Supporting Information

An integrative sustainability assessment of the Tsuji-Trost reaction simulating allylic amination under non-conventional (*vs.* conventional) conditions

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1. General information.

Unless otherwise noted, all manipulations (reactions) were carried out in oven-dried glassware in a glovebox under an atmosphere of dinitrogen. The concentration of reaction mixtures was done under reduced pressure by rotary evaporation at 25–50 °C at an appropriate pressure. Yields refer to purified and spectroscopically characterized compounds unless otherwise stated.

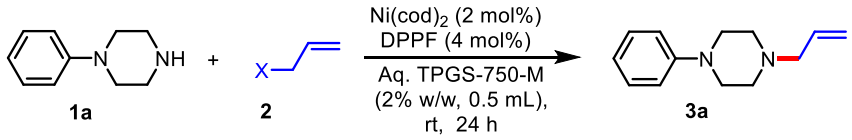
Chemicals and solvents. All the allylic precursors, catalysts, and ligands were purchased from Sigma-Aldrich. Other chemicals were purchased from Sigma-Aldrich, Alfa Aesar, and Spectrochem and used as received unless otherwise stated. Solvents like ethyl acetate, hexane, dichloromethane, methanol, and acetone were purchased from Fisher Scientific and used as received. All the reaction solvents and deuterated solvents were purchased from Sigma Aldrich and used as received.

Purification method. Thin layer chromatography (TLC) was performed using Merck TLC plates pre-coated with 250 μm thickness silica gel 60 F254 plates and visualized by fluorescence quenching under UV light. The compounds were purified using column chromatography (100-200 and or 320-400 mesh size silica) and eluted using EtOAc: Hexane as mobile phase.

Spectroscopic characterization. ^{1}H NMR and ^{13}C NMR spectra were recorded on Brukar 500 MHz and 125 MHz spectrometers respectively using tetramethylsilane (1% v/v) as an internal standard. Both ^{1}H and ^{13}C NMR chemical shifts were reported in parts per million downfield from tetramethylsilane (δ = 0) with the solvent residual peak. Coupling constants (*J*) were reported in hertz (Hz). Standard abbreviations indicating multiplicity were used as follows: s (singlet), b (broad), d (doublet), t (triplet), q (quartet), and m (multiplet). High-resolution mass spectra (HRMS) spectra of compounds were obtained at Agilent Q-TOF spectrometer in positive (ESI^{+}) ion mode. Gas Chromatography-Mass Spectrometry (GC-MS) was performed on an Agilent Technologies 8890 GC system coupled with Agilent Technologies 7010B mass spectrometer (GC/TQ) using Agilent HP-5MS UI column (30 m × 250 μm, 0.25 μm).

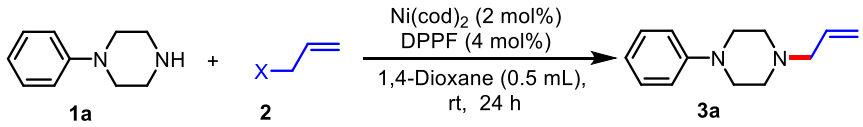
2. Model reaction and conditions to access the allylic precursors

Method A



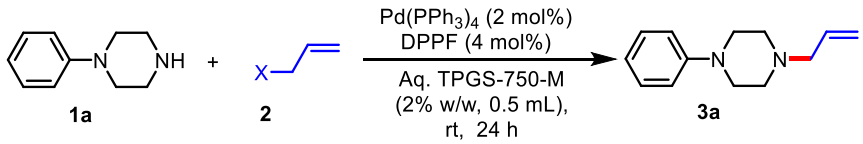
To a well cleaned tube equipped with a stir bar, $Ni(cod)_2$ (1.1 mg, 0.004 mmol, 2 mol%), DPPF (4.4 mg, 0.008 mmol, 4 mol%), 1-phenylpiperazine **1a** (32.4 mg, 30.5 μL, 0.2 mmol), allylic precursor **2** (0.3 mmol, 1.5 equiv), and aqueous TPGS-750-M (2% w/w, 0.5 mL) were added. The resultant mixture was stirred at room temperature for 24 h. The reaction mixture was diluted with EtOAc (2 X 0.5 mL) and vortexed the resultant mixture. The supernatant liquid containing product and other organic residue was removed carefully. The recovered organic layer was dried over anhyd. Na_2SO_4 and concentrated under reduced pressure. The crude products were adsorbed on silica gel and pass through the column (eluent: Hexane/EtOAc) to get analytically pure product **3a** as pale yellow liquid; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.32 – 7.27 (m, 2H), 6.96 (d, J = 7.7 Hz, 2H), 6.89 (t, J = 7.3 Hz, 1H), 5.94 (ddt, J = 16.8, 10.1, 6.6 Hz, 1H), 5.27 (dq, J = 17.2, 1.6 Hz, 1H), 5.24 – 5.21 (m, 1H), 3.25 (t, J = 5.6 Hz, 4H), 3.10 (d, J = 6.7 Hz, 2H), 2.66 (t, J = 5.4 Hz, 4H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 151.2, 134.6, 129.0, 119.6, 118.4, 116.0, 61.7, 52.9, 49.0; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ Calculated for $C_{13}H_{19}N_2^+$ 203.1543, Found 203.1543.

Method B



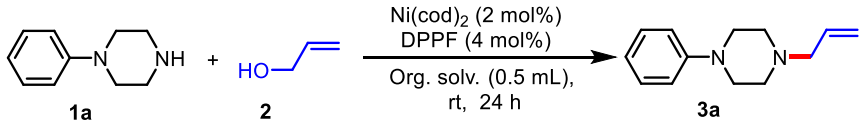
To a well cleaned tube equipped with a stir bar, $Ni(cod)_2$ (1.1 mg, 0.004 mmol, 2 mol%), DPPF (4.4 mg, 0.008 mmol, 4 mol%), 1-phenylpiperazine 1a (32.4 mg, 30.5 μL, 0.2 mmol), allylic precursor 2 (0.3 mmol, 1.5 equiv), and 1,4-dioxane (0.5 mL) were added. The resultant mixture was stirred at room temperature for 24 h. The reaction mixture was diluted with EtOAc (2 X 0.5 mL). The crude products were adsorbed on silica gel and pass through the column (eluent: Hexane/EtOAc) to get analytically pure product **3a**.

Method C



To a well cleaned tube equipped with a stir bar, $Ni(cod)_2$ (1.1 mg, 0.004 mmol, 2 mol%), DPPF (4.4 mg, 0.008 mmol, 4 mol%), 1-phenylpiperazine **1a** (32.4 mg, 30.5 μL, 0.2 mmol), allylic precursor 2 (0.3 mmol, 1.5 equiv), and 1,4-dioxane (0.5 mL) were added. The resultant mixture was stirred at room temperature for 24 h. The reaction mixture was diluted with EtOAc (2 X 0.5 mL) and vortexed the resultant mixture. The supernatant liquid containing product and other organic residue was removed carefully. The recovered organic layer was dried over anhyd. Na_2SO_4 and concentrated under reduced pressure. The crude products were adsorbed on silica gel and pass through the column (eluent: Hexane/EtOAc) to get analytically pure product **3a**.

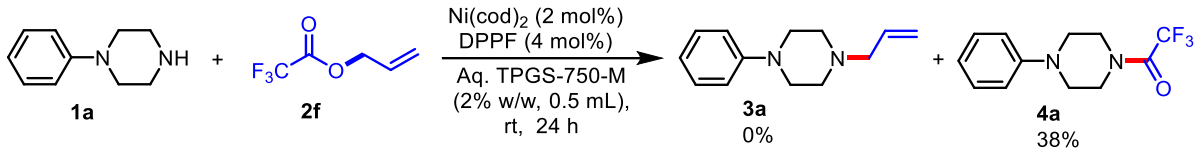
3. Selection of organic solvent for Ni(0)/DPPF-catalyzed allylic amination using 2a.



Entry	Solvent	Isolated yield/3a (%)
1	Toluene	19
2	1,4-Dioxane	48
3	THF	18
4	DMF	traces
5	Acetonitrile	45

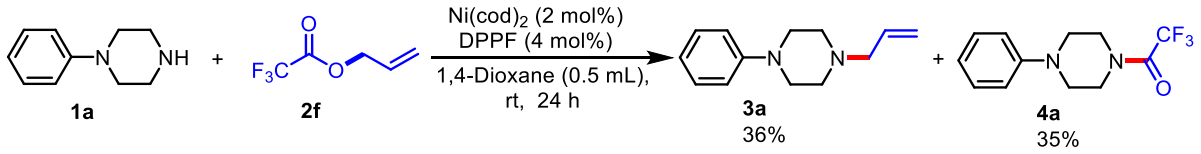
4. Side reaction assessment (selected allylic precursors)

Side reaction assessment of allyl trifluoroacetate (2f) in aqueous medium



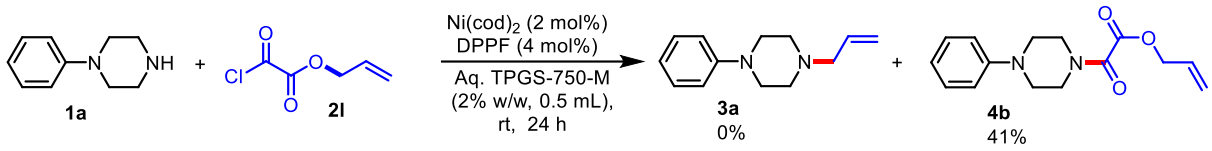
To a well cleaned tube equipped with a stir bar, $Ni(cod)_2$ (1.1 mg, 0.004 mmol, 2 mol%), DPPF (4.4 mg, 0.008 mmol, 4 mol%), 1-phenylpiperazine **1a** (32.4 mg, 30.5 μL, 0.2 mmol), allyl trifluoroacetate **2f** (46.2 mg, 39.07 μL, 0.3 mmol, 1.5 equiv), and aqueous TPGS-750-M (2% w/w, 0.5 mL) were added. The resultant mixture was stirred at room temperature for 24 h. The reaction mixture was diluted with EtOAc (2 X 0.5 mL) and vortexed the resultant mixture. The recovered organic layer was dried over anhyd. Na_2SO_4 and concentrated under reduced pressure. The crude products were adsorbed on silica gel and pass through the column (eluent: Hexane/EtOAc) to get analytically pure 2,2,2-trifluoro-1-(4-phenylpiperazin-1-yl)ethan-1-one **4a** (19.6 mg, 38%) as pale yellow liquid. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.33 – 7.28 (m, 2H), 6.95 (dd, J = 8.2, 6.8 Hz, 3H), 3.88 – 3.83 (m, 2H), 3.77 (t, J = 5.0 Hz, 2H), 3.27 – 3.21 (m, 4H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 150.5, 129.4, 121.1, 116.9, 116.5 (q, J = 286.1 Hz) 49.8, 49.3, 45.74 (q, J = 2.9 Hz), 43.3; **^{19}F NMR** (471 MHz, $CDCl_3$) δ -68.76; **GC-MS:** Rt = 13.485; *m/z*: $[M]^+$ Calculated for $C_{12}H_{13}F_3N_2O^+$ 258.1 Found 257.8

Side reaction assessment of allyl trifluoroacetate (2f) in organic medium



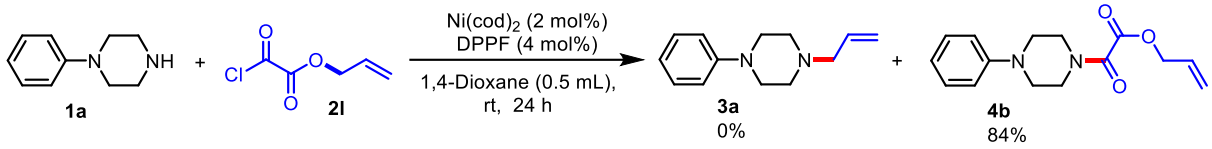
To a well cleaned tube equipped with a stir bar, $Ni(cod)_2$ (1.1 mg, 0.004 mmol, 2 mol%), DPPF (4.4 mg, 0.008 mmol, 4 mol%), 1-phenylpiperazine **1a** (32.4 mg, 30.5 μL, 0.2 mmol), allyl trifluoroacetate **2f** (46.2 mg, 39.07 μL, 0.3 mmol, 1.5 equiv), and 1,4-dioxane (2% w/w, 0.5 mL) were added. The resultant mixture was stirred at room temperature for 24 h. The reaction mixture was diluted with EtOAc (2 X 0.5 mL). The crude products were adsorbed on silica gel and pass through the column (eluent: Hexane/EtOAc) to get analytically pure product **3a** (14.5 mg, 36%) and **4a** (18.0 mg, 35%).

Side reaction assessment of allyl oxalyl chloride (2l) in aqueous medium



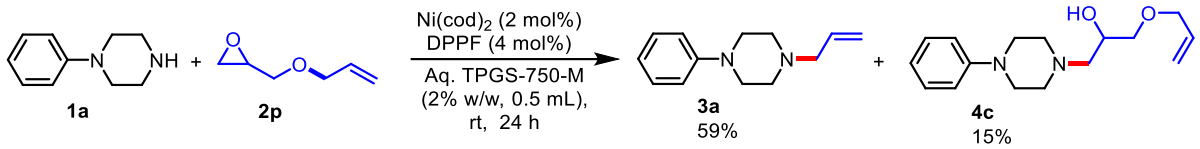
To a well cleaned tube equipped with a stir bar, $Ni(cod)_2$ (1.1 mg, 0.004 mmol, 2 mol%), DPPF (4.4 mg, 0.008 mmol, 4 mol%), 1-phenylpiperazine **1a** (32.4 mg, 30.5 μL, 0.2 mmol), allyl oxalyl chloride **2l** (44.56 mg, 36.7 μL, 0.3 mmol, 1.5 equiv), and aqueous TPGS-750-M (2% w/w, 0.5 mL) were added. The resultant mixture was stirred at room temperature for 24 h. The reaction mixture was diluted with EtOAc (2 X 0.5 mL). The crude products were adsorbed on silica gel and pass through the column (eluent: Hexane/EtOAc) to get analytically pure product **4b** (22.45 mg, 41%) as yellow liquid. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.38 – 7.24 (m, 2H), 7.02 – 6.89 (m, 3H), 6.00 (ddt, J = 17.2, 10.4, 6.0 Hz, 1H), 5.45 (dq, J = 17.2, 1.5 Hz, 1H), 5.36 (dq, J = 10.4, 1.2 Hz, 1H), 4.81 (dt, J = 5.9, 1.3 Hz, 2H), 3.88 – 3.74 (m, 2H), 3.70 – 3.54 (m, 2H), 3.35 – 3.11 (m, 4H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 162.2, 159.8, 150.7, 130.7, 129.3, 121.0, 120.1, 117.0, 66.5, 49.8, 49.2, 46.0, 41.4; **GC-MS:** Rt = 18.228; *m/z*: $[M]^+$ Calculated for $C_{15}H_{18}N_2O_3^+$ 274.1 Found 273.8

Side reaction assessment of allyl oxalyl chloride (2l) in organic medium



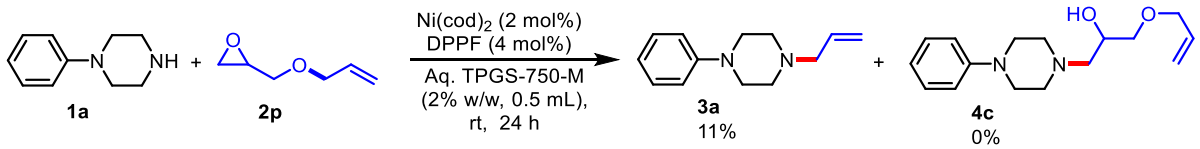
To a well cleaned tube equipped with a stir bar, $Ni(cod)_2$ (1.1 mg, 0.004 mmol, 2 mol%), DPPF (4.4 mg, 0.008 mmol, 4 mol%), 1-phenylpiperazine **1a** (32.4 mg, 30.5 μL, 0.2 mmol), allyl oxalyl chloride **2l** (44.56 mg, 36.7 μL, 0.3 mmol, 1.5 equiv), and aqueous TPGS-750-M (2% w/w, 0.5 mL) were added. The resultant mixture was stirred at room temperature for 24 h. The reaction mixture was diluted with EtOAc (2 X 0.5 mL). The crude products were adsorbed on silica gel and pass through the column (eluent: Hexane/EtOAc) to get analytically pure product **4b** (46 mg, 84%).

Side reaction assessment of allyl glycidyl ether (2p) in aqueous medium



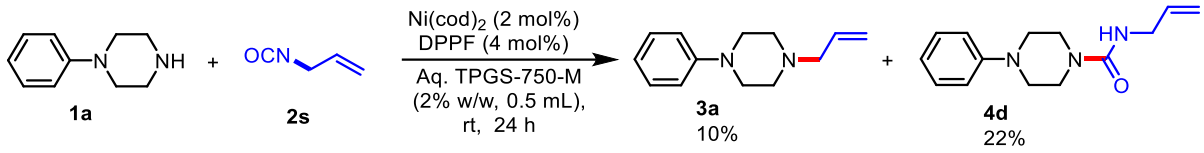
To a well cleaned tube equipped with a stir bar, $Ni(cod)_2$ (1.1 mg, 0.004 mmol, 2 mol%), DPPF (4.4 mg, 0.008 mmol, 4 mol%), 1-phenylpiperazine **1a** (32.4 mg, 30.5 μL, 0.2 mmol), allyl glycidyl ether **2p** (34.2 mg, 35.6 μL, 0.3 mmol, 1.5 equiv), and aqueous TPGS-750-M (2% w/w, 0.5 mL) were added. The resultant mixture was stirred at room temperature for 24 h. The reaction mixture was diluted with EtOAc (2 X 0.5 mL) and vortexed the resultant mixture. The recovered organic layer was dried over anhyd. Na_2SO_4 and concentrated under reduced pressure. The crude products were adsorbed on silica gel and pass through the column (eluent: Hexane/EtOAc) to get analytically pure product **3a** (23.8 mg, 59%) and 1-(allyloxy)-3-(4-phenylpiperazin-1-yl)propan-2-ol **4c** (8.3 mg, 15%) as colourless liquid. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.30 – 7.25 (m, 2H), 6.95 – 6.92 (m, 2H), 6.87 (t, J = 7.3 Hz, 1H), 5.92 (ddt, J = 17.3, 10.4, 5.7 Hz, 1H), 5.29 (dq, J = 17.2, 1.6 Hz, 1H), 5.20 (dq, J = 10.4, 1.4 Hz, 1H), 4.04 (dt, J = 5.7, 1.4 Hz, 2H), 4.00 (dq, J = 9.6, 4.5 Hz, 1H), 3.60 (s, 1H), 3.49 (qd, J = 9.9, 4.9 Hz, 2H), 3.24 (dt, J = 6.4, 4.1 Hz, 4H), 2.89 – 2.83 (m, 2H), 2.71 – 2.64 (m, 2H), 2.62 – 2.57 (m, 1H), 2.52 (dd, J = 12.5, 3.5 Hz, 1H).; **^{13}C NMR** (125 MHz, $CDCl_3$): δ 151.1, 134.6, 129.2, 120.0, 117.4, 116.2, 72.5, 72.4, 66.0, 60.8, 53.3, 49.0; **GC-MS:** Rt = 16.325; *m/z*: $[M]^+$ Calculated for $C_{16}H_{24}N_2O_2^+$ 276.2 Found 275.9.

