_2^+ [M+H^+]$ 345.1364; found 345.1360.





N-((4-Bromophenyl)(5-chlorobenzo[d]oxazol-2-yl)methyl)-*N*-ethylethanamine



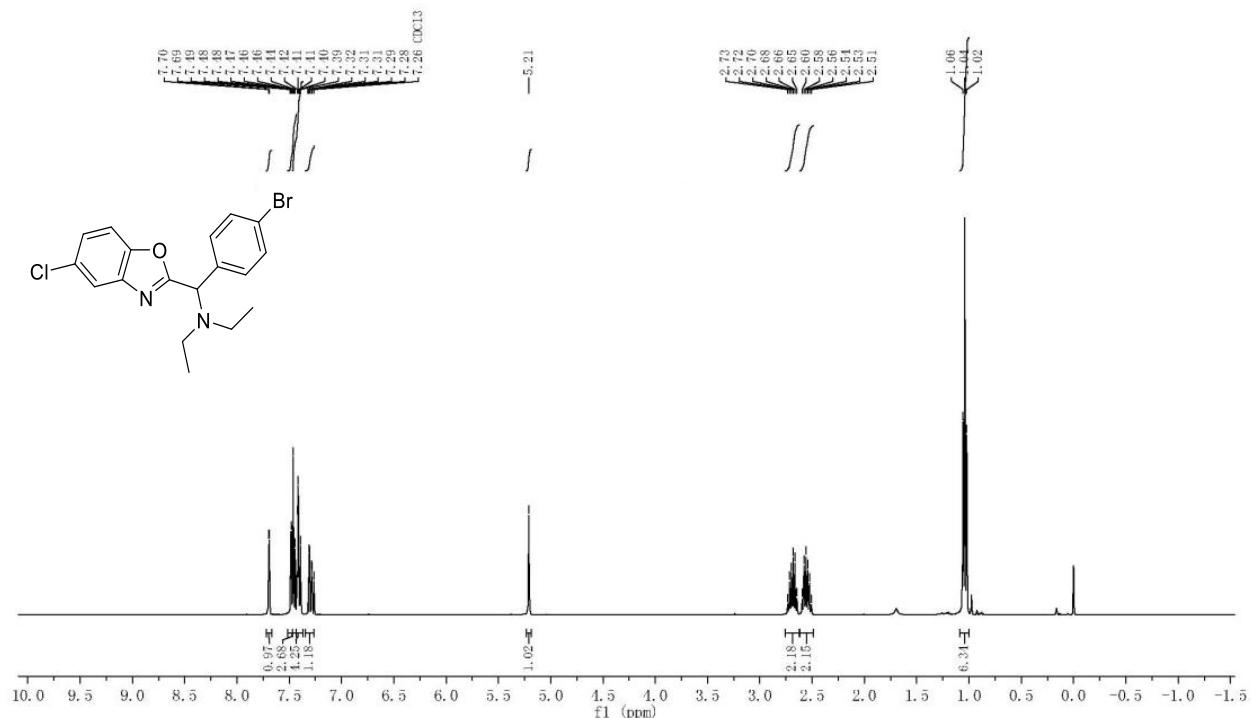
The title compound was prepared according to General Procedure 2 (reaction time: 18 h).

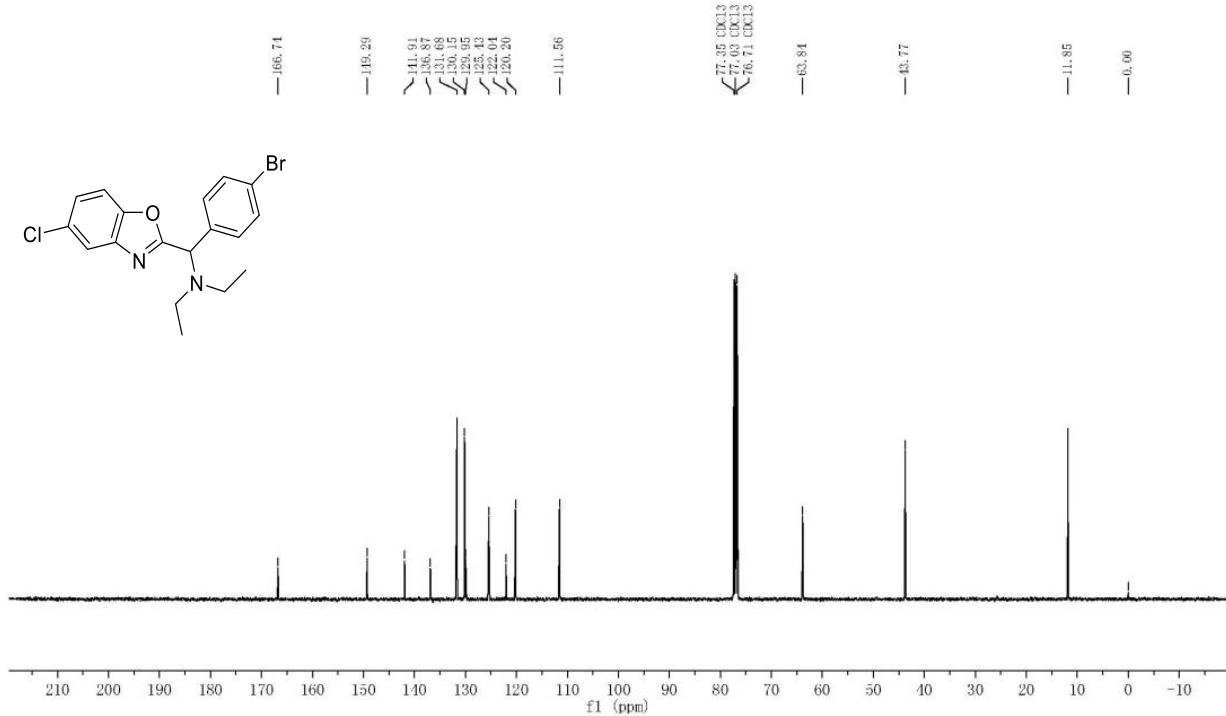
Yield: 280 mg (49%); 57 LCAP before workup/ Prep-HPLC

¹H NMR (400 MHz, Chloroform-d, ppm) δ 7.70 (d, J = 2.1 Hz, 1H), 7.50 – 7.45 (m, 2H), 7.45 – 7.38 (m, 3H), 7.30 (m, 1H), 5.21 (s, 1H), 2.69 (m, 2H), 2.55 (m, 2H), 1.04 (t, J = 7.1 Hz, 6H).

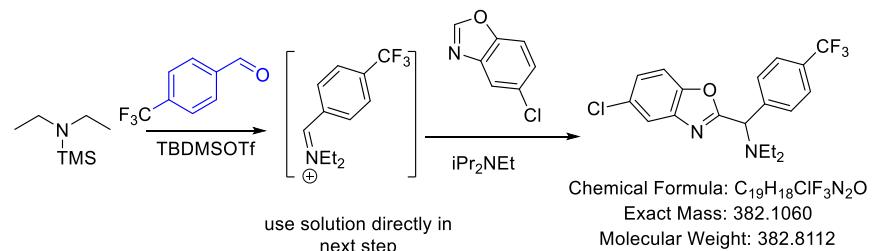
¹³C NMR (101 MHz, Chloroform-d, ppm) δ 166.7, 149.2, 141.9, 136.8, 131.6, 130.1, 129.9, 125.4, 122.0, 120.2, 111.5, 63.8, 43.7, 11.8.

HRMS: Calc. C₁₈H₁₈BrClN₂O⁺ [M+H⁺] 393.0364; found 393.0359.





N-(5-Chlorobenzo[d]oxazol-2-yl)(4-(trifluoromethyl)phenyl)methyl)-*N*-ethylethanamine



The title compound was prepared according to General Procedure 2 (reaction time: 18 h).

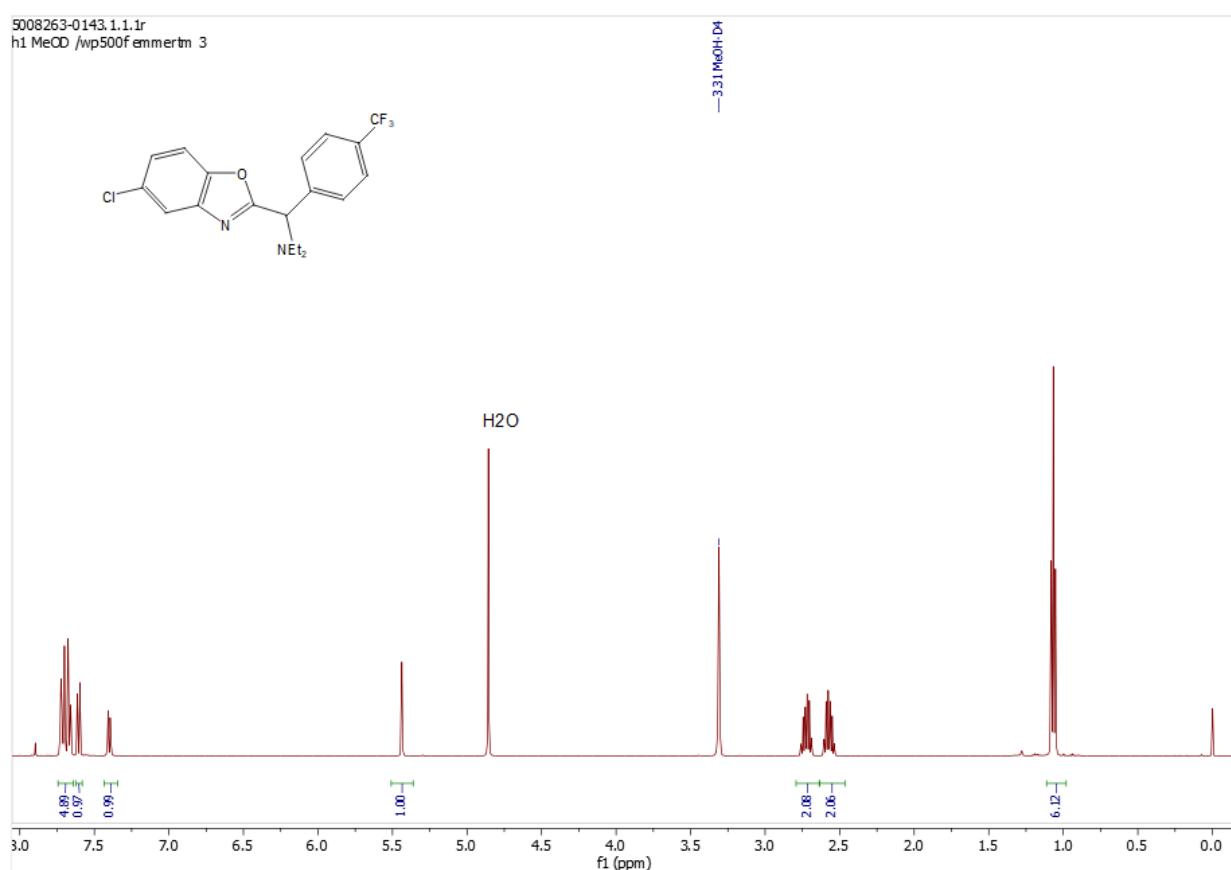
Yield: 189 mg (50%); 68 LCAP before workup/ Pre-HPLC

1H NMR (500 MHz, Methanol- d_4 , ppm) δ 7.77 – 7.63 (m, 5H), 7.61 (d, J = 8.7 Hz, 1H), 7.40 (dd, J = 8.7, 2.1 Hz, 1H), 5.44 (s, 1H), 2.72 (dq, J = 14.4, 7.2 Hz, 2H), 2.57 (dq, J = 13.9, 7.0 Hz, 2H), 1.07 (t, J = 7.1 Hz, 6H).

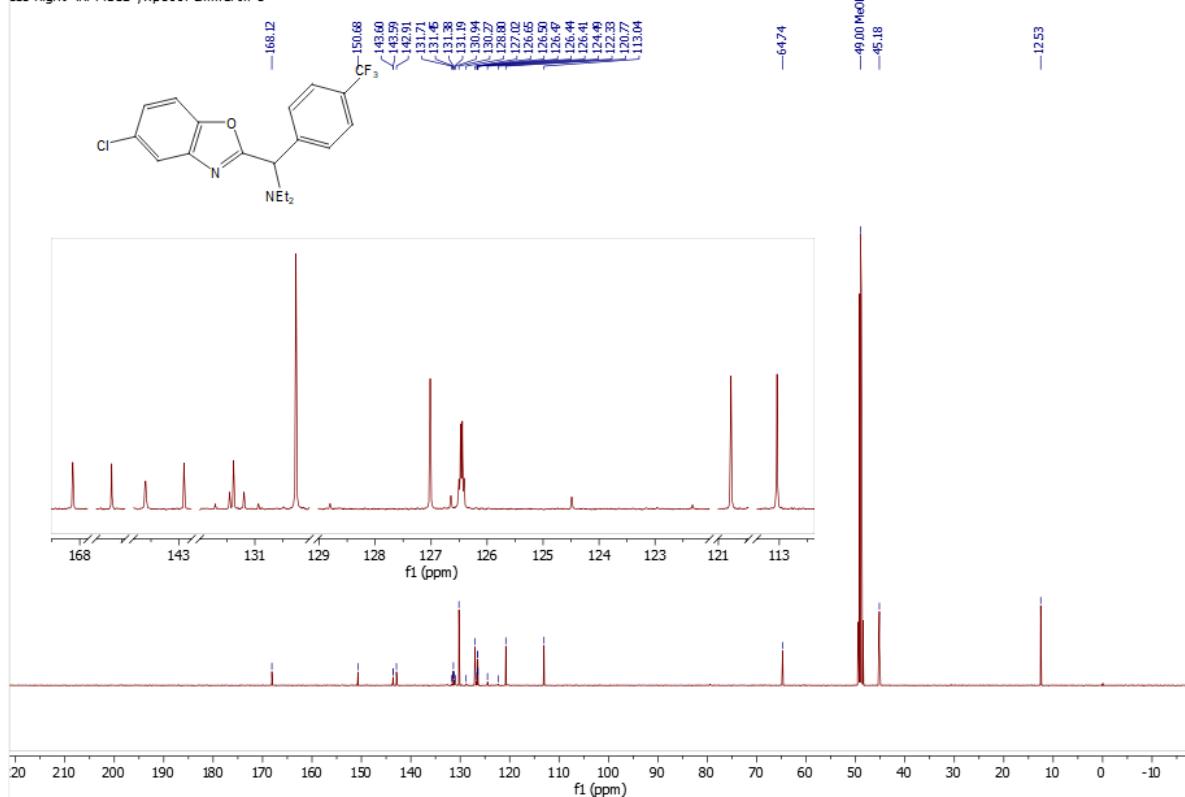
^{13}C NMR (126 MHz, Methanol- d_4 , ppm) δ 168.1, 150.6, 143.6 (m), 142.9, 131.3, 131.3 (q, J = 32.3 Hz), 130.2, 127.0, 126.4 (q, J = 3.8 Hz), 125.5 (q, J = 271.2 Hz), 120.7, 113.0, 64.7, 45.1, 12.5.

