Tin-catalyzed reductive coupling of amines with CO_2 and H_2

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Supporting information

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1. General procedures

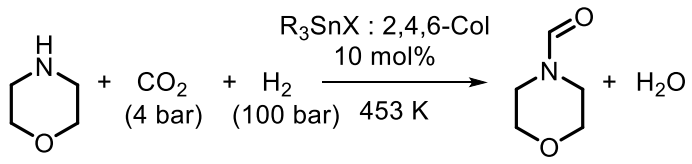
All reagents and solvents were purchased from commercial suppliers (Sigma-Aldrich, Merck, Alpha-Aesar, TCI, Across, abcr, Thermo scientific, Linde gas a.s. and Lach:ner). Specifically, tricyclohexyltin chloride was purchased from Thermo scientific, silver triflate was purchased from Sigma-Aldrich, silver triflimide was purchased from TCI and silver perchlorate was purchased from Thermo scientific. Synthetic reagents were used as received and without further purification including hydrogen gas (99.90%) and carbon dioxide for food industry (99.90%) purchased from Linde gas a.s. Solvents used were reagent grade or better. THF, hexane and DCM were dried on PureSolv MD 5 automated solvent drying system from Inert®. All other solvents were dried and stored over 3Å molecular sieves (20%w/v) and degassed by sparging with dry N_2 for a minimum of 20 minutes before use. All synthetic experiments were carried out using standard Schlenk techniques. Unless otherwise specified ^{1}H, ^{13}C and ^{119}Sn NMRs were taken on a Bruker AVANCE-III (400 MHz) at 298K spectrometer and reported in ppm (δ). Deuterated solvents were purchased from abcr and used as received except for Gutmann-Beckett measurements, where $CDCl_3$ was dried and stored over 3Å molecular sieves (20%w/v). NMR spectroscopy abbreviations: s, singlet; d, doublet; t, triplet; m, multiplet. All the products of catalytic tests were identified by ^{1}H NMR data in comparison with literature, by GC coupled to mass spectrometry on a Shimadzu QP-2010 GC-MS with a Supelcowax 10 column and where necessary by comparison with genuine samples of the targeted compounds.

2. Catalytic tests

2.1 General Procedure:

In air R_3SnX (0.1 mmol), 2,4,6- collidine (0.1 mmol) and morpholine (1 mmol) were dissolved in sulfolane (5 mL) in a steel autoclave. The autoclave was then sealed and purged 5 times with the desired pressure of CO_2. The reaction was then topped up with the desired H_2 reaction pressure. The temperature and stirring rate were set using the Specview program on Parr 5000 series multi reactor system. T = 0 was defined as the time the heating starts. The heating was turned off 2 hours before the end of the stated reaction time and allowed to cool down under pressure over the course of the remaining 2 hours of the test i.e., for a reaction time of 24 hours the heating was turned off after 22 hours and the reaction was depressurized after the 24-hour mark. DCM (1 mmol) was added to the reactor, stirred and an aliquot was taken for ^{1}H NMR analysis in $CDCl_3$. The conversion of morpholine and the yield of N-formylmorpholine were quantified by ^{1}H NMR analysis with the added DCM as the internal standard. Other reaction products were quantified by their respective N-formate signal in ^{1}H NMR and structures confirmed by GC-MS on a Shimadzu QP-2010 GC-MS with a Supelcowax 10 column.

2.2 Typical result(s) of N-formylation of morpholine with CO_2 and H_2:



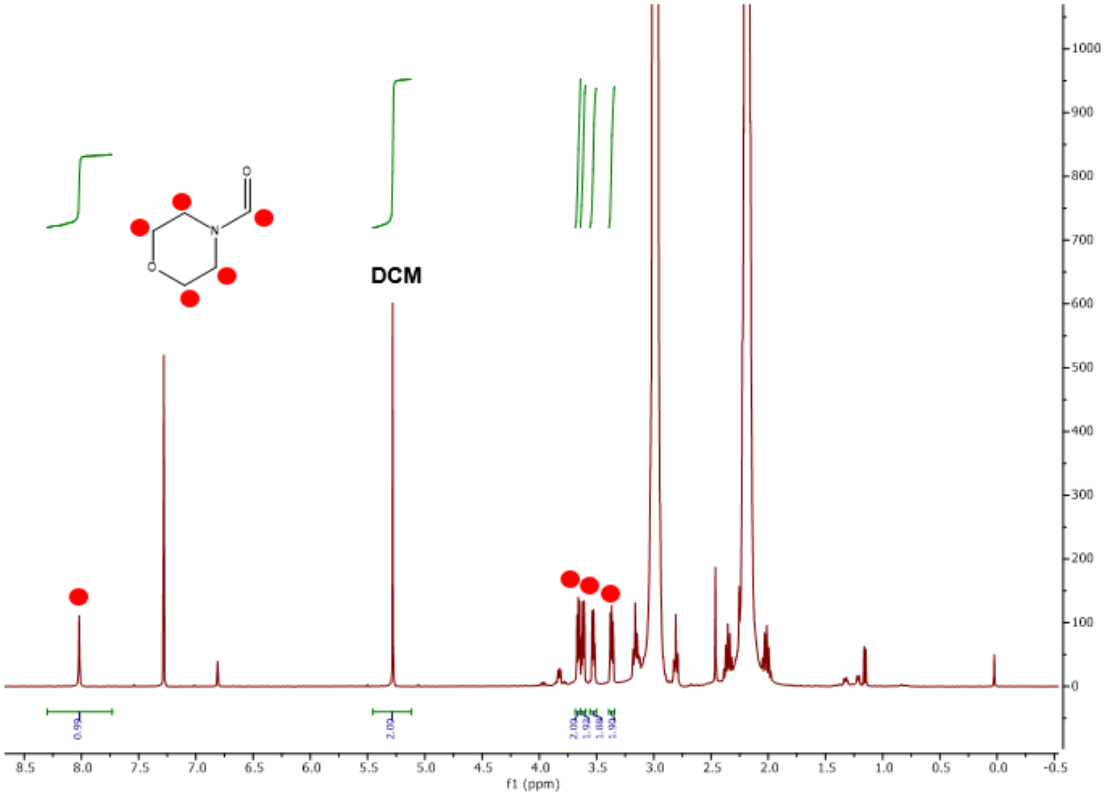
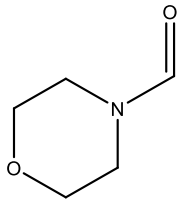


Figure S1: ^{1}H NMR of a reaction mixture at the end of a catalytic test of N-formylation of morpholine, where N-formylmorpholine peaks are marked by red spots. All unmarked peaks can be assigned to the reaction catalyst and sulfolane i.e R_3SnX, 2,4,6-collidine and the reaction solvent.

N-formylmorpholine:



^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.36 (2H), 3.53 (m, 2H), 3.60-3.67 (m, 4H), 8.02 (1H); GC retention time 9.5 to 9.6 minutes; EI-MS (*m/z*) calculated: 115.1, found 115.1 with a 92-98% agreement of EI-MS molecular fragmentation with NIST EI-MS library.

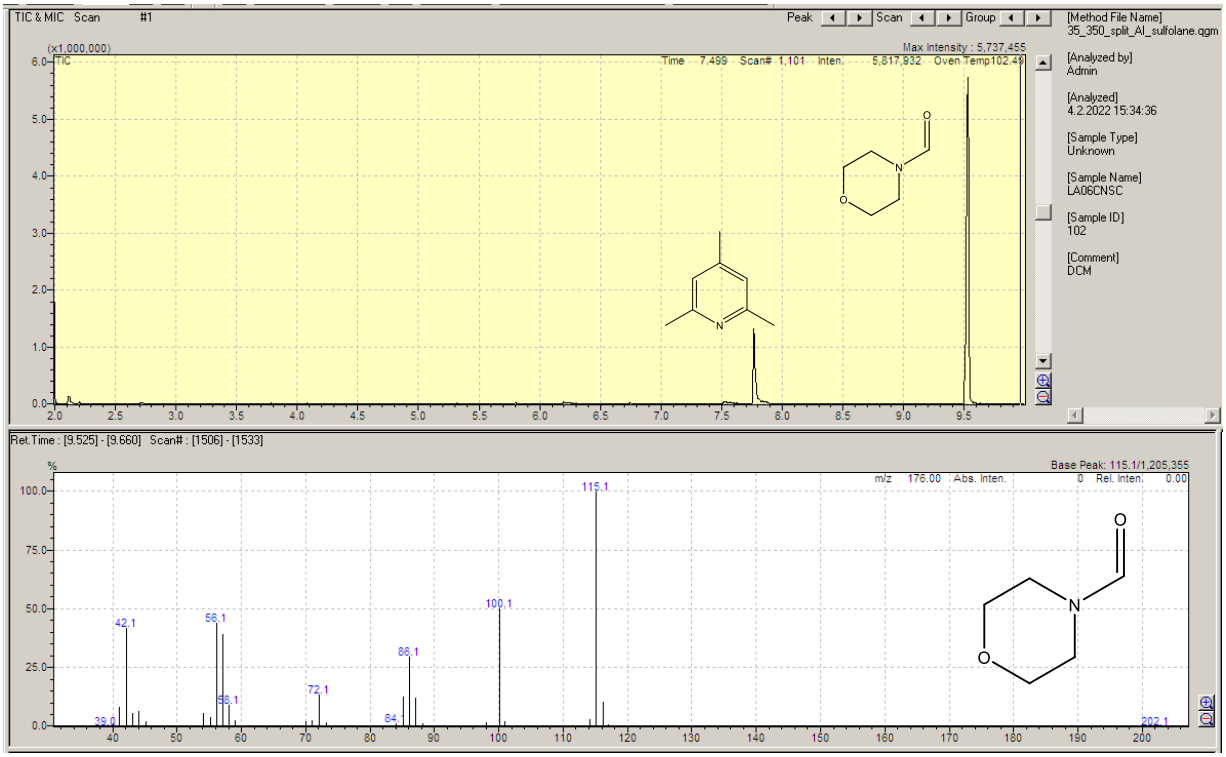


Figure S2: GC-MS analysis of a reaction mixture at the end of a catalytic test of N-formylation of morpholine with R_3SnX : 2,4,6-collidine as the reaction catalyst.

2.3 Optimization of reaction solvent:

$^{i}Pr_3SnOTf$: 2,4,6-collidine (FLP1) have been reported to hydrogenate imines and aldehydes[1,2] in 1,2-dichlorobenzene (DCB) as the solvent. All other reported FLPs also used aromatic or ether solvents such as toluene, fluorobenzene, THF, dioxane or diethylether[2–5] . Nevertheless, initial attempts to N-formylate morpholine with CO_2 and H_2 as the reductant and **FLP1** catalyst in DCB were limited by mass transfer due to poor solubility of morpholinium carbamate salt, which precipitated out of the reaction medium upon addition of CO_2. Thus, we turned to dipolar aprotic solvents namely sulfolane, N-methylpyrrolidone (NMP), ethylene carbonate, dimethylformamide

(DMF) and benzonitrile. It was found that NMP gave the highest conversion, however, it has been shown that it may decompose to a formylated product[6] so would be unreliable in the quantification of further reactions. DMF acted as a formylating reagent as well as the reaction solvent when it was tested so it was also disregarded. Considering this, sulfolane was selected as the reaction solvent as it gave comparable yields to NMP, and it is comparably less toxic.

Table S1: Effect of reaction solvent on the N-formylation of morpholine with FLP1 (10 mol%), H_2 (30 bar) and CO_2 (4 bar).

Catalyst (LA)	Solvent	Temperature (K)	Time (hr)	Yield (%)
$^{i}Pr_3SnOTf$	DCB	453	24	8
$^{i}Pr_3SnOTf$	Benzonitrile	453	24	15
$^{i}Pr_3SnOTf$	Sulfolane	453	24	22
$^{i}Pr_3SnOTf$	NMP	453	24	25
$^{i}Pr_3SnOTf$	Ethylene carbonate	453	24	5

2.4 Optimization of CO_2 pressure:

Table S2: Effect of CO_2 partial pressure on the N-formylation of morpholine with FLP1 (10 mol%) and 5 mL sulfolane.

Catalyst (LA)	H_2 Pressure (bar)	CO_2 Pressure (bar)	Temperature (K)	Time (hr)	Yield (%)
$^{i}Pr_3SnOTf$	30	1	453	24	17
$^{i}Pr_3SnOTf$	30	2	453	24	27
$^{i}Pr_3SnOTf$	30	4	453	24	26
$^{i}Pr_3SnOTf$	30	8	453	24	20
$^{i}Pr_3SnOTf$	60	30	453	24	14

2.5 Optimization of H_2 pressure:

Table S3: Effect of H_2 partial pressure on the N-formylation of morpholine with FLP1 (10 mol%) and 5 mL sulfolane.

Catalyst (LA)	H_2 Pressure (bar)	CO_2 Pressure (bar)	Temperature (K)	Time (hr)	Yield (%)
$^{i}Pr_3SnOTf$	15	4	453	24	10
$^{i}Pr_3SnOTf$	30	4	453	24	21
$^{i}Pr_3SnOTf$	50	4	453	24	50
$^{i}Pr_3SnOTf$	100	4	453	24	56
$^{i}Pr_3SnOTf$	120	4	453	24	56

2.6 Optimization of temperature:

Table S4: Effect of temperature on the N-formylation of morpholine with FLP1 (10 mol%) and 5 mL sulfolane.

Catalyst (LA)	H_2 Pressure (bar)	CO_2 Pressure (bar)	Temperature (K)	Time (hr)	Yield (%)
$^{i}Pr_3SnOTf$	100	4	433	24	26
$^{i}Pr_3SnOTf$	100	4	443	24	36
$^{i}Pr_3SnOTf$	100	4	453	24	56
$^{i}Pr_3SnOTf$	100	4	463	24	54
$^{i}Pr_3SnOTf$	100	4	473	24	53

3. Synthesis of catalysts

3.1 $^{i}Pr_3SnOTf$ synthesis: This procedure was adapted from reference[1]

$^{i}Pr_4Sn$ (5.0 g, 17.2 mmol) and HOTf (3.3 g ,14.6 mmol) were added to $CHCl_3$ (80 mL) and stirred at RT for 5 days. After which the solution was filtered and evaporated under reduced pressure. The resulting solid was washed with heptane (3 x 10 mL) affording $^{i}Pr_3SnOTf$ as a white solid (4.8 g, 83%).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.48 [6H, d, $J_{(1H-1H)}$ = 7.6 Hz, $J_{(117Sn-1H)}$ = 86 Hz, $J_{(119Sn-1H)}$ = 90 Hz, CH_3], 2.18 [1H, sept, $J_{(1H-1H)}$ = 7.6 Hz, $J_{(119Sn-1H)}$ = 39 Hz, CH].

3.2 $^{i}Pr_2Sn(OTf)_2$ synthesis:

$^{i}Pr_4Sn$ (2.0g, 6.9mmol) and HOTf (3.2 g ,14 mmol) were added to $CHCl_3$ (80 mL) and stirred at RT for 5 days. After which the solid was separated, washed with hexane (3 x 10mL) and dried. $^{i}Pr_2Sn(OTf)_2$ was afforded as a white solid in 85% yield.

^{1}H NMR (400 MHz, acetone-d_6) δ: 1.53 (6H), 2.52 (1H); ^{13}C and ^{119}Sn were measured at 600 MHz Brucker NMR instrument. ^{13}C NMR (150 MHz, acetone-d_6) δ: 120.1(q, CF_3) 20.49 (s, CH), 19.4 (s, CH_3); ^{119}Sn NMR (224 MHz, acetone-d_6) δ: -381.4 (s)