Side reaction assessment of allyl glycidyl ether (2p) in organic medium



To a well cleaned tube equipped with a stir bar, $Ni(cod)_2$ (1.1 mg, 0.004 mmol, 2 mol%), DPPF (4.4 mg, 0.008 mmol, 4 mol%), 1-phenylpiperazine **1a** (32.4 mg, 30.5 μL, 0.2 mmol), allyl glycidyl ether **2p** (34.2 mg, 35.6 μL, 0.3 mmol, 1.5 equiv), and aqueous TPGS-750-M (2% w/w, 0.5 mL) were added. The resultant mixture was stirred at room temperature for 24 h. The reaction mixture was diluted with EtOAc (2 X 0.5 mL). The crude products were adsorbed on silica gel and pass through the column (eluent: Hexane/EtOAc) to get analytically pure product **3a** (4.4 mg, 11%).

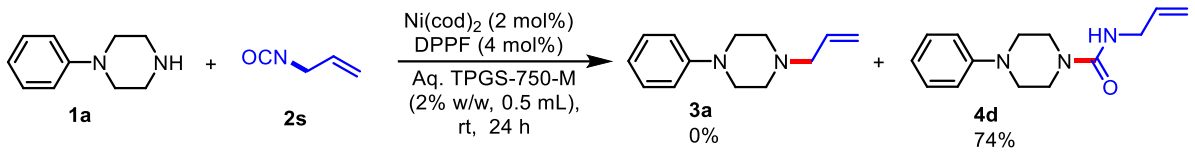
Side reaction assessment of allyl isocyanate (2s) in aqueous medium



1a **2s** **3a** 10% **4d** 22%

To a well cleaned tube equipped with a stir bar, $Ni(cod)_2$ (1.1 mg, 0.004 mmol, 2 mol%), DPPF (4.4 mg, 0.008 mmol, 4 mol%), 1-phenylpiperazine **1a** (32.4 mg, 30.5 μL, 0.2 mmol), allyl isocyanate **2s** (24,9 mg, 26.5 μL, 0.3 mmol, 1.5 equiv), and aqueous TPGS-750-M (2% w/w, 0.5 mL) were added. The resultant mixture was stirred at room temperature for 24 h. The reaction mixture was diluted with EtOAc (2 X 0.5 mL) and vortexed the resultant mixture. The recovered organic layer was dried over anhyd. Na_2SO_4 and concentrated under reduced pressure. The crude products were adsorbed on silica gel and pass through the column (eluent: Hexane/EtOAc) to get analytically pure product **3a** (4.0 mg, 10%) and *N*-allyl-4-phenylpiperazine-1-carboxamide **4d** (10.8 mg, 22%) pale yellow semisolid. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.32 – 7.24 (m, 2H), 7.00 – 6.84 (m, 3H), 5.90 (ddt, J = 17.2, 10.2, 5.7 Hz, 1H), 5.20 (dq, J = 17.1, 1.7 Hz, 1H), 5.12 (dq, J = 10.2, 1.5 Hz, 1H), 4.68 (s, 1H), 3.89 (tt, J = 5.6, 1.6 Hz, 1H), 3.63 – 3.43 (m, 4H), 3.43 – 3.00 (m, 4H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 157.4, 151.0, 135.5, 129.3, 120.4, 116.5, 115.9, 49.2, 43.8, 43.5. **GC-MS:** Rt = 18.187; *m/z*: $[M]^+$ Calculated for $C_{14}H_{19}N_3O^+$ 245.2 Found 244.8.

Side reaction assessment of allyl isocyanate (2s) in organic medium



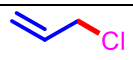
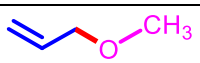
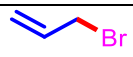
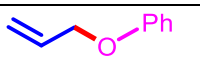
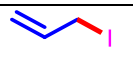
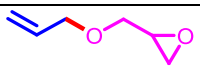
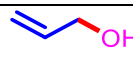
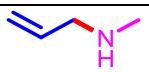
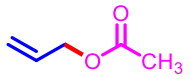
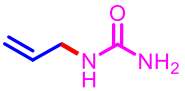
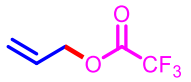
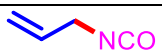
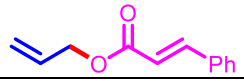
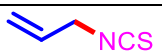
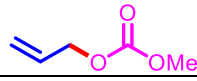
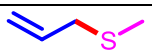
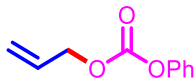
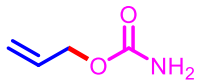
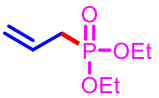
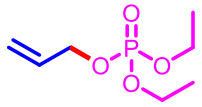
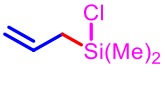
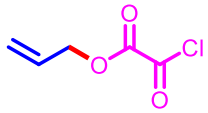
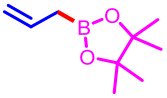
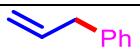
1a **2s** **3a** 0% **4d** 74%

To a well cleaned tube equipped with a stir bar, $Ni(cod)_2$ (1.1 mg, 0.004 mmol, 2 mol%), DPPF (4.4 mg, 0.008 mmol, 4 mol%), 1-phenylpiperazine **1a** (32.4 mg, 30.5 μL, 0.2 mmol), allyl isocyanate **2s** (24,9 mg, 26.5 μL, 0.3 mmol, 1.5 equiv), and aqueous TPGS-750-M (2% w/w, 0.5 mL) were added. The resultant mixture was stirred at room temperature for 24 h. The reaction mixture was diluted with EtOAc (2 X 0.5 mL). The crude products were adsorbed on silica gel and pass through the column (eluent: Hexane/EtOAc) to get analytically pure product **4d** (36.23 mg, 74%).

5. Machine learning predictions of bond dissociation energies (BDEs)

This tool predicts BDEs for single, noncyclic bonds in neutral organic molecules consisting of C, H, O, and N atoms. Mean absolute errors are typically less than 1 kcal/mol for most compounds.

https://bde.ml.nrel.gov/

Code	Allylic Precursor	Bond Dissociation Energy	Code	Allylic Precursor	Bond Dissociation Energy
2a		70.6 Kcal/mol	**2n**		70.8 Kcal/mol
2b		57.4 Kcal/mol	**2o**		55.4 Kcal/mol
2c		40.3 Kcal/mol	**2p**		71.0 Kcal/mol
2d		81.5 Kcal/mol	**2q**		69.1 Kcal/mol
2e		79.1 Kcal/mol	**2r**		78.8 Kcal/mol
2f		82.7 Kcal/mol	**2s**		78.1 Kcal/mol
2g		81.1 Kcal/mol	**2t**		48.9 Kcal/mol
2h		79.6 Kcal/mol	**2u**		60.8 Kcal/mol
2i		80.1 Kcal/mol	**2v**		56.0 Kcal/mol
2j		78.7 kcal/mol	**2w**		77.7 Kcal/mol
2k		79.8 Kcal/mol	**2x**		Not available
2l		82.0 Kcal/mol	**2y**		Not available
2m		70.6 Kcal/mol	**2z**		87.5 Kcal/mol

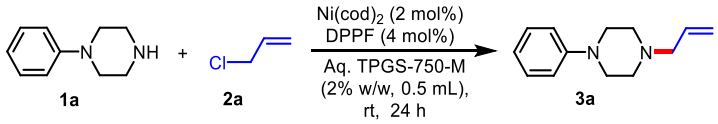
References. St. John, P.C., Guan, Y., Kim, Y., Kim, S., and Paton, R.S. Nat Commun 11, 2328 (2020). https://doi.org/10.1038/s41467-020-16201-z

St. John, P.C., Guan, Y., Kim, Y., Etz, B.D., Kim S., and Paton, R.S. Sci Data 7, 244 (2020). https://doi.org/10.1038/s41597-020-00588-x

6. Calculation of green metrics for active allylic precursors ('in-water' under Ni-catalysis)

Code	Allyl source	E-Factor	%Atom economy	%Atom efficiency	%RME	Relative EcoScale
2a	Allyl chloride	7.07	84.66	14.39	12.38	43.5
2b	Allyl bromide	1.50	71.37	48.53	39.93	69
2c	Allyl iodide	1.97	61.21	42.23	33.62	69.5
2d	Allyl alcohol	0.38	91.75	81.65	72.04	79.5
2e	Allyl acetate	0.79	77.04	66.25	55.56	78
2g	Allyl cinnamate	1.68	57.68	47.29	37.23	81
2h	Allyl methyl carbonate	1.05	72.62	58.82	48.59	75.5
2i	Allyl phenyl carbonate	1.53	59.38	49.87	39.48	82
2j	Allyl carbamate	0.82	76.76	65.24	54.69	82.5
2k	Allyl diethyl phosphate	1.6	56.71	47.63	37.40	82
2m	Allyl imidate	2.9	55.42	32.69	30.93	59.5
2o	Allyl phenyl ether	1.2	68.19	55.23	44.99	70.5
2p	Allyl glycidyl ether	1.8	73.14	41.68	34.52	63.5
2q	N-Allylmethylamine	0.7	86.60	65.81	57.10	86.5
2s	Allyl isocyanate	5.7	82.39	17.30	14.77	45.5
2v	Allyl phenyl sulphone	2.3	58.68	37.55	29.66	72

Calculation of Green metrics for allyl chloride ('in-water' under Ni-catalysis)



Entities	Molecular mass	Quantity used
1a	162.23	32.44 mg
2a	76.52	22.95 mg
3a	202.14	6.86 mg

Atom economy Molecular mass of desired product / Molecular mass of all reactant **X** 100
202.14 / 162.23 + 76.52 X 100 = 84.66%

Atom efficiency %Yield of desired product X %Atom economy / 100
17 X 84.66/ 100 = 14.39%

RME mass of desired product / total mass of reactants **X** 100
6.86 / 55.39 X 100 = 12.38%

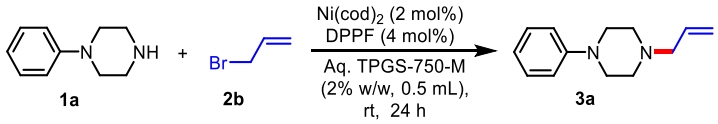
E-factor Amount of organic waste (mg) /Amount of product (mg)
(Total reaction mixture (mg) – Amount of product (mg))/Amount of product (mg)
(55.39 – 6.86)/6.86 = 48.53/6.86 = 7.07

***Relative EcoScale** 100 – sum of individual penalties
100 – 56.5 = 43.5

Calculation of Penalty points	
Parameter	**Penalty points**
1. Yield	(100–17)/2 = 41.5
2. Price of allyl chloride (to obtain 10 mmol of end product)	
Inexpensive (< $10)	0
Expensive (> $10 and < $50)	0
Very expensive (> $50)	5
3. Safety	
N (dangerous for environment)	0
T (toxic)	5
F (highly flammable)	5
E (explosive)	0
F+ (extremely flammable)	0
T+ (extremely toxic)	0
~~**4. Technical setup**~~	
~~**5. Temperature/time**~~	
~~**6. Workup and purification**~~	
Total	**56.5**

*The EcoScale has been represented as a relative EcoScale, wherein the common parameters (Technical setup, Temperature/time, workup, and Purification) have been excluded while calculating the penalty points as they will be the same in all the cases.

Calculation of Green metrics for allyl bromide ('in-water' under Ni-catalysis)



Entities	Molecular mass	Quantity used
1a	162.23	32.44 mg
2b	120.98	36.29 mg
3a	202.14	27.45 mg

Atom economy Molecular mass of desired product / Molecular mass of all reactant **X** 100
202.14 / 162.23 + 120.98 X 100 = 71.37%

Atom efficiency %Yield of desired product X %Atom economy / 100
68 X 71.37/ 100 = 48.53%

RME mass of desired product / total mass of reactants **X** 100
27.45 / 68.73 X 100 = 39.93%

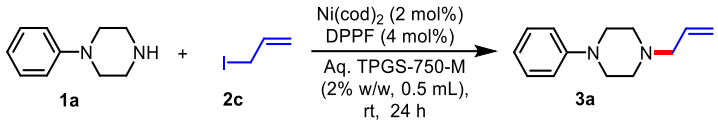
E-factor Amount of organic waste (mg) /Amount of product (mg)
(Total reaction mixture (mg) – Amount of product (mg))/Amount of product (mg)
(68.73 – 27.45)/27.45 = 41.28/27.45 = 1.50

***Relative EcoScale** 100 – sum of individual penalties
100 – 31 = 69

Calculation of Penalty points	
Parameter	**Penalty points**
1. Yield	(100–68)/2 = 16
2. Price of allyl chloride (to obtain 10 mmol of end product)	
Inexpensive (< $10)	0
Expensive (> $10 and < $50)	0
Very expensive (> $50)	5
3. Safety	
N (dangerous for environment)	0
T (toxic)	5
F (highly flammable)	5
E (explosive)	0
F+ (extremely flammable)	0
T+ (extremely toxic)	0
~~**4. Technical setup**~~	
~~**5. Temperature/time**~~	
~~**6. Workup and purification**~~	
Total	**31**

*The EcoScale has been represented as a relative EcoScale, wherein the common parameters (Technical setup, Temperature/time, workup, and Purification) have been excluded while calculating the penalty points as they will be the same in all the cases.

Calculation of Green metrics for allyl Iodide ('in-water' under Ni-catalysis)



Entities	Molecular mass	Quantity used
1a	162.23	32.44 mg
2c	167.98	50.39 mg
3a	202.14	27.85 mg

Atom economy Molecular mass of desired product / Molecular mass of all reactant **X** 100
202.14 / 162.23 + 167.98 X 100 = 61.21%

Atom efficiency %Yield of desired product X %Atom economy / 100
69 X 61.21/ 100 = 42.23%

RME mass of desired product / total mass of reactants **X** 100
27.85 / 82.83 X 100 = 33.62%

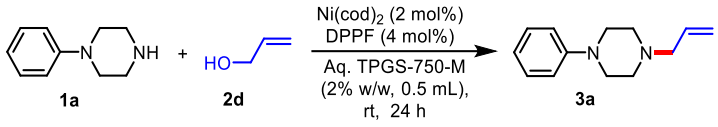
E-factor Amount of organic waste (mg) /Amount of product (mg)
(Total reaction mixture (mg) – Amount of product (mg))/Amount of product (mg)
(82.83 – 27.85)/27.85 = 54.98/27.85 = 1.97

***Relative EcoScale** 100 – sum of individual penalties
100 – 30.5 = 69.5

Calculation of Penalty points	
Parameter	**Penalty points**
1. Yield	(100–69)/2 = 15.5
2. Price of allyl chloride (to obtain 10 mmol of end product)	
Inexpensive (< $10)	0
Expensive (> $10 and < $50)	0
Very expensive (> $50)	5
3. Safety	
N (dangerous for environment)	0
T (toxic)	5
F (highly flammable)	5
E (explosive)	0
F+ (extremely flammable)	0
T+ (extremely toxic)	0
~~**4. Technical setup**~~	
~~**5. Temperature/time**~~	
~~**6. Workup and purification**~~	
Total	**30.5**

*The EcoScale has been represented as a relative EcoScale, wherein the common parameters (Technical setup, Temperature/time, workup, and Purification) have been excluded while calculating the penalty points as they will be the same in all the cases.

Calculation of Green metrics for allyl alcohol ('in-water' under Ni-catalysis)



Entities	Molecular mass	Quantity used
1a	162.23	32.44 mg
2d	58.07	17.42 mg
3a	202.14	35.92 mg

Atom economy Molecular mass of desired product / Molecular mass of all reactant **X** 100
202.14 / 162.23 + 58.07 X 100 = 91.75%

Atom efficiency %Yield of desired product X %Atom economy / 100
89 X 91.75/ 100 = 81.65%

RME mass of desired product / total mass of reactants **X** 100
35.92 / 49.86 X 100 = 72.04%

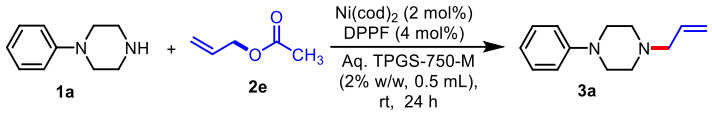
E-factor Amount of organic waste (mg) /Amount of product (mg)
(Total reaction mixture (mg) – Amount of product (mg))/Amount of product (mg)
(49.86 – 35.92)/35.92 = 85.78/35.92 = 0.38

***Relative EcoScale** 100 – sum of individual penalties
100 – 20.5= 79.5

Calculation of Penalty points	
Parameter	**Penalty points**
1. Yield	(100–89)/2 = 5.5
2. Price of allyl chloride (to obtain 10 mmol of end product)	
Inexpensive (< $10)	0
Expensive (> $10 and < $50)	0
Very expensive (> $50)	5
3. Safety	
N (dangerous for environment)	0
T (toxic)	5
F (highly flammable)	5
E (explosive)	0
F+ (extremely flammable)	0
T+ (extremely toxic)	0
~~**4. Technical setup**~~	
~~**5. Temperature/time**~~	
~~**6. Workup and purification**~~	
Total	**20.5**

*The EcoScale has been represented as a relative EcoScale, wherein the common parameters (Technical setup, Temperature/time, workup, and Purification) have been excluded while calculating the penalty points as they will be the same in all the cases.

Calculation of Green metrics for allyl acetate ('in-water' under Ni-catalysis)



Entities	Molecular mass	Quantity used
1a	162.23	32.44 mg
2e	100.12	30.03 mg
3a	202.14	34.71 mg

Atom economy Molecular mass of desired product / Molecular mass of all reactant **X** 100
202.14 / 162.23 + 100.12 X 100 = 77.04%

Atom efficiency %Yield of desired product X %Atom economy / 100
86 X 77.04/ 100 = 66.25%

RME mass of desired product / total mass of reactants **X** 100
34.71 / 62.47 X 100 = 55.56%

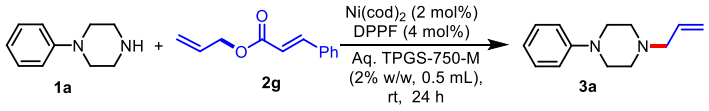
E-factor Amount of organic waste (mg) /Amount of product (mg)
(Total reaction mixture (mg) – Amount of product (mg))/Amount of product (mg)
(62.47 – 34.71)/34.71 = 27.76/34.71 = 0.79

***Relative EcoScale** 100 – sum of individual penalties
100 – 22= 78

Calculation of Penalty points	
Parameter	**Penalty points**
1. Yield	(100–86)/2 = 7
2. Price of allyl chloride (to obtain 10 mmol of end product)	
Inexpensive (< $10)	0
Expensive (> $10 and < $50)	0
Very expensive (> $50)	5
3. Safety	
N (dangerous for environment)	0
T (toxic)	5
F (highly flammable)	5
E (explosive)	0
F+ (extremely flammable)	0
T+ (extremely toxic)	0
~~**4. Technical setup**~~	
~~**5. Temperature/time**~~	
~~**6. Workup and purification**~~	
Total	**22**

*The EcoScale has been represented as a relative EcoScale, wherein the common parameters (Technical setup, Temperature/time, workup, and Purification) have been excluded while calculating the penalty points as they will be the same in all the cases.