^{19}F NMR (470 MHz, Methanol- d_4 , ppm) δ -64.08.

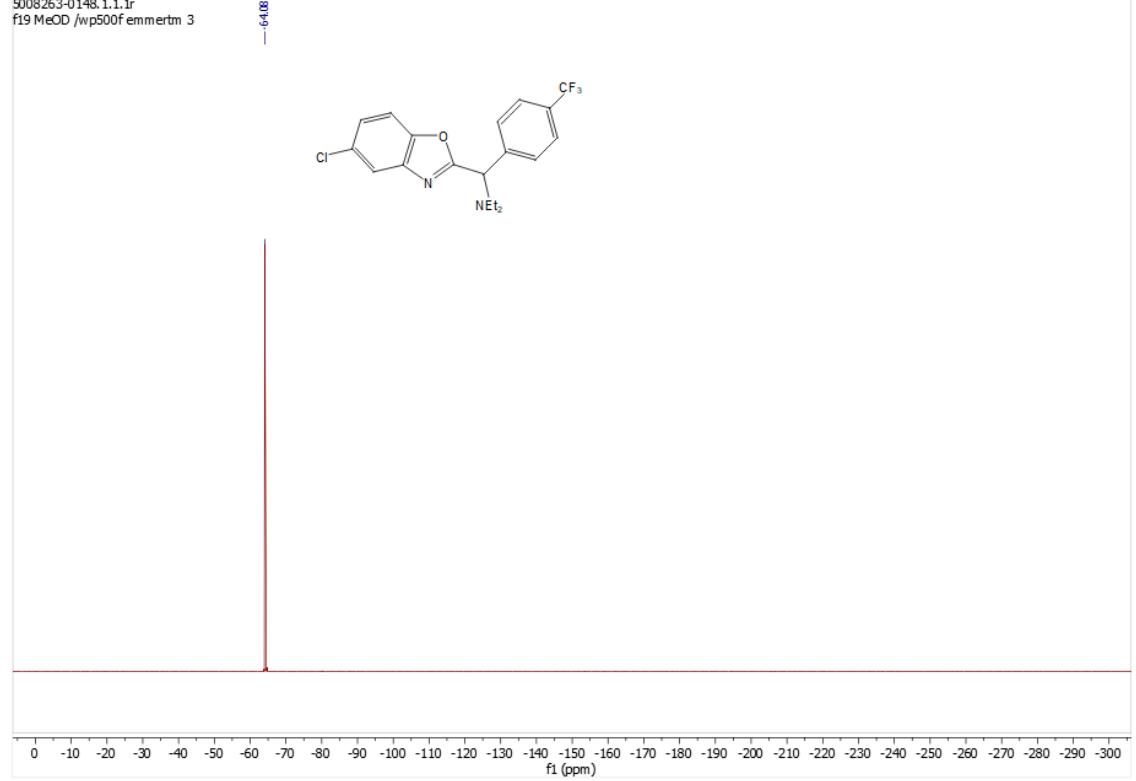
HRMS: Calc. $C_{19}H_{18}ClF_3N_2O^+ [M+H^+]$ 383.1133; found 383.1133.



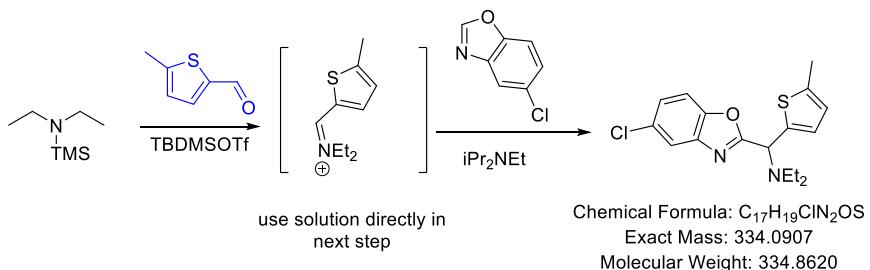
5008263-0148.7.1.r
c13-night-4hr MeOD /wp500f emmertm 3



5008263-0148.1.1.r
f19 MeOD /wp500f emmertm 3



N-((5-Chlorobenzo[d]oxazol-2-yl)(5-methylthiophen-2-yl)methyl)-*N*-ethylethanamine



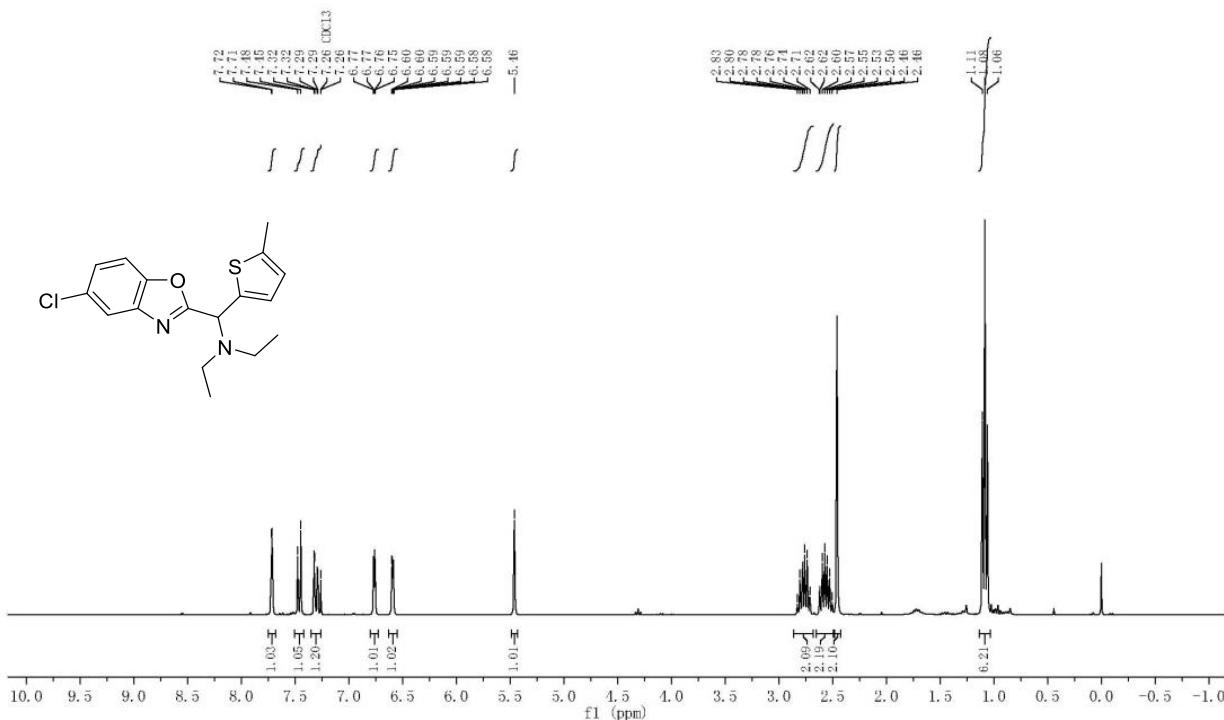
The title compound was prepared according to General Procedure 2 (reaction time: 18 h).

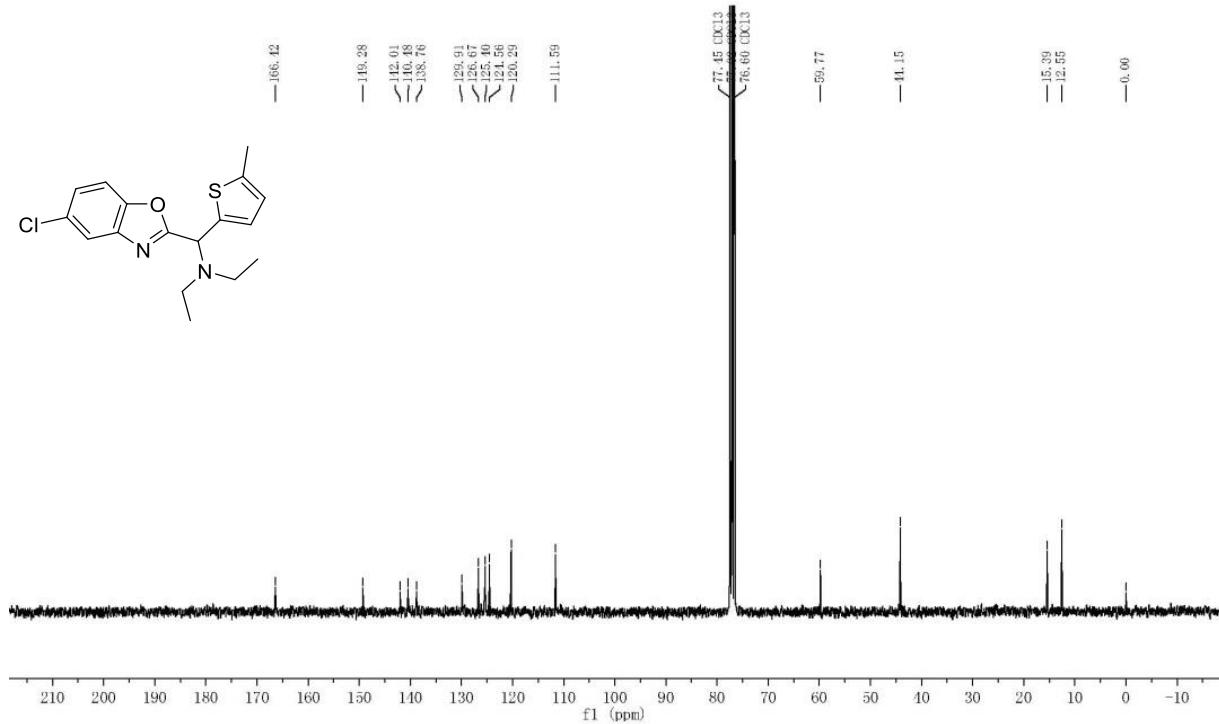
Yield: 120 mg (26 %); 82 LCAP before workup/ Pre-HPLC

¹H NMR (300 MHz, Chloroform-d, ppm) δ 7.73 (d, *J* = 2.1 Hz, 1H), 7.47 (d, *J* = 8.7 Hz, 1H), 7.32 (m, 2.1 Hz, 1H), 6.77 (m, 1H), 6.60 (m, 1H), 5.47 (s, 1H), 2.88 – 2.70 (m, 2H), 2.57 (dq, *J* = 13.8, 7.0 Hz, 2H), 2.47 (s, 3H), 1.10 (t, *J* = 7.1 Hz, 6H).

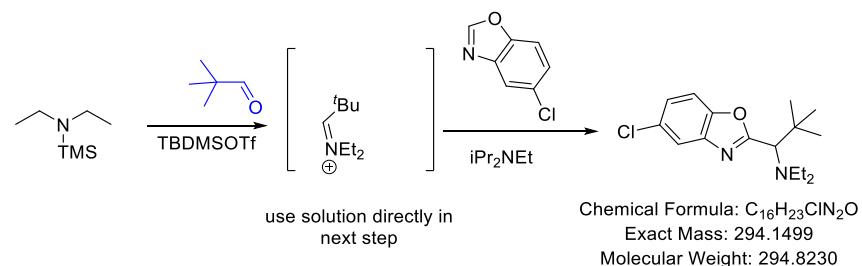
¹³C NMR (75 MHz, Chloroform-d, ppm) δ 166.4, 149.2, 142.0, 140.4, 138.7, 129.9, 126.6, 125.4, 124.5, 120.2, 111.5, 59.7, 44.1, 15.3, 12.5.

HRMS: Calc. C₁₇H₁₉CIN₂OS⁺ [M+H⁺] 335.0979; found 335.0974.





1-(5-Chlorobenzo[d]oxazol-2-yl)-N,N-diethyl-2,2-dimethylpropan-1-amine



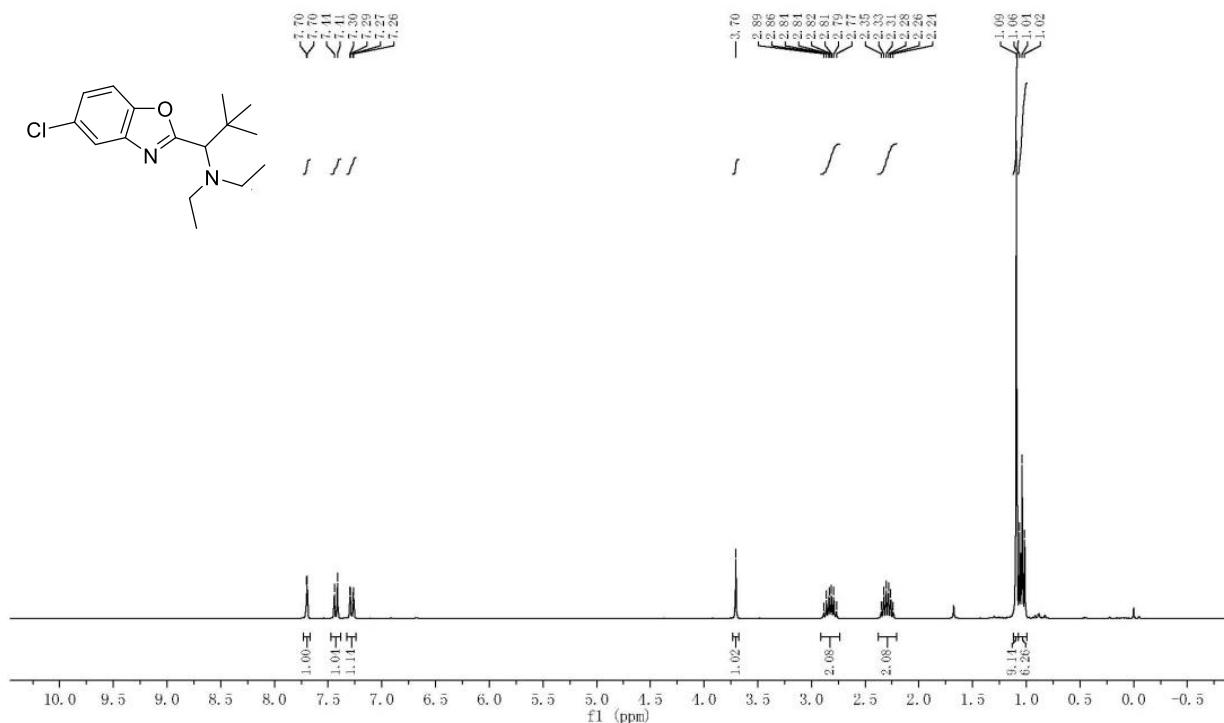
The title compound was prepared according to General Procedure 2 (reaction time: 18 h).

