Supporting Information for:

Vicinal, Double C-H Functionalization of Alcohols via an Imidate Radical-Polar Crossover Cascade

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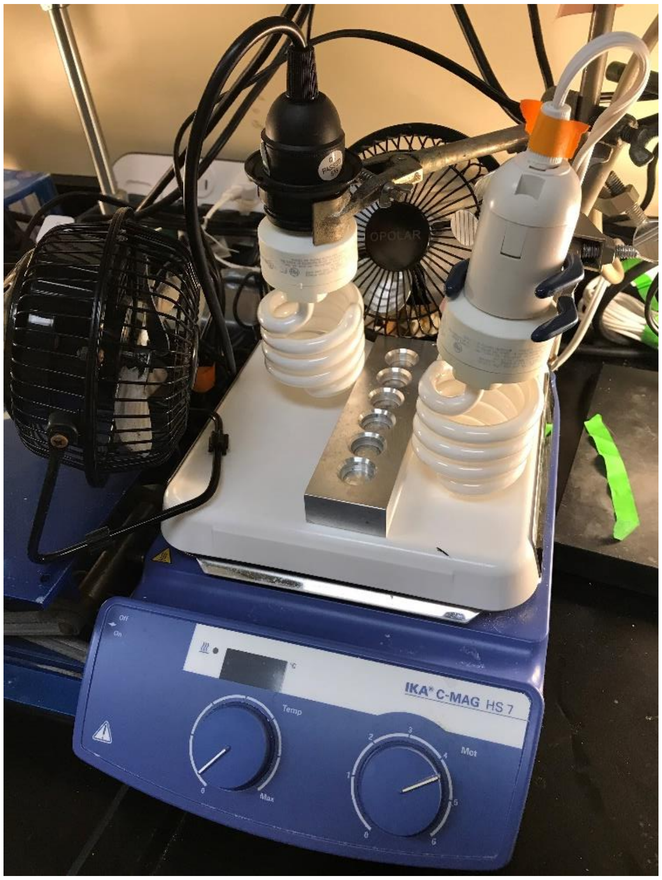
Table of Contents

I. General Information

All chemicals and reagents were purchased from Sigma-Aldrich, Alfa Aesar, Acros, TCI, Oakwood Chemical, or ChemImplex. Sodium iodide and reagents were dried under high vacuum before use. Solvents were purified in the following manner. Acetonitrile and amine bases were distilled over calcium hydride. CH_2Cl_2, THF, Et_2O and DMF were degassed with N_2 and dried by passing through columns containing alumina, copper, or molecular sieves. Flash column chromatography, or preparative thin-layer chromatography, was performed with Silicycle F60 (230-400 mesh) silica gel. Thin layer chromatography (TLC) analyses were performed using EMD 60 F254 TLC plates and visualized by fluorescence quenching or $KMnO_4$ stain. All yields are averages of at least two experimental runs. Cyclic voltammetry was performed with a BioLogic VSP potentiostat in a three-electrode electrochemical cell consisting of a glassy carbon disk working electrode (0.07 cm2, BASi), a Ag/Ag+ quasi-reference electrode (BASi) containing 0.01M AgBF4 (Sigma) in acetonitrile, and a platinum wire counter electrode (23 cm, ALS). Charge/discharge measurements were carried out with a BioLogic VSP potentiostat in a custom glass H-cell. Samples were prepared with 0.02 mmol of analyte in 2.5 mL of 0.5 M tetra-methylammonium tetrafluoroborate in dry, degassed acetonitrile. Data was analyzed using Excel. The onset potential (E_{on}) was measured by calculating the x-intercept potential between the linearly extrapolated fastest rising portion of the current wave (or peak) and the baseline (background) current.

Nuclear magnetic resonance (NMR) spectra (^1H, ^{13}C) were recorded using either a Bruker AVIII 400 or AVIII 600 MHz NMR spectrometer. ^1H and ^{13}C NMR chemical shifts are reported in parts per million and referenced to residual $CHCl_3$ signals in $CDCl_3$ (1H: δ 7.26; ^{13}C: δ 77.), or $CFCl_3$ (^{19}F: δ 0.0). ^1H NMR data are reported as follows: chemical shifts (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet, b = broad, ap = apparent), coupling constant (Hz), relative integral. Data for ^{13}C is reported in terms of chemical shift and multiplicity where appropriate. High-resolution Mass Spectrometry (HRMS) data were obtained using Bruker MicrOTOF (ESI). Infrared (IR) spectra were recorded using a Thermo Fisher Nicolet iS10 FT-IR and are reported in terms of frequency of absorption (cm^{-1}). Melting points were determined using an Electrotherman IA9000.

Photochemical reactions were performed by placing two 26 W compact fluorescent light bulbs (1550 lumens, 5000 K) approximately 2 cm away from the reaction vessel, with 1 fan to the side and another behind the reaction vessel. See a photograph of the set-up below.



II. General Procedures

General Procedure 1 (GP1) – Trichloroacetimidate Formation

To a 100 mL round-bottom flask containing a stir bar, alcohol (1 equiv.), and CH_2Cl_2 (1 M), was added trichloroacetonitrile (1.5 equiv.) and DBU (0.1 equiv.). The solution was stirred overnight and monitored by TLC. Upon completion, the solution was concentrated *in vacuo* before purification by flash chromatography (silica gel, specific eluent conditions noted with each substrate).

Notes:

- Silica gel is loaded with hexanes containing 1% Et_3N to avoid imidate hydrolysis, which also results in quicker compound elution.

General Procedure 2 (GP2) – Benzimidate Formation

(a) To a 4-dram vial equipped with a PTFE septum cap and magnetic stir bar was added alcohol (1 equiv), nitrile (1.1 equiv), PhMe [0.5 M], and trifluoromethanesulfonic acid (1.2 equiv). The solution was heated to 110 °C and stirred. After 24 h the solution was cooled to room temperature, and then stored at –15 °C until crystallization of the trifluoromethanesulfonate salt was observed. The salt was isolated via filtration and washed with cold hexanes and Et_2O. Residual solvent was removed under vacuum.

(b) The salt was suspended in Et_2O, and $NaHCO_3$ (sat. aq) was added dropwise until the dissolution of the salt observed. The aqueous layer was extracted 3x with CH_2Cl_2 (5 mL), and the combined organic layer was dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was purified via column chromatography (silica treated with 1% Et_3N/hexanes to avoid hydrolysis).

Notes:

- The free-based imidate is more prone to hydrolysis than the benzimidate salt, when stored for extended periods of time. For this reason, we suggest storing the benzimidate salt in a freezer and free-basing prior to use.

General Procedure 3 (GP3) – Amino-Iodination

To a 2-dram vial equipped with a PTFE septum cap and magnetic stir bar, was added imidate (1 equiv.) and I_2 (3 equiv.). Dry ${}^tBuOH$ (0.3 M) was degassed using a freeze-pump-thaw technique (3x) or via sparging with N_2 (15 min), then added to the vial. This solution was stirred for 3 minutes, and iodobenzene diacetate (3 equiv.) was added as a solid. The headspace of this vial was evacuated and backfilled with N_2 (3x). The reaction was irradiated with two 26 W (1550 lumens, 5000 K) compact fluorescent light bulbs and cooled by two fans for 1h. Upon completion, the solution was quenched via a reductive workup with 20% $Na_2S_2O_3$. The organic layer was extracted with EtOAc (3x). The combined organic layer was concentrated *in vacuo* before purification by flash chromatography (specific eluent conditions noted with each substrate) to afford amino-iodinated product.

Notes:

- Solvent was degassed using a freeze-pump-thaw technique (3x)
- Pre-stir with imidate, I_2, and ${}^tBuOH$ is needed to fully ensure that I_2 dissolves before adding iodobenzene diacetate to prevent degradation of diastereomeric ratio.
- Iodobenzene diacetate must be sufficiently dry to ensure optimum yields. Typically, the material was left under high vacuum for at least 24h before use.
- The reaction is heavily dependent on light setup. Ensuring optimum light bulb distance as well as obtaining the required light bulbs promote higher yields and diastereomeric ratios.

General Procedure 4 (GP4) – Amino-iodination for rate studies

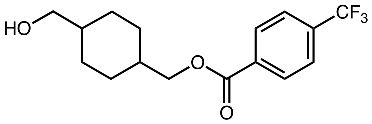
To a 2-dram vial equipped with a PTFE septa cap and magnetic stir bar was added imidate **1** (51.7 mg, 0.2 mmol), I_2 (152.3 mg, 0.6 mmol), ^{t}BuOH (0.7 mL), and dichloroethane as an internal standard (15.5 μL, 0.2 mmol). The solution was stirred at room temperature for 3 min to ensure I_2 had been solubilized. Iodobenzene diacetate was added as a solid, and the vial was immediately irradiated with 2 x 26 W compact fluorescent light bulbs (~ 2cm) and stirred at 900 rpm. After the allotted time, an aliquot (~50 μL) was removed via syringe and immediately quenched in a vial containing 0.5 mL $CDCl_3$ and 1.0 mL $Na_2S_2O_3$ (20%, aq). After all time points had been collected, the organic layer was removed via syringe and dried over anhydrous $MgSO_4$. The solution was directly analyzed by ^{1}H-NMR, 600 MHz, d_1 = 3 seconds.

General Procedure 5 (GP5) – One-step amino-iodination

To a 2-dram vial equipped with a PTFE septa cap and magnetic stir bar was added alcohol (0.2 mmol), I_2 (0.6 mmol), trichloroacetonitrile (0.4 mmol), DBU (0.02 mmol), and $PhCF_3$ (0.7 mL). The solution was stirred at room temperature for 3 min to ensure I_2 had been solubilized. Iodobenzene diacetate (0.2 mmol) was added as a solid, and the vial was immediately irradiated with 2 x 26 W compact fluorescent light bulbs (~ 2cm) and stirred at 900 rpm. After 24h, $PhCF_3$ was removed and replaced with 1.0 mL MeCN and 0.5 mL H_2O. TsOH (1 equiv.) was added, and the reaction was stirred until no oxazoline was observed by thin layer chromatography. Upon completion, the solution was quenched via a reductive workup with 20% $Na_2S_2O_3$ and $NaHCO_3$ (sat. aq.). The organic layer was extracted with EtOAc (3x). The combined organic layer was concentrated *in vacuo* before purification by flash chromatography (specific eluent conditions noted with each substrate) to afford amino-iodinated product.

III. Substrate Synthesis

Alcohols



(4-(hydroxymethyl)cyclohexyl)methyl 4-(trifluoromethyl)benzoate (S12A)

Cyclohexane-1,4-diyldimethanol (7.21 g, 50.0 mmol) was dissolved in THF (75 mL) and cooled to 0°C. NaH (60% dispersion in oil) (2.0 g, 50.0 mmol) was added portionwise, and the suspension was stirred for 1h. At 0°C, 4-(trifluoromethyl)benzoyl chloride (6.95 g, 4.9 mL, 33.3 mmol) was added dropwise by syringe and allowed to stir at room temperature for 6h. The reaction was quenched with H_2O (20 mL) and Et_2O (20 mL). The solution was extracted 5x with Et_2O (20 mL). The combined organic layer was dried over $MgSO_4$ (anhydrous) and concentrated *in vacuo*. The residue was adsorbed onto celite, loaded onto silica gel, and purified by flash column chromatography (isocratic: 20 : 80 EtOAc : hexanes) to yield the target alcohol **S12A** (7.34 g, 70%) as a colorless oil.

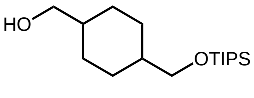
Rf: 0.21 (20% EtOAc/hexanes).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.15 (d, J = 7.9 Hz, 2H), 7.70 (d, J = 8.2 Hz, 2H), 4.29 (d, J = 7.2 Hz, 1H), 4.19 (d, J = 6.4 Hz, 1H), 3.57 (d, J = 7.0 Hz, 1H), 3.48 (d, 6.2 Hz, 1H), 2.07-1.86 (m, 2H), 1.81-1.70 (m, 1H), 1.65-1.58 (m, 2H), 1.55-1.45 (m, 3H), 1.37 (bs, 1H), 1.16-1.09 (m, 1H), 1.06-0.99 (m, 1H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.57, 165.54, 134.52 (q, J = 32.8 Hz), 133.81, 133.78, 130.08, 125.54 (q, 3.5 Hz), 123.77 (q, 272.8 Hz), 70.54, 68.59, 68.31, 66.23, 40.52, 38.19, 37.51, 34.73, 29.20, 28.84, 25.68, 25.24.

HRMS (ESI-TOF) m/z: calc'd for $C_{16}H_{19}F_3O_3$ $[M+Na]^+$ 339.1184, found 339.1171.

IR (film) cm^{-1}: 3345, 3021, 2978, 2922, 2856, 1720, 1324, 1098, 1017, 861.



(4-(((triisopropylsilyl)oxy)methyl)cyclohexyl)methanol (S13A)

Cyclohexane-1,4-diyldimethanol (7.21 g, 50.0 mmol) was dissolved in THF (75 mL) and cooled to 0°C. NaH (60% dispersion in oil) (2.0 g, 50.0 mmol) was added portionwise, and the suspension was stirred for 1h. At 0°C, TIPSCl (6.42 g, 7.1 mL, 33.3 mmol) was added dropwise by syringe and allowed to stir at room temperature for 6h. The reaction was quenched with H_2O (20 mL) and Et_2O (20 mL). The solution was extracted 5x with

Et_2O (20 mL). The combined organic layer was dried over $MgSO_4$ (anhydrous) and concentrated *in vacuo*. The residue was adsorbed onto celite, loaded onto silica gel, and purified by flash column chromatography (isocratic: 20 : 80 EtOAc : hexanes) to yield the target alcohol **S13A** (5.6 g, 56%) as a colorless oil.

Rf: 0.42 (20% EtOAc/hexanes).

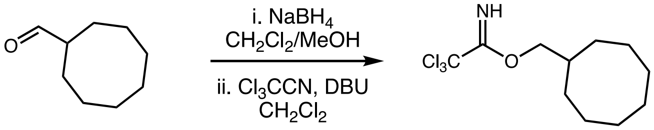
^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.56 (d, J = 5.1 Hz, 1H), 3.55 (d, J = 5.3 Hz, 1H), 3.49 (d, J = 6.2, 1H), 3.45 (d, J = 6.3 Hz, 1H), 1.83-1.81 (m, 3H), 1.71-1.65 (m, 1H), 1.55-1.49 (m, 2H), 1.45-1.41 (m, 4H), 1.36 (bs, 1H), 1.05 (s, 18H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 69.08, 68.91, 66.79, 66.17, 41.06, 40.92, 38.58, 38.19, 29.19, 29.17, 25.71, 25.71, 25.38, 18.19, 12.15.

HRMS (ESI-TOF) m/z: calc'd for $C_{17}H_{36}O_2Si$ $[M+H]^+$ 301.2563, found 301.2537.

IR (film) cm^{-1}: 3329, 2940, 2918, 2864, 1463,1116, 1059, 1032, 881.

Imidates



cyclooctylmethyl 2,2,2-trichloroacetimidate (S6)

Step 1: Aldehyde reduction
To a solution of cyclooctanecarbaldehyde (1.08 mL, 7.13 mmol) in a 1:1 mixture of CH_2Cl_2 and MeOH (35 mL) was slowly added $NaBH_4$ portionwise (1.06 g, 28.5 mmol) at 0°C. The mixture was warmed to room temperature and stirred for 1 h. Upon completion (monitored by TLC), the reaction was quenched with H_2O (35 mL) under vigorous stirring, and extracted with CH_2Cl_2. The combined organic layer was dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude mixture of cyclooctylmethanol was carried forward without further purification.

Step 2: Trichloroacetimidate formation
The crude mixture was subjected to **GP1** without further purification. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 10 : 89 : 1, EtOAc : hexane : Et_3N) to yield imidate **S6** (2.01 g, 98% over two steps) as a colorless oil.

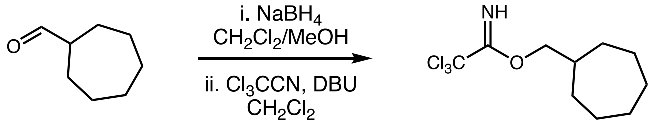
Rf: 0.41 (5% EtOAc/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (bs, 1H), 4.06 (d, J = 6.9 Hz, 2H), 2.08 – 1.99 (m, 1H), 1.76 – 1.67 (m, 4 H), 1.59 – 1.56 (m, 8 H), 1.53 – 1.50 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.32, 91.88, 75.08, 36.81, 29.25, 27.06, 26.48, 25.48.

HRMS (ESI-TOF) m/z: calc'd for $C_{11}H_{18}Cl_3NO$ $[M+Na]^+$ 308.0346, found 308.0348.

IR (neat) cm^{-1}: 3345, 2917, 2850, 1661, 1466, 1075, 793.



cycloheptylmethyl 2,2,2-trichloroacetimidate (S7)

Step 1: Carboxylic acid reduction
To a suspension of $LiAlH_4$ (0.3985 g, 10.5 mmol) in THF (77 mL) under N_2 was slowly added cycloheptanecarboxylic acid (0.96 mL, 7 mmol) in THF (23 mL) dropwise at 0°C. The mixture was warmed to room temperature and stirred overnight. Upon completion

(monitored by TLC), the reaction was diluted with Et_2O and cooled to 0°C. The reaction was quenched by adding H_2O (0.40 mL), 10% NaOH (0.40 mL), and H_2O (1.2 mL) under vigorous stirring. The reaction was allowed to warm to room temperature for 15 minutes, and extracted with Et_2O. The combined organic layer was dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude mixture of cycloheptylmethanol was carried forward without further purification.

Step 2: Trichloroacetimidate formation
The crude mixture was subjected to **GP1** without further purification. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 10 : 89 : 1, EtOAc : hexane : Et_3N) to yield imidate **S7** (1.76 g, 92% over two steps) as a yellow oil.

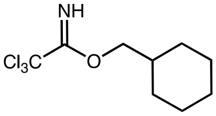
Rf: 0.43 (5% EtOAc/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (bs, 1H), 4.08 (d, J = 6.9 Hz, 2H), 2.05 – 1.95 (m, 1H), 1.86 – 1.79 (m, 2 H), 1.76 – 1.42 (m, 8 H), 1.35 – 1.26 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.36, 91.91, 74.78, 38.54, 31.03, 28.71, 26.45.

HRMS (ESI-TOF) m/z: calc'd for $C_{10}H_{16}Cl_3NO$ $[M+Na]^+$ 294.0190, found 294.0168.

IR (neat) cm^{-1}: 3345, 2921, 2853, 1661, 1461, 1308, 1076, 991.



cyclohexylmethyl 2,2,2-trichloroacetimidate (1)

Cyclohexylmethanol (2.15 mL, 17.5 mmol) was subjected to **GP1**. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 10 : 89 : 1, EtOAc : hexane : Et_3N) to yield imidate **1** (4.52 g, 91%) as a colorless oil.

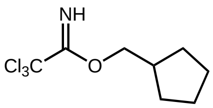
Rf: 0.47 (5% EtOAc/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (bs, 1H), 4.09 (d, J = 6.0 Hz, 2H), 1.86 – 1.66 (m, 6H), 1.34 – 1.00 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.35, 91.88, 74.78, 37.12, 29.69, 26.51, 25.83.

HRMS (ESI-TOF) m/z: calc'd for $C_9H_{14}Cl_3NO$ $[M+Na]^+$ 280.0033, found 280.0025.

IR (neat) cm^{-1}: 3346, 2924, 2852, 1661, 1465, 1075, 821, 793.



cyclopentylmethyl 2,2,2-trichloroacetimidate (S8)

Cyclopentanemethanol (0.5 g, 0.54 mL, 5.0 mmol) was subjected to **GP1**. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 5 : 94 : 1, EtOAc : hexanes : Et_3N) to yield imidate **S8** (1.2 g, 100%) as a light yellow oil.

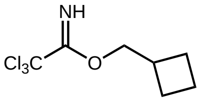
Rf: 0.57 (10% EtOAc / hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (bs, 1H), 4.17 (d, J = 7.0 Hz, 2H), 2.38 (sept, J = 7.5 Hz, 1H), 1.85-1.77 (m, 2H), 1.69-1.54 (m, 4H), 1.40-1.31 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.3, 91.9, 73.5, 38.4, 29.4, 25.5.

HRMS (ESI-TOF) m/z: calc'd for $C_8H_{12}Cl_3NO$ $[M+Na]^+$ 265.9882, found 265.9886.

IR (film) cm^{-1}: 3345, 2952, 2868, 1662, 1076.



cyclobutylmethyl 2,2,2-trichloroacetimidate (S9)

Cyclobutylmethanol (0.66 mL, 7 mmol) was subjected to **GP1**. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 10 : 89 : 1, EtOAc : hexane : Et_3N) to yield imidate **S9** (1.59 g, 99%) as a yellow oil.

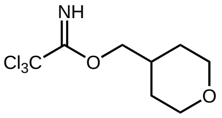
Rf: 0.35 (5% EtOAc/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.22 (bs, 1H), 4.26 (d, J = 6.4 Hz, 2H), 2.84 – 2.73 (m, 1H), 2.15 – 2.08 (m, 2 H), 1.99 – 1.88 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.37, 91.86, 73.12, 34.02, 24.69, 18.61.

HRMS (ESI-TOF) m/z: calc'd for $C_7H_{10}Cl_3NO$ $[M+Na]^+$ 251.9720, found 251.9720.

IR (neat) cm^{-1}: 3346, 2941, 1662, 1460, 1291, 1073, 792.



(tetrahydro-2*H*-pyran-4-yl)methyl 2,2,2-trichloroacetimidate (S10)

(Tetrahydro-2*H*-pyran-4-yl)methanol (0.58 g, 5.0 mmol) was subjected to **GP1**. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 5 : 94 : 1, EtOAc : hexanes : Et_3N) to yield imidate **S10** (1.1 g, 85%) as a colorless oil that solidified over time to give a white solid.

Rf: 0.56 (40% EtOAc / hexanes).

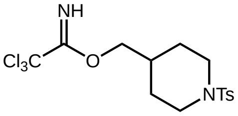
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.26 (bs, 1H), 4.14 (d, J = 6.5 Hz, 2H), 4.02-3.98 (m, 2H), 3.41 (td, J = 17.7, 2.1 Hz, 2H), 2.15-2.04 (m, 1H), 1.73-1.63 (m, 2H), 1.51-1.41 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.10, 91.65, 73.64, 67.61, 34.52, 29.51.

HRMS (ESI-TOF) m/z: calc'd for $C_8H_{12}Cl_3NO_2$ $[M+H]^+$ 260.0012, found 260.0001.

IR (film) cm^{-1}: 3226, 1650, 1104.

MP: 137 – 139 °C.



(1-tosylpiperidin-4-yl)methyl 2,2,2-trichloroacetimidate (S11)

1-tosylpiperidin-4-yl)methanol (1.35 g, 5 mmol) was subjected to **GP1**. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 15 : 84 : 1, EtOAc : hexanes : Et_3N) to yield imidate **S11** (0.83 g, 100%) as a light yellow solid.

Rf: 0.63 (40% EtOAc / hexanes).

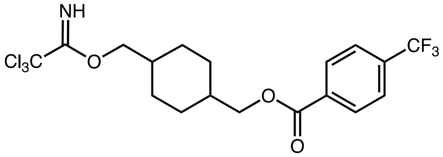
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25 (bs, 1H), 7.65 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 8.5 Hz, 2H), 4.11 (d, J = 6.2, 2H), 3.84-3.81 (m, 2H), 2.43 (s, 3H), 2.29 (td, J = 18.0, 2.6 Hz, 2H), 1.85-1.72 (m, 3H), 1.53-1.43 (m, 2H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 162.93, 143.64, 133.34, 129.76, 127.86, 91.50, 72.90, 46.04, 34.77, 28.18, 21.66.

HRMS (ESI-TOF) m/z: calc'd for $C_{15}H_{19}Cl_3N_2O_3S$ $[M+Na]^+$ 435.0080, found 435.0108.

IR (film) cm^{-1}: 3312, 3051, 1669, 1381, 1163, 1078.

MP: 113 – 114 °C.



(4-((2,2,2-trichloro-1-iminoethoxy)methyl)cyclohexyl)methyl 4-(trifluoromethyl)benzoate (S12)

(4-(hydroxymethyl)cyclohexyl)methyl 4-(trifluoromethyl)benzoate (1.58 g, 5.0 mmol) was subjected to **GP1**. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 5 : 94 : 1, EtOAc : hexanes : Et_3N) to yield imidate **S12** (2.13 g, 93%) as a colorless oil.

Rf: 0.29 (10% EtOAc/hexanes).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.24 (bs J = 9.8 Hz, 1H), 8.15 (d, J = 8.2 Hz, 2H), 7.69 (d, J = 8.3 Hz, 2H), 4.29 (d, J = 7.3 Hz, 1H), 4.23 (d, J = 7.1 Hz, 1H), 4.19 (d, J = 6.4 Hz, 1H), 4.12 (d, J = 6.3 Hz, 1H), 2.10-2.04 (m, 1H), 1.94-1.92 (m, 2H), 1.84-1.79 (m, 1H), 1.68-1.64 (m, 2H), 1.58-1.53 (m, 2H), 1.19-1.12 (m, 2H).

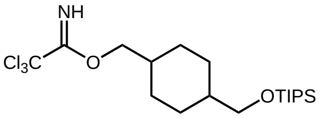
^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.48, 163.22, 163.19, 134.52 (q, 32.6 Hz), 133.76, 130.07, 125.52 (q, 3.8 Hz), 123.77 (q, 272.6 Hz), 91.76, 91.74, 74.33, 72.22, 70.40, 68.24, 37.29, 37.04, 34.70, 34.40, 29.03, 28.81, 25.50, 25.30.

^{19}F NMR (564 MHz, $CDCl_3$): δ = -63.11.

HRMS (ESI-TOF) m/z: calc'd for $C_{18}H_{19}Cl_3F_3NO_3$ $[M+H]^+$ 460.0461, found 460.0462.

IR (film) cm^{-1}: 3230, 2979, 2933, 2854, 1712, 1666, 1274, 1097, 797.

MP: 53.5-56 °C.



(4-(((triisopropylsilyl)oxy)methyl)cyclohexyl)methyl 2,2,2-trichloroacetimidate (S13)

(4-(((triisopropylsilyl)oxy)methyl)cyclohexyl)methanol (0.70 g, 2.3 mmol) was subjected to **GP1**. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 5 : 94 : 1, EtOAc : hexanes : Et_3N) to yield imidate **S13** (0.97 g, 95%) as a colorless oil.

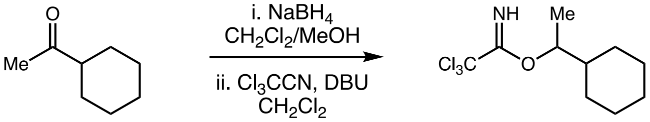
Rf: 0.43 (10% EtOAc / hexanes).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.21 (bs, 1H), 4.21 (d, J = 7.0 Hz, 1H), 4.10 (d, J = 6.5 Hz, 1H), 3.57 (d, J = 7.0 Hz, 1H), 3.50 (d, J = 6.2 Hz, 1H), 1.89-1.84 (m, 3H), 1.81-1.75 (m, 1H), 1.72-1.67 (m, 1H), 1.58-1.53 (m, 3H), 1.48-1.44 (m, 2H), 1.05 (s, 18H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.32, 163.29, 91.87, 74.74, 72.51, 68.99, 66.60, 40.83, 38.33, 37.40, 34.56, 29.17, 29.03, 25.66, 25.66, 25.32, 18.19, 12.15.

HRMS (ESI-TOF) m/z: calc'd for $C_{19}H_{36}Cl_3NO_2Si$ $[M+Na]^+$ 466.1479, found 466.1464.