Calculation of Green metrics for allyl cinnamate ('in-water' under Ni-catalysis)



Entities	Molecular mass	Quantity used
1a	162.23	32.44 mg
2g	188.22	56.46 mg
3a	202.14	33.10 mg

Atom economy Molecular mass of desired product / Molecular mass of all reactant **X** 100
202.14 / 162.23 + 188.22 X 100 = 57.68%

Atom efficiency %Yield of desired product X %Atom economy / 100
82 X 57.68/ 100 = 47.29%

RME mass of desired product / total mass of reactants **X** 100
33.10 / 88.90 X 100 = 37.23%

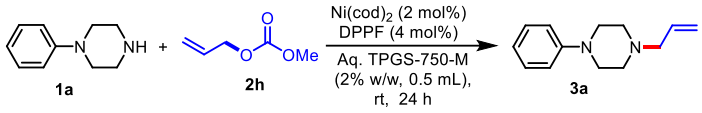
E-factor Amount of organic waste (mg) /Amount of product (mg)
(Total reaction mixture (mg) – Amount of product (mg))/Amount of product (mg)
(88.90 – 33.10)/33.10 = 55.8/33.10 = 1.68

***Relative EcoScale** 100 – sum of individual penalties
100-19 = 81

Calculation of Penalty points	
Parameter	**Penalty points**
1. Yield	(100–82)/2 = 9
2. Price of allyl chloride (to obtain 10 mmol of end product)	
Inexpensive (< $10)	0
Expensive (> $10 and < $50)	0
Very expensive (> $50)	5
3. Safety	
N (dangerous for environment)	0
T (toxic)	5
F (highly flammable)	0
E (explosive)	0
F+ (extremely flammable)	0
T+ (extremely toxic)	0
~~**4. Technical setup**~~	
~~**5. Temperature/time**~~	
~~**6. Workup and purification**~~	
Total	**19**

*The EcoScale has been represented as a relative EcoScale, wherein the common parameters (Technical setup, Temperature/time, workup, and Purification) have been excluded while calculating the penalty points as they will be the same in all the cases.

Calculation of Green metrics for allyl methyl carbonate ('in-water' under Ni-catalysis)



Entities	Molecular mass	Quantity used
1a	162.23	32.44 mg
2h	116.12	34.83 mg
3a	202.14	32.69 mg

Atom economy Molecular mass of desired product / Molecular mass of all reactant **X** 100
202.14 / 162.23 + 116.12 X 100 = 72.62%

Atom efficiency %Yield of desired product X %Atom economy / 100
81 X 72.62/ 100 = 58.82%

RME mass of desired product / total mass of reactants **X** 100
32.69 / 67.27 X 100 = 48.59%

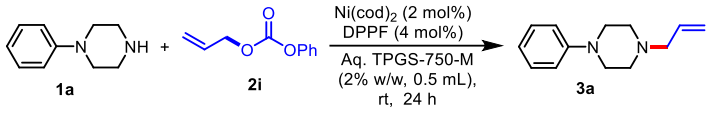
E-factor Amount of organic waste (mg) /Amount of product (mg)
(Total reaction mixture (mg) – Amount of product (mg))/Amount of product (mg)
(67.27 – 32.69)/32.69= 34.58/32.69= 1.05

***Relative EcoScale** 100 – sum of individual penalties
100 – 24.5= 75.5

Calculation of Penalty points	
Parameter	**Penalty points**
1. Yield	(100–81)/2 = 9.5
2. Price of allyl chloride (to obtain 10 mmol of end product)	
Inexpensive (< $10)	0
Expensive (> $10 and < $50)	0
Very expensive (> $50)	5
3. Safety	
N (dangerous for environment)	0
T (toxic)	5
F (highly flammable)	5
E (explosive)	0
F+ (extremely flammable)	0
T+ (extremely toxic)	0
~~**4. Technical setup**~~	
~~**5. Temperature/time**~~	
~~**6. Workup and purification**~~	
Total	**24.5**

*The EcoScale has been represented as a relative EcoScale, wherein the common parameters (Technical setup, Temperature/time, workup, and Purification) have been excluded while calculating the penalty points as they will be the same in all the cases.

Calculation of Green metrics for allyl phenyl carbonate ('in-water' under Ni-catalysis)



Entities	Molecular mass	Quantity used
1a	162.23	32.44 mg
2h	178.18	53.45 mg
3a	202.14	33.91 mg

Atom economy Molecular mass of desired product / Molecular mass of all reactant **X** 100
202.14 / 162.23 + 178.18 X 100 = 59.38%

Atom efficiency %Yield of desired product X %Atom economy / 100
84 X 59.38/ 100 = 49.87%

RME mass of desired product / total mass of reactants **X** 100
33.91 / 85.89 X 100 = 39.48%

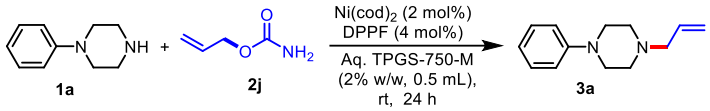
E-factor Amount of organic waste (mg) /Amount of product (mg)
(Total reaction mixture (mg) – Amount of product (mg))/Amount of product (mg)
(85.89 – 33.91)/33.91= 51.98/33.91= 1.53

***Relative EcoScale** 100 – sum of individual penalties
100 – 18= 82

Calculation of Penalty points	
Parameter	**Penalty points**
1. Yield	(100–84)/2 = 8
2. Price of allyl chloride (to obtain 10 mmol of end product)	
Inexpensive (< $10)	0
Expensive (> $10 and < $50)	0
Very expensive (> $50)	5
3. Safety	
N (dangerous for environment)	0
T (toxic)	5
F (highly flammable)	0
E (explosive)	0
F+ (extremely flammable)	0
T+ (extremely toxic)	0
~~**4. Technical setup**~~	
~~**5. Temperature/time**~~	
~~**6. Workup and purification**~~	
Total	**18**

*The EcoScale has been represented as a relative EcoScale, wherein the common parameters (Technical setup, Temperature/time, workup, and Purification) have been excluded while calculating the penalty points as they will be the same in all the cases.

Calculation of Green metrics for allyl carbamate ('in-water' under Ni-catalysis)



Entities	Molecular mass	Quantity used
1a	162.23	32.44 mg
2h	101.10	30.33 mg
3a	202.14	34.31 mg

Atom economy Molecular mass of desired product / Molecular mass of all reactant **X** 100
202.14 / 162.23 + 101.10 X 100 = 76.76%

Atom efficiency %Yield of desired product X %Atom economy / 100
85 X 76.76/ 100 = 65.24%

RME mass of desired product / total mass of reactants **X** 100
34.31 / 62.73 X 100 = 54.69%

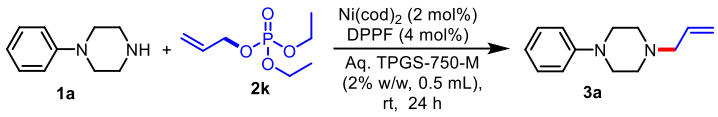
E-factor Amount of organic waste (mg) /Amount of product (mg)
(Total reaction mixture (mg) – Amount of product (mg))/Amount of product (mg)
(62.73 – 34.31)/34.31= 28.42/34.31= 0.82

***Relative EcoScale** 100 – sum of individual penalties
100 – 17.5= 82.5

Calculation of Penalty points	
Parameter	**Penalty points**
1. Yield	(100–85)/2 = 7.5
2. Price of allyl chloride (to obtain 10 mmol of end product)	
Inexpensive (< $10)	0
Expensive (> $10 and < $50)	0
Very expensive (> $50)	5
3. Safety	
N (dangerous for environment)	0
T (toxic)	5
F (highly flammable)	0
E (explosive)	0
F+ (extremely flammable)	0
T+ (extremely toxic)	0
~~**4. Technical setup**~~	
~~**5. Temperature/time**~~	
~~**6. Workup and purification**~~	
Total	**17.5**

*The EcoScale has been represented as a relative EcoScale, wherein the common parameters (Technical setup, Temperature/time, workup, and Purification) have been excluded while calculating the penalty points as they will be the same in all the cases.

Calculation of Green metrics for Diethyl allyl phosphate ('in-water' under Ni-catalysis)



Entities	Molecular mass	Quantity used
1a	162.23	32.44 mg
2h	194.17	58.25 mg
3a	202.14	33.91 mg

Atom economy Molecular mass of desired product / Molecular mass of all reactant **X** 100
202.14 / 162.23 + 194.17 X 100 = 56.71%

Atom efficiency %Yield of desired product X %Atom economy / 100
84 X 56.71/ 100 = 47.63%

RME mass of desired product / total mass of reactants **X** 100
33.91 / 90.65 X 100 = 37.40%

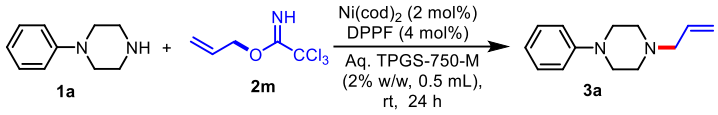
E-factor Amount of organic waste (mg) /Amount of product (mg)
(Total reaction mixture (mg) – Amount of product (mg))/Amount of product (mg)
(90.65 – 33.91)/33.91= 56.74/33.91= 1.6

***Relative EcoScale** 100 – sum of individual penalties
100 – 18= 82

Calculation of Penalty points	
Parameter	**Penalty points**
1. Yield	(100–84)/2 = 8
2. Price of allyl chloride (to obtain 10 mmol of end product)	
Inexpensive (< $10)	0
Expensive (> $10 and < $50)	0
Very expensive (> $50)	5
3. Safety	
N (dangerous for environment)	0
T (toxic)	5
F (highly flammable)	0
E (explosive)	0
F+ (extremely flammable)	0
T+ (extremely toxic)	0
~~**4. Technical setup**~~	
~~**5. Temperature/time**~~	
~~**6. Workup and purification**~~	
Total	**18**

*The EcoScale has been represented as a relative EcoScale, wherein the common parameters (Technical setup, Temperature/time, workup, and Purification) have been excluded while calculating the penalty points as they will be the same in all the cases.

Calculation of Green metrics for allyl imidate ('in-water' under Ni-catalysis)



Entities	Molecular mass	Quantity used
1a	162.23	32.44 mg
2m	202.47	60.74 mg
3a	202.14	23.81 mg

Atom economy Molecular mass of desired product / Molecular mass of all reactant **X** 100
202.14 / 162.23 + 202.47 X 100 = 55.42%

Atom efficiency %Yield of desired product X %Atom economy / 100
59 X 55.42/ 100 = 32.69%

RME mass of desired product / total mass of reactants **X** 100
23.81 / 93.14X 100 = 25.56%

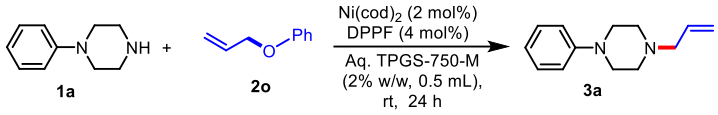
E-factor Amount of organic waste (mg) /Amount of product (mg)
(Total reaction mixture (mg) – Amount of product (mg))/Amount of product (mg)
(93.14 – 23.81)/23.81= 69.33/23.81= 2.9

***Relative EcoScale** 100 – sum of individual penalties
100 – 40.5= 59.5

Calculation of Penalty points	
Parameter	**Penalty points**
1. Yield	(100–59)/2 = 20.5
2. Price of allyl chloride (to obtain 10 mmol of end product)	
Inexpensive (< $10)	0
Expensive (> $10 and < $50)	0
Very expensive (> $50)	5
3. Safety	
N (dangerous for environment)	0
T (toxic)	5
F (highly flammable)	0
E (explosive)	10
F+ (extremely flammable)	0
T+ (extremely toxic)	0
~~**4. Technical setup**~~	
~~**5. Temperature/time**~~	
~~**6. Workup and purification**~~	
Total	**40.5**

*The EcoScale has been represented as a relative EcoScale, wherein the common parameters (Technical setup, Temperature/time, workup, and Purification) have been excluded while calculating the penalty points as they will be the same in all the cases.

Calculation of Green metrics for allyl phenyl ether ('in-water' under Ni-catalysis)



1a 2o 3a

Entities	Molecular mass	Quantity used
1a	162.23	32.44 mg
2o	134.18	40.25 mg
3a	202.14	32.69 mg

Atom economy Molecular mass of desired product / Molecular mass of all reactant **X** 100
202.14 / 162.23 + 134.18 X 100 = 68.19%

Atom efficiency %Yield of desired product X %Atom economy / 100
81 X 68.19/ 100 = 55.23%

RME mass of desired product / total mass of reactants **X** 100
32.69 / 72.65 X 100 = 44.99%

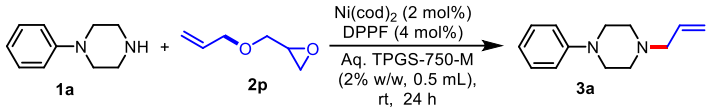
E-factor Amount of organic waste (mg) /Amount of product (mg)
(Total reaction mixture (mg) – Amount of product (mg))/Amount of product (mg)
(72.65 – 32.69)/32.69= 39.96/32.69= 1.2

***Relative EcoScale** 100 – sum of individual penalties
100 – 29.5= 70.5

Calculation of Penalty points	
Parameter	**Penalty points**
1. Yield	(100–81)/2 = 9.5
2. Price of allyl chloride (to obtain 10 mmol of end product)	
Inexpensive (< $10)	0
Expensive (> $10 and < $50)	0
Very expensive (> $50)	5
3. Safety	
N (dangerous for environment)	0
T (toxic)	0
F (highly flammable)	5
E (explosive)	10
F+ (extremely flammable)	0
T+ (extremely toxic)	0
~~**4. Technical setup**~~	
~~**5. Temperature/time**~~	
~~**6. Workup and purification**~~	
Total	**29.5**

*The EcoScale has been represented as a relative EcoScale, wherein the common parameters (Technical setup, Temperature/time, workup, and Purification) have been excluded while calculating the penalty points as they will be the same in all the cases.

Calculation of Green metrics for glycidyl ether ('in-water' under Ni-catalysis)



Entities	Molecular mass	Quantity used
1a	162.23	32.44 mg
2p	114.14	34.24 mg
3a	202.14	23.01 mg

Atom economy Molecular mass of desired product / Molecular mass of all reactant **X** 100
202.14 / 162.23 + 114.14 X 100 = 73.14%

Atom efficiency %Yield of desired product X %Atom economy / 100
57 X 73.14/ 100 = 41.68%

RME mass of desired product / total mass of reactants **X** 100
23.01 / 66.64 X 100 = 34.52%

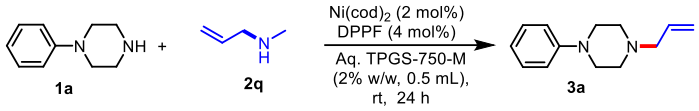
E-factor Amount of organic waste (mg) /Amount of product (mg)
(Total reaction mixture (mg) – Amount of product (mg))/Amount of product (mg)
(66.64 – 23.01)/23.01= 43.63/23.01= 1.8

***Relative EcoScale** 100 – sum of individual penalties
100 – 36.5= 63.5

Calculation of Penalty points	
Parameter	**Penalty points**
1. Yield	(100–57)/2 = 21.5
2. Price of allyl chloride (to obtain 10 mmol of end product)	
Inexpensive (< $10)	0
Expensive (> $10 and < $50)	0
Very expensive (> $50)	5
3. Safety	
N (dangerous for environment)	0
T (toxic)	5
F (highly flammable)	5
E (explosive)	0
F+ (extremely flammable)	0
T+ (extremely toxic)	0
~~**4. Technical setup**~~	
~~**5. Temperature/time**~~	
~~**6. Workup and purification**~~	
Total	**36.5**

*The EcoScale has been represented as a relative EcoScale, wherein the common parameters (Technical setup, Temperature/time, workup, and Purification) have been excluded while calculating the penalty points as they will be the same in all the cases.

Calculation of Green metrics for *N*-Allylmethylamine ('in-water' under Ni-catalysis)



Entities	Molecular mass	Quantity used
1a	162.23	32.44 mg
2q	71.12	21.33 mg
3a	202.14	30.68 mg

Atom economy Molecular mass of desired product / Molecular mass of all reactant **X** 100
202.14 / 162.23 + 71.12 X 100 = 86.60%

Atom efficiency %Yield of desired product X %Atom economy / 100
76 X 86.60/ 100 = 65.81%

RME mass of desired product / total mass of reactants **X** 100
30.68 / 53.73 X 100 = 57.10%

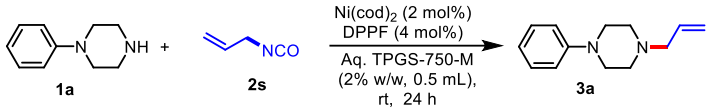
E-factor Amount of organic waste (mg) /Amount of product (mg)
(Total reaction mixture (mg) – Amount of product (mg))/Amount of product (mg)
(53.73 – 30.68)/30.68= 23.05/30.68= 0.7

***Relative EcoScale** 100 – sum of individual penalties
100 – 27= 73

Calculation of Penalty points	
Parameter	**Penalty points**
1. Yield	(100–76)/2 = 12
2. Price of allyl chloride (to obtain 10 mmol of end product)	
Inexpensive (< $10)	0
Expensive (> $10 and < $50)	0
Very expensive (> $50)	5
3. Safety	
N (dangerous for environment)	0
T (toxic)	5
F (highly flammable)	5
E (explosive)	0
F+ (extremely flammable)	0
T+ (extremely toxic)	0
~~**4. Technical setup**~~	
~~**5. Temperature/time**~~	
~~**6. Workup and purification**~~	
Total	**27**

*The EcoScale has been represented as a relative EcoScale, wherein the common parameters (Technical setup, Temperature/time, workup, and Purification) have been excluded while calculating the penalty points as they will be the same in all the cases.

Calculation of Green metrics for allyl isocyanate ('in-water' under Ni-catalysis)



1a 2s 3a

Entities	Molecular mass	Quantity used
1a	162.23	32.44 mg
2s	83.09	24.92 mg
3a	202.14	8.47 mg

Atom economy Molecular mass of desired product / Molecular mass of all reactant **X** 100
202.14 / 162.23 + 83.09 X 100 = 82.39%

Atom efficiency %Yield of desired product X %Atom economy / 100
21 X 82.39/ 100 = 17.30%

RME mass of desired product / total mass of reactants **X** 100
8.47 / 57.32 X 100 = 14.77%

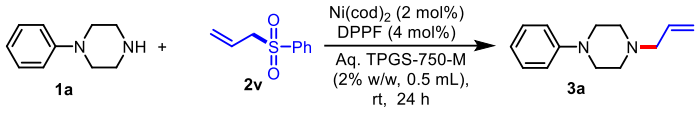
E-factor Amount of organic waste (mg) /Amount of product (mg)
(Total reaction mixture (mg) – Amount of product (mg))/Amount of product (mg)
(57.32– 8.47)/8.47= 48.85/8.47= 5.7

***Relative EcoScale** 100 – sum of individual penalties
100 – 54.5= 45.5

Calculation of Penalty points	
Parameter	**Penalty points**
1. Yield	(100–21)/2 = 39.5
2. Price of allyl chloride (to obtain 10 mmol of end product)	
Inexpensive (< $10)	0
Expensive (> $10 and < $50)	0
Very expensive (> $50)	5
3. Safety	
N (dangerous for environment)	0
T (toxic)	5
F (highly flammable)	5
E (explosive)	0
F+ (extremely flammable)	0
T+ (extremely toxic)	0
~~**4. Technical setup**~~	
~~**5. Temperature/time**~~	
~~**6. Workup and purification**~~	
Total	**54.5**

*The EcoScale has been represented as a relative EcoScale, wherein the common parameters (Technical setup, Temperature/time, workup, and Purification) have been excluded while calculating the penalty points as they will be the same in all the cases.