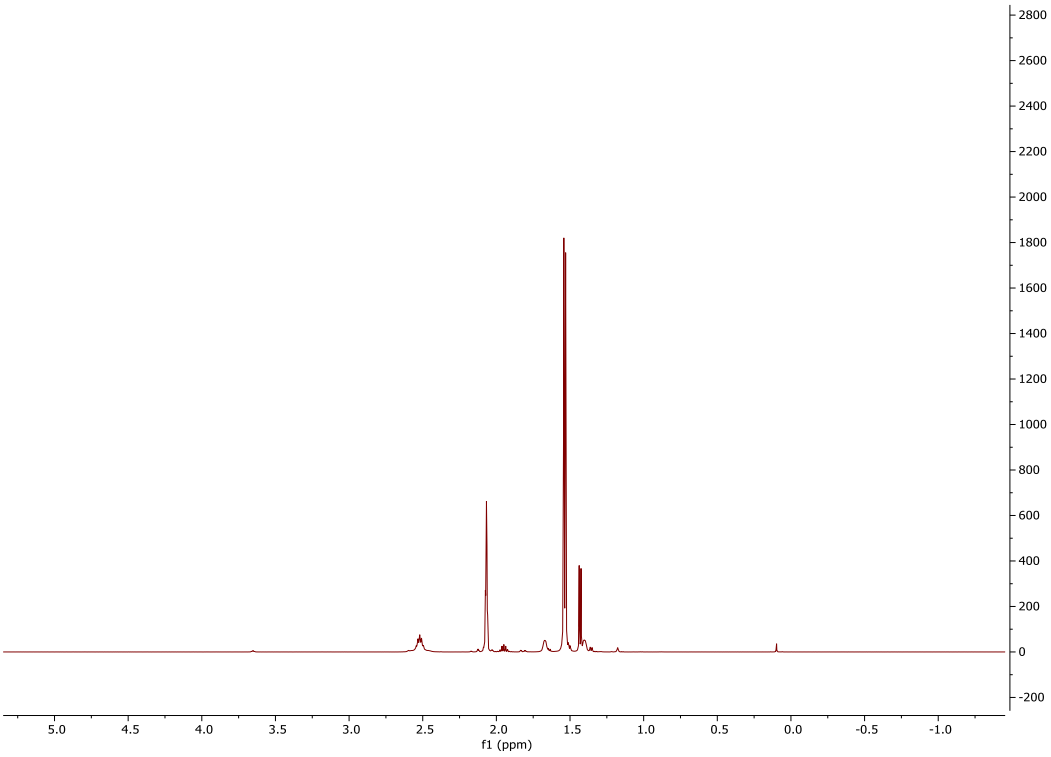


Figure S3: ^{1}H NMR spectrum of $^{i}Pr_2SnOTf_2$

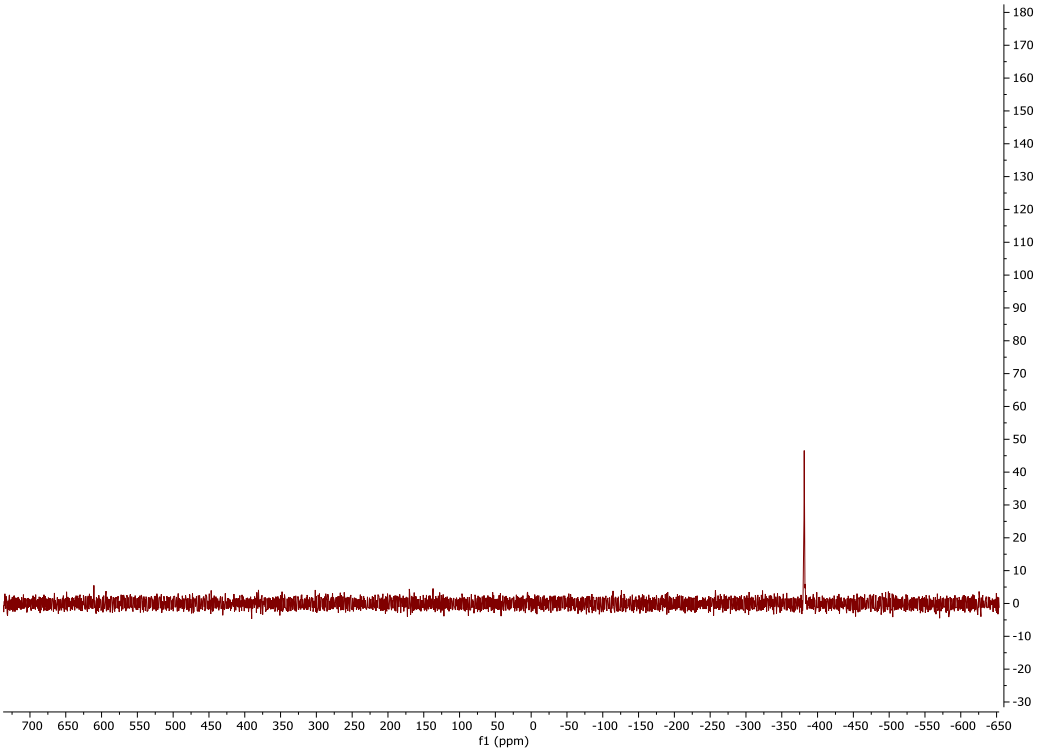


Figure S4: ^{119}Sn NMR spectrum of $^{i}Pr_2SnOTf_2$

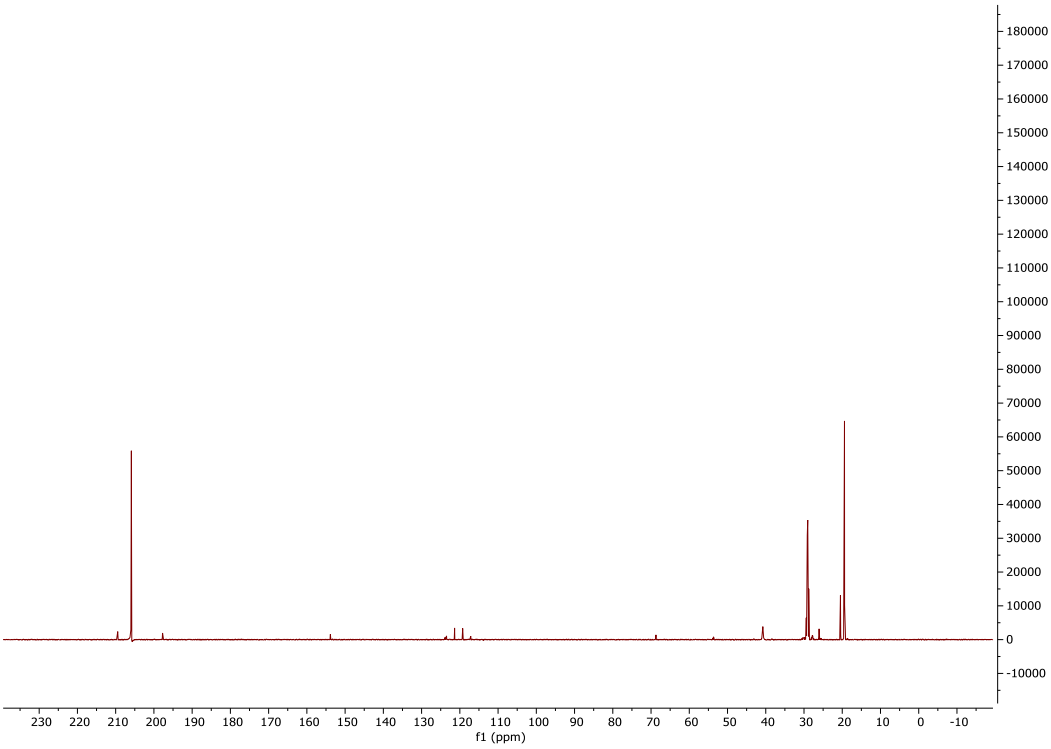


Figure S5: ^{13}C NMR spectrum of $^{i}Pr_2SnOTf_2$

3.3 Cy_3SnX synthesis:

To a solution of Cy_3SnCl (500 mg,1.24 mmol) in CH_2Cl_2 (50mL) was added AgX (1.24 mmol, X = OTf, NTf_2, ClO_4). The reaction was stirred at RT for 3 days. The solution was then filtered and evaporated under reduced pressure affording a white solid.

Cy_3SnOTf:

^1H NMR (400 MHz, $CDCl_3$) δ: 2.29 – 1.21ppm (m, 33H); ^{13}C, ^{19}F and ^{119}Sn were measured at 600 MHz Brucker NMR instrument. ^{13}C NMR (150 MHz, $CDCl_3$) δ: 38.72ppm (s), 30.64ppm (s), 28.76ppm (s), 26.57ppm (s); ^{119}Sn NMR (224 MHz, $CDCl_3$) δ: 73.9ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -77.20ppm (s); HRMS+ for $C_{19}H_{33}F_3O_3SSn$ m/z: 517.2972 (calculated: 517.2352); HRMS- for $CF_3O_3S^-$ m/z: 148.9580 (calculated: 148.9520)

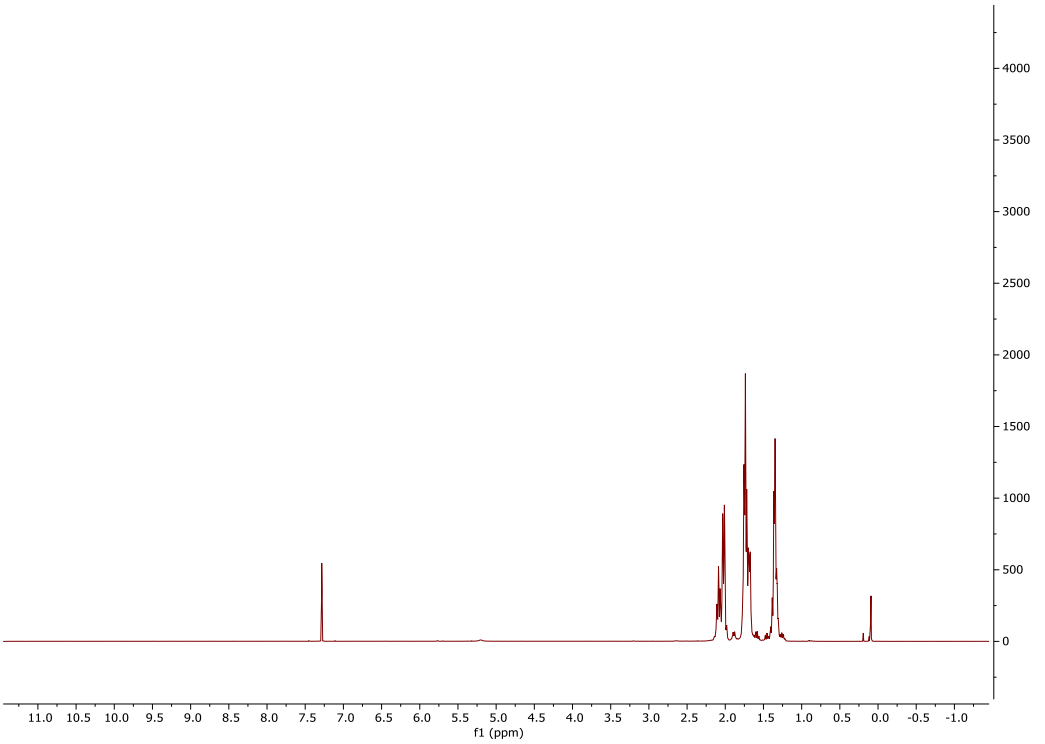


Figure S6: ^{1}H NMR spectrum of Cy_3SnOTf

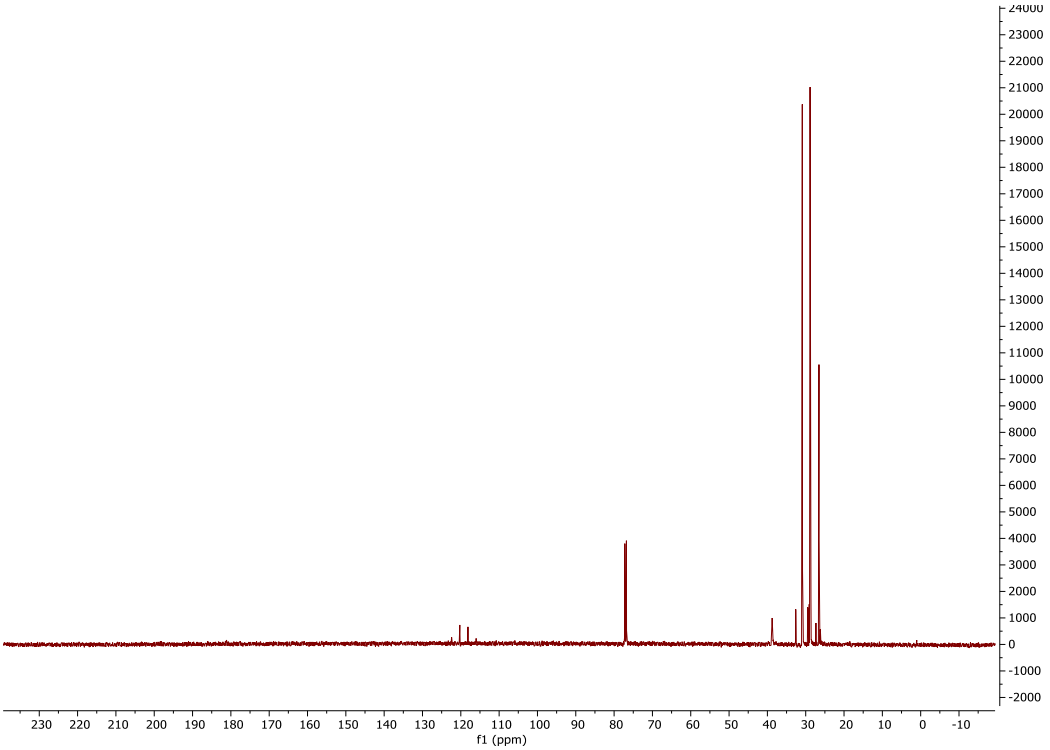


Figure S7: ^{13}C NMR spectrum of Cy_3SnOTf

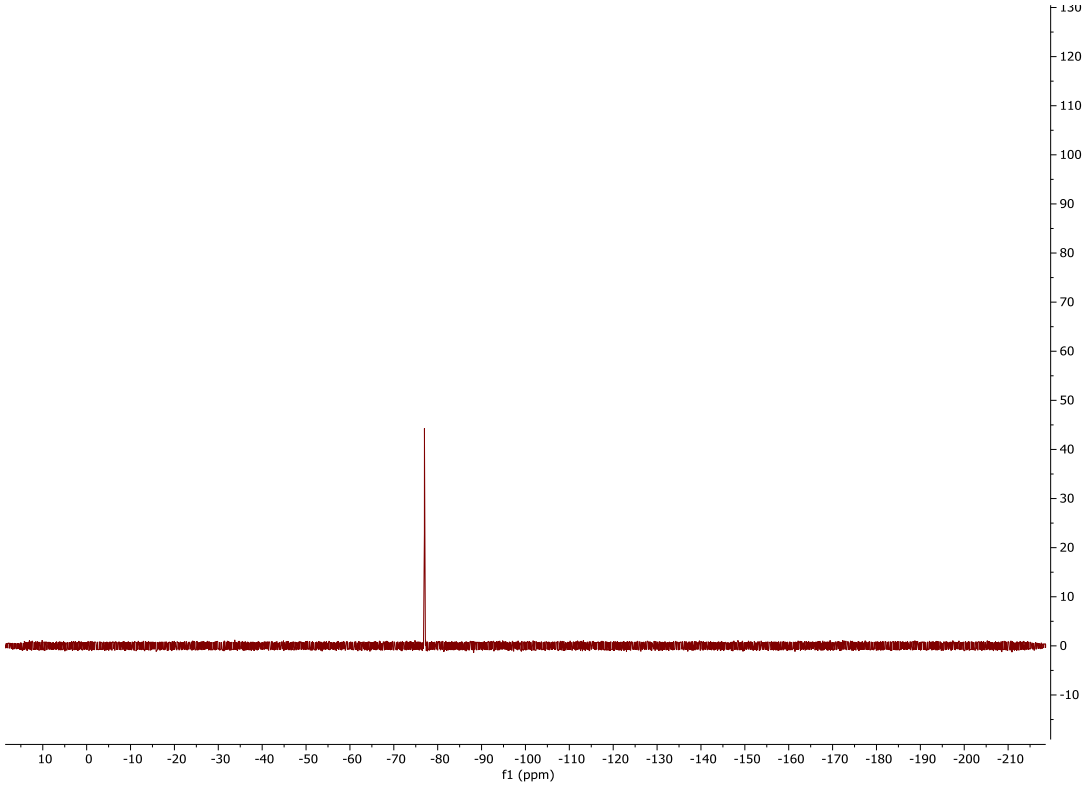


Figure S8: ^{19}F NMR spectrum of Cy_3SnOTf

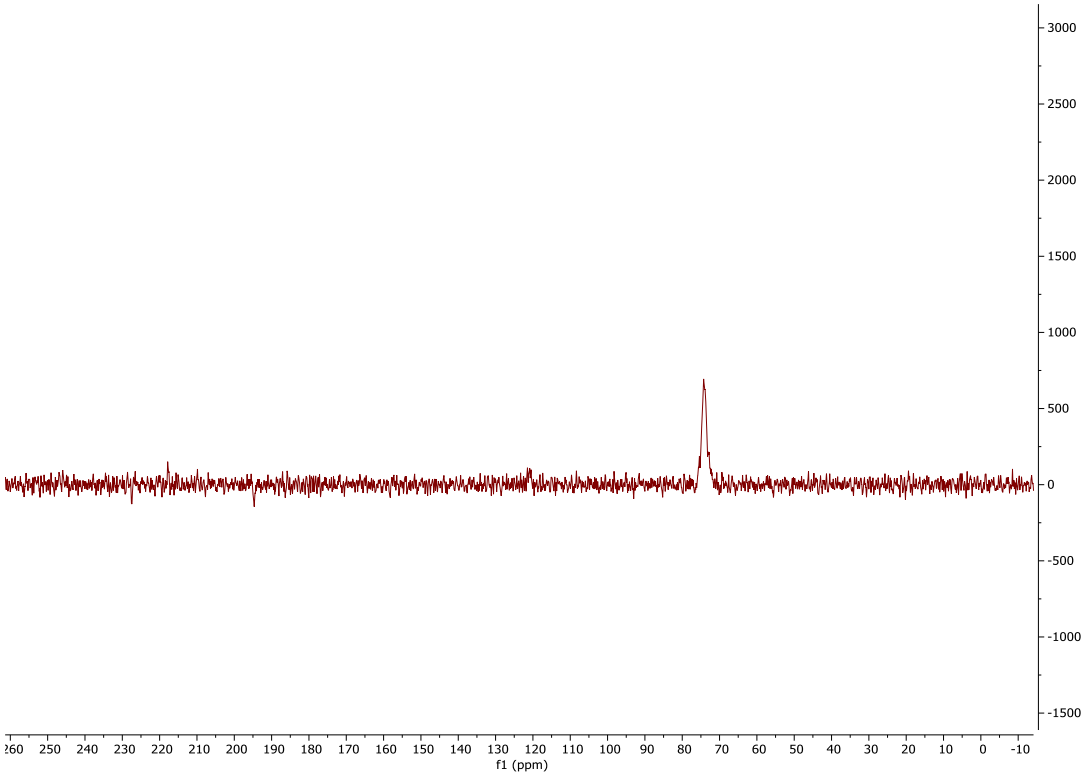


Figure S9: ^{119}Sn NMR spectrum of Cy_3SnOTf

Cy_3SnClO_4:

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.40 – 1.23ppm (m, 33H); ^{13}C, ^{19}F and ^{119}Sn were measured at 600 MHz Brucker NMR instrument. ^{13}C NMR (150 MHz, $CDCl_3$) δ: 38.66ppm (s), 30.66ppm (s), 28.83ppm (s), 26.56ppm (s); ^{119}Sn NMR (224 MHz, $CDCl_3$) δ: 74.3ppm (s); HRMS+ for $C_{18}H_{33}Sn^{+}$ m/z: 369.1661 (calculated: 369.1604); HRMS- for ClO_4^{-} m/z: 98.9501 (calculated: 98.9489)