IR (film) cm^{-1}: 3348, 2940, 2920, 2891, 2864, 1663, 1308, 1080, 795.



1-cyclohexylethyl 2,2,2-trichloroacetimidate (S14)

Step 1: Ketone reduction
To a solution of 1-cyclohexylethan-1-one (0.96 mL, 7 mmol) in a 1:1 mixture of CH_2Cl_2 and MeOH (35 mL) was slowly added $NaBH_4$ portionwise (1.06 g, 28.5 mmol) at 0^{o}C. The mixture was warmed to room temperature and stirred for 1 h. Upon completion (monitored by TLC), the reaction was quenched with H_2O (35 mL) under vigorous stirring and extracted with CH_2Cl_2. The combined organic layer was dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude mixture of 1-cyclohexylethan-1-ol was carried forward without further purification.

Step 2: Trichloroacetimidate formation
The crude mixture was subjected to **GP1** without further purification. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and

purified by flash column chromatography (isocratic: 10 : 89 : 1, EtOAc : hexane : Et_3N) to yield imidate **S14** (0.90 g, 47% over two steps) as a yellow oil.

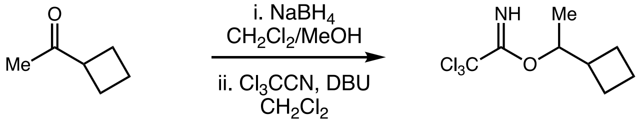
Rf: 0.43 (5% EtOAc/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17 (bs, 1H), 4.85 (quin, J = 6.3 Hz, 1H), 1.91 – 1.88 (m, 1H), 1.79 – 1.56 (m, 5 H), 1.29 (d, J = 6.3 Hz, 3H), 1.27 – 1.05 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.60, 92.35, 80.25, 42.82, 28.75, 28.45, 26.57, 26.23, 26.13, 16.02.

HRMS (ESI-TOF) m/z: calc'd for $C_{10}H_{16}Cl_3NO$ $[M+Na]^+$ 294.0190, found 294.0192.

IR (neat) cm^{-1}: 3347, 2926, 2853, 1657, 1449, 1075, 791.



1-cyclobutylethyl 2,2,2-trichloroacetimidate (S15)

Step 1: Ketone reduction
To a solution of 1-cyclohexylethan-1-one (0.76 mL, 7 mmol) in a 1:1 mixture of CH_2Cl_2 and MeOH (35 mL) was slowly added $NaBH_4$ portionwise (1.06 g, 28.5 mmol) at 0ºC. The mixture was warmed to room temperature and stirred for 1 h. Upon completion (monitored by TLC), the reaction was quenched with H_2O (35 mL) under vigorous stirring and extracted with CH_2Cl_2. The combined organic layer was dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude mixture of 1-cyclohexylethan-1-ol was carried forward without further purification.

Step 2: Trichloroacetimidate formation
The crude mixture was subjected to **GP1** without further purification. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 10 : 89 : 1, EtOAc : hexane : Et_3N) to yield imidate **S15** (0.85 g, 50% over two steps) as a yellow oil.

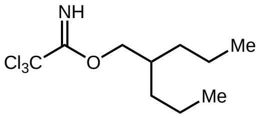
Rf: 0.40 (5% EtOAc/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (bs, 1H), 5.00 (quint, J = 6.4 Hz, 1H), 2.60 – 2.54 (m, 1H), 2.06 – 1.80 (m, 6 H), 1.23 (d, J = 6.3 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.84, 92.31, 79.26, 40.38, 24.28, 24.25, 18.09, 16.28.

HRMS (ESI-TOF) m/z: calc'd for $C_8H_{12}Cl_3NO$ $[M+Na]^+$ 265.9877, found 265.9873.

IR (neat) cm^{-1}: 3347, 2977, 2940, 2867, 1658, 1375, 1284, 1066.



2-propylpentyl 2,2,2-trichloroacetimidate (S16)

2-propylpentan-1-ol (1.3 g, 10.0 mmol) was subjected to **GP1**. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 1 : 98 : 1, EtOAc : hexanes : Et_3N) to yield imidate **S16** (2.74 g, 100%) as a colorless oil.

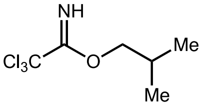
Rf: 0.60 (10% EtOAc / hexanes).

^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.19 (bs, 1H), 4.18 (d, J = 5.6 Hz, 2H), 1.84-1.82 (m, 1H), 1.41-1.31 (m, 8H), 0.92-0.89 (m, 6H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 163.41, 91.88, 72.35, 36.94, 33.67, 19.99, 14.51.

HRMS (ESI-TOF) m/z: calc'd for $C_{10}H_{18}Cl_3NO$ $[M+Na]^+$ 296.0352, found 296.0327.

IR (film) cm^{-1}: 3348, 2957, 2929, 2872, 1662, 1080, 823.



isobutyl 2,2,2-trichloroacetimidate (S17)

2-methylpropan-1-ol (0.65 mL, 7 mmol) was subjected to **GP1**. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 10 : 89 : 1, EtOAc : hexane : Et_3N) to yield imidate **S17** (1.48 g, 97%) as a yellow oil.

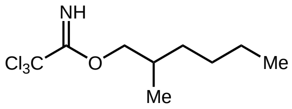
Rf: 0.33 (5% EtOAc/hexanes)

^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.21 (bs, 1H), 4.06 (d, J = 6.8 Hz, 2H), 2.12 (sept, J = 6.7 Hz, 1H), 1.01 (d, J = 6.9 Hz, 6H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 163.29, 91.86, 75.64, 27.81, 19.14.

HRMS (ESI-TOF) m/z: calc'd for $C_6H_{10}Cl_3NO$ $[M+Na]^+$ 239.9720, found 239.9721.

IR (neat) cm^{-1}: 3347, 2962, 2875, 1662, 1471, 1288, 1076, 1001, 824, 793.



2-methylhexyl 2,2,2-trichloroacetimidate (S18)

2-methylhexan-1-ol (0.58 g, 5 mmol) was subjected to **GP1**. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 1 : 98 : 1, EtOAc : hexanes : Et_3N) to yield imidate **S18** (1.3 g, 100%) as a colorless oil.

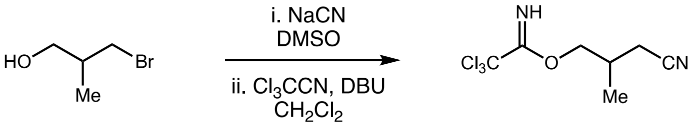
Rf: 0.61 (10% EtOAc / hexanes).

^1H NMR (400 MHz, $CDCl_3$): δ = 8.20 (bs, 1H), 4.15 (dd, J = 10.4, 5.8 Hz, 1H), 4.07 (dd, J = 10.4, 6.7 Hz, 1H), 2.01-1.90 (m, 1H), 1.50-1.20 (m, 6H), 1.01 (d, J = 6.8, 3H), 0.91-0.88 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.35, 91.88, 74.52, 33.04, 32.60, 29.11, 23.00, 17.01, 14.17.

HRMS (ESI-TOF) m/z: calc'd for $C_9H_{16}Cl_3NO$ $[M+Na]^+$ 282.0195, found 282.0182.

IR (film) cm^{-1}: 3348, 2957, 2929, 2872, 1662, 1080, 793.



2-cyanopropyl 2,2,2-trichloroacetimidate (S19)

Step 1: Bromide displacement
To a solution of 3-bromo-2-methylpropan-1-ol (0.15 mL, 1.43 mmol) in DMSO (1.5 mL) was added NaCN (77.2 mg, 1.57 mmol). The mixture was warmed to 60°C and stirred for overnight. Upon completion (monitored by TLC), the reaction was quenched with H_2O and extracted with CH_2Cl_2. The combined organic layer was washed with H_2O and brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude mixture was loaded directly onto silica gel and purified by flash column chromatography (isocratic: 49 : 50 : 1, EtOAc : hexane : Et_3N) to yield 4-hydroxy-3-methylbutanenitrile (84.1 mg, 59% yield) as a yellow oil.

Rf: 0.24 (50% EtOAc/hexanes)

Step 2: Trichloroacetimidate formation

4-hydroxy-3-methylbutanenitrile (0.078 g, 0.79 mmol) was subjected to **GP1**. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 20 : 79 : 1, EtOAc : hexane : Et_3N) to yield imidate **S19** (0.19 g, 100%) as a yellow oil.

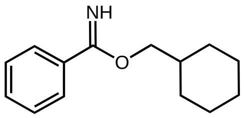
Rf: 0.23 (20% EtOAc/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.38 (bs, 1H), 4.31 (dd, J = 10.9 Hz, 4.5 Hz, 1H), 4.15 (dd, 10.9, J = 7.3 Hz, 1H), 2.60 – 2.53 (m, 1H), 2.47 – 2.38 (m, 2H), 1.21 (d, J = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.58, 118.03, 91.27, 71.61, 30.36, 21.49, 16.15.

HRMS (ESI-TOF) m/z: calc'd for $C_7H_9Cl_3N_2O$ $[M+Na]^+$ 264.9673 found 264.9666.

IR (neat) cm^{-1}: 3342, 2968, 2246, 1729, 1667, 1616, 1463, 1301.



cyclohexylmethyl benzimidate (S20)

2-methylhexan-1-ol (1.14 g, 1.23 mL, 10.0 mmol) and benzonitrile (1.1 g, 1.13 mL 11.0 mmol) was subjected to **GP2**. Upon completion, the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 10 : 89 : 1, EtOAc : hexanes : Et_3N) to yield imidate **S20** (1.91 g, 80%) as a colorless oil.

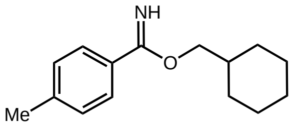
Rf: 0.50 (20% EtOAc / hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75 (d, J = 7.0 Hz, 2H), 7.47-7.38 (m, 3H), 4.07 (d, J = 5.6 Hz, 2H), 1.90-1.68 (m, 6H), 1.36-1.05 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.17, 133.15, 130.89, 128.53, 126.80, 71.41, 37.38, 30.07, 26.61, 25.94.

HRMS (ESI-TOF) m/z: calc'd for $C_{14}H_{19}NO$ $[M+Na]^+$ 240.1364, found 240.1373.

IR (film) cm^{-1}: 3336, 3087, 3026, 2922, 2831, 1631, 1494, 1065.



cyclohexylmethyl 4-methylbenzimidate (S21)

2-methylhexan-1-ol (1.14 g, 1.23 mL, 10.0 mmol) and 4-methylbenzonitrile (1.29 g, 1.31 mL, 11.0 mmol) was subjected to **GP2**. Upon completion, the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 10 : 89 : 1, EtOAc : hexanes : Et_3N) to yield imidate **S21** (1.57 g, 68%) as a colorless oil.

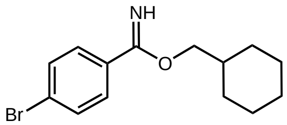
Rf: 0.38 (20% EtOAc/hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65-7.63 (m, 3H), 7.22-7.20 (m, 2H), 4.05 (d, J = 6.1 Hz, 2H), 2.39 (s, 3H), 1.89-1.69 (m, 6H), 1.36-1.08 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.10, 141.19, 130.34, 129.22, 126.77, 71.32, 37.40, 30.10, 26.64, 25.96, 21.50.

HRMS (ESI-TOF) m/z: calc'd for $C_{15}H_{21}NO$ $[M+H]^+$ 232.1701, found 232.1699.

IR (film) cm^{-1}: 3306, 3032, 2922, 2851, 1629, 1328, 1064, 814, 729.



cyclohexylmethyl 4-bromobenzimidate (S22)

2-methylhexan-1-ol (0.46 g, 0.49 mL, 4.0 mmol) and 4-bromobenzonitrile (0.73 g, 4.0 mmol) was subjected to **GP2**. Upon completion, the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 10 : 89 : 1, EtOAc : hexanes : Et_3N) to yield imidate **S22** (0.89 g, 75%) as a colorless oil.

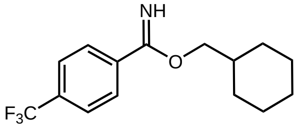
Rf: 0.50 (20% EtOAc / hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, J = 8.6 Hz, 2H), 7.57-7.54 (m, 2H), 4.05 (d, J = 6.0 Hz, 2H), 1.89-1.20 (m, 6H), 1.37-1.20 (m, 3H), 1.12-1.06 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.74, 132.03, 131.74, 128.52, 125.53, 71.45, 37.31, 30.05, 26.57, 25.90.

HRMS (ESI-TOF) m/z: calc'd for $C_{14}H_{18}BrNO$ $[M+H]^+$ 296.0650, found 296.0680.

IR (film) cm^{-1}: 3306, 3041, 2921, 2850, 1630, 1067, 816.



cyclohexylmethyl 4-(trifluoromethyl)benzimidate (S23)

2-methylhexan-1-ol (0.46 g, 0.49 mL, 4.0 mmol) and 4-(trifluoromethyl)benzonitrile (0.68 g, 4.0 mmol) was subjected to **GP2**. Upon completion, the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 10 : 89 : 1, EtOAc : hexanes : Et_3N) to yield imidate **S23** (0.59 g, 52%) as a colorless oil.

Rf: 0.48 (20% EtOAc / hexanes).

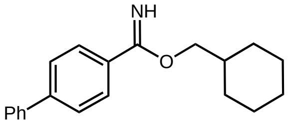
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.86 (bs, 2H), 7.65 (td J = 29.9 Hz, 8.3 Hz, 2H), 4.08 (bs, 2H), 1.87-1.69 (m, 6H), 1.35-1.20 (m, 3H), 1.13-1.07 (m, 2H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 167.27, 136.47, 132.73 (q, $^2J_{CF}$ = 32.6 Hz), 127.30, 125.58, 123.91 (q, $^1J_{CF}$ = 274.4 Hz), 71.92, 37.33, 30.06, 26.57, 25.91.

^{19}F NMR (564 MHz, $CDCl_3$): δ = -62.94.

HRMS (ESI-TOF) m/z: calc'd for $C_{15}H_{18}F_3NO$ $[M+H]^+$ 286.1382, found 286.1410.

IR (film) cm^{-1}: 3364, 3028, 2970, 1644, 1320, 1016, 953.



cyclohexylmethyl [1,1'-biphenyl]-4-carbimidate (S24)

2-methylhexan-1-ol (0.46 g, 0.49 mL, 4.0 mmol) and [1,1'-biphenyl]-4-carbonitrile (0.72 g, 4.0 mmol) was subjected to **GP2**. Upon completion, the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 10 : 89 : 1, EtOAc : hexanes : Et_3N) to yield imidate **S24** (0.94 g, 80%) as a colorless oil.

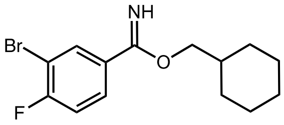
Rf: 0.41 (20% EtOAc / hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (bs, 2H), 7.65-7.60 (m, 4H), 7.48-7.44 (m, 2H), 7.40-7.36 (m, 1H), 4.11 (bs, 2H), 1.93-1.71 (m, 6H), 1.39-1.08 (m, 5H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 168.21, 143.68, 140.22, 131.79, 128.98, 127.96, 127.24, 127.19, 71.54, 37.37, 30.06, 26.59, 25.92.

HRMS (ESI-TOF) m/z: calc'd for $C_{20}H_{23}NO$ $[M+H]^+$ 294.1858, found 294.1878.

IR (film) cm^{-1}: 3349, 3029, 2976, 2924, 1628, 1073, 736.



cyclohexylmethyl 3-bromo-4-fluorobenzimidate (S25)

2-methylhexan-1-ol (1.14 g, 1.23 mL, 10.0 mmol) and 3-bromo-4-fluorobenzonitrile (2.0 g, 10.0 mmol) was subjected to **GP2**. Upon completion, the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 10 : 89 : 1, EtOAc : hexanes : Et_3N) to yield imidate **S25** (2.04 g, 65%) as a colorless oil.

Rf: 0.33 (20% EtOAc/hexanes).

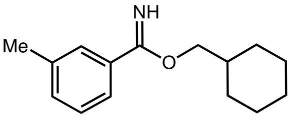
^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.95-7.94 (m, 1H), 7.67-7.67 (m, 1H), 7.46 (bs, 1H), 7.09 (t, J = 8.4 Hz, 1H), 3.97 (d, J = 5.8 Hz, 2H), 1.83-1.79 (m, 6H), 1.31-0.98 (m, 5H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 165.88, 160.59 (d, 252.1 Hz), 132.39, 130.61, 127.73, 116.31 (d, 22.9 Hz), 109.22 (d, 21.7 Hz), 71.72, 37.14, 29.94, 26.46, 25.77.

^{19}F NMR (367 MHz, CDCl$_3$): δ = -103.65.

HRMS (ESI-TOF) m/z: calc'd for $C_{14}H_{17}BrFNO$ $[M+H]^+$ 314.0556, found 314.0538.

IR (film) cm^{-1}: 3290, 3041, 2923, 2851, 1634, 1322, 1070, 730.



cyclohexylmethyl 3-methylbenzimidate (S26)

2-methylhexan-1-ol (1.14 g, 1.23 mL, 10.0 mmol) and 3-methylbenzonitrile (1.29 g, 1.32 mL, 11.0 mmol) was subjected to **GP2**. Upon completion, the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 5 : 94 : 1, EtOAc : hexanes : Et_3N) to yield imidate **S26** (1.25 g, 54%) as a colorless oil.

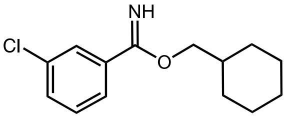
Rf: 0.39 (20% EtOAc/hexanes).

^{1}H NMR (600 MHz, CDCl$_3$): δ = 7.96 (s, 1H), 7.61-7.57 (m, 2H), 7.31-7.26 (m, 2H), 4.00 (d, J = 6.4 Hz, 2H), 2.36 (s, 3H), 1.84-1.65 (m, 6H), 1.33-1.26 (m, 2H), 1.24-1.14 (m, 1H), 1.11-1.04 (m, 2H).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 168.13, 139.77, 134.66, 132.88, 129.87, 128.84, 125.40, 72.24, 38.76, 31.31, 27.90, 27.24, 22.10.

HRMS (ESI-TOF) m/z: calc'd for $C_{15}H_{21}NO$ $[M+H]^+$ 232.1701, found 232.1707.

IR (film) cm^{-1}: 3335, 3044, 2923, 2852, 1632, 1328, 1068, 795.



cyclohexylmethyl 3-chlorobenzimidate (S27)

2-methylhexan-1-ol (1.14 g, 1.23 mL, 10.0 mmol) and 3-chlorobenzonitrile (1.51 g, 11.0 mmol) was subjected to **GP2**. Upon completion, the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 10 : 89 : 1, EtOAc : hexanes : Et_3N) to yield imidate **S27** (1.11 g, 44%) as a colorless oil.

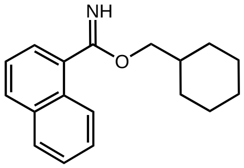
Rf: 0.36 (20% EtOAc/hexanes).

^{1}H NMR (600 MHz, CD$_3$CN): δ = 8.08 (bs, 1H), 7.79-7.78 (m, 1H), 7.72-7.71 (m, 1H), 7.48-7.46 (m, 1H), 7.41-7.38 (m, 1H), 3.98 (d, J = 6.3 Hz, 2H), 1.83-1.65 (m, 6H), 1.32-1.25 (m, 2H), 1.23-1.16 (m, 1H), 1.10-1.04 (m, 2H).

^{13}C NMR (100 MHz, CD$_3$CN): δ = 166.00, 136.40, 135.37, 131.99, 131.49, 128.25, 126.73, 72.78, 38.48, 31.07, 27.68, 27.02.

HRMS (ESI-TOF) m/z: calc'd for $C_{14}H_{18}ClNO$ $[M+H]^+$ 252.1155, found 252.1149.

IR (film) cm^{-1}: 3336, 3047, 2925, 2852, 1633, 1326, 1069, 730.



cyclohexylmethyl 1-naphthimidate (S28)

2-methylhexan-1-ol (1.14 g, 1.23 mL, 10.0 mmol) and 1-naphthonitrile (1.68 g, 11.0 mmol) was subjected to **GP2**. Upon completion, the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 10 : 89 : 1, EtOAc : hexanes : Et_3N) to yield imidate **S28** (0.67 g, 25%) as a colorless oil.

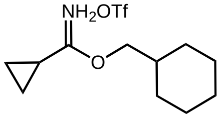
Rf: 0.39 (20% EtOAc/hexanes).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.10 (bd, 8.3 Hz, 1H), 7.89-7.86 (m, 2H), 7.60-7.45 (m, 5H), 4.23 (d, J = 6.4 Hz, 2H), 1.91-1.83 (m, 3H), 1.79-1.76 (m, 2H), 1.71-1.69 (m, 1H), 1.33-1.20 (m, 3H), 1.16-1.09 (m, 2H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.31, 134.02, 133.72, 130.08, 129.91, 128.51, 126.97, 126.27, 125.50, 125.23, 125.02, 71.85, 37.34, 30.09, 26.56, 25.89.

HRMS (ESI-TOF) m/z: calc'd for $C_{18}H_{21}NO$ $[M+H]^+$ 268.1701, found 268.1695.

IR (film) cm^{-1}: 3335, 3044, 2923, 2852, 1632, 1328, 1068, 731.



cyclohexylmethyl cyclopropanecarbimidate triflate (S29)

2-methylhexan-1-ol (1.14 g, 1.23 mL, 10.0 mmol) and cyclopropanecarbonitrile (0.74 g, 0.81 mL, 11.0 mmol) was subjected to **GP2(a)** to yield imidate salt **S29** (1.01 g, 30%) as a white solid.

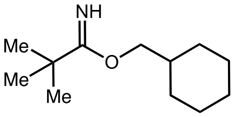
^{1}H NMR (600 MHz, CD_3CN): δ = 9.51 (bs, 1H), 8.64 (bs, 1H), 4.05 (d, J = 6.4 Hz, 2H), 2.02-1.97 (m, 1H), 1.83-1.76 (m, 1H), 1.75-1.65 (m, 5H), 1.32-1.24 (m, 6H), 1.23-1.15 (m, 1H), 1.06-0.99 (m, 2H).

^{13}C NMR (150 MHz, CD_3CN): δ = 182.93, 78.79, 37.53, 29.89, 27.14, 26.49, 14.38, 12.29.

^{19}F NMR (564 MHz, CD_3CN): δ = -79.39.

HRMS (ESI-TOF) m/z: calc'd for $C_{11}H_{19}NO$ [M-OTf]$^+$ 182.1545, found 182.1533.

IR (film) cm^{-1}: 3256, 3098, 2926, 2853, 1704, 1224, 1026, 633.



cyclohexylmethyl pivalimidate (S30)

2-methylhexan-1-ol (1.14 g, 1.23 mL, 10.0 mmol) and pivalonitrile (0.83 g, 1.22 mL, 11.0 mmol) was subjected to **GP2**. Upon completion, the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 10 : 89 : 1, EtOAc : hexanes : Et_3N) to yield imidate **S30** (0.69 g, 35%) as a colorless oil.

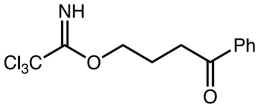
Rf: 0.36 (20% EtOAc/hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.71 (bs, 1H), 3.73 (d, J = 6.4 Hz, 2H), 1.70-1.55 (m, 7H), 1.23-1.09 (m, 2H), 1.07 (s, 9H), 0.97-0.88 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.79, 70.71, 37.84, 37.21, 29.82, 27.67, 26.48, 25.80.

HRMS (ESI-TOF) m/z: calc'd for $C_{12}H_{23}NO$ [M+H]$^+$ 198.1858, found 198.1871.

IR (film) cm^{-1}: 3335, 2923, 2852, 1632, 1328, 1068, 731.



4-oxo-4-phenylbutyl 2,2,2-trichloroacetimidate (33)

4-hydroxy-1-phenylbutan-1-one[1] (1.42 g, 8.6 mmol) was subjected to **GP1**. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 0 : 99 : 1, EtOAc : hexane : Et_3N) to yield imidate **33** (2.24 g, 90%) as a yellow solid.

Rf: 0.36 (20% EtOAc/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.30 (bs, 1H), 7.99 – 7.96 (m, 2H), 7.59 – 7.55 (m, 1H), 7.48 – 7.45 (m, ,2H), 4.42 (t, J = 6.2 Hz, 2H), 3.17 (t, J = 7.2 Hz, 2H), 2.25 (quint, J = 6.7 Hz, 2H).

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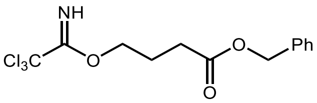
[1] Murphy, S. K.; Dong, V. M. *J. Am. Chem. Soc.* **2013**, *135*, 5553.

^{13}C NMR (100 MHz, CDCl$_3$): δ = 199.18, 162.95, 136.99, 133.28, 128.78, 128.16, 91.68, 68.83, 34.79, 23.10.

HRMS (ESI-TOF) m/z: calc'd for $C_{12}H_{12}Cl_3NO_2$ $[M+Na]^+$ 329.9826, found 329.9825.

IR (neat) cm^{-1}: 3341, 2978, 2942, 2906, 1676, 1662, 1595, 1580, 1474.

MP: 51.3 °C – 54.2 °C.



benzyl 4-(2,2,2-trichloro-1-iminoethoxy)butanoate (35)

Benzyl 4-hydroxybutanoate[2] (3.69 g, 19 mmol) was subjected to **GP1**. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 20 : 79 : 1, EtOAc : hexane : Et_3N) to yield imidate **35** (5.17 g, 80%) as a yellow oil.

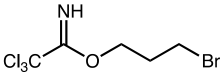
Rf: 0.63 (25% EtOAc/hexanes)

^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.29 (bs, 1H), 7.39 – 7.30 (m, 5H), 5.14 (s, 2H), 4.34 (t, J = 6.2 Hz, 2H), 2.55 (t, J = 7.4 Hz, 2H), 2.18 – 2.11 (m, 2H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 172.75, 162.91, 136.02, 128.73, 128.42, 128.38, 91.56, 68.43, 66.54, 30.77, 23.89.

HRMS (ESI-TOF) m/z: calc'd for $C_{13}H_{14}Cl_3NO_3$ $[M+Na]^+$ 359.9931, found 359.9924.

IR (neat) cm^{-1}: 3340, 2958, 1732, 1663, 1498, 1455, 1304, 1165, 1075.



3-bromopropyl 2,2,2-trichloroacetimidate (37)

3-bromopropan-1-ol (0.90 mL, 10 mmol) was subjected to **GP1**. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 10 : 89 : 1, EtOAc : hexane : Et_3N) to yield imidate **37** (2.07 g, 73%) as a colorless oil.

Rf: 0.42 (5% EtOAc/hexanes)

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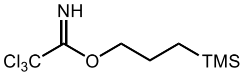
[2] Weber, A. E.; Halgren, T. A.; Doyle, J. J.; Lynch, R. J.; Siegl, P. K. S.; Parsons, W. H.; Greenlee, W. J.; Patchett, A. A. *J. Med. Chem.* **1991**, *34*, 2962.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.33 (bs, 1H), 4.45 (t, J = 5.9 Hz, 2H), 3.70 (t, J = 6.4 Hz, 2H), 2.27-2.21 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.78, 91.48, 66.01, 41.19, 31.44.

HRMS (ESI-TOF) m/z: calc'd for $C_7H_{12}Cl_3NO$ $[M+Na]^+$ 302.8596, found 302.8591.

IR (neat) cm^{-1}: 3335, 2968, 1070, 760, 631.



3-(trimethylsilyl)propyl 2,2,2-trichloroacetimidate (39)

3-(trimethylsilyl)propan-1-ol (1.11 mL, 7 mmol) was subjected to **GP1**. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 10 : 89 : 1, EtOAc : hexane : Et_3N) to yield imidate **39** (1.95 g, 100%) as a colorless oil.