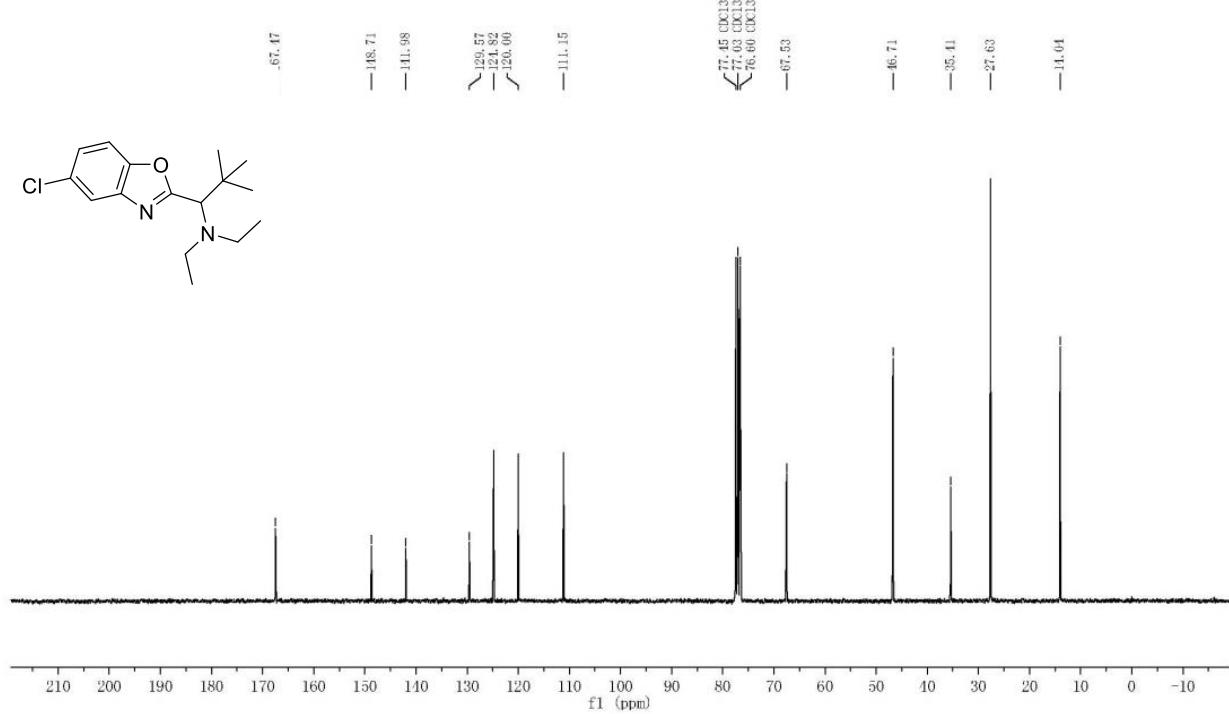
Yield: 53 mg (12 %); 37 LCAP before workup/ Pre-HPLC

¹H NMR (300 MHz, Chloroform-d, ppm) δ 7.70 (d, *J* = 2.1 Hz, 1H), 7.43 (d, *J* = 8.6 Hz, 1H), 7.31 – 7.26 (m, 1H), 3.70 (s, 1H), 2.83 (dq, *J* = 13.0, 7.4 Hz, 2H), 2.29 (dq, *J* = 13.5, 6.8 Hz, 2H), 1.09 (s, 9H), 1.04 (t, *J* = 7.1 Hz, 6H).

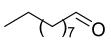
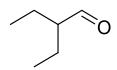
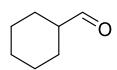
¹³C NMR (75 MHz, Chloroform-d, ppm) δ 167.4, 148.7, 141.9, 129.5, 124.8, 120.0, 111.1, 67.5, 46.7, 35.4, 27.6, 14.0.

HRMS: Calc. C₁₅H₂₁ClN₂O⁺ [M+H⁺] 295.1572; found 295.1569.

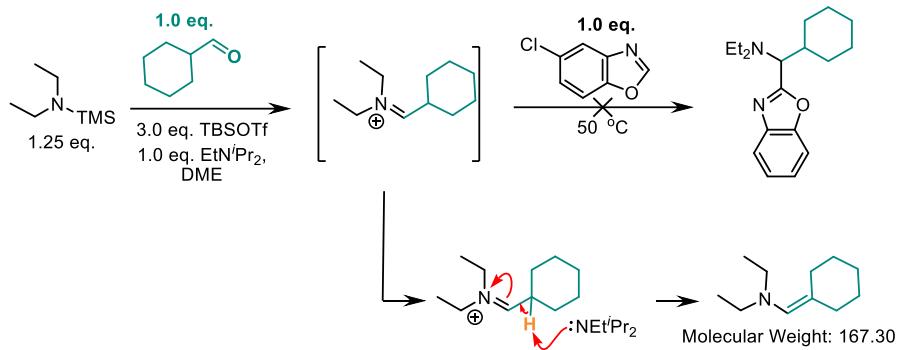




Aldehydes showing no product formation under conditions of General Procedure 2



Experimental data supporting enamine formation for aliphatic aldehydes with acidic β -C-H bonds



Scheme 3. Proposed Mechanism of Enamine Formation

In a glovebox, cyclohexanecarbaldehyde (0.121 mL, 1.00 mmol, 1.00 euquiv.) was reacted with *N,N*-diethyl-1,1,1-trimethylsilanamine (0.237 mL, 1.25 mmol, 1.25 equiv.), and *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.69 mL, 3.00 mmol, 3.00 equiv.) in DME (1.5 mL) for 15 min. The resulting solution was added to a vial containing a mixture of 5-chlorobenzoxazole (0.154 g, 1.00 mmol, 1.00 equiv.) and *N*-ethyl-*N*-isopropylpropan-2-amine (0.174 mL, 1.00 mmol, 1.00 equiv.) in DME (1.5 mL). The reaction vial was sealed, removed from the glovebox, and heated on a hotplate to 50 °C for 48 h. After that time, the crude reaction mixture was cooled to room temperature and concentrated in vacuum (rotary evaporator). 0.6 mL CDCl₃ was added and the resulting mixture was analyzed by 1H NMR. 100 uL of the solution in CDCl₃ was then dilution with 300 uL MeCN and analyzed by UPLC/MS. See below for data and analysis.

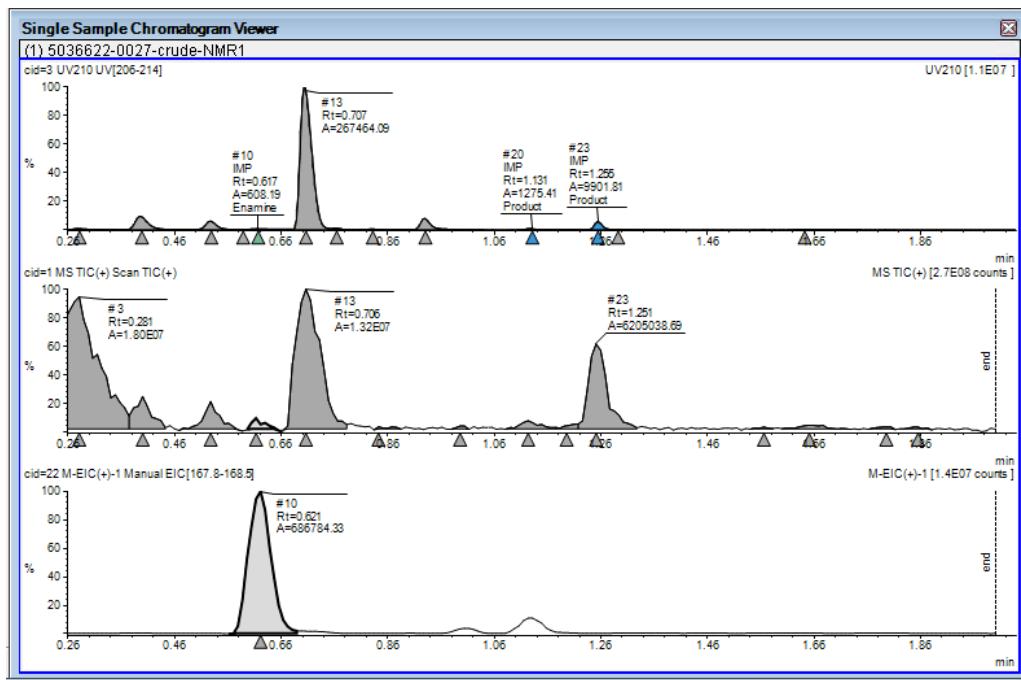


Figure 5. Analysis of crude reaction mixture. A peak at 0.617 min (0.2 LCAP in the 210 nm chromatogram) likely represents the proposed enamine product, as confirmed by massspectroscopic analysis ($M+H$ 168; see TIC spectrum in the second row). The third row shows a mass extracted chromatogram for m/z 168. However, due to the lack of chromophore in the enamine structure, the peak intensity is low in the UV chromatogram.

5036622-0027-crude.1.fid
h1 CDCl₃ /wp500! feltens 46

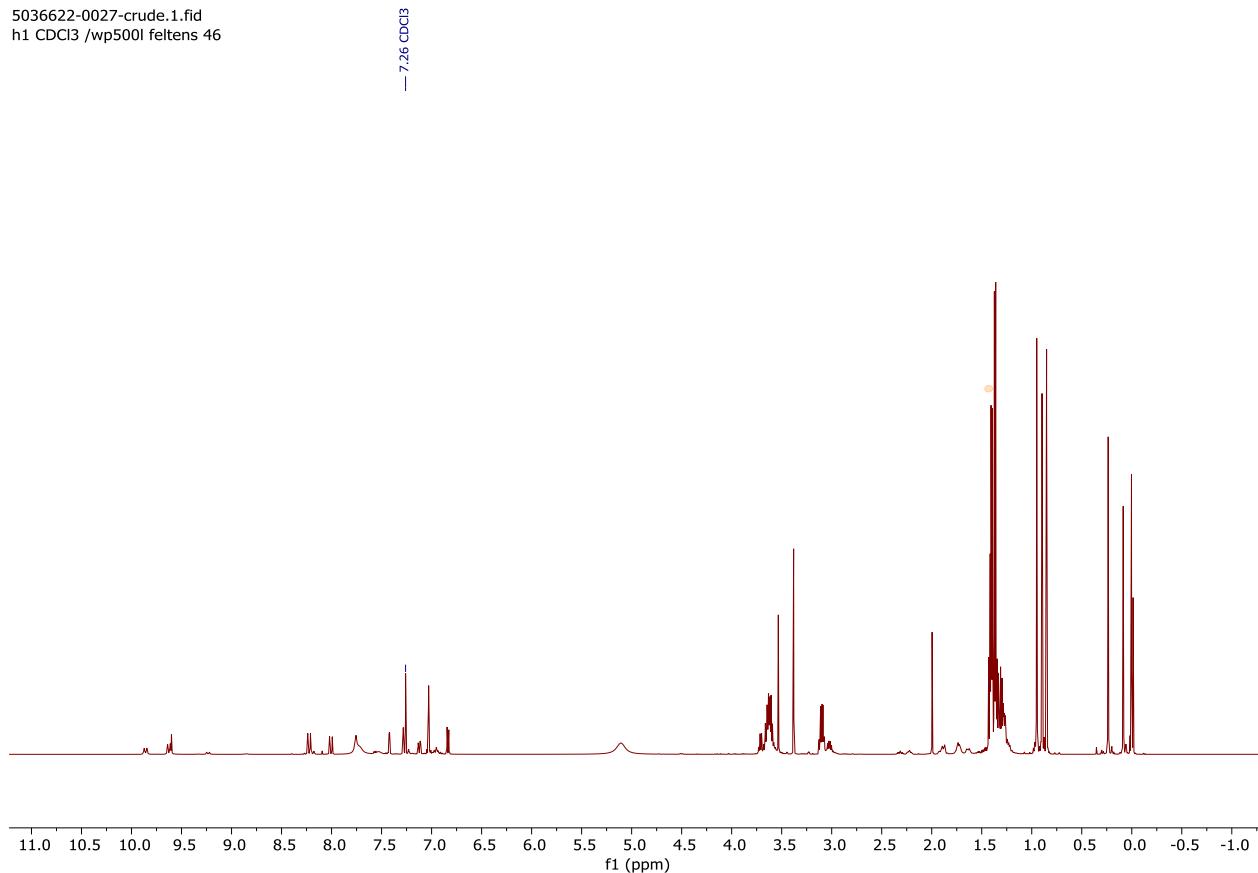


Figure 6. ¹H NMR Spectrum of the crude reaction mixture. The broad peak at 5.11 ppm is characteristic for the enamine product;¹ all the other enamine peaks likely overlap with peaks of other reactants.

¹ A. D. Dilman, P. A. Belyakov, M. I. Struchkova, D. E. Arkhipov, A. A. Korlyukov and V. A. Tartakovskiy, *The Journal of Organic Chemistry*, 2010, **75**, 5367-5370.