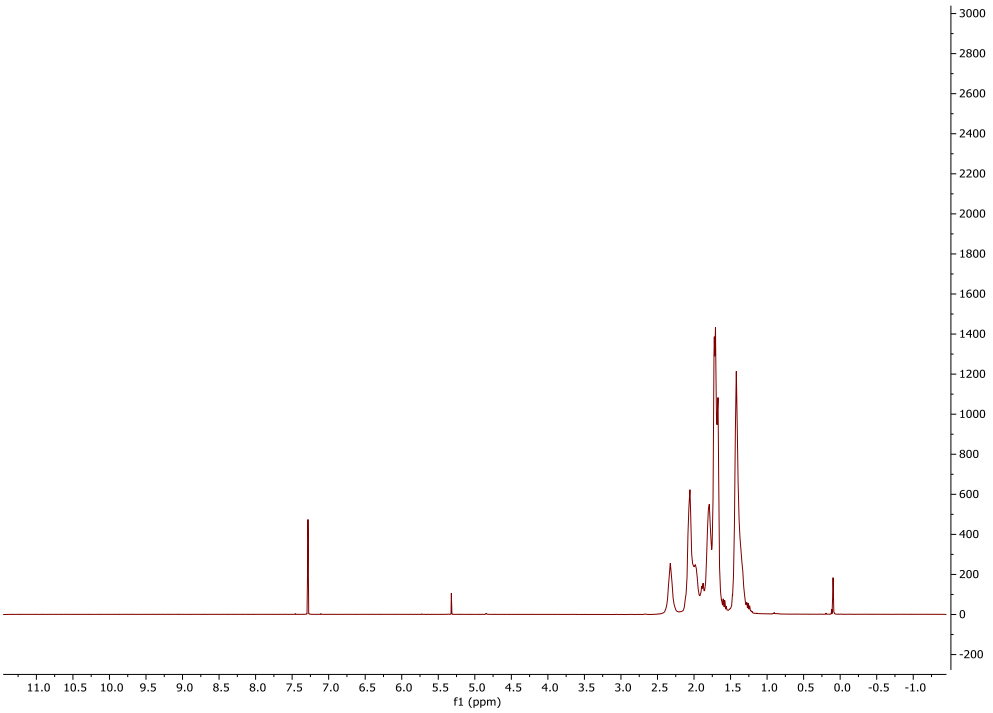


Figure S10: ^{1}H NMR spectrum of Cy_3SnClO_4

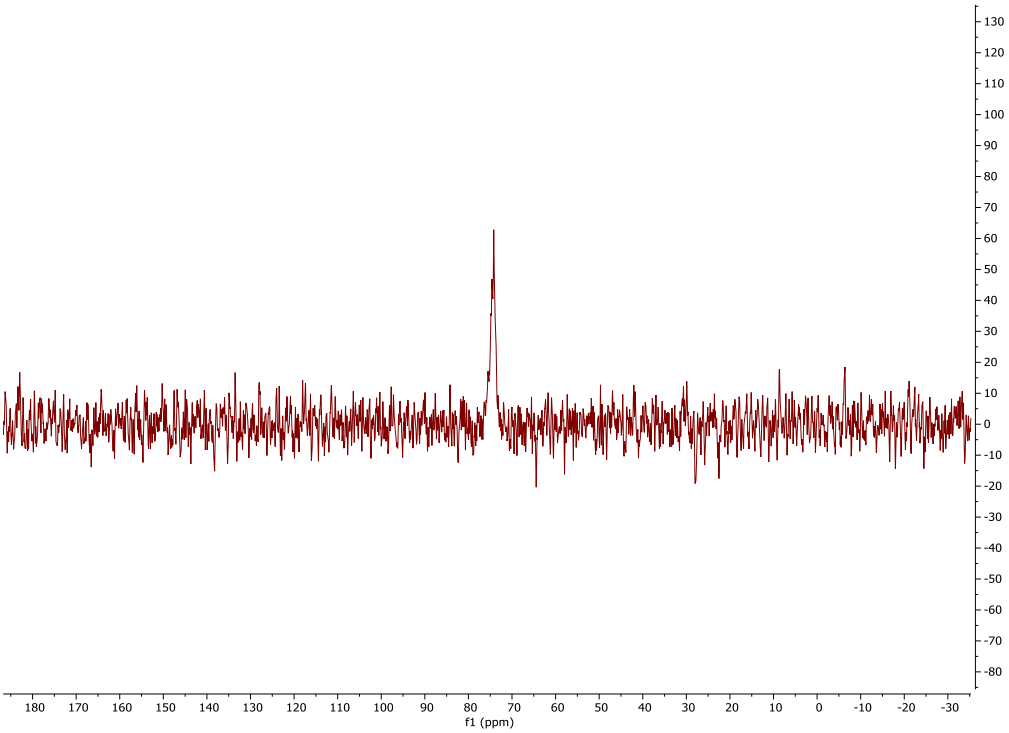


Figure S11: ^{119}Sn NMR spectrum of Cy_3SnClO_4

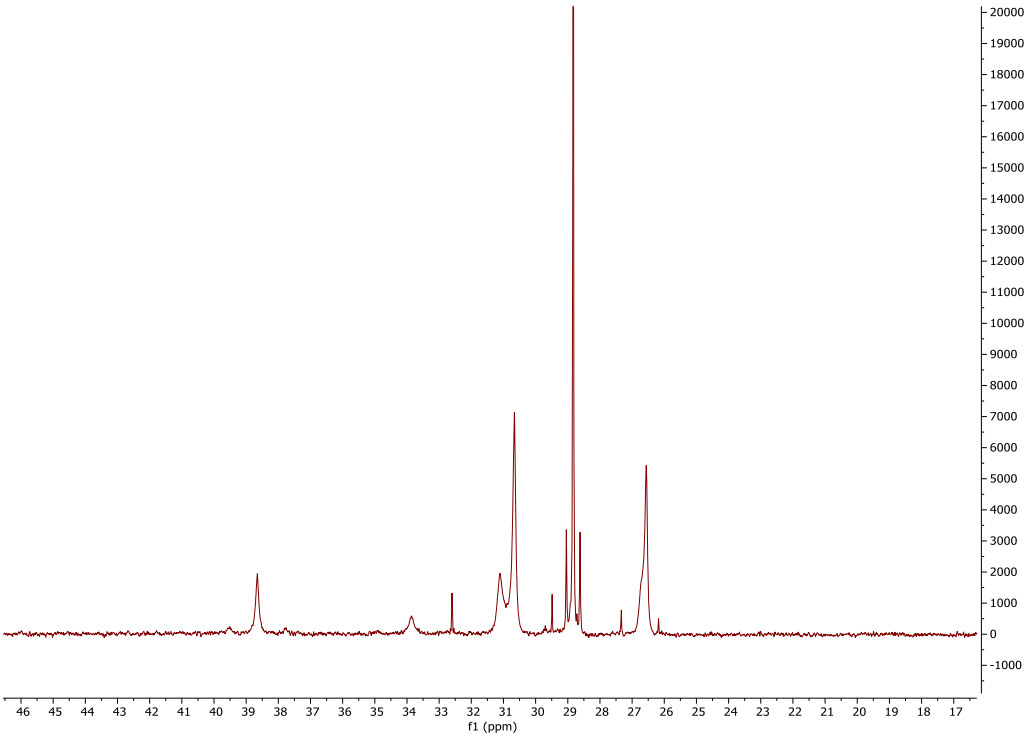


Figure S12: ^{13}C spectrum of Cy_3SnClO_4

Cy_3SnNTf_2:

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.15 – 1.21ppm (m, 33H); ^{13}C, ^{19}F and ^{119}Sn were measured at 600 MHz Brucker NMR instrument. ^{13}C NMR (150 MHz, $CDCl_3$) δ: 118.95 ppm (q) (two peaks of the quartet are obscured by the baseline), 38.78ppm (s), 31.0ppm (s), 28.90ppm (s), 26.50ppm (s); ^{19}F NMR (376 MHz, $CDCl_3$) δ: -78.2ppm (s); HRMS+ for $C_{18}H_{33}Sn^{+}$ m/z: 369.1661 (calculated: 369.1614); HRMS- for $C_2F_6NO_4S_2^{-}$ m/z: 279.9304 (calculated: 279.9173)

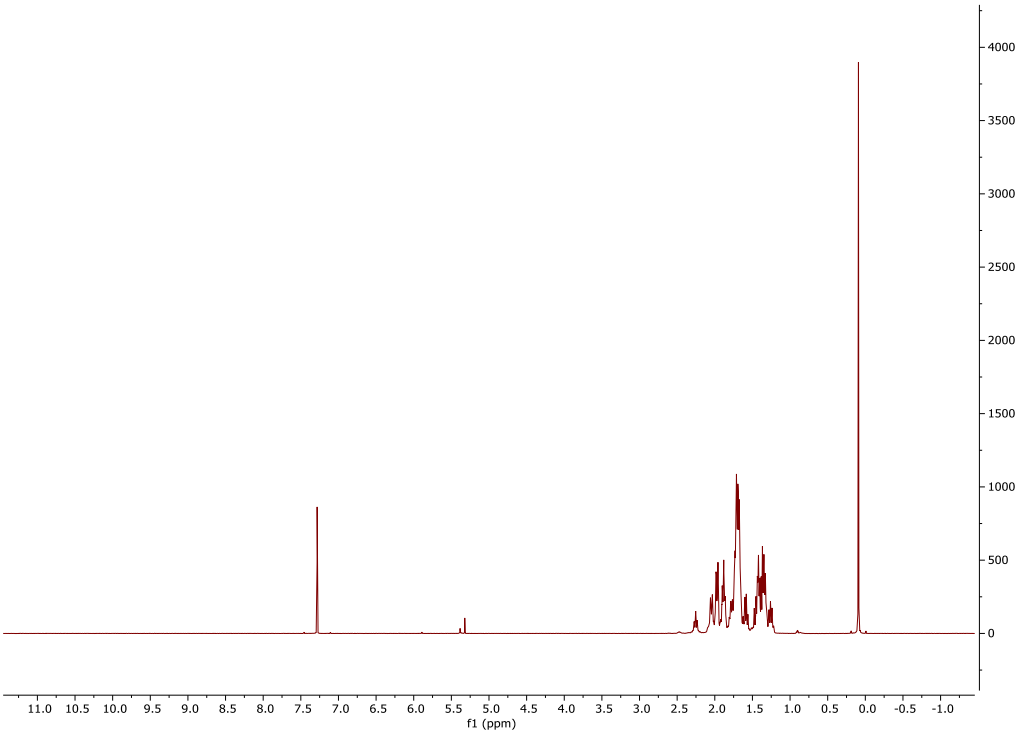


Figure S13: ^{1}H NMR spectrum of Cy_3SnNTf_2

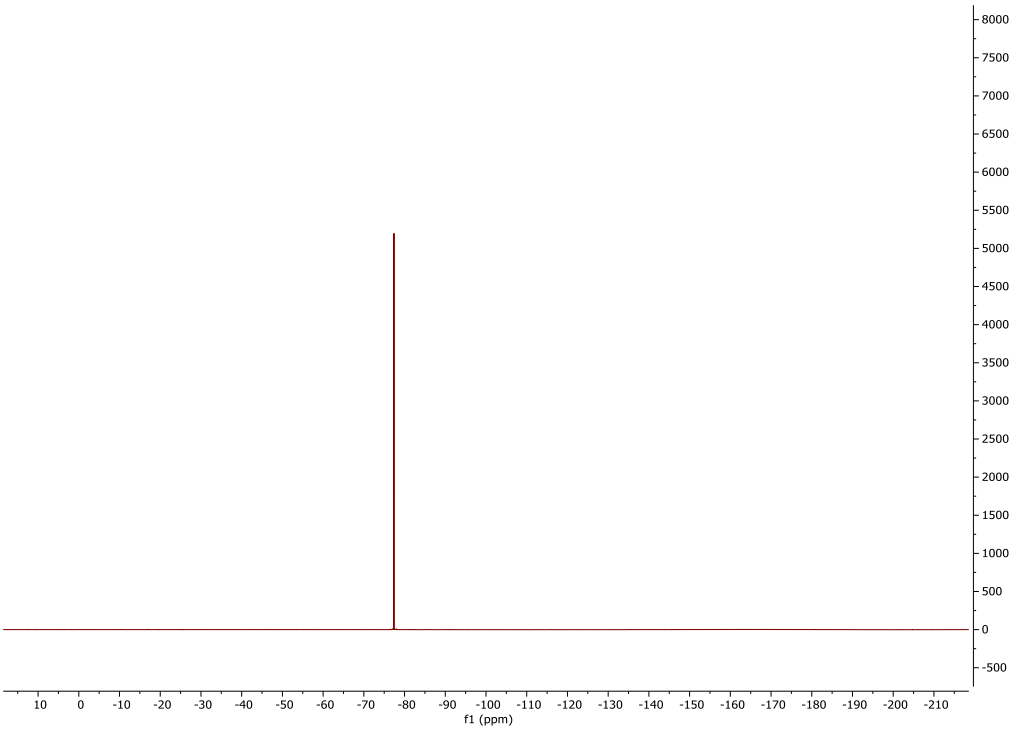


Figure S14: ^{19}F NMR spectrum of Cy_3SnNTf_2

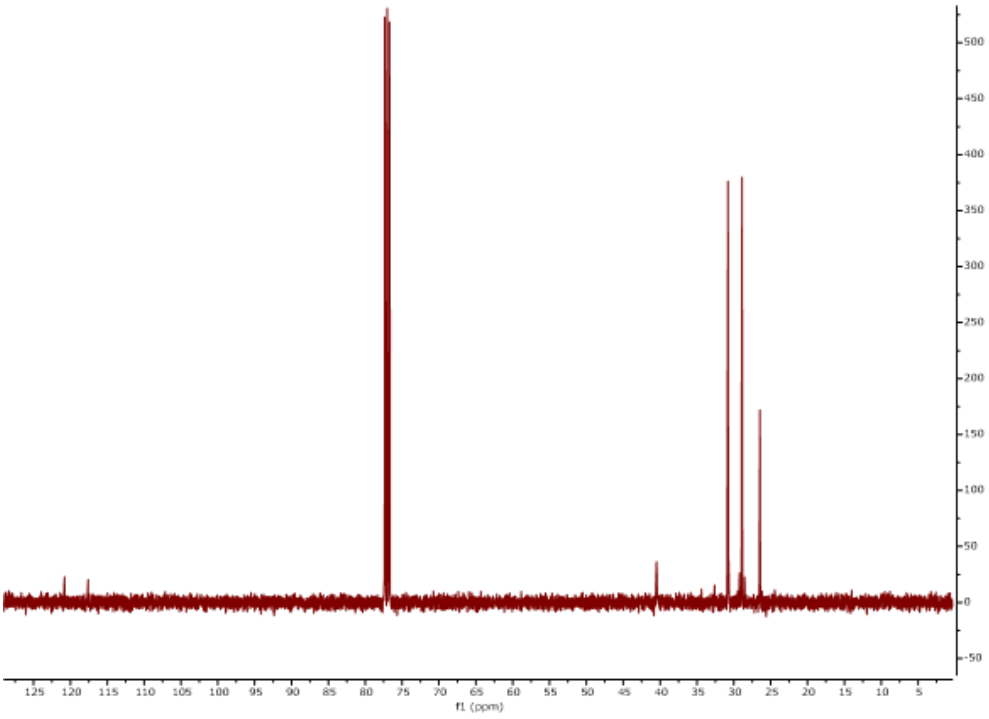


Figure S15: ^{13}C NMR spectrum of Cy_3SnNTf_2

3.4 Synthesis of $^{s}Bu_4Sn$

To a suspension of Mg turnings (3.65 g, 150 mmol) and iodine (50.0 mg) in THF (40 mL) was added 2-chlorobutane (14.4 mL, 135 mmol) at 0 °C with vigorous stirring. After the addition, the solution was warmed to RT and left stirring for 10 h. The suspension was filtered through a frit and washed with THF (2 x 40 mL). The ^{s}BuMgCl solution was added dropwise to a stirred solution of $SnCl_4$ (7.50 g, 28.8 mmol) in THF (50 mL) cooled to 0 °C. After complete addition, the solution was heated to 80 °C for 3 d. After the solution was cooled to RT, H_2O (20 mL) was added carefully.

This synthesis gave a mixture of all six possible diastereomers in a statistical ratio. No attempt was made to separate them. The characterisation data presented are for this mixture.

^{1}H NMR (400 MHz, C_6D_6) δ 0.95 (t, $^{3}J_{1H\text{-}1H}$ = 7.3 Hz, 12H, SnCHCH$_2$C*H*$_3$), 2.25 (d, $^{3}J_{1H\text{-}1H}$ = 7.1 Hz, $^{3}J_{1H\text{-}117/119Sn}$ = 60.2 Hz, 12H, SnCHC*H*$_3$), 1.29-1.44 (m), 1.46-1.64 (m), 1.67-1.87 (m); ^{119}Sn{^{1}H} NMR (149 MHz, C_6D_6) δ −45.5, −45.1, −45.0

3.5 Synthesis of $^{s}Bu_3SnOTf$

To a solution of $^{s}Bu_4Sn$ (2.50 g, 7.20 mmol) in $CHCl_3$ (40 mL) was added HOTf (1.03 g, 6.84 mmol), which was stirred for 19 h at 50 °C. The solvent was removed in vacuo to yield a white gum, which would not dry further. Pentane (10 mL) was added and the solution was cooled to −40 °C and left for 12 h, whereupon a white solid precipitated. The solid was filtered, washed with cold pentane (2 x 10 mL) and dried in vacuo to furnish $^{s}Bu_3SnOTf$ as a free-flowing white powder (2.87 g, 6.53 mmol, 95%).