Calculation of Green metrics for allyl phenyl sulfone ('in-water' under Ni-catalysis)



Entities	Molecular mass	Quantity used
1a	162.23	32.44 mg
2v	182.24	54.67 mg
3a	202.14	25.83 mg

Atom economy Molecular mass of desired product / Molecular mass of all reactant **X** 100
202.14 / 162.23 + 182.24 X 100 = 58.68%

Atom efficiency %Yield of desired product X %Atom economy / 100
64 X 58.68/ 100 = 37.55%

RME mass of desired product / total mass of reactants **X** 100
25.83 / 87.07 X 100 = 29.66%

E-factor Amount of organic waste (mg) /Amount of product (mg)
(Total reaction mixture (mg) – Amount of product (mg))/Amount of product (mg)
(87.07– 25.83)/25.83= 61.24/25.83= 2.3

***Relative EcoScale** 100 – sum of individual penalties
100 – 28= 72

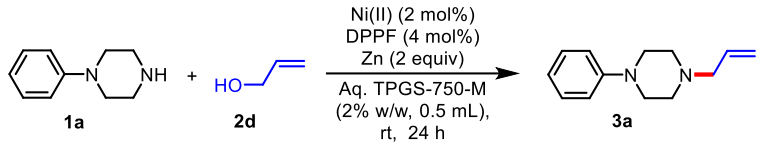
Calculation of Penalty points	
Parameter	**Penalty points**
1. Yield	(100–64)/2 = 18
2. Price of allyl chloride (to obtain 10 mmol of end product)	
Inexpensive (< $10)	0
Expensive (> $10 and < $50)	0
Very expensive (> $50)	5
3. Safety	
N (dangerous for environment)	0
T (toxic)	5
F (highly flammable)	0
E (explosive)	0
F+ (extremely flammable)	0
T+ (extremely toxic)	0
~~**4. Technical setup**~~	
~~**5. Temperature/time**~~	
~~**6. Workup and purification**~~	
Total	**28**

*The EcoScale has been represented as a relative EcoScale, wherein the common parameters (Technical setup, Temperature/time, workup, and Purification) have been excluded while calculating the penalty points as they will be the same in all the cases.

7. Demonstration of 'in-water' allylic amination using Ni(0) pre-catalyst

7.1. Evaluation of Ni(0)-precatalysts, ligands, and optimisation study.

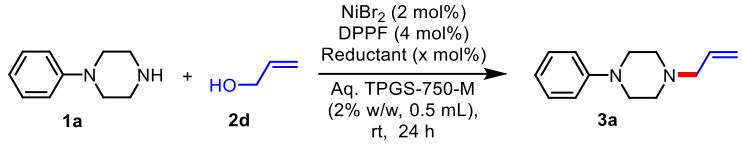
Evaluation of different Ni(0) pre-catalyst



Ni(0) precatalyst	**3a** (%Yield)[a]
NiF_2	14
$NiCl_2$	21
$NiBr_2$	42
$NiCl_2$ glyme	29
$Ni(acac)_2$	25
None	0[b]

Conditions: **1a** is treated with **2d** in presence of different Ni(II) catalysts and DPPF with 2 equiv. of Zn powder in aq. TPGS-750-M micelles. [a]Yield represents the isolated and purified yield of **3a**. [b]Starting **1a** was found intact.

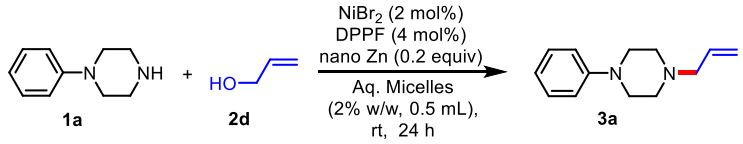
Optimization of reductants and their molar equivalent



Reductant	**3a** (%Yield)[a]
Zn dust (2 equiv)	42
Zn dust (1 equiv)	28
Zn dust (0.5 equiv)	15
Mn dust (2 equiv)	Traces[b]
nano-Zn (0.5 equiv)	67
nano-Zn (0.3 equiv)	68
nano-Zn (0.2 equiv)	67
nano-Zn (0.1 equiv)	Traces[b]

Conditions: **1a** is treated with **2d** in presence of catalytic $NiBr_2$ and DPPF under different reaction conditions in aq. TPGS-750-M micelles. [a]Yield represents the isolated and purified yield of **3a**. [b]Starting **1a** was found intact.

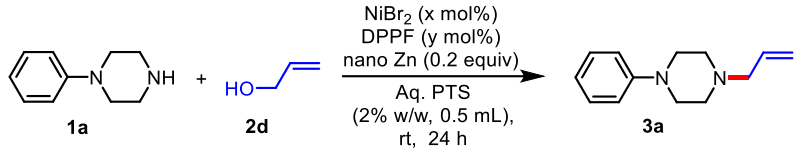
Evaluation of different micellar media



Aq. Micelles (2 % w/w)	**3a** (%Yield)[a]
TPGS-750 M	67
SPGS-550 M	10
PTS	81
HPMC	Traces[b]
SDS	18
SDOSS	46
Tween-40	36
SPAN-40	11
Triton X-100	Traces[b]
none	Traces[b]

Conditions: **1a** is treated with **2d** in presence of catalytic $NiBr_2$ and DPPF with nano Zn (20 mol%) in different aq. micelles. [a]Yield represents the isolated and purified yield of **3a**. [b]Starting **1a** was found intact.

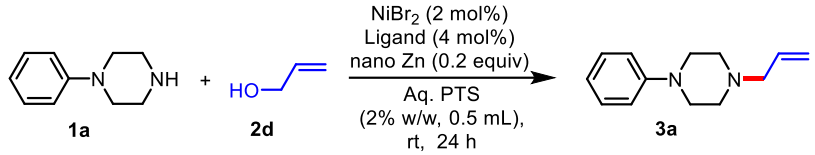
Optimization of amount of $NiBr_2$ and DPPF ligand



$NiBr_2$ (mol%)	**3a (%Yield)[a]**
2	81
1	67
0.5	55
DPPF (mol%)	
4	81
2	61
0.5	Traces[b]

Conditions: **1a** is treated with **2d** in presence of different catalytic amount of $NiBr_2$ and DPPF with nano Zn (20 mol%) in different aq. micelles. [a]Yield represents the isolated and purified yield of **3a**. [b]Starting **1a** was found intact.

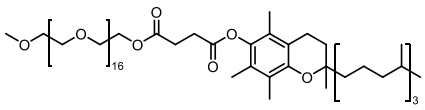
Re-evaluation of different ligands under optimized conditions.



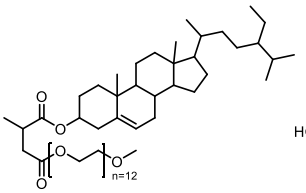
Ligand	**3a (%Yield)[a]**
PPh_3	18
$P(o\text{-}tol)_3$	0[b]
PCy_3	0[b]
DPPM	0[b]
DPPP	0[b]
XPhos	0[b]
RuPhos	0[b]
XantPhos	43
DPEPhos	66
4-4′-diMeO-2-2′-bipyr	0[b]
4,4’-di-^{t}Bu-2,2’-bpyr	0[b]
5,5'-CF_3,2,2'-bipyr	0[b]
BPhen	0[b]
SIPr•HCl	0[b]
SIPr•HBF_4	0[b]
SIMes•HCl	0[b]
IAd•HBF_4	0[b]

Conditions: **1a** is treated with **2d** under optimized conditions in presence of different ligand (4 mol%). [a]Yield represents the isolated and purified yield of **3a**. [b]Starting **1a** was found intact.

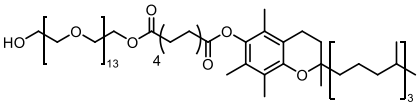
Structure of surfactants used in study.



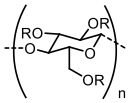
DL-α-Tocopherol methoxypolyethylene glycol succinate
(TPGS-750M)



β-sitosterol methoxypolyethyleneglycol succinate
(SPGS-550M)

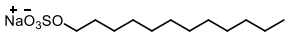


Polyoxyethanyl-α-tocopheryl sebacate
(**PTS**)

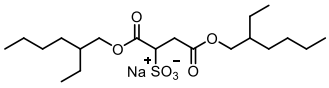


R = H, CH_3, $CH_2CH(OH)CH_3$

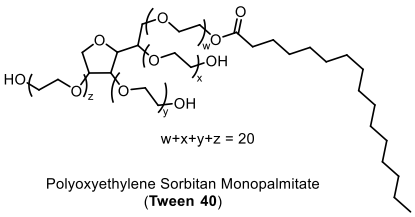
Hydroxypropylmethyl cellulose
(**HMPC**)



Sodium dodecyl sulfate
(SDS)

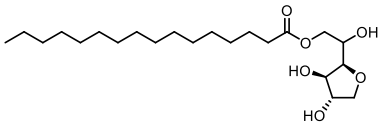


Dioctyl Sodium Sulfosuccinate
(SDOSS)

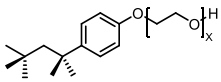


w+x+y+z = 20

Polyoxyethylene Sorbitan Monopalmitate
(**Tween 40**)

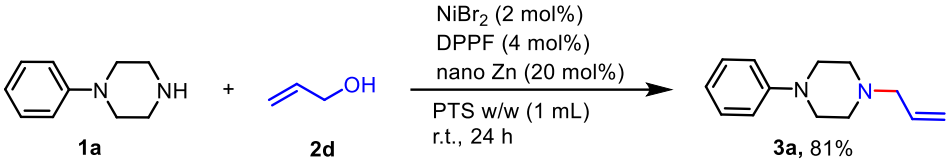


Sorbitan monopalmitate
(SPAN-40)



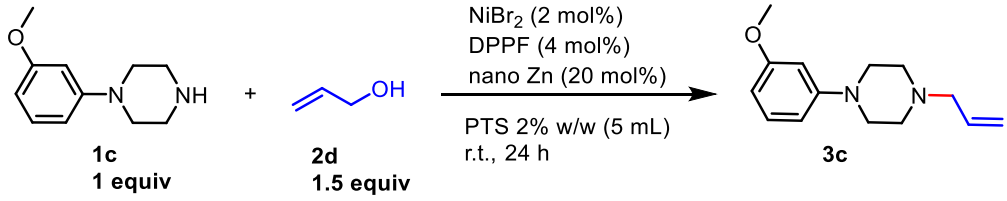
2-[4-(2,4,4-trimethylpentan-2-yl)phenoxy]ethanol
(**Triton X-100**)

Representative experimental procedure for the N-allylation using allyl alcohols in the presence of Ni (0) pre-catalyst in aqueous micellar



To a well clean tube equipped with a stir bar, $NiBr_2$ (0.87 mg, 0.004 mmol, 2 mol%), DPPF (4.4 mg, 0.008 mmol, 4 mol%), nano Zn (2.6 mg, 0.04 mmol, 20 mol%) 1-phenylpiperazine **1a** (32.4 mg, 31.5 µL, 0.2 mmol), allyl alcohol **2d** (17.4 mg, 20.4 µL, 0.3 mmol, 1.5 equiv), and aqueous PTS (2% w/w, 1 mL) were added. The resultant mixture was stirred at room temperature for 24 h. After the stipulated time period, the reaction mixture was diluted with EtOAc (2 X 0.5 mL) and vortexed. The supernatant organic layers containing product and other organic residue were dried over anhyd. Na_2SO_4 and concentrated under reduced pressure. The crude products were adsorbed on silica gel and passed through the column (eluent: Hexane/EtOAc) to get analytically pure product **3a** (81%) as a pale-yellow liquid.

7.2. Scale up study using Ni (0) pre-catalyst in aqueous micellar



	Aq. PTS 2% w/w used	3a (% Yield)
1a (0.5 g)	5 mL	80
1a (1 g)	7 mL	79
1a (5 g)	10 mL	81
1a (10 g)	13 mL	78

Representative procedure (10.0 Gram scale)

To a well clean tube equipped with a stir bar, $NiBr_2$ (269.4 mg, 1.2 mmol, 2 mol%), DPPF (1.36 g, 2.4 mmol, 4 mol%), nano Zn (806.0 mg, 12.32 mmol, 20 mol%), 1-phenylpiperazine **1a** (10.0 g, 9.4 mL, 61.6 mmol), allyl alcohol **2d** (5.3 g, 6.29 mL, 92.4 mmol, 1.5 equiv), and aqueous PTS (2% w/w, 13 mL) were added. The resultant mixture was stirred at room temperature for 24 h. After the stipulated time period, the reaction mixture was diluted with EtOAc (2 X 100 mL) and vortexed. The supernatant organic layers containing product and other organic residue were dried over anhyd. Na_2SO_4 and concentrated under reduced pressure. The crude products were adsorbed on silica gel and passed through the column (eluent: Hexane/EtOAc) to get analytically pure product **3c** (9.72 g, 78%) as a pale-yellow liquid.

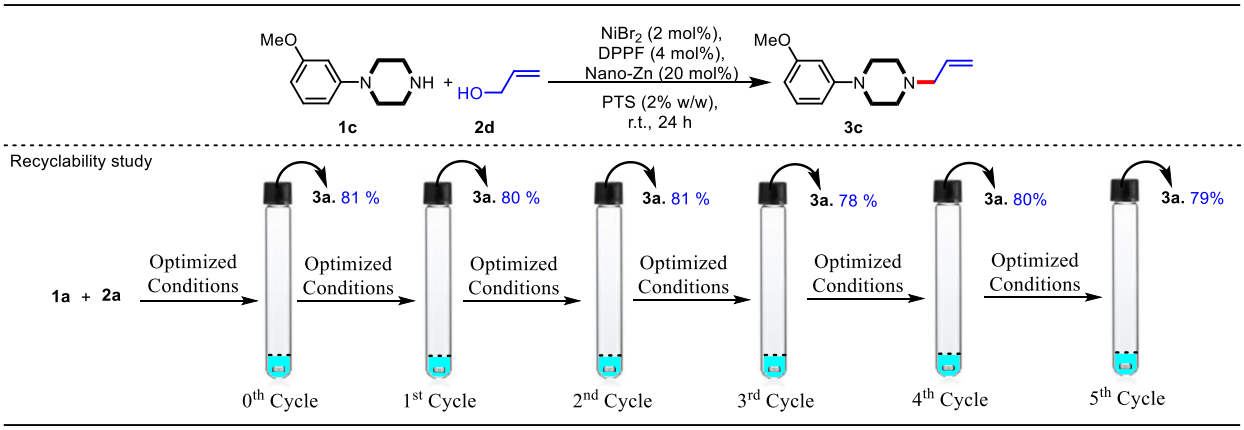
7.2. ICP-MS study

The ICH categorized the various elemental impurities in four different classifications to facilitate decisions during the risk assessment process. Nickel falls under Class 2a with 200 mg/L (for oral application) and set according to the permitted daily exposure limits (PDE).

Sample	Ni (ppm)
MCSHL-ICPMS	0.040285

7.3. Recyclability study under Ni (0) pre-catalyst in aqueous micellar

Procedure: To a well cleaned and dried seal tube equipped with a stir bar, $NiBr_2$ (4.3 mg, 0.02 mmol, 2 mol%), DPPF (22.1 mg, 0.04 mmol, 4 mol%), 1-(3-methoxyphenyl)piperazine **1c** (192.2 mg, 168.6 µL, 1 mmol), allyl alcohol **2d** (87.12 mg, 102.01 µL, 1.5 mmol, 1.5 equiv), and aqueous PTS (2% w/w, 5 mL) were added. The resultant mixture was stirred at room temperature for 24 h. After the stipulated time period, the reaction mixture was diluted with EtOAc (3 X 5 mL) and vortexed. The supernatant organic layers containing product and other organic residue were dried over anhyd. Na_2SO_4 and concentrated under reduced pressure. The crude products were adsorbed on silica gel and passed through the column (eluent: Hexane/EtOAc) to get analytically pure product **3c** (0.18 g, 81%) as a pale-yellow liquid. To the remaining aqueous layer same protocol as mentioned above was repeated except addition of fresh aqueous PTS (2% w/w), for product formation in the next consecutive cycles as summarized below.



7.4. Determination of Average particle size and Particle Distribution Index (PDI) of PTS-derived micelles (0 cycle vs. 6th cycle) using the Zeta sizer

Sample preparation: About 0.5 mL of freshly prepared aqueous solutions (2% w/w) of PTS were pipetted out and diluted one time (1x) with miliQ water in microcentrifuge tube. This was further filtered through Fluoropore Membrane Filter (MF-Millipore™, 0.22 µm pore size, hydrophobic PTFE, 47 mm membrane). The filtrate collected were used as final sample. All the sample measurements were made at 25 ± 2 °C in triplicate using disposable cuvette, and the results were analyzed using Zetasizer 633 nm and angle (173°). In a similar manner, recovered aqueous PTS (after 5th run) was analysed.

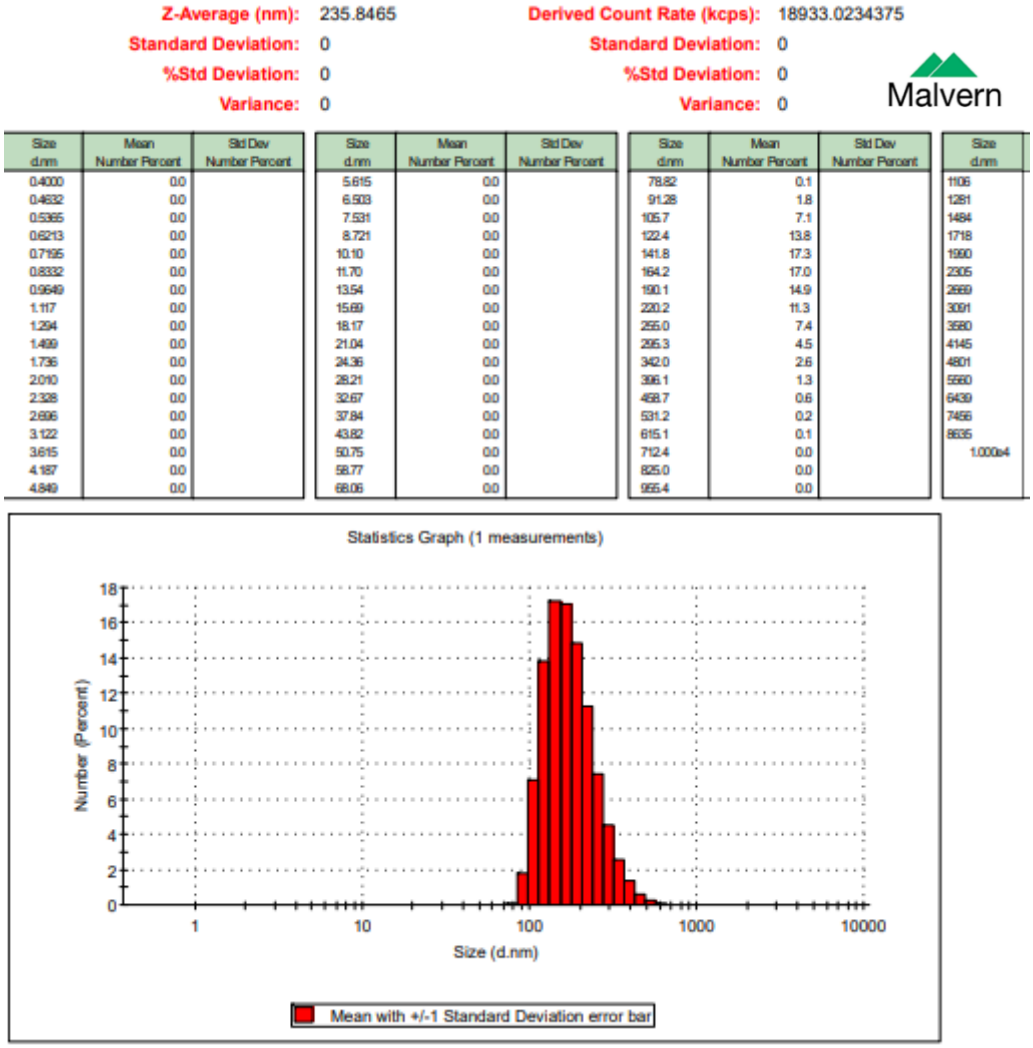


Fig S1. Zeta sizer analysis (Particle size distribution) of freshly prepared aq. PTS micelles (2% w/w)