Experiments in support of proposed mechanism: Observation of azole-TBS adduct and H/D exchange

In the glovebox, an oven dried 4 mL vial equipped with a stirbar was charged with 5-chlorobenzoxazole (80 mg, 0.520 mmol) and DME (1.6 mL). 100 uL of this solution was diluted with 300 uL MeCN and then analyzed by UPLC/MS.

tert-Butyldimethylsilyl trifluoromethanesulfonate (0.120 mL, 0.520 mmol) was added to the solution, which was stirred for 5 min. 100 uL of the solution was diluted with 300 uL MeCN and analyzed by UPLC/MS.

Then, *N*-ethyl-*N*-isopropylpropan-2-amine (0.190 mL, 1.094 mmol) and trifluoromethanesulfonic acid-d₁ (0.046uL, 0.520 mmol) were added. The reaction was stirred at room temperature. After 2 h, 100 uL of the solution was diluted with 300 uL MeCN and analyzed by UPLC/MS.

KF (80 mg, 1.4 mmol) was added to convert any silylated azole back to the starting material and the mixture was heated to 50 C for 5 h. 100 uL of the resulting mixture was diluted with 300 uL MeCN and analyzed by UPLC/MS.

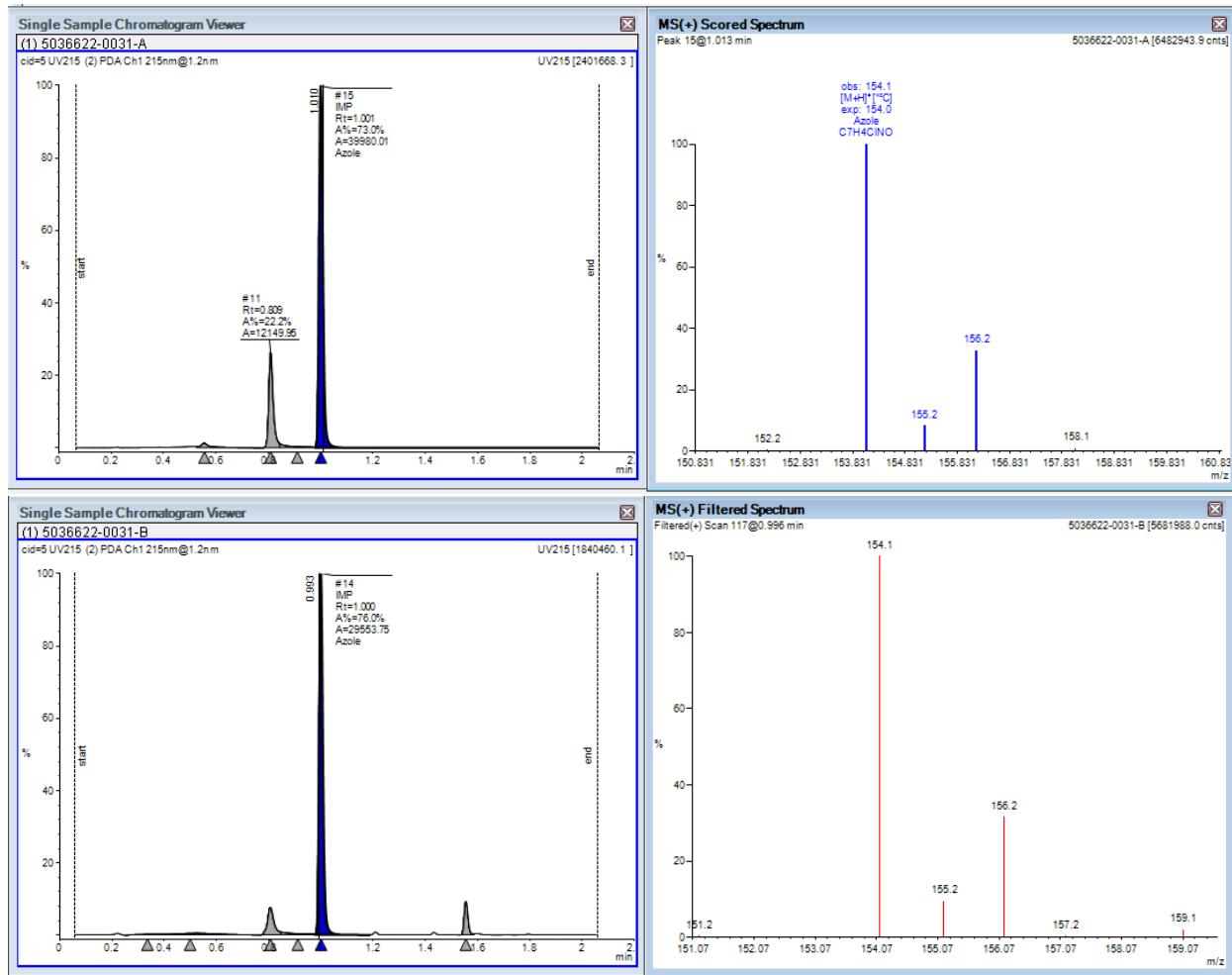


Figure 7. Left side: UPLCMS chromatograms of 4-chlorobenzoxazole in DME (top) and 4-chlorobenzoxazole + TBSOTf in DME. Right side: mass spectra of 4-chlorobenzoxazole peak at 1.0 min.

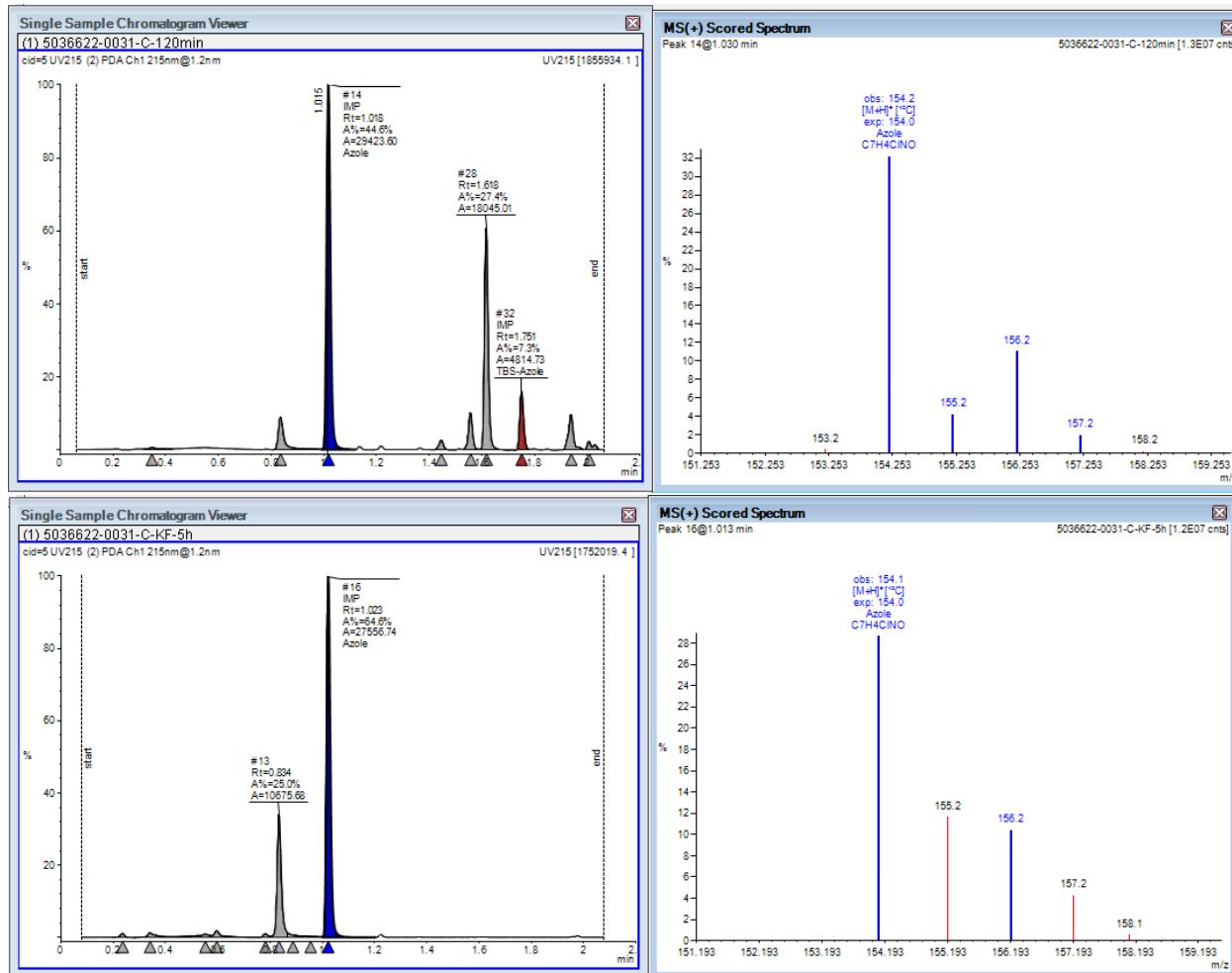
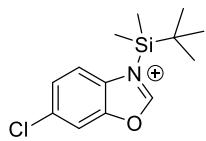


Figure 8. Left side: UPLCMS chromatograms of 4-chlorobenzoxazole + TBSOTf + TfOH-D1 + *i*Pr₂NEt in DME after 2 h (top) and after quenching with KF (bottom). Right side: mass spectra of 4-chlorobenzoxazole peak at 1.0 min showing an increase in the M+2 and M+4 peaks due to deuterium incorporation.

Table 1. Detailed H/D exchange results.

m/z	Calculated m/z abundance azole [M+H]	Measured azole starting material	Measured Azole + TBSOTf	Measured Azole + TBSOTf + TfOD+ <i>i</i> Pr ₂ NEt (2 h, RT)	Measured reaction mixture + KF (5 h @ 50 °C)
154	100%	100%	100%	100%	100%
155	7.6%	8%	10%	13%	41%
156	32.0%	33%	39%	34%	36%
157	2.4%	0%	2%	6%	15%



m/z: 268.09 (100.0%), 270.09 (32.0%),
269.10 (14.1%), 269.09 (5.1%), 271.09
(4.5%), 270.09 (3.3%), 271.09 (1.6%),
272.09 (1.1%)

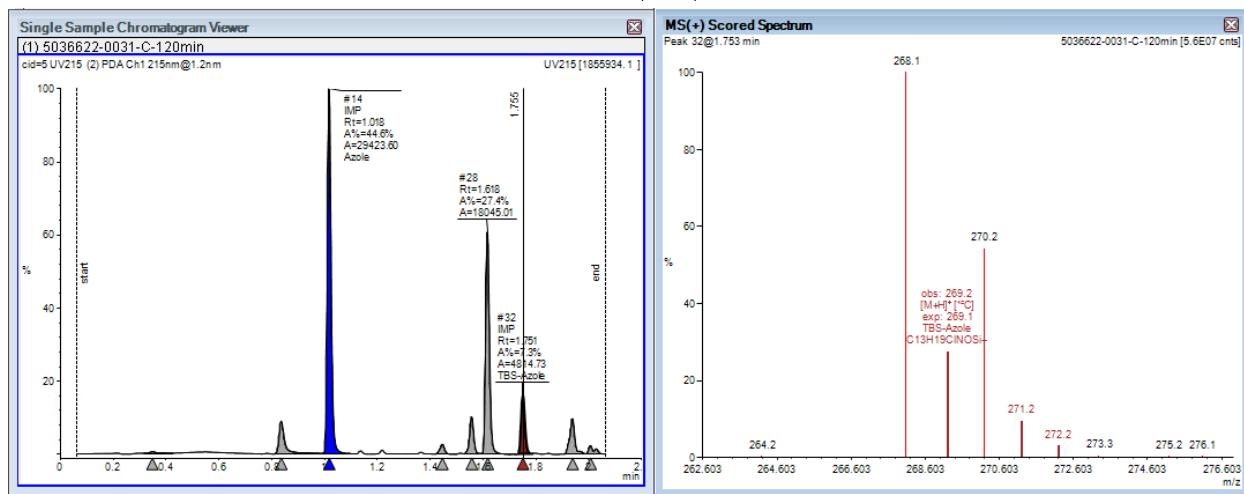
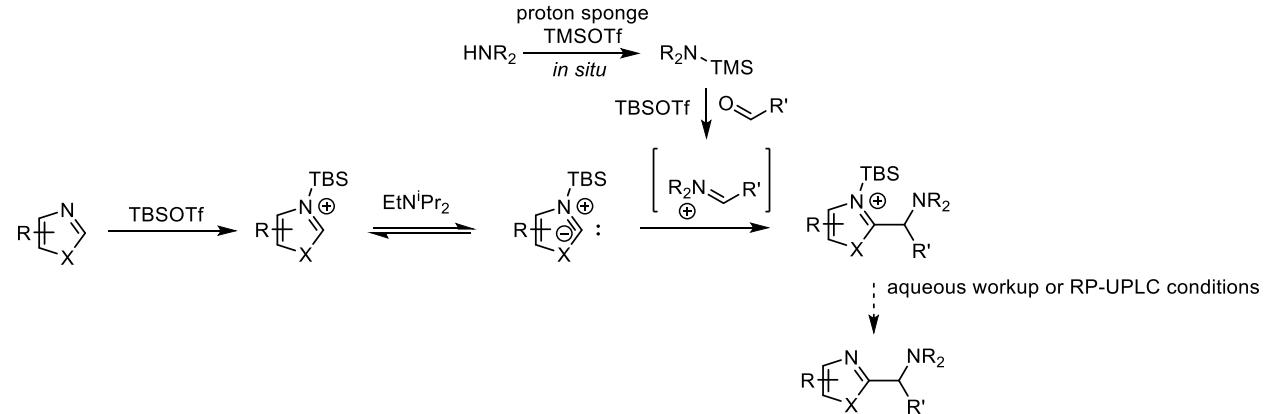


Figure 9. Mass Spectrum showing TBS-azole adduct m/z 268 at 1.75 min and predicted mass distribution for TBS-azole adduct.