This synthesis gave a mixture of all four possible diastereomers in statistical ratio. No attempt was made to separate these. The characterisation data presented are for this mixture.

^{1}H NMR (400 MHz, C_6D_6) δ 1.04 (t, $^{3}J_{1H\text{-}1H}$ = 7.3 Hz, 9H, SnCHCH$_2$C*H*$_3$), 1.46 (d, $^{3}J_{1H\text{-}1H}$ = 7.4 Hz, $^{3}J_{1H\text{-}117/119Sn}$ = 85.1 Hz, 9H, SnCHC*H*$_3$), 1.77-1.96 (m), 2.06-2.23 (m, 3H, SnC*H*); ^{119}Sn{^{1}H} NMR (149 MHz, C_6D_6) δ 214.7, 215.7; MS (APCI) m/z = 369 ($^{s}Bu_3SnOSO_2^{+}$), 219 ($^{s}Bu_3Sn^{+}$)

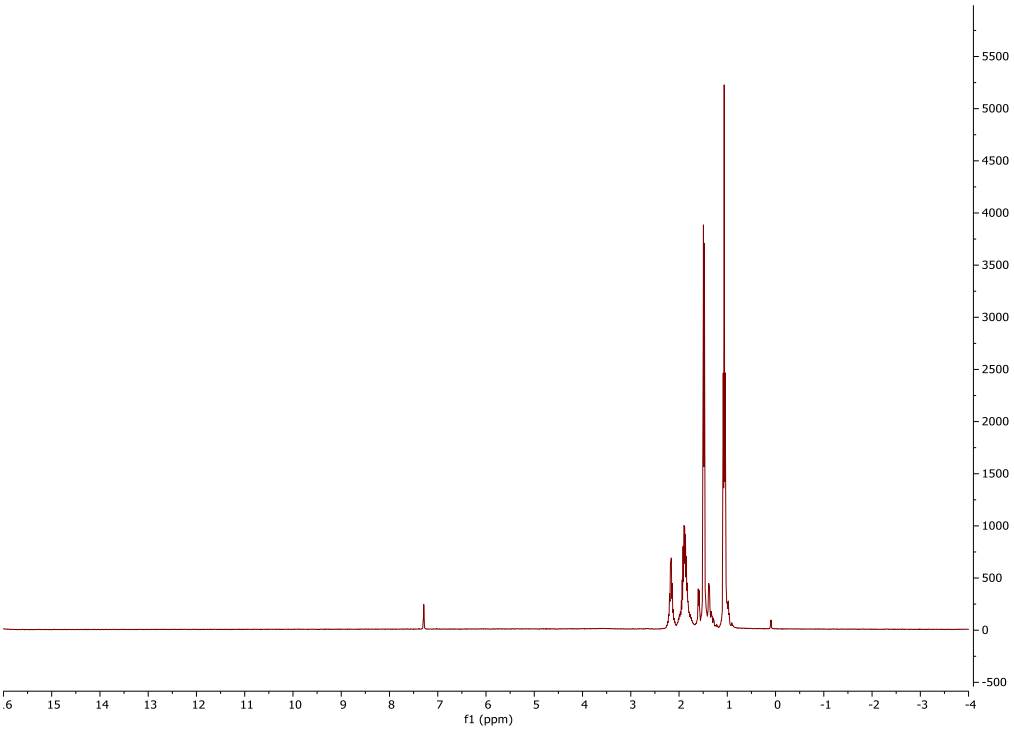


Figure S16: ^{1}H NMR spectrum of $^{s}Bu_3SnOTf$

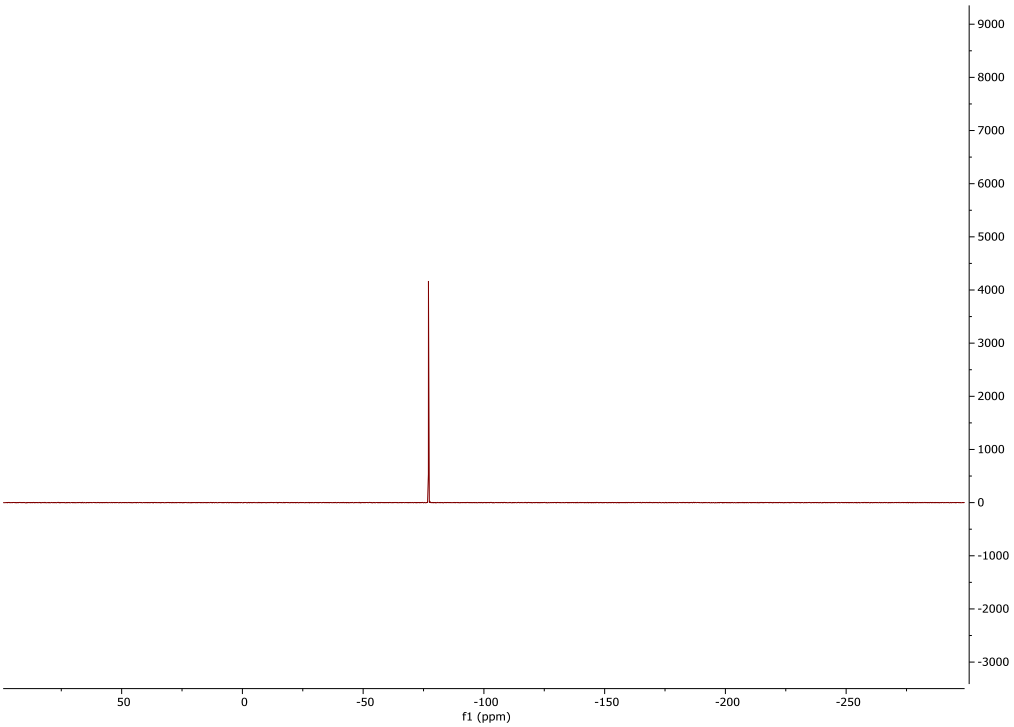


Figure S17: ^{19}F NMR spectrum of $^{s}Bu_3SnOTf$

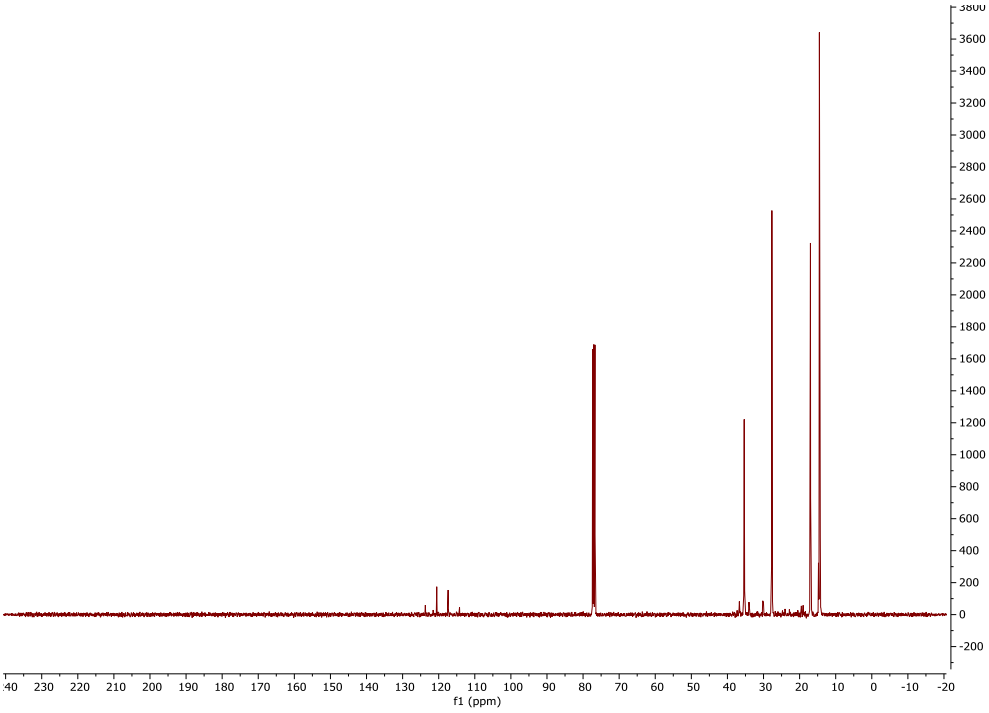


Figure S18: ^{13}C NMR spectrum of $^{s}Bu_3SnOTf$

3.6 Synthesis of $(Nph)_4Sn$

Neophylmagnesium chloride was prepared by heating magnesium turnings (7.50 g, 309 mmol) and neophylchloride (49.0 mL, 51.3 g, 304 mmol) in Et_2O (100mL) at reflux for 24 hrs. The Grignard solution was then filtered and stirred over an ice bath. $SnCl_4$ (5.85 mL, 13.0 g, 50.0 mmol) in benzene (40 mL) was added dropwise, and the suspension stirred at room temperature for 60 hrs. The excess Grignard was quenched carefully with water (250 mL) before the product was extracted with Et_2O (3x150 mL), washed with water (400 mL), dried (Na_2SO_4), and the solvent removed in vacuo. Addition of an ethanol/benzene solution (3:1) resulted in the precipitation of the product, which was filtered, washed with cold ethanol (3x15 mL) and cold pentane (3x15 mL), then dried in vacuo. The product was subsequently recrystallised from pentane at −45◦C, yielding $(Nph)_4Sn$ as white crystals (26.4 g, 39.5 mmol, 79 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 [t, $^{3}J_{1H-1H}$ = 7.5 Hz, 8H, *m* – CH], 7.16 [t, $^{3}J_{1H-1H}$ = 7.2 Hz, 4H, *p* – CH], 7.11 [d, $^{3}J_{1H-1H}$ = 7.5 Hz, 8H, *o* – CH], 1.14 [s, 24H, CH_3], 0.79 [s, $^{2}J_{119|117Sn-1H}$ = 47.7 Hz, 8H, CH_2]; $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 151.6 [*i* – C], 128.2 [*m* – CH], 125.7 [*o* – CH], 125.5 [*p* – CH], 38.5 [$C(CH_3)_2$], 33.5 [CH_3], 31.2 [$^{1}J_{119Sn-13C}$ = 302 Hz, $^{1}J_{117Sn-13C}$ = 289 Hz, CH_2]; $^{119}Sn\{^{1}H\}$ NMR (149 MHz, $CDCl_3$): δ -52.6 (s)

3.7 $(Nph)_3SnOTf$

Trifluoromethanesulfonic acid (0.68 mL, 1.15 g, 7.67 mmol) suspended in $CHCl_3$ (5 mL) was added dropwise to a solution of $(Nph)_4Sn$ (5.00g, 7.67 mmol) in $CHCl_3$ (40 mL) with rapid stirring. The

mixture was heated to 60◦C for 48 hours, the solution was filtered, the solvent removed in vacuo, and the solid thoroughly washed with pentane (3x30 mL). The product was subsequently recrystallised from Et_2O at −45◦C, yielding $(Nph)_3SnOTf$ as colourless needles (4.06 g, 6.08 mmol, 79 %).

^1H NMR (400 MHz, $CDCl_3$): δ 7.35-7.25 [m, 9H, *m* – CH, *p* – CH], 6.91 [m, 6H, *o* – CH], 1.35 [s, $^2J_{119|117Sn-1H}$ = 45.6 Hz, 6H, CH_2], 1.21 [s, 18H, CH_3]; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 150.4 [*i* – C], 129.0 [*m* – CH], 126.6 [*p* – CH], 125.1 [*o* – CH], 41.1 [$^1J_{119|117Sn-13C}$ = 307 Hz, CH_2], 37.6 [$C(CH_3)_2$], 32.9 [CH_3]; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$): δ -77.7 (s); $^{119}Sn\{^1H\}$ NMR (149 MHz, $CDCl_3$): δ 250 (s); HRMS (EI) found (calculated) for $C_{31}H_{39}F_3O_3SSn$ m/z: 668.1589 (668.1594)

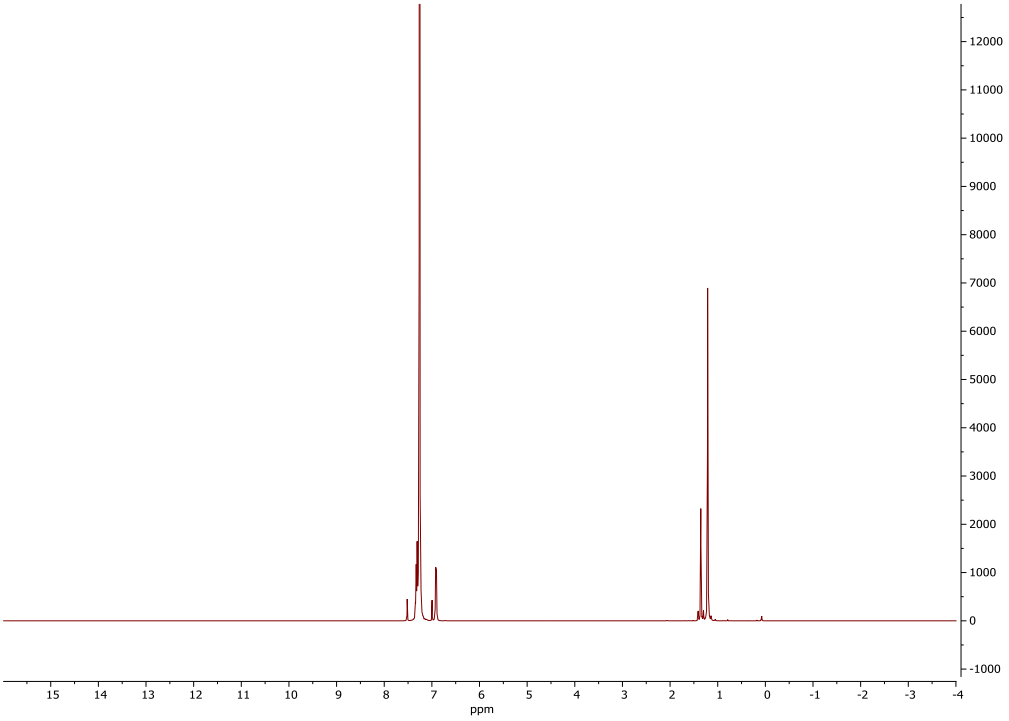


Figure S19: ^1H NMR spectrum of NPh_3SnOTf

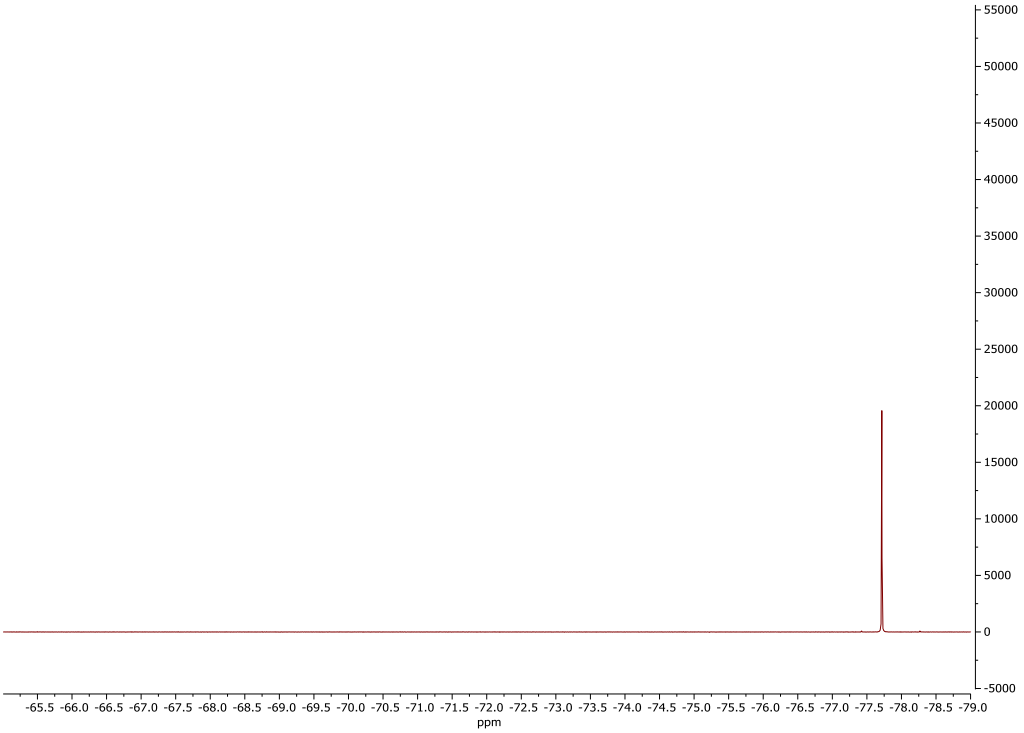


Figure S20: ^{19}F NMR spectrum of NPh_3SnOTf

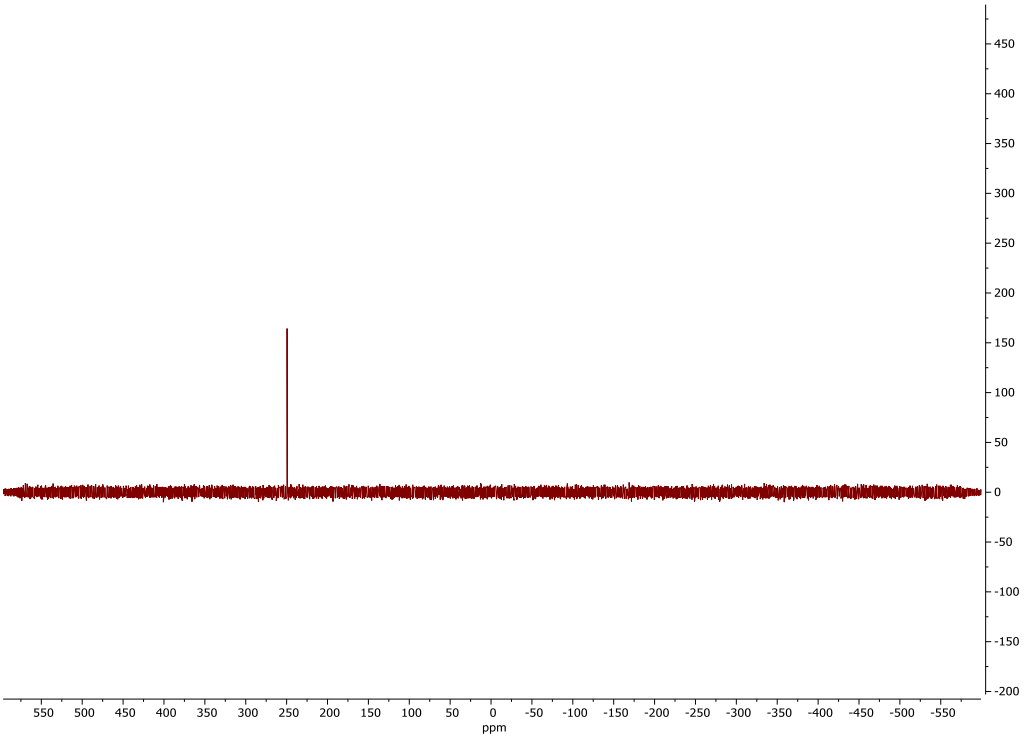


Figure S21: ^{119}Sn NMR spectrum of NPh_3SnOTf

4. Catalyst stability testing

4.1 General procedure for catalyst stability testing

Morpholine (1mmol), and 1 mol% of catalyst were dissolved in sulfolane under standard reaction conditions (100 bar H_2, 4 bar CO_2 and at 453 K). The reaction was run for a week at which point the autoclave was degassed, an aliquot was taken and if no morpholine remained in the sample another 1 mmol of morpholine was added and the autoclave was repressurized. This process was repeated until the catalyst stopped fully converting starting material. The Cy_3SnOTf was stopped at 300 turnovers (3 week long reaction) as this was enough to conclude it was more stable than $^{i}Pr_3SnOTf$ which only reached 162 (2 week long reaction) turnovers.