Z-Average (nm):	1278.486	Derived Count Rate (kcps):	29459.0611979...
Standard Deviation:	0	Standard Deviation:	0
%Std Deviation:	0	%Std Deviation:	0
Variance:	0	Variance:	0

Malvern

Size d.nm	Mean Number Percent	Std Dev Number Percent	Size d.nm	Mean Number Percent	Std Dev Number Percent	Size d.nm	Mean Number Percent	Std Dev Number Percent	Size d.nm
0.4000	0.0		5.615	0.0		78.82	16.7		1106
0.4632	0.0		6.503	0.0		91.28	14.4		1281
0.5365	0.0		7.531	0.0		105.7	15.6		1484
0.6213	0.0		8.721	0.0		122.4	17.4		1718
0.7195	0.0		10.10	0.0		141.8	14.7		1990
0.8332	0.0		11.70	0.0		164.2	9.6		2305
0.9649	0.0		13.54	0.0		190.1	3.0		2669
1.117	0.0		15.69	0.0		220.2	0.2		3091
1.294	0.0		18.17	0.0		255.0	0.0		3580
1.499	0.0		21.04	0.0		295.3	0.0		4145
1.736	0.0		24.36	0.0		342.0	0.0		4801
2.010	0.0		28.21	0.0		396.1	0.0		5560
2.328	0.0		32.67	0.0		458.7	0.0		6439
2.696	0.0		37.84	0.0		531.2	0.0		7456
3.122	0.0		43.82	0.0		615.1	0.0		8635
3.615	0.0		50.75	0.0		712.4	0.0		1.000e4
4.187	0.0		58.77	0.0		825.0	0.0		
4.849	0.0		68.06	8.3		955.4	0.0		

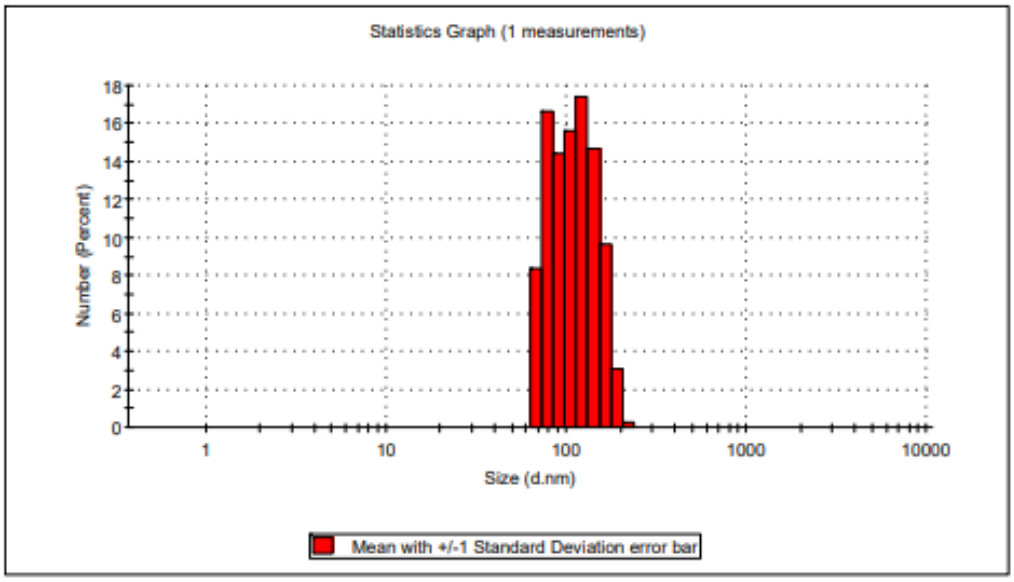
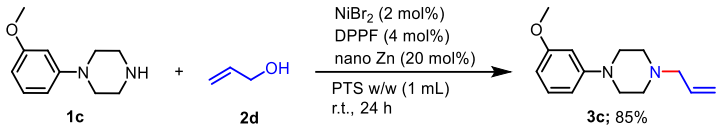


Fig S2. Zeta sizer analysis (Particle size distribution) of aq. PTS micelles (2% w/w) after 5th cycle.

7.5. Calculation of Green metrics for 1-(3-methoxyphenyl)piperazine ('in-water' under Ni-catalysis)



Entities	Molecular mass	Quantity used
1a	192.12	38.42 mg
2d	58.08	17.4 mg
3a	232.15	39.49 mg

Atom economy Molecular mass of desired product / Molecular mass of all reactant **X** 100
232.15 / 192.12 + 58.08 X 100 = 92.72%

Atom efficiency %Yield of desired product X %Atom economy / 100
85 X 92.72 / 100 = 78.81%

RME mass of desired product / total mass of reactants **X** 100
39.49 / 55.82 X 100 = 70.74%

E-factor Amount of organic waste (mg) /Amount of product (mg)
(Total reaction mixture (mg) – Amount of product (mg))/Amount of product (mg)
(55.82 – 39.49) /39.49 = 0.4

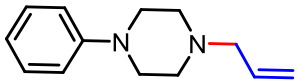
EcoScale 100 – sum of individual penalties
100 – 24 = 76

Calculation of Penalty points	
Parameter	**Penalty points**
1. Yield	(100 – 85) / 2 = 7.5
2. Price of reaction components (to obtain 10 mmol of end product)	
Inexpensive (< $10)	0
Expensive (> $10 and < $50)	0
Very expensive (> $50)	5
3. Safety	
N (dangerous for environment)	0
T (toxic)	5
F (highly flammable)	0
E (explosive)	0
F+ (extremely flammable)	0
T+ (extremely toxic)	0
4. Technical setup	
Common setup	0
Instruments for controlled addition of chemicals	0
Unconventional activation technique	0
Pressure equipment, > 1 atm	0
Any additional special glassware	0
(Inert) gas atmosphere	0
Glove box	0

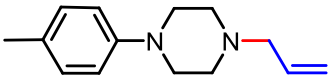
5. Temperature/time	
Room temperature, < 1 h	0
Room temperature, < 24 h	1
Heating, < 1 h	0
Heating, > 1 h	0
Cooling to 0°C	0
Cooling, < 0°C	0
6. Workup and purification	
None	0
Cooling to room temperature	0
Adding solvent	0
Simple filtration	0
Removal of solvent with bp < 150°C	0
Crystallization and filtration	0
Removal of solvent with bp > 150°C	0
Solid phase extraction	0
Distillation	0
Sublimation	0
Liquid-liquid extraction	3
Classical chromatography	10
Total points	**24**

8. Spectroscopic characterization data

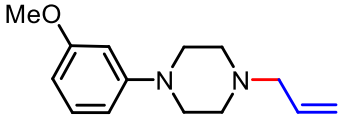
1-Allyl-4-phenylpiperazine (3a); Pale yellow liquid (32.80 mg, 81%); **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.32 – 7.28 (m, 2H), 6.96 (d, *J* = 7.7 Hz, 2H), 6.89 (t, *J* = 7.3 Hz, 1H), 5.9 (ddt, *J* = 16.8, 10.1, 6.6 Hz, 1H), 5.27 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.24 – 5.21 (m, 1H), 3.26 – 3.24 (m, 4H), 3.10 (d, *J* = 6.7 Hz, 2H), 2.67 – 2.65 (m, 4H); **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 151.2, 134.6, 129.0, 119.6, 118.4, 116.0, 61.7, 52.9, 49.0; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ Calculated for $C_{13}H_{19}N_2^+$ 203.1548 Found 203.1505.



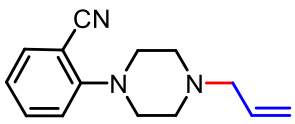
1-Allyl-4-(p-tolyl)piperazine (3b): Pale yellow liquid (38.03 mg, 87%); **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.09 – 7.07 (m, 2H), 6.87 – 6.84 (m, 2H), 5.91 (ddt, *J* = 16.8, 10.1, 6.6 Hz, 1H), 5.26 – 5.18 (m, 2H), 3.18 – 3.16 (m, 4H), 3.07 (dt, *J* = 6.7, 1.3 Hz, 2H), 2.64 – 2.62 (m, 4H), 2.27 (s, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 149.2, 134.7, 129.6, 129.2, 118.3, 116.4, 61.7, 53.1, 49.6, 20.4. **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ Calculated for $C_{14}H_{21}N_2^+$ 217.1699 Found 217.1705.



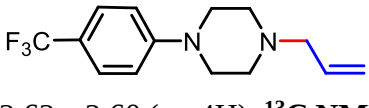
1-Allyl-4-(3-methoxyphenyl)piperazine (3c): Pale yellow liquid (39.49 mg, 85%);**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.17 (t, *J* = 8.2 Hz, 1H), 6.55 (ddd, *J* = 8.2, 2.3, 0.8 Hz, 1H), 6.47 (t, *J* = 2.4 Hz, 1H), 6.41 (ddd, *J* = 8.2, 2.4, 0.8 Hz, 1H), 5.90 (ddt, *J* = 16.8, 10.2, 6.6 Hz, 1H), 5.24 – 5.17 (m, 2H), 3.79 (s, 3H), 3.22 – 3.20 (m, 4H), 3.06 (dt, *J* = 6.7, 1.3 Hz, 2H), 2.61 – 2.59 (m, 4H); **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 160.5, 152.7, 134.8, 129.7, 118.3, 108.8, 104.3, 102.4, 61.8, 55.1, 53.0, 49.0; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ Calculated for $C_{14}H_{21}N_2O^+$ 233.1648 Found 233.1649.



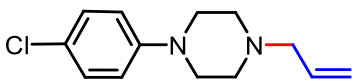
2-(4-Allylpiperazin-1-yl)benzonitrile (3d): Pale yellow liquid (31.81 mg, 70%); **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.55 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.47 (ddd, *J* = 8.9, 7.4, 1.7 Hz, 1H), 7.02 – 6.97 (m, 2H), 5.89 (ddt, *J* = 16.9, 10.1, 6.7 Hz, 1H), 5.25 – 5.17 (m, 2H), 3.26 – 3.24 (m, 4H), 3.09 (dt, *J* = 6.7, 1.3 Hz, 2H), 2.69 – 2.67 (m, 4H); **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 155.7, 134.6, 134.3, 133.8, 121.7, 118.6, 118.4, 106.0, 61.6, 53.0, 51.5; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ Calculated for $C_{14}H_{18}N_3^+$ 228.1495 Found 228.1502.



1-Allyl-4-(4-(trifluoromethyl)phenyl)piperazine (3e): Pale yellow liquid (38.91mg, 72%); **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.48 – 7.47 (m, 2H), 6.93 – 6.91 (m, 2H), 5.89 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.26 – 5.19 (m, 2H), 3.31 – 3.29 (m, 4H), 3.07 (dt, *J* = 6.6, 1.3 Hz, 2H), 2.62 – 2.60 (m, 4H); **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 153.2, 134.5, 126.3 (q, $^{3}J_{C-F}$ = 3.77 Hz), 101.9 (q, $^{1}J_{C-F}$ = 270.92 Hz), 120.4 (q, $^{2}J_{C-F}$ = 32.50 Hz), 118.5, 114.5, 61.6, 52.7, 47.9; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ Calculated for $C_{14}H_{18}F_3N_2^+$ 271.1417, Found 271.1422.

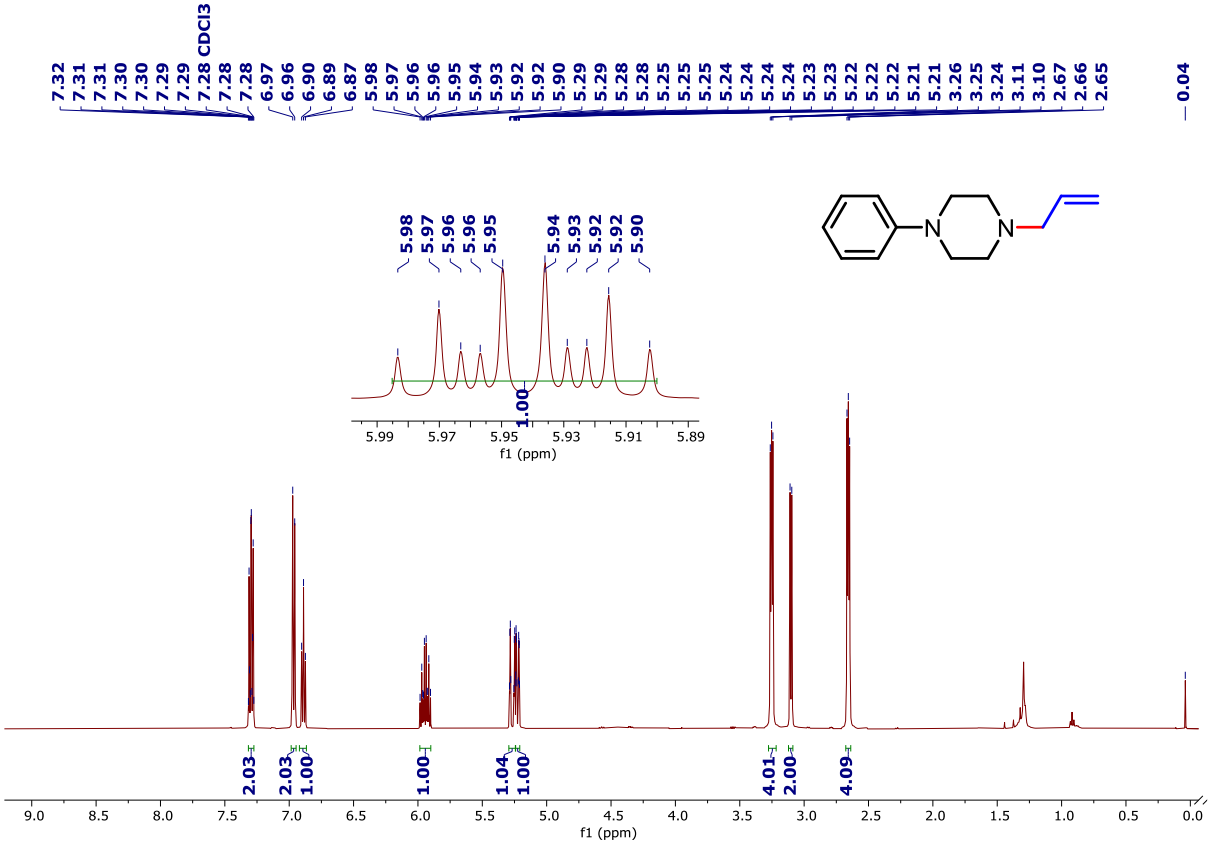


1-Allyl-4-(4-chlorophenyl)piperazine (3f): Pale yellow liquid (42.62 mg, 90%); **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.21 – 7.18 (m, 2H), 6.85 – 6.82 (m, 2H), 5.89 (ddt, *J* = 16.8, 10.2, 6.6 Hz, 1H), 5.25 – 5.17 (m, 2H), 3.19 – 3.17 (m, 4H), 3.06 (dt, *J* = 6.6, 1.3 Hz, 2H), 2.61– 2.59 (m, 4H); **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 149.9, 134.7, 128.9, 124.4, 118.3, 117.2, 61.7, 52.9, 49.1; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ Calculated for $C_{13}H_{18}ClN_2^+$ 237.1153 Found 237.1154.

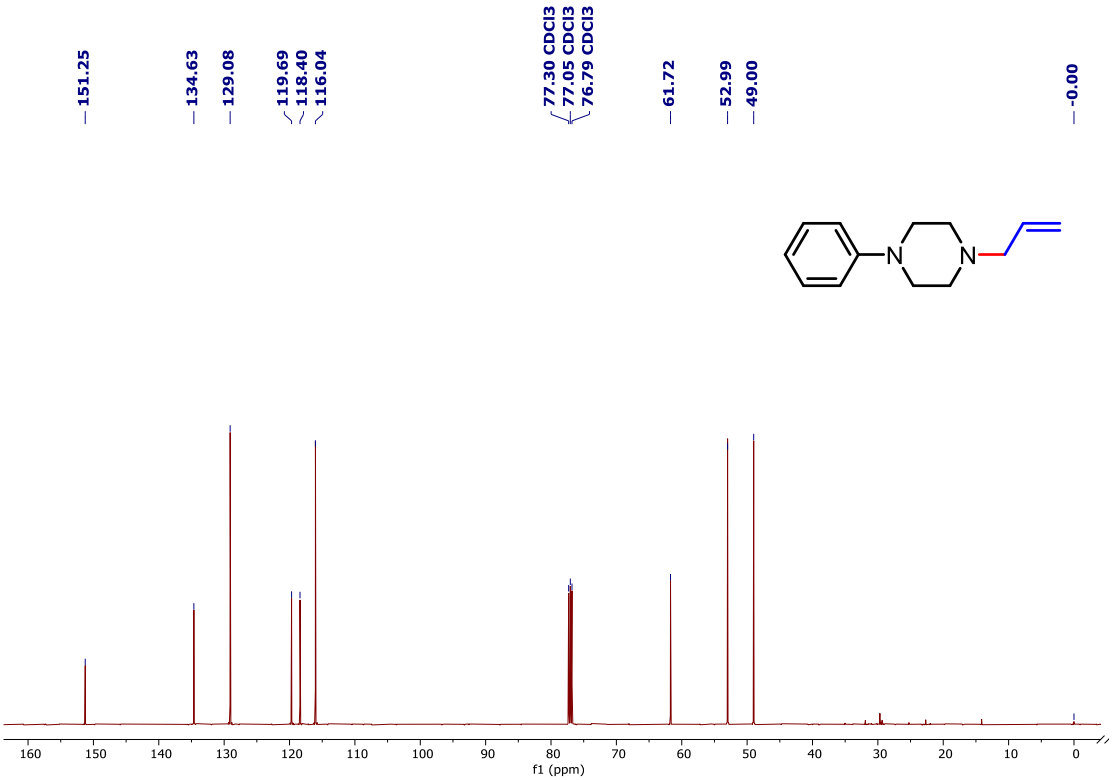


9. NMR spectra (^{1}H, ^{13}C, ^{19}F)

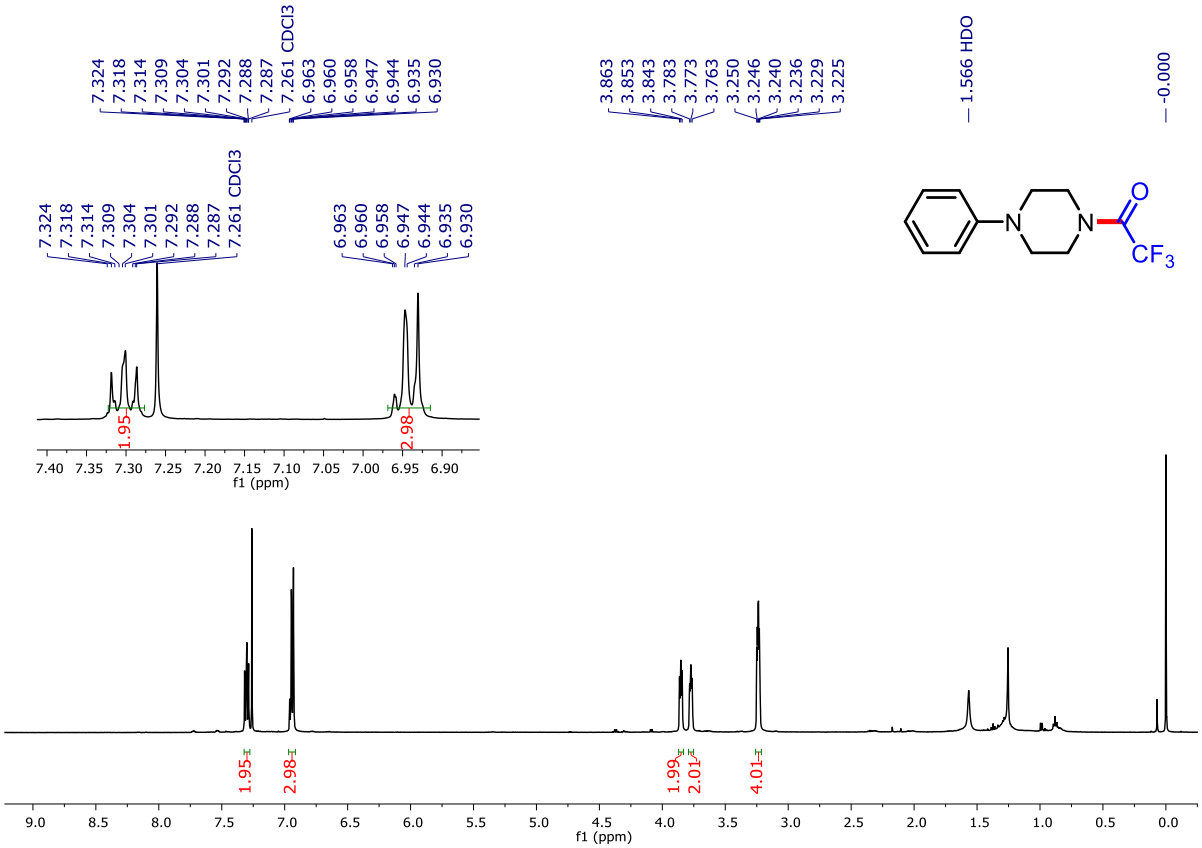
1-Allyl-4-phenylpiperazine (3a): ^{1}H NMR (500 MHz, $CDCl_3$)



