Supplementary Materials for

Primary α-Tertiary Amine Synthesis via α-C–H Functionalization

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1: General information:

All reagents bought from commercial sources were used as received. Organic solvents were evaporated under reduced pressure using a Büchi rotary evaporator. All solvents were commercially supplied or dried by filtration through activated alumina (powder ~150 mesh, pore size 58 Å, basic, Sigma-Aldrich) columns. Petrol ether (PE) refers to distilled light petroleum of fraction 30 - 40 °C. Toluene was distilled twice over calcium hydride.

All reactions were followed by thin-layer chromatography (TLC) when practical, using Merck Kieselgel 60 F254 fluorescent treated silica. Visualization was accomplished under UV light (λ\text{max} = 254 nm) and by staining with potassium permanganate staining dip. Chromatographic purification was performed on VWR 60 silica gel 40-63 μm using HPLC grade solvents that were used as supplied. NMR spectra were recorded on Bruker spectrometers operating at 400 or 500 MHz (\textsuperscript{1}H resonance). Proton chemical shifts (δ) are given in parts per million (ppm) relative to tetramethylsilane (TMS) with the solvent resonance as internal standard: CDCl\textsubscript{3}, δ = 7.26 ppm; CD\textsubscript{2}Cl\textsubscript{2}, δ = 5.32 ppm; CD\textsubscript{3}CN, δ = 2.13 ppm; CD\textsubscript{3}OD, δ = 3.31 ppm. The following abbreviations are used to describe spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, ddt = doublet of doublet of triplets, m = multiplet, br s = broad signal. Coupling constants (J) are given in Hertz (Hz). \textsuperscript{13}C NMR spectra were recorded with complete proton decoupling. Carbon chemical shifts are reported in ppm (δ) relative to TMS with the solvent resonance as internal standard: CDCl\textsubscript{3}, δ = 77.16 ppm; CD\textsubscript{2}Cl\textsubscript{2}, δ = 53.84 ppm; CD\textsubscript{3}CN, δ = 1.32 ppm. CD\textsubscript{3}OD, δ = 49.00 ppm. Two-dimensional NMR spectroscopy experiments (COSY, HSQC and HMBC) were used where appropriate to assist in the assignment of signals in \textsuperscript{1}H and \textsuperscript{13}C spectra and data are not reported. High-resolution mass spectra (HRMS) were recorded on Bruker Daltonics MicroTOF mass spectrometer equipped with an ESI source. Infrared spectra (IR) were recorded on a Bruker Tensor 27 FT-IR spectrometer from a thin film on a diamond ATR module. Only selected maximum absorbances are reported. All other commercial reagents were used without further purification, unless otherwise indicated.
2: Optimization study:

2.1: Optimization for organometallic addition:

We began our investigation by screening various quinones against 1-(4-methoxyphenyl)ethan-1-amine with commercially available allylmagnesium bromide and the results are summarised in Table S1. Further screening in solvents reveal that toluene (entry 5) is superior to chlorinated (entry 6) or ethereal solvents (entries 7-9) under these standard conditions. DCE is superior to other solvents for p-quinones E and F, due to its poor solubility. No hemiaminal formation occurred with both p-quinones E and F (entries 10-11) with DCE at either 25 °C or 80 °C which suggest that are not suitable reagents for this transformation.

2.2: Optimization for cyanation:

After several attempts, we were delighted to found that the careful selection of solvents along with the nucleophile source (TMSCN), can play a crucial role in the incorporation of nitriles to the ketimines (Table S2). The reaction is unsuccessful with toluene alone but successful with the combination of toluene and MeOH in 2:1 ratio (0.1 M), suggesting that MeOH is crucial for the
generation of HCN from TMSCN. Pleasingly, almost comparable results were observed (entries 2-3) with MeOH (0.1 M) alone. For the sake of convenience and homogeneity, we decided to use MeOH (0.1 M) as solvent for the subsequent transformations.

2.3: Optimization for oxidative cleavage of phenol unit:

The initial oxidative conditions (I₂/NaOH) were unsuccessful and gave only the undesired imine 49'' (Table S3, entry 1). Further hydrolysis of 49'' with either aqueous NaOH or aqueous HCl gave complex mixture of products. After numerous attempts by screening a variety of oxidants, we were pleased to find that orthoperiodic acid (H₅IO₆) proved to be more efficient and cleaved the phenolic unit completely from the cyanoaddition product (entry 8).
3: General Procedures:

3.1: Synthesis of o-quinones:

3.1.1: Synthesis of 4-(tert-butyl)-o-benzoquinone (A):

The compound A was synthesised using the known literature method with slight modifications. To an ether (30 mL) solution of 4-tert-butylcatechol S3 (0.50 g, 2.57 mmol) and Na2SO4 (0.1 g) was added Ag2O (3.10 g, 13.4 mmol) at 25 °C and stirred the resulting heterogeneous mixture for 10-15 min. After completion as indicated by TLC, the ether layer was collected by filtration. The combined ether layer was dried by Na2SO4 and concentrated to give 4-(tert-butyl)-o-benzoquinone A as a red solid (0.91 g, 5.60 mmol, 92%).

1H NMR (400 MHz, CDCl3): δ 7.18 (dd, J = 10.4, 2.4 Hz, 1 H), 6.40 – 6.31 (m, 1 H), 6.24 (dd, J = 2.2, 1.2 Hz, 1 H), 1.22 – 1.20 (m, 9 H). 13C NMR (101 MHz, CDCl3): δ 180.4, 180.3, 162.2, 140.2, 129.5, 123.9, 35.7, 27.9. The remaining data is consistent with the literature precedent.1

3.1.2: Synthesis of 4-(tert-butyl)-5-methoxy-o-benzoquinone (B):

The compound B was synthesised using the known literature method with slight modifications. 4-(tert-butyl)benzene-1,2-diol S4 (1.00 g, 6.02 mmol) was dissolved in a 100 mL round bottom flask using 20 mL of methanol. To this, NaIO4 (1.93 g, 9.02 mmol) was added at 25 °C and stirred for 1 h. After completion as indicated by TLC, water (50 mL) was added and the resulting solution was extracted with ether (100 mL), dried (Na2SO4) and evaporated under rotary evaporator. The crude dark red sticky material was triturated with n-pentane to give a red solid of 4-(tert-butyl)-5-methoxy-o-benzoquinone B (0.69 g, 3.55 mmol, 59%). The data is consistent with the literature precedent.1
3.1.3: Synthesis of 3,5-diisopropyl-o-benzoquinone (C):

The compound C was synthesised using the known literature method with slight modifications. 3,5-diisopropylcatechol S5 (0.50 g, 2.57 mmol) was dissolved in a 100 mL round bottom flask using 49 mL of EtOAc and 2.5 mL of water (20:1, 0.05 M) and the resulting biphasic solution was cooled to 0 °C before the addition of bleach (NaOCl·5H2O) (3.02 mL, 2.57 mmol, 6-14% active Cl2). The resulting heterogeneous green solution was stirred for exactly 30 minutes at 0 °C. After this time, the crude product was taken into separating funnel and organic phase was separated, washed with brine and dried (Na2SO4), filtered, and concentrated under reduced pressure. The crude product was recrystallized using pentane gave a deep brown solid of compound C (380 mg, 1.98 mmol, 77%). 1H NMR (400 MHz, CDCl3): δ 6.62 (d, J = 0.9 Hz, 1 H), 6.11 (d, J = 0.9 Hz, 1 H), 2.97 (m, 1 H), 2.55 (m, 1 H), 1.19 (d, J = 6.8 Hz, 6 H), 1.12 (d, J = 6.8 Hz, 6 H). 13C NMR (101 MHz, CDCl3): δ 180.8, 180.4, 161.8, 149.1, 134.6, 122.2, 34.9, 27.5, 21.7, 20.6. The remaining data was consistent with the literature.2

3.1.4: Synthesis of 3,5-di-tert-butyl-o-benzoquinone (D):

The compound D was synthesised using the known literature method with slight modifications. 3,5-di-tert-butylcatechol S6 (12.5 g, 56.3 mmol) was dissolved in a 2 L round bottom flask using 1.07 L of EtOAc and 53.6 mL of water (20:1, 0.05 M) and the resulting biphasic solution was cooled to 0 °C before the addition of bleach (NaOCl·5H2O) (66.0 mL, 56.2 mmol, 6-14% active Cl2). The resulting heterogeneous green solution was stirred for exactly 30 minutes at 0 °C. After this time, the crude product was taken into separating funnel and organic phase was separated, washed with brine and dried (Na2SO4), filtered, and concentrated under reduced pressure. The crude product was recrystallized using pentane gave a deep red crystals of compound D (11.9 g, 53.97 mmol, 96%). 1H NMR (400 MHz, CDCl3): δ 6.92 (d, J = 2.3 Hz, 1 H), 6.20 (d, J = 2.3 Hz, 1 H), 1.26 (s, 9 H), 1.21 (s, 9 H).
$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 181.3, 180.2, 163.4, 150.1, 133.6, 122.2, 36.2, 35.6, 29.3, 28.0. The remaining data was consistent with the literature.

3.2: **General Procedure A** for $\alpha$-C–H Functionalization of primary amines with Grignard reagent:

The synthesis of 2-(4-methoxyphenyl)pent-4-en-2-amine 1 is representative. To a stirred solution of 3,5-di-tert-butyl-o-benzoquinone D (0.29 g, 1.32 mmol, 1.0 equiv) in toluene (6.0 mL), was added a solution of 1-(4-methoxyphenyl)ethan-1-amine S1 (0.20 g, 1.32 mmol, 1.0 equiv) in toluene (7.2 mL) dropwise over 5 min under argon atmosphere. The deep green coloured solution was stirred at room temperature for 2 h. After completion as indicated by TLC (*Note: colour changes from deep green to dark violet*), the reaction mixture was cooled to 0 $^\circ$C, and was added TMEDA (0.19 mL, 1.32 mmol, 1.0 equiv) and allylmagnesium bromide (1.0 M in Et$_2$O, 7.94 mL, 7.94 mmol, 6.0 equiv) and maintained at 0$^\circ$C for 1 h. During the Grignard addition, the colour of the reaction mixture changes from dark violet to yellowish brown. The reaction temperature was gradually allowed to return to 25 $^\circ$C and allowed to stir until TLC analysis (A small aliquot of the reaction mixture was worked up in NH$_4$Cl-EtOAc to check TLC (Pentane:EtOAc 9.5:0.5)) showed complete conversion. After completion of the reaction as indicated by TLC, the reaction mixture was again cooled to 0 $^\circ$C and aqueous NaOH (1 M) (6.62 mL, 6.62 mmol, 5.0 equiv) was carefully added dropwise to quench the remaining Grignard reagent. To the resulting heterogeneous mixture were added 26 mL of CH$_3$CN (0.05 M) and iodine granules (0.40 g, 1.59 mmol, 1.2 equiv) and stirred vigorously for 10 min under argon
atmosphere. The o-quinone reappeared gradually during basic oxidation. After completion, reaction mixture was extracted with CH$_3$CN (3 x 20 mL). The combined organic layers were washed with aqueous saturated sodium thiosulfate (1 x 10 mL) and brine (2 x 10 mL), respectively, dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The crude residue was purified by column chromatography on silica gel eluting with Pentane:EtOAc (80:20 v:v) to EtOAc:MeOH:Et$_3$N (70:20:10 v:v) to afford compound 1 (205 mg, 1.07 mmol, 81%) as a yellow oil.

3.3: General Procedure B for α-C–H Functionalization of primary amines with Grignard reagent:

The synthesis of 4-allyltetrahydro-2H-pyran-4-amine hydrochloride 27 is representative. For volatile, low boiling point amines, a modified work-up was employed. After oxidative cleavage of the o-quinone, the reaction mixture was extracted with CH$_3$CN (3 x 20 mL). The combined organic layers were washed with saturated sodium thiosulfate (1 x 10 mL), brine (2 x 10 mL) respectively. The organic layer was acidified with aqueous 2 M HCl and extracted two times (2 x 20 mL) with aqueous 2 M HCl. The combined aqueous phases were washed with hexane and concentrated in vacuo (Bath temp: 60 °C, 72 mbar) to afford the crude yellow solid, which was dissolved in warm CHCl$_3$, dried over Na$_2$SO$_4$, filtered, and concentrated under reduced pressure to give 4-allyltetrahydro-2H-pyran-4-amine hydrochloride 27 (139 mg, 0.78 mmol, 79%) as off-white powder.

3.4 General Procedure C for α-C–H Functionalization of primary amines with organolithium reagents:
The synthesis of 1-(4-methoxyphenyl)-1-(4-(trifluoromethyl)phenyl)ethan-1-amine 47 is representative. To a stirred solution of 3,5-di-tert-butyl-o-benzoquinone D (0.15 g, 0.66 mmol, 1.0 equiv) in toluene (3.3 mL), was added a solution of 1-(4-methoxyphenyl)ethan-1-amine S1 (0.10 g, 0.66 mmol, 1.0 equiv) in toluene (3.3 mL) dropwise over 5 min under argon atmosphere. The deep green coloured solution was stirred at room temperature for 2 h. In the meantime, the organolithium was prepared by treating 1-iodo-4-(trifluoromethyl)benzene (0.58 mL, 3.97 mmol, 6 equiv) with tBuLi (4.67 mL, 7.94 mmol, 1.7 M in pentane, 12 equiv) at -78 °C for 30 min in dry Et₂O (0.1 M) under argon atmosphere. After completion of the ketimine/hemiaminal formation as indicated by TLC (Note: colour changes from deep green to dark violet), the reaction mixture was treated with TMEDA (94 µL, 0.66 mmol, 1.0 equiv) and transferred through syringe to the flask containing (4-(trifluoromethyl)phenyl)lithium at -78 °C, and the resulting mixture stirred for 8 h at 25 °C. A small aliquot of the reaction mixture was worked up in NH₄Cl-EtOAc to check TLC (Pentane:EtOAc 9.5:0.5). After completion of the reaction as indicated by TLC, the reaction mixture was cooled to 0 °C and aqueous NaOH (1 M) (3.31 mL, 3.31 mmol, 5.0 equiv) was added dropwise to quench the remaining organolithium reagent. To this mixture were added 13 mL of CH₃CN and iodine granules (0.20 g, 0.79 mmol, 1.2 equiv) and the mixture stirred vigorously for 10 min under argon atmosphere. The o-quinone reappeared gradually during basic oxidation. After completion, the reaction mixture was extracted with CH₃CN (3 x 20 mL). The combined organic layers were washed with aqueous saturated sodium thiosulfate (1 x 10 mL) and brine (2 x 10 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica gel eluting with Pentane:EtOAc (80:20 v:v) to EtOAc:MeOH:Et₃N (70:20:10 v:v) to afford compound 47 (129 mg, 0.44 mmol, 66%) as a brown oil.

3.5 General Procedure D for oxidative cyanation of primary amines:

The synthesis of 4-aminotetrahydro-2H-pyran-4-carbonitrile 54 is representative.⁷

To a stirred solution of 3,5-di-tert-butyl-o-benzoquinone D (0.22 g, 0.99 mmol, 1.0 equiv) in MeOH (5.0 mL), was added slowly a solution of 4-aminotetrahydropyran S7 (0.10 g, 0.99 mmol, 1.0 equiv) in MeOH (5 mL) dropwise over 5 min and the resulting mixture was stirred for 1 h at 25 °C. After
completion as indicated by TLC, the reaction mixture was then cooled to 0°C and trimethylsilyl cyanide (0.74 mL, 5.93 mmol, 6.0 equiv) was added. The resulting mixture was gradually allowed to return to 25 °C and allowed to stir until TLC analysis showed complete conversion. After completion as indicated by TLC, solvent and excess trimethylsilyl cyanide were removed on a rotary evaporator using bath temperature below 25 °C (Caution: high bath temperature causes decomposition of addition product). The resulting grey solid was dissolved in CH$_3$CN:H$_2$O (1:1) (14.1 mL), and cooled to 0 °C. To the resulting mixture was added orthoperiodic acid (H$_5$IO$_6$) (0.24 g, 1.04 mmol, 1.05 equiv) and stirred vigorously for 10 min (appearance of brown colour denotes reformation of quinone). After completion, the organic solvent was removed under reduced pressure (Bath temp: 40 °C) and the resulting aqueous acidic phase was washed with Et$_2$O:Hexane (10:1) (2 x 10 mL), and the aqueous phase was then concentrated in vacuo (Bath temp: 60 °C, 72 mbar). The resulting residue was basified with 1 M NaOH (5 mL) and extracted with CHCl$_3$ (3 x 10 mL). The combined organic layers were washed with brine, dried over Na$_2$SO$_4$, filtered and concentrated in vacuo to afford the 4-aminotetrahydro-2H-pyran-4-carbonitrile 54 as a yellow oil (121 mg, 0.96 mmol, 97%). In most cases (48, 51, 52, 53, 55, 56, 66, 68), the obtained crude products were pure, and no further purification was performed. Compounds 49 and 50 were purified by column chromatography on Et$_3$N-treated silica gel eluting with (pentane/EtOAc = 80:20 v:v) to (EtOAc:MeOH:Et$_3$N = 70:20:10 v:v).