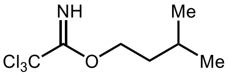
Rf: 0.46 (5% EtOAc/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.22 (bs, 1H), 4.25 (d, J = 6.9 Hz, 2H), 1.81 – 1.73 (m, 2H), 0.61 – 0.53 (m, 2H), 0.01 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.20, 91.86, 72.20, 23.03, 12.44, -1.63.

HRMS (ESI-TOF) m/z: calc'd for $C_8H_{16}Cl_3NOSi$ $[M+Na]^+$ 297.9959, found 297.9952.

IR (neat) cm^{-1}: 3348, 2953, 1662, 1386, 1291, 1248, 1080.



isopentyl 2,2,2-trichloroacetimidate (41)

3-methylbutan-1-ol (0.76 mL, 7 mmol) was subjected to **GP1**. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 10 : 89 : 1, EtOAc : hexane : Et_3N) to yield imidate **41** (1.53 g, 94%) as a colorless oil.

Rf: 0.38 (5% EtOAc/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.22 (bs, 1H), 4.32 (d, J = 6.7 Hz, 2H), 1.85 – 1.75 (m, 1H), 1.67 (q, J = 6.7 Hz, 2H), 0.96 (d, J = 6.7 Hz, 6H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 163.25, 91.82, 68.37, 37.10, 25.23, 22.62.

HRMS (ESI-TOF) m/z: calc'd for $C_7H_{12}Cl_3NO$ $[M+Na]^+$ 253.9877, found 253.9878.

IR (neat) cm^{-1}: 3347, 2958, 2871, 1662, 1465, 1308, 1078, 794.

IV. Amino-halogenation Optimization

Imidate (**1**) (51.7 mg, 0.2 mmol) was subjected to **GP3**. Upon completion, the combined organic layer was concentrated and the yields and diastereomeric ratios were determined by ^{1}H-NMR using dichloroethane as an internal standard.

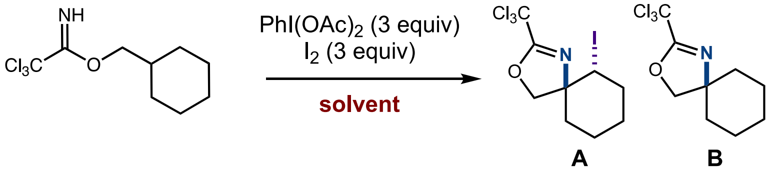


Table S1: Solvent Effects

Entry	Solvent	A	B
1	MeCN	30%, 20 : 1 dr	28%
2	CH_2Cl_2	43%, 20 : 1 dr	15%
3	$PhCF_3$	55%, 3 : 1 dr	8%
4	HFIP	0%	38%
5	HFIP:CH_2Cl_2 (3:1)	0%	83%
6	**^{t}BuOH**	**84%, 19 : 1 dr**	**<5%**

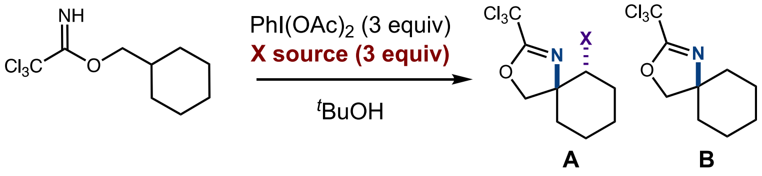


Table S2: Effect of halogen source and oxidant

Entry	"X" (3 equiv)	Oxidant (3 equiv)	A	B
1	LiCl	$PhI(OAc)_2$	0%	0%
2	LiBr	$PhI(OAc)_2$	31%	<5%
3	NaI	$PhI(OAc)_2$	92%, 1.3 : 1 dr	<5%
5	CsI	$PhI(OAc)_2$	90%, 1.5 : 1 dr	<5%
5	**I_2**	**$PhI(OAc)_2$**	**84%, 19 : 1 dr**	**<5%**
6	I_2	$PhI(OPiv)_2$	44%, 1.3 : 1 dr	0%
7	I_2	PIFA	17%	<5%
8	I_2	none	0%	0%

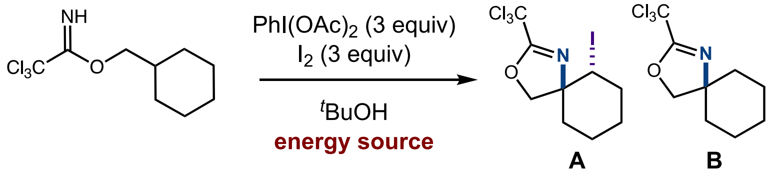


Table S3: Effect of energy source

Entry	Light	A	B
1	dark, rt	0	0
2	dark, 50 °C	20%	0
3	white LED	84%, 2 : 1 dr	<5%
4	**white CFL**	**84%, 19 : 1 dr**	**<5%**
5	white CFL, no fans	86%, 9 : 1 dr	<5%

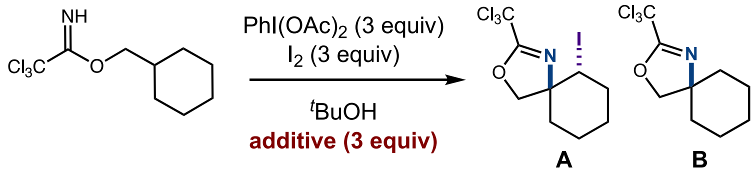


Table S4: Effect of base additives

Entry	Base Additive	Solvent	A	B
1	pyridine	CH_2Cl_2	47%, 4 : 1 dr	<5%
2	collidine	CH_2Cl_2	69%, 2 : 1 dr	<5%
3	2,6-ditertbutyl pyridine	CH_2Cl_2	83%, 1.3 : 1 dr	11%
4	2,6-lutidine	CH_2Cl_2	84%, 2 : 1 dr	5%
5	2,6-lutidine	^{t}BuOH	90%, 2 : 1 dr	6%
6	**none**	**^{t}BuOH**	**84%, 19 : 1 dr**	**<5%**

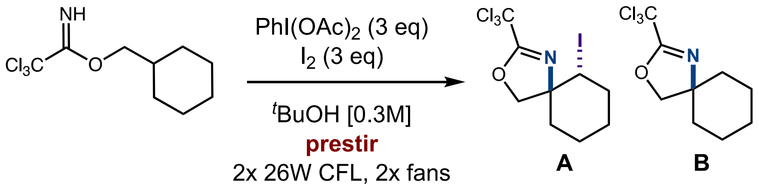


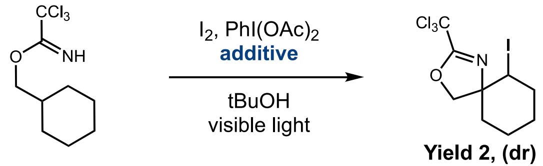
Table S5: Effect of prestir

Entry	Pre-stir time	A	B
1	0 min	90%, 4 : 1 dr	<5%
2	**3 min**	**84%, 19 : 1 dr**	**<5%**

Note: with a zero minute prestir, results were inconsistent.

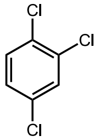
V. Functional Group Tolerance and Additive Screen

Imidate (**1**) (51.7 mg, 0.2 mmol) was subjected to **GP3** with the following modifications: an additive (1 equiv.) was introduced during the 3 min prestir. Upon completion, dichloroethane or isopropyl acetate was added as an internal standard, and the crude mixture was analyzed by ^{1}H-NMR.

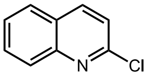


Key: 66-100 %
34-66 %
0-33 %

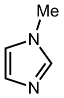
arenes



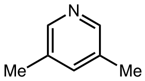
Prod: 83% (12:1)
Additive: 102%



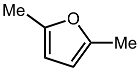
Prod: 67% (20 : 1)
Additive: 101%



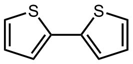
Prod: 78% (10 : 1)
Additive: 71%



Prod: 71% (6 : 1)
Additive: 104%

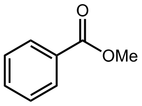


Prod: 20% (nd)
Additive: 0%

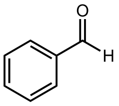


Prod: 17% (nd)
Additive (%): 0%

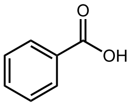
carbonyl derivatives



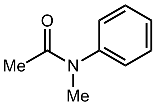
Prod: 83% (12 : 1)
Additive: 99%



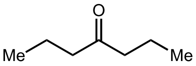
Prod: 71% (12 : 1)
Additive: 84%



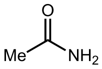
Prod: 59% (17 : 1)
Additive: 100%



Prod: 76% (19 : 1)
Additive: 100%

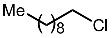


Prod: 75% (16 : 1)
Additive: 98%

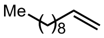


Prod: 60% (11 : 1)
Additive: 73%

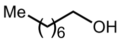
other



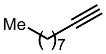
Prod: 78% (11 : 1)
Additive: 100%



Prod: 92% (4 : 1)
Additive: 0%

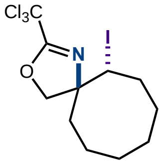


Prod: 71% (6 : 1)
Additive: 68%



Prod: 89% (4 : 1)
Additive: 0%

VI. Amino-iodination Characterization



6-iodo-2-(trichloromethyl)-3-oxa-1-azaspiro[4.7]dodec-1-ene (6)

Imidate **S6** (57.3 mg, 0.2 mmol) was subjected to **GP3** with the following changes: NaI (90 mg, 0.6 mmol). Upon completion, the combined organic layer was concentrated *in vacuo* to afford amino-iodinated product **6** (70%, 5 : 1 d.r. – NMR yield) as an orange oil with 15% amination product.

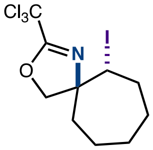
Rf: Diastereomer **A** (major): 0.32 (5% EtOAc/hexanes), Diastereomer **B** (minor): 0.27 (5% EtOAc/hexanes)

^{1}H NMR (400 MHz, CDCl$_3$): Diastereomer **A** (major) δ = 4.61 (dd, J = 9.2 Hz, J = 2.3 Hz, 1H), 4.49 (ap s, 2 H), 2.82 – 2.73 (m, 1H), 2.60 – 2.54 (m, 1H), 2.39 – 2.32 (m, 1H), 1.89 – 1.83 (m, 1H), 1.81 – 1.55 (m, 7H), 1.41 – 1.34 (m, 1H).

^{13}C NMR (100 MHz, CDCl$_3$): Diastereomer **A** (major) δ = 161.62, 87.00, 83.33, 79.14, 43.46, 37.81, 33.15, 29.44, 27.58, 24.55, 22.16.

HRMS (ESI-TOF) m/z: calc'd for $C_{11}H_{15}Cl_3INO$ $[M+Na]^+$ 431.9156, found 431.9139.

IR (neat) cm^{-1}: 2921, 2854, 1663, 1466, 1444, 1269, 998, 789.



6-iodo-2-(trichloromethyl)-3-oxa-1-azaspiro[4.6]undec-1-ene (7)

Imidate **S7** (54.5 mg, 0.2 mmol) was subjected to **GP3** with the following changes: NaI (90 mg, 0.6 mmol). Upon completion, the combined organic layer was concentrated *in vacuo* to afford amino-iodinated product **7** (82%, 1.4 : 1 d.r. – NMR yield) as an yellow oil with 10% amination product.

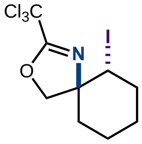
Rf: Diastereomer **A** (major): 0.39 (5% EtOAc/hexanes), Diastereomer **B** and amination product (minor): 0.45 (5% EtOAc/hexanes)

^{1}H NMR (400 MHz, CDCl$_3$): Diastereomer **A** (major) δ = 4.45 (d, J = 8.3 Hz, 1H), 4.42 (d, J = 8.2 Hz, 1H), 4.21 (dd, J = 10.3 Hz, 2.3 Hz, 1H), 2.60 – 2.41 (m, 2H), 2.10 – 2.04 (m, 1H), 1.98 – 1.69 (m, 4H), 1.61 – 1.34 (m, 3H).
Diastereomer **B** δ = 4.65 (d, J = 8.8 Hz, 1 H), 4.57 (dd, J = 10.0 Hz, 2.5 Hz, 1 H), 4.37 (d, J = 8.8 Hz, 1 H), 2.58 – 2.51 (m, 1 H), 2.05 – 2.02 (m, 2 H), 1.99 – 1.90 (m, 1 H), 1.80 – 1.40 (m, 6 H).

^{13}C NMR (150 MHz, CDCl$_3$): Diastereomer **A** (major) δ = 161.26, 83.42, 78.21, 45.22, 37.28, 36.96, 31.07, 29.02, 27.55, 20.82.
Diastereomer **B** (minor) δ = 161.05, 80.87, 78.39, 45.35, 37.49, 35.98, 35.40, 27.34, 26.09, 20.79.

HRMS (ESI-TOF) m/z: calc'd for $C_{10}H_{13}Cl_3INO$ $[M+Na]^+$ 417.9000, found 417.9023.

IR (neat) cm^{-1}: 2924, 2856, 1661, 1457, 1363, 997, 789.



6-iodo-2-(trichloromethyl)-3-oxa-1-azaspiro[4.5]dec-1-ene (2)

Imidate **1** (51.7 mg, 0.2 mmol) was subjected to **GP3**. Upon completion, the combined organic layer was concentrated *in vacuo* before purification by flash chromatography (isocratic: 1 : 99 EtOAc : hexanes) to afford amino-iodinated product **2** (64.3 mg, 84%, 19 : 1 d.r.) as a white solid.

Note: The product may appear as a yellow oil with the presence of trace amounts of impurities.

Rf: 0.38 (5% EtOAc/hexanes)

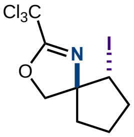
^{1}H NMR (400 MHz, CDCl$_3$): δ = 4.68 (d, J = 8.8 Hz, 1H), 4.53 (dd, J = 11.7 Hz, J = 4.0 Hz, 1H), 4.42 (d, J = 8.8 Hz, 1H), 2.51 – 2.44 (m, 1H), 2.12 – 2.06 (m, 1H), 1.98 – 1.80 (m, 3H), 1.68 – 1.55 (m, 1H), 1.51 – 1.42 (m, 1H), 1.37 – 1.25 (m, 1H).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 161.64, 86.76, 79.51, 75.50, 41.08, 36.18, 36.14, 26.99, 21.96.

HRMS (ESI-TOF) m/z: calc'd for $C_9H_{11}Cl_3INO$ $[M+Na]^+$ 403.8843, found 403.8856.

IR (neat) cm^{-1}: 2936, 2858, 1657, 1446, 1301, 1240, 999, 777.

MP: 58.0 °C – 60.6 °C.



6-iodo-2-(trichloromethyl)-3-oxa-1-azaspiro[4.4]non-1-ene (8)

Imidate **S8** (48.9 mg, 0.2 mmol) was subjected to **GP3** with the following changes: NaI (90 mg, 0.6 mmol). Upon completion, the combined organic layer was concentrated *in vacuo* before purification by flash chromatography (isocratic: 1 : 99 EtOAc : hexanes) to afford amino-iodinated product **8** (72.6 mg, 99%, 1 : 1 d.r.) as a yellow oil for one diastereomer (**A**) and a white solid for the other diastereomer (**B**).

Rf: Diastereomer **A**: 0.34 (5% EtOAc/hexanes), Diastereomer **B**: 0.24 (5% EtOAc/hexanes)

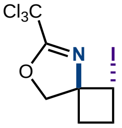
^{1}H NMR (400 MHz, CDCl$_3$): Diastereomer **A** δ = 4.81 (d, J = 9.2 Hz, 1 H), 4.40 (d, J = 9.2 Hz, 1 H), 4.34 (ap t, J = 6.3 Hz, 1 H), 2.62 – 2.54 (m, 1 H), 2.18 – 2.02 (m, 3 H), 1.96 – 1.88 (m, 2 H).
Diastereomer **B** δ = 4.48 (d, J = 8.8 Hz, 1 H), 4.44 (d, J = 8.9 Hz, 1 H), 3.96 (dd, J = 11.0 Hz, J = 7.7 Hz, 1 H), 2.47 – 2.31 (m, 2 H), 2.18 – 2.10 (m, 1 H), 2.05 – 1.97 (m, 1 H), 1.86 – 1.72 (m, 2 H).

^{13}C NMR (100 MHz, CDCl$_3$): Diastereomer **A** δ = 162.51, 86.77, 82.08, 81.66, 38.08, 36.48, 35.68, 22.08.
Diastereomer **B** δ = 161.91, 86.82, 80.42, 77.40, 36.27, 35.97, 34.96, 23.11.

HRMS (ESI-TOF) m/z: calc'd for $C_8H_9Cl_3INO$ $[M+H]^+$ 367.8867, found 367.8864.

IR (neat) cm^{-1}: 2982, 2958, 1654, 1466, 1444, 1271, 996, 788, 773.

MP (Diastereomer **B):** 113.0 °C – 114.8 °C.



1-iodo-6-(trichloromethyl)-7-oxa-5-azaspiro[3.4]oct-5-ene (9)

Imidate **S9** (46.1 mg, 0.2 mmol) was subjected to **GP3** with the following changes: PhI(OAc)$_2$ (257.3 mg, 0.8 mmol) and I$_2$ (101.5 mg, 0.4 mmol). Upon completion, the combined organic layer was concentrated *in vacuo* before purification by flash chromatography (isocratic: 1 : 99 EtOAc : hexanes) to afford amino-iodinated product **9** (64.4 mg, 91%, 1 : 1 d.r.) as a white solid for diastereomer **A** (major) and a yellow oil for diastereomer **B** (minor).

Rf: Diastereomer **A**: 0.25 (5% EtOAc/hexanes), Diastereomer **B**: 0.20 (5% EtOAc/hexanes)

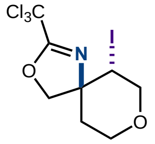
^{1}H NMR (400 MHz, CDCl$_3$): Diastereomer **A** δ = 5.13 (d, J = 9.4 Hz, 1 H), 4.87 (dd, J = 9.0 Hz, 9.0 Hz, 1 H), 4.58 (d, J = 9.3 Hz, 1 H), 2.78 – 2.70 (m, 1 H), 2.65 – 2.57 (m, 1 H), 2.39 – 2.33 (m, 1 H), 2.16 – 2.04 (m, 1 H).
Diastereomer **B** δ = 4.45 (dd, J = 10.0 Hz, 8.0 Hz, 1 H), 4.36 (d, J = 9.8 Hz, 1 H), 4.32 (d, J = 9.6 Hz, 1 H), 2.80 – 2.70 (m, 1 H), 2.55 – 2.46 (m, 2 H), 2.38 – 2.30 (m, 1 H).

^{13}C NMR (100 MHz, CDCl$_3$): Diastereomer **A** δ = 163.45, 86.41, 83.14, 76.13, 34.04, 28.93, 27.42.
Diastereomer **B** δ = 163.12, 86.53, 78.34, 77.06, 34.29, 29.04, 25.60.

HRMS (ESI-TOF) m/z: calc'd for $C_7H_7Cl_3INO$ $[M+H]^+$ 353.8711, found 353.8708.

IR (film) cm^{-1}: 2923, 2853, 1711, 1654, 1506, 1461, 819, 792.

MP (Diastereomer **A**)**:** 114.4 °C – 117.0 °C.



6-iodo-2-(trichloromethyl)-3,8-dioxa-1-azaspiro[4.5]dec-1-ene (10)

Imidate **S10** (52.1 mg, 0.2 mmol) was subjected to **GP3** with the following changes: the reaction time was extended to 2h. Upon completion, the combined organic layer was concentrated *in vacuo* before purification by flash chromatography (isocratic: 5 : 94 EtOAc : hexanes) to afford amino-iodinated product **10** (53.9 mg, 70%, 1.6 : 1 d.r.) as a yellow oil with 5% amination product.

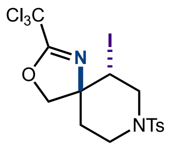
Rf: Diastereomer **A** & **B**: 0.32 (15% EtOAc/hexanes)

^{1}H NMR (400 MHz, CDCl$_3$): Diastereomer **A** & **B** δ = 4.73 (d, J = 8.9 Hz, 1H), 4.50 – 4.44 (m, 3.5 H), 4.25 – 4.17 (m, 4 H), 4.12 – 4.02 (m, 5.6 H), 3.96 – 3.92 (m, 1.4 H), 3.55 – 3.46 (m, 2 H), 2.33 – 2.10 (m, 5.6 H).

^{13}C NMR (100 MHz, CDCl$_3$): Diastereomer **A** & **B** δ = 162.76, 162.28, 86.78, 86.58, 81.51, 79.66, 73.30, 72.28, 71.11, 71.05, 64.66, 64.39, 39.05, 38.28, 37.52, 37.05, 36.70, 29.83.

HRMS (ESI-TOF) m/z: calc'd for $C_8H_9Cl_3INO_2$ $[M+Na]^+$ 405.8636, found 405.8645.

IR (neat) cm^{-1}: 2962, 2847, 1735, 1659, 1465, 1436, 1243, 1095, 1007, 785.



6-iodo-8-tosyl-2-(trichloromethyl)-3-oxa-1,8-diazaspiro[4.5]dec-1-ene (11)

Imidate (**S11**) (82.7 mg, 0.2 mmol) was subjected to **GP3**. Upon completion, the combined organic layer was concentrated and the residue was loaded directly onto silica gel and purified by flash column chromatography (isocratic: 10 : 90, EtOAc : hexanes) to yield amino-iodinated product **11** (79.6 mg, 74%, 14:1) as a pale yellow solid.

Rf: 0.40 (20% EtOAc / hexanes).

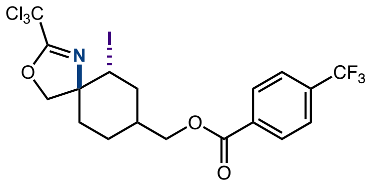
^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.66 (d, J = 8.2 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 4.49 (d, J = 9.0 Hz, 1H), 4.39 (dd, J = 8.7, 3.7 Hz, 1H), 4.25 (d, J = 9.3 Hz, 1H), 3.88-3.85 (m, 1H), 3.57-3.54 (m, 1H), 3.05-3.00 (m, 1H), 2.86-2.82 (m, 1H), 2.45 (s, 3H), 2.28-2.22 (m, 1H), 2.15-2.06 (m, 1H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 162.77, 144.24, 133.91, 130.13, 127.64, 86.44, 79.97, 73.25, 51.14, 42.52, 35.01, 34.00, 21.73.

HRMS (ESI-TOF) m/z: calc'd for $C_{15}H_{16}Cl_3IN_2O_3S$ [M+Na]$^+$ 558.8890, found 558.8890.

IR (film) cm^{-1}: 3065, 3048, 2971, 2925, 2859, 2361, 1723, 1667, 1352, 1152, 786.

MP: 208.1 - 209.0 ^{o}C.



6-iodo-2-(trichloromethyl)-3-oxa-1-azaspiro[4.5]dec-1-en-8-yl)methyl 4-(trifluoromethyl)benzoate (12)

Imidate **S12** (92.1 mg, 0.2 mmol) was subjected to **GP3**. Upon completion, the combined organic layer was concentrated *in vacuo* before purification by flash chromatography (isocratic: 10 : 90, EtOAc : hexanes) to afford amino-iodinated product **12** (95.9 mg, 82%, 13:1) as a white solid.

Rf: 0.58 (15% EtOAc/hexanes)

^{1}H NMR (600 MHz, CDCl$_3$): δ = 8.16 (d, J = 8.1 Hz, 2H), 7.71 (d, J = 8.3 Hz, 2H), 4.50-4.49 (m, 1H), 4.46 (d, J = 9.1 Hz, 1H), 4.35-4.32 (m, 2H), 4.26 (d, J = 9.2 Hz, 1H), 2.48-2.41 (m, 1H), 2.37-2.32 (m, 1H), 2.29-2.24 (m, 1H), 2.13-2.10 (m, 1H), 1.85-1.81 (m, 2H), 1.73-1.71 (m, 1H).

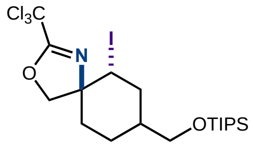
^{13}C NMR (150 MHz, CDCl$_3$): δ = 165.36, 161.78, 134.68 (q, 32.6 Hz), 133.53, 130.15, 125.60 (q, 3.7 Hz), 123.75 (q, 272.5 Hz), 87.05, 83.46, 74.34, 68.60, 39.12, 35.76, 33.25, 33.25, 33.00, 24.31.

^{19}F NMR (564 MHz, CDCl$_3$): δ = -63.12.

HRMS (ESI-TOF) m/z: calc'd for $C_{18}H_{16}Cl_3F_3INO_3$ $[M+H]^+$ 460.0461, found 460.0462.

IR (film) cm^{-1}: 3058, 2946, 1721, 1658, 1271, 774.

MP: 126.0-128.0 °C.



6-iodo-2-(trichloromethyl)-8-(((triisopropylsilyl)oxy)methyl)-3-oxa-1-azaspiro[4.5]dec-1-ene (13)

Imidate (**S13**) (89 mg, 0.2 mmol) was subjected to **GP3**. Upon completion, the combined organic layer was concentrated and the residue was loaded directly onto silica gel and purified by flash column chromatography (isocratic: 5 : 94 : 1, EtOAc : hexanes : Et$_3$N) to yield imidate X (89.9 mg, 79%) as a colorless oil.

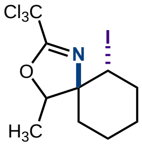
Rf: 0.46 (10% EtOAc / hexanes).

^{1}H NMR (400 MHz, CDCl$_3$): δ =4.53-4.50 (m, 1H), 4.49 (d, J = 9.0 Hz, 1H), 4.28 (d, J = 4.5 Hz, 1H), 3.66 (dd, J = 6.0, 2.0 Hz, 2H), 2.30-2.23 (m, 1H), 2.19-2.11 (m, 1H), 2.09-2.02 (m, 2H), 1.84-1.74 (m, 2H), 1.61-1.57 (m, 1H), 1.07-1.06 (m, 2H).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 161.50, 87.10, 83.01, 74.84, 66.48, 40.44, 36.72, 36.11, 33.17, 28.85, 23.92, 18.18, 12.11.

HRMS (ESI-TOF) m/z: calc'd for $C_{19}H_{33}Cl_3INO_2Si$ $[M+Na]^+$ 590.0289, found 590.0272.

IR (film) cm^{-1}: 2941, 2891, 2863, 1659, 1099, 996, 792.



6-iodo-4-methyl-2-(trichloromethyl)-3-oxa-1-azaspiro[4.5]dec-1-ene (14)

Imidate **S14** (54.5 mg, 0.2 mmol) was subjected to **GP3** with the following changes: NaI (90 mg, 0.6 mmol). Upon completion, the combined organic layer was concentrated *in vacuo* before purification by flash chromatography (isocratic: 1 : 99 EtOAc : hexanes) to afford amino-iodinated product **14** (42.6 mg, 54%, 1.3 : 1 d.r.) as an orange oil for both diastereomers with 5% amination product.

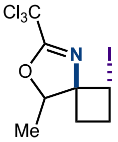
Rf: Diastereomer **A** (major): 0.34 (5% EtOAc/hexanes), Diastereomer **B** (minor): 0.29 (5% EtOAc/hexanes)

^{1}H NMR (400 MHz, CDCl$_3$): Diastereomer **A** (major) δ = 4.78 (q, J = 6.6 Hz, 1H), 4.41 – 4.39 (m, 1H), 2.45 – 2.37 (m, 1H), 2.03 – 1.50 (m, 7H), 1.40 (d, J = 6.5 Hz, 3H).
Diastereomer **B** (minor) δ = 4.91 (q, J = 6.6 Hz, 1 H), 4.20 (dd, J = 12.1 Hz, J = 4.2 Hz, 1H), 2.67 – 2.57 (m, 1H), 2.43 – 2.37 (m, 1H), 2.01 – 1.84 (m, 2H), 1.72 – 1.64 (m, 2H), 1.58 – 1.51 (m, 1H), 1.44 – 1.33 (m, 1H), 1.36 (d, J = 6.7 Hz, 3H).