5. Gutman-Beckett acidity measurements

5.1 General procedure for Gutman-Beckett acidity measurements

0.02 mL of a stock solution of Triethylphosphine oxide (30 mg, 0.22 mmol,) in 2 mL of dry $CDCl_3$ was added to a solution of Lewis acid (0.1 mmol) in 0.5mL of $CDCl_3$. ^{31}P (^{1}H) NMRs wertr then measured, after which more Lewis acid was added, the sample was then remeasured, and this process was repeated until the peak positions remained constant.

The acceptor numbers were calculated using the formula from reference[7]

Acceptor number = [$\delta^{31}P$ [^{1}H]/ppm (sample) – 41.0] x 2.22

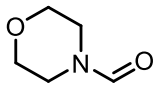
5.2 Results of Gutman-Beckett acidity measurements

Table S5*:* Summary of the acceptor numbers for Cy_3SnX Lewis acids.

Catalyst (LA)	$\delta^{31}P$ [^{1}H]/ppm	Acceptor number
Cy_3SnOTf	68.1	60.2
Cy_3SnNTf_2	76.9	79.7
Cy_3SnClO_4	71.6	67.9

6. Substrate scope

6.1 N-formylmorpholine



^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.36 (2H), 3.53 (m, 2H), 3.60-3.67 (m, 4H), 8.02 (1H); GC retention time 9.5 to 9.6 minutes; EI-MS (*m/z*) calculated: 115.1, found 115.1 with a 92-98% agreement of EI-MS molecular fragmentation with NIST EI-MS library.

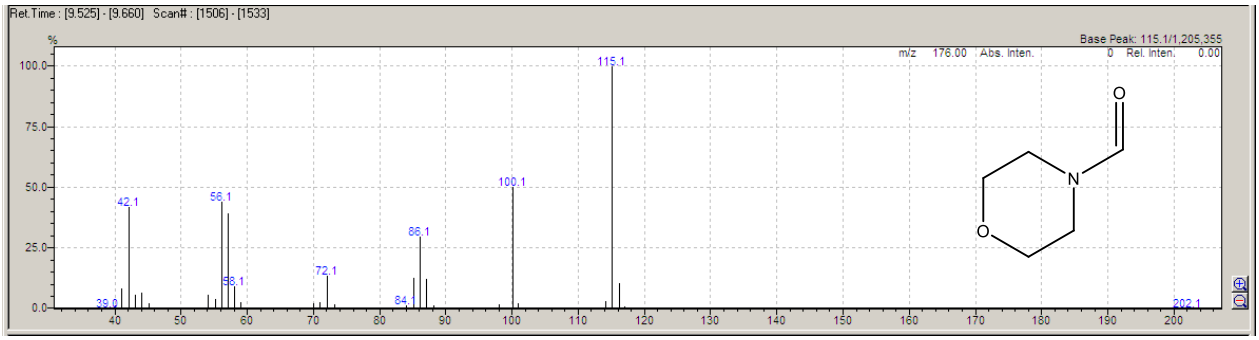
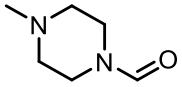


Figure S22: EI-MS analysis of the reaction product of N-formylation of morpholine with CO_2 and H_2.

6.2 1-Formyl-4-methylpiperazine



^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.03 (1H) 3.60-3.67 (m, 4H), 3.62 (m, 2H), 3.55 (2H); GC retention time 13.3 to 13.5 minutes; EI-MS (*m/z*) calculated: 128.1, found 128.1

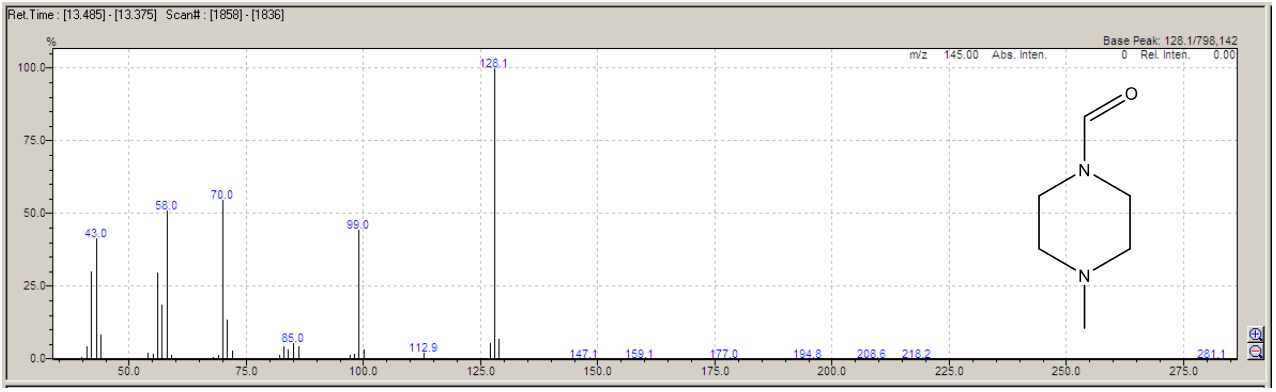
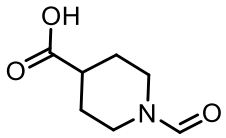


Figure S23: EI-MS analysis of the reaction product of N-formylation of 1-methylpiperazine with CO_2 and H_2.

6.3 N-Formylpiperidine-4-carboxylic acid



^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.98 (s 1H), all other peaks were obscured by the reaction solvent; GC retention time 16.7 to 17.3 minutes; EI-MS (*m/z*) calculated: 157.1, found 157.1

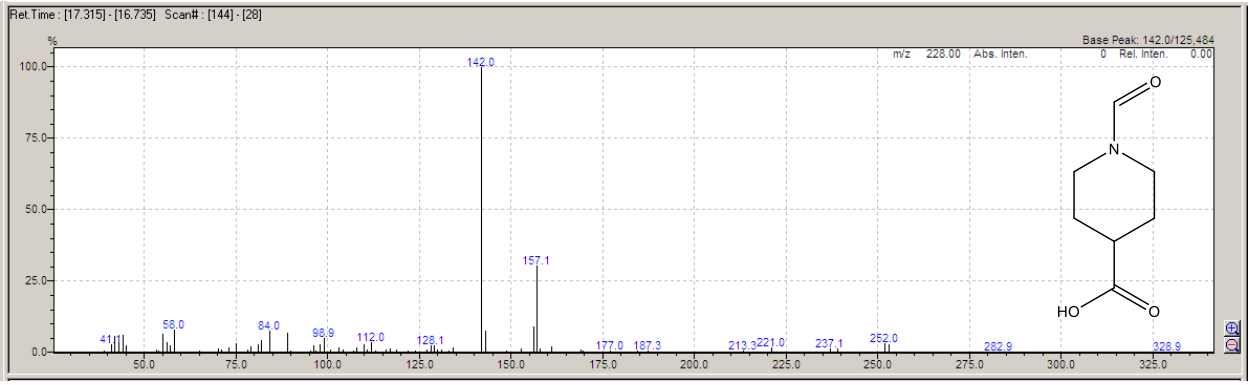
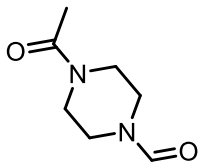


Figure S24: EI-MS analysis of the reaction product of N-formylation of piperidine-4-carboxylic acid with CO_2 and H_2.

6.4 4-Acetylpiperazine-1-carbaldehyde



^{1}H NMR (400 MHz, $CDCl_3$) δ:8.09 (s,1H), all other peaks were obscured by the reaction solvent; GC retention time 25.7 to 25.8 minutes; EI-MS (*m/z*) calculated: 156.1, found 156.1

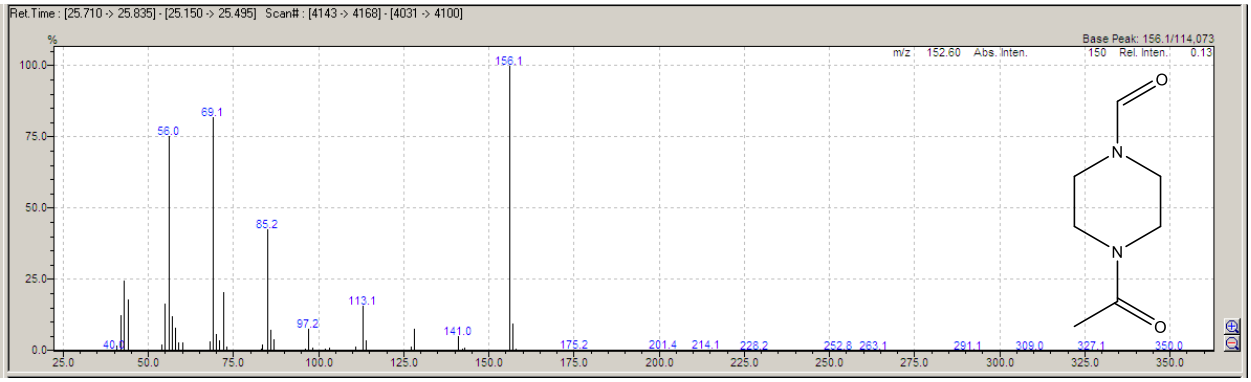
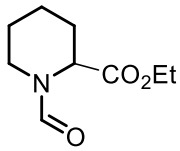


Figure S25: EI-MS analysis of the reaction product of N-formylation of 1-Acetylpiperazine with CO_2 and H_2.

6.5 Ethyl 1-formylpiperidine-2-carboxylate



^{1}H NMR (400 MHz, $CDCl_3$) mixture of rotamers δ: 8.03 (s, 1H (rotamer 1)) 7.99 (s, 1H (rotamer 2)) 7.93 (s,1H (rotamer 3)), 5.63 (s, 1H (rotamer 2)), 5.06 (d, 1H (rotamer 3)) , 4.23 (s, 1H (rotamer 1), all other peaks were obscured by the reaction solvent; GC retention time 16.3 to 16.4 minutes; EI-MS (*m/z*) calculated: 185.2, found 185.1. The reaction product was also compared to a genuine sample of ethyl 1-formylpiperidine-2-carboxylate GC retention time 16.3 to 16.4 minutes; EI-MS (*m/z*) calculated: 185.2, found 185.1

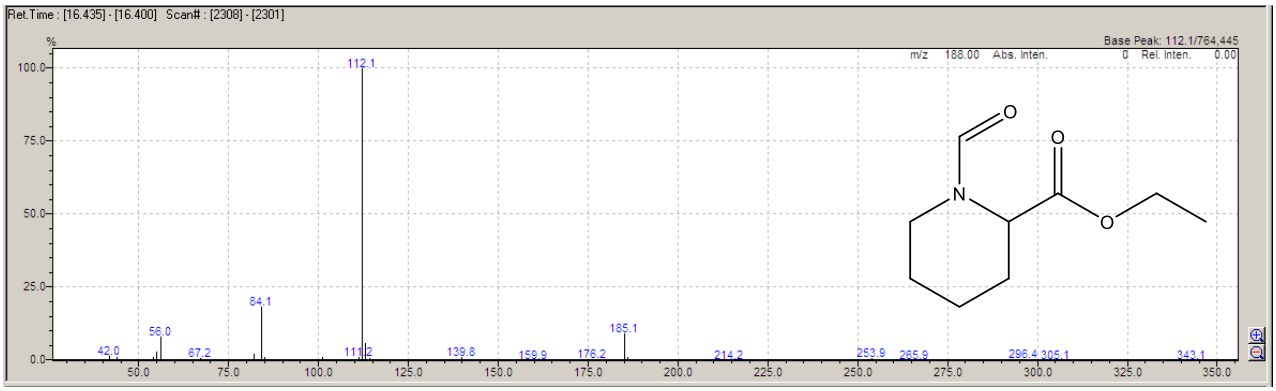


Figure S26: EI-MS analysis of the reaction product of N-formylation of 1-(piperidin-2-yl)butan-1-one with CO_2 and H_2.

The reaction results in a mixture of products of ethyl 1-formylpiperidine-2-carboxylate and N-formylpiperidine (70:30) with the N-formylpiperidine ^{1}H NMR peaks at 8.02 (s, 1H) 8.00 (s, 1H) 7.97 (s, 1H), all other peaks were obscured by the reaction solvent; GC retention time 12.38 to 12.29 minutes; EI-MS (*m/z*) calculated: 113.1, found 113.1

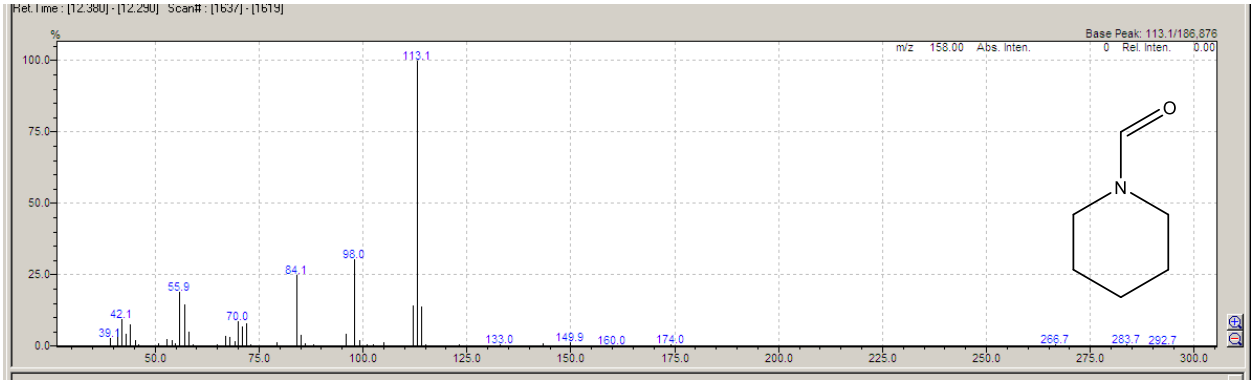
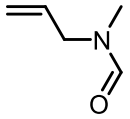


Figure S27: EI-MS analysis of the reaction side product of N-formylation of 1-(piperidin-2-yl)butan-1-onewith CO_2 and H_2.

6.6 N-allyl-N-methylformamide



^{1}H NMR (400 MHz, $CDCl_3$) δ (mixture of rotamers): 8.08 (1H), 5.67-5.81 (m, 1H), 5.16-5.29 (m, 2H); 3.95 (d, J_{1H-1H} = 5.81 Hz, 1H), 3.83 (d, J_{1H-1H} = 6.15 Hz, 1H), 2.91 (s, 3H), 2.84 (s, 3H); GC retention time 9.4 to 9.7 minutes; EI-MS (*m/z*) calculated: 99.1, found 99.0

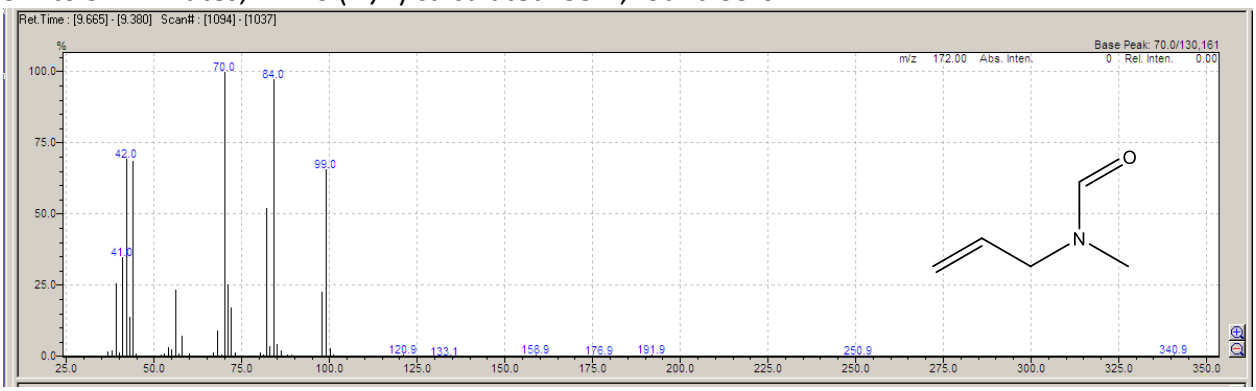
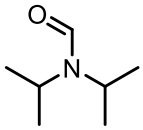


Figure S28: EI-MS analysis of the reaction product of N-formylation of N-methylprop-2-en-1-amine with CO_2 and H_2.