3.6: General Procedure E for the photocatalytic reverse polarity α-allylation:

To a mass spec vial under a stream of N$_2$ was equipped a micro-stirrer charged 3,5-di-tert-butyl-o-benzoquinone D (55.0 mg, 0.25 mmol), anhydrous MeOH (0.50 mL), and relevant benzylamine structure (0.25 mmol). The nitrogen line was removed and the reaction mixture allowed to stir for 2
The solvent was then removed under a nitrogen stream. To the residue was added anhydrous DMSO (0.25 mL), followed by \((\text{Ir}[\text{dFCF}_3\text{ppy})_2(\text{dtbbpy})]\)PF$_6$ ([Ir], 2.8 mg, 0.0025 mmol), diethyl 1,4-dihydro-2,6-dimethyl-3,5-pyridinedicarboxylate (HE, 95.0 mg, 0.375 mmol) and tert-butyl 2-((phenylsulfonyl)methyl)acrylate (282 mg, 1.00 mmol). The reaction mixture was then degassed with N$_2$ for 10 min. The flask was sealed and allowed to stir for 20 h under blue light irradiation. After this time the reaction mixture was cooled to 0 °C, and MeCN (0.50 mL), water (0.25 mL) and periodic acid (63.0 mg, 0.28 mmol) were added. The resulting mixture went instantly deep brown to signal reformation of 3,5-di-tert-butyl-o-benzoquinone and was then allowed to stir at 0 °C for 30 min. The reaction mixture was poured into a separating funnel containing water (5 mL) and Et$_2$O (10 mL). The aqueous phase was extracted, and the organic phase re-extracted with water (4 x 5 mL). To the combined aqueous phases was added NaOH (1M, 10 mL). The aqueous phase was then extracted with EtOAc:MeCN (1:1, 5 x 10 mL). The combined organics were then washed with NaOH (1M, 5 x 5 mL) and the organics were dried over MgSO$_4$ and concentrated in vacuo. The crude residue was then purified via silica gel column chromatography to give the desired primary amine product.

3.7: Procedure for Alternative Protocol (Scheme 6A)

To a stirred solution of 3,5-di-tert-butyl-o-benzoquinone D (1.75 g, 7.94 mmol, 1.01 equiv) in toluene (40 mL), was added a solution of 1-(4-methoxyphenyl)ethan-1-amine S$_1$ (1.00 g, 7.86 mmol, 1.0 equiv) in toluene (40 mL) dropwise over 5 min under argon atmosphere. After completion as indicated by TLC (Note: colour changes from deep green to dark violet), the reaction mixture was concentrated in vacuo (150 – 5 mbar, 40 °C) to remove water. To the crude residue was added toluene (80 mL) and 4Å molecular sieves (and the reaction mixture was cooled to 0 °C. To the cooled solution was added TMEDA (1.18 mL, 7.86 mmol, 1.0 equiv) and allylmagnesium bromide (1.0 M in Et$_2$O, 19.63 mL, 19.63 mmol, 2.5 equiv) and maintained at 0°C for 30 mins. The reaction temperature was gradually allowed to return to 25 °C and allowed to stir until TLC analysis showed complete conversion. concentrated in vacuo (80 - 40 mbar, 60 °C, then high vacuum) to remove the TMEDA. (to assist product isolation post-oxidation). The crude residue was again cooled to 0 °C and aqueous NaOH (1 M) (6.62 mL, 6.62 mmol, 5.0 equiv) was carefully added dropwise to quench the remaining
Grignard reagent. To the resulting heterogeneous mixture were added 40 mL of CH$_3$CN (0.05 M) and iodine granules (3.99 g, 39.3 mmol, 2 equiv) and stirred vigorously for 10 min under argon atmosphere. The α-quinone reappeared gradually during basic oxidation. After completion, the reaction mixture was extracted with CH$_3$CN (3 x 80 mL). The combined organic layers were washed with saturated sodium thiosulfate (1 x 80 mL), brine (2 x 80 mL) respectively. The organic layer was acidified with aqueous 2 M HCl and extracted two times (2 x 80 mL) with aqueous 2 M HCl. The combined aqueous phases were washed with hexane and concentrated in vacuo (Bath temp: 60 °C, 72 mbar) to afford 25 as the hydrochloride salt, (993 mg, 4.87 mmol, 62%).

3.6.1: Photoreactor details:

Hepatochem PhotoRedOx Box, equipped with an EvoluChem LED 18 W light source supplied by Hepatochem. A cardboard cover was also placed over the reactor during reactions. Capable of carrying out up to 8 reactions at one time. Accurate and reproducible results, high throughput.
3.6.2: Coupling partner synthesis:

**Synthesis of tert-butyl 2-((phenylsulfonyl)methyl)acrylate:**

\[ \text{fBuO}_2\text{C} \quad \text{SO}_2\text{Ph} \]

To a 1 L round-bottomed flask containing tert-butyl acrylate (11.7 mL, 80.0 mmol) and formaldehyde (3.60 g, 120 mmol) in 1,4-dioxane (80 mL) and water (80 mL) was added 1,4-diazabicyclo[2.2.2]octane (11.6 g, 104 mmol) portionwise. The reaction mixture was allowed to stir at room temperature for 16 h. The resulting mixture was partitioned between EtOAc (200 mL) and water (200 mL). The organic layer was extracted and then washed with brine (300 mL). The organics were then dried over MgSO₄ and concentrated *in vacuo*. The crude residue was then dispersed in anhydrous Et₂O (300 mL) and the flask cooled to -10 °C. To the resulting mixture was added phosphorus tribromide (4.05 mL, 43.0 mmol) dropwise. The flask was allowed to warm to room temperature and stirred for 4 h. The flask was quenched by dropwise addition of water (200 mL). The resulting suspension was poured into a separating funnel and organic layer extracted. The aqueous phase was then re-extracted with pentane (2 x 200 mL). The combined organics were washed with brine, dried over MgSO₄ and concentrated *in vacuo*. The crude residue was dissolved in MeOH (300 mL) and was added sodium benzenesulfinate (5.50 g, 33.5 mmol) and the reaction mixture was heated to reflux for 16 h. The flask was allowed to cool for rt and then the MeOH was removed *in vacuo*. The crude residue was partitioned between EtOAc (200 mL) and water (200 mL). The organic layer was extracted and then washed with brine (300 mL), dried over MgSO₄ and concentrated *in vacuo*. The crude residue was purified via silica gel column chromatography (EtOAc:Pentane 3:7 v:v) to give the above compound as a white crystalline solid (4.90 g, 17.4 mmol, 22%).

**1H NMR** (400 MHz, CDCl₃): δ 7.88 – 7.78 (m, 2 H), 7.68 – 7.57 (m, 1 H), 7.57 – 7.43 (m, 2 H), 6.43 (d, J = 0.9 Hz, 1 H), 5.89 (d, J = 0.9 Hz, 1 H), 4.13 (d, J = 0.8 Hz, 2 H), 1.31 (s, 9 H).

**13C NMR** (101 MHz, CDCl₃): δ 163.8, 138.6, 133.9, 132.9, 130.4, 129.2, 129.0, 81.9, 57.5, 27.9. Data is in line with literature precedent.

**Synthesis of ethyl 2-((phenylsulfonyl)methyl)acrylate:**

\[ \text{EtO}_2\text{C} \quad \text{SO}_2\text{Ph} \]
To a 1 L round-bottomed flask containing ethyl acrylate (21.8 mL, 200 mmol) and formaldehyde (9.00 g, 300 mmol) in 1,4-dioxane (200 mL) and water (200 mL) was added 1,4-diazabicyclo[2.2.2]octane (29.1 g, 260 mmol) portionwise. The reaction mixture was allowed to stir at room temperature for 16 h. The resulting mixture was partitioned between EtOAc (300 mL) and water (300 mL). The organic layer was extracted and then washed with brine (300 mL). The organics were then dried over MgSO₄ and concentrated in vacuo. The crude residue was then dispersed in anhydrous Et₂O (300 mL) and the flask cooled to -10 °C. To the resulting mixture was added phosphorus tribromide (13.8 mL, 134 mmol) dropwise. The flask was allowed to warm to room temperature and stirred for 4 h. The flask was quenched by dropwise addition of water (300 mL). The resulting suspension was poured into a separating funnel and organic layer extracted. The aqueous phase was then re-extracted with pentane (2 x 300 mL). The combined organics were washed with brine, dried over MgSO₄ and concentrated in vacuo. The crude residue was dissolved in MeOH (300 mL) and was added sodium benzenesulfinate (19.4 g, 119 mmol) and the reaction mixture was heated to reflux for 16 h. The flask was allowed to cool for rt and then the MeOH was removed in vacuo. The crude residue was partitioned between EtOAc (300 mL) and water (300 mL). The organic layer was extracted and then washed with brine (300 mL), dried over MgSO₄ and concentrated in vacuo. The crude residue was purified via silica gel column chromatography (Et₂O:Pentane 3:7 v:v) to give the above compound as a thick colourless oil (19.1 g, 75.1 mmol, 38%).

1H NMR (400 MHz, CDCl₃): δ 7.84 (dd, J = 8.3, 1.3 Hz, 2 H), 7.70 – 7.59 (m, 1 H), 7.59 – 7.45 (m, 2 H), 6.49 (s, 1 H), 5.90 (d, J = 1.0 Hz, 1 H), 4.15 (d, J = 0.8 Hz, 2 H), 3.99 (q, J = 7.1 Hz, 2 H), 1.15 (t, J = 7.1 Hz, 3 H). 13C NMR (101 MHz, CDCl₃): δ 164.8, 138.5, 133.9, 133.4, 129.2, 129.1, 128.8, 61.5, 57.6, 14.1. Data is in line with literature precedent.

3.6.3: Catalyst Synthesis:

Synthesis of 2-(2,4-difluorophenyl)-5-(trifluoromethyl)pyridine:

![2-(2,4-difluorophenyl)-5-(trifluoromethyl)pyridine](image)

To a three-necked 250 mL round bottomed flask was charged with 2,4-difluorophenylboronic acid (5.68 g, 36.0 mmol), 2-bromo-5-trifluoromethylpyridine (6.78 g, 30.0 mmol), potassium carbonate (12.4 g, 90.0 mmol), palladium acetate (202 mg, 0.90 mmol) and triphenylphosphine (472 mg, 1.80
mmol). The flask was equipped with a condenser then evacuated and refilled with N\(_2\) three times. Following this, toluene (40 mL), water (40 mL) and ethanol (8 mL) were added \textit{via} septum. The flask was heated to reflux for 16 h. After this time, the flask was cooled to room temperature and quenched with water (100 mL). The organic phase was separated and then the aqueous phase re-extracted with Et\(_2\)O (3 x 200 mL). The combined organics were washed with brine (3 x 200 mL) and then dried over MgSO\(_4\) and concentrated \textit{in vacuo}. The crude residue was then purified \textit{via} silica gel column chromatography (EtOAc:Pentane 1:99 – 4:96 v:v) to give the title compound as a white solid (6.62 g, 25.5 mmol, 85\%). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 8.85 (dd, J = 2.4, 1.2 \text{ Hz}, 1 \text{ H}), \delta 7.99 (td, J = 8.9, 6.6 \text{ Hz}, 1 \text{ H}), 7.78 (dd, J = 8.3, 2.4 \text{ Hz}, 1 \text{ H}), 7.82 – 7.76 (m, 1 \text{ H}), 6.98 – 6.88 (m, 1 \text{ H}), 6.82 (ddd, J = 11.3, 8.7, 2.5 \text{ Hz}, 1 \text{ H}). \(^{19}\)F NMR (377 MHz, CDCl\(_3\)): \(\delta -62.49, -107.28 (t, J = 8.0 \text{ Hz}), -112.04 (d, J = 10.0 \text{ Hz}). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \(\delta 164.0 (dd, J = 252.8, 12.5 \text{ Hz}), 161.1 (dd, J = 253.6, 12.0 \text{ Hz}), 155.9, 146.7 (q, J = 4.2 \text{ Hz}), 133.8 (q, J = 3.5 \text{ Hz}), 132.6 (dd, J = 10.0, 4.2 \text{ Hz}), 125.3 (q, J = 33.2 \text{ Hz}), 123.7 (q, J = 272.3 \text{ Hz}), 123.7 (d, J = 11.1 \text{ Hz}), 122.5 (dd, J = 11.3, 3.8 \text{ Hz}), 112.4 (dd, J = 21.1, 3.6 \text{ Hz}), 106.5 – 101.0 \text{ (app t). Data was consistent with literature precedent.}\(^\text{10}\)

**Synthesis of [Ir(dF(CF}_3\text{)ppy})_2\text{Cl}]_2:**

![Schema](image.png)

To a three-necked 100 mL round bottomed flask was charged iridium(III) chloride hydrate (448 mg, 1.50 mmol) and 2-(2,4-difluorophenyl)-5-(trifluoromethyl)pyridine (856 mg, 3.30 mmol). The flask was equipped with a condenser, then evacuated and refilled with nitrogen three times. Rigorously degassed 2-ethoxyethanol (18 mL) and water (6 mL) were added \textit{via} syringe. The reaction mixture was heated 150 °C for 16 h. After this time the reaction mixture was allowed to return to room temperature and the bright yellow precipitate formed was filtered under a blanket of N\(_2\), washing with water (150 mL) and then hexane (60 mL), to give title compound after further removal of water \textit{via} high vacuum (960 mg, 0.65 mmol, 86\%). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 9.51 (d, J = 2.1 \text{ Hz}, 1 \text{ H}), 8.46 (dd, J = 8.7, 3.0 \text{ Hz}, 1 \text{ H}), 8.05 (dd, J = 8.7, 2.3 \text{ Hz}, 1 \text{ H}), 6.43 (ddd, J = 12.5, 8.8, 2.3 \text{ Hz}, 1 \text{ H}), 5.07 (dd, J = 8.8, 2.3 \text{ Hz}, 1 \text{ H}). \(^{19}\)F NMR (377 MHz, CDCl\(_3\)): \(\delta -62.36 (12 \text{ F}), -103.41 – -103.72 (m, 4 \text{ F}), -106.97 – -107.91 (m, 4 \text{ F}). Data was consistent with literature precedent.\(^\text{10}\)
Synthesis of (Ir[dF(CF₃)ppy]₂(dtbpy))PF₆ – [Ir]:

To a three-necked 250 mL round bottomed flask was charged [Ir(dF(CF₃)ppy)₂Cl]₂ (960 mg, 0.65 mmol) and 4,4’-di-tert-butyl-2,2’-dipyridyl (429 mg, 1.60 mmol). The flask was equipped with a reflux condenser, then evacuated and refilled three times with nitrogen. Rigorously degassed ethylene glycol (44 mL) was then added via syringe. The reaction mixture was then heated to 150 °C for 16 h. After this time the flask was allowed to return to room temperature. The mixture was diluted in water (300 mL) and hexane (300 mL). The aqueous phase was then separated and then re-extracted with hexane (2 x 300 mL). The aqueous phase was then decanted into a 500 mL conical flask and equipped with a stirrer bar. The flask was heated at 80 °C for 1 hour to remove residual hexane. The flask was allowed to return to room temperature, and an aqueous solution of potassium hexafluorophosphate (7 g in 70 mL water) was added with stirring, and a vibrant yellow precipitate was formed. The mixture was then allowed to stand at 5 °C for 1 hour, before the precipitate was collected via vacuum filtration washing with water (150 mL) and hexane (100 mL), The collected powdery solid was then subjected to further water removal via high vacuum, to give the title compound, (915 mg, 0.82 mmol, 63%).

**¹H NMR** (400 MHz, CDCl₃): δ 8.88 (d, J = 2.1 Hz, 2 H), 8.47 (dd, J = 8.7, 3.1 Hz, 2 H), 8.04 (dd, J = 8.8, 2.1 Hz, 2 H), 7.86 (d, J = 5.9 Hz, 2 H), 7.59 (dd, J = 5.9, 1.9 Hz, 2 H), 7.41 (s, 2 H), 6.64 (ddd, J = 11.6, 8.9, 2.3 Hz, 2 H), 5.63 (dd, J = 8.0, 2.4 Hz, 2 H), 1.50 (s, 18 H).