^{13}C NMR (100 MHz, CDCl$_3$): Diastereomer **A** (major) δ = 160.44, 89.63, 87.29, 74.72, 44.60, 33.92, 29.38, 23.80, 22.06, 16.13.
Diastereomer **B** (minor) δ = 161.00, 89.87, 87.40, 74.92, 44.98, 37.59, 32.48, 29.10, 21.75, 15.47.

HRMS (ESI-TOF) m/z: calc'd for $C_{10}H_{13}Cl_3INO$ $[M+H]^+$ 395.9180, found 395.9182.

IR (neat) cm^{-1}: 2964, 2858, 1700, 1656, 1445, 1380, 1249, 824, 789.



1-iodo-8-methyl-6-(trichloromethyl)-7-oxa-5-azaspiro[3.4]oct-5-ene (15)

Imidate **S15** (48.9 mg, 0.2 mmol) was subjected to **GP3** with the following changes: NaI (90 mg, 0.6 mmol). Upon completion, the combined organic layer was concentrated *in vacuo* before purification by flash chromatography (isocratic: 1 : 99 EtOAc : hexanes) to afford amino-iodinated product **15** (42.6 mg, 54%, 3.3 : 3.2 : 1 d.r.) as an orange oil for both diastereomers with 5% of another diastereomer.

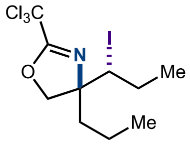
Rf: Diastereomer **A** (major): 0.28 (5% EtOAc/hexanes), Diastereomer **B** (minor): 0.18 (5% EtOAc/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): Diastereomer **A** (major) δ = 5.21 (q, J = 6.6 Hz, 1H), 4.21 (ap t, J = 8.3 Hz, 1H), 2.76 – 2.68 (m, 1H), 2.55 – 2.34 (m, 3H), 1.49 (d, J = 6.5 Hz, 3H).
Diastereomer **B** (minor) δ = 4.57 (q, J = 6.7 Hz, 1 H), 4.37 (dd, J = 10.0 Hz, J = 8.0 Hz, 1H), 2.80 – 2.70 (m, 1H), 2.51 – 2.26 (m, 3H), 1.36 (d, J = 6.5 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$): Diastereomer **A** (major) δ = 162.43, 89.08, 86.73, 77.90, 29.72, 29.40, 28.94, 16.95.
Diastereomer **B** (minor) δ = 162.42, 86.87, 85.35, 79.77, 29.95, 29.25, 26.16, 16.19.

HRMS (ESI-TOF) m/z: calc'd for $C_8H_9Cl_3INO$ $[M+H]^+$ 367.8867, found 367.8840.

IR (film) cm^{-1}: 2969, 2932, 1710, 1466, 1378, 1340, 1305.



4-((1-iodopropyl)-4-propyl-2-(trichloromethyl)-4,5-dihydrooxazole (16)

Imidate (**16**) (74.9 mg, 0.2 mmol) was subjected to **GP3**. Upon completion, the combined organic layer was concentrated and the residue was loaded directly onto silica gel and purified by flash column chromatography (isocratic: hexanes) to yield amino-iodinated product **16** (66.9 mg, 82%, 1.1:1) as a pale yellow oil.

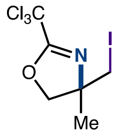
Rf: 0.53 (10% EtOAc / hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = Diastereomer **A**: 4.64 (d, J = 9.3 Hz, 1H), 4.34 (d, J = 9.2 Hz, 1H), 4.20-4.16 (m, 1H), 2.03-1.30 (m, 6H), 0.96 (t, J = 7.3 Hz, 6H).
Diastereomer **B**: 4.50 (d, J = 9.0 Hz, 1H), 4.44 (d, J = 9.0 Hz, 1H), 4.20-4.16 (m, 1H), 2.03-1.30 (m, 6H), 1.08 (t, J = 7.1 Hz, 6H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 161.94, 161.74, 86.86, 79.94, 78.21, 77.87, 77.82, 51.34, 47.63, 43.93, 38.21, 27.72, 27.31, 17.13, 16.66, 15.20, 15.07, 14.43, 14.29.

HRMS (ESI-TOF) m/z: calc'd for $C_{10}H_{15}Cl_3INO$ $[M+Na]^+$ 419.9162, found 419.9140.

IR (film) cm^{-1}: 2964, 2937, 2874, 1770, 1659, 998, 816, 750.



4-(iodomethyl)-4-methyl-2-(trichloromethyl)-4,5-dihydrooxazole (17)

Imidate **S17** (43.7 mg, 0.2 mmol) was subjected to **GP3** with the following changes: $PhI(OAc)_2$ (322.1 mg, 1.0 mmol) and NaI (90 mg, 0.6 mmol). In addition, the reaction time was extended to 2h. Upon completion, the combined organic layer was concentrated *in vacuo* before purification by flash chromatography (isocratic: 5 : 94 EtOAc : hexanes) to afford amino-iodinated product **17** (34.4 mg, 50%) as a yellow solid.

Rf: 0.22 (5% EtOAc/hexanes)

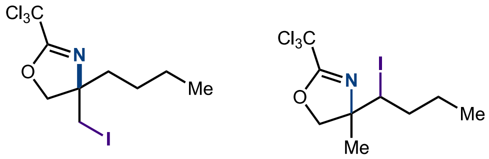
^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.58 (d, J = 8.4 Hz, 1H), 4.30 (d, J = 8.8 Hz, 1H), 3.39 (ap q, J = 8.1 Hz, 2H), 1.60 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.68, 86.61, 81.27, 71.11, 26.04, 15.46.

HRMS (ESI-TOF) m/z: calc'd for $C_6H_7Cl_3INO$ $[M+H]^+$ 341.8711, found 341.8701.

IR (neat) cm^{-1}: 2975, 1652, 1471, 1290, 788, 776.

MP: 59.0 °C – 62.7 °C.



4-(1-iodobutyl)-4-methyl-2-(trichloromethyl)-4,5-dihydrooxazole (18)

Imidate (**18)** (52.1 mg, 0.2 mmol) was subjected to **GP3**. Upon completion, the combined organic layer was concentrated and the residue was loaded directly onto silica gel and purified by flash column chromatography (isocratic: 1 : 99 EtOAc : hexanes) to yield amino-iodinated product **18** (56.9 mg, 74%, 1.1:1 dr, 8:1 rr) as a pale yellow oil.

Rf: 0.36 (10% EtOAc / hexanes).

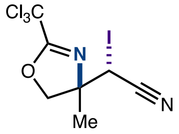
^{1}H NMR (400 MHz, $CDCl_3$): δ = Diastereomer **A**: 4.70 (d, J = 9.1 Hz, 1H), 4.28 (d, J = 9.1 Hz, 1H), 4.21 (dd, J = 11.3 Hz, 2.9 Hz, 1H), 1.94-1.28 (m, 6H), 0.98-0.92 (m, 3H).
Diastereomer **B**: 4.51 (d, J = 8.8 Hz, 1H), 4.33 (d, J = 8.8 Hz, 1H), 4.14 (dd, J = 11.3 Hz, 2.5 Hz, 1H), 1.94-1.28 (m, 6H), 0.98-0.92 (m, 3H).

Regioisomer **2**: 4.51 (d, J = 8.9 Hz, 1H), 4.39 (d, J = 8.9 Hz, 1H), 3.40 (dd, J = 17.6, 10.4 Hz, 2H), 1.94-1.28 (m, 6H), 0.98-0.92 (m, 3H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 161.97, 161.95, 161.89, 86.67, 83.03, 80.03, 76.48, 75.36, 74.90, 74.42, 73.68, 71.32, 47.19, 45.32, 39.41, 36.50, 36.11, 31.59, 29.34, 25.95, 23.59, 23.51, 23.33, 23.28, 23.07, 14.22, 13.23, 13.20.

HRMS (ESI-TOF) m/z: calc'd for $C_9H_{13}Cl_3INO$ $[M+Na]^+$ 405.9005, found 405.8994.

IR (film) cm^{-1}: 2926, 2855, 2359, 1660, 999, 795.



2-(4-(iodomethyl)-2-(trichloromethyl)-4,5-dihydrooxazol-4-yl)acetonitrile (19)

Imidate **S19** (48.7 mg, 0.2 mmol) was subjected to **GP3** with the following changes: $PhI(OAc)_2$ (257.3 mg, 0.8 mmol). Upon completion, the combined organic layer was concentrated and the yield was determined by ^{1}H-NMR using dichloroethane as an internal standard (75%, 1:1). Compound **19** was isolated using preparatory thin-layer chromatography (10 : 90 EtOAc : hexanes) as a yellow oil

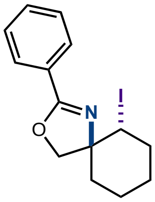
Rf: Diastereomer **A**: 0.21 (10% EtOAc/hexanes), Diastereomer **B**: 0.19 (10% EtOAc/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): Diastereomer **A** δ = 4.75 (d, J = 9.5 Hz, 1 H), 4.54 (s, 1 H), 4.46 (d, J = 9.4 Hz, 1 H), 1.80 (s, 3 H).
Diastereomer **B** δ = 4.76 (d, J = 9.5 Hz, 1 H), 4.44 (s, 1 H), 4.41 (d, J = 9.5 Hz, 1 H), 1.68 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): Diastereomer **A** δ = 164.00, 116.80, 86.07, 80.02, 73.11, 24.14, 8.97.
Diastereomer **B** δ = 164.46, 116.44, 80.01, 79.45, 73.57, 26.34, 7.09.

HRMS (ESI-TOF) m/z: calc'd for $C_7H_6Cl_3IN_2O$ $[M+Na]^+$ 388.8483, found 388.8465.

IR (neat) cm^{-1}: 2975, 1652, 1471, 1290, 788, 776.



6-iodo-2-phenyl-3-oxa-1-azaspiro[4.5]dec-1-ene (20)

Imidate **(S20)** (43.5 mg, 0.2 mmol) was subjected to **GP3**. Upon completion, the combined organic layer was concentrated and the residue was loaded directly onto silica gel and purified by flash column chromatography (isocratic: 5 : 95 EtOAc : hexanes) to yield amino-iodinated product **20** (59.4 mg, 87%, >20:1) as a pale yellow oil.

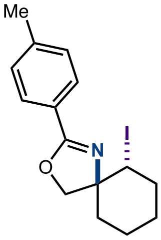
Rf: 0.30 (10% EtOAc / hexanes).

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.95-7.93 (m, 2H), 7.50-7.46 (m, 1H), 7.42-7.38 (m, 2H), 4.56 (dd, J = 11.3 Hz, 3.9 Hz, 1H), 4.47 (d, J = 8.6 Hz, 1H), 4.21 (d, J = 8.6 Hz, 1H), 2.54-2.47 (m, 1H), 2.09-2.05 (m, 1H), 1.96-1.84 (m, 3H), 1.65-1.59 (m, 1H), 1.52-1.27 (m, 2H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 163.05, 131.58, 128.55, 128.44, 127.81, 76.44, 75.06, 44.26, 36.88, 36.33, 27.08, 22.42.

HRMS (ESI-TOF) m/z: calc'd for $C_{14}H_{16}INO$ [M+H]$^+$ 342.0355, found 342.0329.

IR (film) cm^{-1}: 3060, 2932, 2856, 1648, 1321, 1060, 1024, 693.



6-iodo-2-(*p*-tolyl)-3-oxa-1-azaspiro[4.5]dec-1-ene (21)

Imidate **(S21)** (46.3 mg, 0.2 mmol) was subjected to **GP3**. Upon completion, the combined organic layer was concentrated and the residue was loaded directly onto silica gel and purified by flash column chromatography (isocratic: 5 : 95 EtOAc : hexanes) to yield amino-iodinated product **21** (61.1 mg, 87%, >20:1) as a white solid.

Rf: 0.50 (20% EtOAc / hexanes).

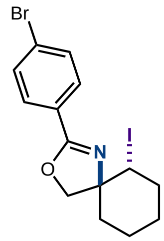
^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.83 (d, J = 8.2 Hz, 2H), 7.21 (d, J = 7.9 Hz, 2H), 4.54 (dd, J = 11.3, 3.9 Hz, 1H), 4.44 (d, J = 8.6 Hz, 1H), 4.18 (d, J = 8.6 Hz, 1H), 2.53-2.46 (m, 1H), 2.38 (s, 3H), 2.10-2.04 (m, 1H), 1.94-1.84 (m, 3H), 1.64-1.59 (m, 1H), 1.51-1.32 (m, 2H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 163.04, 141.93, 129.15, 128.50, 125.06, 75.00, 44.52, 36.94, 36.36, 27.13, 22.47, 21.70.

HRMS (ESI-TOF) m/z: calc'd for $C_{15}H_{18}INO$ [M+H]$^+$ 356.0511, found 356.0496.

IR (film) cm^{-1}: 3034, 2981, 2954, 1643, 1070, 827, 727.

MP: 89.0-91.0 °C.



2-(4-bromophenyl)-6-iodo-3-oxa-1-azaspiro[4.5]dec-1-ene (22)

Imidate **(S22)** (59.2 mg, 0.2 mmol) was subjected to **GP3**. Upon completion, the combined organic layer was concentrated and the residue was loaded directly onto silica gel and purified by flash column chromatography (isocratic: 5 : 95 EtOAc : hexanes) to yield imidate **22** (59.7 mg, 71%, >20:1) as a pale yellow oil.

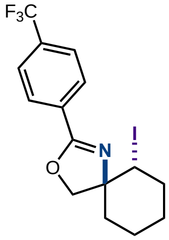
Rf: 0.33 (10% EtOAc / hexanes).

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.82-7.79 (m, 2H), 7.55-7.53 (m, 2H), 4.53 (dd, J = 11.3, 3.9 Hz, 1H), 4.46 (d, J = 8.6 Hz, 1H), 4.20 (d, J = 8.6 Hz, 1H), 2.53-2.47 (m, 1H), 2.10-2.05 (m, 1H), 1.94-1.84 (m, 3H), 1.65-1.61 (m, 1H), 1.52-1.30 (m, 2H).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 162.23, 131.75, 130.12, 126.86, 126.30, 76.63, 75.26, 44.06, 36.90, 36.29, 27.09, 22.43.

HRMS (ESI-TOF) m/z: calc'd for $C_{14}H_{15}BrINO$ [M+H]$^+$ 419.9460, found 419.9450.

IR (film) cm^{-1}: 3032, 2933, 2856, 1647, 1070, 726.



6-iodo-2-(4-(trifluoromethyl)phenyl)-3-oxa-1-azaspiro[4.5]dec-1-ene (23)

Imidate **(S23)** (57.1 mg, 0.2 mmol) was subjected to **GP3**. Upon completion, the combined organic layer was concentrated and the residue was loaded directly onto silica gel and purified by flash column chromatography (isocratic: 5 : 95 EtOAc : hexanes) to yield amino-iodinated product **23** (67.1 mg, 82%, >20:1) as a white solid.

Rf: 0.33 (10% EtOAc / hexanes).

^{1}H NMR (600 MHz, CDCl$_3$): δ = 8.06 (d, J = 8.1 Hz, 2H), 7.67 (d, J = 8.2 Hz, 2H), 4.54 (dd, J = 11.3, 3.9 Hz, 1H), 4.49 (d, J = 8.6 Hz, 1H), 4.24 (d, J = 8.4 Hz, 1H), 2.53-2.48 (m, 1H), 2.10-2.06 (m, 1H), 1.94-1.86 (m, 3H), 1.65-1.61 (m, 1H), 1.51-1.44 (m, 1H), 1.39-1.33 (m, 1H).

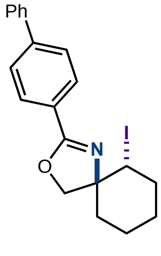
^{13}C NMR (150 MHz, CDCl$_3$): δ = 161.79, 133.20 (q, 32.5 Hz), 131.29, 128.95, 125.43 (q, 3.8 Hz), 123.93 (q, 272.5 Hz), 76.73, 75.39, 43.77, 36.88, 36.27, 27.09, 22.37.

^{19}F NMR (367 MHz, CDCl$_3$): -62.98.

HRMS (ESI-TOF) m/z: calc'd for $C_{15}H_{15}F_3INO$ [M+H]$^+$ 410.0229, found 410.0214.

IR (film) cm^{-1}: 3003, 2955, 2864, 1646, 1318, 1073, 848, 676.

MP: 109.1-110.3 °C.



2-([1,1'-biphenyl]-4-yl)-6-iodo-3-oxa-1-azaspiro[4.5]dec-1-ene (24)

Imidate **(S24)** (58.7 mg, 0.2 mmol) was subjected to **GP3**. Upon completion, the combined organic layer was concentrated and the residue was loaded directly onto silica gel and purified by flash column chromatography (isocratic: 5 : 95, EtOAc : hexanes) to yield amino-iodinated product **22** (63.4 mg, 76%, >20:1) as a white solid.

Rf: 0.39 (10% EtOAc / hexanes).

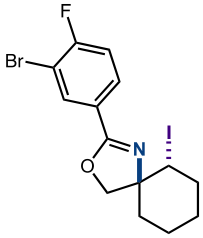
^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.03-8.01 (m, 2H), 7.65-7.61 (m, 4H), 7.47-7.44 (m, 2H), 7.39-7.36 (m, 1H), 4.58 (dd, J = 11.3, 3.9 Hz, 1H), 4.49 (d, J = 8.6 Hz, 1H), 4.23 (d, J = 8.6 Hz, 1H), 2.54-2.50 (m, 1H), 2.12-2.08 (m, 1H), 1.97-1.88 (m, 3H), 1.66-1.62 (m, 1H), 1.52-1.45 (m, 1H), 1.41-1.34 (m, 1H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 162.84, 144.34, 140.42, 129.05, 129.00, 128.02, 127.34, 127.17, 126.72, 76.47, 45.16, 44.38, 36.97, 36.38, 27.15, 22.48.

HRMS (ESI-TOF) m/z: calc'd for $C_{20}H_{20}INO$ $[M+H]^+$ 418.0668, found 418.0651.

IR (film) cm^{-1}: 3031, 3029, 2985, 2980, 1639, 1068, 825, 721.

MP: 81.3-83.2 °C.



2-(3-bromo-4-fluorophenyl)-6-iodo-3-oxa-1-azaspiro[4.5]dec-1-ene (25)

Imidate **(S25)** (62.8 mg, 0.2 mmol) was subjected to **GP3**. Upon completion, the combined organic layer was concentrated and the residue was loaded directly onto silica gel and purified by flash column chromatography (isocratic: 5 : 95, EtOAc : hexanes) to yield amino-iodinated product **25** (66.1 mg, 75%, 13:1) as a white solid.

Rf: 0.53 (15% EtOAc / hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18 (dd, J = 6.7, 2.1 Hz, 1H), 7.86 (qd, J = 7.3, 2.1 Hz, 1H), 7.14 (t, J = 8.4 Hz, 1H), 4.51 (d, J = 11.3 Hz, 1H), 4.46 (d, J = 8.7 Hz, 1H), 4.20 (d, J = 8.7 Hz, 1H), 2.53-2.46 (m, 1H), 2.09-2.03 (m, 1H), 1.93-1.83 (m, 3H), 1.65-1.60 (m, 1H), 1.52-1.29 (m, 2H).

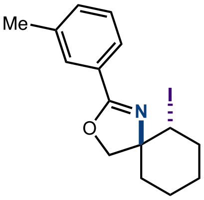
^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.18 (d, 252.7 Hz), 160.96, 134.05, 129.50 (d, J = 8.1 Hz), 125.53 (d, J = 3.7 Hz), 116.53 (d, J = 23.0 Hz), 109.36 (d, J = 21.6 Hz), 77.36, 75.33, 43.89, 36.89, 36.27, 27.05, 22.40.

^{19}F NMR (367 MHz): δ = -102.42.

HRMS (ESI-TOF) m/z: calc'd for $C_{14}H_{14}BrFINO$ $[M+H]^+$ 437.9366, found 437.9362.

IR (film) cm^{-1}: 3078, 2979, 2938, 2858, 1649, 1492, 830.

MP: 82-83 °C.



6-iodo-2-(*m*-tolyl)-3-oxa-1-azaspiro[4.5]dec-1-ene (26)

Imidate **(S26)** (46.3 mg, 0.2 mmol) was subjected to **GP3**. Upon completion, the combined organic layer was concentrated and the residue was loaded directly onto silica gel and purified by flash column chromatography (isocratic: 5 : 95, EtOAc : hexanes) to yield amino-iodinated product **26** (63.4 mg, 89%, 9:1) as a pale yellow oil.

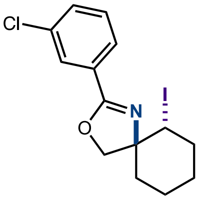
Rf: 0.55 (15% EtOAc / hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (m, 1H), 7.74-7.71 (m, 1H), 7.30-7.28 (m, 2H), 4.55 (dd, J = 11.4, 3.9 Hz, 1H), 4.46 (d, J = 8.6 Hz, 1H), 4.20 (d, J = 8.7 Hz, 1H), 2.54-2.48 (m, 1H), 2.38 (s, 3H), 2.10-2.04 (m, 1H), 1.96-1.84 (m, 3H), 1.67-1.60 (m, 1H), 1.52-1.31 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.16, 138.23, 132.38, 129.09, 128.37, 127.75, 125.65, 76.32, 75.07, 44.35, 36.98, 36.41, 27.18, 22.47, 21.37.

HRMS (ESI-TOF) m/z: calc'd for $C_{15}H_{18}INO$ $[M+H]^+$ 356.0511, found 356.0501.

IR (film) cm^{-1}: 3039, 2932, 2857, 1647, 1063, 712.



2-(3-chlorophenyl)-6-iodo-3-oxa-1-azaspiro[4.5]dec-1-ene (27)

Imidate **(S27)** (50.3 mg, 0.2 mmol) was subjected to **GP3**. Upon completion, the combined organic layer was concentrated and the residue was loaded directly onto silica gel and purified by flash column chromatography (isocratic: 5 : 95 EtOAc : hexanes) to yield amino-iodinated **27** (75.1 mg, 83%, 9:1) as a pale yellow solid.

Rf: 0.53 (15% EtOAc / hexanes).

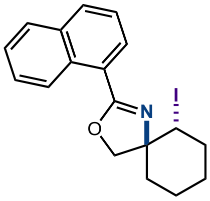
^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.95-7.94 (m, 1H), 7.83-7.81 (m, 1H), 7.46-7.43 (m, 1H), 7.36-7.32 (m, 1H), 4.53 (dd, J = 11.3, 3.9 Hz, 1H), 4.47 (d, J = 8.7 Hz, 1H), 4.21 (d, J = 8.7 Hz, 1H), 2.53-2.47 (m, 1H), 2.09-2.04 (m, 1H), 1.93-1.83 (m, 3H), 1.65-1.61 (m, 1H), 1.53-1.31 (m, 2H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 161.84, 134.56, 131.61, 129.76, 129.65, 128.65, 126.64, 76.70, 75.24, 43.92, 36.87, 36.26, 27.03, 22.38.

HRMS (ESI-TOF) m/z: calc'd for $C_{14}H_{15}ClINO$ $[M+H]^+$ 375.9965, found 375.9956.

IR (film) cm^{-1}: 3078, 2944, 2921, 2853, 1643, 1315, 973, 754.

MP: 96.3-97.5 °C.



6-iodo-2-(naphthalen-1-yl)-3-oxa-1-azaspiro[4.5]dec-1-ene (28)

Imidate (**S28)** (83.5 mg, 0.2 mmol) was subjected to **GP3**. Upon completion, the combined organic layer was concentrated and the residue was loaded directly onto silica gel and purified by flash column chromatography (isocratic: 5 : 95, EtOAc : hexanes) to yield amino-iodinated product **28** (78.3 mg, 70%, 9:1) as a white solid.

Rf: 0.66 (15% EtOAc / hexanes).

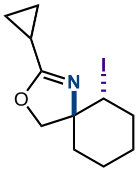
^{1}H NMR (400 MHz, CDCl$_3$): δ = 9.08-9.06 (m, 1H), 8.08-8.06 (m, 1H), 7.97-7.95 (m, 1H), 7.88-7.86 (m, 1H), 7.63-7.58 (m, 1H), 7.54-7.47 (m, 2H), 4.67 (dd, J = 11.0, 3.9 Hz, 1H), 4.51 (d, J = 8.6 Hz, 1H), 4.26 (d, J = 8.6 Hz, 1H), 2.60-2.53 (m, 1H), 2.22-2.16 (m, 1H) 2.06-1.91 (m, 3H), 1.72-1.65 (m, 1H), 1.58-1.41 (m, 2H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 163.01, 133.86, 132.00, 131.28, 129.08, 128.48, 127.39, 126.64, 126.22, 124.87, 124.77, 77.36, 75.90, 44.39, 36.98, 36.26, 26.94, 22.45.

HRMS (ESI-TOF) m/z: calc'd for $C_{18}H_{18}INO$ $[M+H]^+$ 392.0511, found 392.0497.

IR (film) cm^{-1}: 3091, 3049, 2968, 2933, 2850, 1640, 1509, 1121, 1005, 774.

MP: 99-100 °C.



2-cyclopropyl-6-iodo-3-oxa-1-azaspiro[4.5]dec-1-ene (29)

Imidate **(S29)** (66.3 mg, 0.2 mmol) was subjected to **GP3**. Upon completion, the combined organic layer was concentrated and the residue was loaded directly onto silica gel and purified by flash column chromatography (isocratic: 10 : 90, EtOAc : hexanes) to yield amino-iodinated product **29** (48.2 mg, 80%, 19:1) as a colorless oil.

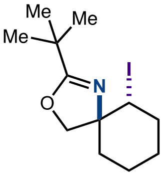
Rf: 0.43 (15% EtOAc / hexanes).

^{1}H NMR (700 MHz, CDCl$_3$): δ = 4.39 (dd, J = 11.4, 3.9 Hz, 1H), 4.20 (d, J = 8.6 Hz, 1H), 3.94 (d, J = 8.6 Hz, 1H), 2.41 (dq, J = 12.9, 4.1 Hz, 1H), 1.96-1.93 (m, 1H), 1.81-1.75 (m, 3H), 1.61-1.53 (m, 2H), 1.40-1.35 (m, 1H), 1.28-1.23 (m, 1H), 0.96-0.95 (m, 2H), 0.84-0.83 (m, 2H).

^{13}C NMR (175 MHz, CDCl$_3$): δ = 168.34, 76.13, 74.27, 44.96, 36.97, 22.59, 8.75, 7.38, 7.11.

HRMS (ESI-TOF) m/z: calc'd for $C_{11}H_{16}INO$ [M+H]$^+$ 306.0355, found 306.0344.

IR (film) cm^{-1}: 2930, 2857, 1728, 1658, 1171.



2-(*tert*-butyl)-6-iodo-3-oxa-1-azaspiro[4.5]dec-1-ene (30)

Imidate (**S30)** (39.5 mg, 0.2 mmol) was subjected to **GP3**. Upon completion, the combined organic layer was concentrated and the residue was loaded directly onto silica gel and purified by flash column chromatography (isocratic: 10 : 90, EtOAc : hexanes) to yield amino-iodinated product **30** (55.1 mg, 86%, 12:1) as a colorless oil.

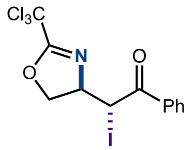
Rf: 0.61 (15% EtOAc / hexanes).