DFT Results

Proposed Mechanism



Scheme 4. Proposed Mechanism

Computational Methods

All density functional theory (DFT) calculations were performed using Gaussian 16². Geometry optimizations and frequency calculations were performed at the M06-2X/6-31G(d) level of theory^{3,4}, with the SMD model⁵ to account for solvation effects. Normal vibrational mode analysis confirmed the optimized structures are minima or transition structures. Transition structures are verified by intrinsic reaction coordinate (IRC) calculations. Truhlar's quasiharmonic correction was used to compute molecular entropies to reduce error caused by the breakdown of the harmonic oscillator approximation, by setting all positive frequencies that are less than 100 cm⁻¹ to 100 cm⁻¹.⁶ M06-2X/def2TZVPP single-point energies were computed on the M06-2X-optimized structures. MacroModel⁷ was used to perform conformational searches with the OPLS3e force field.⁸ 3D renderings of stationary points were generated using CYLview 1.0⁹ and PyMOL 2.3¹⁰.

² Gaussian 16, Revision C.01, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams-Young, D.; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Ragahavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. Gaussian, Inc., Wallingford CT, 2016.

³ Zhao, Y.; Truhlar, D. G. *Theor. Chem. Acc.* 2008, 120, 215

⁴ Zhao, Y.; Truhlar, D. G. *Acc. Chem. Res.* 2008, 41, 157

⁵ Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem. B* 2009, 113, 6378

⁶ Zhao, Y.; Truhlar, D. G. *Phys. Chem. Chem. Phys.* 2008, 10, 2813

⁷ Schrödinger Release 2019-3: MacroModel, Schrödinger, LLC, New York, NY, 2019.

⁸ Roos, K.; Wu, C.; Damm, W.; Reboul, M.; Stevenson, J.M.; Lu, C.; Dahlgren, M.K.; Mondal, S.; Chen, W.; Wang, L.; Abel, R.; Friesner, R.A.; Harder, E.D., *J. Chem. Theory Comput.*, 2019, 1863–1874

⁹ Legault, C. Y. CYLview, version 1.0b; Université de Sherbrooke: Quebec, Canada, 2009; <http://www.cylview.org>.

¹⁰ The PyMOL Molecular Graphics System, Version 2.0 Schrödinger, LLC.

Calculated Transition States for C-C Bond Formation Step

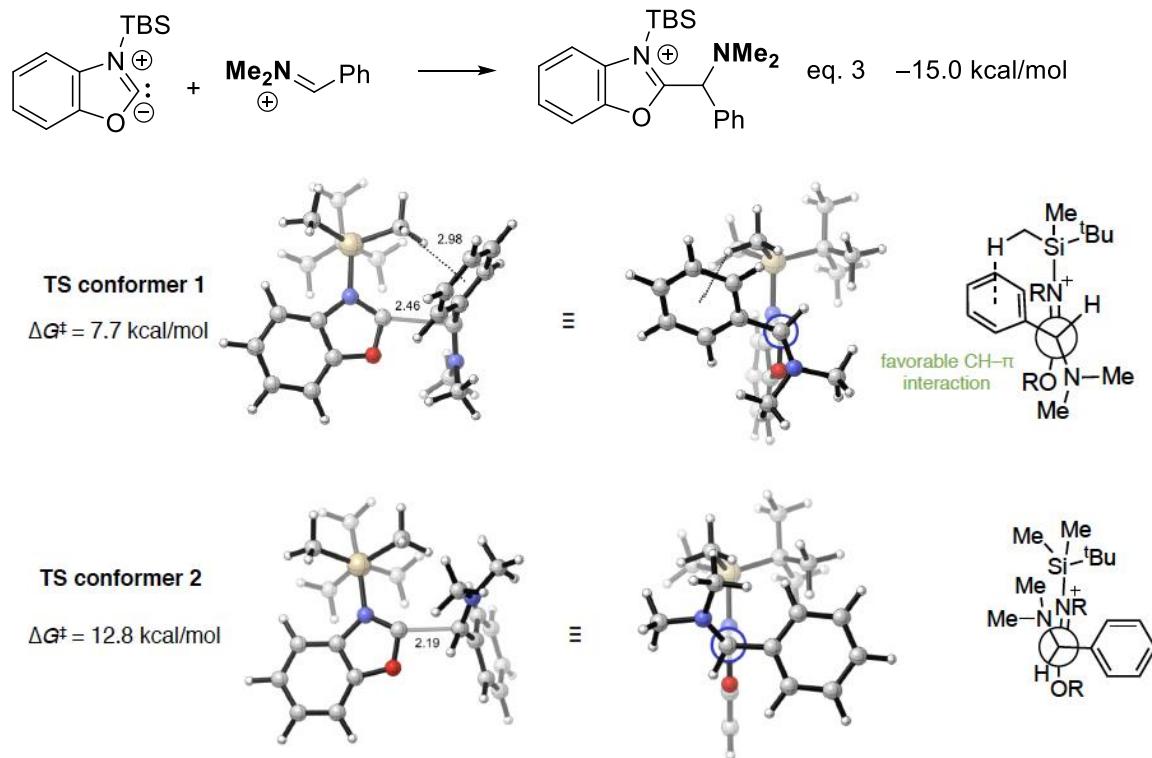
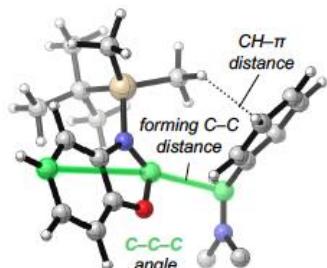


Figure 10. Important TS conformations about the C-C forming bond between **3** and the truncated N-benzylidene-N-methylmethanaminium.

Table 2. Key C-C bond forming distances and angles of the lowest energy transition state structures for 9 iminium electrophiles reacting with **3**.



TS	ΔG^\ddagger (kcal/mol)	C-C_distance (Å)	CH-π_distance (Å)	C-C-C_angle
Cy2NH	20.3	2.48	2.89	160.9
CyNH2	10.9	2.53	3.21	151.5
pyrrolidine	9.9	2.46	2.79	137.4
piperazine	9.8	2.47	2.87	159.6
azetidine	9.1	2.42	2.92	157.1
azepane	8.7	2.41	2.81	157.8
morpholine	8.5	2.48	2.91	156.3
Me2NH	7.7	2.46	2.98	156.3
Et2NH	7.6	2.45	2.79	159.4

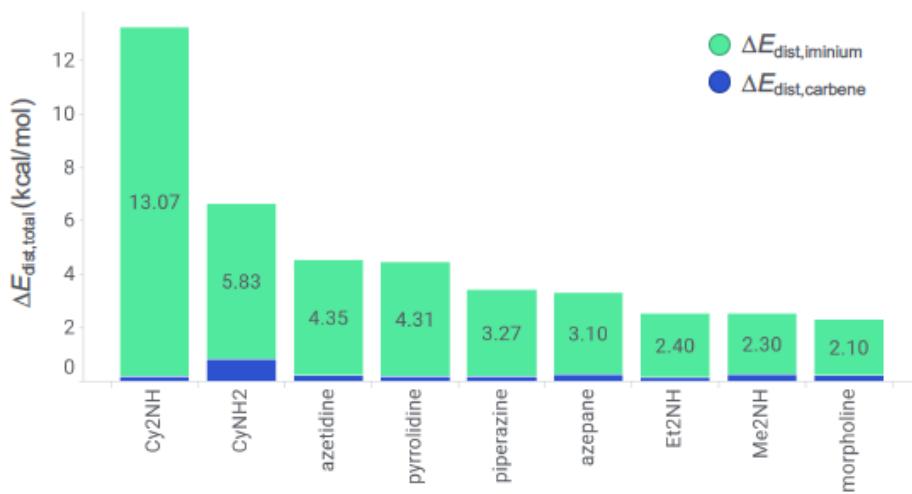


Figure 11. Distortion energies of silylated carbene **3** and 9 iminium electrophiles going from reactant to transition state geometries.

Insights into Azole Reactivity: Calculated Deprotonation Equilibria with Successful and Unsuccessful Substrates

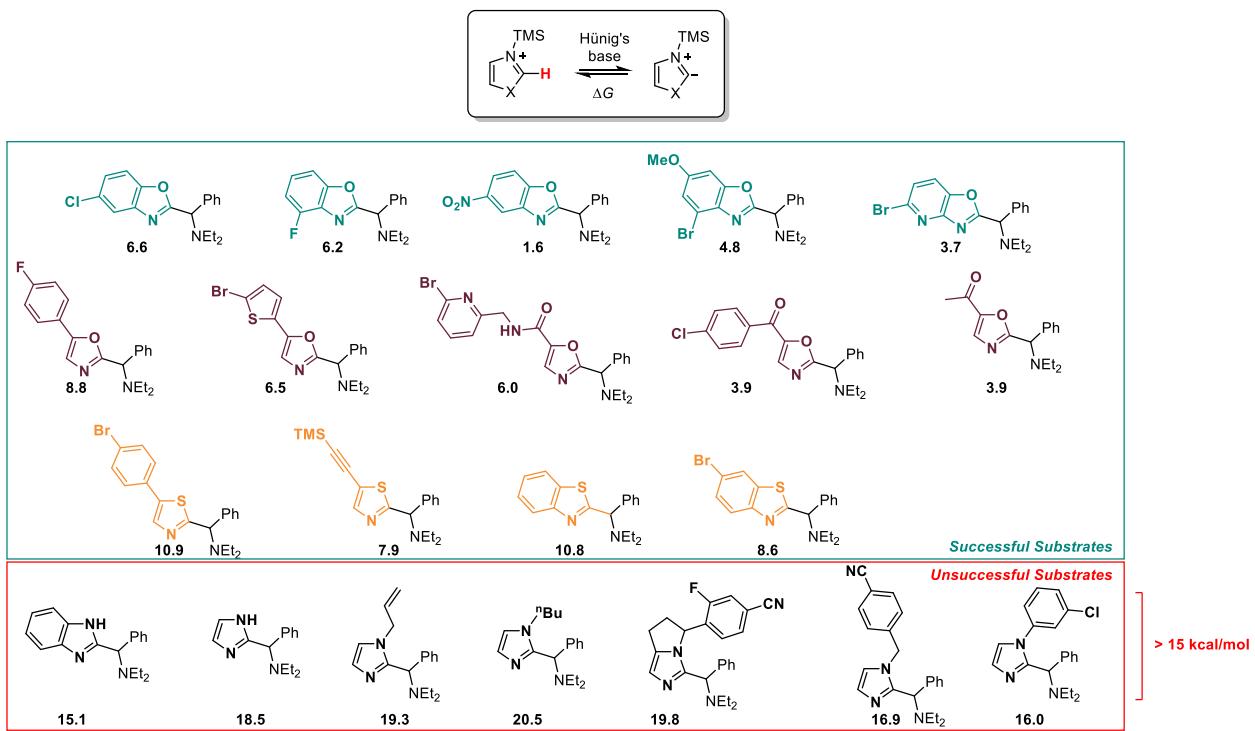


Figure 12. Calculated Free Enthalpies ΔG for Deprotonation of the Parent Azole Substrate for the Azole Substrate Scope. Desired products are shown. All numbers under the desired product are shown in kcal/mol.

Cartesian Coordinates for Transition State				H	-1.45834	-0.97664	-1.37397
Structures in the Amine Scope				H	4.26922	-2.35687	1.11114
azepane_TS				H	3.57995	-1.04675	2.07392
C	2.14353	4.10748	1.82519	H	4.83544	-0.70451	0.86498
C	3.94835	-1.30921	1.07620	H	0.99124	-2.67897	0.85847
C	1.42316	-2.57741	-0.14392	H	0.60244	-2.47504	-0.85963
C	3.29049	-0.83493	-1.95086	H	1.95740	-3.50716	-0.37296
Si	2.60891	-1.13958	-0.21811	C	2.14411	-0.81585	-2.97048
C	0.91163	3.62687	1.39041	C	4.26045	-1.97785	-2.28970
C	3.30644	3.32694	1.73834	C	4.04137	0.50234	-2.00512
C	3.28842	2.03592	1.21875	H	0.00391	4.21735	1.44322
O	-0.13534	1.61515	0.37140	N	-2.56031	0.43030	-0.42737
C	0.91701	2.34072	0.87743	C	-3.30939	0.94148	0.73367
C	2.05385	1.55170	0.79097	C	-4.60629	1.64223	0.33253
N	1.62017	0.33737	0.21942	C	-5.43345	0.89319	-0.72274
C	-1.49389	-1.31144	2.00749	C	-5.06196	1.26749	-2.16201
C	-1.41216	-2.31093	2.96976	C	-3.66845	0.82800	-2.61163
C	-1.63118	-3.64319	2.61641	C	-2.54384	1.23725	-1.66175
C	-1.92304	-3.97834	1.29649	H	-3.54004	0.08367	1.36741
C	-1.98857	-2.98266	0.32649	H	-2.65480	1.62010	1.29152
C	0.30246	0.39756	-0.03146	H	-5.18145	1.74798	1.25788
C	-1.79002	-1.64509	0.68099	H	-4.40134	2.66121	-0.01566
C	-1.83530	-0.65173	-0.40865	H	-5.33547	-0.19132	-0.57298
H	2.20664	5.10959	2.23612	H	-6.49075	1.13229	-0.57190
H	4.24755	3.74198	2.08357	H	-5.79772	0.83783	-2.85029
H	4.19495	1.44544	1.15124	H	-5.14020	2.35794	-2.26359
H	-1.29751	-0.27740	2.27706	H	-3.63294	-0.26262	-2.73059
H	-1.17157	-2.05203	3.99585	H	-3.45067	1.26048	-3.59409
H	-1.56569	-4.42058	3.37134	H	-1.56344	1.08846	-2.12298
H	-2.08579	-5.01455	1.01838	H	-2.61821	2.28932	-1.37492
H	-2.19271	-3.24220	-0.70928				