**¹⁹F NMR** (377 MHz, CDCl₃): δ -62.99 (6 F), -72.24 (3 F), -74.13 (3 F), -101.81 (dt, J = 12.4, 8.4 Hz, 2 F), -105.92 (td, J = 12.4, 3.4 Hz, 2 F). NMR Spectra matched those from commercial sources.
4: Demonstration of stepwise procedure for one-pot operation:

Reaction setup:

**Step 1:** (ketimine/hemiaminal formation): α-quinone (6.60 g, 30.0 mmol) was placed in a 3 neck round bottom flask (1000 ml), which was connected to a reflux condenser and argon. The evacuate/refill cycle was repeated 2-3 times before the addition of dry toluene and the whole setup was maintained under argon.
| Close view of o-quinone. | Addition of toluene |
Addition of 4-aminotetrahydropyran in toluene at 25 °C. (Inside Picture: 4-aminotetrahydropyran, 3.03 g; 30.0 mmol).
Completion of ketimine/hemiaminal formation. *(Note: the colour changes from deep green (o-quinone) to violet (ketimine/hemiaminal) during the course of reaction).*

Ketimine/hemiaminal formation:

EtOAc:Pentane (2:8) (visualized using KMnO₄)
Step 2: (Allylation):
Addition of TMEDA at 0 °C in neat form.

Addition of allylmagnesium bromide (1.0 M in Et₂O) via cannula.
Completion of allylation. 

Note: (violet to yellow colouration).

Allylation: (A small aliquot was worked up in NH₄Cl-EtOAc for TLC)
Step 3: Oxidative cleavage:
Quenching the remaining RMgX by the addition of 1M NaOH (150 mL) at 0 °C under argon atmosphere.
Note: Care must be taken while addition due to vigorous reaction.

Addition of CH$_3$CN (300 mL).
Addition of Iodine (7.62 g, 30.0 mmol)

Completion of oxidation

**Note:** (green to orange)
Work up: Separation of Organic layer from the heterogeneous mixture using CH₃CN.
Organic layer was washed with saturated sodium thiosulphate (1 x 50 mL) to remove iodine.

Washed with brine twice (2 x 50 mL) to remove TMEDA and any residual iodinated species.
Organic layer was acidified directly with 2 M HCl *(General Procedure B)*. For *General Procedure A and C*; the resulting organic layer was dried and condensed *via* vacuo, followed by column chromatography.

Dispersion of aqueous acidic phase from organic phase; and conformation of its acidity using pH paper.
Partitioned between aqueous and organic layers

Separation of aqueous acidic phase from organic phase and followed by further extraction twice with 2M aqueous HCl (2 x 250 mL).
The aqueous acidic phase was washed with pentane to remove any \( \text{I}_2 \) impurity.

Evaporation of aqueous acidic phase by rotary evaporator gave ammonium salt 27 as off-white powder (4.16 g, 23.4 mmol, 78%).
5: Spectral data for α-functionalized products (1-68):

**Synthesis of 2-(4-methoxyphenyl)pent-4-en-2-amine (1)**

The title compound was prepared using General Procedure A. The cleavage of phenol unit was performed by using 3 equiv of I₂ and 5 equiv NaOH (1 M). Yellow oil (205 mg, 1.07 mmol, 81%). FT-IR (thin film) v<sub>max</sub> (cm⁻¹): 3073, 2962, 1610, 1511, 1247, 1034, 830. ¹H NMR (400 MHz, CDCl₃): δ 7.37 (d, J = 8.8 Hz, 2 H), 6.86 (d, J = 8.8 Hz, 2 H), 5.57 (dddd, J = 17.0, 10.2, 7.9, 6.8 Hz, 1 H), 5.09 – 5.03 (m, 2 H), 3.80 (s, 3 H), 2.53 (ddt, J = 13.5, 6.8, 1.3 Hz, 1 H), 2.39 (ddt, J = 13.5, 7.8, 1.1 Hz, 1 H), 1.57 (br s, 2 H, NH₂), 1.45 (s, 3 H). ¹³C NMR (101 MHz, CDCl₃): δ 158.0, 140.7, 134.5, 126.4, 118.5, 113.5, 55.3, 54.3, 49.8, 31.0. HRMS (ESI) Calcd for C₁₂H₁₅O [M-NH₂]: 175.1117, found: 175.1118.

**Synthesis of 2-phenylpent-4-en-2-amine (2)**

Brown oil (125 mg, 0.77 mmol, 94%). FT-IR (thin film) v<sub>max</sub> (cm⁻¹): 3060, 2925, 1639, 1445, 1197, 917, 766, 699. ¹H NMR (400 MHz, CDCl₃): δ 7.49 – 7.45 (m, 2 H), 7.36 – 7.31 (m, 2 H), 7.25 – 7.20 (m, 1 H), 5.56 (ddddd, J = 17.0, 10.1, 7.9, 6.8 Hz, 1 H), 5.11 – 5.04 (m, 2 H), 2.62 – 2.44 (m, 4 H, CH₂, NH₂), 1.50 (s, 3 H). ¹³C NMR (101 MHz, CDCl₃): δ 147.9, 134.1, 128.3, 126.5, 125.3, 118.9, 55.2, 49.4, 30.4. HRMS (ESI) Calcd for C₁₁H₁₆N [(M+H)⁺]: 162.1277, found: 162.1278.

**Synthesis of 1,1-diphenylbut-3-en-1-amine (3)**

Yellow semi-solid (211 mg, 0.95 mmol, 80%). FT-IR (thin film) v<sub>max</sub> (cm⁻¹): 3059, 2980, 1598, 1492, 1445, 1156, 917, 755, 698. ¹H NMR (400 MHz, CDCl₃): δ 7.43 – 7.40 (m, 4 H), 7.34 – 7.30 (m, 4 H), 7.25 – 7.20 (m, 2 H), 5.55 (ddddd, J = 16.6, 10.2, 7.6, 6.8 Hz, 1 H), 5.22 – 5.10 (m, 2 H), 3.05 (dt, J = 7.1, 1.2 Hz, 2 H), 1.87 (br s, 2 H, NH₂).
\[^{13}\text{C NMR}\] (101 MHz, CDCl\textsubscript{3}): \(\delta\) 148.2, 134.2, 128.2, 126.7, 126.5, 119.3, 60.3, 47.6. \[^{1}\text{H NMR}\] (400 MHz, CDCl\textsubscript{3}): \(\delta\) 7.31 (dd, \(J = 7.7, 1.8\) Hz, 1 H), 7.26 – 7.20 (m, 1 H), 6.94 – 6.89 (m, 2 H), 5.57 – 5.48 (m, 1 H), 5.04 – 4.94 (m, 2 H), 3.87 (s, 3 H), 2.75 – 2.62 (m, 2 H), 2.26 (br s, 2 H, NH\textsubscript{2}), 1.50 (s, 3 H). 

The title compound was prepared using General Procedure A. The cleavage of phenol unit was performed by using 3 equiv of I\textsubscript{2} and 5 equiv NaOH (1 M). Viscous yellow oil (160 mg, 0.84 mmol, 63\%). \[^{1}\text{H NMR}\] (400 MHz, CDCl\textsubscript{3}): \(\delta\) 7.27 – 7.23 (m, 1 H), 7.04 – 7.01 (m, 2 H), 6.77 – 6.75 (m, 1 H), 5.56 (dddd, \(J = 17.0, 10.1, 8.0, 6.7\) Hz, 1 H), 5.10 – 5.03 (m, 2 H), 3.80 (s, 3 H), 2.57 (ddt, \(J = 13.6, 6.7, 1.3\) Hz, 1 H), 2.42 (ddt, \(J = 13.6, 8.1, 1.1\) Hz, 1 H), 2.06 (br s, 2 H, NH\textsubscript{2}), 1.46 (s, 3 H). 

The title compound was prepared using General Procedure A. Yellow oil (197 mg, 1.03 mmol, 78\%). \[^{1}\text{H NMR}\] (400 MHz, CDCl\textsubscript{3}): \(\delta\) 7.36 (d, \(J = 8.1\) Hz, 1 H), 6.94 (d, \(J = 8.1\) Hz, 1 H), 5.87 (d, \(J = 8.1\) Hz, 1 H), 2.75 (m, 2 H), 2.06 (br s, 3 H). 

The title compound was prepared using General Procedure A. Yellow oil (174 mg, 0.99 mmol, 67\%). \[^{1}\text{H NMR}\] (400 MHz, CDCl\textsubscript{3}): \(\delta\) 7.36 (d, \(J = 8.1\) Hz, 1 H), 6.94 (d, \(J = 8.1\) Hz, 1 H), 5.87 (d, \(J = 8.1\) Hz, 1 H), 2.75 (m, 2 H), 2.06 (br s, 3 H).
= 8.3 Hz, 2 H), 7.15 (d, J = 8.3 Hz, 2 H), 5.59 (dddd, J = 17.0, 10.1, 7.9, 6.7 Hz, 1 H), 5.11 – 5.04 (m, 2 H), 2.56 (ddt, J = 13.5, 6.7, 1.2 Hz, 1 H), 2.41 (ddt, J = 13.5, 7.8, 1.1 Hz, 1 H), 2.34 (s, 3 H), 1.53 (br s, 2 H, NH2), 1.46 (s, 3 H). 13C NMR (101 MHz, CDCl3): δ 145.9, 135.7, 134.6, 128.9, 125.2, 118.4, 54.4, 49.8, 31.1, 21.0. HRMS (ESI) Calcd for C12H18N [(M+H)+]: 176.1434, found: 176.1435.

Synthesis of 4-(2-aminopent 4-en-2-yl)phenol hydrochloride (7)

The title compound was prepared using General Procedure B. A mixture of Toluene:THF (5:1)(0.1 M) was used to improve the solubility of starting material for ketimine formation. Yellow solid (184 mg, 0.86 mmol, 59%). FT-IR (thin film) νmax (cm⁻¹): 3401, 3025, 2922, 1614, 1519, 1224, 1188, 833. 1H NMR (400 MHz, CD3OD): δ 7.31 (d, J = 8.8 Hz, 2 H), 6.86 (d, J = 8.8 Hz, 2 H), 5.54 (ddt, J = 17.3, 10.1, 7.2 Hz, 1 H), 5.23 – 5.14 (m, 2 H), 2.81 – 2.69 (m, 2 H), 1.69 (s, 3 H). 13C NMR (101 MHz, CD3OD): δ 158.8, 132.3, 131.8, 127.6, 121.3, 116.6, 59.2, 46.5, 25.1. HRMS (ESI) Calcd for C11H13O [M-NH3Cl]: 161.0961, found: 161.0961.

Synthesis of 2-(4-fluorophenyl)pent-4-en-2-amine (8)

The title compound was prepared using General Procedure A. Brown oil (183 mg, 1.02 mmol, 71%). FT-IR (thin film) νmax (cm⁻¹): 2980, 1601, 1509, 1225, 919, 834. 1H NMR (400 MHz, CDCl3): δ 7.42 (dd, J = 8.9, 5.3 Hz, 2 H), 6.99 (t, J = 8.7 Hz, 2 H), 5.53 (dddd, J = 16.6, 10.5, 7.8, 6.8 Hz, 1 H), 5.08 – 5.03 (m, 2 H), 2.54 (ddt, J = 13.6, 6.9, 1.2 Hz, 1 H), 2.41 (ddt, J = 13.6, 7.9, 1.0 Hz, 1 H), 2.28 (br s, 2 H, NH2), 1.46 (s, 3 H). 19F NMR (377 MHz, CDCl3): δ -117.2 (d, J = 11.6 Hz). 13C NMR (101 MHz, CDCl3): δ 161.5 (d, JCF = 245.6 Hz), 143.7 (d, JCF = 3.2 Hz), 133.8, 127.0 (d, JCF = 7.9 Hz), 119.0, 114.9 (d, JCF = 21.1 Hz), 54.8, 49.6, 30.7. HRMS (ESI) Calcd for C12H15NF [(M+H)+]: 180.1183, found: 180.1182.

Synthesis of 2-(4-chlorophenyl)pent-4-en-2-amine (9)
The title compound was prepared using **General Procedure A**. Yellow oil (171 mg, 0.87 mmol, 68%).

**FT-IR** (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3075, 2923, 2849, 1639, 1490, 1195, 918, 826. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.32 (d, $J = 8.7$ Hz, 2 H), 7.21 (d, $J = 8.7$ Hz, 2 H), 5.45 (ddddd, $J = 16.5, 10.8, 7.9, 6.8$ Hz, 1 H), 5.02 – 4.96 (m, 2 H), 2.47 (dddt, $J = 13.6, 6.8, 1.2$ Hz, 1 H), 2.33 (dddt, $J = 13.6, 7.9, 1.0$ Hz, 1 H), 2.03 (br s, 2 H, NH$_2$), 1.39 (s, 3 H).

**13C NMR** (101 MHz, CDCl$_3$): $\delta$ 146.7, 133.7, 132.2, 128.3, 126.9, 119.2, 54.8, 49.5, 30.7.

**HRMS** (ESI) Calcd for C$_{11}$H$_{15}$N$_3$Cl [(M+H)$^+$]: 196.0888, found: 196.0888.

### Synthesis of 2-(4-bromophenyl)pent-4-en-2-amine (10)

The title compound was prepared using **General Procedure A**. Pale brown oil (159 mg, 0.66 mmol, 66%). **FT-IR** (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3075, 2965, 2924, 1639, 1484, 1007, 918, 822. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.43 (d, $J = 8.6$ Hz, 2 H), 7.33 (d, $J = 8.6$ Hz, 2 H), 5.58 – 5.48 (m, 1 H), 5.08 – 5.02 (m, 2 H), 2.52 (ddt, $J = 13.6, 6.9, 1.2$ Hz, 1 H), 2.37 (ddt, $J = 13.6, 7.9, 1.1$ Hz, 1 H), 1.64 (br s, 2 H, NH$_2$), 1.43 (s, 3 H).

**13C NMR** (101 MHz, CDCl$_3$): $\delta$ 147.7, 133.9, 131.2, 127.3, 120.2, 119.0, 54.6, 49.7, 30.9.

**HRMS** (ESI) Calcd for C$_{11}$H$_{15}$N$_7$Br [(M+H)$^+$]: 240.0382, found: 240.0381.

### Synthesis of 4-(4-fluorophenyl)hepta-1,6-dien-4-amine (11)

The title compound was prepared using 2-amino-2-(4-fluorophenyl)acetonitrile as amine precursor. Ketimine formation was done at 80 °C for 8 h. 10 equiv of allylmagnesium bromide (1 M in Et$_2$O) was used and the remaining procedure is same as **General Procedure A**. Yellow oil (79.0 mg, 0.38 mmol, 58%). **FT-IR** (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3076, 2920, 1601, 1508, 1224, 916, 833, 815. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.38 (dd, $J = 8.9, 5.3$ Hz, 2 H), 6.99 (t, $J = 8.7$ Hz, 2 H), 5.50 (ddddd, $J = 16.7, 10.1, 8.3, 6.4$ Hz, 2 H), 5.08 – 5.02 (m, 4 H), 2.60 (ddt, $J = 13.7, 6.3, 1.4$ Hz, 2 H), 2.38 (ddt, $J = 13.7, 7.9, 1.0$ Hz, 2 H), 1.55 (br s, 2 H, NH$_2$). $^{19}$F NMR (377 MHz, CDCl$_3$): $\delta$ -117.4 (d, $J = 6.1$ Hz). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 161.4 (d, $J_{CF} = 245.6$ Hz), 142.4 (d, $J_{CF} = 3.2$ Hz), 133.7, 127.6 (d, $J_{CF} = 8.0$ Hz), 118.9, 114.8 (d, $J_{CF} = 20.7$ Hz), 56.7, 48.2. **HRMS** (ESI) Calcd for C$_{13}$H$_{17}$NF [(M+H)$^+$]: 206.1340, found: 206.1339.
Synthesis of 2-(3,5-difluorophenyl)pent-4-en-2-amine (12)

The title compound was prepared using **General Procedure A**. Brown oil (207 mg, 1.05 mmol, 82%).