^{1}H NMR (400 MHz, CDCl$_3$): δ = 4.47 (dd, J = 12.3, 4.0 Hz, 1H), 4.27 (d, J = 8.6 Hz, 1H), 4.00 (d, J = 8.6 Hz, 1H), 2.48-2.41 (m, 1H), 1.95-1.76 (m, 4H), 1.56-1.52 (m, 1H), 1.43-1.27 (m, 2H), 1.22 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 173.20, 75.50, 74.34, 44.94, 37.16, 36.82, 33.31, 28.00, 27.79, 22.62.

HRMS (ESI-TOF) m/z: calc'd for $C_{12}H_{20}INO$ [M+H]$^+$ 322.0668, found 322.0661.

IR (film) cm^{-1}: 2954, 2930, 2858, 1730, 1655, 1125, 1097, 990.



2-iodo-1-phenyl-2-(2-(trichloromethyl)-4,5-dihydrooxazol-4-yl)ethan-1-one (34)

Imidate **(33)** (61.7 mg, 0.2 mmol) was subjected to **GP3** with the following modifications: NaI (3 equiv) was used in place of I_2, and PhI(OAc)$_2$ (3.5 equiv) was used. Upon completion, the combined organic layer was concentrated and the yield was determined by ^{1}H-NMR using dichloroethane as an internal standard (59%, 1.5:1). Compound **34** was isolated using preparatory thin-layer chromatography (10 : 90 EtOAc : hexanes) as a colorless oil.

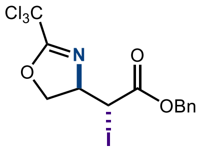
Rf: 0.36 (15% EtOAc / hexanes).

^{1}H NMR (600 MHz, CDCl$_3$): δ = 7.99-7.97 (m, 2H), 7.63-7.61 (m, 1H), 7.52-7.49 (m, 2H), 6.06 (d, J = 2.9 Hz, 1H), 5.03 (dd, J = 9.8, 9.8 Hz, 1H), 4.71 (dd, J = 9.8, 7.6 Hz, 1H), 4.29 (ddd, J = 9.6, 7.8, 3.0 Hz, 1H).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 193.89, 164.82, 134.40, 133.36, 129.09, 128.97, 86.64, 78.08, 67.15, 33.23.

HRMS (ESI-TOF) m/z: calc'd for $C_{12}H_9Cl_3INO_2$ [M+H]$^+$ 431.8822, found 431.8817.

IR (film) cm^{-1}: 3061, 2980, 2924, 2853, 1770, 1709, 1669, 1233, 986, 795.



benzyl 2-iodo-2-(2-(trichloromethyl)-4,5-dihydrooxazol-4-yl)acetate (36)

Imidate **35** (67.7 mg, 0.2 mmol) was subjected to **GP3** with the following changes: $PhI(OAc)_2$ (257.7 mg, 0.8 mmol). In addition, the reaction time extended to 4 hours. Upon completion, the combined organic layer was concentrated and the yield was determined by ^{1}H-NMR using dichloroethane as an internal standard (55%, 1:1). Compound **36** was isolated using preparatory thin-layer chromatography (10 : 90 EtOAc : hexanes) as a yellow oil.

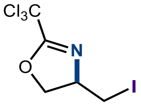
Rf: 0.21 (10% EtOAc/hexanes)

^{1}H NMR (600 MHz, $CDCl_3$): Diastereomer **A** δ = 7.42 – 7.35 (m, 5 H), 5.23 (d, J = 12.1Hz, 1 H), 5.19 (d, J = 12.1Hz, 1 H), 4.95 (d, J = 4.4Hz, 1 H), 4.81 (dd, J = 9.7 Hz, 4.7 Hz, 1H), 4.63 (dd, J = 9.7 Hz, 7.6 Hz, 1H), 4.34 (ddd, J = 9.7 Hz, 7.5 Hz, 4.4 Hz, 1H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = Diastereomer **A** δ = 169.69, 164.82, 134.87, 128.85, 128.81, 128.39, 68.13, 67.47, 26.81.

HRMS (ESI-TOF) m/z: calc’d for $C_{13}H_{11}Cl_3INO_3$ $[M+Na]^+$ 483.8741, found 483.8734.

IR (neat) cm^{-1}: 2934, 1719, 1702, 1658, 1498, 1455, 1380, 1326, 1212, 1188.



4-(iodomethyl)-2-(trichloromethyl)-4,5-dihydrooxazole (38,40)

Procedure A: Imidate **37** (55.0 mg, 0.2 mmol) was subjected to **GP3** with the following changes: NaI (90 mg, 0.4 mmol). Upon completion, the combined organic layer was concentrated *in vacuo* before purification by flash chromatography (1% EtOAc/hexanes with 1% Et_3N) to afford amino-iodinated product **38** (49.3 mg, 75%) as a yellowish solid.

Procedure B: Imidate **39** (55.3 mg, 0.2 mmol) was subjected to **GP3** with the following changes: NaI (90 mg, 0.4 mmol). Upon completion, the combined organic layer was concentrated *in vacuo* before purification by flash chromatography (1% EtOAc/hexanes with 1% Et_3N) to afford amino-iodinated product **40** (46.0 mg, 70%) as a yellowish solid.

Rf: 0.37 (20% EtOAc/hexanes)

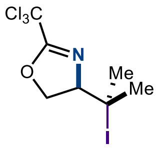
^{1}H NMR (400 MHz, CDCl$_3$): δ = 4.72 (dd, J = 9.2 Hz, 8.8 Hz, 1H), 4.58 – 4.51 (m, 1H), 4.42 (dd, J = 8.8 Hz, J = 7.3 Hz, 1H), 3.46 (dd, J = 10.4 Hz, 3.6 Hz, 1H), 3.32 (dd, J = 10.5 Hz, 7.3 Hz, 1H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 164.31, 86.64, 67.00, 31.07, 8.74.

HRMS (ESI-TOF) m/z: calc'd for $C_5H_5Cl_3INO$ [M+Na]$^+$ 349.8374, found 349.8396.

IR (neat) cm^{-1}: 3007, 2962, 2904, 1701, 1656, 1466, 1414, 1355, 1329.

MP: 48.7 °C – 50.6 °C.



4-(2-iodopropan-2-yl)-2-(trichloromethyl)-4,5-dihydrooxazole (42)

Imidate **41** (46.5 mg, 0.2 mmol) was subjected to **GP3** with the following changes: NaI (60 mg, 0.4 mmol). In addition, the reaction time shortened to 20 minutes. Upon completion, the combined organic layer was concentrated *in vacuo* before purification by flash chromatography (1 : 98 : 1 EtOAc : hexanes : Et_3N) to afford amino-iodinated product **42** (32.1 mg, 45%) as a white solid.

Rf: 0.26 (5% EtOAc/hexanes)

^{1}H NMR (400 MHz, CDCl$_3$): δ = 4.72 (dd, J = 10.0 Hz, J = 9.3 Hz, 1H), 4.62 (dd, J = 9.2 Hz, J = 7.6 Hz, 1H), 4.19 (dd, J = 9.8 Hz, J = 7.5 Hz, 1H), 2.04 (s, 3H), 1.95 (s, 3H).

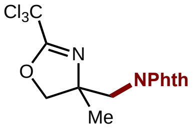
^{13}C NMR (100 MHz, CDCl$_3$): δ = 163.92, 78.64, 76.33, 50.54, 35.17, 32.10.

HRMS (ESI-TOF) m/z: calc'd for $C_7H_9Cl_3INO$ [M+Na]$^+$ 377.8687, found 377.8703.

IR (neat) cm^{-1}: 2989, 2966, 2924, 2866, 1763, 1662, 1451.

MP: 87.6 °C – 89.2 °C.

VII. Post-Synthetic Functionalization Characterization



2-((4-methyl-2-(trichloromethyl)-4,5-dihydrooxazol-4-yl)methyl)isoindoline-1,3-dione (43)

To a 2-dram vial equipped with a PTFE septum cap and magnetic stir bar was added oxazoline **17** (40 mg, 0.117 mmol) and KPhthalimide (43.3 mg, 0.234 mmol). Dry DMF (1.67 mL) was added to the vial, and the reaction was stirred at 100°C for 24h. Upon completion, the solution was cooled to room temperature then concentrated *in vacuo.* The solution was then diluted with CH_2Cl_2, and washed with 1 M NaOH (2x), and brine (1x). The combined organic layer was concentrated *in vacuo* before purification by flash chromatography (15% EtOAc/hexanes) to afford product **43** (27.1 mg, 64%) as a white solid.

Rf: 0.13 (15% EtOAc/hexanes)

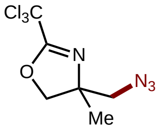
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 – 7.85 (m, 2H), 7.78 – 7.72 (m, 2H), 4.97 (d, J = 8.9 Hz, 1H), 4.21 (d, J = 9.0 Hz, 1H), 3.95 (AB q, J = 11.1, 2H), 1.50 (s, 3H).

^{13}C NMR (400 MHz, $CDCl_3$): δ = 168.56, 162.69, 134.38, 131.93, 123.64, 80.04, 72.76, 45.61, 29.83, 24.29.

HRMS (ESI-TOF) m/z: calc'd for $C_{14}H_{11}Cl_3N_2O_3$ $[M+Na]^+$ 382.9727, found 382.9724.

IR (film) cm^{-1}: 3185, 3059, 2919, 2850, 1773, 1706, 1661, 1604, 1467, 1051, 727, 712.

MP: 156.0 °C – 159.6 °C



4-(azidomethyl)-4-methyl-2-(trichloromethyl)-4,5-dihydrooxazole (44)

To a 2-dram vial equipped with a PTFE septum cap and magnetic stir bar was added oxazoline **17** (68.5 mg, 0.2 mmol) and sodium azide (26 mg, 0.4 mmol). Dry DMF (1 mL) was added to the vial, and the reaction was stirred at 80°C for 24h. Upon completion, the solution was cooled to RT then dumped into H_2O. The aqueous layer was extracted 3x with CH_2Cl_2 (5 mL). The organic layer was washed 5x with H_2O (5 mL). The combined organic layer was concentrated *in vacuo* before purification by flash chromatography (isocratic: 15 : 85, EtOAc : hexanes) to afford product **44** (44.7 mg, 87%) as a colorless oil.

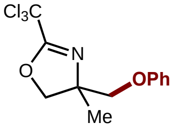
Rf: 0.25 (10% EtOAc / hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.57 (d, J = 8.6 Hz, 1H), 4.23 (d, J = 8.6 Hz, 1H), 3.57 (d, J = 12.5 Hz, 1H), 3.27 (d, J = 12.5 Hz, 1H), 1.41 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.11, 86.42, 78.65, 72.32, 58.42, 24.17.

HRMS (ESI-TOF) m/z: calc'd for $C_6H_7Cl_3N_4O$ $[M+Na]^+$ 278.9583, found 278.9563.

IR (film) cm^{-1}: 2097, 1658, 998.



4-methyl-4-(phenoxymethyl)-2-(trichloromethyl)-4,5-dihydrooxazole (45)

To a 2-dram vial equipped with a PTFE septum cap and magnetic stir bar was added oxazoline **17** (68.5 mg, 0.2 mmol) and NaOPh (46.4 mg, 0.4 mmol). Dry DMF (1 mL) was added to the vial, and the reaction was stirred at 100°C for 15h. Upon completion, the solution was cooled to room temperature then dumped into H_2O. The aqueous layer was extracted 3x with CH_2Cl_2 (5 mL). The organic layer was washed with 10% NaOH (aq) followed by 5x H_2O (5 mL). The combined organic layer was concentrated *in vacuo* before purification by flash chromatography (isocratic: 20 : 80, EtOAc : hexanes) to afford product **45** (57.4 mg, 93%) as a white solid.

Rf: 0.27 (10% EtOAc / hexanes).

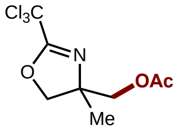
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30 – 7.27 (m, 2H), 6.99-6.95 (m, 1H), 6.91 – 6.88 (m, 2H), 4.78 (d, J = 8.5 Hz, 1H), 4.32 (d, J = 8.5 Hz, 1H), 4.03 (d, J = 9.2 Hz, 1H), 3.96 (d, J = 9.2 Hz, 1H), 1.52 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.89, 158.63, 129.65, 121.46, 114.73, 78.96, 77.35, 72.70, 71.78, 23.35.

HRMS (ESI-TOF) m/z: calc'd for $C_{12}H_{12}Cl_3NO_2$ $[M+Na]^+$ 329.9800, found 329.9822.

IR (film) cm^{-1}: 2976, 2930, 2871, 1665, 1236, 1080.

MP: 111 – 112 °C.



(4-methyl-2-(trichloromethyl)-4,5-dihydrooxazol-4-yl)methyl acetate (46)

To a 2-dram vial equipped with a PTFE septum cap and magnetic stir bar was added oxazoline **17** (68.5 mg, 0.2 mmol) and KOAc (78.5 mg, 0.8 mmol). Dry DMF (1 mL) was added to the vial, and the reaction was stirred at 100ºC for 48 h. Upon completion, the solution was cooled to room temperature then dumped into H_2O. The aqueous layer was extracted 3x with CH_2Cl_2 (5 mL). The organic layer was washed 5x with H_2O (5 mL). The combined organic layer was concentrated *in vacuo* before purification by flash chromatography (isocratic: 20 : 80, EtOAc : hexanes) to afford product **46** (54.9 mg, 100%) as a colorless oil.

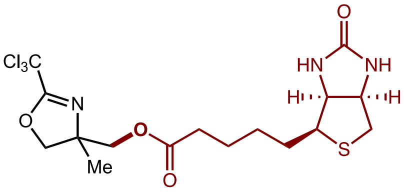
Rf: 0.25 (10% EtOAc / hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.57 (d, J = 8.6 Hz, 1H), 4.24 (d, J = 8.6 Hz, 1H), 4.16 (d, J = 11.4 Hz, 1H), 4.09 (d, J = 11.4 Hz, 1H), 2.06 (s, 3H), 1.42 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.69, 169.82, 86.54, 78.46, 77.36, 71.09, 68.58, 23.06, 20.80.

HRMS (ESI-TOF) m/z: calc'd for $C_8H_{10}Cl_3NO_3$ $[M+Na]^+$ 295.9600, found 295.9620.

IR (film) cm^{-1}: 1735, 1660, 1160.



(4-methyl-2-(trichloromethyl)-4,5-dihydrooxazol-4-yl)methyl 5-((3a*S*,4*S*,6a*R*)-2-oxohexahydro-1*H*-thieno[3,4-*d*]imidazol-4-yl)pentanoate (47)

To a 2-dram vial equipped with a PTFE septum cap and magnetic stir bar was added oxazoline **17** (68.5 mg, 0.2 mmol), D-biotin (97.7 mg, 0.4 mmol), and K_2CO_3 (110.6 mg, 0.8 mmol). Dry DMF (1 mL) was added to the vial, and the reaction was stirred at 110ºC for 7 h. Upon completion, the solution was cooled to room temperature and concentrated *in vacuo* before purification by flash chromatography (isocratic: 5 : 95, MeOH : CH_2Cl_2) to afford product **47** (69.7 mg, 76%, 1:1 dr) as a pale yellow oil.

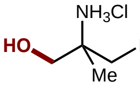
Rf: 0.22 (5% MeOH / CH_2Cl_2).

^{1}H NMR (600 MHz, $CDCl_3$): (1:1 mixture of two diastereomers) δ = 5.55 (bs, 1H), 5.50 (bs, 1H), 5.09 (bs, 2H), 4.57 (d, J = 8.6 Hz, 1H), 4.57 (d, J = 8.6 Hz, 1H), 4.52-4.50 (m, 2H), 4.32-4.30 (m, 2H), 4.25 (d, J = 8.6 Hz, 1H), 4.25 (d, J = 8.6 Hz, 1H), 4.18 (d, J = 11.4 Hz, 1H), 4.17 (d, J = 11.4 Hz, 1H), 4.13 (d, J = 11.4 Hz, 1H), 4.12 (d, J = 11.4 Hz, 1H), 3.16-3.13 (m, 2H), 2.93-2.90 (m, 2H), 2.74-2.72 (m, 2H), 2.37-2.35 (m, 4H), 1.74-1.61 (m, 10H), 1.50-1.45 (m, 2H), 1.43 (s, 3H), 1.43 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 173.79, 173.33, 173.31, 163.77, 163.72, 162.76, 86.56, 78.46, 71.12, 68.47, 62.09, 62.07, 60.45, 60.24, 55.54, 55.52, 55.47, 40.68, 40.65, 34.07, 33.86, 33.82, 28.48, 28.45, 28.37, 24.92, 24.81, 24.78, 23.16, 14.39.

HRMS (ESI-TOF) m/z: calc'd for $C_{16}H_{22}Cl_3N_3O_4S$ $[M+Na]^+$ 480.0294, found 480.0302.

IR (film) cm^{-1}: 3271, 3054, 2932, 2863, 2357, 1733, 1695, 1667, 1147, 1089, 1017, 731.



2-(chloro-λ^5-azaneyl)-3-iodo-2-methylpropan-1-ol (48)

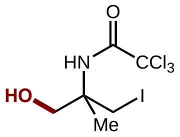
To a 2-dram vial equipped with a PTFE septum cap and magnetic stir bar was added oxazoline **17** (68.5 mg, 0.2 mmol) and MeOH (1 mL). 2M HCl (aq) (0.2 mL, 0.4 mmol) was added to the vial, and the reaction was stirred at room temperature for 16h. The reaction was concentrated *in vacuo* and rinsed with hexanes to afford product **X** (50.3 mg, 100%) as a light yellow solid.

^{1}H NMR (400 MHz, d_4-MeOD): δ = 8.22 (bs, 3H), 3.69 (dd, J = 22.1, 11.5 Hz, 2H), 3.50 (dd, J = 11.9, 11.1 Hz, 2H), 1.41 (s, 3H).

^{13}C NMR (100 MHz, d_4-MeOD): δ = 65.77, 57.66, 21.58, 8.76.

HRMS (ESI-TOF) m/z: calc'd for $C_4H_{11}ClINO$ $[M-Cl]^+$ 215.9900, found 215.9891.

IR (film) cm^{-1}: 2971, 2827, 2732, 1595, 1054, 818.



2,2,2-trichloro-*N*-(1-hydroxy-3-iodo-2-methylpropan-2-yl)acetamide (49)

To a 2-dram vial equipped with a PTFE septum cap and magnetic stir bar was added oxazoline **17** (68.5 mg, 0.2 mmol) and TsOH monohydrate (38 mg, 0.2 mmol). MeCN (1 mL) and H_2O (0.5 mL) were added to the vial, and the reaction was stirred at room temperature for 8 min. Upon completion, the solution was dumped into H_2O and quenched with $NaHCO_3$ (aq). The aqueous layer was extracted 3x with CH_2Cl_2 (5 mL). The combined organic layer was concentrated *in vacuo* before purification by flash chromatography (isocratic: 15 : 85, EtOAc : hexanes) to afford product **49** (71.4 mg, 99%) as a yellow oil.

Rf: 0.33 (40% EtOAc / hexanes).

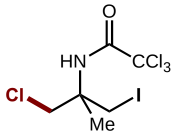
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.02 (bs, 1H), 3.92 (d, J = 11.4 Hz, 1H), 3.79 (d, J = 11.3 Hz, 1H), 3.70 (d, J = 10.6, 1H), 3.56 (d, J = 10.6 Hz, 1H), 2.73 (bs, 1H), 1.51 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.67, 92.76, 66.85, 57.75, 22.04, 12.20.

HRMS (ESI-TOF) m/z: calc'd for $C_6H_9Cl_3INO_2$ $[M+Na]^+$ 358.8700, found 358.8721.

IR (film) cm^{-1}: 3462, 3376, 1697, 1045, 816.

MP: 102 – 104 °C.



2,2,2-trichloro-*N*-(1-chloro-3-iodo-2-methylpropan-2-yl)acetamide (50)

To a 2-dram vial equipped with a PTFE septum cap and magnetic stir bar was added oxazoline **17** (68.5 mg, 0.2 mmol) and CH_2Cl_2 (1.3 mL). 4M HCl in dioxane (0.2 mL, 0.8 mmol) was added to the vial, and the reaction was stirred at room temperature for 12h. The reaction was quenched with saturated $NaHCO_3$ (aq). The aqueous layer was extracted 3x with CH_2Cl_2 (5 mL). The combined organic layer was concentrated *in vacuo* before purification by flash chromatography (isocratic: 10 : 90, EtOAc : hexanes) to afford product **50** (74.0 mg, 98%) as a white solid.

Rf: 0.40 (10% EtOAc / hexanes).

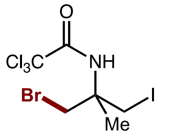
^{1}H NMR (400 MHz, CDCl$_3$): δ = 6.74 (bs, 1H), 4.08 (d, J = 11.4, 1H), 3.84 (d, J = 10.6 Hz, 1H), 3.78 (d, J = 11.4 Hz, 1H), 3.54 (d, J = 10.6 Hz, 1H), 1.63 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 161.0, 92.5, 57.1, 47.8, 22.8, 11.7.

HRMS (ESI-TOF) m/z: calc'd for $C_6H_8Cl_4INO$ $[M+Na]^+$ 399.8302, found 399.8302.

IR (film) cm^{-1}: 3289, 1693, 1528, 844, 820.

MP: 81 – 82 °C.



2,2,2-trichloro-*N*-(1-bromo-3-iodo-2-methylpropan-2-yl)acetamide (51)

To a 2-dram vial equipped with a PTFE septum cap and magnetic stir bar was added oxazoline **17** (68.5 mg, 0.2 mmol) and CH_2Cl_2 (0.5 mL). TMSBr (52 μL, 0.4 mmol) was added to the vial, and the reaction was stirred at room temperature for 30 min. The reaction was concentrated *in vacuo* before purification by flash chromatography (isocratic: 10 : 90, EtOAc : hexanes) to afford product **51** (78.7 mg, 93%) as a white solid.

Rf: 0.50 (15% EtOAc / hexanes).

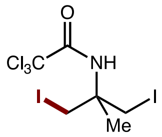
^{1}H NMR (600 MHz, CDCl$_3$): δ = 6.74 (bs, 1H), 4.03 (d, J = 10.7 Hz, 1H), 3.91 (d, J = 10.6 Hz, 1H), 3.69 (d, J = 10.7 Hz, 1H), 3.57 (d, J = 10.6 Hz, 1H), 1.67 (s, 3H).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 161.05, 92.51, 56.31, 36.88, 23.74, 11.92.

HRMS (ESI-TOF) m/z: calc'd for $C_6H_8BrCl_3INO$ $[M+Na]^+$ 443.7797, found 443.7775.

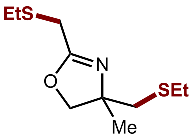
IR (film) cm^{-1}: 3293, 2981, 2924, 1692, 1528, 1256, 819.

MP: 99 – 101 °C.



2,2,2-trichloro-*N*-(1,3-diiodo-2-methylpropan-2-yl)acetamide (51A)

To a 2-dram vial equipped with PTFE septa cap and magnetic stir bar, was added hexamethyldisilane (0.4 mmol) and I_2 (0.4 mmol) under N_2. The reaction was refluxed for 1 hour. After cooling to room temperature, oxazoline **17** (68.5 mg, 0.2 mmol) was added as a solution in CH_2Cl_2 (1 mL) and stirred for 12 hours. The reaction was concentrated *in vacuo* before purification by flash chromatography (isocratic: 10 : 90, EtOAc : hexanes) to afford product **X** (50.8 mg, 54%) as a white solid.



2,4-bis((ethylthio)methyl)-4-methyl-4,5-dihydrooxazole (52)

To a 2-dram vial equipped with a PTFE septum cap and magnetic stir bar was added oxazoline **17** (40 mg, 0.117 mmol) and K_2CO_3 (80.8 mg, 0.585 mmol). The vial was evacuated and refilled with N_2 (3x). Ethanethiol (0.042 mL, 0.585 mmol) and DMF (1.67 mL) were added to the vial, and the reaction was stirred under N_2 at 100°C for 48h. Upon completion, the solution was cooled to room temperature, then diluted with H_2O and extracted with CH_2Cl_2 (3x). The aqueous layer was extracted (3x) with CH_2Cl_2 (5 mL). The organic layer was washed with H_2O, 1 M NaOH, and brine, then dried over $MgSO_4$. The combined organic layer was concentrated *in vacuo* before purification by flash chromatography (15% EtOAc/hexanes) to afford product **52** (24.9 mg, 91%) as a colorless oil.

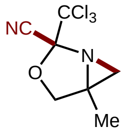
Rf: 0.15 (15% EtOAc/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.28 (d, J = 8.4 Hz, 1H), 3.95 (d, J = 8.4 Hz, 1H), 3.27 (s, 2H), 2.71 (s, 2H), 2.66 (q, J = 7.4 Hz, 2H), 2.58 (q, J = 7.5, 2H), 1.35 (s, 3H), 1.29 – 1.21 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.27, 77.35, 71.46, 42.79, 27.95, 27.92, 26.85, 26.73, 15.02, 14.42.

HRMS (ESI-TOF) m/z: calc'd for $C_{10}H_{19}NOS_2$ $[M+Na]^+$ 256.0800, found 256.0796.

IR (film) cm^{-1}: 2965, 2925, 2870, 1666, 1451, 1409, 1374, 1267, 730.



5-methyl-2-(trichloromethyl)-3-oxa-1-azabicyclo[3.1.0]hexane-2-carbonitrile (53)

To a 2-dram vial equipped with a PTFE septum cap and magnetic stir bar was added oxazoline **17** (68.5 mg, 0.2 mmol) and NaCN (49.0 mg, 1.0 mmol). Dry DMF (1 mL) was added to the vial, and the reaction was stirred at 50°C for 12 h. Upon completion, the solution was cooled to room temperature then dumped into aqueous $NaHCO_3$ (5 mL) and Et_2O (5 mL). The aqueous layer was extracted 3x with EtOAc (5 mL). The organic layer was washed 5x with H_2O (5 mL). The combined organic layer was concentrated *in vacuo* before purification by flash chromatography (isocratic: 20 : 80, EtOAc : hexanes) to afford product **53** (40.1 mg, 83%, 8 : 1) as a colorless oil.

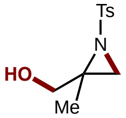
Rf: 0.35 (20% EtOAc / hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.41 (d, J = 8.2 Hz, 1H), 4.20 (dd, J = 8.1, 1.7 Hz, 1H), 2.35 (d, 1.3 Hz, 1H), 2.14 (t, 1.4 Hz, 1H), 1.51 (s, 3H).

^{13}C NMR (175 MHz, $CDCl_3$): δ = 113.79, 104.73, 75.74, 52.28, 38.46, 29.84, 16.96.

HRMS (ESI-TOF) m/z: calc'd for $C_7H_7Cl_3N_2O$ $[M+Na]^+$ 262.9522, found 262.9521.

IR (film) cm^{-1}: 2973, 2906, 2357, 1177, 1021, 839, 819.



(2-methyl-1-tosylaziridin-2-yl)methanol (54)

To a 2-dram vial equipped with a PTFE septum cap and magnetic stir bar was added oxazoline **17** (68.5 mg, 0.2 mmol) and 6M HCl (0.3 mL). MeOH (1 mL) was added to the vial, and the reaction was stirred at room temperature until starting material was consumed as determined by TLC (1h). The solution was concentrated *in vacuo*, and the residue was dissolved in MeOH (1 mL) and excess $KHCO_3$ was added. The suspension was stirred at room temperature for 45 mins before being concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (1 mL) and cooled to 0°C followed by addition of TsCl (46 mg, 0.24 mmol) and Et_3N (34 μL, 0.24 mmol). The solution was stirred for 1.5 hr before being dumped into H_2O. The aqueous layer was extracted 3x with CH_2Cl_2 (5 mL). The combined organic layer was concentrated *in vacuo* before purification by flash chromatography (isocratic: 50 : 50, EtOAc : hexanes) to afford product **54** (29.4 mg, 61%) as an off-white solid.