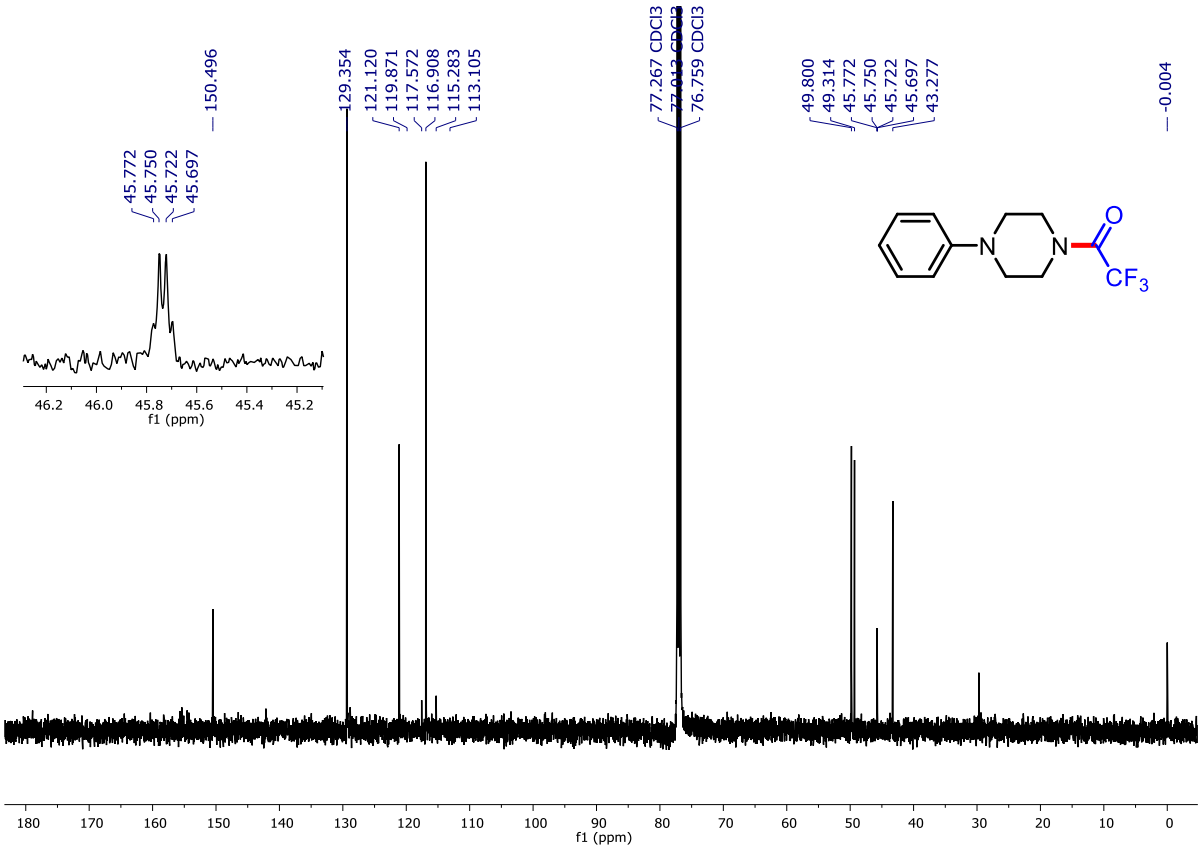
1-Allyl-4-phenylpiperazine (3a): ^{13}C NMR (125 MHz, $CDCl_3$)



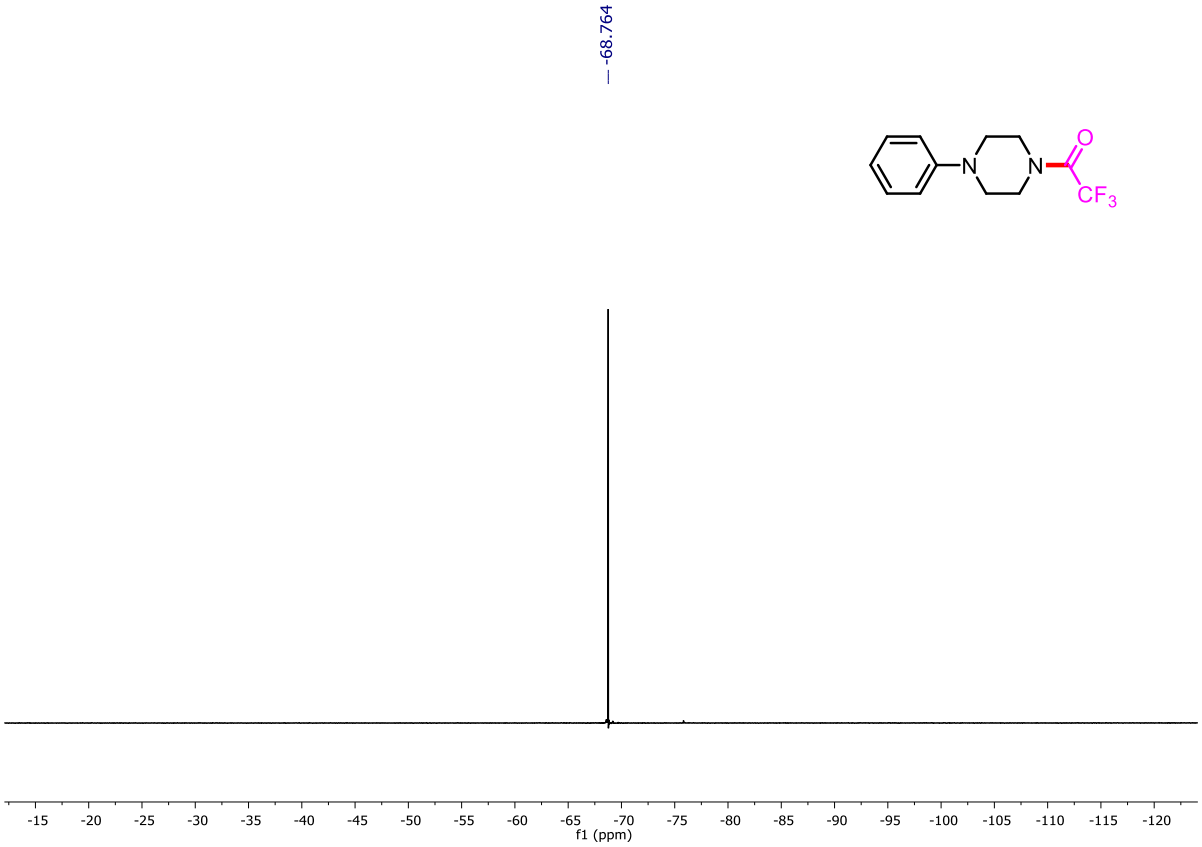
2,2,2-Trifluoro-1-(4-phenylpiperazin-1-yl)ethan-1-one (4a): ^{1}H NMR (500 MHz, $CDCl_3$)



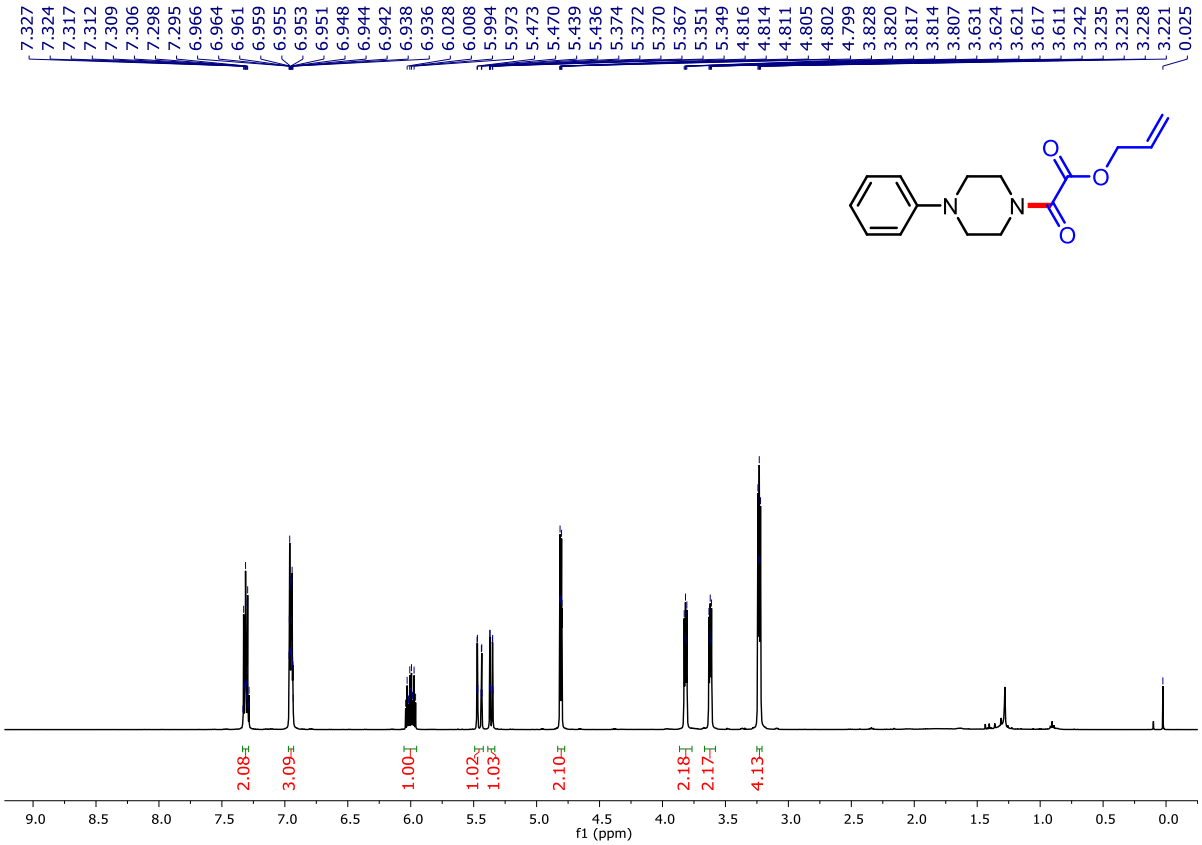
2,2,2-Trifluoro-1-(4-phenylpiperazin-1-yl)ethan-1-one (4a): ^{13}C NMR (125 MHz, $CDCl_3$)



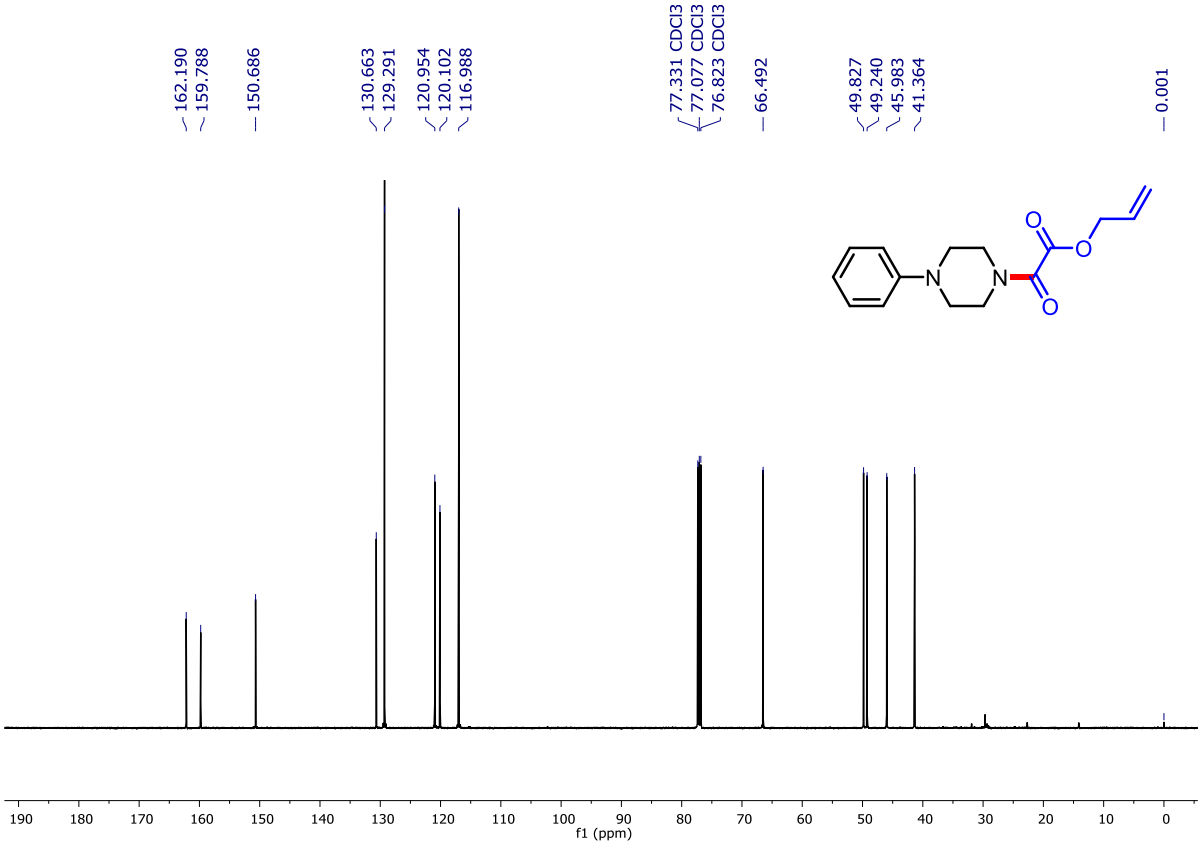
2,2,2-Trifluoro-1-(4-phenylpiperazin-1-yl)ethan-1-one (4a): ^{19}F NMR (471 MHz, $CDCl_3$)



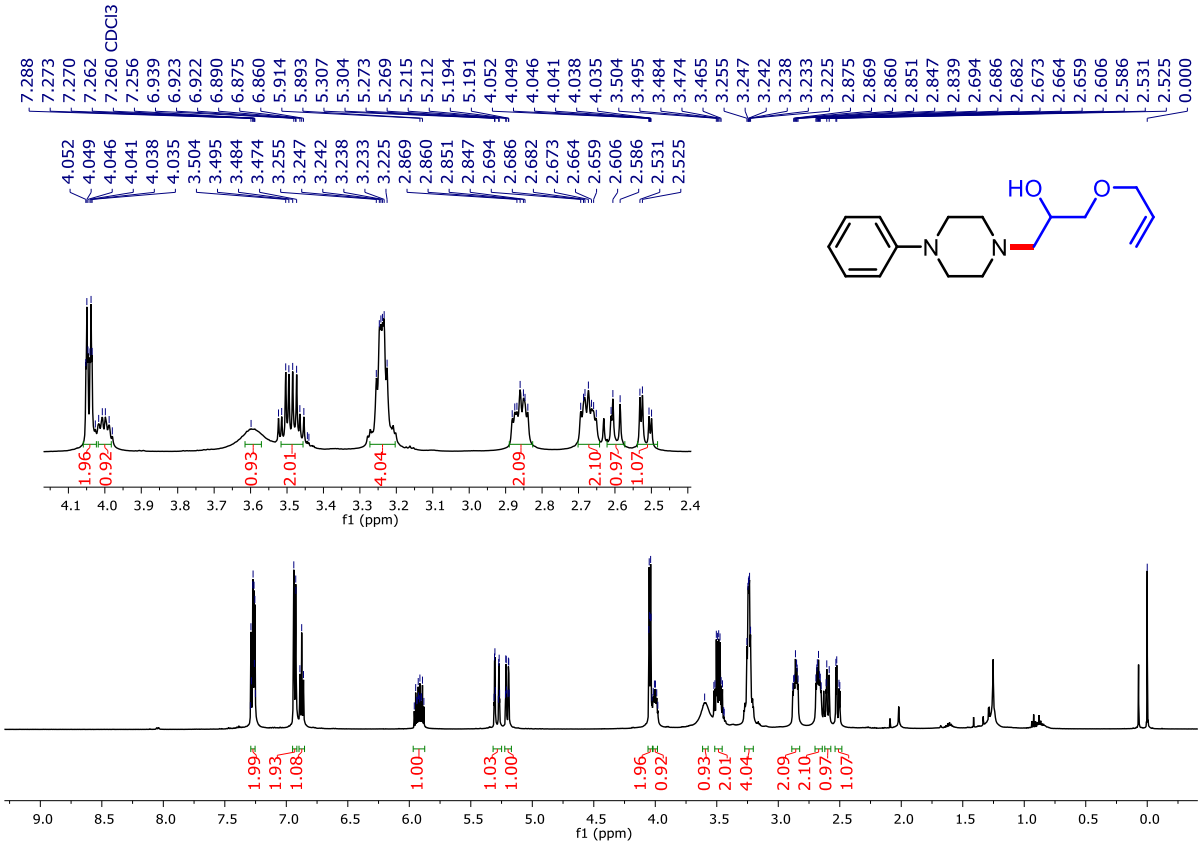
Allyl 2-oxo-2-(4-phenylpiperazin-1-yl)acetate (4b): ^{1}H NMR (500 MHz, $CDCl_3$)



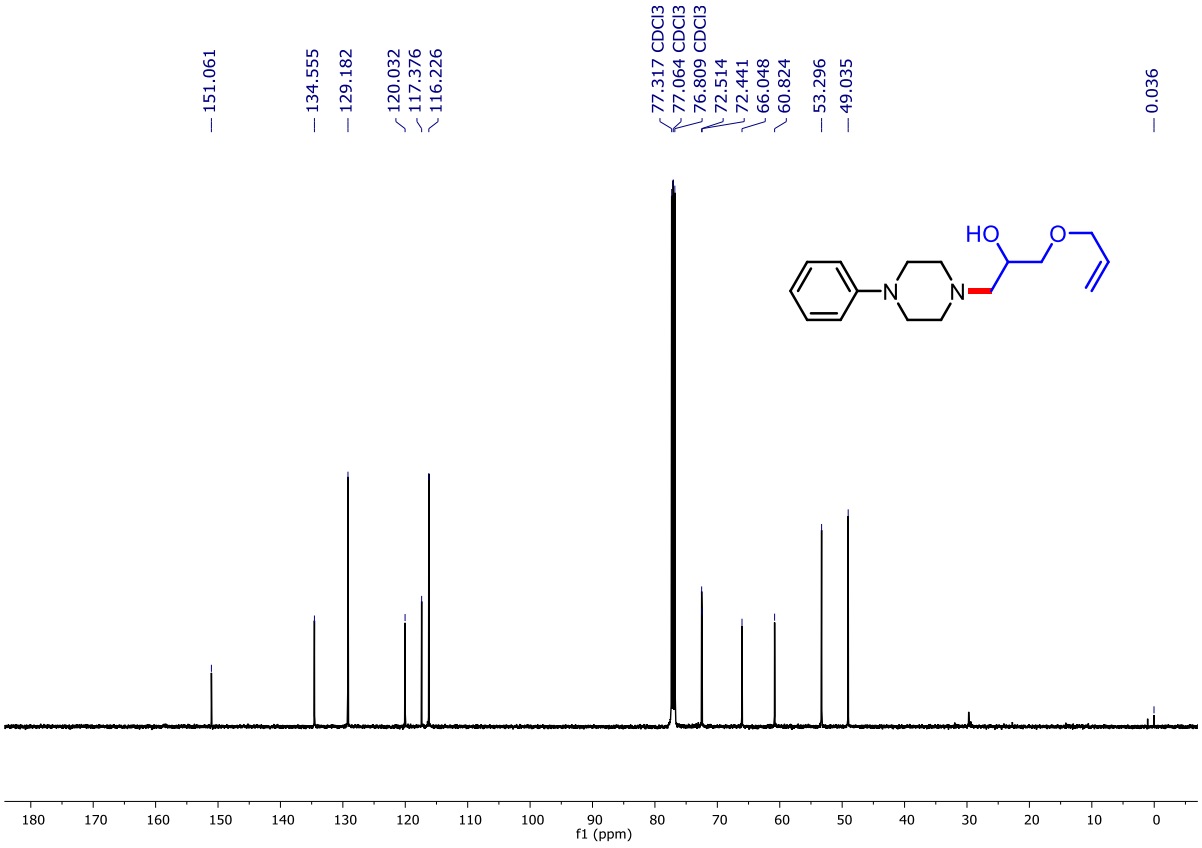
Allyl 2-oxo-2-(4-phenylpiperazin-1-yl)acetate (4b): ^{13}C NMR (125 MHz, $CDCl_3$)



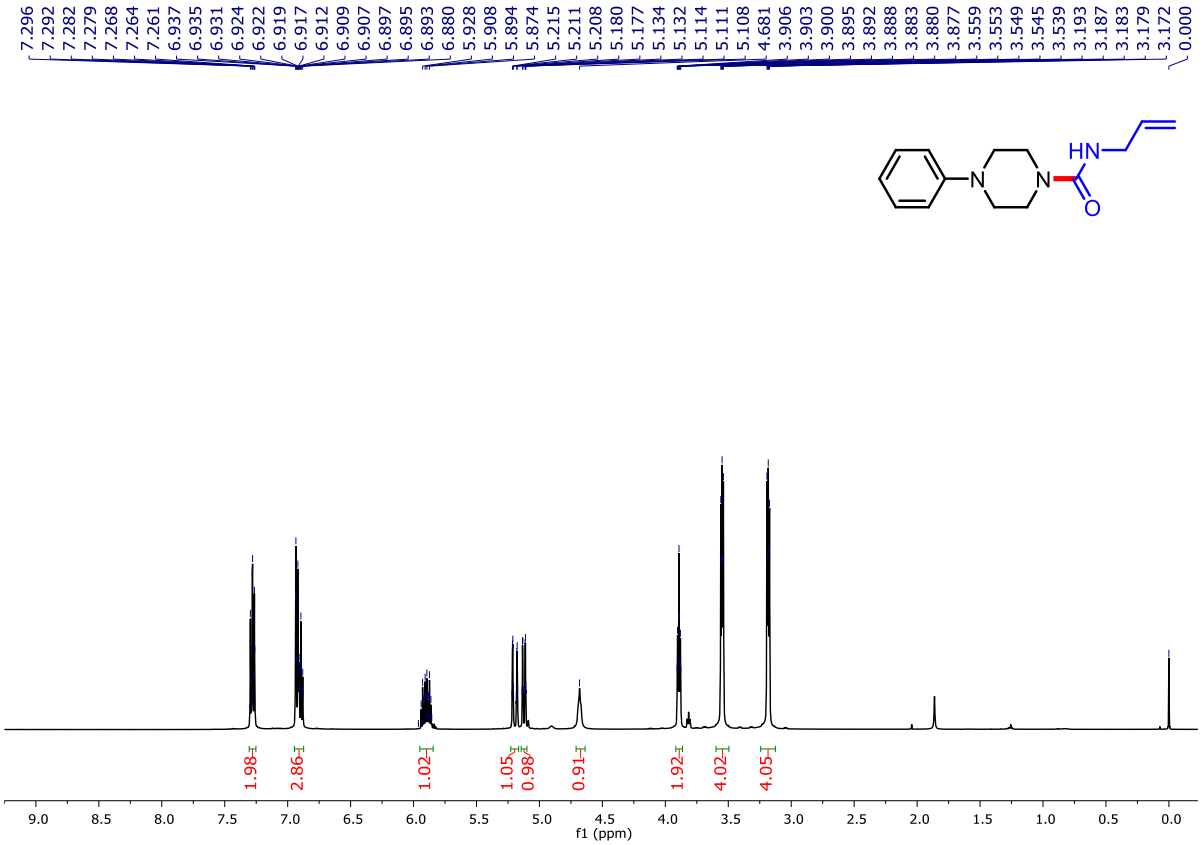
1-(allyloxy)-3-(4-phenylpiperazin-1-yl)propan-2-ol (4c): ^{1}H NMR (500 MHz, $CDCl_3$)



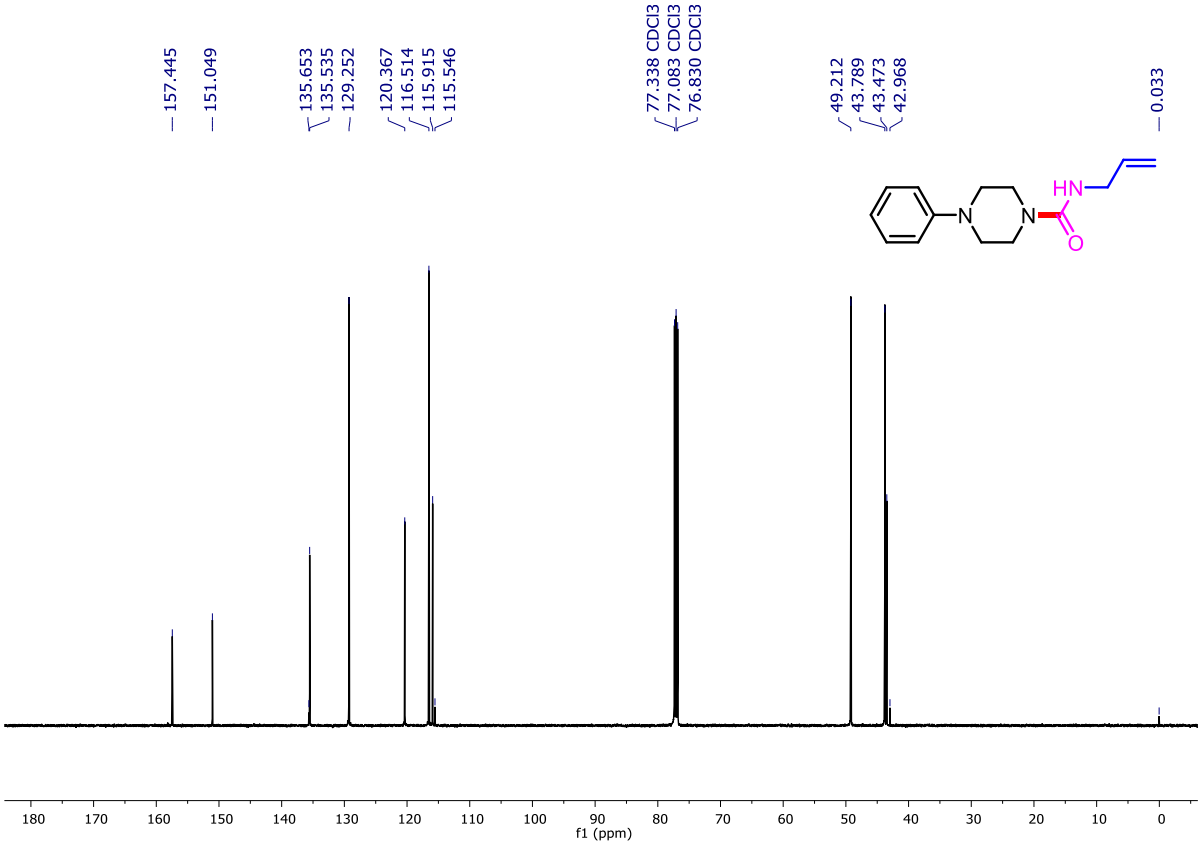
1-(allyloxy)-3-(4-phenylpiperazin-1-yl)propan-2-ol (4c): ^{13}C NMR (125 MHz, $CDCl_3$)



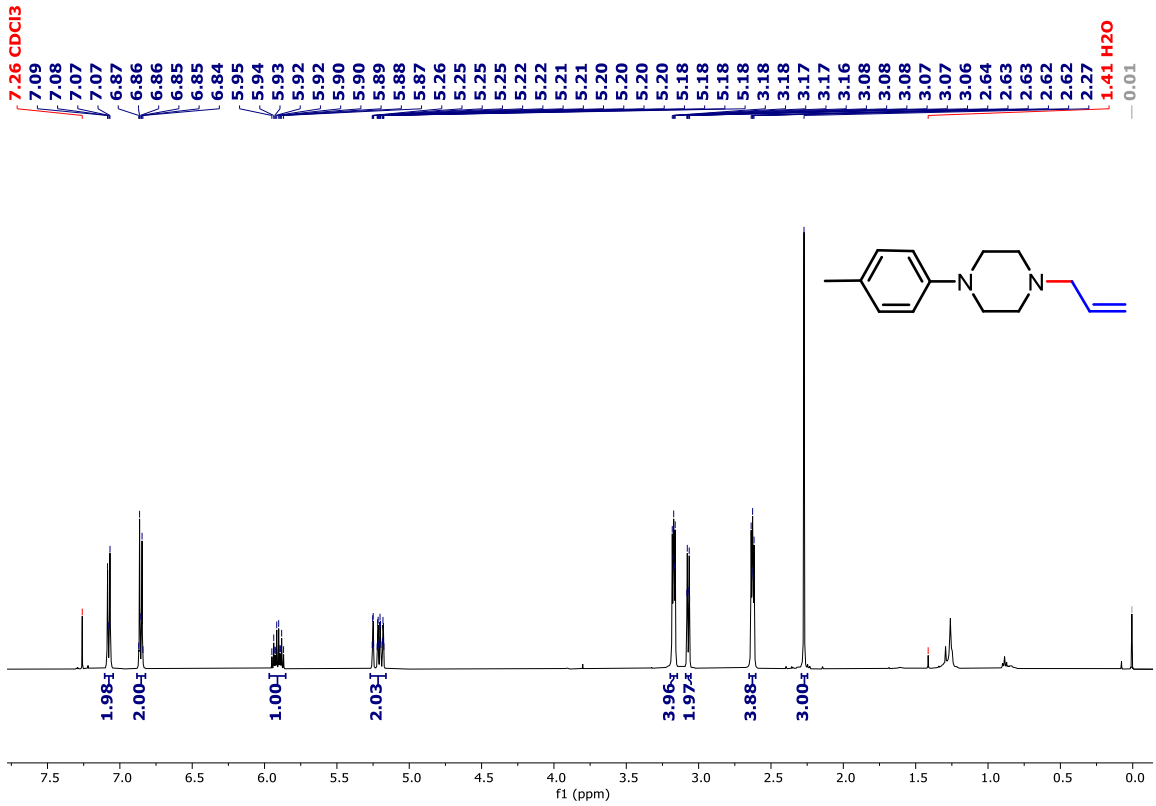
***N*-allyl-4-phenylpiperazine-1-carboxamide (4d):** ^{1}H NMR (500 MHz, $CDCl_3$)



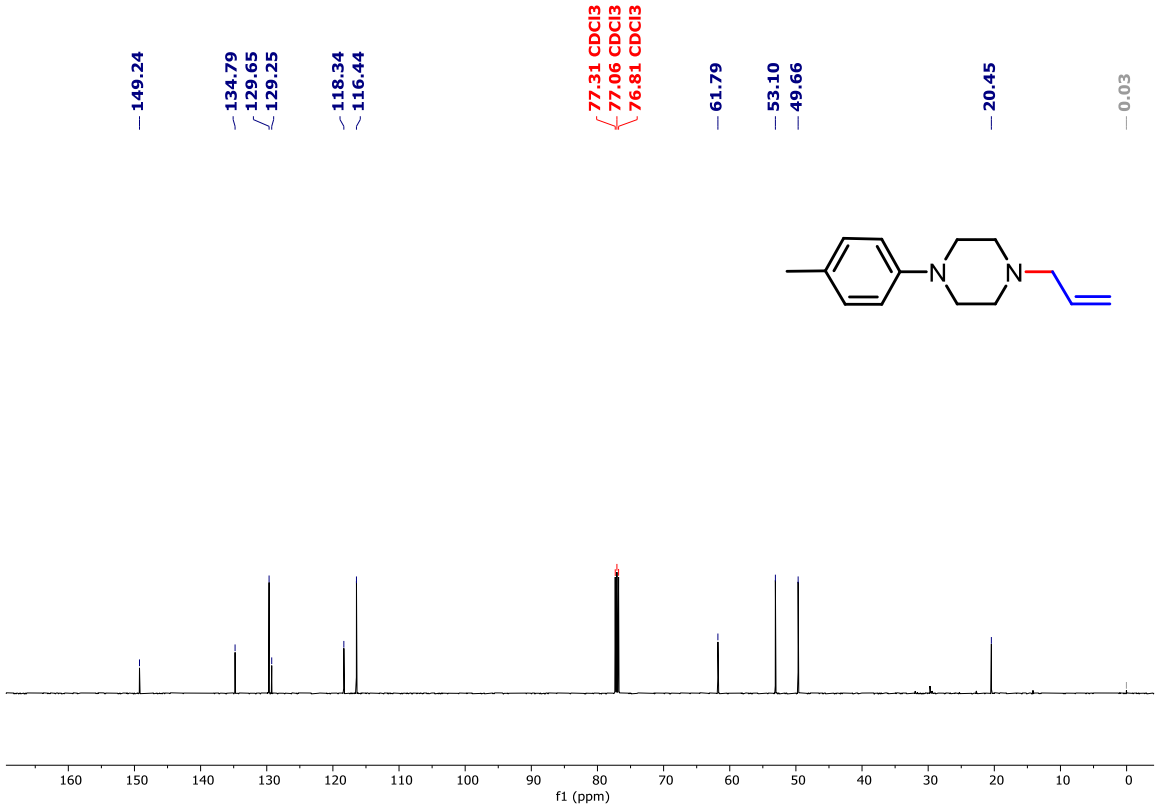
***N*-allyl-4-phenylpiperazine-1-carboxamide (4d):** ^{13}C NMR (125 MHz, $CDCl_3$)



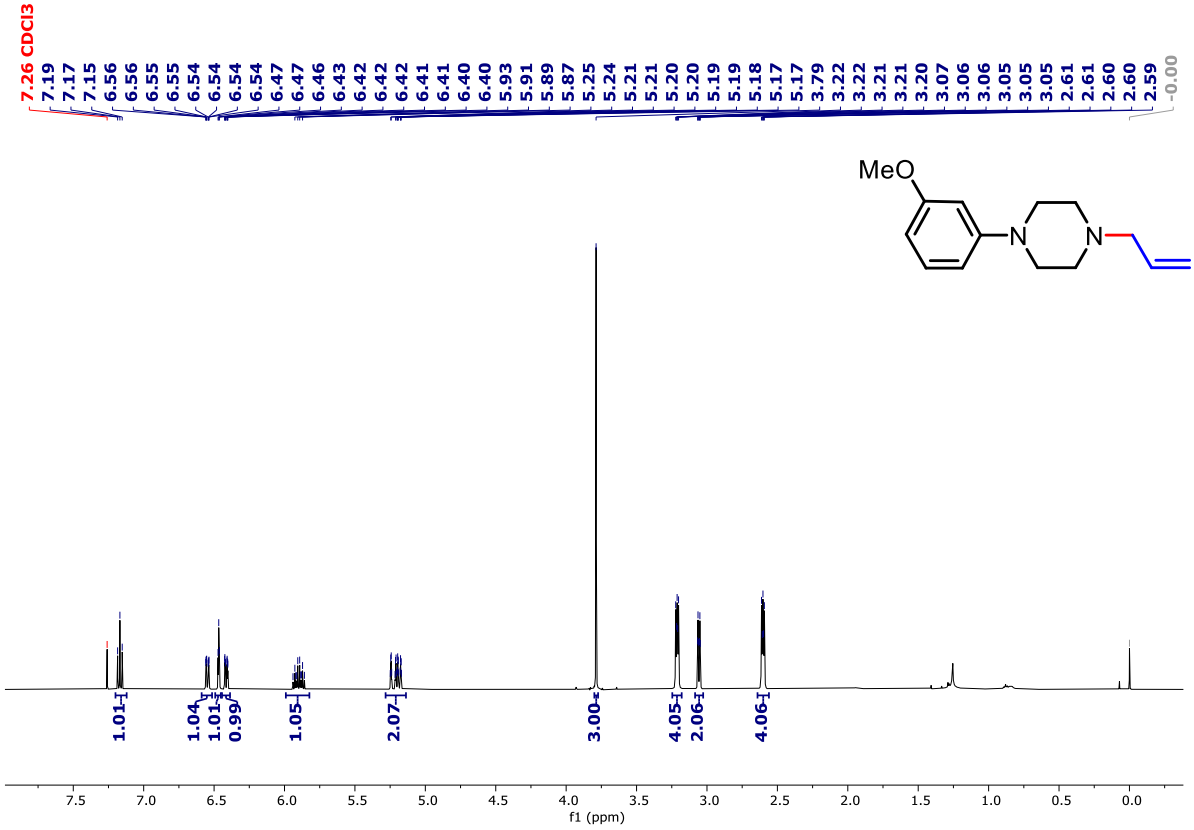
1-allyl-4-(p-tolyl)piperazine (3b): ^{1}H NMR (500 MHz, $CDCl_3$)