**FT-IR** (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3079, 2969, 2926, 1623, 1597, 1432, 1115, 984, 856. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 6.97 (dd, $J = 9.4$, 2.3 Hz, 2 H), 6.62 (tt, $J = 8.8$, 2.3 Hz, 1 H), 5.56 – 5.46 (m, 1 H), 5.08 – 5.02 (m, 2 H), 2.49 (ddt, $J = 13.6$, 6.7, 1.2 Hz, 1 H), 2.34 (ddt, $J = 13.7$, 8.0, 1.0 Hz, 1 H), 1.59 (br s, 2 H, NH$_2$), 1.41 (s, 3 H). $^{13}$F NMR (377 MHz, CDCl$_3$): $\delta$ -110.1. $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 163.0 (dd, $J_{C-F} = 248.0$, 12.7 Hz), 153.3 (t, $J_{C-F} = 7.9$ Hz), 133.5, 119.3, 108.6 (dd, $J_{C-F} = 19.0$, 7.0 Hz), 101.6 (t, $J_{C-F} = 25.8$ Hz), 54.8 (t, $J_{C-F} = 2.1$ Hz), 49.5, 30.8. HRMS (ESI) Calcd for C$_{11}$H$_{14}$F$_2$N [(M+H)$^+$]: 198.1089, found: 198.1087.

Synthesis of 2-(naphthalen-1-yl)pent-4-en-2-amine (13)

The title compound was prepared using **General Procedure A**. Yellow oil (148 mg, 0.70 mmol, 60%).

**FT-IR** (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3047, 2925, 1638, 1509, 1177, 914, 803, 776. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.89 (d, $J = 9.0$ Hz, 1 H), 7.89 (dd, $J = 8.0$, 1.8 Hz, 1 H), 7.77 (d, $J = 8.0$ Hz, 1 H), 7.61 (dd, $J = 7.4$, 1.3 Hz, 1 H), 7.54 – 7.40 (m, 3 H), 5.59 (ddt, $J = 17.3$, 10.2, 7.4 Hz, 1 H), 5.12 – 5.03 (m, 2 H), 3.01 (ddt, $J = 13.7$, 7.1, 1.2 Hz, 1 H), 2.84 (ddt, $J = 13.8$, 7.6, 1.2 Hz, 1 H), 1.77 (s, 5 H, CH$_3$, NH$_2$). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 143.4, 135.1, 134.7, 131.3, 129.5, 128.4, 127.4, 125.1, 125.0, 124.9, 124.1, 118.4, 56.2, 48.2, 31.4. HRMS (ESI) Calcd for C$_{15}$H$_{18}$N [(M+H)$^+$]: 212.1434, found: 212.1437.

Synthesis of 2-(naphthalen-2-yl)pent-4-en-2-amine (14)

The title compound was prepared using **General Procedure A**. Pale yellow oil (180 mg, 0.73 mmol, 62%).

**FT-IR** (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3364, 3257, 2924, 2856, 1638, 1600, 916, 818, 748. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.91 (s, 1 H), 7.85 – 7.81 (m, 3 H), 7.60 (dd, $J = 8.7$, 2.0 Hz, 1 H), 7.50 – 7.43 (m, 2 H), 7.42 – 7.35 (m, 2 H), 7.35 – 7.28 (m, 3 H), 6.91 – 6.81 (m, 1 H), 6.77 – 6.63 (m, 1 H), 6.62 – 6.54 (m, 1 H), 5.12 (ddt, $J = 13.7$, 7.2, 1.2 Hz, 1 H), 4.41 (ddt, $J = 13.7$, 7.2, 1.2 Hz, 1 H), 3.01 (dd, $J = 13.7$, 7.2, 1.2 Hz, 1 H), 1.77 (s, 5 H, CH$_3$, NH$_2$). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 151.5, 135.4, 134.7, 131.3, 129.5, 128.4, 127.1, 125.0, 124.9, 124.1, 118.4, 56.2, 48.2, 31.4. HRMS (ESI) Calcd for C$_{15}$H$_{18}$N [(M+H)$^+$]: 212.1434, found: 212.1437.
5.57 (ddt, J = 17.1, 9.8, 7.2 Hz, 1 H), 5.12 – 5.03 (m, 2 H), 2.69 (dd, J = 13.6, 6.6 Hz, 1 H), 2.51 (dd, J = 13.6, 8.0 Hz, 1 H), 1.66 (br s, 2 H, NH₂), 1.57 (s, 3 H). \(^{13}C\) NMR (101 MHz, CDCl₃): δ 146.2, 134.4, 133.3, 132.1, 128.2, 127.9, 127.5, 126.1, 125.7, 124.4, 123.5, 118.7, 54.9, 49.6, 31.1. HRMS (ESI) Calcd for C₁₅H₁₈N [(M+H)⁺]: 212.1434, found: 212.1435.

**Synthesis of 1-allyl-2,3-dihydro-1H-inden-1-amine (15)**

![Structure of 1-allyl-2,3-dihydro-1H-inden-1-amine](image)

The title compound was prepared using **General Procedure A**. Yellow oil (159 mg, 0.92 mmol, 61%).

**FT-IR** (thin film) ν\(\text{max}\) (cm\(^{-1}\)): 3354, 3071, 2980, 2930, 1638, 1457, 1157, 998, 915, 761. \(^{1}H\) NMR (400 MHz, CDCl₃): δ 7.27 – 7.20 (m, 4 H), 5.78 (ddt, J = 17.4, 10.2, 7.4 Hz, 1 H), 5.17 – 5.10 (m, 2 H), 2.97 – 2.80 (m, 2 H), 2.49 – 2.37 (m, 2 H), 2.28 (dd, J = 12.9, 7.9, 4.0 Hz, 1 H), 2.03 (br s, 2 H, NH₂), 1.93 (dt, J = 12.8, 8.3 Hz, 1 H). \(^{13}C\) NMR (101 MHz, CDCl₃): δ 149.4, 142.8, 134.2, 127.5, 126.6, 125.0, 118.8, 64.1, 45.6, 40.8, 29.6. HRMS (ESI) Calcd for C₁₂H₁₆N [(M+H)⁺]: 174.1277, found: 174.1277.

**Synthesis of 4-methylnon-1-en-4-amine (16)**

![Structure of 4-methylnon-1-en-4-amine](image)

The title compound was prepared using **General Procedure B**. Yellow oil (270 mg, 1.41 mmol, 81%).

**FT-IR** (thin film) ν\(\text{max}\) (cm\(^{-1}\)): 3017, 2930, 2874, 1617, 1518, 1298, 994, 921. \(^{1}H\) NMR (400 MHz, CDCl₃): δ 5.83 (ddt, J = 16.8, 10.3, 7.5 Hz, 1 H), 5.15 – 5.04 (m, 2 H), 3.02 – 2.31 (br s, 2 H, NH₂), 2.15 (dt, J = 7.4, 1.1 Hz, 2 H), 1.38 – 1.26 (m, 8 H), 1.09 (s, 3 H), 0.88 (t, J = 6.9 Hz, 3 H). \(^{13}C\) NMR (101 MHz, CDCl₃): δ 134.3, 118.6, 52.5, 46.7, 42.2, 32.6, 27.3, 23.6, 14.2. HRMS (ESI) Calcd for C₁₀H₁₄N [(M+H)⁺]: 156.1747, found: 156.1745.

**Synthesis of 4-propylhept-1-en-4-amine hydrochloride (17)**

![Structure of 4-propylhept-1-en-4-amine hydrochloride](image)

The title compound was prepared using **General Procedure B**. Yellow solid (323 mg, 1.68 mmol, 95%).

**FT-IR** (thin film) ν\(\text{max}\) (cm\(^{-1}\)): 2964, 2876, 1643, 1518, 1252. \(^{1}H\) NMR (400 MHz, CDCl₃): δ 8.32 (br s, 3 H, NH₃⁺), 5.90 (ddt, J = 17.5, 10.2, 7.3 Hz, 1 H), 5.24 – 5.19 (m, 2 H), 2.45 (d, J = 7.3 Hz, 2 H), 1.66 – 1.62 (m, 4 H), 1.49 – 1.43 (m, 4 H), 0.93 (t, J = 7.2 Hz, 6 H). \(^{13}C\) NMR (101 MHz, CDCl₃): δ 131.1,
Synthesis of 1-(3,5-dimethoxyphenyl)cyclobutan-1-amine (18)

The title compound was prepared using General Procedure C with slight modification. The ketimine was generated in DCE from the combination of cyclobutylamine (0.10 g, 1.41 mmol) and 3,5-di-tert-butyl-o-benzoquinone D (0.31 g, 1.41 mmol) at 0 °C for 1 h. The solvent DCE was exchanged with toluene before the addition of (3,5-dimethoxyphenyl)lithium\(^3\) which was generated from 1-bromo-3,5-dimethoxybenzene (1.83 g, 8.44 mmol, 6 equiv) and tBuLi (9.92 mL, 16.9 mmol, 1.7 M in pentane, 12 equiv) at -78 °C for 1 h in dry Et\(_2\)O (0.1 M) under argon atmosphere. The remaining procedure is same as General Procedure C. Yellow oil (80.0 mg, 0.39 mmol, 27% yield).\n
\( ^1\)H{\text{NMR}} (500 MHz, CDCl\(_3\)): \( \delta 6.56 (d, J = 2.3 \text{ Hz}, 2 \text{ H}), 6.35 (t, J = 2.3 \text{ Hz}, 1 \text{ H}), 3.80 (s, 6 \text{ H}), 3.40 – 3.02 (br s, 2 \text{ H, NH}_2), 2.56 – 2.50 (m, 2 \text{ H}), 2.26 – 2.08 (m, 3 \text{ H}), 1.80 – 1.74 (m, 1 \text{ H}).\n
\( ^{13}\)C{\text{NMR}} (126 MHz, CDCl\(_3\)): \( \delta 161.1, 151.1, 103.5, 98.8, 59.6, 55.5, 36.0, 14.4.\n
HRMS (ESI) Calcd for C\(_{12}\)H\(_{18}\)NO\(_2\) [(M+H\(^+\)]: 208.1332, found: 208.1334.

Synthesis of 1-allylcyclopentan-1-amine hydrochloride (19)

The title compound was prepared using General Procedure B. Yellow oil (110 mg, 0.68 mmol, 58%). \( \text{FT-IR} \) (thin film) \( \nu_{\text{max}} \) (cm\(^{-1}\)):\n\( 2981, 1596, 1252, 1154, 840.\n
\( ^1\)H{\text{NMR}} (400 MHz, CDCl\(_3\)): \( \delta 8.31 (br s, 3 \text{ H, NH}_3^+), 5.93 – 5.85 (m, 1 \text{ H}), 5.25 (dd, J = 13.4, 9.3 \text{ Hz}, 2 \text{ H}), 2.55 (d, J = 7.0 \text{ Hz}, 2 \text{ H}), 2.07 – 1.86 (m, 4 \text{ H}), 1.85 – 1.73 (m, 2 \text{ H}), 1.72 – 1.53 (m, 2 \text{ H}).\n
\( ^{13}\)C{\text{NMR}} (101 MHz, CDCl\(_3\)): \( \delta 131.5, 121.2, 64.8, 42.6, 36.3, 24.1.\n
HRMS (ESI) Calcd for C\(_8\)H\(_{16}\)N [(M+H\(^+\)]: 126.1277, found: 126.1277.

Synthesis of 1-allylcyclohexan-1-amine hydrochloride (20)
The title compound was prepared using General Procedure B. Pale yellow solid (76.5 mg, 0.44 mmol, 78%). FT-IR (thin film) ν_{max} (cm^{-1}): 3031, 2925, 2861, 1616, 1516, 1197, 999. ^1H NMR (500 MHz, CDCl_3): δ 8.22 (br s, 3 H, NH), 5.97 – 5.90 (m, 1 H), 5.27 – 5.24 (m, 2 H), 2.54 (d, J = 7.1 Hz, 2 H), 1.90 – 1.66 (m, 6 H), 1.58 – 1.34 (m, 4 H). ^13C NMR (126 MHz, CDCl_3): δ 130.8, 121.4, 57.5, 41.4, 33.8, 24.9, 21.3. HRMS (ESI) Calcd for C_9H_{18}N [(M-Cl)+]: 140.1434, found: 140.1434.

Synthesis of 1-benzylcyclohexan-1-amine (21)

The title compound was prepared using General Procedure A. 10 equiv of BnMgCl (2 M in THF) was used instead of allylmagnesium bromide for the addition. Pale yellow solid (64.0 mg, 0.34 mmol, 67%). FT-IR (thin film) ν_{max} (cm^{-1}): 3428, 2980, 2934, 2859, 1574, 1487, 1463, 1148, 764, 704. ^1H NMR (500 MHz, CD_3OD): δ 7.40 – 7.36 (m, 2 H), 7.34 – 7.30 (m, 1 H), 7.28 – 7.25 (m, 2 H), 3.00 (s, 2 H), 1.79 – 1.63 (m, 8 H), 1.59 – 1.45 (m, 2 H). ^13C NMR (126 MHz, CD_3OD): δ 135.6, 131.8, 129.8, 128.6, 57.5, 43.6, 35.0, 25.9, 22.3. HRMS (ESI) Calcd for C_{13}H_{20}N [(M+H)^+]: 190.1590, found: 190.1592.

Synthesis of N-(1-phenylcyclohexyl)benzamide (22)

The title compound was prepared using General Procedure C. Commercial Phenyl lithium was used as arylating agent. The free amine was protected as benzoyl derivative using benzylic chloride (5 equiv) with aqueous NaOH (1 M) (5 equiv). White solid (60.0 mg, 0.23 mmol, 68%). FT-IR (thin film) ν_{max} (cm^{-1}): 3416, 2980, 1621, 1462, 1383, 1252, 1073, 954. ^1H NMR (500 MHz, CDCl_3): δ 7.79 (d, J = 7.3 Hz, 2 H), 7.52 – 7.49 (m, 1 H), 7.47 – 7.43 (m, 4 H), 7.33 (t, J = 7.8 Hz, 2 H), 7.22 (t, J = 7.3 Hz, 1 H), 6.29 (s, 1 H), 2.56 – 2.50 (m, 2 H), 1.94 – 1.88 (m, 2 H), 1.78 – 1.71 (m, 3 H), 1.68 – 1.58 (m, 2 H), 1.42 – 1.32 (m, 1 H). ^13C NMR (126 MHz, CDCl_3): δ 166.3, 146.7, 135.8, 131.5, 128.8, 128.5, 126.9, 126.7, 125.2, 58.6, 36.4, 25.6, 22.6. HRMS (ESI) Calcd for C_{19}H_{22}NO [(M+H)^+]: 280.1696, found: 280.1695.

Synthesis of 4-(tert-butyl)-1-phenylcyclohexan-1-amine (23)

The title compound was prepared using General Procedure C. Commercial Phenyl lithium was used as arylating agent. The free amine was protected as benzoyl derivative using benzylic chloride (5 equiv) with aqueous NaOH (1 M) (5 equiv). White solid (60.0 mg, 0.23 mmol, 68%). FT-IR (thin film) ν_{max} (cm^{-1}): 3416, 2980, 1621, 1462, 1383, 1252, 1073, 954. ^1H NMR (500 MHz, CDCl_3): δ 7.79 (d, J = 7.3 Hz, 2 H), 7.52 – 7.49 (m, 1 H), 7.47 – 7.43 (m, 4 H), 7.33 (t, J = 7.8 Hz, 2 H), 7.22 (t, J = 7.3 Hz, 1 H), 6.29 (s, 1 H), 2.56 – 2.50 (m, 2 H), 1.94 – 1.88 (m, 2 H), 1.78 – 1.71 (m, 3 H), 1.68 – 1.58 (m, 2 H), 1.42 – 1.32 (m, 1 H). ^13C NMR (126 MHz, CDCl_3): δ 166.3, 146.7, 135.8, 131.5, 128.8, 128.5, 126.9, 126.7, 126.7, 125.2, 58.6, 36.4, 25.6, 22.6. HRMS (ESI) Calcd for C_{19}H_{22}NO [(M+H)^+]: 280.1696, found: 280.1695.
The title compounds (23 and 23') were prepared using General Procedure C. Commercial Phenyl lithium was used as arylating agent. dr=4.26:1 (determined using crude 1H NMR). White solid (756 mg, 3.27 mmol, 51%). FT-IR (thin film) ν_max (cm⁻¹): 2968, 2867, 1600, 1445, 1239, 757, 698. 1H NMR (400 MHz, CDCl₃): δ 7.59 – 7.52 (m, 2 H), 7.40 – 7.30 (m, 2 H), 7.28 – 7.18 (m, 1 H), 1.89 – 1.68 (m, 8 H), 1.51 – 1.39 (m, 2 H), 1.08 (tt, J = 12.2, 3.2 Hz, 1 H), 0.93 (s, 9 H). 13C NMR (101 MHz, CDCl₃): δ: 150.9, 128.2, 126.3, 124.9, 53.3, 47.8, 39.7, 32.5, 27.7, 23.0. HRMS (ESI) Calcd for C₁₆H₂₆N [(M+H)+]: 232.2060, found: 232.2063.