H	1.40612	-0.03685	-2.73925	C	3.87182	-0.43594	-1.40102
H	2.53781	-0.60997	-3.97477	C	3.65689	-2.93197	-1.29756
H	1.62167	-1.77869	-3.01224	H	2.30196	-1.20435	2.63171
H	5.11168	-2.00832	-1.59906	H	3.81821	-1.29668	1.71157
H	3.76733	-2.95727	-2.26438	H	2.87549	-2.75689	2.01464
H	4.66288	-1.83998	-3.30204	H	0.14739	4.45445	0.55956
H	4.86787	0.54006	-1.28507	C	-2.73532	-0.45973	1.37125
H	4.47299	0.64749	-3.00456	C	-3.13387	-1.26054	2.43508
H	3.37799	1.35245	-1.80660	C	-3.51222	-2.58503	2.21135
azetidine_TS				C	-3.48202	-3.11480	0.92331
C	2.08816	4.01761	1.44154	C	-3.06981	-2.32196	-0.14306
C	0.35188	-2.64713	0.17864	C	-2.70795	-0.98974	0.07694
C	2.88069	-1.60651	-1.34645	H	-2.40595	0.55900	1.55252
C	2.79892	-1.68793	1.78364	H	-3.14232	-0.85429	3.44140
Si	1.81445	-1.49079	0.20572	H	-3.82255	-3.20647	3.04559
C	0.89711	3.70644	0.79167	H	-3.76835	-4.14696	0.74970
C	3.04680	3.03279	1.72419	H	-3.02926	-2.73280	-1.14825
C	2.85654	1.69926	1.37399	C	-2.30182	-0.19475	-1.09332
O	-0.32963	1.78162	-0.19309	N	-2.75354	0.99236	-1.33188
C	0.72892	2.37434	0.45349	C	-2.55649	1.87766	-2.49164
C	1.66163	1.38631	0.72911	C	-3.46067	2.92444	-1.80224
N	1.10201	0.19551	0.22063	C	-3.50553	2.00328	-0.56118
C	-0.09271	0.45323	-0.33536	H	-1.85306	-0.70802	-1.93965
H	2.28094	5.04486	1.73241	H	-2.92334	1.43778	-3.42092
H	3.96375	3.31838	2.22906	H	-1.50472	2.15970	-2.59056
H	3.60778	0.94957	1.59395	H	-4.42735	3.05326	-2.28749
H	0.70055	-3.68662	0.18620	H	-2.99399	3.89370	-1.63427
H	-0.26832	-2.50290	-0.71039	H	-2.93449	2.37101	0.29321
H	-0.27992	-2.49866	1.06192	H	-4.48252	1.63701	-0.23839
C	1.99126	-1.57871	-2.59664	H	1.38327	-0.66620	-2.64414

H	2.61309	-1.60900	-3.50131	C	-2.27979	0.06259	-0.00000
H	1.31455	-2.44045	-2.63214	N	-1.60538	1.15703	-0.00000
H	4.52120	-0.40220	-0.51741	H	3.05682	1.21100	-0.00000
H	4.52265	-0.53848	-2.27972	H	3.02923	-1.24899	0.00000
H	3.35821	0.52938	-1.48209	H	0.87227	-2.51498	0.00000
H	4.33290	-2.97758	-0.43537	H	0.93313	2.52295	-0.00000
H	2.98692	-3.79929	-1.24985	H	-3.35571	-0.05140	-0.00000
H	4.26932	-3.04095	-2.20248	bzox-tms-imin-adduct			
bzoxazole-1-				C	-2.90245	3.66851	0.06801
H	-0.86449	2.51811	0.00000	C	-3.68518	-1.69290	-0.90577
H	-0.85926	-2.50084	-0.00000	C	-0.97267	-2.79303	-1.56938
H	-3.00980	-1.22536	0.00000	C	-1.95616	-2.65553	1.45904
H	-3.01028	1.24166	0.00000	Si	-1.94825	-1.91605	-0.24746
N	1.66136	1.13483	0.00000	C	-1.55262	3.42944	-0.15408
C	2.44890	0.07391	-0.00001	C	-3.81214	2.61514	0.26014
O	1.58692	-1.10786	-0.00000	C	-3.42485	1.28163	0.22127
C	-0.86687	1.43110	0.00000	O	0.06919	1.57155	-0.33747
C	0.33448	0.72101	0.00000	C	-1.19330	2.09375	-0.18449
C	0.31301	-0.68218	-0.00000	C	-2.07423	1.03268	-0.02660
C	-0.86723	-1.41470	-0.00000	N	-1.29113	-0.14300	-0.12083
C	-2.06331	-0.69133	0.00000	C	2.75160	1.14135	0.71078
C	-2.06247	0.70978	0.00000	C	3.99389	1.76544	0.77058
bzoxazole				C	4.98963	1.43745	-0.14802
C	2.10153	0.69585	-0.00000	C	4.73901	0.48328	-1.12989
C	2.08692	-0.71046	0.00000	C	3.49496	-0.13975	-1.19057
C	0.89673	-1.43105	0.00000	C	-0.04256	0.25886	-0.27406
C	-0.26065	-0.66778	0.00000	C	2.49179	0.18174	-0.27425
C	-0.27408	0.72742	-0.00000	C	1.19000	-0.60309	-0.33840
C	0.92683	1.43804	-0.00000	C	1.03973	-1.20087	2.04192
O	-1.56038	-1.08818	0.00000	C	1.98434	-2.73793	0.46875

N	1.01186	-1.66502	0.65711	C	2.59660	-2.00540	-1.04478
H	-3.25984	4.69168	0.10698	Si	1.49486	-1.57006	0.42388
H	-4.85400	2.84894	0.45097	C	1.19111	3.73431	0.33474
H	-4.14336	0.49184	0.39074	C	3.15918	2.95018	1.54141
H	1.98482	1.41304	1.43093	C	2.83722	1.61230	1.33147
H	4.18340	2.51098	1.53649	O	-0.17505	1.84856	-0.53679
H	5.95709	1.92739	-0.09867	C	0.89079	2.39728	0.13693
H	5.50840	0.22419	-1.85043	C	1.66985	1.35461	0.61601
H	3.29932	-0.88355	-1.95958	N	1.01166	0.17934	0.19966
H	1.15801	-1.09979	-1.31901	C	-2.85975	0.34458	1.15000
H	0.31047	-0.39717	2.19722	C	-3.37585	-0.14186	2.34492
H	0.75785	-2.03619	2.68860	C	-3.96715	-1.40513	2.39059
H	2.03237	-0.84494	2.35360	C	-4.02959	-2.19204	1.24294
H	1.69415	-3.58798	1.09316	C	-3.49682	-1.71800	0.04846
H	3.00548	-2.43411	0.74456	C	-0.09205	0.49345	-0.49786
H	1.99228	-3.05728	-0.57761	C	-2.92892	-0.44098	-0.00712
H	-3.76341	-0.91165	-1.66911	C	-2.36586	-0.01876	-1.29981
H	-4.43135	-1.50747	-0.12902	C	-3.31768	2.23843	-1.29787
H	-3.95949	-2.64049	-1.38584	C	-1.97673	1.39820	-3.18651
H	-0.81042	-2.15521	-2.44569	N	-2.59762	1.11363	-1.89389
H	-0.01548	-3.18308	-1.22185	H	2.64457	5.01954	1.24448
H	-1.57711	-3.64379	-1.90644	H	4.05980	3.19408	2.09524
H	-1.02085	-3.17529	1.67907	H	3.47010	0.81791	1.70983
H	-2.78109	-3.37305	1.53417	H	-2.37338	1.31567	1.12298
H	-2.11758	-1.88752	2.22374	H	-3.31175	0.46188	3.24430
H	-0.82562	4.22191	-0.28665	H	-4.36961	-1.77931	3.32667
bzox-TS				H	-4.47915	-3.17894	1.27916
C	2.35364	3.99142	1.05625	H	-3.52040	-2.33639	-0.84506
C	2.38703	-1.69579	2.06222	H	-1.91713	-0.79227	-1.91396
C	-0.10962	-2.52283	0.45019	H	-3.84629	2.75719	-2.09912

H	-4.03559	1.88014	-0.56201	C	2.68144	0.59794	3.37237
H	-2.60593	2.92553	-0.83160	C	4.56397	-0.36647	2.15770
H	-2.75286	1.67043	-3.90519	C	3.80190	-0.58725	1.01493
H	-1.43195	0.52122	-3.53657	O	0.62504	0.66579	1.97908
H	-1.28336	2.23505	-3.06363	C	1.94462	0.37295	2.22171
H	2.33886	-2.73453	2.40923	C	2.46339	-0.20359	1.07372
H	1.91370	-1.07242	2.82861	N	1.39185	-0.24260	0.15529
H	3.44480	-1.42237	1.99743	C	0.30246	0.30292	0.71875
H	-0.74494	-2.18780	1.27812	H	4.65044	0.36271	4.18180
H	-0.67349	-2.40285	-0.47984	H	5.61125	-0.64961	2.15423
H	0.09010	-3.59137	0.59228	H	4.23476	-1.03670	0.12847
C	3.19118	-3.40180	-0.80466	H	-0.05890	0.81130	-2.42901
C	3.73325	-0.98208	-1.17579	H	-1.02616	-0.53737	-1.77947
C	1.76908	-2.01647	-2.33697	H	-0.22699	-0.68591	-3.35574
H	0.55896	4.52560	-0.05261	H	3.17100	0.72056	-2.06857
H	3.81899	-3.69384	-1.65700	H	3.85212	-0.91737	-2.13362
H	3.82180	-3.42810	0.09202	H	2.82640	-0.33155	-3.44570
H	2.41280	-4.16695	-0.69470	C	2.56891	-3.37487	-0.57874
H	4.39888	-1.26663	-2.00167	C	1.45947	-3.39703	-2.82002
H	3.35377	0.02392	-1.39041	C	0.07649	-3.29946	-0.72943
H	4.34630	-0.92772	-0.26774	H	2.24108	1.04829	4.25456
H	2.41748	-2.23206	-3.19676	C	-1.19305	3.04838	-1.65328
H	0.98943	-2.78678	-2.31052	C	-0.53447	4.09062	-2.29670
H	1.28605	-1.04797	-2.52082	C	0.46327	4.80464	-1.63519
cy1_TS				C	0.79822	4.48193	-0.32113
C	4.01688	0.21152	3.31421	C	0.14194	3.44211	0.32516
C	-0.12393	-0.27817	-2.34375	C	-0.85137	2.71102	-0.33856
C	2.96615	-0.31574	-2.35867	H	-1.97482	2.51717	-2.18883
C	1.38204	-2.83761	-1.38902	H	-0.80552	4.34888	-3.31519
Si	1.41432	-0.95433	-1.53489	H	0.97373	5.61765	-2.14178

H	1.56726	5.04204	0.20068	H	-0.01617	-2.91602	0.29443	
H	0.39712	3.19008	1.35114	H	-0.80548	-2.98011	-1.29754	
C	-1.53063	1.63698	0.41239	cy2_TS				
N	-2.57648	1.00189	-0.05212	C	-2.32704	-3.51803	2.95934	
C	-3.32944	0.00464	0.71598	C	-4.74697	1.31875	0.95153	
C	-4.83171	0.23969	0.57070	C	-2.46028	2.43081	-0.78266	
C	-5.61366	-0.82558	1.34533	C	-4.20043	0.07854	-1.87419	
C	-5.22474	-2.23864	0.90373	Si	-3.46584	0.91882	-0.35189	
C	-3.71704	-2.46207	1.03981	C	-1.17752	-3.05114	2.32822	
C	-2.93502	-1.40161	0.26146	C	-3.57316	-2.90605	2.75549	
H	-1.44427	1.66143	1.49499	C	-3.72372	-1.80385	1.91883	
H	-2.76937	1.02591	-1.05134	O	-0.41003	-1.29206	0.74979	
H	-3.03719	0.14165	1.76429	C	-1.35124	-1.95476	1.50069	
H	-5.09389	0.18499	-0.49582	C	-2.57223	-1.33177	1.29174	
H	-5.08527	1.24580	0.92052	N	-2.30111	-0.27852	0.39321	
H	-6.68736	-0.66237	1.20911	C	-0.99405	-0.27344	0.07480	
H	-5.40817	-0.71151	2.41829	H	-2.25906	-4.37530	3.62081	
H	-5.51778	-2.38347	-0.14516	H	-4.44591	-3.30399	3.26272	
H	-5.77198	-2.98131	1.49344	H	-4.69465	-1.34638	1.76685	
H	-3.43839	-3.45915	0.68281	H	-5.55619	0.58420	1.00890	
H	-3.43497	-2.41174	2.10012	H	-5.20147	2.28696	0.71129	
H	-1.85546	-1.53197	0.38839	H	-4.29248	1.40850	1.94435	
H	-3.15812	-1.49556	-0.81195	H	-2.02481	2.88668	0.11345	
H	2.54674	-4.47293	-0.57897	H	-1.64844	2.20679	-1.48065	
H	3.53247	-3.06954	-1.00367	H	-3.11247	3.17686	-1.25247	
H	2.53485	-3.04702	0.46621	C	-3.11044	-0.11512	-2.93661	
H	1.43233	-4.49426	-2.79111	C	-5.30941	0.98320	-2.43404	
H	0.61752	-3.06579	-3.43944	C	-4.79814	-1.28576	-1.50461	
H	2.38884	-3.10535	-3.32408	H	-0.20612	-3.51267	2.46844	
H	0.05352	-4.39606	-0.67361	C	0.53121	2.15346	1.35832	