6.7 N,N-diisopropylformamide



^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.10 (1H), 3.62 (m, 2H), 1.21(d, 6H); GC retention time 9.5 to 9.7 minutes; EI-MS (*m/z*) calculated: 129.2, found 129.1

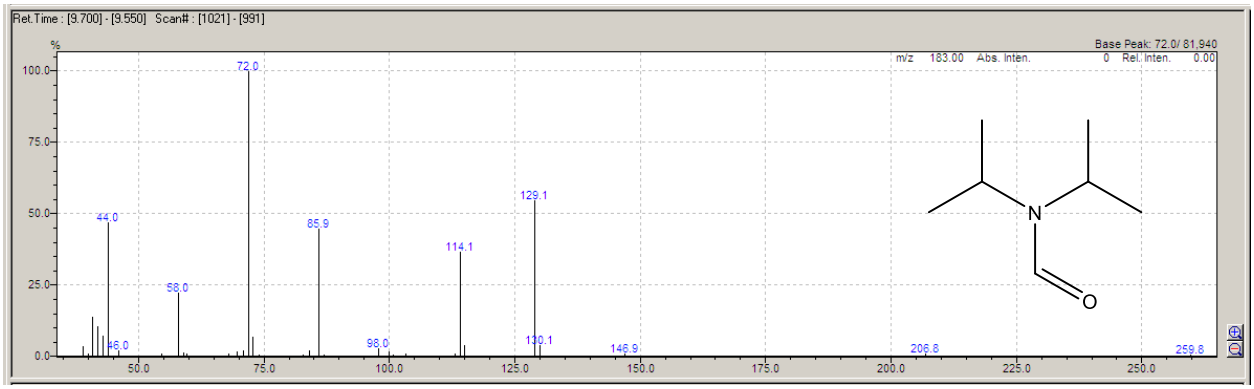
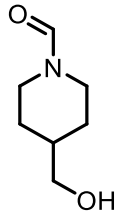


Figure S29: EI-MS analysis of the reaction product of N-formylation of diisopropylamine with CO_2 and H_2.

6.8 N-Formyl-4-piperidinemethanol



^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00 (s,1H), 4.41(dt, 1H), 3.63 (dp,1H), 3.50 (m, 2H), 2.62 (td, 1H), 1.14 (m, 2H) All other peaks were obscured by the reaction solvent.; GC retention time 21.7 to 21.9 minutes; EI-MS (*m/z*) calculated: 143.2, found 143.1

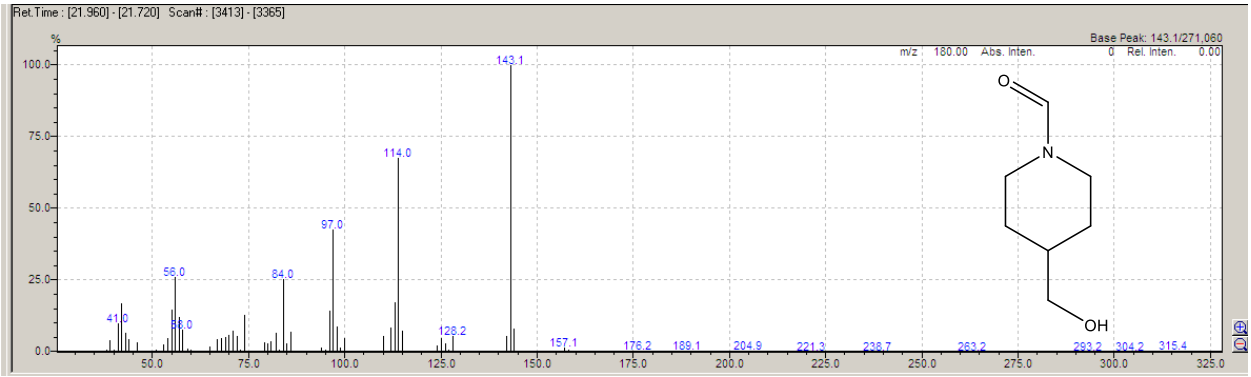
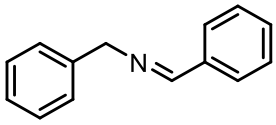


Figure S30: EI-MS analysis of the reaction product of N-formylation of 4-hydroxymethylpiperidine with CO_2 and H_2.

6.9 Attempted N-formylation of benzylamine

Attempted N-formylation of benzylamine with CO_2, H_2 and Cy_3SnOTf as the reaction catalyst did not yield the expected product N-formylbenzylamine but rather the homocoupled product N-benzyl-1-phenylmethanimine and its hydrogenated analogue dibenzylamine.

N-benzyl-1-phenylmethanimine



^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.05 (s, 1H); GC retention time 18.6 to 18.8 minutes; EI-MS (*m/z*) calculated: 195.3, found 195.1

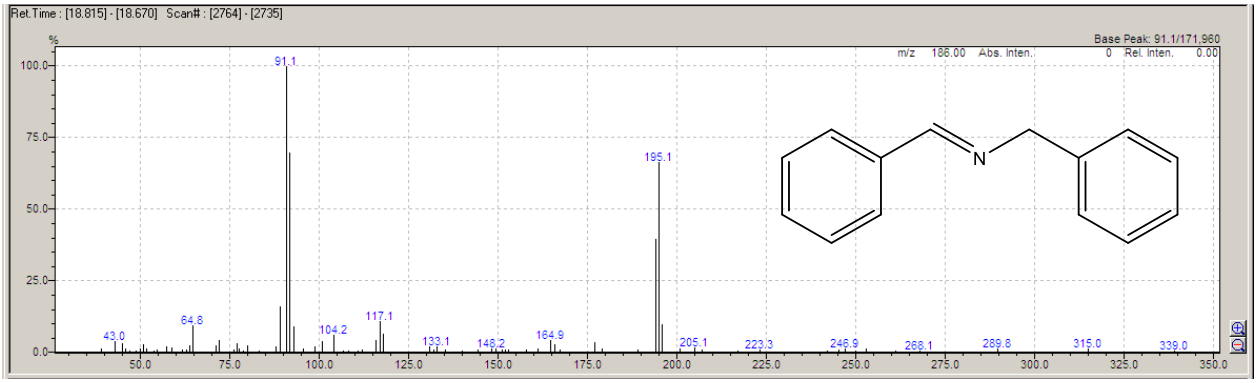
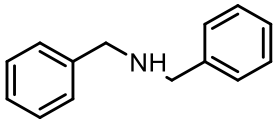


Figure S31: EI-MS analysis of the reaction product 1 of attempted N-formylation of benzylamine with CO_2 and H_2.

Dibenzylamine



GC retention time 18.6 to 18.8 minutes; EI-MS (*m/z*) calculated: 197.3, found 197.1

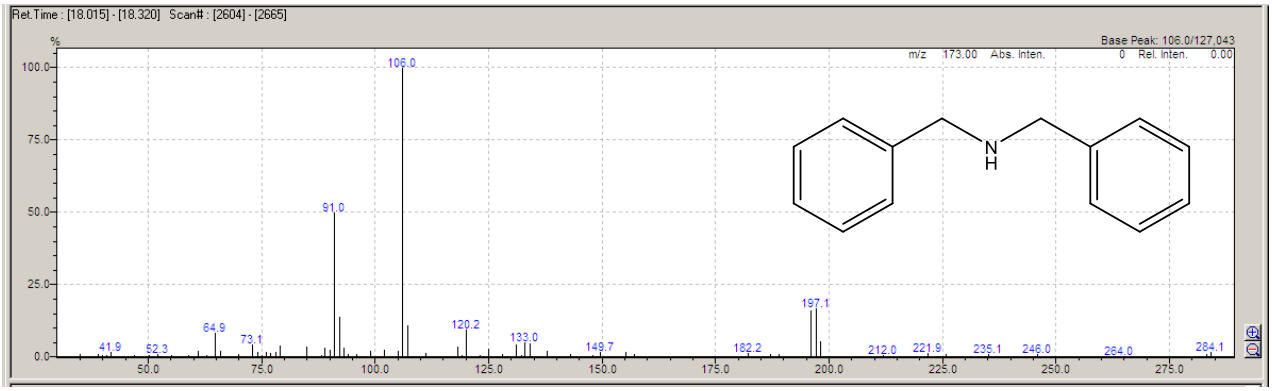


Figure S31: EI-MS analysis of the reaction product 2 of attempted N-formylation of benzylamine with CO_2 and H_2.

7. Synthesis of 4-hydroxymethylpiperidine.

The procedure was adapted from reference.[8]

In a Schlenk flask, to a stirred suspension of $LiAlH_4$ (6.64 g, 175 mmol) in THF (200 mL) was added isonipecotic acid (7.54 g, 58.3 mmol). The reaction was stirred at room temperature for 24h after which 10 mL of H_2O, 10 mL 15% w/w NaOH in H_2O and 10 mL of H_2O were carefully added in sequence. A colourless precipitate gradually formed. After which diethyl ether (200mL) was added, the solid was then

filtered. The solids were washed with ethyl acetate and the filtrate was collected and evacuated under reduced pressure. This afforded a colourless solid in a yield of 5.20 g (72% yield).

^{1}H NMR (400 MHz, $CDCl_3$): 3.43ppm (d, 2H), 3.07ppm (dt,2H), 2.58ppm (td, 2H), 2.48ppm (br s, 2H), 1.71ppm (d, 2H), 1.58ppm (m, 1H), 1.11 (qd, 2H)

8. Heterocycle hydrogenation

In air, to the autoclave, Cy_3SnOTf (0.1 mmol), 2,4,6-collidine (0.1 mmol) were dissolved in sulfolane (5 mL). The autoclave was then sealed and purged 5 times with the desired pressure of CO_2. The reaction is then topped up with the desired H_2 reaction pressure. The temperature and stirring rate were set using the Specview program on Parr 5000 series multi reactor system. The reaction was allowed to warm to 453K and was held there for 30 mins after which the heating was turned off and the reactor was allowed to cool to room temperature. DCM (1 mmol) was added to the reactor, stirred and an aliquot was taken for ^1H NMR in $CDCl_3$. The conversion was quantified by comparing the integral of the formate peak and the integral of DCM.

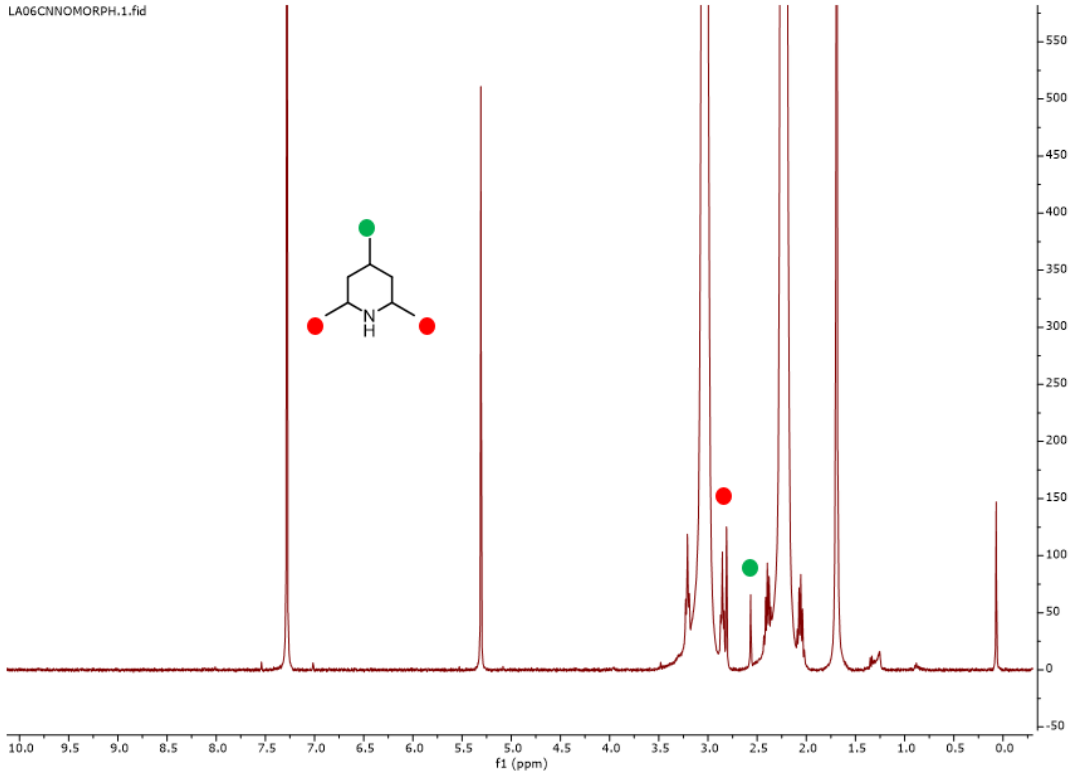


Figure S32: ^1H NMR spectrum of the reaction of 10mol% of Cy_3SnOTf and of 2,4,6-collidine at 100 bar H_2, 4 bar CO_2 and 453 K in the absence of morpholine.

Normally the aromatic hydrogen peak occurs at 6.9ppm however no such peak can be seen here but the alkyl groups are still present suggesting the base didn't precipitate out as a salt.

9. Mechanism investigation: Formate transfer

9.1 $Cy_3SnOCOH$ synthesis: The procedure was adapted from reference[9]

Cy_3SnOH (0.620 g, 1.61 mmol) was added to toluene (25 mL) and heated until the solids dissolved (ca. 328K). Under rapid stirring formic acid (0.6 mL, 15.9 mmol, 98%) was added dropwise to the solution. The solution was then stirred overnight, and the volatiles were removed under reduced pressure, which afforded a white solid in a yield of 84%. This solid was used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.34ppm (s,1H), 2.06 – 1.85 ppm(m,), 1.76-1.63ppm(m,), 1.45-1.27ppm(m,); ^{13}C and ^{119}Sn were measured at 600 MHz Brucker NMR instrument. ^{13}C NMR $\{^{1}H\}$ (150 MHz, $CDCl_3$) δ: 166.3ppm (s, HO**C**OSn), 33.9 (s, H**C**Sn), 31.0 (s, CH_2) 28.9 (s, CH_2), 26.8 (s, CH_2); ^{119}Sn NMR $\{^{1}H\}$ (224 MHz, $CDCl_3$) δ: 32.3 (s)