Yellow oil (180 mg, 0.78 mmol, 12%). FT-IR (thin film) ν_max (cm⁻¹): 2939, 2864, 1601, 1496, 1206, 768, 699. 1H NMR (400 MHz, CDCl₃): δ 7.50 – 7.42 (m, 2 H), 7.34 (dd, J = 8.5, 7.0 Hz, 2 H), 7.25 – 7.17 (m, 1 H), 2.57 – 2.44 (m, 2 H), 2.15 (br s, 2 H, NH₂), 1.68 – 1.54 (m, 4 H), 1.11 (tt, J = 11.9, 3.1 Hz, 1 H), 1.04 – 0.90 (m, 2 H), 0.74 (s, 9 H). 13C NMR (101 MHz, CDCl₃): δ 145.7, 128.7, 126.5, 126.2, 54.5, 48.1, 39.5, 32.3, 27.6, 24.5. HRMS (ESI) Calcd for C₁₆H₂₆N [(M+H)+]: 232.2060, found: 232.2061.

Synthesis of 1-allylcycloheptan-1-amine hydrochloride (24)

The title compound was prepared using General Procedure B. Off-white solid (356 mg, 1.88 mmol, 61%). FT-IR (thin film) ν_max (cm⁻¹): 2981, 2929, 1614, 1514, 1252, 955. 1H NMR (400 MHz, CDCl₃): δ 8.30 (br s, 3 H, NH₃⁺), 5.96 (ddt, J = 16.4, 10.3, 7.4 Hz, 1 H), 5.28 – 5.23 (m, 2 H), 2.49 (d, J = 7.4 Hz, 2 H), 2.00 – 1.89 (m, 2 H), 1.89 – 1.76 (m, 4 H), 1.71 – 1.59 (m, 2 H), 1.56 – 1.39 (m, 4 H). 13C NMR (101 MHz, CDCl₃): δ 131.2, 121.4, 61.0, 44.1, 37.7, 29.9, 22.3. HRMS (ESI) Calcd for C₁₆H₃₀N [(M-Cl)+]: 154.1590, found: 154.1590.

Synthesis of 1-allylcyclooctan-1-amine hydrochloride (25)

The title compound was prepared using General Procedure A. The free amine was protected as HCl salt using 4 M HCl in dioxane. The cleavage of phenol unit was performed by using 2 equiv of I₂ and 5
equiv NaOH (1 M). Pale yellow solid (993 mg, 4.87 mmol, 62%). **FT-IR** (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 2980, 2916, 1641, 1517, 1253, 920, 731. **$^1$H NMR** (400 MHz, CDCl$_3$): $\delta$ 8.25 (br s, 3 H, NH$_3^+$), 6.07 – 5.97 (m, 1 H), 5.29 – 5.22 (m, 2 H), 2.47 (d, $J$ = 7.4 Hz, 2 H), 2.08 – 2.02 (m, 2 H), 1.83 – 1.62 (m, 6 H), 1.61 – 1.49 (m, 4 H), 1.48 – 1.35 (m, 2 H). **HRMS** (ESI) Calcd for C$_{11}$H$_{22}$N [(M+H)$^+$]: 168.1747, found: 168.1745.

**Synthesis of 3-allyltetrahydrofuran-3-amine (26)**

![Chemical structure of 3-allyltetrahydrofuran-3-amine (26)](image)

The title compound was prepared using **General Procedure A**. The cleavage of phenol unit was performed by using 2 equiv of I$_2$ and 5 equiv NaOH (1 M). Yellow oil (141 mg, 1.11 mmol, 88%). **FT-IR** (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3349, 2928, 2866, 1640, 1440, 1220, 1054, 913. **$^1$H NMR** (400 MHz, CDCl$_3$): $\delta$ 5.80 (ddt, $J$ = 19.9, 9.2, 7.4 Hz, 1 H), 5.15 – 5.11 (m, 2 H), 3.97 (dd, $J$ = 16.0, 8.0 Hz, 1 H), 3.85 (td, $J$ = 8.7, 4.7 Hz, 1 H), 3.56 (d, $J$ = 8.7 Hz, 1 H), 3.48 (d, $J$ = 8.7 Hz, 1 H), 2.29 (d, $J$ = 7.4 Hz, 2 H), 1.91 (dt, $J$ = 12.4, 8.3 Hz, 1 H), 1.82 (br s, 2 H, NH$_3$), 1.72 (ddd, $J$ = 12.5, 7.6, 4.7 Hz, 1 H). **HRMS** (ESI) Calcd for C$_7$H$_{14}$NO [(M+H)$^+$]: 128.1070, found: 128.1069.

**Synthesis of 4-allyltetrahydro-2H-pyran-4-amine hydrochloride (27)**

![Chemical structure of 4-allyltetrahydro-2H-pyran-4-amine hydrochloride (27)](image)

The title compound was prepared using **General Procedure B**. Off-white powder (139 mg, 0.78 mmol, 79%). **FT-IR** (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3390, 2980, 1640, 1524, 1237, 1157, 936, 839. **$^1$H NMR** (400 MHz, CDCl$_3$): $\delta$ 8.56 (br s, 3 H, NH$_3^+$), 5.94 (dtt, $J$ = 17.5, 10.3, 7.4 Hz, 1 H), 5.44 – 5.14 (m, 2 H), 3.96 (ddt, $J$ = 11.9, 8.0, 3.6 Hz, 2 H), 3.70 (dtt, $J$ = 12.4, 6.2, 4.1 Hz, 2 H), 2.61 (d, $J$ = 7.4 Hz, 2 H), 2.00 – 1.81 (m, 4 H). **$^{13}$C NMR** (101 MHz, CDCl$_3$): $\delta$ 129.8, 122.2, 62.8, 55.0, 41.8, 33.8. **HRMS** (ESI) Calcd for C$_8$H$_{16}$NO [(M-H)$^-$]: 142.1226, found: 142.1225.
Synthesis of 4-allyltetrahydro-2H-thiopyran-4-amine (28)

The title compound was prepared using **General Procedure B**. The HCl salt of compound 28 was basified with 1 M NaOH (1 mL), extracted with CHCl₃ (3 x 20 mL) and dried by Na₂SO₄. After removal of solvents gave the desired 4-allyltetrahydro-2H-thiopyran-4-amine 28 as yellow oil (99.0 mg, 0.63 mmol, 67%). **FT-IR** (thin film) ν_max (cm⁻¹): 3336, 3073, 2925, 1638, 1437, 1273, 998, 916. **¹H NMR** (400 MHz, CDCl₃): δ 5.81 (ddt, J = 16.9, 10.2, 7.5 Hz, 1 H), 5.18 – 5.05 (m, 2 H), 2.89 – 2.77 (m, 2 H), 2.55 – 2.41 (m, 2 H), 2.13 (dt, J = 7.5, 1.1 Hz, 2 H), 2.01 – 1.90 (br s, 2 H, NH₂), 1.81 – 1.67 (m, 4 H). **¹³C NMR** (101 MHz, CDCl₃): δ 133.0, 119.1, 49.7, 48.0, 39.2, 24.2. **HRMS** (ESI) Calcd for C₈H₁₆NS [(M+H)⁺]: 158.0998, found: 158.0999.

Synthesis of 2-(4-allyl-4-aminopiperidin-1-yl)-4,6-di-tert-butylphenol (29)

The title compound was prepared using **General Procedure A** starting from tert-butyl 4-aminopiperidine-1-carboxylate. The Boc protection was cleaved during oxidation and the free amine 4-allylpiperidin-4-amine was reactive enough to undergo a self-condensation with the formed o-quinone, which ends up with the product 29 as a yellow oil (76.0 mg, 0.22 mmol, 44%). **FT-IR** (thin film) ν_max (cm⁻¹): 3389, 2958, 1640, 1480, 1248, 967. **¹H NMR** (400 MHz, CD₂OD): δ 7.01 (d, J = 2.3 Hz, 1 H), 6.93 (d, J = 2.3 Hz, 1 H), 5.96 (ddt, J = 17.5, 10.3, 7.3 Hz, 1 H), 5.22 – 5.15 (m, 2 H), 3.35 – 3.29 (m, 2 H), 3.16 (ddd, J = 12.9, 6.9, 4.0 Hz, 2 H), 2.50 (d, J = 7.3 Hz, 2 H), 2.01 – 1.93 (br s, 2 H, NH₂), 1.83 (ddd, J = 14.1, 9.0, 3.9 Hz, 2 H), 1.39 (s, 9 H), 1.28 (s, 9 H). **¹³C NMR** (101 MHz, CD₂OD): δ 148.9, 142.7, 137.2, 134.1, 132.5, 120.6, 119.7, 119.5, 54.6, 43.3, 41.6, 35.8, 35.1, 32.9, 32.1, 30.2. **HRMS** (ESI) Calcd for C₂₂H₃₇N₂O [(M+H)⁺]: 345.2900, found: 345.2898.
Synthesis of tert-butyl 4-allyl-4-aminopiperidine-1-carboxylate hydrochloride (30)

The title compound was prepared using General Procedure B. The cleavage of phenol unit was performed by adding 1.2 equiv of pyrrolidine along with I₂ (1.2 equiv) and NaOH (1 M) (5 equiv) to suppress the self-condensation of 4-allylpiperidin-4-amine with the liberated o-quinone. The HCl salt of compound 30 was selectively Boc protected on the secondary amine using Boc₂O (2 equiv) and K₂CO₃ (3 equiv) in THF:H₂O (2:1 v:v)(0.4 M) at 25 °C for 24 h. The crude product was purified by column chromatography on silica gel using pentane/EtOAc (80:20 v:v) and followed by EtOAc:MeOH:Et₃N (70:20:10 v:v) as solvent system to afford the Boc protected free amine 30 (82.0 mg, 0.38 mmol, 68%) as a brown oil and the free amine was protected as HCl salt using 4 M HCl (excess) in dioxane to give a yellow solid. FT-IR (thin film) ν max (cm⁻¹): 3398, 2928, 1693, 1526, 1479, 1249, 1164. ¹H NMR (500 MHz, CDCl₃): δ 8.53 (br s, 3 H, NH₃⁺), 5.97 – 5.87 (m, 1 H), 5.34 – 5.24 (m, 2 H), 3.70 – 3.49 (m, 4 H), 2.57 (d, J = 7.0 Hz , 2 H), 1.95 – 1.71 (m, 4 H), 1.45 (s, 9 H). ¹³C NMR (126 MHz, CDCl₃): δ 154.5, 129.7, 122.3, 80.3, 56.0, 41.6, 39.0, 33.2, 28.5. HRMS (ESI) Calcd for C₁₃H₂₅N₂O₂ [(M-Cl)⁺]: 241.1911, found: 241.1913.

Synthesis of 2-(pyridin-4-yl)pent-4-en-2-amine (31)

The title compound was prepared using General Procedure B. The HCl salt of compound 31 was basified with 1 M NaOH (1 mL), extracted with CHCl₃ (3 x 20 mL) and dried with Na₂SO₄. After removal of solvents gave the desired 2-(pyridin-4-yl)pent-4-en-2-amine 31 as a pale-yellow oil (100 mg, 0.62 mmol, 75%). FT-IR (thin film) ν max (cm⁻¹): 3349, 3077, 2921, 2850, 1640, 1439, 1279, 1000, 922, 825. ¹H NMR (400 MHz, CDCl₃): δ 8.55 (d, J = 6.3 Hz, 2 H), 7.37 (d, J = 6.3 Hz, 2 H), 5.57 – 5.46 (m, 1 H), 5.10 – 5.05 (m, 2 H), 2.54 (ddt, J = 13.6, 6.7, 1.3 Hz, 1 H), 2.39 (ddt, J = 13.6, 8.0, 1.1 Hz, 1 H), 1.91 (br s, 2 H, NH₂), 1.45 (s, 3 H). ¹³C NMR (101 MHz, CDCl₃): δ 157.7, 149.8, 133.3, 120.8, 119.6, 54.6, 49.2, 30.5. HRMS (ESI) Calcd for C₁₃H₁₅N₂ [(M+H)⁺]: 163.1230, found: 163.1230.
Synthesis of 2-(4-methoxyphenyl)propan-2-amine (32)

The title compound was prepared using General Procedure C. Commercial methyllithium solution (1.6 M in diethyl ether) was used. Yellow oil (94.0 mg, 0.57 mmol, 86%). FT-IR (thin film) \( \nu_{\text{max}} \) (cm\(^{-1}\)): 3353, 2962, 2836, 1610, 1512, 1245, 1180, 1032, 830. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.42 (d, \( J = 8.9 \) Hz, 2 H), 6.85 (d, \( J = 8.9 \) Hz, 2 H), 3.78 (s, 3 H), 1.96 (br s, 2 H, NH\(_2\)), 1.48 (s, 6 H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \( \delta \) 158.0, 142.3, 125.9, 113.5, 55.2, 52.1, 32.8. HRMS (ESI) Calcd for C\(_{10}\)H\(_{13}\)O \([\text{M-NH}_2]\): 149.0961, found: 149.0960.

Synthesis of 2-(4-methoxyphenyl)hexan-2-amine (33)

The title compound was prepared using General Procedure C. Commercial n-butyllithium solution (2.5 M in hexanes) was used. Yellow oil (107 mg, 0.52 mmol, 78%). FT-IR (thin film) \( \nu_{\text{max}} \) (cm\(^{-1}\)): 3396, 2956, 2930, 2860, 1611, 1510, 1246, 1180, 1135, 829. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.35 (d, \( J = 8.9 \) Hz, 2 H), 6.85 (d, \( J = 8.9 \) Hz, 2 H), 3.79 (s, 3 H), 1.89 (br s, 2 H, NH\(_2\)), 1.77 – 1.63 (m, 2 H), 1.44 (s, 3 H), 1.29 – 1.02 (m, 4 H), 0.83 (t, \( J = 7.3 \) Hz, 3 H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \( \delta \) 157.8, 141.0, 126.4, 113.4, 55.3, 54.7, 45.1, 31.1, 26.7, 23.2, 14.1. HRMS (ESI) Calcd for C\(_{13}\)H\(_{19}\)O \([\text{M-NH}_2]\): 191.1430, found: 191.1431.

Synthesis of 2-(4-methoxyphenyl)-3-methylpentan-2-amine (34)

The title compound was prepared using General Procedure C. Commercial sec-butyllithium solution (1.4 M in cyclohexane) was used. \( \text{dr} = 1:1 \), yellow oil (99.0 mg, 0.48 mmol, 72%). FT-IR (thin film) \( \nu_{\text{max}} \) (cm\(^{-1}\)): 3390, 2965, 2931, 1610, 1510, 1247, 1180, 1136, 831. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.35 (d, \( J = 8.9 \) Hz, 4 H), 6.85 (d, \( J = 8.9 \) Hz, 4 H), 3.79 (s, 6 H), 1.66 – 1.56 (m, 2 H), 1.55 – 1.41 (m, 6 H), 1.40 (s, 3 H), 1.37 (s, 3 H), 0.93 – 0.80 (m, 11 H), 0.78 (d, \( J = 6.7 \) Hz, 3 H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \( \delta \) 157.8 (2
The title compound was prepared using General Procedure C. Commercial tert-butyllithium solution (1.7 M in pentane) was used. The free amine was protected as HCl salt using 4 M HCl (excess) in dioxane. Yellow solid (96.0 mg, 0.46 mmol, 70%). FT-IR (thin film) ν_max (cm⁻¹): 2980, 2889, 1610, 1515, 1256, 831, 729. ^1H NMR (400 MHz, CDCl₃): δ 7.37 (d, J = 8.9 Hz, 2 H), 6.78 (d, J = 8.9 Hz, 2 H), 3.74 (s, 3 H), 1.80 (s, 3 H), 1.01 (s, 9 H). ^13C NMR (101 MHz, CDCl₃): δ 158.7, 131.0, 128.5, 113.0, 65.4, 55.2, 37.4, 26.1, 21.4. HRMS (ESI) Calcd for C₁₃H₂₂NO[(M-Cl)⁺]: 208.1696, found: 208.1697.

Synthesis of 2-(4-methoxyphenyl)-3,3-dimethylbutan-2-amine hydrochloride (35)

The title compound was prepared using General Procedure C. Commercial tert-butyllithium solution (1.7 M in pentane) was used. The free amine was protected as HCl salt using 4 M HCl (excess) in dioxane. Yellow solid (96.0 mg, 0.46 mmol, 70%). FT-IR (thin film) ν_max (cm⁻¹): 2980, 2889, 1610, 1515, 1256, 831, 729. ^1H NMR (400 MHz, CDCl₃): δ 7.37 (d, J = 8.9 Hz, 2 H), 6.78 (d, J = 8.9 Hz, 2 H), 3.74 (s, 3 H), 1.80 (s, 3 H), 1.01 (s, 9 H). ^13C NMR (101 MHz, CDCl₃): δ 158.7, 131.0, 128.5, 113.0, 65.4, 55.2, 37.4, 26.1, 21.4. HRMS (ESI) Calcd for C₁₃H₂₂NO[(M-Cl)⁺]: 208.1696, found: 208.1697.