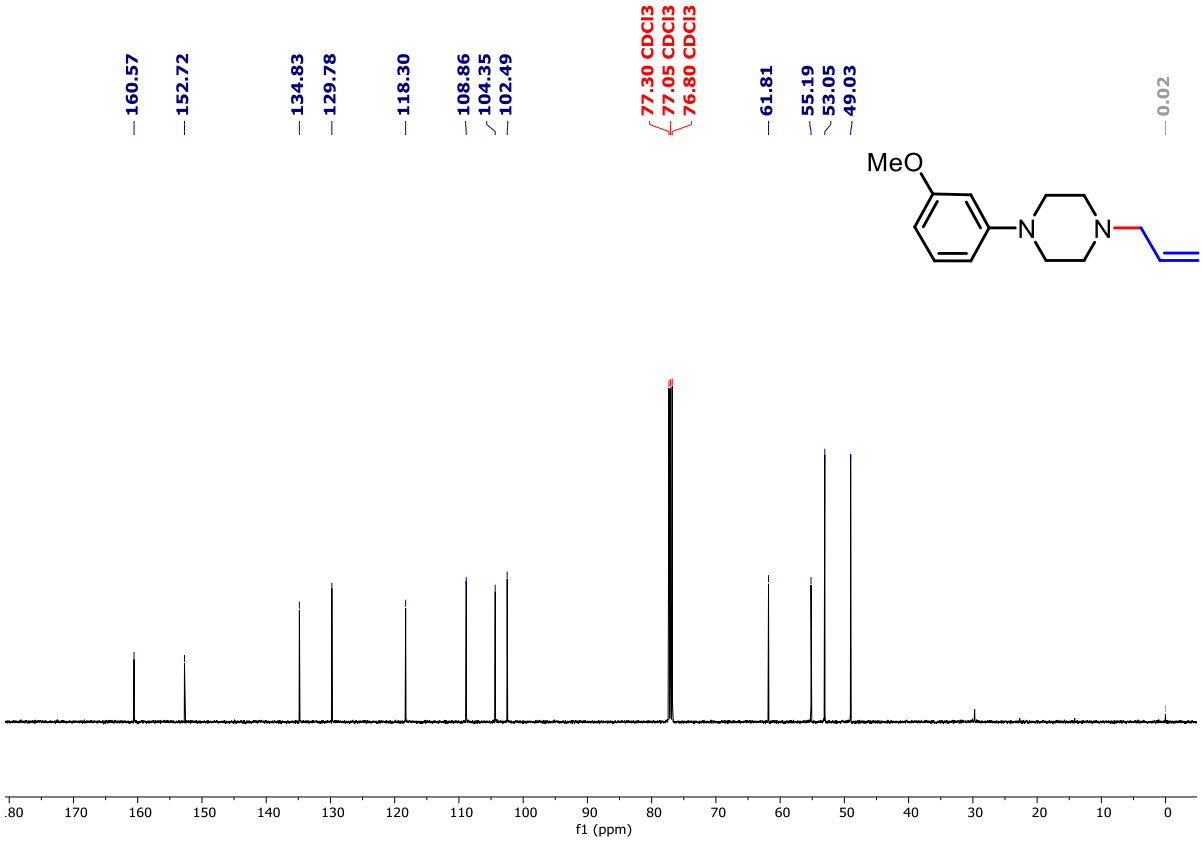
1-allyl-4-(p-tolyl)piperazine (3b): ^{13}C NMR (125 MHz, $CDCl_3$)



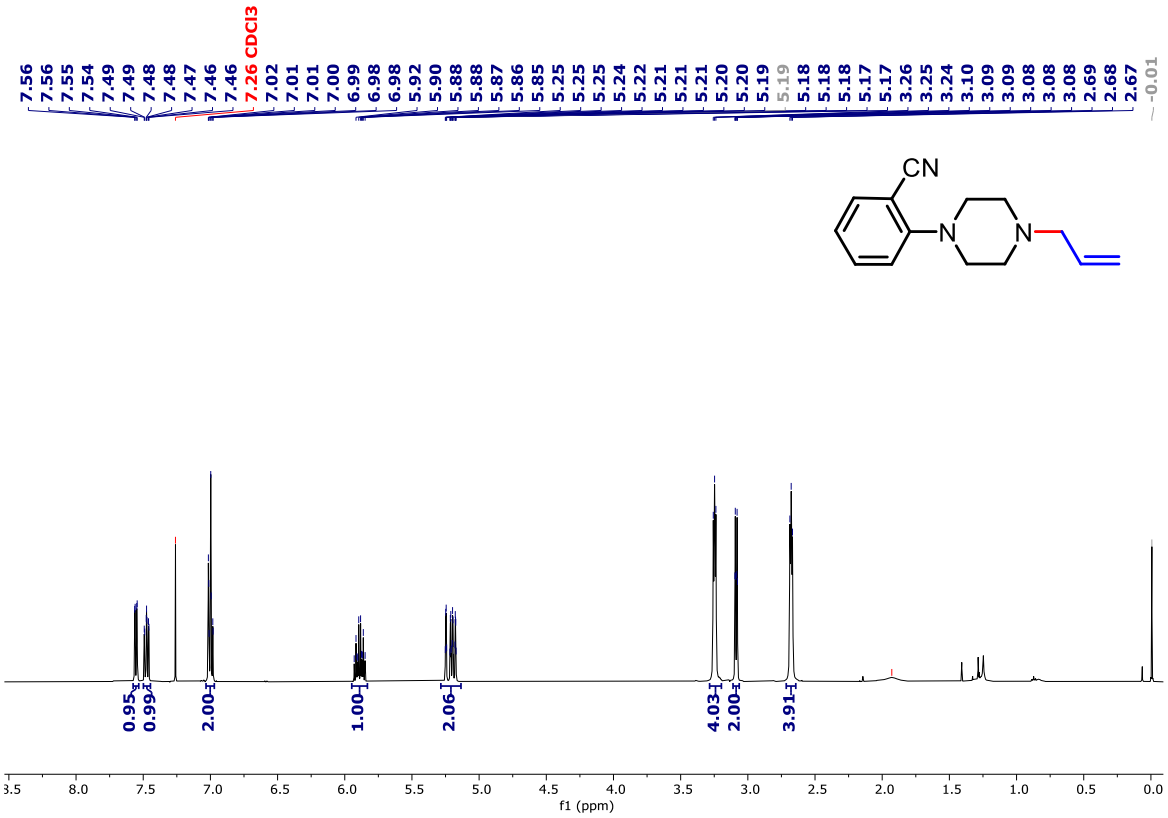
1-allyl-4-(3-methoxyphenyl)piperazine (3c): ^{1}H NMR (500 MHz, $CDCl_3$)



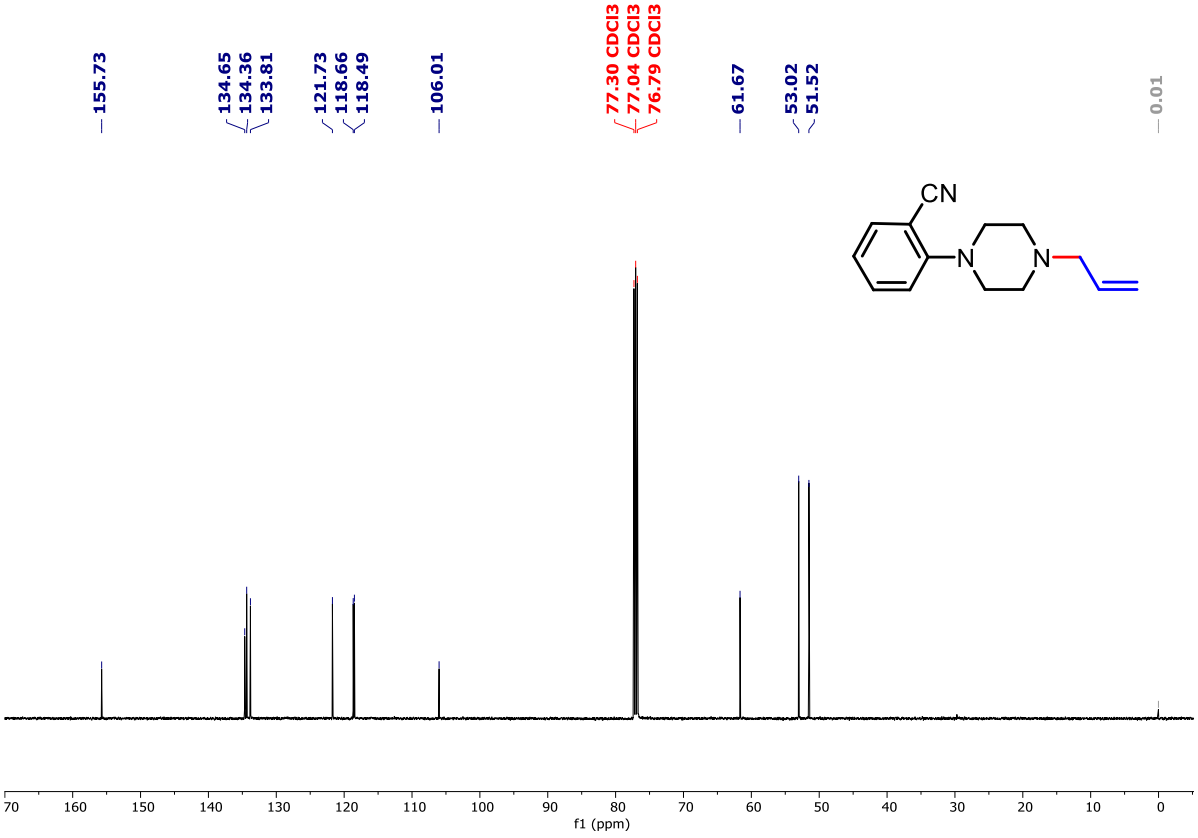
1-allyl-4-(3-methoxyphenyl)piperazine (3c): ^{13}C NMR (125 MHz, $CDCl_3$)



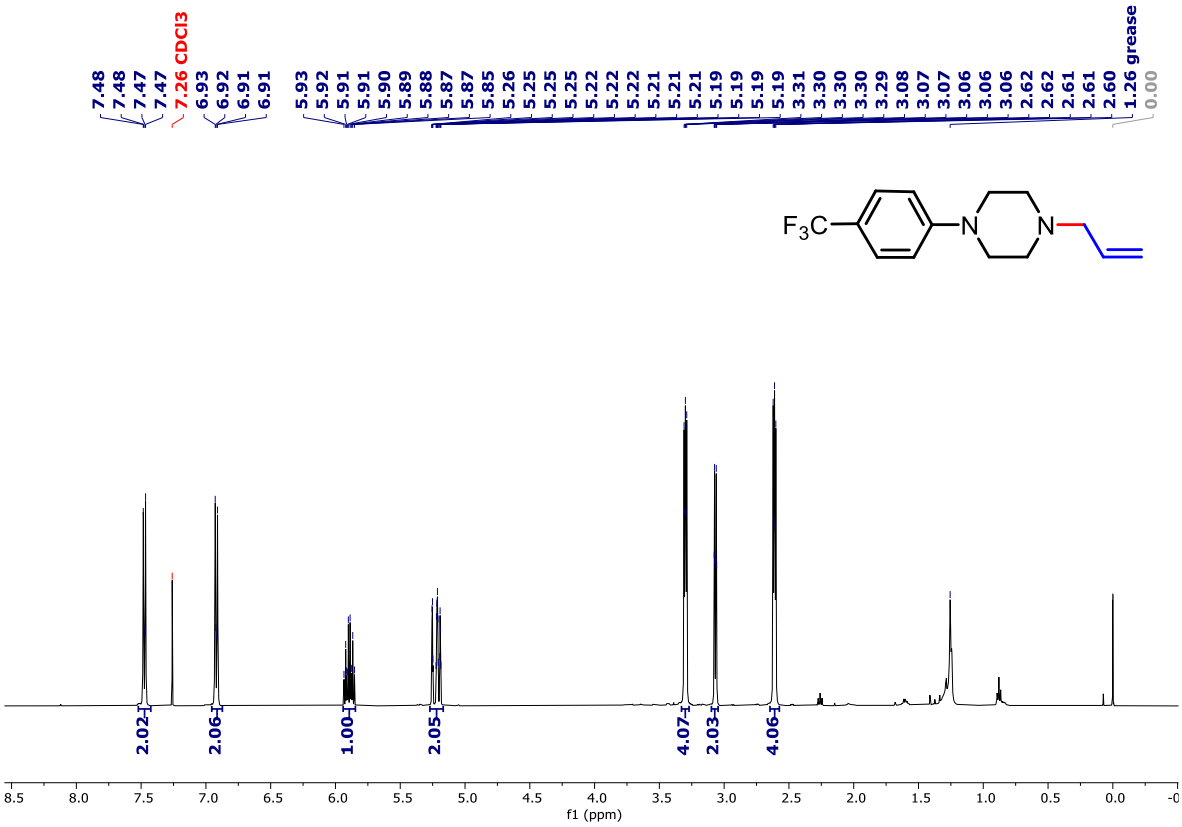
2-(4-allylpiperazin-1-yl)benzonitrile (3d): ^{1}H NMR (500 MHz, $CDCl_3$)



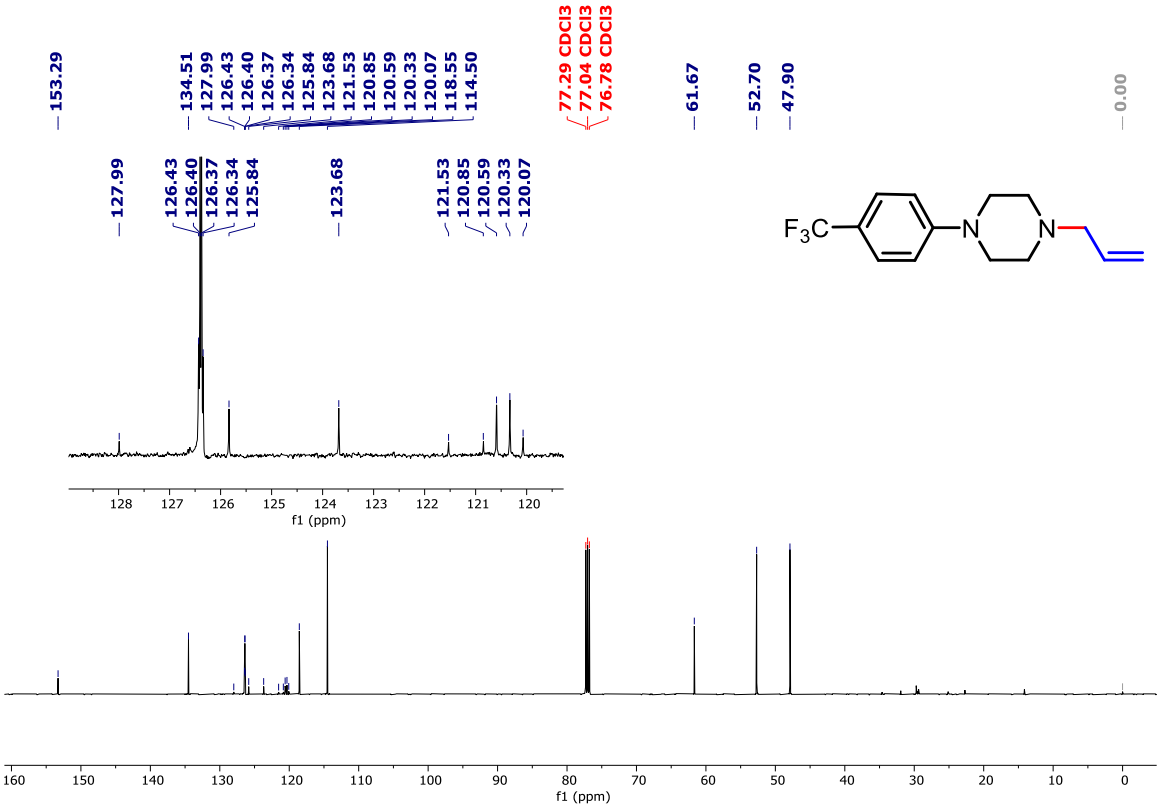
2-(4-allylpiperazin-1-yl)benzonitrile (3d): ^{13}C NMR (125 MHz, $CDCl_3$)



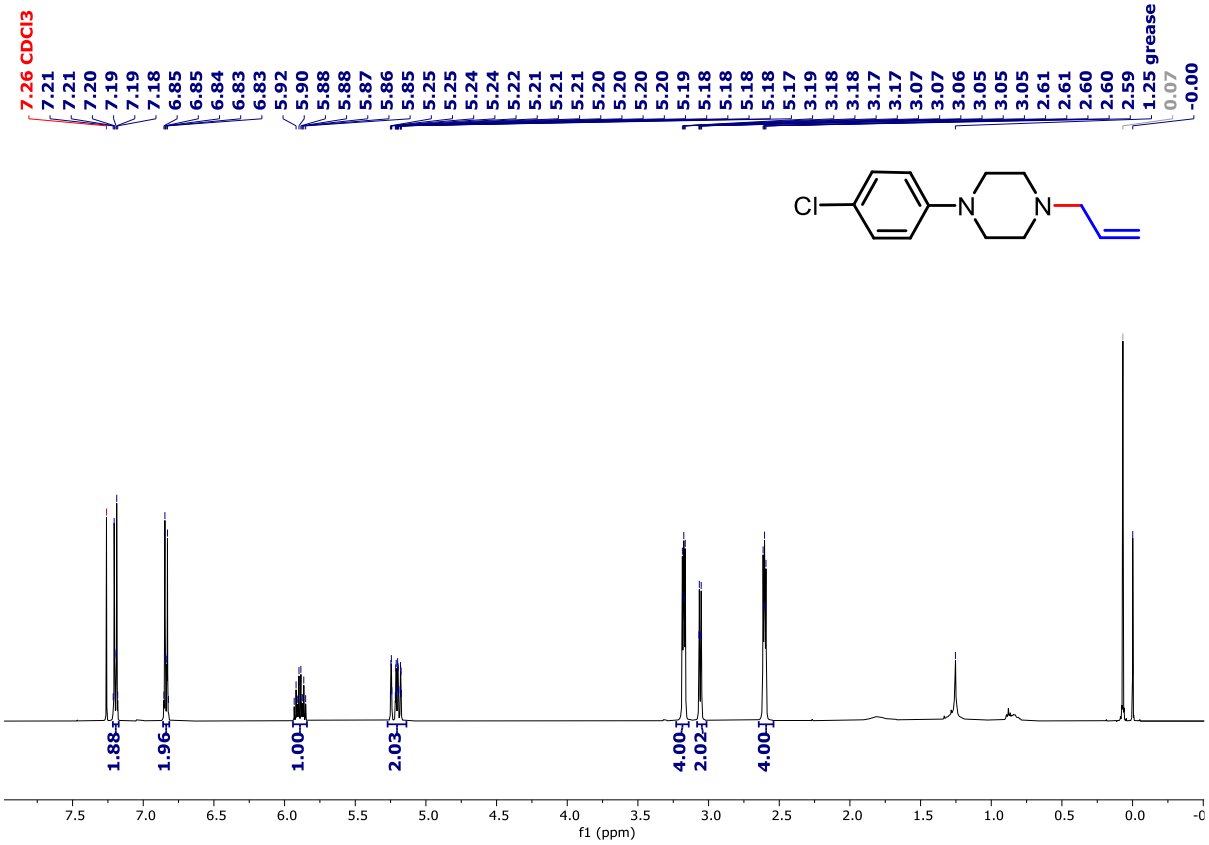
1-allyl-4-(4-(trifluoromethyl)phenyl)piperazine (3e): ^{1}H NMR (500 MHz, $CDCl_3$)



1-allyl-4-(4-(trifluoromethyl)phenyl)piperazine (3e): ^{13}C NMR (125 MHz, $CDCl_3$)



1-allyl-4-(4-chlorophenyl)piperazine (3f): ^{1}H NMR (500 MHz, $CDCl_3$)



1-allyl-4-(4-chlorophenyl)piperazine (3f): ^{13}C NMR (125 MHz, $CDCl_3$)