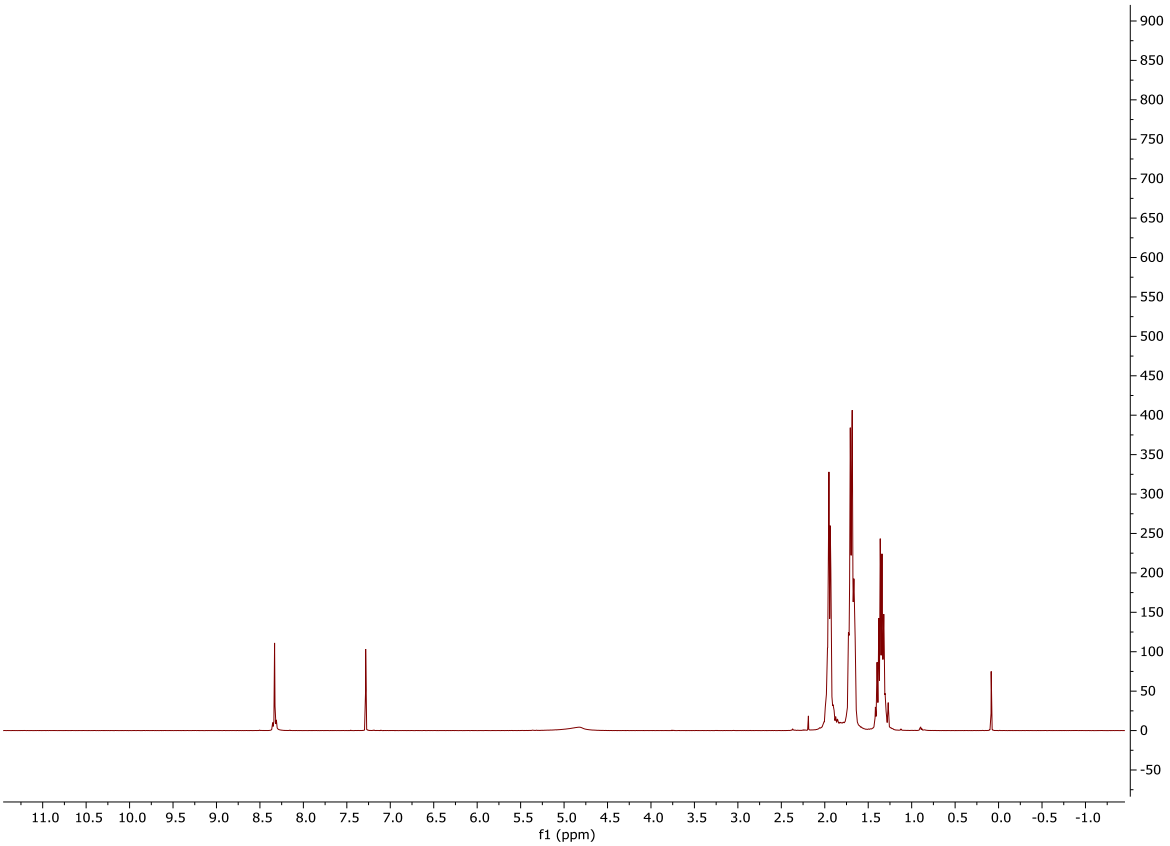


Figure S33: ^{1}H NMR spectrum of $Cy_3SnOCOH$

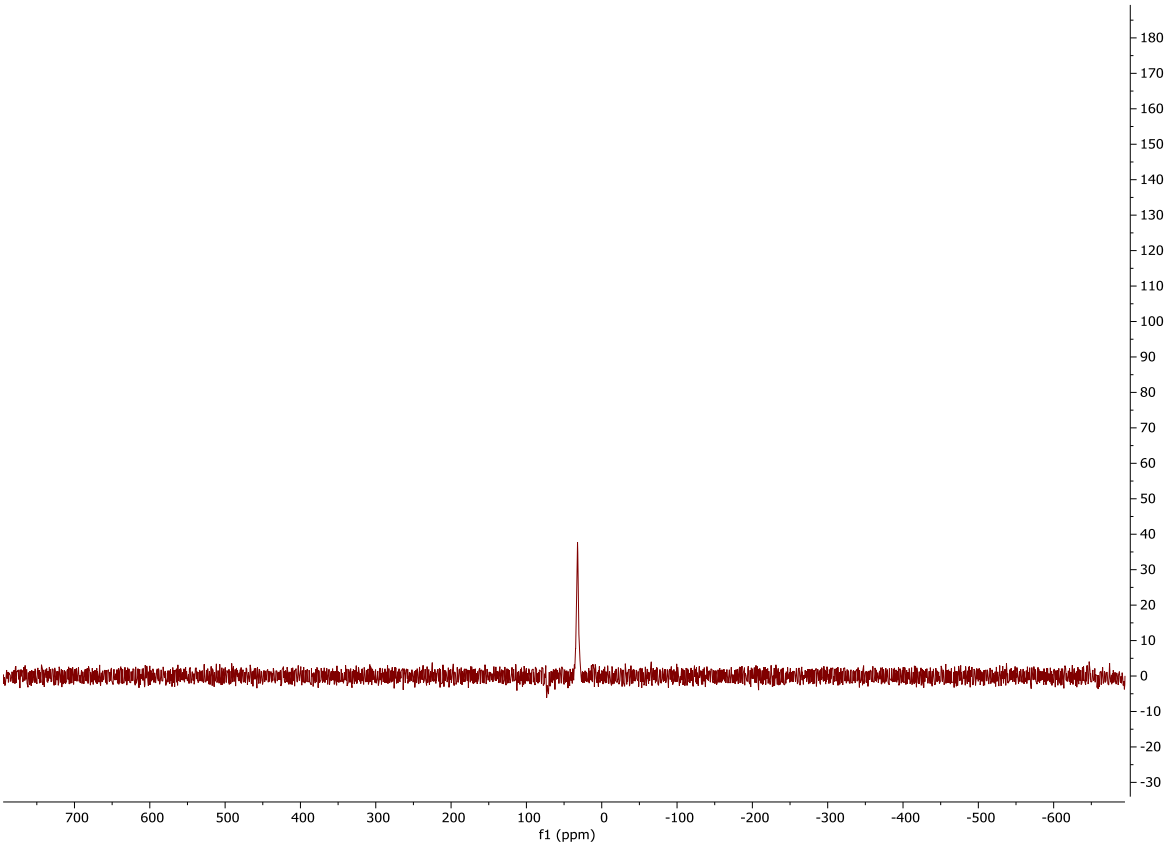


Figure S34: ^{119}Sn NMR spectrum of $Cy_3SnOCOH$

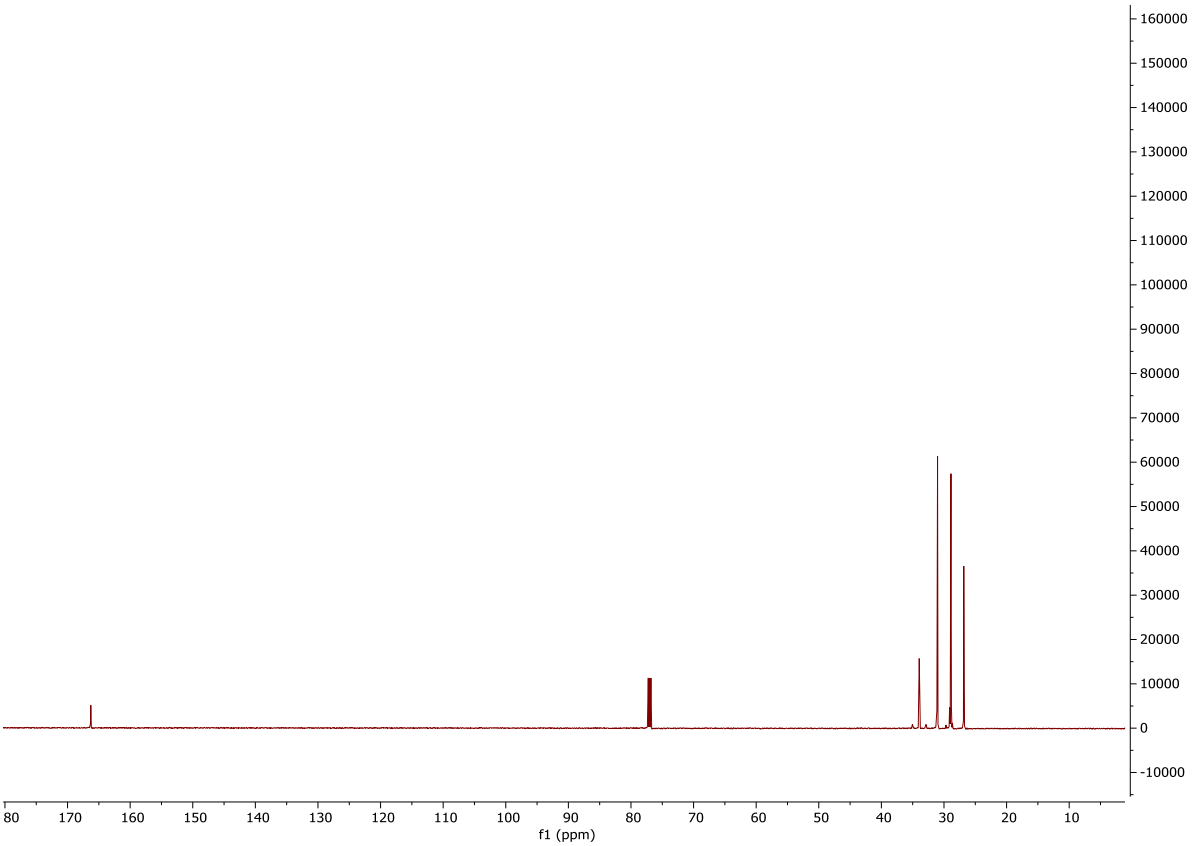


Figure S35: ^{13}C NMR spectrum of $Cy_3SnOCOH$

9.2 Standard procedure for direct reaction of $Cy_3SnOCOH$ with morpholine:

In air, to the autoclave, $Cy_3SnOCOH$ (0.1 mmol), 2,4,6-collidine (0.1 mmol) and morpholine (1 mmol) were dissolved in sulfolane (5 mL). The autoclave was then sealed and purged 5 times with the desired pressure of CO_2. The reaction is then topped up with the desired H_2 reaction pressure. The temperature and stirring rate were set using the Specview program on Parr 5000 series multi reactor system. The reaction was allowed to warm to 453K and was held there for 30 mins after which the heating was turned off and the reactor was allowed to cool to room temperature. DCM (1 mmol) was added to the reactor, stirred and an aliquot was taken for ^1H NMR in $CDCl_3$. The conversion was quantified by comparing the integral of the formate peak and the integral of DCM.

9.3 Formate transfer experiments:

Table S6: Effect of H_2 and CO_2 on the formate transfer of $Cy_3SnOCOH$ (10 mol%) to morpholine in the presence of 2,4,6-collidine (10 mol%) in 5 mL sulfolane.

Catalyst (LA)	H_2 Pressure (bar)	CO_2 Pressure (bar)	Temperature (K)	Time (min)	Yield (%)
$Cy_3SnOCOH$	0	6	453	30	6
$Cy_3SnOCOH$	0	30	453	30	6
$Cy_3SnOCOH$	100	6	453	30	10
$Cy_3SnOCOH$	100	30	453	30	10
$Cy_3SnOCOH$	0	0	453	30	4

10. Mechanism investigation: Cy_3SnOH reaction with morpholinium triflate

10.1 Standard procedure for direct reaction of Cy_3SnOH with morpholinium triflate:

In air, to the autoclave, Cy_3SnOH (0.1mmol), 2,4,6-collidine (0.1mmol), morpholinium triflate (0.1mmol) and morpholine (0.9mmol) were dissolved in sulfolane (5ml). The autoclave was then sealed and purged 5 times with the desired pressure of CO_2. The reaction is then topped up with the desired H_2 reaction pressure. The temperature and stirring rate were set using **Specview program connected to the Parr 5000 series multi reactor system.** T = 0 was defined as the time the heating starts. The heating was turned off 2 hours before the end of the end of the stated reaction time i.e., for a reaction time of 24hours the heating was turned off 22 hours in and the reaction was degassed at the 24-hour mark. DCM (1mmol) was added to the reactor, stirred and an aliquot was taken for NMR in $CDCl_3$. The conversion was quantified by comparing the integral of the formate peak and the integral of DCM. Other reaction products were determined by GC-MS.

10.2 Cy_3SnOH synthesis:

The procedure was adapted from reference[10]

A 5% solution of NaOH in water (15mL) was slowly added to a solution of Cy_3SnCl (807mg, 2mmol) in Et_2O (15mL). The mixture was stirred for 1h and subsequently filtered. The ether layer was separated from the aqueous layer and the aqueous was washed with Et_2O (3x10mL). The combined ether layers were evaporated under reduced pressure and the solids were combined with the original solids. The combined solids were recrystallized from EtOH. After which EtOH was filtered, and the solids were dried. The white solid was collected in an 87% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.98 – 1.86 ppm(m,), 1.79-1.60ppm(m,), 1.45-1.24ppm(m,), -0.33ppm (s,1H); ^{13}C, ^{19}F and ^{119}Sn were measured at 600 MHz Brucker NMR instrument. ^{13}C NMR (150 MHz, $CDCl_3$) δ: 32.0 (s), 31.10 (s), 28.80 (s), 27.0 (s); ^{119}Sn (224 MHz, $CDCl_3$) δ: 10.48 ppm

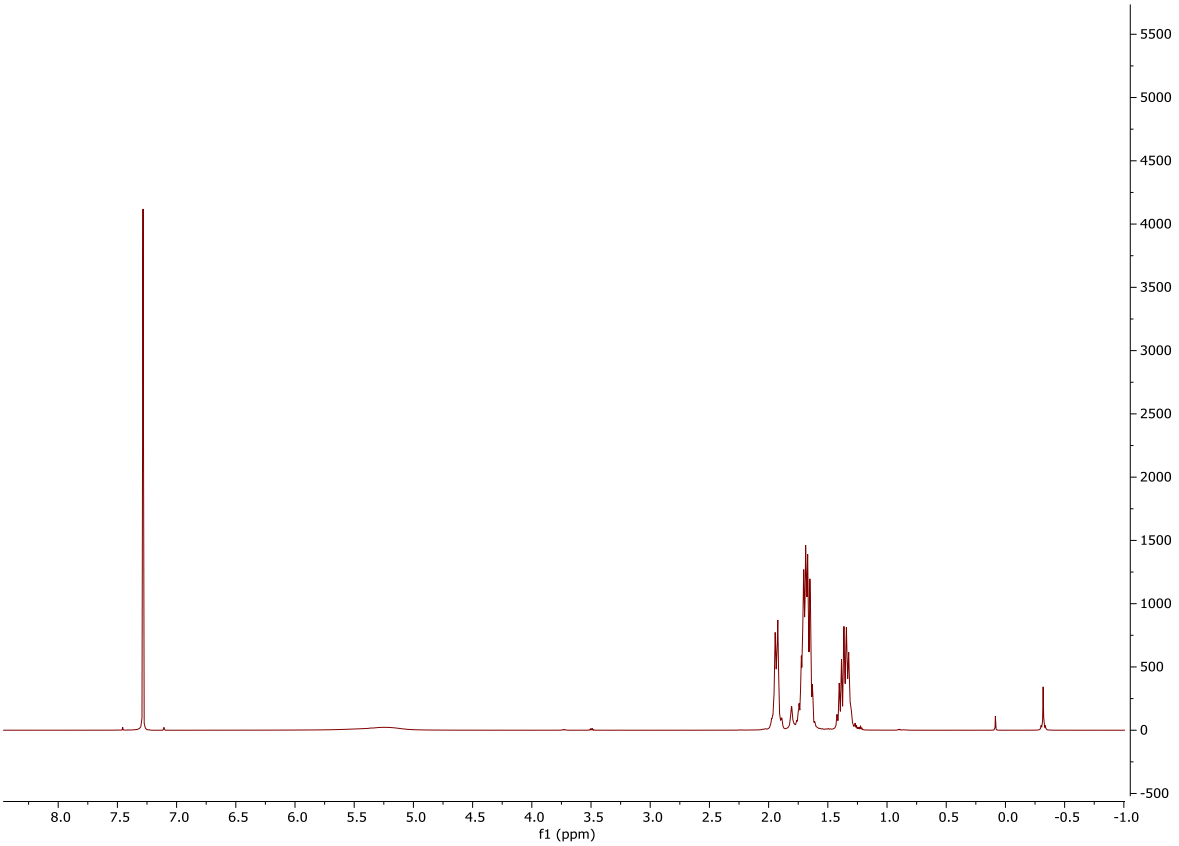


Figure S36: ^{1}H NMR spectrum of Cy_3SnOH

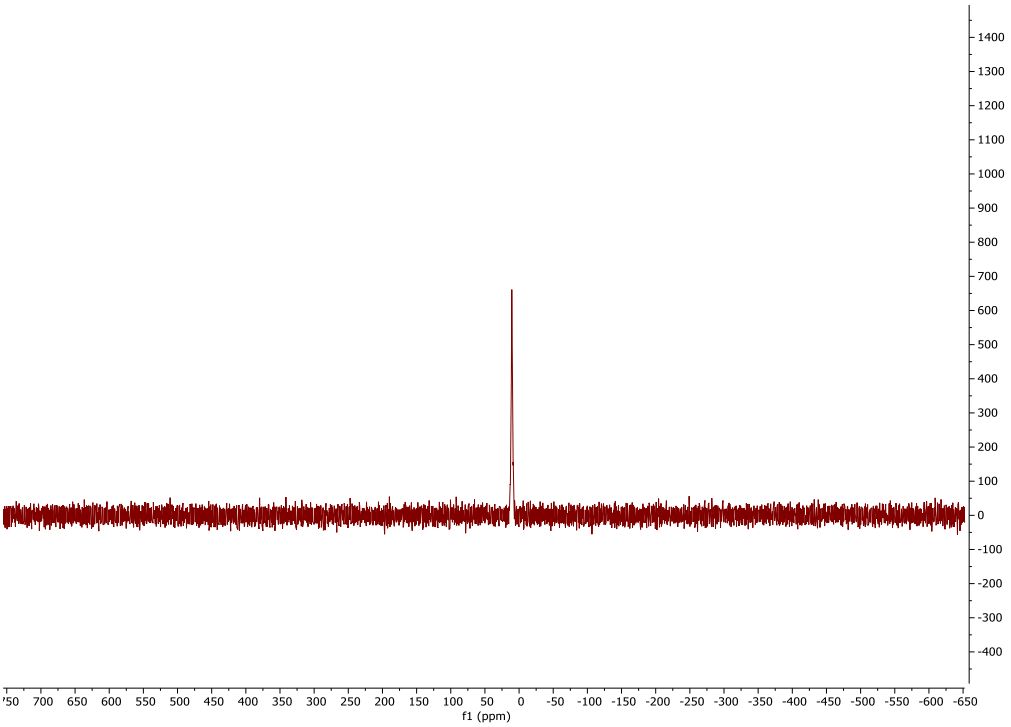


Figure S37: ^{119}Sn NMR spectrum of Cy_3SnOH

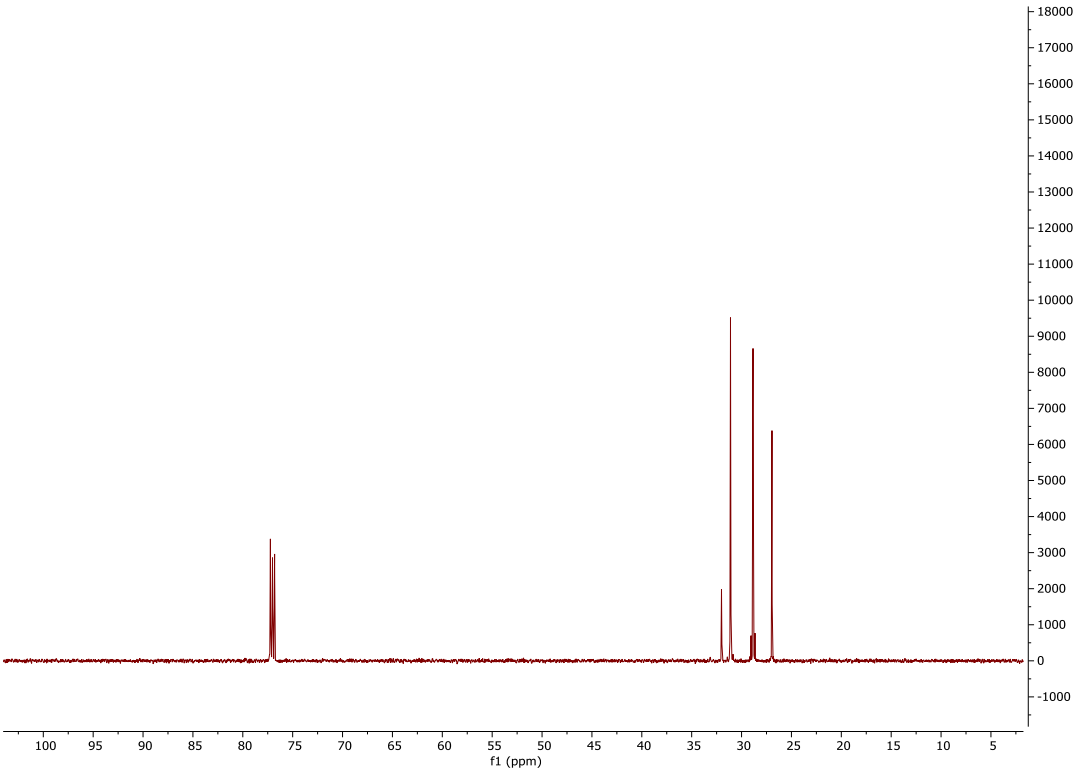


Figure S38: ^{13}C NMR spectrum of Cy_3SnOH

11. Mechanism investigation: In-situ ^{1}H NMR of the reaction mixture

^{1}H NMR spectra of the reaction mixture were measured on a Bruker AVANCE-III (400 MHz) spectrometer in 10 mm sapphire tubes from Wilmad with custom-made stainless-steel caps. The measurements were performed in the absence of a deuterated solvent and hence without a signal lock. Position of ^{1}H NMR signals of sulfolane was then aligned with sulfolane peaks recorded in $CDCl_3$.