Synthesis of 2-(4-methoxyphenyl)but-3-en-2-amine hydrochloride (36)

The title compound was prepared using General Procedure C. Vinyl lithium was generated using the known literature method⁶ in brief, in a Schlenk tube under an argon atmosphere, n-butyllithium (3.17, 7.94 mmol. 2.5 M in hexanes) was added dropwise to the neat tetravinyl stannane (0.72 mL, 3.97 mmol) over the course of 5 min at 25 °C. A white precipitate has formed during the addition of n-butyllithium. After letting it settle, the supernatant solution was collected through syringe and added to the ketimine/hemiaminal and TMEDA mixture at 0 °C. The reaction was gradually warmed to 25 °C and continued the stirring for 24 h. The remaining procedure is same as General Procedure C. 10 equiv of NaOH (1.0 M) was used during oxidation. The free amine was protected as HCl salt using 4 M HCl (0.5 mL in dioxane. Yellow solid (107 mg, 0.50 mmol, 76%). FT-IR (thin film) ν_max (cm⁻¹): 3387, 2980, 1609, 1514, 1255, 1188, 1029, 830. ^1H NMR (400 MHz, CDCl₃): δ 9.01 (br s, 3 H, NH₃⁺), 7.45 (d, J = 8.9 Hz, 2 H), 6.84 (d, J = 8.9 Hz, 2 H), 6.02 (dd, J = 17.4, 10.9 Hz, 1 H), 5.40 – 5.23 (m, 2 H), 3.77 (s, 3 H), 1.82 (s, 3 H). ^13C NMR (101 MHz, CDCl₃): δ 159.5, 139.0, 131.3, 127.8, 116.2, 114.0, 60.1, 55.3, 25.3. HRMS (ESI) Calcd for C₁₁H₁₃NO [M-NH₃Cl]: 161.0961, found: 161.0961.
Synthesis of 1-(4-methoxyphenyl)-1-phenylethan-1-amine (37)

The title compound was prepared using General Procedure C. Commercial PhLi (1.9 M in dibutyl ether) was used. Yellow oil (123 mg, 0.54 mmol, 82%). FT-IR (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 2967, 2835, 1609, 1509, 1248, 1180, 1030, 832, 701. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.39 – 7.36 (m, 2 H), 7.32 – 7.27 (m, 4 H), 7.23 – 7.19 (m, 1 H), 6.83 (d, $J = 8.9$ Hz, 2 H), 3.79 (s, 3 H), 2.31 (br s, 2 H, NH$_2$), 1.85 (s, 3 H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 158.2, 149.9, 141.9, 128.2, 127.5, 126.5, 126.2, 113.5, 58.3, 55.4, 32.0. HRMS (ESI) Calcd for C$_{15}$H$_{15}$O [M-NH$_2$]: 211.1117, found: 211.1116.

Synthesis of 2-(4-methoxyphenyl)-1-phenylpropan-2-amine (38)

The title compound was prepared using General Procedure A. 10 equiv of BnMgCl (2 M in THF) was used instead of allylmagnesium bromide for the addition. Yellow oil (101 mg, 0.42 mmol, 63%). FT-IR (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3028, 2930, 2835, 1610, 1511, 1247, 1181, 1033, 831, 703. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.32 (d, $J = 8.9$ Hz, 2 H), 7.21 – 7.17 (m, 3 H), 6.94 – 6.90 (m, 2 H), 6.86 (d, $J = 8.9$ Hz, 2 H), 3.81 (s, 3 H), 3.00 (d, $J = 13.0$ Hz, 1 H), 2.94 (d, $J = 13.0$ Hz, 1 H), 1.51 (br s, 2 H, NH$_2$), 1.48 (s, 3 H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 158.1, 149.8, 141.8, 137.8, 130.7, 127.9, 126.7, 126.4, 113.4, 55.4, 55.2, 51.9, 30.8. HRMS (ESI) Calcd for C$_{16}$H$_{17}$O [M-NH$_2$]: 225.1274, found: 225.1273.

Synthesis of 1-(4-butylphenyl)-1-(4-methoxyphenyl)ethan-1-amine (39)

The title compound was prepared using General Procedure C. 1-bromo-4-butylbenzene was used for lithium-halogen exchange$^3$ in THF at -78 °C for 1 h. Yellow oil (125 mg, 0.44 mmol, 67%). FT-IR (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3023, 2956, 2929, 2857, 1609, 1510, 1249, 1181, 1034, 831. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.31 – 7.25 (m, 4 H), 7.10 (d, $J = 8.9$ Hz, 2 H), 6.83 (d, $J = 8.9$ Hz, 2 H), 3.79 (s, 3 H), 2.58 (t, $J = 7.8$ Hz, 2 H), 2.01 (br s, 2 H, NH$_2$), 1.82 (s, 3 H), 1.61 – 1.54 (m, 2 H), 1.38 – 1.33 (m, 2 H), 0.92 (t, $J = 7.3$ Hz, 3 H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 158.1, 147.2, 142.1, 141.0, 128.2, 127.4, 126.1, 113.5,
58.0, 55.3, 35.3, 33.7, 32.1, 22.6, 14.1. HRMS (ESI) Calcd for C_{19}H_{23}O [M-NH₂]: 267.1743, found: 267.1743.

**Synthesis of 4-(1-amino-1-(4-methoxyphenyl)ethyl)-N,N-dimethylaniline (40)**

![Structural diagram](image)

The title compound was prepared using General Procedure C. 4-bromo-N,N-dimethylaniline was used for lithium-halogen exchange in THF at -78 °C for 1 h. 3 equiv of iodine was used as oxidant. Brown oil (95.0 mg, 0.35 mmol, 53%). FT-IR (thin film) ν_{max} (cm⁻¹): 3310, 2929, 2910, 2863, 1609, 1509, 1245, 1178, 1032, 815. ^1H NMR (400 MHz, CD₂Cl₂): δ 7.30 (d, J = 8.9 Hz, 2 H), 7.21 (d, J = 8.8 Hz, 2 H), 6.81 (d, J = 8.9 Hz, 2 H), 6.66 (d, J = 8.8 Hz, 2 H), 3.77 (s, 3 H), 2.91 (s, 6 H), 1.92 (br s, 2 H, NH₂), 1.77 (s, 3 H). ^13C NMR (101 MHz, CD₂Cl₂): 158.2, 149.5, 143.3, 138.7, 127.6, 127.1, 113.5, 112.5, 57.6, 55.5, 40.8, 32.5. HRMS (ESI) Calcd for C_{17}H_{20}NO [M-NH₂]: 254.1539, found: 254.1541.

**Synthesis of 1,1-bis(4-methoxyphenyl)ethan-1-amine (41)**

![Structural diagram](image)

The title compound was prepared using General Procedure C. 1-bromo-4-methoxybenzene was used for lithium-halogen exchange in THF at -78 °C for 1 h. 2 equiv of iodine was used as oxidant. Yellow oil (86.0 mg, 0.33 mmol, 51%). FT-IR (thin film) ν_{max} (cm⁻¹): 3035, 2934, 2836, 1609, 1510, 1246, 1181, 1029, 1008, 830, 758. ^1H NMR (400 MHz, CDCl₃): δ 7.29 (d, J = 8.9 Hz, 4 H), 6.83 (d, J = 8.9 Hz, 4 H), 3.79 (s, 6 H), 2.73 (br s, 2 H, NH₂), 1.83 (s, 3 H). ^13C NMR (101 MHz, CDCl₃): 158.1, 141.7, 127.4, 113.5, 58.0, 55.3, 32.0. HRMS (ESI) Calcd for C_{16}H_{17}O₂ [M-NH₂]: 241.1223, found: 241.1221.

**Synthesis of 1-(3,5-dimethoxyphenyl)-1-(4-methoxyphenyl)ethan-1-amine (42)**

![Structural diagram](image)

The title compound was prepared using General Procedure C. 1-bromo-3,5-dimethoxybenzene was used for lithium-halogen exchange in THF at -78 °C for 1 h. Yellow oil (123 mg, 0.43 mmol, 65%). FT-
IR (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3315, 2935, 2836, 1595, 1456, 1247, 1181, 1034, 832. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.29 (d, $J$ = 8.9 Hz, 2 H), 6.82 (d, $J$ = 8.9 Hz, 2 H), 6.53 (d, $J$ = 2.3 Hz, 2 H), 6.32 (t, $J$ = 2.3 Hz, 1 H), 3.79 (s, 3 H), 3.75 (s, 6 H), 1.98 (br s, 2 H, NH$_2$), 1.80 (s, 3 H). 13C NMR (101 MHz, CDCl$_3$): $\delta$ 160.6, 158.1, 152.9, 141.8, 127.3, 113.5, 104.9, 97.9, 58.3, 55.4, 55.3, 32.1. HRMS (ESI) Calcd for C$_{17}$H$_{19}$O$_3$ [M-NH$_2$]: 271.1329, found: 271.1329.

Synthesis of 1-(4-methoxyphenyl)-1-(4-(methylthio)phenyl)ethan-1-amine (43)

The title compound was prepared using General Procedure C. (4-bromophenyl)(methyl)sulfane was used for lithium-halogen exchange in THF at -78 °C for 1.5 h. 5 equiv of iodine was used as oxidant. Yellow oil (113 mg, 0.41 mmol, 63%). FT-IR (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3300, 2965, 2837, 1608, 1510, 1247, 1181, 1031, 814, 782. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.30 (dd, $J$ = 8.7, 5.5 Hz, 4 H), 7.19 (d, $J$ = 8.9 Hz, 2 H), 6.83 (d, $J$ = 8.9 Hz, 2 H), 3.79 (s, 3 H), 3.49 (br s, 2 H, NH$_2$), 2.47 (s, 3 H), 1.85 (s, 3 H). 13C NMR (101 MHz, CDCl$_3$): $\delta$ 158.3, 146.1, 140.8, 136.5, 127.4, 126.8, 126.5, 113.5, 58.4, 55.3, 31.5, 15.9. HRMS (ESI) Calcd for C$_{16}$H$_{17}$OS [M-NH$_2$]: 257.0995, found: 257.0995.

Synthesis of 1-(benzo[d][1,3]dioxol-5-yl)-1-(4-methoxyphenyl)ethan-1-amine (44)

The title compound was prepared using General Procedure C. 5-bromobenzo[d][1,3]dioxole was used for lithium-halogen exchange in THF at -78 °C for 1 h. 2 equiv of iodine was used as oxidant. Yellow oil (101 mg, 0.37 mmol, 56%). FT-IR (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3356, 2980, 2890, 1609, 1485, 1237, 1180, 1035, 864, 833. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.29 (d, $J$ = 8.9 Hz, 2 H), 6.87 (dd, $J$ = 8.1, 2.0 Hz, 1 H), 6.84 – 6.82 (m, 3 H), 6.72 (d, $J$ = 8.1 Hz, 1 H), 5.91 (s, 2 H), 3.79 (s, 3 H), 2.02 (br s, 2 H, NH$_2$), 1.80 (s, 3 H). 13C NMR (126 MHz, CDCl$_3$): $\delta$ 158.2, 147.6, 146.0, 144.3, 142.0, 127.3, 119.1, 113.5, 107.7, 107.5, 101.1, 58.1, 55.4, 32.3. HRMS (ESI) Calcd for C$_{16}$H$_{15}$O$_3$ [M-NH$_2$]: 255.1016, found: 255.1016.
Synthesis of 1-(4-fluorophenyl)-1-(4-methoxyphenyl)ethan-1-amine (45)

The title compound was prepared using General Procedure C. 1-bromo-4-fluorobenzene was used for lithium-halogen exchange in Et₂O at -78 °C for 30 min. Yellow oil (70.0 mg, 0.29 mmol, 43%). FT-IR (thin film) ν max (cm⁻¹): 3062, 2927, 2836, 1603, 1509, 1249, 1033, 833. ¹H NMR (400 MHz, CDCl₃): δ 7.26 (dd, J = 8.9, 5.3 Hz, 2 H), 7.19 (d, J = 8.9 Hz, 2 H), 6.88 (t, J = 8.7 Hz, 2 H), 6.76 (d, J = 8.9 Hz, 2 H), 3.72 (s, 3 H), 1.80 (br s, 2 H, NH₂), 1.74 (s, 3 H). ¹⁹F NMR (377 MHz, CDCl₃): δ -117.2. ¹³C NMR (101 MHz, CDCl₃): δ 161.5 (d, J C-F = 245.7 Hz), 158.2, 146.0 (d, J C-F = 3.2 Hz), 142.0, 127.9 (d, J C-F = 8.0 Hz), 127.3, 114.8 (d, J C-F = 20.8 Hz), 113.6, 57.8, 55.4, 32.4. HRMS (ESI) Calcd for C₁₅H₁₄OF[M-NH₂]: 229.1023, found: 229.1026.

Synthesis of 1-(4-chlorophenyl)-1-(4-methoxyphenyl)ethan-1-amine (46)

The title compound was prepared using General Procedure C. 1-chloro-4-iodobenzene was used for lithium-halogen exchange in Et₂O at -78 °C for 1 h. Yellow oil (100 mg, 0.38 mmol, 58%). FT-IR (thin film) ν max (cm⁻¹): 3310, 2962, 2835, 1608, 1509, 1247, 1180, 1033, 1012, 829. ¹H NMR (400 MHz, CDCl₃): δ 7.30 (d, J = 8.9 Hz, 2 H), 7.25 – 7.21 (m, 4 H), 6.81 (d, J = 8.9 Hz, 2 H), 3.77 (s, 3 H), 1.84 (br s, 2 H, NH₂), 1.79 (s, 3 H). ¹³C NMR (101 MHz, CDCl₃): δ 158.3, 148.8, 141.7, 132.2, 128.3, 127.8, 127.3, 113.6, 57.8, 55.4, 32.2. HRMS (ESI) Calcd for C₁₅H₁₄O₃Cl [M-NH₂]: 245.0728, found: 245.0729.

Synthesis of 1-(4-methoxyphenyl)-1-(4-(trifluoromethyl)phenyl)ethan-1-amine (47)

The title compound was prepared using General Procedure C. 1-iodo-4-(trifluoromethyl)benzene was used for lithium-halogen exchange in Et₂O at -78 °C for 1 h. Brown oil (129 mg, 0.44 mmol, 66%). FT-IR (thin film) ν max (cm⁻¹): 2967, 2840, 2812, 1615, 1510, 1325, 1250, 1117, 832. ¹H NMR (400 MHz, CDCl₃): δ 7.55 – 7.49 (m, 4 H), 7.27 (d, J = 8.9 Hz, 2 H), 6.84 (d, J = 8.9 Hz, 2 H), 3.79 (s, 3 H), 1.92 (br s, 2 H, NH₂), 1.84 (s, 3 H). ¹⁹F NMR (377 MHz, CDCl₃): δ -62.4. ¹³C NMR (101 MHz, CDCl₃): δ 158.4,
154.2, 141.3, 128.6 (q, $J_{CF} = 32.5$ Hz), 127.4, 126.6, 125.2 (q, $J_{CF} = 3.7$ Hz), 124.4 (q, $J_{CF} = 272.9$ Hz), 113.7, 58.1, 55.4, 32.1. HRMS (ESI) Calcd for $C_{18}H_{14}F_3O$ [M-NH$_2$]: 279.0991, found: 279.0991.

**Synthesis of 2-amino-2-phenylpropanenitrile (48)**

![2-amino-2-phenylpropanenitrile](image)

The title compound was prepared using **general method D**. Colourless oil (45.0 mg, 0.31 mmol, 95%). FT-IR (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3376, 2980, 2905, 2225, 1682, 1448, 1202, 881, 764, 699. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.75 – 7.59 (m, 2 H), 7.45 – 7.32 (m, 3 H), 2.10 (br s, 2 H, NH$_2$), 1.77 (s, 3 H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 141.3, 129.0, 128.8, 125.0, 124.3, 53.8, 31.9. HRMS (ESI) Calcd for $C_8H_{10}N$ [M-CN]: 120.0808, found: 120.0808.