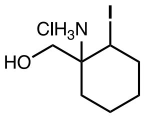
Rf: 0.26 (40% EtOAc / hexanes).

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.82 (d, J = 8.3, 2H), 7.33 (d, J = 8.5, 2H), 3.85 (dd, J = 12.6, 6.9 Hz, 1H), 3.70 (dd, J = 12.7, 6.9 Hz, 1H), 2.62 (s, 1H), 2.53 (s, 1H), 2.44 (s, 3H), 2.33 (t, J = 7.0, 1H), 1.64 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 144.41, 137.60, 129.83, 127.51, 65.33, 51.78, 38.83, 21.80, 17.38.

HRMS (ESI-TOF) m/z: calc'd for $C_{11}H_{15}NO_3S$ $[M+Na]^+$ 264.0700, found 264.0669.

IR (film) cm^{-1}: 3295, 3035, 1693, 1382, 1157.



(1-amino-2-iodocyclohexyl)methanol chloride salt (56)

To a 2-dram vial equipped with a PTFE septum cap and magnetic stir bar was added oxazoline **2** (360 mg, 0.94 mmol) and MeOH (5 mL). 2M HCl (aq) (1.0 mL, 1.9 mmol) was added to the vial, and the reaction was stirred at room temperature for 16h. The reaction was concentrated *in vacuo* and rinsed with hexanes to afford product **56** (209.2 mg, 100%) as a white solid. A single crystal was prepared using methanol and ether through vapor diffusion at room temperature.

^{1}H NMR (400 MHz, d$_4$-MeOD): δ = 4.42 (dd, J = 11.4, 4.4 Hz), 3.95 (d, J = 11.7 Hz), 3.78 (dd, J = 11.7, 1.1 Hz), 2.33-2.25 (m, 2H), 2.11-2.04 (m, 1H), 1.77-1.70 (m, 1H), 1.63-1.44 (m, 4H).

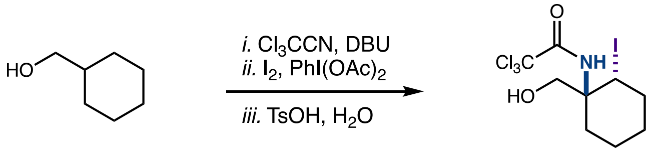
^{13}C NMR (100 MHz, d$_4$-MeOD): δ = 63.98, 60.96, 37.48, 34.12, 31.30, 28.27, 21.93.

HRMS (ESI-TOF) m/z: calc'd for $C_4H_{11}ClINO$ $[M-Cl]^+$ 256.0198, found 256.0170.

IR (film) cm^{-1}: 3222, 3070, 2980, 2883, 1600, 1524, 1062.

MP: 191 – 193 °C.

VIII. One-pot Procedure



2,2,2-trichloro-*N*-(1-(hydroxymethyl)-2-iodocyclohexyl)acetamide (55)

Cyclohexylmethanol (2.15 mL, 0.2 mmol) was subjected to **GP1**. Upon completion (monitored by TLC) the reaction was concentrated and subjected to **GP2**. Upon completion, the reaction was concentrated. TsOH monohydrate (38 mg, 0.2 mmol), MeCN (1 mL) and H_2O (0.5 mL) were added to the vial, and the reaction was stirred at room temperature. Upon completion (as determined by TLC), the solution was dumped into H_2O and quenched with $NaHCO_3$ (aq). The aqueous layer was extracted 3x with CH_2Cl_2 (5 mL). The combined organic layer was concentrated *in vacuo* before purification by flash chromatography (isocratic: 15 : 85, EtOAc : hexanes) to afford product **55** (57.7 mg, 72%) as a pale yellow solid.

Rf: 0.37 (20% EtOAc / hexanes).

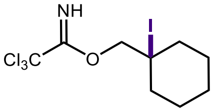
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.24 (bs, 1H), 5.09 (dd, J = 10.7, 4.3 Hz, 1H), 4.09 (d, J = 12.0 Hz, 1H), 3.94 (d, J = 11.9 Hz, 1H), 2.68 (bs, 1H), 2.36 (m, 1H), 2.22-2.18 (m, 1H), 2.15-2.09 (m, 2H), 1.72-1.64 (m, 2H), 1.56-1.50 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.42, 93.03, 66.16, 60.69, 35.93, 34.61, 30.59, 26.81, 21.54.

HRMS (ESI-TOF) m/z: calc'd for $C_9H_{13}Cl_3INO_2$ $[M+Na]^+$ 421.8954, found 421.8956.

IR (film) cm^{-1}: 3368, 2939, 2865, 1697, 1510, 818.

IX. C-H Iodination



(1-iodocyclohexyl)methyl 2,2,2-trichloroacetimidate (4)

To a 2-dram vial equipped with a PTFE septum cap and magnetic stir bar, was added imidate **1** (51.7 mg, 0.2 mmol), iodobenzene diacetate (77.3 mg. 0.24 mmol) and NaI (36.0 mg, 0.24 mmol). This vial was evacuated and backfilled with N_2 (3x). Dry, degassed ^{t}BuOH (0.66 mL) was added to the vial under N_2. The reaction was irradiated with two 26 W compact fluorescent light bulbs and cooled by two fans for 1h. Upon completion, the solution was quenched via a reductive workup with 20% $Na_2S_2O_3$. The aqueous layer was extracted with EtOAc (3x). The combined organic layer was concentrated *in vacuo* before purification by flash chromatography (1% EtOAc/hexanes with 1% Et_3N) to afford iodinated product **4** (57.2 mg, 74%) as a yellow oil.

Rf: 0.44 (5% EtOAc/hexanes)

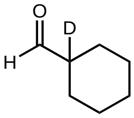
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.36 (bs, 1H), 4.60 (s, 2H), 2.14 – 2.10 (m, 2H), 1.81 – 1.71 (m, 6H), 1.44 – 1.37 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.41, 91.39, 79.46, 57.58, 39.53, 25.43, 24.25.

HRMS (ESI-TOF) m/z: calc'd for $C_9H_{13}Cl_3INO$ $[M+H]^+$ 383.9180, found 383.9197.

IR (neat) cm^{-1}: 3343, 2929, 2857, 1663, 1446, 1301, 1284, 1076, 792.

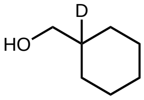
X. Rate Experiments



cyclohexane-1-*d*-1-carbaldehyde

To a 10 mL pressure tube equipped with a magnetic stir bar was added cyclohexane carbaldehyde (610 μL, 5 mmol) and D_2O. The reaction was heated to 100°C and allowed to stir overnight. After cooling to room temperature, 1M HCl (3 mL) and CH_2Cl_2 (12 mL) were added. The aqueous layer was extracted 3x with CH_2Cl_2 (10 mL). The combined organic layer was washed with $NaHCO_3$ (sat. aq) and brine before being dried on anhydrous $MgSO_4$. The organic layer was concentrated *in vacuo*. ^{1}H-NMR analysis indicated a deuterium incorporation of 75%.

The crude mixture was subjected to the above procedure one additional time to afford the title compound with 98% deuterium incorporation which was carried forward without any additional purification.



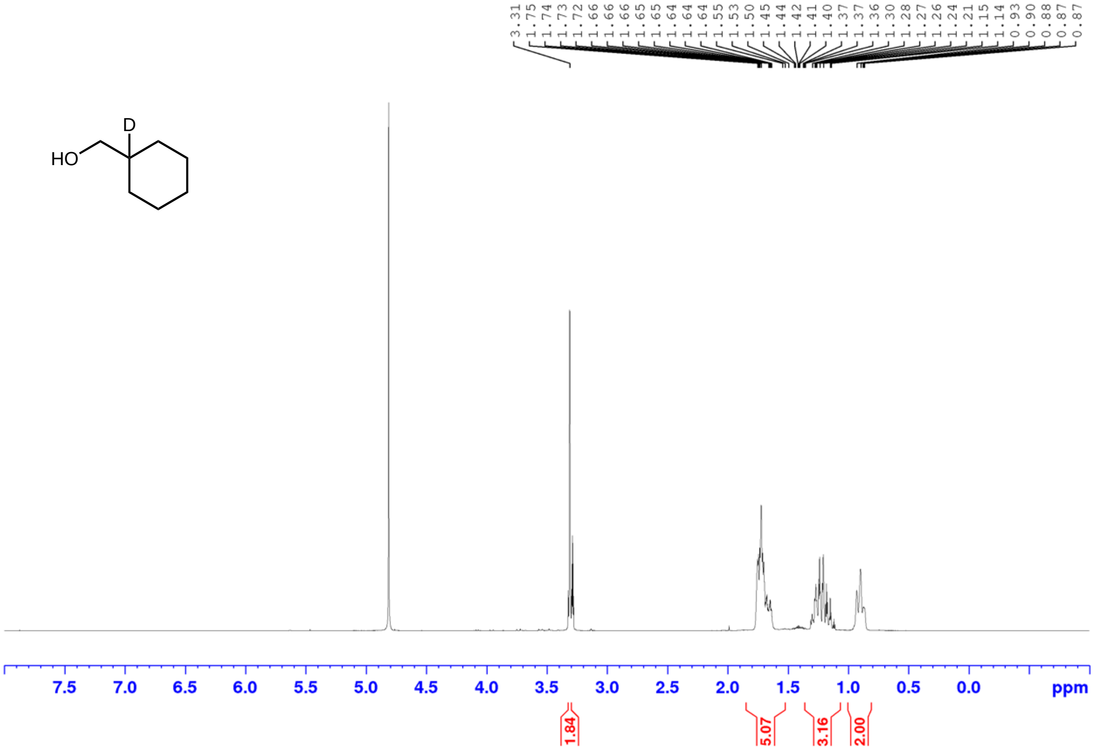
(cyclohexyl-1-*d*)methanol

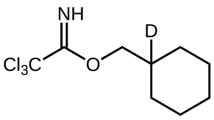
To a 10 mL round bottom flask equipped with a magnetic stir bar was added aldehyde (226 mg, 2.0 mmol) and *d*$_4$-MeOD (2.0 mL). The mixture was brought to 0°C, and $NaBH_4$ (151 mg, 4.0 mmol) was added portionwise. The solution was brought to room temperature and allowed to stir 1h. After starting material had been consumed, the reaction was quenched with brine. The aqueous layer was extracted 3x with CH_2Cl_2 (10 mL), and the combine organic layer was dried over anhydrous $MgSO_4$ and concentrated *in vacuo* to yield the title compound as a colorless oil. ^{1}H-NMR analysis indicated a deuterium incorporation of >95%. Spectroscopic data matches literature reports.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.31 (s, 2H), 1.75-1.64 (m, 5H), 1.30-1.14 (m, 3H), 0.930.87 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 68.79, 41.18 (t, J = 19.1Hz), 30.74, 27.77, 27.02.

Note: If MeOH was used in lieu of *d*$_4$-MeOD, erosion of deuterium incorporation was observed.





(cyclohexyl-1-*d*)methyl 2,2,2-trichloroacetimidate (1-*D*)

Alcohol (461 mg, 5 mmol) was subjected to **GP1**. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified by flash column chromatography (isocratic: 1 : 98 : 1, EtOAc : hexanes : Et_3N) to yield imidate 1-*D* (1.3 g, 100%) as a colorless oil.

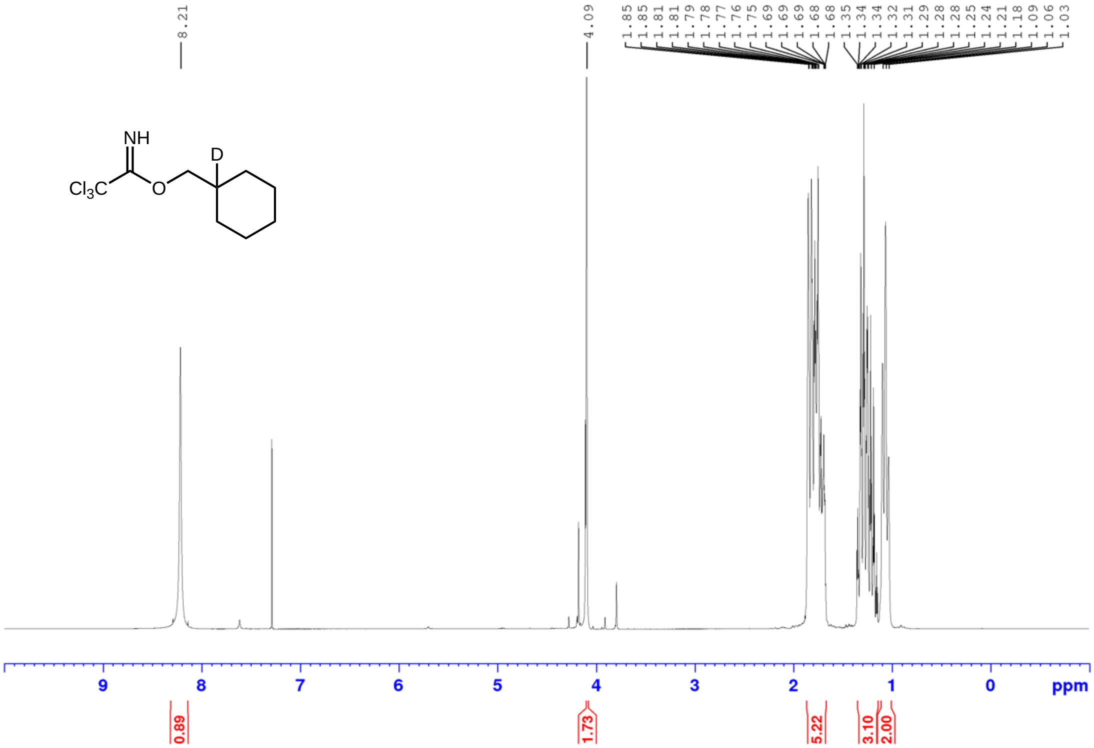
Rf: 0.47 (10% EtOAc / hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (bs, 1H), 4.08 (s, 2H), 1.83-1.79 (m, 2H), 1.77-1.67 (m, 3H), 1.37-1.17 (m, 3H), 1.08-1.02 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.27, 91.85, 74.67, 36.57 (t, J = 19.3 Hz), 29.54, 26.48, 25.78.

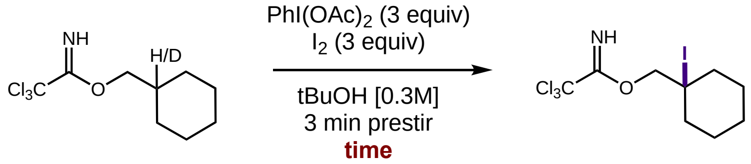
HRMS (ESI-TOF) m/z: calc'd for $C_9H_{13}DCl_3NO$ $[M+H]^+$ 259.0282, found 259.0277.

IR (film) cm^{-1}: 3345, 2923, 2852, 1662, 1078, 793.



Intramolecular KIE (HAT)

Initial rate for C-H iodination



Imidate **1** (51.7 mg, 0.2 mmol) was subjected to **GP4**. The ^{1}H-NMR of each sample was collected and analyzed for formation of alkyl iodide intermediate.

Analysis: The NMR yields of alkyl iodide **4** were plotted against time in seconds. The slope was utilized to calculate the initial rate of the reaction. The procedure was repeated, and the average of two trials was taken. Calculated values are tabulated below.

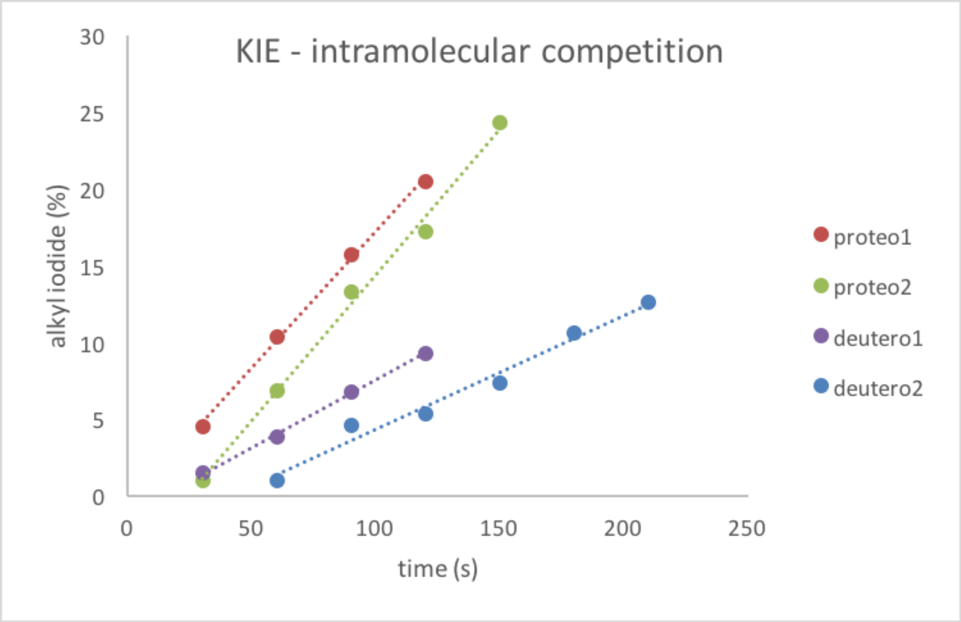
Initial rates for β-H cyclohexylmethanol imidate

Run	H-initial rate	R^2
1	0.1777	0.998
2	0.1897	0.994
Avg.	**0.1837**	

Initial rates for β-D cyclohexylmethanol imidate

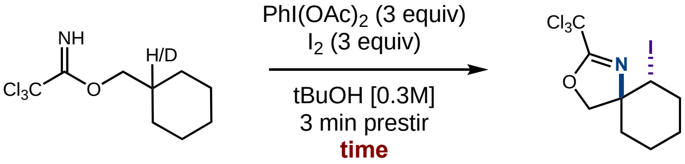
Run	D-initial rate	R^2
1	0.0877	0.999
2	0.0743	0.979
Avg.	**0.081**	

KIE (HAT) = K_H/K_D = 2.3



Intramolecular KIE (amino-iodination)

Initial rate for amino-iodination (from imidate 1-*D*)



Imidate **1** (51.7 mg, 0.2 mmol) was subjected to **GP4**. The ^{1}H-NMR of each sample was collected and analyzed. The ^{1}H-NMR of each sample was collected and analyzed for formation of amino-iodinated product.

Analysis: The NMR yields of amino-iodinated product **2** were plotted against time in seconds. The slope was utilized to calculate the initial rate of the reaction. The procedure was repeated, and the average of three trials was taken. Calculated values are tabulated below.

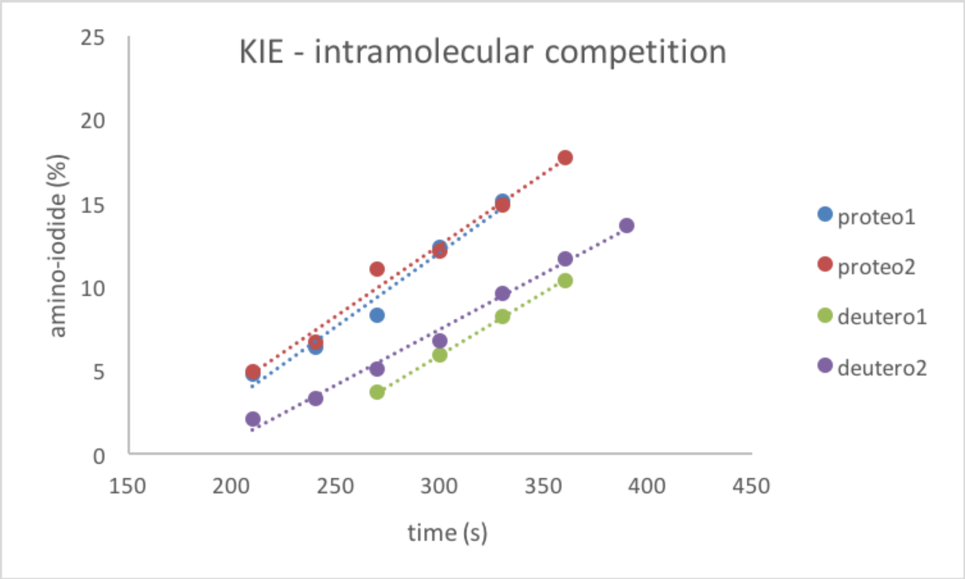
Initial rates for β-H cyclohexylmethanol imidate

Run	H-initial rate	R^2
1	0.0853	0.983
2	0.0887	0.971
Avg.	**0.0870**	

Initial rates for β-D cyclohexylmethanol imidate

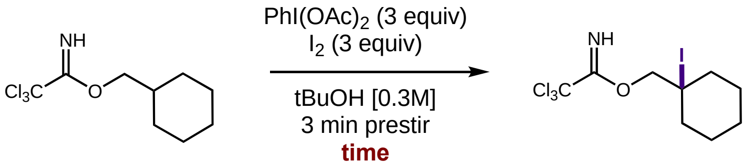
Run	D-initial rate	R^2
1	0.0747	0.9999
2	0.0743	0.990
Avg.	**0.0745**	

KIE = K_H/K_D = 1.2



Relative Rate Studies

Initial rate for C-H iodination (from imidate 1)



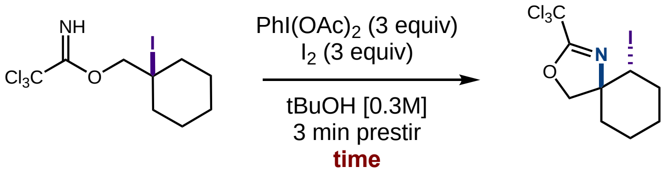
Imidate **1** (51.7 mg, 0.2 mmol) was subjected to **GP4**. The ^{1}H-NMR of each sample was collected and analyzed. The ^{1}H-NMR of each sample was collected and analyzed for formation of alkyl iodide intermediate.

Analysis: The NMR yields of alkyl iodide **4** were plotted against time in seconds. The slope was utilized to calculate the initial rate of the reaction. The procedure was repeated, and the average of three trials was taken. Calculated values are tabulated below.

Initial rates for cyclohexylmethanol imidate iodination

Run	**Initial rate**	**R^2**
1	0.1777	0.998
2	0.1897	0.994
Avg.	**0.1837 (k_1)**	

Initial rate for amino-iodination (from iodo-imidate 4)



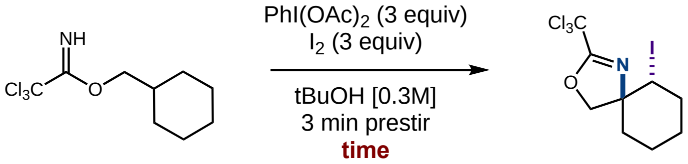
Imidate **4** (51.7 mg, 0.2 mmol) was subjected to **GP4**. The ^{1}H-NMR of each sample was collected and analyzed. The ^{1}H-NMR of each sample was collected and analyzed for formation of amino-iodinated product.

Analysis: The NMR yields of amino iodinated product **2** were plotted against time in seconds. The slope was utilized to calculate the initial rate of the reaction. The procedure was repeated, and the average of three trials was taken. Calculated values are tabulated below.

Initial rates for amino-iodination from iodo-imidate

Run	**Initial rate**	**R^2**
1	0.1059	0.912
2	0.1220	0.973
3	0.1085	0.973
Avg.	**0.1107 (k_2)**	

Initial rate for amino-iodination (from imidate 1)

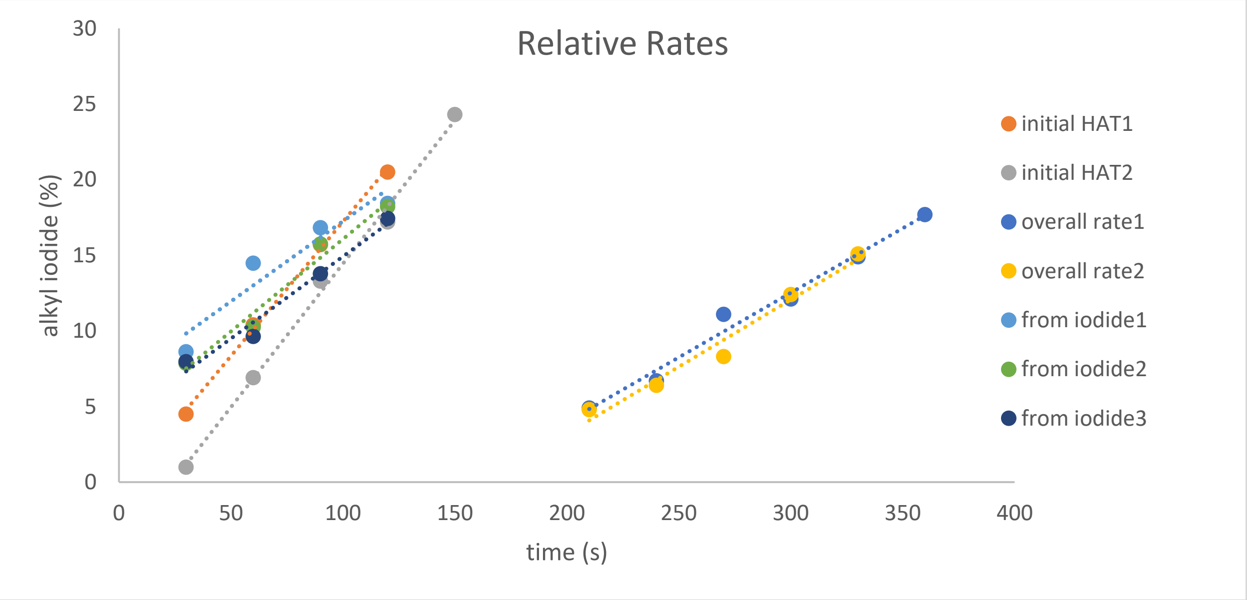


Imidate **1** (51.7 mg, 0.2 mmol) was subjected to **GP4**. The ^{1}H-NMR of each sample was collected and analyzed. The ^{1}H-NMR of each sample was collected and analyzed for formation of amino-iodinated product.

Analysis: The NMR yields of amino-iodinated product **4** were plotted against time in seconds. The slope was utilized to calculate the initial rate of the reaction. The procedure was repeated, and the average of three trials was taken. Calculated values are tabulated below.

Initial rates for cyclohexylmethanol imidate amino-iodination

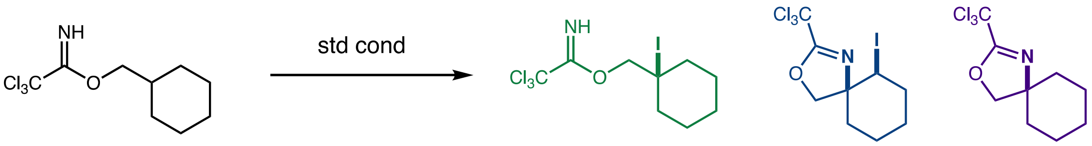
Run	**Initial rate**	**R^2**
1	0.0853	0.983
2	0.0887	0.971
Avg.	**0.0870 (k_3)**	



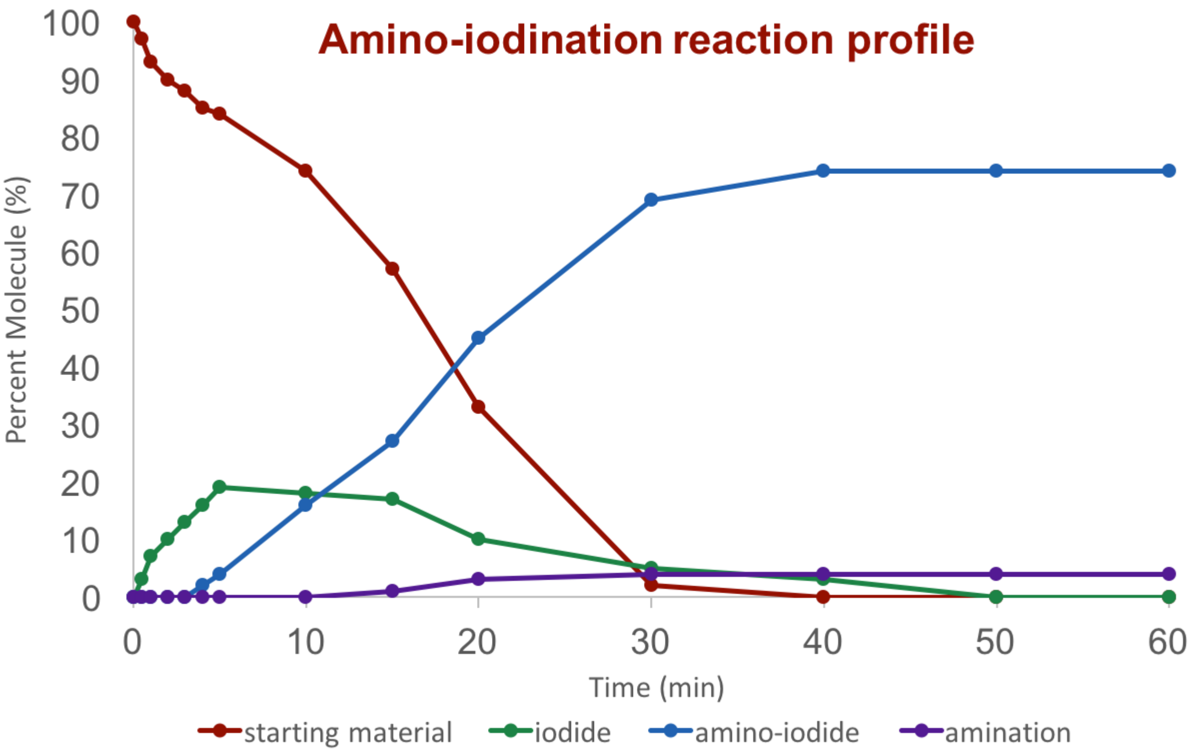
k	**Initial rate (avg)**	**Relative Rate**
1	0.1837	**2.1**
2	0.1107	**1.3**
3	0.0870	**1.0**

XI. Mechanistic Experiments and Reaction Profile

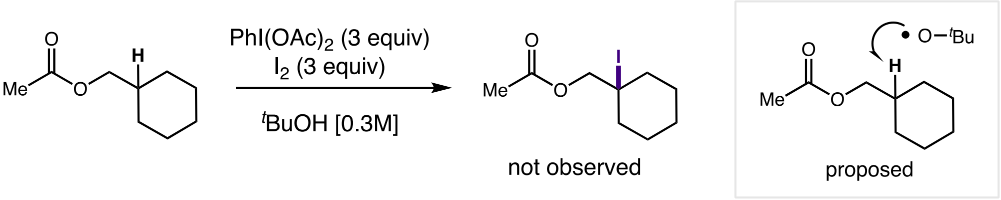
Amino-iodination reaction profile



Imidate **1** (51.7 mg, 0.2 mmol) was subjected to **GP4**. The ^{1}H-NMR of each sample was collected and analyzed. The ^{1}H-NMR of each sample was collected and analyzed for product distribution.



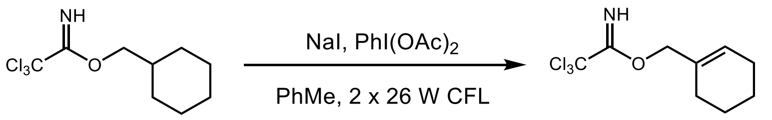
Intramolecular vs intermolecular C-H abstraction



Cyclohexylmethyl acetate was subjected to **GP3**. After 1h, the reaction was diluted with CH_2Cl_2 and quenched with $Na_2S_2O_3$ (20%, aq). The aqueous layer was extracted 3x with CH_2Cl_2 (5 mL). The organic layer was concentrated, and the crude mixture was analyzed by ^{1}H-NMR using dichloroethane as internal standard. Starting cyclohexylmethyl acetate was observed as 100% with no product formation.

Analysis: Modeled after **imidate 1**, the ester contains a tertiary C-H of similar strength. If the C-H abstraction were to occur by intermolecular HAT from an *in situ* generated alkoxy radical, an alkyl iodide product should be observed. However, when subjected to reaction conditions, 100% of the starting material remained, indicating this intermolecular HAT is likely not operating in the reaction. These data support directed reactivity via an imidate radical.

Probing allyl imidate as a competent intermediate

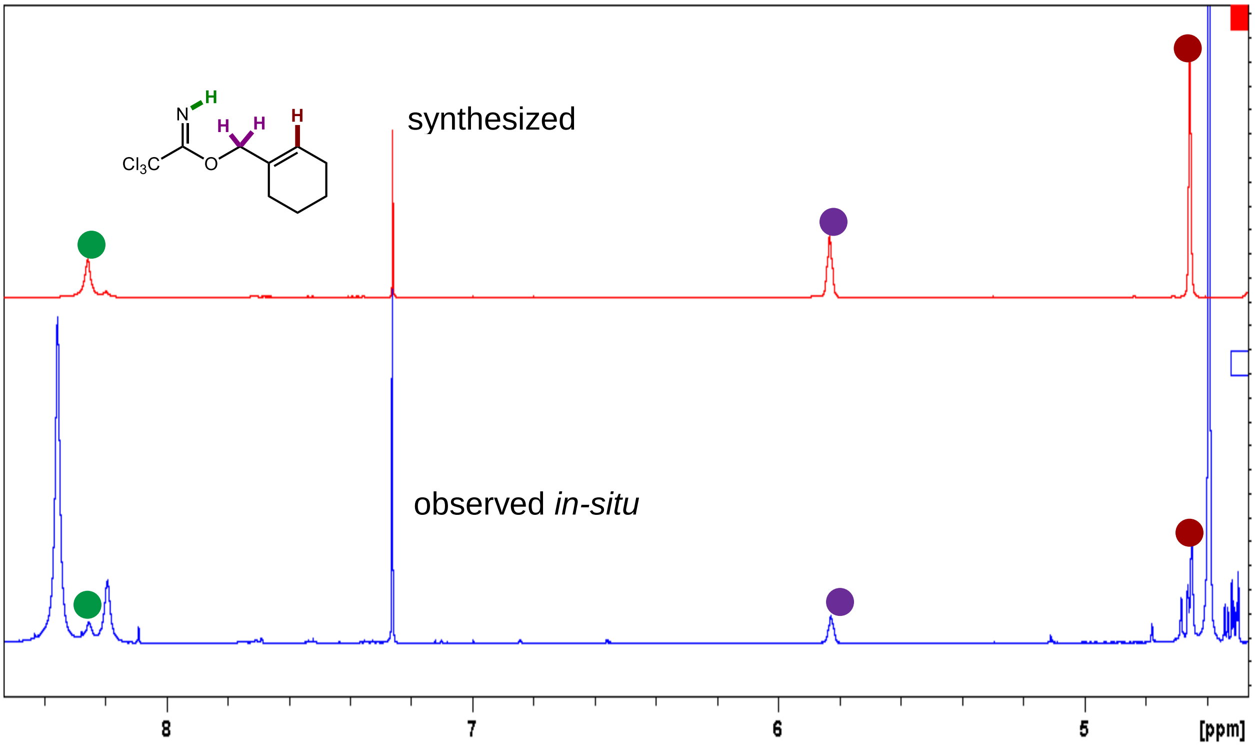


50% iodide intermediate (**4)**
12% S.M. (**1)**
7% amino-iodinated product (**2**)
4% olefin (5)

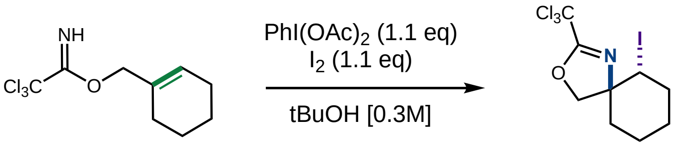
cyclohex-1-en-1-ylmethyl 2,2,2-trichloroacetimidate (5)

To a 2-dram vial equipped with a PTFE septum cap and magnetic stir bar, was added imidate **1** (51.7 mg, 0.2 mmol), iodobenzene diacetate (193 mg. 0.6 mmol) and NaI (90 mg, 0.6 mmol). This vial was evacuated and backfilled with N_2 (3x). Dry, degassed PhMe (1 mL) was added to the vial under N_2. The reaction was irradiated with two 26 W compact fluorescent light bulbs and cooled by two fans for 2.66h. Upon completion, the solution was quenched via a reductive workup with 20% $Na_2S_2O_3$. The organic layer was extracted with EtOAc (3x). The combined organic layer was concentrated *in vacuo* to afford 4% of the observed desaturated product **5**, along with 50% of the alkyl iodide intermediate **4**, 12% remaining starting material **1**, and 7% of the amino-iodinated product **2**.

Note: PhMe was used as a solvent in lieu of ^{t}BuOH because the rate of the reaction was observed to be slower in PhMe, allowing for observation of the desaturated product *in-situ*.



Subjecting allyl imidate to modified reaction conditions



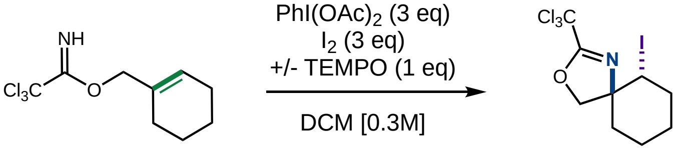
To a 2-dram vial equipped with a PTFE septum cap and magnetic stir bar was added Cyclohexenylmethanol imidate **5** (51.3 mg, 0.2 mmol) and ^{t}BuOH (0.7 mL). Iodobenzene diacetate (71 mg, 0.22 mmol) and I_2 (56 mg, 0.22 mmol) were added, and the reaction was irriadiated with 2x 26W CFLs, cooled with 2x fans, and stirred at room temperature for 30 mins. Upon completion, the solution was quenched with $Na_2S_2O_3$ (20%, aq), and the aqueous layer was extracted with CH_2Cl_2 3x (5 mL). The combined organic layer was concentrated *in vacuo*, and the crude mixture was analyzed by ^{1}H-NMR using dichloroethane as an internal standard, showing 59% (>20 : 1 dr) of the title compound **2**.

Note 1: In a separate control experiment, it was found that I_2 rapidly decomposes the allyl imidate when iodobenzene diacetate is not present. For this reason, no prestir was used in this experiment.

Note 2: When subjecting allyl imidate **5** to standard reaction conditions **(GP3)**, low mass balance was observed. We attribute this to the high level of oxidant present in the mixture. As evident from the reaction profile, there is a high concentration of alkyl iodide intermediate generated before any olefin intermediate is formed. Because of this, I_2 in the reaction has been at least partially consumed before olefin is generated.

Analysis: allyl imidate **5** is a competent intermediate in this reaction.

On the Origin of Diastereoselectivity



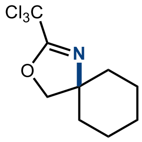
(Procedure 1) To a 2-dram vial equipped with a PTFE septum cap and magnetic stir bar was added Cyclohexenylmethanol imidate **5** (51.3 mg, 0.2 mmol) and CH_2Cl_2 (0.7 mL). Iodobenzene diacetate (193 mg, 0.6 mmol), I_2 (152 mg, 0.6 mmol), and TEMPO (31 mg, 0.2 mmol) were added. The reaction was irriadiated with 2x 26W CFLs, cooled with 2x fans, and stirred at room temperature for 30 mins. Upon completion, the solution was quenched with $Na_2S_2O_3$ (20%, aq), and the aqueous layer was extracted with CH_2Cl_2 3x (5 mL). The combined organic layer was concentrated *in vacuo*, and the crude mixture was analyzed by ^{1}H-NMR using dichloroethane as an internal standard, showing 84% (>20 : 1) of the title compound **2**.

(Procedure 2) To a 2-dram vial equipped with a PTFE septum cap and magnetic stir bar was added Cyclohexenylmethanol imidate **5** (51.3 mg, 0.2 mmol) and CH_2Cl_2 (0.7 mL). Iodobenzene diacetate (193 mg, 0.6 mmol), and I_2 (152 mg, 0.6 mmol) were added to the vial. The reaction was irriadiated with 2x 26W CFLs, cooled with 2x fans, and stirred at room temperature for 30 mins. Upon completion, the solution was quenched with $Na_2S_2O_3$ (20%, aq), and the aqueous layer was extracted with CH_2Cl_2 3x (5 mL). The combined organic layer was concentrated *in vacuo*, and the crude mixture was analyzed by ^{1}H-NMR using dichloroethane as an internal standard, showing 83% (5 : 1) of the title compound **2**.

Note: In a separate control experiment, it was found that I_2 rapidly decomposes the allyl imidate when iodobenzene diacetate is not present. For this reason, no prestir was used in this experiment.

Analysis: Using CH_2Cl_2 as a solvent in this reaction consistently yielded the title compound in 5 : 1 dr. As no prestir is used in these experiments, all I_2 is not fully solubilized. Because of this, a lower diastereomeric ratio is observed, likely due to competing radical and ionic mechanistic pathways. With the addition of a radical trap, we believe the diastereomeric ratio is greatly increased (>20 : 1) due to suppression of the radical-mediated 5-exo-trig cyclization pathway. Based on these data, we believe our amino-iodination reaction proceeds through an ionic cyclization, resulting in increased diastereomeric ratios. This is supported by enhanced solubility of I_2 in ^{t}BuOH over CH_2Cl_2.

Probing an "amination-first" mechanism



2-(trichloromethyl)-3-oxa-1-azaspiro[4.5]dec-1-ene (3)

To a 2-dram vial equipped with a PTFE septum cap and magnetic stir bar, was added imidate **3** (51.7 mg, 0.2 mmol), iodobenzene diacetate (193 mg. 0.6 mmol) and NaI (90 mg, 0.6 mmol). This vial was evacuated and backfilled with N_2 (3x). Dry, degassed hexafluoro-2-propanol (0.75 mL) and CH_2Cl_2 (0.25 mL) was added to the vial under N_2. The reaction was irradiated with two 26 W compact fluorescent light bulbs and cooled by two fans for 1h. Upon completion, the solution was quenched via a reductive workup with 20% $Na_2S_2O_3$. The aqueous layer was extracted with EtOAc (3x). The combined organic layer was concentrated *in vacuo* before purification by flash chromatography (1% EtOAc/hexanes with 1% Et_3N) to afford aminated product **3** (30.1 mg, 59%) as a yellow oil.

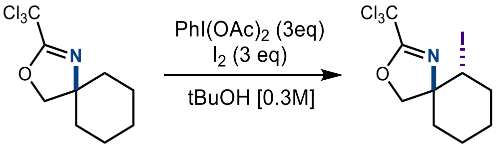
Rf: 0.27 (5% EtOAc/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.32 (s, 2H), 1.83 – 1.76 (m, 4H), 1.66 – 1.54 (m, 3H), 1.40 – 1.23 (m, 3H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 160.71, 87.05, 80.43, 72.42, 36.62, 25.00, 22.73.

HRMS (ESI-TOF) m/z: calc'd for $C_9H_{12}Cl_3NO$ $[M+H]^+$ 256.0057, found 256.0032.

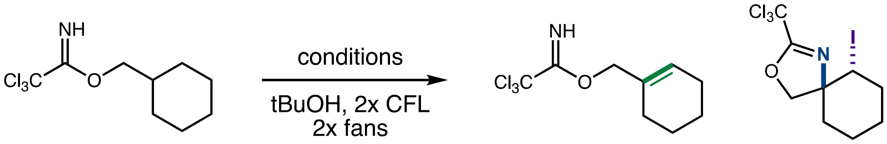
IR (neat) cm^{-1}: 2931, 2856, 1766, 1661, 1450, 1358, 1230, 994.



Amination product **3** (25.3 mg, 0.1 mmol) was subjected to **GP3**. Upon completion, the combined organic layer was concentrated *in vacuo* to achieve recovery of the starting material **3** (77% – ^{1}H-NMR).

Analysis: The aminated product was subjected to reaction conditions to test the hypothesis that the amination product could undergo β scission to generate a reactive olefin that would then be amino-iodinated in an "amination first" mechanism. No target molecule was formed indicating this side product does not lead to target product.

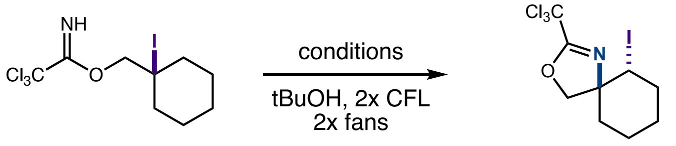
Examining elimination mechanism

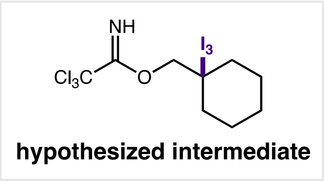


(Procedure 1) Cyclohexenylmethanol imidate **1** (51.3 mg, 0.2 mmol) was subjected to **GP3.** Upon completion, the solution was quenched with $Na_2S_2O_3$ (20%, aq), and the organic layer was extracted with CH_2Cl_2 3x (5 mL). The combined organic layer was concentrated *in vacuo*, and the crude mixture was analyzed by ^{1}H-NMR using dichloroethane as an internal standard. The results are tabulated below.

Entry	Additive	Starting Material
1	NaOAc	100%
2	HOAc	100%
3	**NaOAc/I$_2$**	**86% (13% iodoamination)**
4	HOAc/I$_2$	100%
5	NaOAc/PhI(OAc)$_2$	100%
6	HOAc/PhI(OAc)$_2$	100%
7	I$_2$	100%
8	PhI(OAc)$_2$	100%

Analysis: These experiments served as controls to probe is the starting material imidate is consumed under modified reaction conditions. This was critical, as the tertiary iodide intermediate is not isolable from starting imidate, so a mixture of the two was used in following experiments. If the starting material imidate had been consumed under modified conditions, false positive results may be observed. Entry 3 was the only set of conditions that gave conversion of starting material to any extent; a mixture of NaOAc and I_2 is able to promote some conversion of starting material to product **2**. This is likely due to small amounts of AcOI being generated throughout the course of the reaction.





hypothesized intermediate

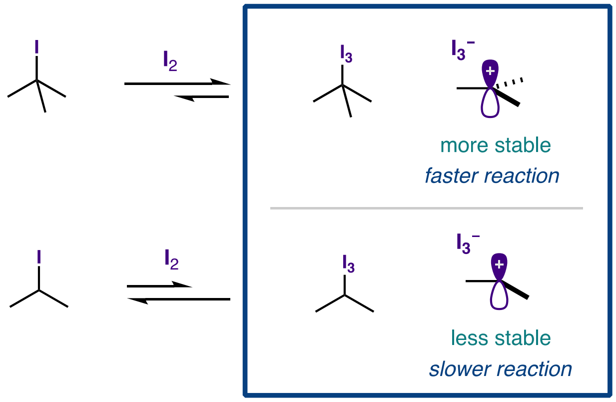
(Procedure 2) To a 2-dram vial equipped with a PTFE septum cap and magnetic stir bar was added iodinated starting material **(4)** (0.2 mmol, 3:1 mixture with imidate **(1)** and ^{t}BuOH (0.7 mL). The desired additive(s) were added (3 equiv) to the vial. The reaction was irriadiated with 2x 26W CFLs, cooled with 2x fans, and stirred at room temperature for 1h. Upon completion, the solution was quenched with $Na_2S_2O_3$ (20%, aq), and the aqueous layer was extracted with CH_2Cl_2 3x (5 mL). The combined organic layer was concentrated *in vacuo*, and the crude mixture was analyzed by ^{1}H-NMR using dichloroethane as an internal standard. The results are tabulated below.

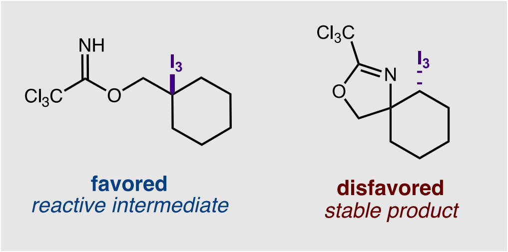
Entry	**Additive**	**Starting Material**
1	NaOAc	100%
2	HOAc	100%
3	**NaOAc, I_2**	**63% (36% iodoamination)**
4	**HOAc, I_2**	**3%**
5	NaOAc, $PhI(OAc)_2$	92%
6	HOAc, $PhI(OAc)_2$	94%
7	$PhI(OAc)_2$	84%
8	**I_2**	**0%**
9	**$PhI(OAc)_2$, I_2**	**0% (98% iodoamination)**

Analysis: Controls using only base or acid showed no consumption of the alkyl iodide, indicating that direct elimination is unlikely. Additionally, using $PhI(OAc)_2$ does not consume starting material. This disfavors the possibility of direct oxidation of the alkyl iodide by $PhI(OAc)_2$ to promote the desired elimination. However, in the presence of I_2, consumption of alkyl iodide is observed, supporting an iodine mediated elimination. We believe this intermediate to be critical for this reaction mechanism, as the formation of alkyl-I_3 complexes are far more rapid with tertiary than secondary iodides. With both I_2 and NaOAc, we hypothesize that consumption of iodine by acetate makes this elimination a slower process. As poor yields of amino-iodinated product 2 are observed (trichloroacetamide is the major byproduct), it is clear that I_2 is required for the elimination step, but I_2 alone is not able to perform the desired amino-iodination. When I_2 and

PhI(OAc)$_2$ are used together, nearly quantitative conversion of alkyl iodide to amino-iodination is observed.

On Product Stability: Work by Keefer et al shows that alkyl iodides form complexes with I_2.[3] The stability of this complex in polar solvents is relatively unaffected by the structure of the alkyl iodide. However, in non-polar solvents, this complex stability is directly related to the structure of the alkyl iodide (*tertiary* > *secondary*). This is due to the cationic character on the carbon atom, where a highly substituted cation is more stable than a less substituted cation. As solvent polarity drops, the structure of the alkyl iodide plays a large role in stabilizing the cation, whereas in polar solvents, solvation assists stabilization.





As the tertiary iodide (intermediate) forms a complex with I_2 more strongly, the alkyl iodide should be expected to react faster than in the case of secondary alkyl iodides (product) leading to relative stability of products during the reaction.

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[3] Keefer, R. M.; Andrews, L. J. *J. Am. Chem. Soc.* **1952**, *74* (8), 1891–1893. ; Bujake, J. E.; Noyes, R. M. *J. Am. Chem. Soc*, **1960**, *83*, 1555.

XII. UV/Vis and NMR Experiments

UV/Vis analysis was performed on pre-stirred (5 minutes) samples of each substrate or reaction mixture dissolved in CH_2Cl_2. Each sample was prepared and diluted to the same concentrations. Below is the spectra for 2,6-lutidine with varying equivalents of I_2.

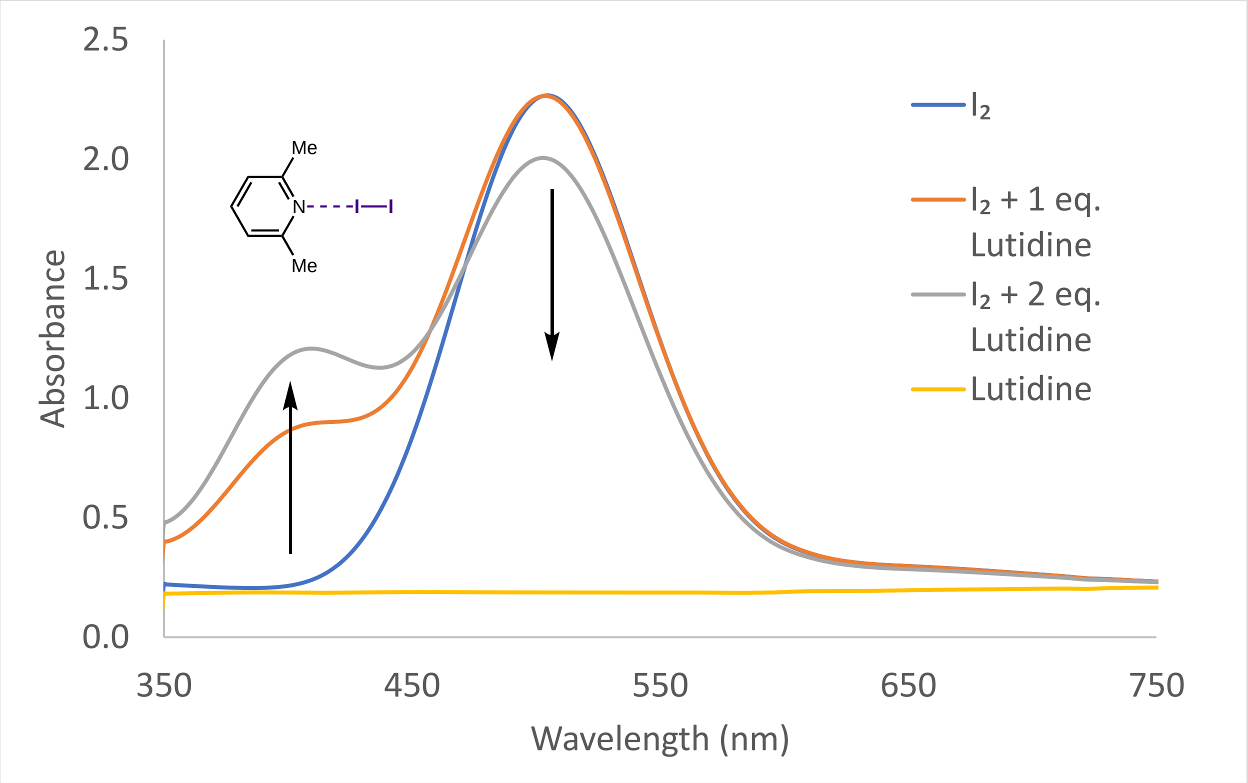


Figure 1: UV/Vis absorbance of I_2 and 2,6-lutidine.

NMR analysis was performed in pre-stirred (5 minutes) samples of substrate reaction mixture dissolved in $CDCl_3$ and diluted to the same concentrations. Below is the spectra for 2,6-lutidine with varying equivalents of I_2.

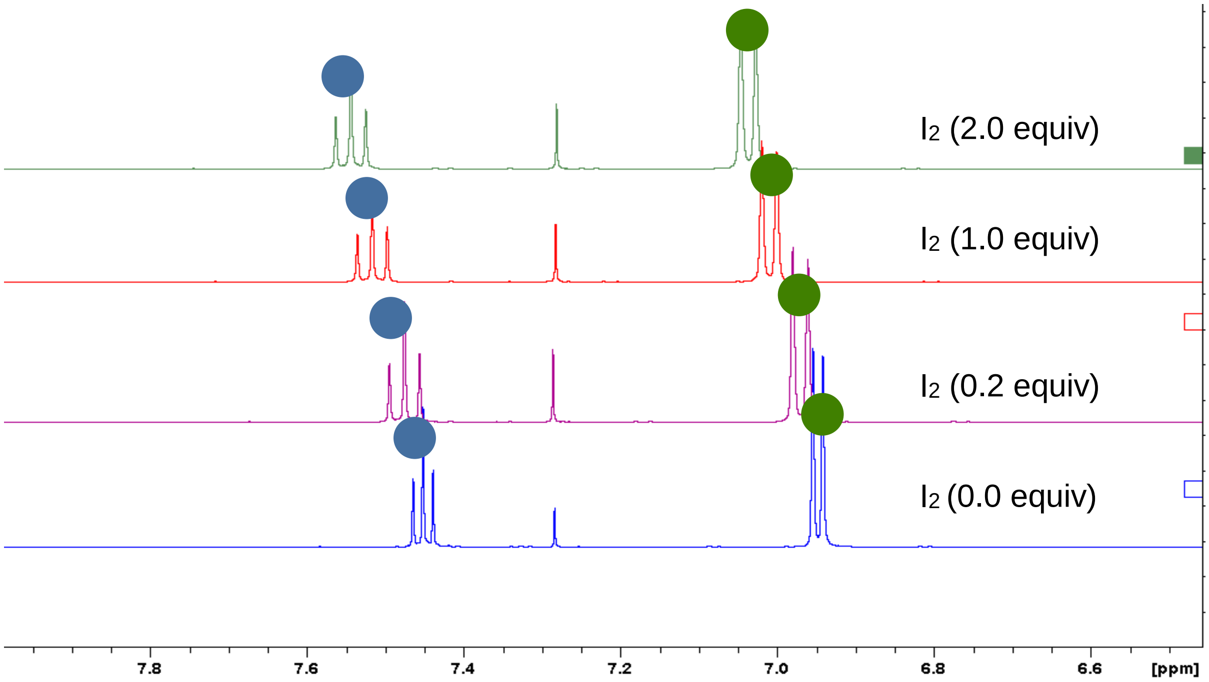
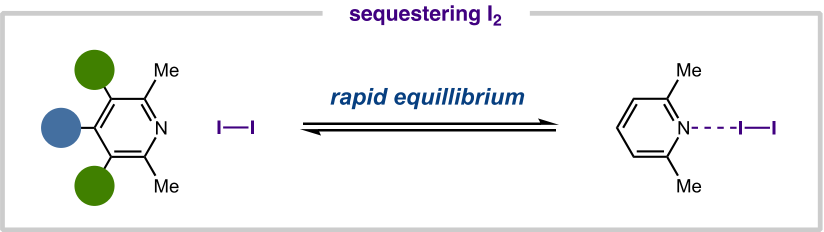


Figure 2: NMR spectra of 2,6-lutidine with varying amounts of I_2.



Analysis: The performed UV/Vis experiments indicate the presence of an I_2-lutidine complex in solution by the appearance of a new band at 420nm.[4] NMR experiments also support this complexation by the downfield shift of the aryl protons in lutidine in the presence of I_2. We believe this helps explain lower diastereomeric ratios in the presence of pyridine bases by lowering the effective concentration of I_2.

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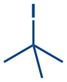
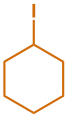
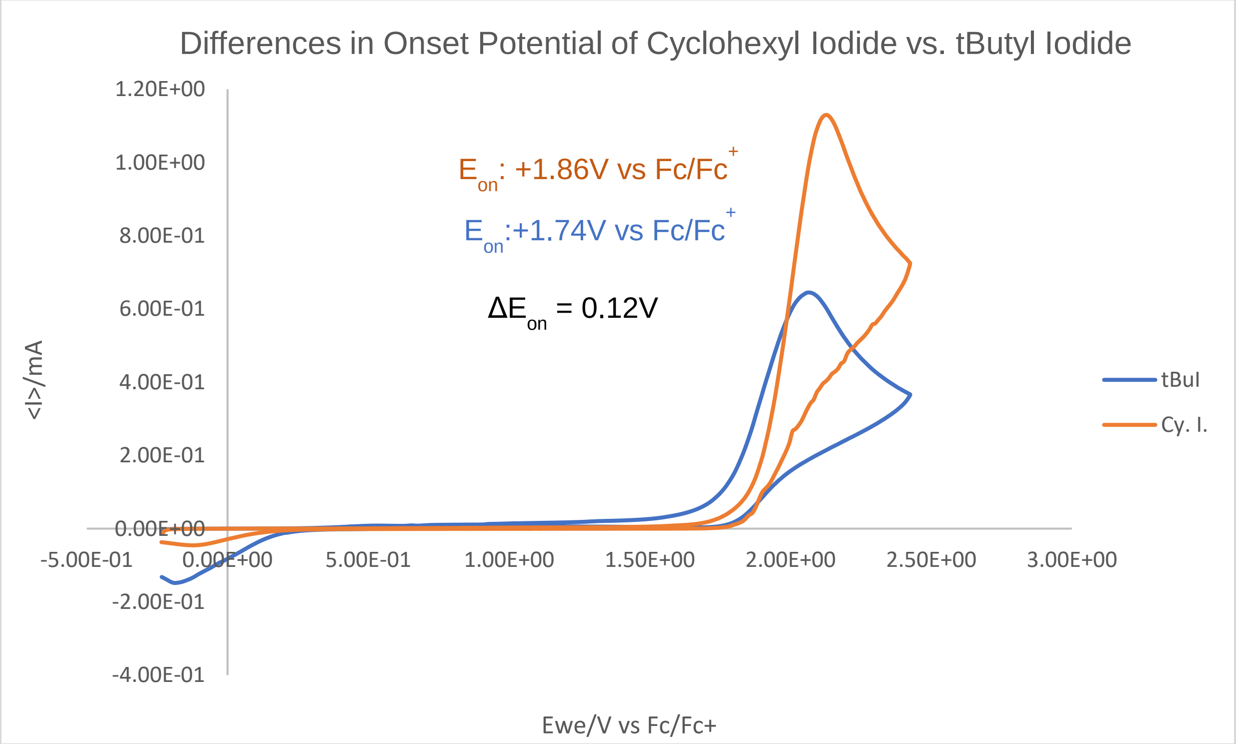
[4] Aloisi, G. G.; Beggiato, G.; Mazzucato, U. *Trans. Faraday Soc*. **1970**, *66*, 3075.

XIII. Electrochemical Data

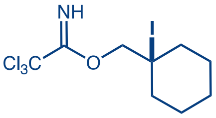
Cyclic voltammetry was performed with a BioLogic VSP potentiostat in a three-electrode electrochemical cell consisting of a glassy carbon disk working electrode (0.07 cm2, BASi), a Ag/Ag+ quasi-reference electrode (BASi) containing 0.01M AgBF4 (Sigma) in acetonitrile, and a platinum wire counter electrode (23 cm, ALS). Charge/discharge measurements were carried out with a BioLogic VSP potentiostat in a custom glass H-cell. Samples were prepared with 0.02 mmol of analyte in 2.5 mL of 0.5 M potassium hexafluorophosphate in dry, degassed acetonitrile. Data was analyzed using Excel. The onset potential (E_{on}) was measured by calculating the x-intercept potential between the linearly extrapolated fastest rising portion of the current wave (or peak) and the baseline (background) current.

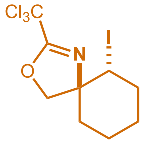


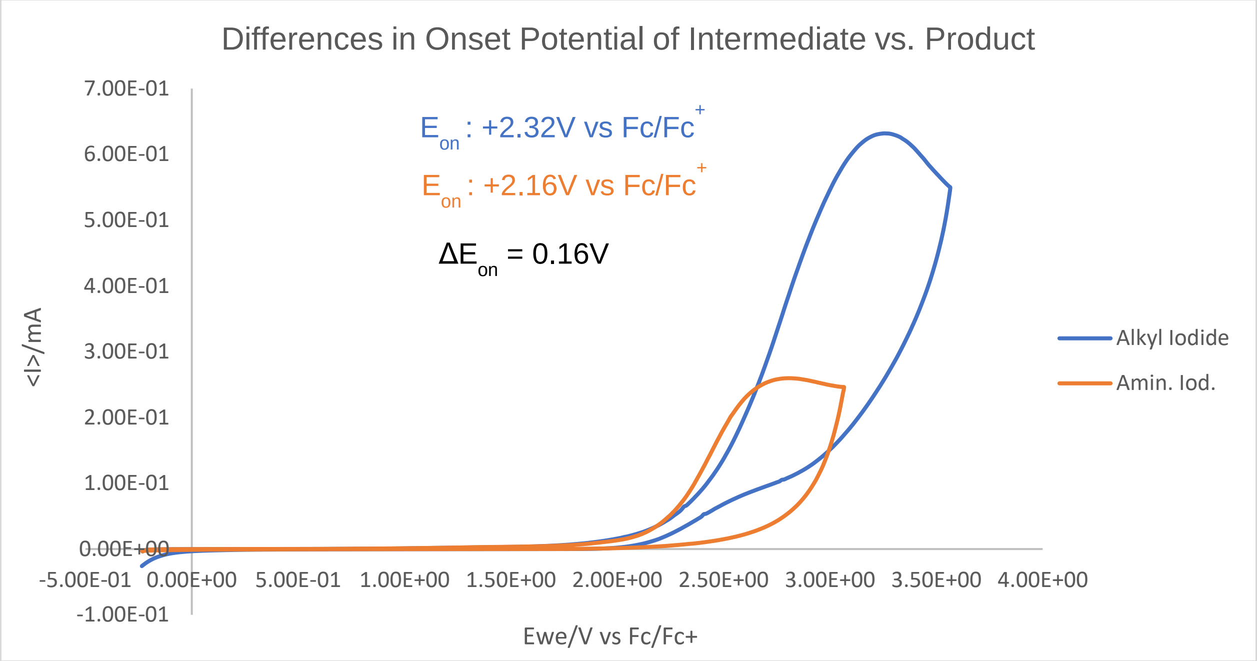




E_{on} = +1.74V (*t*BuI) and +1.86V (Cy. I.)







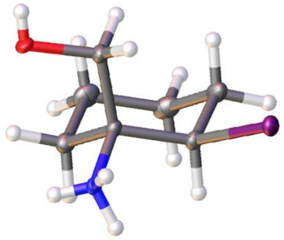
E_{on} = +2.32V (alkyl iodide) and +2.16V (amino-iod.)

Analysis: Cyclic voltammetry was conducted on the alkyl iodide intermediate and the amino-iodinated product to probe if a difference in oxidation potentials was the defining factor in favoring elimination of the iodide in the intermediate and not the iodide in the product. Compared to a model cyclic voltammetry experiment between cyclobutyl iodide and tert-butyl iodide, there was no appreciable difference between the tertiary iodide generated in the intermediate and the secondary iodide generated in the amino-iodinated product. This disfavors the possibility of single electron oxidation of the alkyl iodide to promote the desired elimination.

XIV. X-ray Crystallographic Data

A colorless block 0.21 x 0.14 x 0.09 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using omega scans. Crystal-to-detector distance was 50 mm and exposure time was 0.50 seconds per frame using a scan width of 0.5°. Data collection was 100% complete to 26.365° in θ. A total of 17913 reflections were collected covering the indices -15<=h<=15, -8<=k<=8, -16<=l<=16. 2038 reflections were founded to be symmetry independent, with an R_{int} of 0.0489. Indexing and unit cell refinement indicated a primitive, monoclinic lattice. The space group was found to be P 21/n (No. 14). The data were integrated using the CrysAlis^{Pro} 1.171.39.46e software program and scaled using the SCALE3 ABSPACK scaling algorithm. Solution by intrinsic phasing (SHELXT-2015) produced a heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014.

Table 1. Crystal data and structure refinement.



Empirical formula	C7 H15 Cl I N O	
Formula weight	291.55	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/n	
Unit cell dimensions	a = 12.0579(3) Å	α= 90°.
	b = 6.4915(2) Å	β= 108.766(3)°.
	c = 13.4589(4) Å	γ = 90°.
Volume	997.48(5) Å^3	
Z	4	
Density (calculated)	1.941 Mg/m^3	
Absorption coefficient	3.429 mm^{-1}	
F(000)	568	
Crystal size	0.210 x 0.140 x 0.090 mm^3	
Theta range for data collection	3.197 to 26.365°.	
Index ranges	-15<=h<=15, -8<=k<=8, -16<=l<=16	
Reflections collected	17913	
Independent reflections	2038 [R(int) = 0.0489]	
Completeness to theta = 26.365°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.74075	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2038 / 0 / 116	
Goodness-of-fit on F^2	1.056	
Final R indices [I>2sigma(I)]	R1 = 0.0211, wR2 = 0.0542	
R indices (all data)	R1 = 0.0224, wR2 = 0.0548	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.995 and -0.669 e.Å^{-3}	

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

	x	y	z	U(eq)
C(1)	6189(2)	2959(4)	4479(2)	16(1)
C(2)	7001(2)	1204(4)	5022(2)	13(1)
C(3)	8299(2)	1740(4)	5274(2)	15(1)
C(4)	8668(2)	1938(5)	4294(2)	20(1)
C(5)	8409(3)	-80(5)	3666(2)	23(1)
C(6)	7119(3)	-648(5)	3390(2)	22(1)
C(7)	6765(2)	-798(4)	4372(2)	16(1)
Cl(1)	4113(1)	5981(1)	2694(1)	15(1)
I(1)	8801(1)	4498(1)	6237(1)	18(1)
N(1)	6769(2)	732(4)	6031(2)	12(1)
O(1)	5002(2)	2328(3)	4217(2)	17(1)

Table 3. Bond lengths [Å] and angles [°].

C(1)-O(1)	1.420(3)
C(1)-C(2)	1.526(4)
C(1)-H(1D)	0.9900
C(1)-H(1E)	0.9900
C(2)-N(1)	1.503(3)
C(2)-C(3)	1.530(3)
C(2)-C(7)	1.542(4)
C(3)-C(4)	1.527(4)
C(3)-I(1)	2.179(3)
C(3)-H(3)	1.0000
C(4)-C(5)	1.535(4)
C(4)-H(4A)	0.9900
C(4)-H(4B)	0.9900
C(5)-C(6)	1.524(4)
C(5)-H(5A)	0.9900
C(5)-H(5B)	0.9900
C(6)-C(7)	1.517(4)
C(6)-H(6A)	0.9900
C(6)-H(6B)	0.9900
C(7)-H(7A)	0.9900
C(7)-H(7B)	0.9900
N(1)-H(1A)	0.87(4)
N(1)-H(1B)	0.83(4)
N(1)-H(1C)	0.73(4)
O(1)-H(1)	0.63(3)
O(1)-C(1)-C(2)	110.1(2)
O(1)-C(1)-H(1D)	109.6
C(2)-C(1)-H(1D)	109.6
O(1)-C(1)-H(1E)	109.6
C(2)-C(1)-H(1E)	109.6
H(1D)-C(1)-H(1E)	108.2
N(1)-C(2)-C(1)	107.9(2)
N(1)-C(2)-C(3)	108.7(2)

C(1)-C(2)-C(3)	112.9(2)
N(1)-C(2)-C(7)	106.7(2)
C(1)-C(2)-C(7)	112.6(2)
C(3)-C(2)-C(7)	107.8(2)
C(4)-C(3)-C(2)	112.9(2)
C(4)-C(3)-I(1)	110.00(18)
C(2)-C(3)-I(1)	112.77(17)
C(4)-C(3)-H(3)	106.9
C(2)-C(3)-H(3)	106.9
I(1)-C(3)-H(3)	106.9
C(3)-C(4)-C(5)	109.9(2)
C(3)-C(4)-H(4A)	109.7
C(5)-C(4)-H(4A)	109.7
C(3)-C(4)-H(4B)	109.7
C(5)-C(4)-H(4B)	109.7
H(4A)-C(4)-H(4B)	108.2
C(6)-C(5)-C(4)	110.6(2)
C(6)-C(5)-H(5A)	109.5
C(4)-C(5)-H(5A)	109.5
C(6)-C(5)-H(5B)	109.5
C(4)-C(5)-H(5B)	109.5
H(5A)-C(5)-H(5B)	108.1
C(7)-C(6)-C(5)	110.8(2)
C(7)-C(6)-H(6A)	109.5
C(5)-C(6)-H(6A)	109.5
C(7)-C(6)-H(6B)	109.5
C(5)-C(6)-H(6B)	109.5
H(6A)-C(6)-H(6B)	108.1
C(6)-C(7)-C(2)	112.9(2)
C(6)-C(7)-H(7A)	109.0
C(2)-C(7)-H(7A)	109.0
C(6)-C(7)-H(7B)	109.0
C(2)-C(7)-H(7B)	109.0
H(7A)-C(7)-H(7B)	107.8
C(2)-N(1)-H(1A)	112(2)
C(2)-N(1)-H(1B)	115(2)

H(1A)-N(1)-H(1B)	104(3)
C(2)-N(1)-H(1C)	112(3)
H(1A)-N(1)-H(1C)	104(4)
H(1B)-N(1)-H(1C)	108(4)
C(1)-O(1)-H(1)	105(3)

Symmetry transformations used to generate equivalent atoms:

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

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	12(1)	16(1)	18(1)	3(1)	1(1)	-2(1)
C(2)	10(1)	16(1)	10(1)	1(1)	1(1)	-2(1)
C(3)	12(1)	17(1)	14(1)	0(1)	1(1)	-2(1)
C(4)	14(1)	29(2)	17(1)	7(1)	4(1)	-1(1)
C(5)	21(2)	32(2)	16(2)	3(1)	7(1)	5(1)
C(6)	25(2)	26(2)	14(2)	-3(1)	3(1)	1(1)
C(7)	15(1)	15(1)	17(1)	-1(1)	2(1)	-1(1)
Cl(1)	15(1)	13(1)	13(1)	-2(1)	-1(1)	2(1)
I(1)	16(1)	18(1)	17(1)	2(1)	0(1)	-6(1)
N(1)	11(1)	12(1)	11(1)	-1(1)	1(1)	-2(1)
O(1)	10(1)	16(1)	20(1)	7(1)	-2(1)	1(1)

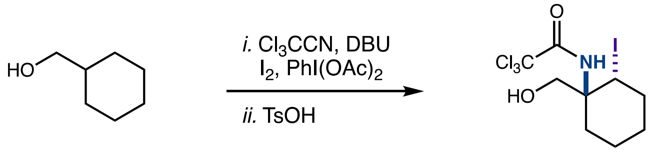
Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3).

	x	y	z	U(eq)
H(1D)	6327	4170	4951	19
H(1E)	6360	3365	3834	19
H(3)	8756	569	5694	18
H(4A)	9516	2249	4500	24
H(4B)	8235	3085	3853	24
H(5A)	8613	79	3014	28
H(5B)	8898	-1200	4085	28
H(6A)	6635	409	2915	27
H(6B)	6976	-1986	3017	27
H(7A)	7203	-1941	4813	20
H(7B)	5920	-1129	4168	20
H(1)	4710(30)	3040(50)	3930(30)	7(9)
H(1A)	7360(30)	120(60)	6480(30)	22(9)
H(1B)	6650(30)	1750(60)	6350(30)	20(9)
H(1C)	6280(30)	20(60)	5950(30)	19(9)

Table 6. Torsion angles [°].

O(1)-C(1)-C(2)-N(1)	-63.0(3)
O(1)-C(1)-C(2)-C(3)	176.9(2)
O(1)-C(1)-C(2)-C(7)	54.5(3)
N(1)-C(2)-C(3)-C(4)	171.5(2)
C(1)-C(2)-C(3)-C(4)	-68.8(3)
C(7)-C(2)-C(3)-C(4)	56.3(3)
N(1)-C(2)-C(3)-I(1)	-63.0(2)
C(1)-C(2)-C(3)-I(1)	56.7(3)
C(7)-C(2)-C(3)-I(1)	-178.26(17)
C(2)-C(3)-C(4)-C(5)	-57.9(3)
I(1)-C(3)-C(4)-C(5)	175.11(18)
C(3)-C(4)-C(5)-C(6)	56.4(3)
C(4)-C(5)-C(6)-C(7)	-56.3(3)
C(5)-C(6)-C(7)-C(2)	57.1(3)
N(1)-C(2)-C(7)-C(6)	-172.3(2)
C(1)-C(2)-C(7)-C(6)	69.5(3)
C(3)-C(2)-C(7)-C(6)	-55.7(3)

XV. One-Step Strategy



2,2,2-trichloro-*N*-(1-(hydroxymethyl)-2-iodocyclohexyl)acetamide (55)

Cyclohexylmethanol (25 µL, 0.2 mmol) was subjected to **GP5**. The aqueous layer was extracted 3x with EtOAc (5 mL). The combined organic layer was concentrated *in vacuo* before purification by flash chromatography (isocratic: 10 : 90, EtOAc : hexanes) to afford product **55** (55.3 mg, 69%, 3:1 diastereomeric ratio) as a pale yellow oil.

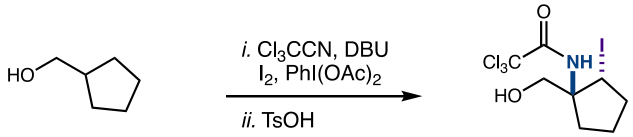
Rf: 0.37 (20% EtOAc / hexanes).

^{1}H NMR (400 MHz, CDCl$_3$): δ = Diastereomer A: δ = 7.25 (br s, 1H), 5.09 (dd, J = 10.7 Hz, 4.3 Hz), 4.09 (d, J = 11.9 Hz, 1H), 3.94 (d, J = 11.9, 1H), 2.69 (br s, 1H), 2.38-2.32 (m, 1H), 2.22-2.08 (m, 3H), 1.74-1.49 (m, 4H).
Diastereomer B: δ = 6.93 (br s, 1H), 4.76 (dd, J = 11.1 Hz, 4.1 Hz, 1H), 4.13-4.07 (m, 1H), 3.64 (dd, J = 11.4 Hz, 5.9 Hz, 1H), 2.72-2.65 (m, 2H), 2.38-2.32 (m, 1H), 2.22-2.08 (m, 1H), 1.79-1.46 (m, 4H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = Diastereomer A: δ = 161.40, 93.04, 66.10, 60.69, 35.94, 34.61, 30.55, 26.83, 21.55.
Diastereomer B: δ = 161.80, 93.04, 66.14, 61.25, 39.96, 36.44, 28.68, 27.52, 21.06.

HRMS (ESI-TOF) m/z: calc'd for $C_9H_{13}Cl_3INO_2$ $[M+Na]^+$ 421.8954, found 421.8956.

IR (film) cm^{-1}: 3368, 2939, 2865, 1697, 1510, 818.



2,2,2-trichloro-*N*-1-(hydroxymethyl)-2-iodocyclopentyl)acetamide (57)

Cyclopentylmethanol (22 µL, 0.2 mmol) was subjected to **GP5**. The aqueous layer was extracted 3x with EtOAc (5 mL). The combined organic layer was concentrated *in vacuo* before purification by flash chromatography (isocratic: 10 : 90, EtOAc : hexanes) to afford product **57** (39.4 mg, 51%, 20:1 diastereomeric ratio) as a pale yellow oil.

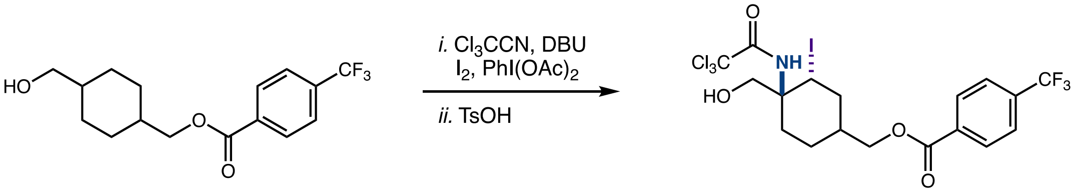
Rf: 0.39 (20% EtOAc / hexanes).

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.43 (br s, 1H), 4.72 (dd, J = 10.1 Hz, 7.2 Hz, 1H), 4.00 (d, 12.0 Hz, 1H), 3.63 (d, 12.0 Hz, 1H), 2.63 (br s, 1H), 2.50-2.42 (m, 1H), 2.34-2.28 (m, 1H), 2.15-1.95 (m, 2H), 1.85-1.72 (m, 2H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 161.52, 92.89, 69.02, 66.00, 37.66, 31.24, 30.38, 23.43.

HRMS (ESI-TOF) m/z: calc'd for $C_8H_{11}Cl_3INO_2$ $[M+Na]^+$ = 407.8798, found 407.8800.

IR (film) cm^{-1}: 3357, 2959, 2882, 1682, 818.



4-(hydroxymethyl)-3-iodo-4-(2,2,2-trichloroacetamido)cyclohexyl)methyl 4-(trifluoromethyl)benzoate (58)

Alcohol S12A (63.3 mg, 0.2 mmol) was subjected to **GP5**. The aqueous layer was extracted 3x with EtOAc (5 mL). The combined organic layer was concentrated *in vacuo* before purification by flash chromatography (isocratic: 10 : 90, EtOAc : hexanes) to afford product **58** (78.3 mg, 65%, 13:1 diastereomeric ratio) as a pale yellow oil.

Rf: 0.31 (20% EtOAc / hexanes).

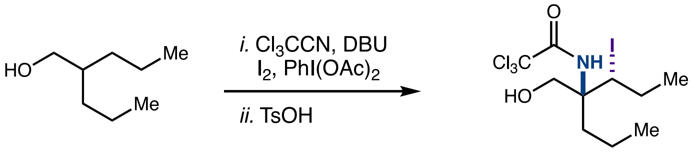
^{1}H NMR (400 MHz, CDCl$_3$): δ = δ = 8.13 (d, J = 8.1 Hz, 2H), 8.17 (d, J = 8.2 Hz, 2H), 6.71 (br s, 1H), 5.15-5.13 (m, 1H), 4.33 (d, J = 5.9 Hz, 2H), 4.00 (dd, J = 23.7 Hz, 11.7 Hz, 2H), 2.54-2.42 (m, 2H), 2.23-2.17 (m, 2H), 2.12-1.86 (m, 3H), 1.58 (br s, 1H), 1.49-1.39 (m, 1H).

^{19}F NMR (367 MHz, CDCl3): δ = -63.14.

^{13}C NMR (100 MHz, CDCl$_3$): δ = 165.35, 161.41, 125.68 (q, J = 4.0 Hz), 92.75, 68.36, 60.40, 35.57, 33.59, 29.67, 27.34, 23.84.

HRMS (ESI-TOF) m/z: calc'd for $C_{18}H_{18}Cl_3F_3INO_4$ $[M+Na]^+$ = 623.9196, found 623.9181.

IR (film) cm^{-1}: 3310, 3014, 2989, 1723, 1683, 1080, 1013, 837.



2,2,2-trichloro-*N*-4-(hydroxymethyl)-3-iodoheptan-4-ylacetamide (59)

2-propylpentan-1-ol (26 mg, 0.2 mmol) was subjected to **GP5**. The aqueous layer was extracted 3x with EtOAc (5 mL). The combined organic layer was concentrated *in vacuo* before purification by flash chromatography (isocratic: 10 : 90, EtOAc : hexanes) to afford product **59** (58.3 mg, 70%, 2:1 diastereomeric ratio) as a pale yellow oil.

Rf: 0.44 (20% EtOAc / hexanes).

^{1}H NMR (400 MHz, CDCl$_3$): δ = Diastereomer A: δ = 7.34 (br s, 1H), 4.54 (dd, J = 8.3 Hz, 5.5 Hz, 1H), 4.15 (dd, J = 12.2 Hz, 4.6 Hz, 1H), 3.35 (dd, J = 9.0 Hz, 4.8 Hz), 2.18-2.10 (m, 1H), 2.00-1.31 (m, 5H), 1.11 (t, J = 7.1 Hz, 3H), 0.96 (t, J = 7.2 Hz, 3H).
Diastereomer B: δ = 7.03 (br s, 1H), 4.76 (dd, J = 11.3 Hz, 2.1 Hz, 1H), 4.04 (dd, J = 12.5 Hz, 4.2 Hz, 1H), 3.94 (dd, J = 12.4 Hz, 9.8 Hz, 1H), 2.00-1.31 (m, 6H), 1.11 (t, J = 7.1 Hz, 3H), 0.99 (t, J = 7.3 Hz, 3H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 162.24, 161.91, 93.03, 64.98, 64.81, 64.94, 63.96, 50.40, 48.58, 38.74, 37.68, 28.51, 27.97, 17.03, 16.40, 15.87, 15.60, 14.64, 14.48.

HRMS (ESI-TOF) m/z: calc'd for $C_{10}H_{17}Cl_3INO_2$ $[M+Na]^+$ = 437.9267, found 437.9293.

IR (film) cm^{-1}: 3368, 2956, 2942, 2897, 1694, 868.