C	0.43574	3.35619	2.05200	H	4.26340	1.25054	3.01068
C	0.67411	4.56434	1.39856	H	5.76630	0.32856	2.96904
C	0.99236	4.57183	0.04207	H	3.78449	-1.16513	3.33493
C	1.07863	3.37282	-0.65857	H	4.62307	-1.55422	1.83511
C	0.87404	2.15873	0.00464	H	2.17903	-1.52597	1.44314
H	0.31293	1.21714	1.86048	H	2.06626	0.11292	2.09231
H	0.16566	3.34874	3.10318	H	0.83096	-0.93165	-2.23046
H	0.59835	5.50008	1.94349	H	2.80786	0.36088	-3.21111
H	1.16365	5.51092	-0.47427	H	2.40571	-1.21491	-3.88419
H	1.31708	3.37705	-1.71927	H	4.77913	-0.65465	-2.03190
C	0.97810	0.93843	-0.82778	H	4.80878	-1.06555	-3.73346
N	1.90834	0.03173	-0.78146	H	5.27719	-3.07840	-2.31872
C	3.05415	-0.00293	0.17206	H	3.82828	-3.27661	-3.30059
C	3.81706	1.32239	0.27144	H	3.92566	-2.62618	-0.31115
C	5.12006	1.08089	1.04063	H	3.35158	-4.09928	-1.05413
C	4.83034	0.50957	2.43038	H	1.47698	-3.07381	-2.08204
C	4.01911	-0.78405	2.33580	H	1.42905	-2.58117	-0.40106
C	2.71803	-0.57968	1.54978	H	-2.27831	-0.72293	-2.55818
C	1.85053	-1.02051	-1.84711	H	-3.52524	-0.63121	-3.81281
C	2.82197	-0.71477	-3.00036	H	-2.70418	0.84351	-3.28004
C	4.25226	-1.22880	-2.80455	H	-6.12556	1.11955	-1.71433
C	4.25190	-2.71917	-2.45369	H	-4.93160	1.97485	-2.71106
C	3.42041	-3.01626	-1.20249	H	-5.73995	0.53229	-3.33810
C	1.99414	-2.46391	-1.33025	H	-5.58179	-1.19921	-0.74190
H	0.37055	0.93687	-1.72677	H	-5.25646	-1.74440	-2.39124
H	3.74249	-0.70321	-0.29729	H	-4.03574	-1.97988	-1.13175
H	3.23071	2.07621	0.80432	etnipr2_1			
H	4.01961	1.70685	-0.73572	N	0.00232	0.27293	-0.21486
H	5.67534	2.02086	1.11994	C	-1.03427	-0.77057	-0.19864
H	5.75460	0.37964	0.48061	C	-0.30903	1.45644	0.57924

C	1.38475	-0.19731	-0.05867	C	-1.75515	-0.72435	1.26789
C	-1.66415	-1.06642	1.17155	C	-2.17286	-0.40266	-1.19951
C	-2.12294	-0.42572	-1.21584	C	0.61735	2.69386	-0.12250
C	0.27438	2.73065	-0.02478	C	1.50131	-1.10096	1.27681
C	1.64864	-1.06440	1.17945	C	1.75434	-1.23605	-1.23483
C	1.86230	-0.90546	-1.32680	H	-0.70686	-1.70577	-0.32876
H	-0.54760	-1.69129	-0.53984	H	0.05860	1.37293	1.51991
H	0.01817	1.35455	1.63005	H	-1.25335	1.78046	0.40418
H	-1.39740	1.56793	0.60818	H	2.07922	0.50050	-0.02838
H	1.99188	0.70929	0.04566	H	-1.01507	-0.83092	2.06283
H	-0.91094	-1.26321	1.93898	H	-2.34731	0.17633	1.45056
H	-2.28827	-0.23379	1.51412	H	-2.43316	-1.58019	1.32652
H	-2.31019	-1.94816	1.09931	H	-3.00117	-1.11177	-1.12457
H	-2.88432	-1.21230	-1.26079	H	-2.58104	0.60569	-1.07040
H	-2.62747	0.50990	-0.94622	H	-1.74503	-0.48869	-2.20382
H	-1.68678	-0.29996	-2.21117	H	0.34033	3.61490	0.39663
H	-0.02444	3.60455	0.56369	H	1.69561	2.56416	-0.00964
H	1.36816	2.71318	-0.05511	H	0.38448	2.82817	-1.18396
H	-0.09015	2.85651	-1.04903	H	1.23794	-0.47924	2.13659
H	1.31901	-0.56728	2.09806	H	0.88311	-2.00352	1.28101
H	1.13435	-2.02950	1.10536	H	2.54218	-1.41132	1.40226
H	2.72082	-1.26740	1.27594	H	2.78869	-1.57218	-1.12640
H	2.93281	-1.12751	-1.26186	H	1.12051	-2.12594	-1.29174
H	1.34055	-1.85646	-1.48240	H	1.67852	-0.68356	-2.17745
H	1.68752	-0.27270	-2.20201	H	0.02656	0.52037	-1.26664
Hetnipr2_1				morpholine_TS			
N	0.02235	0.25951	-0.27235	C	-1.71494	4.02119	2.05226
C	-1.14288	-0.72524	-0.12683	C	-1.30676	-2.58622	-0.18990
C	-0.18870	1.55352	0.47240	C	-3.22274	-0.75473	-1.86669
C	1.40172	-0.35596	-0.04381	C	-3.75260	-1.29922	1.16888

Si	-2.46721	-1.12494	-0.17800	H	1.93925	-4.28665	3.34812
C	-0.54089	3.53956	1.47985	H	2.26037	-5.04002	1.00550
C	-2.89633	3.26445	2.04639	H	2.27296	-3.38439	-0.83491
C	-2.95487	1.99719	1.47346	C	2.00754	-0.76676	-0.66861
O	0.36141	1.55816	0.27873	N	2.72940	0.30600	-0.79436
C	-0.62214	2.27764	0.91591	C	3.59152	0.89153	0.24376
C	-1.77821	1.51194	0.90680	C	4.91914	1.29921	-0.38914
N	-1.42627	0.31780	0.24458	C	3.99044	1.52973	-2.50095
C	-0.13805	0.36392	-0.13332	C	2.60539	1.14027	-2.00084
H	-1.71699	5.00491	2.50986	H	1.52972	-1.11707	-1.57755
H	-3.79083	3.67880	2.49962	H	3.07614	1.76658	0.65335
H	-3.87464	1.42395	1.47269	H	3.75943	0.15988	1.03301
H	-1.86248	-3.50339	-0.41792	H	5.52035	1.82986	0.35206
H	-0.51486	-2.47519	-0.93636	H	5.46491	0.39994	-0.71155
H	-0.83489	-2.71529	0.79114	H	3.89468	2.23475	-3.32908
C	-2.13533	-0.78426	-2.94894	H	4.52614	0.63553	-2.85315
C	-3.89143	0.62686	-1.85307	H	2.04861	0.58486	-2.75878
C	-4.27772	-1.83003	-2.16986	H	2.03890	2.03336	-1.71522
H	-3.32403	-1.11793	2.16062	O	4.72318	2.17159	-1.47965
H	-4.61196	-0.63488	1.03598	H	-2.56738	-0.51893	-3.92309
H	-4.13081	-2.32821	1.15904	H	-1.32922	-0.06954	-2.73820
H	0.37941	4.11259	1.46969	H	-1.68928	-1.78099	-3.04657
C	1.83328	-1.26720	1.79897	H	-4.38255	0.81365	-2.81754
C	1.80182	-2.20277	2.82574	H	-4.66084	0.70514	-1.07505
C	1.96419	-3.55960	2.54238	H	-3.16329	1.43070	-1.69276
C	2.14453	-3.98435	1.22826	H	-4.71376	-1.65864	-3.16303
C	2.15696	-3.05378	0.19383	H	-3.84798	-2.83945	-2.17125
C	2.02139	-1.69102	0.47779	H	-5.09844	-1.81194	-1.44301
H	1.67762	-0.21420	2.01638	ph-iminium			
H	1.64306	-1.87447	3.84778	H	3.96254	-0.65576	0.73714

H	3.34089	-1.60460	-0.65007	O	0.69874	-1.17880	0.34565
H	3.96026	0.05377	-0.89958	C	-0.04009	-2.12029	1.02220
H	2.98436	1.41149	1.19772	C	-1.36194	-1.70169	1.01612
H	2.14187	2.03853	-0.23933	N	-1.35976	-0.47976	0.31136
H	1.20222	1.47037	1.17818	C	-0.11119	-0.18428	-0.09061
H	1.21374	-1.76770	-0.54013	H	-0.31890	-4.99091	2.71275
H	-0.10391	1.76559	-0.66374	H	-2.67672	-4.28455	2.71454
H	-2.50091	2.29085	-0.46728	H	-3.39252	-2.17492	1.63214
H	-4.12172	0.52044	0.14826	H	-2.85248	3.03979	-0.47647
H	-3.34672	-1.80658	0.52535	H	-1.30467	2.39507	-1.04967
H	-0.93985	-2.35477	0.30141	H	-1.58239	2.62514	0.68673
N	2.09254	-0.04895	0.02322	C	-3.74054	-1.54544	-1.65640
C	3.42883	-0.61048	-0.21426	C	-4.77222	0.70571	-2.04576
C	2.09494	1.31146	0.57510	C	-2.45904	0.22000	-2.88524
C	1.03219	-0.74001	-0.23027	H	-4.63004	1.39130	1.26772
C	-0.35592	-0.32188	-0.12998	H	-3.49663	0.46708	2.25842
C	-0.80061	0.99004	-0.36622	H	-4.66203	-0.37242	1.21277
C	-2.15431	1.28159	-0.27204	H	1.43688	-3.59029	1.60176
C	-3.06599	0.28118	0.06699	C	1.36167	2.04895	1.59933
C	-2.63346	-1.02718	0.27994	C	1.12603	3.00210	2.58315
C	-1.28574	-1.33454	0.15901	C	0.89692	4.33220	2.22932
piperazine_TS				C	0.89436	4.70858	0.88858
C	-0.59354	-4.05964	2.22860	C	1.11438	3.75507	-0.10141
C	-2.05373	2.32204	-0.25530	C	1.36411	2.42624	0.25259
C	-3.46066	-0.03956	-1.75221	H	1.51638	1.00852	1.87213
C	-3.99884	0.49506	1.28523	H	1.11382	2.70553	3.62692
Si	-2.76852	0.60391	-0.11882	H	0.71243	5.07285	3.00103
C	0.39415	-3.29265	1.61700	H	0.70810	5.74088	0.61071
C	-1.93718	-3.65578	2.22977	H	1.09074	4.04054	-1.14986
C	-2.35063	-2.47248	1.62431	C	1.56351	1.46927	-0.85501

N	2.62137	0.73760	-1.03151	C	1.04649	-2.59023	-0.15347
C	3.77279	0.64364	-0.11892	C	3.26637	-0.89576	-1.56567
C	4.09969	-0.81404	0.17225	C	3.26206	-1.28786	1.53933
N	4.34863	-1.52631	-1.07336	Si	2.22677	-1.15265	-0.01306
C	4.76792	-2.89427	-0.81600	C	0.22348	3.63631	1.10733
C	3.15660	-1.49954	-1.90974	C	2.47551	3.34490	1.99396
C	2.78462	-0.06291	-2.25686	C	2.57459	2.04799	1.49828
H	0.91326	1.56971	-1.71733	O	-0.56807	1.61117	-0.09703
H	3.56751	1.20176	0.79171	C	0.34425	2.34464	0.62352
H	4.61588	1.10643	-0.64309	C	1.47060	1.55653	0.80479
H	3.27785	-1.27163	0.75145	N	1.17531	0.33491	0.16468
H	5.00574	-0.84171	0.78516	C	-0.05254	0.38665	-0.37890
H	3.99644	-3.47913	-0.28346	H	1.29322	5.13124	2.20894
H	4.98565	-3.39495	-1.76377	H	3.31368	3.76467	2.54029
H	5.67829	-2.89028	-0.20980	H	3.47144	1.45835	1.64798
H	2.30239	-1.99737	-1.41956	H	1.61069	-3.51884	-0.30076
H	3.36607	-2.02796	-2.84507	H	0.35525	-2.47577	-0.99371
H	3.58827	0.39772	-2.84057	H	0.45640	-2.70091	0.76362
H	1.85025	-0.02500	-2.82016	C	2.36947	-0.94808	-2.80933
H	-4.18794	-1.90227	-2.59382	C	3.98463	0.45930	-1.51097
H	-2.82254	-2.12124	-1.48915	C	4.30880	-2.02275	-1.63568
H	-4.44393	-1.78341	-0.84923	H	2.69029	-1.01050	2.43172
H	-5.18578	0.37192	-3.00672	H	4.17275	-0.68172	1.50900
H	-5.53066	0.51436	-1.27730	H	3.57077	-2.33291	1.66069
H	-4.62326	1.79050	-2.11291	H	-0.67260	4.22530	0.94634
H	-2.84583	-0.18520	-3.82981	C	-2.05268	-1.13178	1.59089
H	-2.28390	1.29208	-3.03378	C	-2.08692	-2.03226	2.64917
H	-1.49113	-0.26072	-2.69155	C	-2.31004	-3.38881	2.41065
pyrrolidine_TS				C	-2.48434	-3.84947	1.10800
C	1.32445	4.12462	1.80539	C	-2.43064	-2.95495	0.04367

C	-2.23378	-1.59047	0.28126		tms-bzoxazole-1-		
H	-1.84121	-0.08498	1.78462	H	-1.30493	-2.01184	-1.57976
H	-1.93320	-1.67512	3.66237	H	-1.99185	-0.62645	-2.44277
H	-2.33739	-4.08713	3.24137	H	-3.05780	-1.77194	-1.61303
H	-2.64752	-4.90525	0.91756	H	-1.99187	-0.62640	2.44278
H	-2.54175	-3.31443	-0.97583	H	-3.05777	-1.77194	1.61306
C	-2.18459	-0.72000	-0.90831	H	-1.30490	-2.01179	1.57981
H	-1.74351	-1.13857	-1.80862	H	-3.19526	1.78391	0.88462
N	-2.88096	0.35786	-1.07765	H	-4.29339	0.70728	-0.00001
C	-3.69716	1.06254	-0.06107	H	-3.19526	1.78389	-0.88466
C	-4.17664	2.32307	-0.78901	H	0.53270	-2.22635	-0.00001
C	-4.13925	1.93837	-2.27089	H	3.87647	1.53195	0.00001
C	-2.87552	1.09261	-2.35846	H	4.61943	-0.86046	0.00001
H	-3.09244	1.29689	0.81379	H	2.97268	-2.69109	-0.00000
H	-4.51703	0.40052	0.23264	C	-2.09436	-1.25322	-1.55025
H	-5.16638	2.63094	-0.44839	C	-2.09435	-1.25319	1.55028
H	-3.47653	3.14295	-0.60098	C	-3.28910	1.14706	-0.00001
H	-5.01199	1.33305	-2.53514	Si	-2.01514	-0.21113	0.00000
H	-4.09940	2.80267	-2.93559	N	-0.38600	0.57556	-0.00001
H	-1.97036	1.71104	-2.38449	C	-0.22485	1.92259	-0.00000
H	-2.85407	0.38241	-3.18640	O	1.12348	2.13305	-0.00000
H	1.57620	-0.19065	-2.77237	C	1.25211	-1.41363	-0.00001
H	2.96634	-0.75927	-3.71166	C	0.85810	-0.07827	-0.00001
H	1.89627	-1.93006	-2.92580	C	1.79776	0.94196	-0.00000
H	4.62812	0.54959	-0.62724	C	3.16415	0.71434	0.00000
H	4.62642	0.57733	-2.39438	C	3.56081	-0.62152	0.00000
H	3.27721	1.29679	-1.50386	C	2.62271	-1.66381	-0.00000
H	4.99820	-1.99401	-0.78341		tms-bzoxazole		
H	3.84175	-3.01506	-1.66054	C	2.60523	1.68294	0.00000
H	4.90993	-1.92100	-2.54898	C	3.55559	0.64520	0.00000

C	3.18447	-0.69366	-0.00000	Si	-1.40918	0.17589	0.73179
C	1.81855	-0.91783	-0.00000	C	3.73443	0.51319	-0.46997
C	0.86541	0.09126	-0.00001	C	3.11491	-1.73784	0.22753
C	1.23948	1.43340	-0.00000	C	1.78791	-1.37273	0.44259
O	1.15238	-2.12400	0.00000	O	1.80263	2.06976	-0.42322
C	-0.13224	-1.83997	0.00000	C	2.41037	0.85564	-0.25107
N	-0.38612	-0.55642	-0.00000	C	1.45216	-0.04321	0.19639
Si	-2.06918	0.27545	0.00000	N	0.26525	0.70770	0.28037
C	-2.06539	1.26742	-1.57064	C	0.48148	1.99187	-0.10295
C	-2.06538	1.26743	1.57063	H	5.09463	-1.14189	-0.37287
C	-3.26854	-1.14221	0.00001	H	3.41482	-2.76503	0.40885
H	2.95163	2.71058	0.00000	H	1.05817	-2.09765	0.78508
H	4.61026	0.89811	0.00001	H	-2.18263	-1.25014	2.57725
H	3.90153	-1.50620	0.00000	H	-0.44805	-0.95495	2.73537
H	0.51205	2.23785	-0.00000	H	-1.04716	-2.16660	1.58469
H	-0.84598	-2.65438	0.00000	H	-1.75876	1.98644	2.37616
H	-1.90719	0.62155	-2.44075	H	-2.27665	2.51047	0.76806
H	-3.03555	1.76212	-1.69357	H	-3.30206	1.41515	1.72214
H	-1.29373	2.04407	-1.57310	C	-2.54092	0.72655	-1.78101
H	-1.90717	0.62157	2.44075	C	-3.55401	-1.14959	-0.46148
H	-3.03555	1.76213	1.69357	C	-1.32520	-1.45140	-1.56390
H	-1.29373	2.04409	1.57308	H	4.45812	1.24095	-0.81976
H	-4.28656	-0.73611	0.00001	H	-1.63372	1.28829	-2.03436
H	-3.17043	-1.76931	-0.89211	H	-2.98124	0.36053	-2.71878
H	-3.17042	-1.76931	0.89212	H	-3.25369	1.42793	-1.33210
TBS_bzox-1-				H	-3.37982	-2.02737	0.17250
C	4.07155	-0.81466	-0.21810	H	-4.23690	-0.47676	0.07207
C	-1.24328	-1.17989	2.01607	H	-4.07528	-1.49423	-1.36505
C	-2.26708	1.66493	1.46046	H	-1.06678	-2.30655	-0.92665

H	-1.83039	-1.84973	-2.45461	H	3.10915	-2.66803	0.96835
H	-0.39196	-0.98220	-1.89645	H	3.70453	-4.18659	-0.89629
TBS_Et2_TS_conf_1				H	3.46392	-3.42047	-3.24417
C	-2.48444	4.00891	-1.24659	H	2.63533	-1.13094	-3.72429
C	-3.07323	-1.71309	-1.70297	H	2.04069	0.38793	-1.86207
C	-0.45844	-2.64831	-0.36391	H	1.72902	-0.67495	1.65991
C	-2.84616	-1.70420	1.41956	C	3.02944	2.88206	-0.54496
Si	-1.94032	-1.52443	-0.22679	H	4.44542	2.08995	0.88105
C	-1.22825	3.71363	-0.72443	H	4.11803	1.00592	-0.47365
C	-3.43850	3.00471	-1.47097	C	3.31182	1.19996	3.46795
C	-3.17822	1.66672	-1.18940	H	1.33242	1.37667	2.57860
O	0.13918	1.79668	0.07039	H	2.41872	2.71577	2.19616
C	-0.99192	2.37700	-0.45085	H	-3.15675	-2.77888	-1.94591
C	-1.91812	1.36939	-0.67387	H	-2.67110	-1.20660	-2.58719
N	-1.27647	0.18036	-0.26835	H	-4.08604	-1.33978	-1.52222
C	3.02197	-2.32874	-0.06057	H	0.10600	-2.44953	-1.28223
C	3.35287	-3.18228	-1.10894	H	0.22257	-2.53402	0.48402
C	3.21764	-2.75064	-2.42627	H	-0.78957	-3.69301	-0.39461
C	2.75538	-1.46241	-2.69786	C	-3.55688	-3.06686	1.42776
C	2.43592	-0.60224	-1.65370	C	-3.88531	-0.58703	1.58486
C	-0.03960	0.45995	0.17768	C	-1.84546	-1.64202	2.58105
C	2.57691	-1.03148	-0.33029	H	-0.48043	4.47648	-0.53902
C	2.22279	-0.18603	0.82540	H	-4.08139	-3.21060	2.38175
C	3.66186	1.72151	0.21113	H	-4.30316	-3.14274	0.62786
C	2.37076	1.63660	2.35499	H	-2.85126	-3.89885	1.31401
N	2.72096	0.98903	1.07636	H	-4.43453	-0.72474	2.52593
H	-2.73246	5.03872	-1.48138	H	-3.41858	0.40457	1.61802
H	-4.40789	3.27836	-1.87423	H	-4.62396	-0.58851	0.77420
H	-3.92685	0.90217	-1.36199	H	-2.37673	-1.71678	3.53929

H	-1.12342	-2.46594	2.54011	C	2.88544	1.80857	1.07544
H	-1.28624	-0.69733	2.58691	C	1.40222	0.86647	2.81831
H	2.29019	2.53778	-1.27090	N	2.09324	0.66790	1.54655
H	3.81948	3.41583	-1.08048	H	-2.88435	4.73568	-1.88441
H	2.54252	3.58975	0.13171	H	-4.45250	2.84175	-1.97042
H	4.35049	1.44226	3.22481	H	-3.77620	0.56716	-1.28320
H	3.04830	1.71609	4.39487	H	3.55115	-1.62895	0.95478
H	3.23626	0.12212	3.64039	H	5.12867	-2.56536	-0.71485
bzox-TBS-Et2-imin-adduct				H	4.80123	-2.09672	-3.13226
C	-2.54279	3.75229	-1.57985	H	2.88883	-0.69496	-3.86771
C	-2.72649	-1.79972	-1.86034	H	1.31374	0.22005	-2.22181
C	-0.17465	-2.81950	-0.57014	H	0.98088	-0.98955	1.11768
C	-2.52732	-1.88839	1.28619	C	4.23838	1.86659	1.77402
Si	-1.63169	-1.67741	-0.35271	H	3.04293	1.69857	-0.00115
C	-1.23482	3.59625	-1.13860	H	2.34331	2.75422	1.21718
C	-3.43678	2.66939	-1.63143	H	2.14577	1.23349	3.53296
C	-3.06657	1.38426	-1.25529	H	1.08289	-0.11957	3.17863
O	0.31551	1.86456	-0.28423	C	0.20646	1.82418	2.81499
C	-0.89115	2.30725	-0.77102	H	-2.36633	-1.17682	-2.68618
C	-1.74949	1.21887	-0.82634	H	-3.77278	-1.54868	-1.66434
N	-1.00503	0.10754	-0.35856	H	-2.69795	-2.84081	-2.20252
C	3.40759	-1.43654	-0.10511	H	-0.59960	-3.81827	-0.73465
C	4.29306	-1.95478	-1.04286	H	0.41365	-2.57097	-1.45887
C	4.10838	-1.69260	-2.40081	H	0.49962	-2.89327	0.28672
C	3.03611	-0.90900	-2.81372	C	-3.66436	-0.86841	1.42733
C	2.14657	-0.38797	-1.87335	C	-1.54699	-1.73059	2.45534
C	0.19205	0.57043	-0.04116	C	-3.11164	-3.31191	1.29091
C	2.32581	-0.65362	-0.51650	H	-0.52972	4.41693	-1.07861
C	1.39086	-0.13058	0.57202	H	-3.28917	0.16118	1.47296

H	-4.21586	-1.05744	2.35725	C	-5.26574	1.82943	-0.16634
H	-4.38163	-0.93621	0.60073	C	-4.49486	2.27834	-1.23985
H	-2.07497	-1.87132	3.40732	C	-3.10954	2.16700	-1.19587
H	-0.73816	-2.47012	2.41622	C	-0.47692	0.31763	0.69318
H	-1.09998	-0.72846	2.47493	C	-2.48045	1.59340	-0.08684
H	-3.65451	-3.48235	2.22940	C	-0.95672	1.53417	-0.08376
H	-3.82037	-3.46865	0.46858	C	1.00882	3.00182	-0.08566
H	-2.32965	-4.07708	1.22064	C	-0.69301	3.30328	1.65919
H	4.80937	2.73147	1.42227	N	-0.38717	2.79844	0.31842
H	4.13042	1.95845	2.85924	H	1.49768	-2.63898	4.88028
H	4.81278	0.95981	1.56232	H	1.16688	-4.34462	3.13798
H	0.48091	2.81787	2.44756	H	0.26064	-3.76322	0.91265
H	-0.62759	1.45449	2.20565	H	-2.78455	0.71230	1.86183
H	-0.17197	1.93811	3.83561	H	-5.23727	0.93200	1.79064
OTf-bzox-TBS-Et2-imin-adduct				H	-6.34746	1.91574	-0.20009
C	1.09005	-2.34172	3.92002	H	-4.97417	2.71687	-2.10977
C	-1.00777	-0.52185	-2.65411	H	-2.50147	2.52858	-2.02222
C	0.54508	-2.98497	-1.64177	H	-0.62429	1.35391	-1.10885
C	-2.50074	-2.70331	-1.05578	C	1.15362	3.19046	-1.59014
Si	-0.85148	-1.79431	-1.29980	H	1.34343	3.91553	0.41560
C	0.78435	-1.00489	3.69736	H	1.65247	2.18646	0.27285
C	0.89941	-3.31510	2.92548	H	0.14151	3.10918	2.34876
C	0.38796	-3.00162	1.67204	H	-1.55820	2.76737	2.05775
O	-0.08274	0.50382	1.94067	C	-1.01451	4.79230	1.61391
C	0.27713	-0.72002	2.44352	H	-0.09088	0.06615	-2.74332
C	0.06390	-1.66372	1.45115	H	-1.87644	0.13622	-2.56060
N	-0.44209	-0.95651	0.33690	H	-1.12329	-1.08653	-3.58789
C	-3.25531	1.15845	0.98760	H	0.74713	-2.95721	-2.71912
C	-4.64438	1.27736	0.94921	H	1.47591	-2.70449	-1.14092

H	0.29168	-4.01715	-1.38022	C	3.70485	-0.25392	-0.17756
C	-2.83950	-3.29334	-2.43861	C	4.61112	-1.28973	0.01710
C	-3.62287	-1.75366	-0.62383	C	4.16988	-2.61186	0.01636
C	-2.42081	-3.85133	-0.04115	C	2.82420	-2.90161	-0.20247
H	0.94242	-0.23153	4.43955	C	1.91367	-1.87407	-0.42086
H	-3.02844	-2.51189	-3.18292	C	2.34911	-0.54394	-0.38122
H	-3.75053	-3.90149	-2.36275	C	1.38466	0.51950	-0.69352
H	-2.04307	-3.94477	-2.82100	C	1.79273	1.89861	1.29026
H	-4.58689	-2.28029	-0.65190	C	0.34958	2.68514	-0.59711
H	-3.46923	-1.40398	0.40168	N	1.23009	1.62480	-0.05213
H	-3.70881	-0.87164	-1.27100	H	4.05574	0.77366	-0.20921
H	-3.38326	-4.38017	-0.01405	H	5.66250	-1.06390	0.16310
H	-1.65319	-4.58921	-0.30154	H	4.87925	-3.41835	0.17477
H	-2.22021	-3.48939	0.97332	H	2.48254	-3.93154	-0.21171
H	2.17689	3.48773	-1.83418	H	0.86182	-2.08230	-0.58526
H	0.95255	2.26710	-2.14151	H	0.74367	0.38958	-1.56539
H	0.46929	3.97216	-1.93668	C	0.81277	1.41574	2.35271
H	-0.18481	5.36740	1.18978	H	2.75219	1.39815	1.38959
H	-1.89838	4.96492	0.99210	H	1.95742	2.97645	1.34783
H	-1.21091	5.17734	2.61990	C	1.18640	3.75231	-1.28767
S	2.87705	-0.33968	-0.40752	H	-0.35304	2.21019	-1.28343
O	2.61926	0.09019	0.97474	H	-0.22004	3.08756	0.24257
O	3.43492	-1.68680	-0.56140	H	1.20864	1.67506	3.33850
C	4.25687	0.74530	-0.94060	H	-0.17214	1.87265	2.22972
O	1.79566	0.00270	-1.35342	H	0.68546	0.33231	2.28720
F	3.93464	2.03520	-0.80283	H	1.72643	3.32860	-2.13938
F	5.34691	0.51385	-0.20836	H	1.90883	4.21029	-0.60537
F	4.56165	0.53115	-2.22088	H	0.52305	4.53906	-1.65636
OTf-et2_iminium				S	-1.82000	0.02655	-0.06307

O	-1.63448	0.26038	-1.50626
O	-0.82425	-0.88515	0.52831
C	-3.37591	-0.93878	0.01321
O	-2.11410	1.22768	0.72797
F	-3.25965	-2.07471	-0.67639
F	-4.38942	-0.24131	-0.50052
F	-3.67856	-1.24660	1.27485