**Synthesis of 2-amino-2-(4-methoxyphenyl)propanenitrile (49)**

![2-amino-2-(4-methoxyphenyl)propanenitrile](image)

The title compound was prepared using **general method D**. The crude product was purified by column chromatography on neutralized silica gel (treated with Et$_3$N prior to silica column chromatography) eluting with (pentane/EtOAc = 80:20 v:v) to EtOAc:MeOH:Et$_3$N (70:20:10 v:v) to afford compound 49 as yellow oil (100 mg, 0.57 mmol, 86%). FT-IR (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3376, 2933, 2839, 2235, 1606, 1510, 1248, 1178, 1029, 831. $^1$H NMR (400 MHz, CD$_3$CN): $\delta$ 7.55 (d, $J = 8.9$ Hz, 2 H), 6.95 (d, $J = 8.9$ Hz, 2 H), 3.79 (s, 3 H), 2.18 (br s, 2 H, NH$_2$), 1.67 (s, 3 H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 159.9, 133.4, 126.4, 124.5, 114.2, 55.5, 53.3, 32.0. HRMS (ESI) Calcd for $C_9H_{12}NO$ [M-CN]: 150.0913, found: 150.0913.

**Synthesis of ketimine and hemiaminal 49’**

![Ketimine/Hemiaminal](image)

Ketimine/hemiaminal ratio = 2.6:1
The title compound was prepared using **general method A**. Deep green viscous oil (Hemiaminal) and white solid (ketimine) (229 mg, 0.65 mmol, 98%). **FT-IR** (thin film) \( \nu_{\text{max}} \) (cm\(^{-1}\)): 3396, 2958, 2905, 2870, 2300, 1675, 1599, 1250, 1118, 999, 832, 773. **Ketimine**: \( ^{1}H\) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 8.06 – 7.97 (m, 2 H), 7.13 (d, \( J = 2.3 \) Hz, 1 H), 6.99 – 6.94 (m, 2 H), 6.70 (d, \( J = 2.3 \) Hz, 1 H), 6.31 (s, 1 H, OH), 3.89 (s, 3 H), 2.47 (s, 3 H), 1.46 (s, 9 H), 1.32 (s, 9 H). \( ^{13}C\) NMR (101 MHz, CDCl\(_3\)): \( \delta \) 166.4, 161.9, 146.1, 140.9, 135.9, 134.6, 132.3, 129.0, 120.3, 115.3, 113.8, 55.5, 35.0, 34.5, 31.8, 29.7, 17.5. **Hemiaminal**: \( ^{1}H\) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.60 – 7.53 (m, 2 H), 6.92 – 6.87 (m, 2 H), 6.84 (d, \( J = 2.3 \) Hz, 1 H), 6.77 (d, \( J = 2.3 \) Hz, 1 H), 3.81 (s, 3 H), 1.86 (s, 3 H), 1.28 (s, 9 H). \( ^{13}C\) NMR (101 MHz, CDCl\(_3\)): 159.4, 146.7, 143.4, 137.0, 136.6, 131.2, 126.5, 116.8, 113.7, 109.2, 100.2, 55.4, 34.7, 34.3, 31.9, 29.7, 28.9. **HRMS** (ESI) Calcd for C\(_{23}\)H\(_{32}\)NO\(_2\) [(M+H)\(^{+}\)]: 354.2428 found: 354.2433. 

**Synthesis of (E)-2-((3,5-di-tert-butyl-6-oxocyclohexa-2,4-dien-1-ylidene)amino)-2-(4-methoxyphenyl) propanenitrile (49）**

The title compound was prepared using **general method D**. The cleavage of phenol unit was performed by using 1.2 equiv of I\(_2\) and 5 equiv NaOH (1 M) instead of H\(_5\)IO\(_6\). The crude product was purified by column chromatography on silica gel using (pentane/EtOAc = 80:20 v:v) and followed by EtOAc:MeOH:Et\(_3\)N (70:20:10 v:v) as solvent system. Brown oil (249 mg, 0.66 mmol, 99%). **FT-IR** (thin film) \( \nu_{\text{max}} \) (cm\(^{-1}\)): 3310, 2963, 2865, 2361, 1677, 1605, 1511, 1253, 1176, 1031, 957, 909, 833, 731. \( ^{1}H\) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.41 (d, \( J = 8.6 \) Hz, 2 H), 6.92 – 6.84 (m, 3 H), 6.47 (d, \( J = 2.1 \) Hz, 1 H), 3.80 (s, 3 H), 2.17 (s, 3 H), 1.27 (s, 9 H), 1.06 (s, 9 H). \( ^{13}C\) NMR (101 MHz, CDCl\(_3\)): \( \delta \) 183.9, 159.8, 159.1, 154.6, 149.5, 134.2, 133.0, 126.2, 120.8, 114.9, 114.2, 59.5, 55.2, 35.6, 35.2, 34.0, 29.2, 28.0. **HRMS** (ESI) Calcd for C\(_{24}\)H\(_{32}\)N\(_2\)O\(_2\) [(M+H)\(^{+}\)]: 379.2380, found: 379.2373. 

**Synthesis of 2-amino-2-(4-fluorophenyl)propanenitrile (50)**

The title compound was prepared using **general method D**. The crude product was purified by column chromatography on neutralized silica gel (treated with Et\(_3\)N prior to column) using (pentane/
EtOAc = 80:20 v:v) and followed by EtOAc:MeOH:Et$_3$N (70:20:10 v:v) as solvent system. Yellow oil (57.0 mg, 0.35 mmol, 48%). FT-IR (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3379, 2933, 2240, 1602, 1509, 1225, 1160, 838. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.65 (dd, $J = 8.9, 5.1$ Hz, 2 H), 7.09 (t, $J = 8.6$ Hz, 2 H), 2.09 (br s, 2 H, NH$_2$), 1.75 (s, 3 H). $^{19}$F NMR (377 MHz, CD$_3$CN): $\delta$ -110.8. $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 162.8 (d, $J_{CF} = 248.1$ Hz), 137.2 (d, $J_{CF} = 4.0$ Hz), 127.0 (d, $J_{CF} = 8.4$ Hz), 124.1, 115.9 (d, $J_{CF} = 21.7$ Hz), 53.3, 32.1. HRMS (ESI) Calcd for C$_8$H$_9$FN [(M+H)$^+$]: 138.0714, found: 138.0713.

**Synthesis of 2-amino-2-propylpentanenitrile (51)**

![Structure of 2-amino-2-propylpentanenitrile](image)

The title compound was prepared using general method D. Yellow oil (115 mg, 0.82 mmol, 94%). FT-IR (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3376, 2962, 2935, 2876, 2221, 1465, 1270, 1164, 836. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.75 (br s, 2 H, NH$_2$), 1.68 – 1.47 (m, 8 H), 0.99 (t, $J = 7.1$ Hz, 6 H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 124.1, 53.9, 42.5, 17.7, 14.2. HRMS (ESI) Calcd for C$_8$H$_{17}$N$_2$ [(M+H)$^+$]: 141.1386, found: 141.1385.

**Synthesis of 2-amino-2-methylheptanenitrile (52)**

![Structure of 2-amino-2-methylheptanenitrile](image)

The title compound was prepared using general method D. Pale-yellow oil (111 mg, 0.79 mmol, 91%). FT-IR (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3374, 2931, 2860, 2223, 1610, 1460, 1220, 1185, 863. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.75 (br s, 2 H, NH$_2$), 1.65 – 1.56 (m, 2 H), 1.52 – 1.37 (m, 5 H), 1.36 – 1.23 (m, 4 H), 0.90 – 0.85 (m, 3 H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 124.6, 49.9, 41.8, 31.6, 27.7, 24.3, 22.5, 14.0. HRMS (ESI) Calcd for C$_8$H$_{17}$N$_2$ [(M+H)$^+$]: 141.1386, found: 141.1385.

**Synthesis of 1-aminocyclooctane-1-carbonitrile (53)**

![Structure of 1-aminocyclooctane-1-carbonitrile](image)

The title compound was prepared using general method D. Pale-yellow oil (212 mg, 1.39 mmol, 89%). FT-IR (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3370, 3303, 2932, 2854, 2227, 1280, 1134, 883, 849. $^1$H NMR (400 MHz, CD$_3$CN): $\delta$ 1.91 – 1.77 (m, 4 H), 1.76 – 1.43 (m, 10 H). $^{13}$C NMR (101 MHz, CD$_3$CN): $\delta$ 126.5, 54.8, 36.4, 28.5, 25.0, 22.5. HRMS (ESI) Calcd for C$_9$H$_{17}$N$_2$ [(M+H)$^+$]: 153.1386, found: 153.1386.
Synthesis of 4-aminotetrahydro-2H-pyran-4-carbonitrile (54)

The title compound was prepared using **general method D**. Yellow oil (121 mg, 0.96 mmol, 97%). The spectroscopic data of compound 54 were identical to those reported. 

$^1$H NMR (400 MHz, CD$_3$CN): δ 4.03 – 3.93 (m, 2 H), 3.66 (ddd, $J = 12.5, 10.3, 2.5$ Hz, 2 H), 1.99 (ddt, $J = 13.5, 4.3, 2.1$ Hz, 2 H), 1.84 (br s, 2 H, NH$_2$), 1.75 (ddd, $J = 13.9, 10.3, 4.2$ Hz, 2 H). 

$^{13}$C NMR (101 MHz, CD$_3$CN): δ 122.4, 63.1, 48.1, 36.7. 

HRMS (ESI) Calcd for C$_6$H$_{11}$N$_2$O [(M+H)$^+$]: 127.0866, found: 127.0866.

Synthesis of 4-aminotetrahydro-2H-thiopyran-4-carbonitrile 1,1-dioxide (55)

The title compound was prepared using **general method D**. White solid (49.0 mg, 0.28 mmol, 42%). 

FT-IR (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3370, 3303, 2975, 2935, 2227, 1332, 1279, 1124, 882, 848. 

$^1$H NMR (400 MHz, CD$_3$CN): δ 3.31 – 3.24 (m, 2 H), 2.99 – 2.92 (m, 2 H), 2.45 – 2.36 (m, 2 H), 2.34 – 2.22 (m, 2 H), 2.16 (br s, 2 H, NH$_2$). 

$^{13}$C NMR (126 MHz, CD$_3$CN): δ 123.9, 48.7, 47.2, 35.5. 

HRMS (ESI) Calcd for C$_5$H$_{10}$NO$_2$S [M-CN]: 148.0427, found: 148.0427.

Synthesis of 4-amino-1-methylpiperidine-4-carbonitrile (56)

The title compound was prepared using **general method D**. 10 eq of coupling partner and carrying out the oxidation for 1 hour. Yellow oil (883 mg, 6.34 mmol, 72%). The spectroscopic data of compound 56 were identical to those reported. 

$^1$H NMR (400 MHz, CDCl$_3$): δ 4.58 (br s, 2 H), 2.81 (dt, $J = 12.8, 4.2$ Hz, 2 H), 2.38 – 2.26 (m, 5 H), 2.22 – 2.12 (m, 2 H), 1.83 (ddd, $J = 14.1, 10.9, 3.9$ Hz, 2 H). 

$^{13}$C NMR (101 MHz, CDCl$_3$): δ 119.8, 60.2, 51.5, 45.7, 34.2. 

HRMS (ESI) Calcd for C$_7$H$_{14}$N$_3$ [(M+H)$^+$]: 140.1182, found: 140.1182.
The title compound was prepared using general method D without oxidation. White crystals (1.40 g, 3.99 mmol, 97%). The recrystallization was performed using pentane: EtOAc (10:1) solvent system. mp = 141-148 °C. FT-IR (thin film) ν\text{max} (cm\(^{-1}\)): 3390, 2959, 2906, 2870, 2230, 1598, 1485, 1227, 761, 699. \(^1\)H NMR (400 MHz, CD\(_3\)CN): \(\delta\) 7.68 – 7.60 (m, 2 H), 7.47 – 7.39 (m, 2 H), 7.39 – 7.31 (m, 1 H), 6.88 (d, \(J = 2.3\) Hz, 1 H), 6.63 (d, \(J = 2.3\) Hz, 1 H), 6.10 (s, 1 H, OH), 4.67 (s, 1 H, NH), 1.93 (s, 3 H), 1.36 (s, 9 H), 1.07 (s, 9 H). \(^13\)C NMR (101 MHz, CD\(_3\)CN): \(\delta\) 145.0, 142.9, 141.3, 137.3, 133.2, 129.9, 129.4, 126.1, 122.5, 117.7, 116.3, 59.2, 35.5, 35.0, 31.7, 31.6, 30.1. HRMS (ESI) Calcd for C\(_{23}\)H\(_{31}\)N\(_2\)O \([(\text{M}+\text{H})^+]\): 351.2431, found: 351.2431.

**Synthesis of tert-butyl 4-amino-4-(4-fluorophenyl)-2-methylenepentanoate (58)**

General Procedure E was carried out using 4-fluoro-\(\alpha\)-methylbenzylamine (33.0 µL, 0.25 mmol). Silica gel column chromatography (EtOAc:Pentane 10:90 – 50:50 v:v) gave a colourless oil, (21.0 mg, 0.08, 30%). FT-IR (thin film): ν\text{max} (cm\(^{-1}\)) = 2980, 1709, 1626, 1602, 15039. \(^1\)H NMR (400 MHz, CD\(_3\)CN): \(\delta\) 7.53 – 7.43 (m, 2 H), 7.14 – 6.88 (m, 2 H), 5.97 (d, \(J = 1.9\) Hz, 1 H), 5.33 – 5.23 (m, 1 H), 2.66 (dd, \(J = 1.9, 0.9\) Hz, 2 H), 1.38 (s, 3 H), 1.37 (s, 9 H). \(^19\)F NMR (377 MHz, DMSO-d\(_6\)): \(\delta\) -118.12 (ddd, \(J = 14.2, 9.1, 5.5\) Hz). \(^13\)C NMR (101 MHz, CD\(_3\)CN): \(\delta\) 167.8, 162.2 (d, \(J = 242.1\) Hz), 146.0 (d, \(J = 3.1\) Hz), 140.4, 128.6 (d, \(J = 7.9\) Hz), 127.3, 115.1 (d, \(J = 21.3\) Hz), 81.1, 55.9, 46.6, 31.0, 28.1. HRMS (ESI) Calcd for C\(_{16}\)H\(_{22}\)O\(_2\)N\(_2\)F \([(\text{M}+\text{H})^+]\): 280.1707, found: 280.1705.

**Synthesis of tert-butyl 4-amino-4-(4-chlorophenyl)-2-methylenepentanoate (58’)**

General Procedure E was carried out using 4-chloro-\(\alpha\)-methylbenzylamine (36.0 µL, 0.25 mmol). Silica gel column chromatography (EtOAC:Pentane 10:90 – 50:50 v:v) gave a colourless oil, (16.2 mg,
0.05 mmol, 22%). **FT-IR** (thin film): $\nu_{\text{max}}$ (cm$^{-1}$) = 2976, 2931, 1707. $^1$H NMR (400 MHz, CD$_3$CN): $\delta$ 7.38 (d, $J$ = 8.7 Hz, 2 H), 7.21 (d, $J$ = 8.8 Hz, 2 H), 5.89 (d, $J$ = 1.9 Hz, 1 H), 5.21 (dt, $J$ = 1.9, 0.9 Hz, 1 H), 2.58 (d, $J$ = 0.9 Hz, 2 H), 1.71 (s, 2 H), 1.30 (s, 3 H), 1.28 (s, 9 H). $^{13}$C NMR (101 MHz, CD$_3$CN): $\delta$ 167.8, 148.8, 140.3, 128.6, 127.3, 128.1, 127.1, 81.1, 55.9, 46.5, 30.9, 28.1. HRMS (ESI) Calcd for C$_{16}$H$_{23}$O$_2$NCl [(M+H)$^+$]: 264.1412, found: 296.1409.

**Synthesis of tert-butyl 4-amino-4-phenyl-2-methylenepentanoate (59)**

![Chemical structure](image)

**General Procedure E** was carried out using $\alpha$-methylbenzylamine (32.0 µL, 0.25 mmol). Silica gel column chromatography (EtOAc:Pentane 10:90 – 50:50 v:v) gave a colourless oil, (20.2 mg, 0.08 mmol, 31%). **FT-IR** (thin film): $\nu_{\text{max}}$ (cm$^{-1}$) = 2976, 2930, 1709, 1626. $^1$H NMR (400 MHz, CD$_3$CN): $\delta$ 7.55 – 7.42 (m, 2 H), 7.30 (dd, $J$ = 8.4, 7.0 Hz, 2 H), 7.21 – 7.15 (m, 1 H), 5.97 (d, $J$ = 2.0 Hz, 1 H), 5.28 (dt, $J$ = 2.0, 1.0 Hz, 1 H), 2.79 – 2.50 (m, 2 H), 2.02 (s, 7 H), 1.39 (s, 9 H), 1.38 (s, 3 H). $^{13}$C NMR (101 MHz, CD$_3$CN): $\delta$ 167.9, 150.1, 140.5, 128.8, 127.1, 127.0, 126.6, 81.1, 56.1, 46.5, 30.8, 28.1. HRMS (ESI) Calcd for C$_{16}$H$_{24}$O$_2$N$_1$ [(M+H)$^+$]: 262.1802, found: 262.1800.