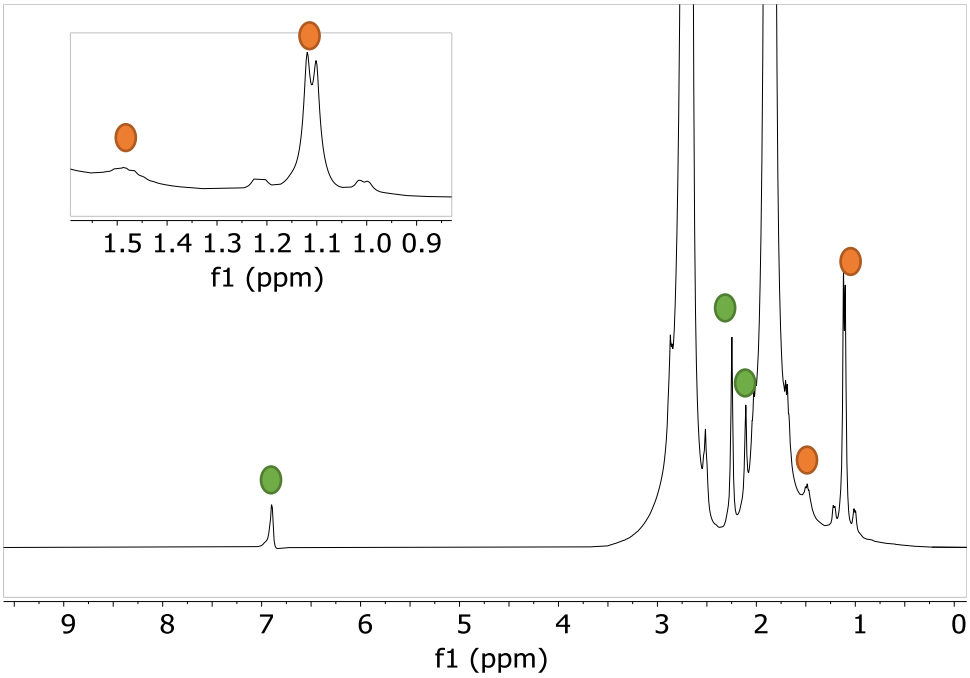


Figure S39: Reference ^{1}H NMR spectrum of FLP1 in sulfolane at 303 K; orange = $^{i}Pr_3SnOTf$, green = 2,4,6-collidine

Interaction of $^{i}Pr_3SnOTf$ and 2,4,6-collidine was not observed (Figure S 13), which confirms that a FLP forms between the LA and the LB rather than a classical LA-LB adduct. However, addition of morpholine to the NMR tube resulted in splitting of $^{i}Pr_3SnOTf$ signals into two set of peaks, which indicates that morpholine binds, at least in part, to the LA (Figure S S 14). This observation is in line with the lower steric profile of morpholine in comparison to 2,4,6-collidine and might also partially explain the requirement for the high reaction temperature, which is not required in the hydrogenation of bulky imines with FLP1[1]. Nevertheless, presence of CO_2 diminishes the interaction as observed by the reformation of the original $^{i}Pr_3SnOTf$ signals upon addition of CO_2 and the formation of new signals that can be attributed to morpholine-4-carboxylic acid (carbamic acid) (Figure S S 15).

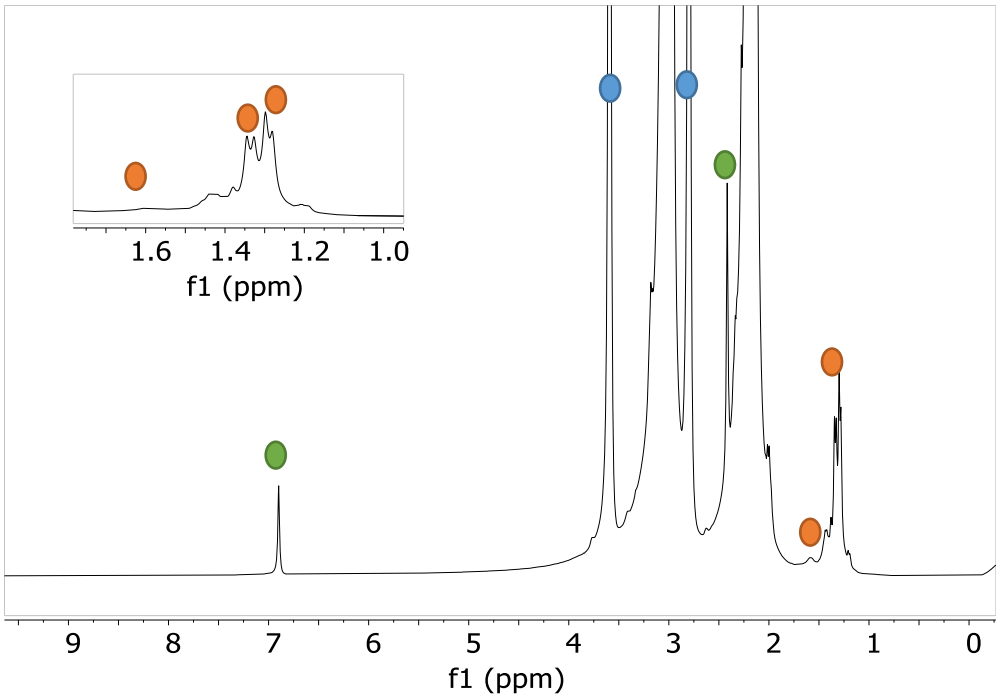


Figure S40: ^{1}H NMR spectrum of FLP1 (0.02 mmol) and morpholine (0.2 mmol) in sulfolane at 303 K; orange = $^{i}Pr_3SnOTf$, green = 2,4,6-collidine, blue = morpholine

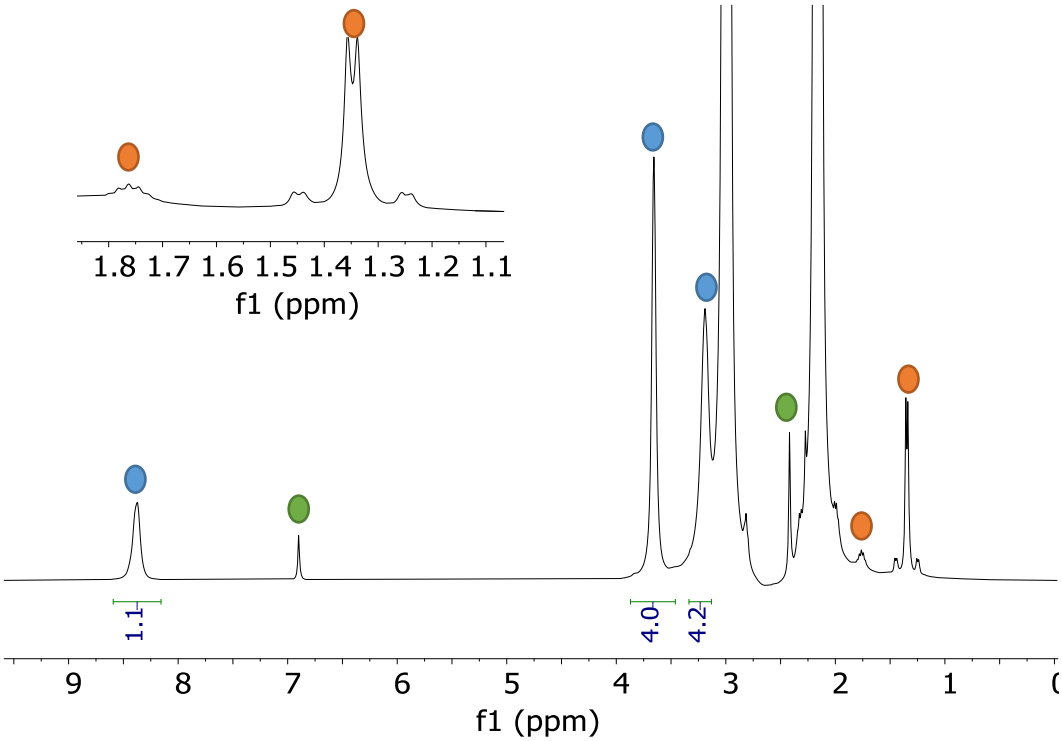


Figure S41: ^{1}H NMR spectrum of FLP1 (0.02 mmol) and morpholine (0.2 mmol) in sulfolane at 303 K in the presence of CO_2 (4 bar) and H2 (96 bar); orange = $^{i}Pr_3SnOTf$, green = 2,4,6-collidine, blue = morpholine carbamic acid

Heating of the reaction mixture in-situ to 393 K results in gradual collapse of the carbamic acid peaks at 3.2, 3.6 and 8.4 ppm and the formation of new peaks at 3.6 and 4.6 ppm, which cannot be attributed to morpholine nor its carbamic acid. Interaction with the reaction catalyst, however, does not take place as $^{i}Pr_3SnOTf$ remains the same even after heating of the reaction mixture at 393 K in-situ for 21 h and further heating at 453 K ex-situ prior to further measurements. No intermediates were observed during the reaction only the slow and gradual formation of the desired reaction product N-formylmorpholine, which indicates that hydrogen activation is the rate-determining step.

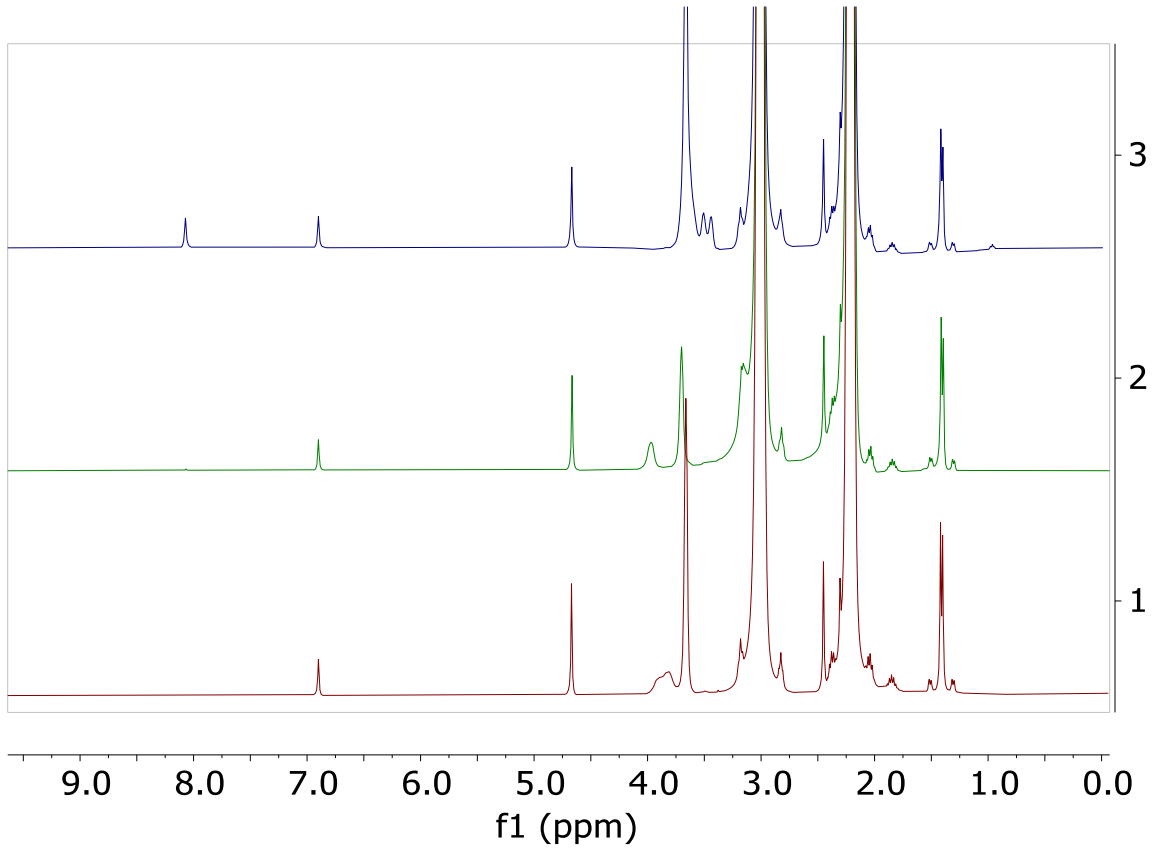


Figure S42: ^{1}H NMR spectrum of FLP1 (0.02 mmol) and morpholine (0.2 mmol) in sulfolane at 393 K in the presence of CO_2 (4 bar) and H_2 (96 bar); red spectrum = t(0 h), green spectrum = t(6 h) @ 393 K and blue spectrum = t(21 h) @ 393 K + t(5 h) @ 453 K

12. References:

(1) Scott, D. J.; Phillips, N. A.; Sapsford, J. S.; Deacy, A. C.; Fuchter, M. J.; Ashley, A. E. Versatile Catalytic Hydrogenation Using A Simple Tin(IV) Lewis Acid. *Angew. Chem. - Int. Ed.* **2016**, *55* (47). https://doi.org/10.1002/anie.201606639.

(2) Sapsford, J.; Scott, D.; Allcock, N.; Fuchter, M.; Ashley, A.; Tighe, C. Direct Reductive Amination of Carbonyl Compounds Catalyzed by a Moisture Tolerant Tin(IV) Lewis Acid. *Adv. Synth. Catal.* **2018**,

360 (6). https://doi.org/10.1002/adsc.201701418.

(3) Gyömöre, Á.; Bakos, M.; Földes, T.; Pápai, I.; Domján, A.; Soós, T. Moisture-Tolerant Frustrated Lewis Pair Catalyst for Hydrogenation of Aldehydes and Ketones. *ACS Catal.* **2015**, *5* (9). https://doi.org/10.1021/acscatal.5b01299.

(4) Hamza, A.; Sorochkina, K.; Kótai, B.; Chernichenko, K.; Berta, D.; Bolte, M.; Nieger, M.; Repo, T.; Pápai, I. Origin of Stereoselectivity in FLP-Catalyzed Asymmetric Hydrogenation of Imines. *ACS Catal.* **2020**, *10* (23). https://doi.org/10.1021/acscatal.0c04263.

(5) Sapsford, J. S.; Csókás, D.; Turnell-Ritson, R. C.; Parkin, L. A.; Crawford, A. D.; Pápai, I.; Ashley, A. E. Transition Metal-Free Direct Hydrogenation of Esters via a Frustrated Lewis Pair. *ACS Catal.* **2021**, *11* (15). https://doi.org/10.1021/acscatal.1c01940.

(6) Lennon, G.; Willox, S.; Ramdas, R.; Funston, S. J.; Klun, M.; Pieh, R.; Fairlie, S.; Dobbin, S.; Cobice, D. F. Assessing the Oxidative Degradation of N-Methylpyrrolidone (Nmp) in Microelectronic Fabrication Processes by Using a Multiplatform Analytical Approach. *J. Anal. Methods Chem.* **2020**, *2020*. https://doi.org/10.1155/2020/8265054.

(7) Erdmann, P.; Greb, L. What Distinguishes the Strength and the Effect of a Lewis Acid: Analysis of the Gutmann–Beckett Method. *Angew. Chem. - Int. Ed.* **2022**, *61* (4). https://doi.org/10.1002/anie.202114550.

(8) Arlegui, A.; Torres, P.; Cuesta, V.; Crusats, J.; Moyano, A. A PH-Switchable Aqueous Organocatalysis with Amphiphilic Secondary Amine–Porphyrin Hybrids. *European J. Org. Chem.* **2020**, *2020* (28), 4399–4407. https://doi.org/10.1002/EJOC.202000648.

(9) Ellis, B. D.; Atkins, T. M.; Peng, Y.; Sutton, A. D.; Gordon, J. C.; Power, P. P. Synthesis and Thermolytic Behavior of Tin(IV) Formates: In Search of Recyclable Metal-Hydride Systems. **2010**. https://doi.org/10.1039/c0dt00812e.

(10) Howie, R. A.; Moura, M. V. H.; Wardell, J. L.; Wardell, S. M. S. V. Further Study of Tris(Cyclohexyl)Stannane Compounds, Cy3SnX. Syntheses of the Compounds with X = Br, I, N3 and NCS and Redetermination of the Crystal Structures of Cy3SnX (X = Br and I). *Polyhedron* **2004**, *23* (14), 2331–2336. https://doi.org/10.1016/J.POLY.2004.08.001.