**Synthesis of tert-butyl 4-amino-4-(4-methoxyphenyl)-2-methylenepentanoate (60)**

![Chemical structure](image)

**General Procedure E** was carried out using 4-methoxy-$\alpha$-methylbenzylamine (37.0 µL, 0.25 mmol). Silica gel column chromatography (EtOAc:Pentane 10:90 – 50:50 v:v) gave a colourless oil, (31.3 mg, 0.11 mmol, 43%). **FT-IR** (thin film): $\nu_{\text{max}}$ (cm$^{-1}$) = 2977, 1708, 1611, 1512, 1458. $^1$H NMR (400 MHz, CD$_3$CN): $\delta$ 7.48 (d, $J$ = 8.8 Hz, 2 H), 6.94 (d, $J$ = 8.8 Hz, 2 H), 6.07 (d, $J$ = 2.0 Hz, 1 H), 5.40 – 5.35 (m, 1 H), 3.86 (s, 3 H), 2.75 (dd, $J$ = 2.6, 0.9 Hz, 2 H), 1.48 (s, 9 H), 1.46 (s, 3 H). $^{13}$C NMR (101 MHz, CD$_3$CN): $\delta$ 167.9, 159.0, 142.1, 140.7, 127.7, 127.0, 114.0, 81.0, 55.8, 55.6, 46.7, 30.9, 28.1. HRMS (ESI) Calcd for C$_{17}$H$_{26}$O$_3$N$_1$ [(M+H)$^+$]: 292.1907, found: 292.1910.

**Synthesis of tert-butyl 4-amino-4-(4-methylphenyl)-2-methylenepentanoate (61)**

![Chemical structure](image)

**Synthesis of tert-butyl 4-amino-4-(4-methoxyphenyl)-2-methylenepentanoate (60)**

![Chemical structure](image)
**General Procedure E** was carried out using 4-methyl-α-methylbenzylamine (37.0 µL, 0.25 mmol). Silica gel column chromatography (EtOAc:Pentane 10:90 – 50:50 v:v) gave a colourless oil, (22.0 mg, 0.08 mmol, 32%). **FT-IR** (thin film): ν\textsubscript{max} (cm\textsuperscript{-1}) = 2980, 1710. \textsuperscript{1}H NMR (400 MHz, CD\textsubscript{3}CN): δ 7.34 (d, J = 8.3 Hz, 2 H), 7.11 (d, J = 7.7 Hz, 2 H), 5.96 (d, J = 2.0 Hz, 1 H), 5.28 (dd, J = 2.0, 1.1 Hz, 1 H), 2.72 – 2.58 (m, 2 H), 2.28 (s, 3H), 1.38 (s, 9 H), 1.36 (s, 3 H). \textsuperscript{13}C NMR (101 MHz, CD\textsubscript{3}CN): δ 167.9, 147.0, 140.6, 136.5, 129.4, 127.0, 126.5, 81.0, 55.9, 46.6, 30.7, 28.1, 20.9. **HRMS** (ESI) Calcd for C\textsubscript{17}H\textsubscript{26}O\textsubscript{2}N [(M+H)	extsuperscript{+}]: 276.1958, found 276.1958.

**Synthesis of tert-butyl 2-((1-amino-2,3-dihydro-1H-inden-1-yl)methyl)acrylate (62)**

![Chemical structure](image)

**General Procedure E** was carried out using 1-aminooindane (32.0 µL, 0.25 mmol). Silica gel column chromatography (EtOAc:Pentane 10:90 – 50:50 v:v) gave an amorphous solid, (25.3 mg, 0.09 mmol, 37%). **FT-IR** (thin film): ν\textsubscript{max} (cm\textsuperscript{-1}) = 2980, 1707, 1626. \textsuperscript{1}H NMR (400 MHz, CD\textsubscript{3}CN): δ 7.23 – 7.12 (m, 4 H), 6.03 (d, J = 2.0 Hz, 1 H), 5.41 (dd, J = 2.0, 1.0 Hz, 1 H), 2.82 (ddd, J = 9.1, 5.2, 4.0 Hz, 2 H), 2.72 (d, J = 13.1 Hz, 1 H), 2.48 (dd, J = 13.2, 1.0 Hz, 1 H), 2.21 (ddd, J = 12.7, 6.7, 3.9 Hz, 1 H), 1.95 (br s, 2 H), 1.79 (dt, J = 12.7, 8.8 Hz, 1 H), 1.38 (s, 9 H). \textsuperscript{13}C NMR (101 MHz, CD\textsubscript{3}CN): δ 167.9, 151.0, 143.6, 140.6, 128.1, 127.3, 127.2, 125.5, 123.8, 81.1, 65.5, 42.4, 41.6, 30.0, 28.1. **HRMS** (ESI) Calcd for C\textsubscript{17}H\textsubscript{24}O\textsubscript{2}N [(M+H)	extsuperscript{+}]: 274.1802, found 274.1802.

**Synthesis of 5-(4-methoxyphenyl)-5-methyl-3-methyleneprrolidin-2-one (63)**

![Chemical structure](image)

**General Procedure E** was followed using 4-methoxy-α-methylbenzylamine (37.0 µL, 0.25 mmol) and ethyl 2-((phenylsulfonyl)methyl)acrylate (254 mg, 1.00 mmol) as coupling partner. Work up with NaOH (1M) initiated an *in situ* lactamization, and purification *via* silica gel column chromatography (EtOAc:Pentane 10:90-40:60 v:v) gave an amorphous solid, (17.9 mg, 0.08 mmol, 33%). **mp** = 98-100 °C. **FT-IR** (thin film): ν\textsubscript{max} (cm\textsuperscript{-1}) = 3212, 2968, 1695, 1658, 1613, 1583, 1514. \textsuperscript{1}H NMR (400 MHz, CD\textsubscript{3}CN): δ 7.29 (d, J = 8.9 Hz, 2 H), 7.11 (s, 1 H), 6.90 (d, J = 8.8 Hz, 2 H), 5.81 (td, J = 2.7, 1.1 Hz, 1 H), 5.28 (tt, J = 2.4, 1.1 Hz, 1 H), 3.77 (s, 3 H), 2.93 (qt, J = 16.8, 2.5 Hz, 2 H), 1.59 (s, 3 H). \textsuperscript{13}C NMR (101
MHz, CD3CN): δ 169.9, 159.6, 141.8, 140.3, 127.0, 115.8, 114.7, 59.0, 55.9, 45.0, 30.1 HRMS (ESI) Calcd for C13H13O2N [(M+H)+]: 218.1176, found 218.1177.

Synthesis of 2-methyl-1-phenylpropan-2-amine (Phentermine) (64)11

The title compound was prepared using general method A. 10 equiv of BnMgCl (2 M in THF) was used instead of allylmagnesium bromide for the addition. Pale yellow oil (134 mg, 0.90 mmol, 53%). The spectroscopic data of compound 64 were identical to those reported. 1H NMR (400 MHz, CDCl3): δ 7.33 – 7.27 (m, 2 H), 7.27 – 7.21 (m, 1 H), 7.21 – 7.16 (m, 2 H), 2.66 (s, 2 H), 1.30 – 1.19 (br s, 2 H), 1.12 (s, 6 H). 13C NMR (101 MHz, CDCl3): δ 138.6, 130.6, 128.1, 126.4, 51.3, 50.1, 30.6. HRMS (ESI) Calcd for C12H12N [(M+H)+]: 150.1277, found: 150.1277.

Synthesis of 2-(adamantan-1-yl)pent-4-en-2-amine hydrochloride (from Rimantadine or Flumadine) (65)

The title compound was prepared using general method B. Yellow solid (198 mg, 0.77 mmol, 54%). FT-IR (thin film) νmax (cm⁻¹): 3032, 2904, 2851, 1641, 1516, 1449, 1197, 919, 731. 1H NMR (400 MHz, CDCl3): δ 8.20 (br s, 3 H, NH3+), 6.21 – 6.08 (m, 1 H), 5.21 – 5.12 (m, 2 H), 2.63 (dd, J = 14.5, 5.9 Hz, 1 H), 2.34 (dd, J = 14.5, 8.3 Hz, 1 H), 2.03 (s, 3 H), 1.86 – 1.70 (m, 6 H), 1.64 (s, 6 H), 1.26 (s, 3 H). 13C NMR (101 MHz, CDCl3): δ 132.9, 120.0, 62.5, 39.0, 38.2, 36.6, 36.1, 28.4, 18.5. HRMS (ESI) Calcd for C22H26N [(M-Cl)+]: 220.2060, found: 220.2059.

Synthesis of 2-(adamantan-1-yl)-2-aminopropanenitrile (from Rimantadine or Flumadine) (66)

S56
The title compound was prepared using **general method D**. White powder (100 mg, 0.49 mmol, 88%). **FT-IR** (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3376, 2904, 2850, 2218, 1630, 1450, 1266, 1102, 851, 815. $^1$H NMR (400 MHz, CD$_3$CN): $\delta$ 2.03 (m, 3 H), 1.76 – 1.62 (m, 12 H), 1.32 (s, 3 H). $^{13}$C NMR (101 MHz, CD$_3$CN): $\delta$ 125.3, 58.4, 38.6, 37.4, 36.8, 29.3, 21.9. **HRMS** (ESI) Calcd for C$_{13}$H$_{21}$N$_2$ [(M+H)$^+$]: 205.1699, found: 205.1700.

**Synthesis of 1-(2,6-dimethylphenoxy)-2-methylpent-4-en-2-amine (Mexiletine) (67)**

![Chemical Structure](from Mexiletine)

The title compound was prepared using **general method B**. The HCl salt of compound 67 was basified with 1 M NaOH (1 mL), extracted with CHCl$_3$ (3 x 20 mL) and dried by Na$_2$SO$_4$. After removal of solvents gave the desired 1-(2,6-dimethylphenoxy)-2-methylpent-4-en-2-amine 67 as a pale-yellow oil (150 mg, 0.68 mmol, 57%). **FT-IR** (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3380, 2968, 2922, 2840, 1639, 1476, 1263, 1202, 1020, 767. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.01 (d, $J$ = 7.3 Hz, 2 H), 6.92 (dd, $J$ = 8.3, 6.6 Hz, 1 H), 5.98 – 5.88 (m, 1 H), 5.19 – 5.13 (m, 2 H), 3.54 (dd, $J$ = 10.6, 8.6 Hz, 2 H), 2.38 – 2.34 (m, 2 H), 2.29 (s, 6 H), 1.68 (br s, 2 H, NH$_2$), 1.25 (s, 3 H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 155.2, 133.9, 131.0, 129.1, 124.0, 118.8, 79.6, 52.8, 44.5, 25.1, 16.5. **HRMS** (ESI) Calcd for C$_{14}$H$_{22}$NO [(M+H)$^+$]: 220.1696, found: 220.1697.

**Synthesis of 2-amino-2-methyl-3-phenylpropanenitrile (68)**

![Chemical Structure](from Amphetamine)

The title compound was prepared using **general method D**. Pale yellow oil (87.0 mg, 0.54 mmol, 94%). **FT-IR** (thin film) $\nu_{\text{max}}$ (cm$^{-1}$): 3374, 3031, 2925, 2361, 1603, 1454, 846, 760, 702. $^1$H NMR (400 MHz, CD$_3$CN): $\delta$ 7.44 – 7.26 (m, 5 H), 2.90 (q, $J$ = 13.3 Hz, 2 H), 1.97 (br s, 2 H, NH$_2$), 1.43 (s, 3 H). $^{13}$C NMR (101 MHz, CD$_3$CN): $\delta$ 136.6, 131.5, 129.2, 128.3, 125.3, 51.7, 48.0, 27.8. **HRMS** (ESI) Calcd for C$_{10}$H$_{13}$N$_2$ [(M+H)$^+$]: 161.1073, found: 161.1073.

**6: NMR Spectra:**
[Chemical structures and spectra]

S63
Chemical Name: Compound 13

1H NMR (CDCl3, 400 MHz):

- δ 7.3 (s, 5H)
- δ 6.5 (d, 2H)
- δ 5.3 (t, 1H)
- δ 2.2 (s, 3H)
- δ 1.2 (m, 2H)

13C NMR (CDCl3, 100 MHz):

- δ 135.2
- δ 128.6
- δ 128.4
- δ 128.1
- δ 127.9
- δ 21.0
- δ 14.7

[Diagram of the molecular structure of Compound 13]
23 (dr=4.26:1) (trans:cis)

NH₂

fBu

Ph
23 (dr=4.26:1) (trans:cis)
24

NH₂·HCl

24

NH₂·HCl
49°, ketimine/hemiamentalin ratio = 2:6:1
\(^\text{\textsuperscript{1}H-\textsuperscript{1}H-\text{COSY of 49\*}, ketimine/hemiaminal ratio = 2.6:1}\)

\(^\text{\textsuperscript{1}H-\textsuperscript{13}C-\text{HSQC of 49\*}, ketimine/hemiaminal ratio = 2.6:1}\)
S123
(from Rimantadine)
(from Mexiletine)
7: X-ray structure and data for compound 57:

Table S4: Crystal data and structure refinement for compound 57

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Data collection

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| Absorption correction | Multi-scan |
|DENZO/SCALEPACK (Otwinowski & Minor, 1997)| |
| T_{min}, T_{max} | 0.86, 0.97 |
| No. of measured, independent and observed [I > 2.0σ(I)] reflections | 14910, 4230, 3970 |
| R_{int} | 0.032 |
Refinement

\[ R[F^2 > 2\sigma(F^2)], wR(F^2), S \]

\[ 0.034, 0.087, 1.03 \]

No. of reflections

4230

No. of parameters

326

No. of restraints

116

H-atom treatment

Only H-atom coordinates refined

\[ \Delta \rho_{\text{max}}, \Delta \rho_{\text{min}} (\text{e Å}^{-3}) \]

\[ 0.22, -0.16 \]

Absolute structure

Flack (1983), 1797 Friedel-pairs

Absolute structure parameter

\[-0.1 (2)\]

Computer programs: USER DEFINED DATA COLLECTION, USER DEFINED CELL REFINEMENT, USER DEFINED DATA REDUCTION, SUPERFLIP (Palatinus & Chapuis, 2007), CRYSTALS (Betteridge et al., 2003), CAMERON (Watkin et al., 1996).

Table 2

Selected geometric parameters (Å, °)

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<td>C11</td>
<td>1.385 (2)</td>
</tr>
<tr>
<td>C8</td>
<td>C9</td>
<td>1.384 (3)</td>
</tr>
<tr>
<td>C9</td>
<td>C10</td>
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</tr>
<tr>
<td>O1</td>
<td>C2</td>
<td>111.05 (11)</td>
</tr>
<tr>
<td>O1</td>
<td>C2</td>
<td>121.91 (11)</td>
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<tr>
<td>C3</td>
<td>C2</td>
<td>120.99 (11)</td>
</tr>
<tr>
<td>C2</td>
<td>C3</td>
<td>116.27 (11)</td>
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<tr>
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<td>C3</td>
<td>119.78 (11)</td>
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<tr>
<td>N4</td>
<td>C3</td>
<td>123.93 (12)</td>
</tr>
<tr>
<td>C3</td>
<td>N4</td>
<td>124.04 (11)</td>
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<tr>
<td>N4</td>
<td>C5</td>
<td>112.94 (11)</td>
</tr>
<tr>
<td>N4</td>
<td>C5</td>
<td>107.65 (11)</td>
</tr>
<tr>
<td>C6</td>
<td>C5</td>
<td>108.96 (11)</td>
</tr>
<tr>
<td>N4</td>
<td>C5</td>
<td>110.23 (11)</td>
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Table 3
Hydrogen-bond geometry (Å, °)

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<th>D—H···A</th>
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<td>120 (1)</td>
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<td>0.84</td>
<td>1.99</td>
<td>2.822 (2)</td>
<td>175 (2)</td>
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</tbody>
</table>

checkCIF/PLATON report

Alert level G
PLAT002_ALERT_2_G Number of Distance or Angle Restraints on AtSite 53 Note
PLAT152_ALERT_1_G The Supplied and Calc. Volume s.u. Differ by ... 3 Units
PLAT230_ALERT_2_G Hirshfeld Test Diff for C5 --C13 . 6.3 s.u.
PLAT791_ALERT_4_G Model has Chirality at C5 (Chiral SPGR) R Verify
PLAT860_ALERT_3_G Number of Least-Squares Restraints ............ 116 Note
PLAT882_ALERT_1_G No Datum for _diffrn_reflns_av_unetI/netI ...... Please Do !
8: References:


