Electronic Supplementary Information

Tertiary Amine Synthesis via Reductive Coupling of Amides with Grignard Reagents

Lan-Gui Xie and Darren Dixon*

Department of Chemistry, Chemistry Research Laboratory
University of Oxford, Mansfield Road, Oxford OX1 3TA, UK

E-mail: darren.dixon@chem.ox.ac.uk

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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 F<sub>254</sub> fluorescent treated silica. Visualisation was accomplished under UV light (λ<sub>max</sub>= 254 nm) and by staining with KMnO<sub>4</sub> staining dip. Chromatographic purification was performed on VWR 60 silica gel 40-63 μm using HPLC grade solvents that were used as supplied. High resolution mass spectra (HRMS) were recorded on a Bruker Daltonics MicroTOF mass spectrometer equipped with an ESI source or on a Micromass GCT equipped with an EI source unless otherwise specified. Infrared absorption spectra (IR) were recorded on a Bruker Tensor 27 FT-IR spectrometer from a thin film on a diamond ATR module. Only selected bands (ν<sub>max</sub>) are reported in wavenumbers (cm<sup>-1</sup>). NMR spectra were recorded on Bruker spectrometers operating at 400 or 500 MHz (1H resonance). Proton chemical shifts (δ) are given in parts per million (ppm) relative to tetramethylsilane (TMS) with the solvent resonance (CDCl<sub>3</sub>, δ = 7.26 ppm) as internal standard. 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, m = multiplet, br = broad signal. Coupling constants (J) are given in Hertz (Hz). <sup>13</sup>C-NMR spectra were recorded with complete proton decoupling. Carbon chemical shifts are reported in ppm (δ) relative to TMS with the solvent resonance (CDCl<sub>3</sub>, δ = 77.16 ppm) as internal standard.

2. Preparation of amides

General procedure for the synthesis of amides

To a solution of the amine (1.1 eq) and Et<sub>3</sub>N (1.5 eq) in dichloromethane (2 mL/mmol), acyl chloride (1 eq) was added in dropwise at 0 °C. The reaction mixture was stirred overnight at room temperature. The solution, diluted with dichloromethane, was washed with 1N HCl, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure for silica gel column.

Synthesis of phenyl(pyrrolidin-1-yl)methanone (S2)<sup>1</sup>
According to the general procedure, using benzoyl chloride (422 mg, 3 mmol) and pyrrolidine (235 mg, 3.3 mmol), phenyl(pyrrolidin-1-yl)methanone was obtained as a colourless oil after flash column chromatography on silica gel (499 mg, 95% yield).

Synthesis of azepan-1-yl(phenyl)methanone (S3)

According to the general procedure, using benzoyl chloride (422 mg, 3 mmol) and azepane (327 mg, 3.3 mmol), azepan-1-yl(phenyl)methanone was obtained as a colourless oil after flash column chromatography on silica gel (555 mg, 91% yield).

Synthesis of azocan-1-yl(phenyl)methanone (S4)

According to the general procedure, using benzoyl chloride (422 mg, 3 mmol) and azocane (374 mg, 3.3 mmol), azocan-1-yl(phenyl)methanone was obtained as a colourless oil after flash column chromatography on silica gel (554 mg, 85% yield).

Synthesis of morpholino(phenyl)methanone (S5)

According to the general procedure, using benzoyl chloride (422 mg, 3 mmol) and morpholine (288 mg, 3.3 mmol), morpholino(phenyl)methanone was obtained as a colourless oil after flash column chromatography on silica gel (528 mg, 92% yield).
Synthesis of (6,7-dimethoxy-3,4-dihydroisoquinolin-2(1H)-yl)(phenyl)methanone (S6)\(^4\)

![Chemical structure](image)

According to the general procedure, using benzoyl chloride (422 mg, 3 mmol) and 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (638 mg, 3.3 mmol), (6,7-dimethoxy-3,4-dihydroisoquinolin-2(1H)-yl)(phenyl)methanone was obtained as a white solid after flash column chromatography on silica gel (794 mg, 89% yield).

**Synthesis of N-benzyl-N-methylbenzamide (S7)\(^1\)**

![Chemical structure](image)

According to the general procedure, using benzoyl chloride (422 mg, 3 mmol) and N-methylbenzylamine (400 mg, 3.3 mmol), N-benzyl-N-methylbenzamide was obtained as a colourless oil after flash column chromatography on silica gel (588 mg, 87% yield).

**Synthesis of N-methoxy-N-methylbenzamide (S8)\(^5\)**

![Chemical structure](image)

According to the general procedure, using benzoyl chloride (422 mg, 3 mmol) and N,O-dimethylhydroxylamine hydrochloride (322 mg, 3.3 mmol), N-methoxy-N-methylbenzamide was obtained as a colourless oil after flash column chromatography on silica gel (421 mg, 85% yield).

**Synthesis of N-Methyl-N-phenylbenzamide (S9)\(^1\)**
According to the general procedure, using benzoyl chloride (169 mg, 1.2 mmol) and N-methylaniline (108 μL, 1 mmol), N-methyl-N-phenylbenzamide was obtained as a colourless oil after flash column chromatography on silica gel (157 mg, 74% yield).

**Synthesis of \(\text{N,N-dimethyldecanamide (S10)\textsuperscript{6}}\)**

According to the general procedure, using decanoyl chloride (622 μL, 3 mmol) and dimethylamine hydrochloride (270 mg, 3.3 mmol), N,N-dimethyldecanamide was obtained as a colourless oil after flash column chromatography on silica gel (455 mg, 76% yield).

**Synthesis of \(\text{N,N-dimethylcyclohexanecarboxamide (S11)\textsuperscript{7}}\)**

According to the general procedure, using cyclohexyl carbonyl chloride (267 μL, 2 mmol) and dimethylamine hydrochloride (180 mg, 2.2 mmol), N,N-dimethylcyclohexylcarboxamide was obtained as a yellowish oil after flash column chromatography on silica gel (263 mg, 85% yield).

**Synthesis of \(\text{N,N-dimethylpivalamide (S12)\textsuperscript{8}}\)**

According to the general procedure, using pivaloyl chloride (370 μL, 3 mmol) and dimethylamine hydrochloride (270 mg, 3.3 mmol), N,N-dimethylpivalamide was obtained as a yellowish oil after flash column chromatography on silica gel (296 mg, 76% yield).

**Synthesis of \(\text{N,N-dimethyl-3,5-bis(trifluoromethyl)benzamide (S14)}\)**
According to the general procedure, using 3,5-bis(trifluoromethyl)benzoyl chloride (830 mg, 3 mmol) and dimethylamine hydrochloride (269 mg, 3.3 mmol), N,N-dimethyl-3,5-bis(trifluoromethyl)benzamide was obtained as a colourless oil after flash column chromatography on silica gel (719 mg, 84% yield).

IR (neat) $\nu_{\text{max}}$: 2920, 1646, 1364, 1279, 1174, 1130, 905, 682;

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.92 (s, 1H), 7.89 (s, 2H), 3.15 (s, 3H), 2.99 (s, 3H);

$^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 168.4, 138.3, 132.5 (q, $J_{CF} = 33.4$ Hz), 127.5 (2C), 124.3 (q, $J_{CF} = 273.0$ Hz), 123.4 (q, $J_{CF} = 3.9$ Hz), 39.4, 35.5;

$^{19}$F-NMR (376 MHz, CDCl$_3$): $\delta$ -63.0;

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{11}$H$_{10}$ONF$_6$) requires $m/z$ 286.0661, found $m/z$ 286.0660.

**Synthesis of N,N-dimethyl-4-methoxy-benzamide (S15)**

According to the general procedure, using 4-anisoyl chloride (270 μL, 2 mmol) and dimethylamine hydrochloride (180 mg, 2.2 mmol), N,N-dimethyl-4-methoxy-benzamide was obtained as colourless gel after flash column chromatography on silica gel (340 mg, 95% yield).

**Synthesis of N,N-dimethyl-4-bromo-benzamide (S16)**

According to the general procedure, using 3,5-bis(trifluoromethyl)benzoyl chloride (830 mg, 3 mmol) and dimethylamine hydrochloride (269 mg, 3.3 mmol), N,N-dimethyl-3,5-bis(trifluoromethyl)benzamide was obtained as a colourless oil after flash column chromatography on silica gel (719 mg, 84% yield).
According to the general procedure, using 4-bromobenzoyl chloride (658 mg, 3 mmol) and dimethylamine hydrochloride (269 mg, 3.3 mmol), \( N,N \)-dimethyl-4-bromo-benzamide was obtained as a white solid after flash column chromatography on silica gel (617 mg, 91% yield).

**Synthesis of \( N,N \)-dimethyl-4-iodo-benzamide (S17)**

\[
\text{CONMe}_2
\]

According to the general procedure, using 4-iodobenzoyl chloride (799 mg, 3 mmol) and dimethylamine hydrochloride (269 mg, 3.3 mmol), \( N,N \)-dimethyl-4-iodo-benzamide was obtained as a white solid after flash column chromatography on silica gel (776 mg, 94% yield).

**Synthesis of \( N,N \)-dimethyl-4-chloro-benzamide (S18)**

\[
\text{CONMe}_2\text{Cl}^-
\]

According to the general procedure, using 4-chlorobenzoyl chloride (256 μL, 2 mmol) and dimethylamine hydrochloride (180 mg, 2.2 mmol), \( N,N \)-dimethyl-4-chloro-benzamide was obtained as a white crystalline solid after flash column chromatography on silica gel (325 mg, 89% yield).

**Synthesis of \( N,N \)-dimethylfuran-2-carboxamide (S19)**

\[
\text{CONMe}_2
\]

According to the general procedure, using 2-furoyl chloride (295 μL, 3 mmol) and dimethylamine hydrochloride (270 mg, 3.3 mmol), \( N,N \)-dimethylfuran-2-carboxamide was obtained as a colourless oil after flash column chromatography on silica gel (356 mg, 85% yield).

**Synthesis of \( N,N \)-dimethyl-4-cyano-benzamide (S20)**

\[
\text{CONMe}_2
\]
According to the general procedure, using 4-cyanobenzoyl chloride (497 mg, 3 mmol) and dimethylamine hydrochloride (269 mg, 3.3 mmol), N,N-dimethyl-4-cyano-benzamide was obtained as a white crystalline solid after flash column chromatography on silica gel (423 mg, 81% yield).

**Synthesis of (2-benzoylphenyl)(piperidin-1-yl)methanone (S21)**

According to the general procedure, using 2-benzoyl-benzoyl chloride (734 mg, 3 mmol) and piperidine (281 mg, 3.3 mmol), (2-benzoylphenyl)(piperidin-1-yl)methanone was obtained as a white crystalline solid after flash column chromatography on silica gel (748 mg, 85% yield).

**IR (neat) ν<sub>max</sub>:** 2937, 2855, 1662, 1628, 1432, 1275, 930, 726, 703;

**<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.81-7.78 (m, 2H), 7.58-7.50 (m, 3H), 7.45-7.38 (m, 4H), 3.52 (br, 2H), 3.27 (br, 2H), 1.63-1.55 (m, 6H);

**<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>):** δ 196.8, 169.1, 138.1, 137.3, 137.2, 133.1, 131.0, 130.3, 129.9, 128.4, 128.3, 127.2, 48.6, 42.7, 26.0, 25.3, 24.6;

**HRMS (ESI+):** exact mass calculated for [M+H]<sup>+</sup> (C<sub>19</sub>H<sub>20</sub>NO<sub>2</sub>) requires m/z 294.1489, found m/z 294.1486.

**Synthesis of N-Benzoyl-4-N-Boc-piperazine (S23)**
According to the general procedure, using benzoyl chloride (169 mg, 1.2 mmol) and N-Boc-piperazine (186 mg, 1 mmol), N-Benzoyl-4-N-Boc-piperazine was obtained as a white crystalline solid after recrystallization from EtOAc / PE (273 mg, 94% yield).

Synthesis of N-benzoyl-L-proline methyl ester (S24)

According to the general procedure, using benzoyl chloride (169 mg, 1.2 mmol) and L-proline methyl ester hydrochloride (166 mg, 1 mmol), N-benzoyl-L-proline methyl ester was obtained as colourless oil after flash column chromatography on silica gel (191 mg, 82% yield).

Synthesis of phenyl(piperidin-1-yl)methanone (S25)

According to the general procedure, using benzoyl chloride (422 mg, 3 mmol) and piperidine (281 mg, 3.3 mmol), phenyl(piperidin-1-yl)methanone was obtained as a colourless oil after flash column chromatography on silica gel (551 mg, 97% yield).

Synthesis of (2-methoxyphenyl)(piperidin-1-yl)methanone (S26)

According to the general procedure, using 2-methoxybenzoyl chloride (512 mg, 3 mmol) and piperidine (281 mg, 3.3 mmol), (2-methoxyphenyl)(piperidin-1-yl)methanone was obtained as a colourless crystalline solid after flash column chromatography on silica gel (539 mg, 82% yield).

Synthesis of (2-fluorophenyl)(pyrrolidin-1-yl)methanone (S27)
According to the general procedure, using 2-fluorobenzoyl chloride (476 mg, 3 mmol) and pyrrolidine (235 mg, 3.3 mmol), (2-fluorophenyl)(pyrrolidin-1-yl)methanone was obtained as a colourless oil after flash column chromatography on silica gel (441 mg, 76% yield).

**Synthesis of N-benzyl-N-ethylbenzamide (S28)**

According to the general procedure, using benzoyl chloride (422 mg, 3 mmol) and N-ethylbenzylamine (446 mg, 3.3 mmol), N-benzyl-N-ethylbenzamide was obtained as a colourless oil after flash column chromatography on silica gel (624 mg, 87% yield).

**Synthesis of (4-cyclohexylpiperazin-1-yl)(phenyl)methanone (S29)**

According to the general procedure, using benzoyl chloride (422 mg, 3 mmol) and 1-cyclohexylpiperazine (555 mg, 3.3 mmol), (4-cyclohexylpiperazin-1-yl)(phenyl)methanone was obtained as a white solid after flash column chromatography on silica gel (736 mg, 90% yield).

**Synthesis of (4-cinnamylpiperazin-1-yl)(phenyl)methanone (S38)**
According to the general procedure, using benzoyl chloride (422 mg, 3 mmol) and 1-cinnamylpiperazine (668 mg, 3.3 mmol), (4-cinnamylpiperazin-1-yl)(phenyl)methanone was obtained as a white solid after flash column chromatography on silica gel (808 mg, 88% yield).

3. Preparation of \((3aR,5R,6R,6aR)-5-(2,2\text{-dimethyl}-1,3\text{-dioxolan-4-yl})-6-((4\text{-iodobenzyl})\text{oxy})-2,2\text{-dimethyltetrahydrofuro}[2,3-d][1,3]dioxole (S43)\).

Under N\(_2\), 1,2:5,6-Di-O-isopropylidene-\(\alpha\)-D-glucofuranose (780.8 mg, 3 mmol) was added into a mixture of NaH (144 mg, 60 % dispersion in mineral oil, 3.6 mmol) and DMF (5 mL) at 0 °C. After warming to room temperature, the mixture was stirring 15 mins. 4-Iodobenzyl bromide (1.1 g, 3.6 mmol) solution in DMF (5 mL) was added dropwise. The result solution was heated to 80 °C for overnight and quenched with water, extracted with ether, dried over Na\(_2\)SO\(_4\), filtrated and the solvent was removed in vacuum. Title compound was obtained as a white solid after silica gel column chromatography (857 mg, 60% yield).

IR (neat) \(\nu_{\text{max}}\): 2985, 2934, 2361, 1485, 1381, 1256, 1073, 1006, 846, 733, 635;

\(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.66 (d, \(J = 8.3\) Hz, 2H), 7.10 (d, \(J = 8.2\) Hz, 2H), 5.89 (d, \(J = 3.7\) Hz, 1H), 4.64-4.55 (m, 3H), 4.35 (dd, \(J = 14.0, 5.9\) Hz, 1H), 4.12-4.08 (m, 2H), 4.00 (dd, \(J = 8.6, 5.6\) Hz, 2H), 1.48 (s, 3H), 1.41 (s, 3H), 1.35 (s, 3H), 1.30 (s, 3H);
13C-NMR (100 MHz, CDCl₃): δ 137.5, 137.4, 129.6, 111.9, 109.1, 105.3, 93.4, 82.7, 81.8, 81.3, 72.4, 71.7, 67.6, 26.9, 26.3, 25.5;

HRMS (ESI+): exact mass calculated for [M+H]⁺ (C₁₉H₂₆O₁₀) requires m/z 477.0769, found m/z 477.0768.

4. Preparation of (3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 4-iodobenzoate (S44)

Under N₂, Cholesterol (1.16 g, 3 mmol) and triethylamine (0.51 mL, 3.6 mmol) were charged into a 100 mL flask with 40 mL DCM at 0 °C. 4-Iodobenzoyl chloride (0.96 g, 3.6 mmol) was then added. The result solution was stirred at room temperature for overnight and quenched with water, extracted with DCM, dried over Na₂SO₄, filtrated and the solvent was removed in vacuum. Title compound was obtained as a white solid after silica gel column chromatography (1.67 g, 90% yield).

IR (neat) νmax: 2940, 2925, 2868, 2848, 2361, 1706, 1584, 1466, 1279, 1102, 1005, 849, 758;

1H-NMR (400 MHz, CDCl₃): δ 7.80 (d, J = 8.6 Hz, 2H), 7.75 (d, J = 8.6 Hz, 2H), 5.42 (d, J = 4.3 Hz, 1H), 4.88-4.80 (m, 1H), 2.46 (d, J = 7.8 Hz, 2H), 2.03-0.99 (m, 29H), 0.93 (d, J = 6.4 Hz, 3H), 0.88 (d, J = 1.5 Hz, 3H), 0.86 (d, J = 1.5 Hz, 3H), 0.68 (s, 3H);

13C-NMR (100 MHz, CDCl₃): δ 165.6, 139.6, 137.7, 131.2, 130.4, 123.0, 100.6, 75.1, 56.8, 56.3, 50.1, 42.4, 39.9, 39.7, 38.3, 37.1, 36.8, 36.3, 35.9, 32.1, 32.0, 28.4, 28.2, 28.0, 24.4, 24.0, 23.0, 22.7, 21.2, 19.5, 18.9, 12.0;

HRMS (EI): exact mass calculated for [M+H]⁺ (C₃₄H₅₀O₁₀) requires m/z 617.2850, found m/z 617.2847.
5. General procedure for preparation of Grignard by magnesium/iodine exchange

A dry vacuum and N₂ refilled 10 mL flask, equipped with a magnetic stirrer and a septum, was charged with (hetero)aryl iodide (0.36 mmol). Dry THF (2 mL) was then added. The solution was cooled to 0 °C with an ice bath, and 1PrMgBr (0.4 mL, 1M in THF, 0.4 mmol) was then added dropwise. The mixture was stirred at that temperature for 30 mins, and used directly.

6. General procedure for preparation of alkynyl Grignard

A dry vacuum and N₂ refilled 10 mL flask, equipped with a magnetic stirrer and a septum, was charged with terminal alkyne (0.36 mmol). Dry THF (2 mL) was then added. The solution was cooled to 0 °C with an ice bath, and EtMgBr (0.13 mL, 3 M in Et₂O, 0.39 mmol) was then added dropwise. The mixture was warmed to room temperature and stirred for 1 h, and then was used directly.

7. General procedure for amide-reductive Grignard addition

Vaska’s catalyst (required amount) and amide (0.3 mmol, 1.0 eq) was charged into a dry 25 mL flask. Vacuum and N₂ refilling was repeated for three time. Dry DCM (3 mL, 0.1 M) was injected by syringe, then TMDS (0.6 mmol, 2.0 eq) while stirring at room temperature. The result mixture was stirred for 15 mins, before cooled down to -78 °C. Grignard reagent (2.0 or 1.2 eq) was added dropwise. The solution was stirred at -78 °C for 2-5 mins more, then warmed to room temperature and stirred for 4 h or 0 °C and stirred for 6 h according to Figure 2 and 3 in the main text. The reaction mixture was quenched with saturated aqueous NH₄Cl-solution and extracted with DCM (3 x 5 mL). The combined organic layers were dried over Na₂SO₄, filtrated and the solvent was removed under vacuum. 1-Bromo-3,5-dimethoxybenzene (32.6 mg, 0.15 mmol) was added as internal standard for NMR yield. The residue was: A purified by flash column chromatography; B treated with 5 mL of 1 M HCl/water solution with stirring, washed with Et₂O (10 mL), then treated with K₂CO₃ saturated aqueous solution (6 mL), extracted with DCM, washed with brine, dried over Na₂SO₄, filtrated and purified by flash column chromatography after removing the solvent under vacuum. Known compounds were consistent with the reported NMR spectrum.
8. Characterization of amine products

*N,N-Dimethyl-1,2-diphenylethananine (1)*[^20]

According to the general procedure for amide-reductive Grignard addition, *N,N*-dimethyl benzoylamide (45.0 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a colourless oil (60 mg, 89% yield).

\(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta 7.20-7.12 \text{ (m, 3H)}\), 7.09-7.01 \((\text{m, 5H})\), 6.91 \((\text{d, } J = 6.6 \text{ Hz, 2H})\), 3.42 \((\text{dd, } J = 9.6, 5.0 \text{ Hz, 1H})\), 3.29 \((\text{dd, } J = 13.3, 5.0 \text{ Hz, 1H})\), 2.93 \((\text{dd, } J = 13.2, 9.7 \text{ Hz, 1H})\), 2.21 \((\text{s, 6H})\);

\(^13\)C-NMR (100 MHz, CDCl\(_3\)): \(\delta 139.7, 139.6, 129.4, 128.8, 128.0, 127.9, 127.1, 125.8, 72.84, 43.1, 40.1\).

*1-(1,2-Diphenylethyl)pyrrolidine (2)*[^20]

According to the general procedure for amide-reductive Grignard addition, phenyl(pyrrolidin-1-yl)methanone (52.6 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a colourless oil (53 mg, 70% yield).

\(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta 7.23-7.17 \text{ (m, 3H)}\), 7.14-7.08 \((\text{m, 5H})\), 6.88 \((\text{dt, } J = 7.4, 2.0 \text{ Hz, 2H})\), 3.40 \((\text{dd, } J = 12.7, 4.2 \text{ Hz, 1H})\), 3.33 \((\text{dd, } J = 10.0, 4.2 \text{ Hz, 1H})\), 2.95 \((\text{dd, } J = 12.7, 10.0 \text{ Hz, 1H})\), 2.70-2.65 \((\text{m, 2H})\), 2.49-2.45 \((\text{m, 2H})\), 1.84-1.77 \((\text{m, 4H})\);

\(^13\)C-NMR (100 MHz, CDCl\(_3\)): \(\delta 142.4, 139.2, 129.6, 128.4, 127.9 \text{ (2C)}\), 126.9, 125.8, 73.5, 53.1, 43.1, 23.5.

*1-(1,2-Diphenylethy)azepane (3)*[^20]
According to the general procedure for amide-reductive Grignard addition, azepan-1-yl(phenyl)methanone (61.0 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a colourless oil (75 mg, 89% yield).

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.18-7.06 (m, 7H), 7.03-6.97 (m, 3H), 3.83 (dd, $J = 8.4$, 6.1 Hz, 1H), 3.22 (dd, $J = 13.7$, 6.1 Hz, 1H), 2.92 (dd, $J = 13.6$, 8.5 Hz, 1H), 2.69-2.64 (m, 2H), 2.54-2.49 (m, 2H), 1.46 (br, 8H);

$^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 141.3, 140.4, 129.4, 128.6, 128.0, 127.8, 126.8, 125.7, 70.8, 52.2, 39.5, 29.3, 27.1.

1-(1,2-Diphenylethyl)azocane (4)

According to the general procedure for amide-reductive Grignard addition, azocan-1-yl(phenyl)methanone (65.2 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a colourless oil (77 mg, 87% yield).

IR (neat) $\nu_{max}$: 2917, 2849, 2361, 1495, 1452, 1129, 734, 698;

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.50-7.38 (m, 7H), 7.35-6.28 (m, 3H), 4.10 (dd, $J = 8.8$, 6.0 Hz, 1H), 3.54 (dd, $J = 13.7$, 6.0 Hz, 1H), 3.26 (dd, $J = 13.6$, 8.8 Hz, 1H), 2.86 (br, 2H), 2.79 (br, 2H), 1.73 (br, 10H);

$^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 141.6, 140.3, 129.4, 128.8, 128.0, 127.8, 126.7, 125.7, 71.2, 50.8, 39.3, 28.6, 27.9, 26.0;
HRMS (ESI+): exact mass calculated for [M+H]+ (C_{21}H_{28}N) requires m/z 294.2216, found m/z 294.2215.

4-(1,2-Diphenylethyl)morpholine (5)

According to the general procedure for amide-reductive Grignard addition, morpholino(phenyl)methanone (57.4 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a colourless oil (72 mg, 90% yield).

IR (neat) ν_{max}: 2955, 2851, 2805, 1494, 1451, 1284, 1116, 754, 699;

^{1}H-NMR (400 MHz, CDCl_{3}): δ 7.15-7.07 (m, 3H), 7.05-6.97 (m, 5H), 6.85 (dt, J = 6.4, 1.6 Hz, 2H), 3.61 (m, 4H), 3.40 (dd, J = 9.4, 5.2 Hz, 1H), 3.27 (dd, J = 13.2, 5.2 Hz, 1H), 2.87 (dd, J = 13.2, 9.4 Hz, 1H), 2.46-2.35 (m, 4H);

^{13}C-NMR (100 MHz, CDCl_{3}): δ 139.8, 139.3, 129.5, 128.8, 128.0, 127.2, 125.9, 72.6, 67.3, 51.4, 39.4;

HRMS (ESI+): exact mass calculated for [M+H]+ (C_{18}H_{22}NO) requires m/z 268.1696, found m/z 268.1697.

2-(1,2-Diphenylethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (6)

According to the general procedure for amide-reductive Grignard addition, (6,7-dimethoxy-3,4-dihydroisoquinolin-2(1H)-yl)(phenyl)methanone (89.2 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method A was applied. Title compound was obtained as a white solid (100 mg, 89% yield).
IR (neat) ν_max: 2933, 2833, 1610, 1516, 1494, 1285, 1255, 1125, 737, 699;

$^1$H-NMR (400 MHz, CDCl$_3$): δ 7.20-7.12 (m, 5H), 7.08-7.02 (m, 3H), 6.92 (dt, $J = 6.6$, 1.6 Hz, 2H), 6.51 (s, 1H), 6.43 (s, 1H), 3.76 (s, 3H), 3.74 (s, 3H), 3.71-3.65 (m, 2H), 3.56 (d, $J = 14.2$ Hz, 1H), 3.41 (dd, $J = 13.2$, 5.0 Hz, 1H), 3.00 (dd, $J = 13.2$, 9.7 Hz, 1H), 2.85-2.57 (m, 4H);

$^{13}$C-NMR (100 MHz, CDCl$_3$): δ 147.5, 147.2, 140.0, 139.5, 129.4, 128.8, 128.0, 127.1, 127.0, 126.5, 125.8, 111.4, 109.7, 71.6, 55.9, 53.4, 48.0, 39.9, 29.1;

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{25}$H$_{28}$NO$_2$) requires $m/z$ 374.2115, found $m/z$ 374.2116.

**N-Benzyl-N-methyl-1,2-diphenylethanamine (7)**

\[
\text{Ph} \quad \text{N} \quad \text{Ph}
\]

According to the general procedure for amide-reductive Grignard addition, (N-benzyl-N-methylbenzamide (63.4 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a colourless oil (77 mg, 85% yield).

IR (neat) ν_max: 3027, 2917, 2789, 1602, 1494, 1452, 1030, 736, 698;

$^1$H-NMR (400 MHz, CDCl$_3$): δ 7.24-7.05 (m, 13H), 6.99 (dt, $J = 6.6$, 1.5 Hz, 2H), 3.78 (t, $J = 6.8$ Hz, 1H), 3.59 (d, $J = 13.3$ Hz, 1H), 3.33-3.23 (m, 2H), 2.98 (dd, $J = 13.1$, 8.7 Hz, 1H), 2.12 (s, 3H);

$^{13}$C-NMR (100 MHz, CDCl$_3$): δ 140.0, 139.3, 129.5, 129.0, 128.9, 128.3, 128.1, 128.0, 127.2, 126.9, 125.9, 69.7, 58.9, 39.0, 38.1;

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{22}$H$_{24}$N) requires $m/z$ 302.1903, found $m/z$ 302.1899.

**N-(1,2-Diphenylethyl)-N,O-dimethylhydroxylamine (8)**
According to the general procedure for amide-reductive Grignard addition, \( N \)-methoxy-\( N \)-methylbenzamide (49.6 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method A was applied. Title compound was obtained as a colourless oil (63 mg, 87% yield).

IR (neat) \( \nu_{\text{max}} \): 2935, 2854, 1495, 1453, 1046, 753, 698;

\(^1\)H-NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.17 (brs, 3H), 7.12-7.05 (m, 5H), 6.90 (d, \( J = 6.52 \) Hz, 2H), 3.64 (d, \( J = 8.3 \) Hz, 1H), 3.57 (s, 3H), 3.51 (d, \( J = 12.9 \) Hz, 1H), 2.95 (t, \( J = 11.6 \) Hz, 1H), 2.42 (s, 3H);

\(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \( \delta \) 140.0, 139.2, 129.6, 128.9, 128.1, 128.0, 127.4, 125.9, 76.0, 60.6, 43.1, 40.6;

HRMS (ESI\(^+\)): exact mass calculated for \([\text{M+H}]^+\) \( (C\text{\textsubscript{1}}\text{\textsubscript{6}}H\text{\textsubscript{20}}NO) \) requires \( m/z \) 242.1539, found \( m/z \) 242.1540.

\( \text{N-(1,2-Diphenylethyl)-N-methylaniline (9)} \)

According to the general procedure for amide-reductive Grignard addition, \( N \)-Methyl-\( N \)-phenylbenzamide (63.4 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method A was applied. Title compound was obtained as a yellowish oil (49 mg, 57% yield).

IR (neat) \( \nu_{\text{max}} \): 3025, 2851, 1597, 1501, 1450, 1100, 746, 694;

\(^1\)H-NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.32-7.12 (m, 13H), 6.67 (t, \( J = 8.5 \) Hz, 2H), 5.28 (dd, \( J = 8.9 \), 6.3 Hz, 1H), 3.39-3.26 (m, 2H), 2.72 (s, 3H);
\textsuperscript{13}C-NMR (100 MHz, CDCl\textsubscript{3}): \( \delta \) 150.5, 141.2, 139.3, 129.1, 128.6, 128.5 (2C), 127.4, 127.2, 126.3, 116.9, 113.6, 63.7, 37.9, 32.6; 

HRMS (ESI\textsuperscript{+}): exact mass calculated for [M+H]\textsuperscript{+} (C\textsubscript{21}H\textsubscript{22}N) requires \( m/z \) 288.1747, found \( m/z \) 288.1746.

\textit{N,N-Dimethyl-1-phenylundecan-2-amine (10)}

\begin{center}
\begin{tikzpicture}
\end{tikzpicture}
\end{center}

According to the general procedure for amide-reductive Grignard addition, \textit{N,N}-dimethyldecanamide (59.8 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a colourless oil (48 mg, 58% yield).

IR (neat) \( \nu_{\text{max}} \): 2924, 2853, 2778, 1494, 1469, 1152, 738, 698;

\textsuperscript{1}H-NMR (400 MHz, CDCl\textsubscript{3}): \( \delta \) 7.32 (t, \( J = 7.1 \) Hz, 2H), 7.22 (t, \( J = 7.9 \) Hz, 3H), 2.97 (dd, \( J = 13.2, 4.4 \) Hz, 1H), 2.69-2.62 (m, 1H), 2.39-2.36 (m, 1H), 2.34 (s, 6H), 1.33-1.20 (m, 14H), 0.92 (t, \( J = 7.1 \) Hz, 3H);

\textsuperscript{13}C-NMR (100 MHz, CDCl\textsubscript{3}): \( \delta \) 141.4, 129.3, 128.4, 125.7, 66.2, 40.6, 34.8, 32.0, 30.6, 29.9, 29.7, 29.5, 27.0, 22.8, 14.3;

HRMS (ESI\textsuperscript{+}): exact mass calculated for [M+H]\textsuperscript{+} (C\textsubscript{19}H\textsubscript{34}N) requires \( m/z \) 276.2686, found \( m/z \) 276.2682.

\textit{1-Cyclohexyl-N,N-dimethyl-2-phenylethanamine (11)}\textsuperscript{21}

\begin{center}
\begin{tikzpicture}
\end{tikzpicture}
\end{center}

According to the general procedure for amide-reductive Grignard addition, \textit{N,N}-dimethylcyclohexanecarboxamide (46.6 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a colourless oil (60 mg, 86% yield).
1H-NMR (400 MHz, CDCl3): δ 7.27-7.19 (m, 4H), 7.16 (tt, J = 7.1, 1.6 Hz, 1H), 2.85 (dd, J = 13.9, 5.1 Hz, 1H), 2.58-2.49 (m, 2H), 2.26 (s, 6H), 1.90 (d, J = 12.8 Hz, 1H), 1.74-1.60 (m, 4H), 1.49-1.41 (m, 1H), 1.22-0.94 (m, 5H);

13C-NMR (100 MHz, CDCl3): δ 143.0, 129.1, 128.3, 125.5, 71.1, 41.8, 41.2, 32.9, 31.3, 31.1, 26.8, 26.7.

N,N,3,3-Tetramethyl-1-phenylbutan-2-amine (12)

According to the general procedure for amide-reductive Grignard addition, N,N-dimethylpivalamide (38.8 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a colourless oil (30 mg, 50% yield).

IR (neat) νmax: 2952, 2865, 2785, 2337, 1064, 1454, 1361, 1020, 728, 697;

1H-NMR (400 MHz, CDCl3): δ 7.29 (d, J = 4.4 Hz, 4H), 7.21-7.16 (m, 1H), 2.88-2.75 (m, 2H), 2.67 (dd, J = 9.1, 4.0 Hz, 1H), 2.34 (s, 6H), 0.99 (s, 9H);

13C-NMR (100 MHz, CDCl3): δ 143.2, 129.3, 128.2, 125.5, 74.1, 43.8, 37.6, 31.9, 28.4;

HRMS (ESI+): exact mass calculated for [M+H]+ (C14H24N) requires m/z 206.1903, found m/z 206.1903.

1-Phenethylpiperidine (13)

According to the general procedure for amide-reductive Grignard addition, formylpiperidine (34 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a colourless oil (46 mg, 83% yield).

1H-NMR (400 MHz, CDCl3): δ 7.15-7.11 (m, 2H), 7.06-7.02 (m, 3H), 2.69-2.64 (m, 2H), 2.43-2.38 (m, 2H), 2.32 (br, 4H), 1.50-1.45 (m, 4H), 1.31 (br, 2H);
\( ^{13} \text{C-NMR} (100 \text{ MHz, CDCl}_3): \delta 140.8, 128.8, 128.4, 126.0, 61.6, 54.7, 33.8, 26.1, 24.6. \)

1-(3,5-Bis(trifluoromethyl)phenyl)-\( N,N \)-dimethyl-2-phenylethanamine (14)

According to the general procedure for amide-reductive Grignard addition, \( N,N \)-dimethyl-3,5-bis(trifluoromethyl)benzamide (85.6 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a colourless oil (99 mg, 91% yield).

IR (neat) \( \nu_{\text{max}}: \) 2928, 2778, 1339, 1277, 1169, 1227, 899, 699;

\( ^1 \text{H-NMR} (400 \text{ MHz, CDCl}_3): \delta 7.68 (s, 1H), 7.50 (s, 2H), 7.16-7.10 (m, 3H), 6.84 (dd, \( J = 7.8, 2.1 \) Hz, 2H), 3.51 (dd, \( J = 9.8, 5.0 \) Hz, 1H), 3.41 (dd, \( J = 13.1, 5.1 \) Hz, 1H), 2.81 (dd, \( J = 13.1, 9.9 \) Hz, 1H), 2.30 (s, 6H);

\( ^{13} \text{C-NMR} (100 \text{ MHz, CDCl}_3): \delta 144.1, 138.0, 131.6 (q, J_{\text{CF}} = 32.8 \text{ Hz}), 129.3, 128.6, 128.4, 127.6 (q, J_{\text{CF}} = 271.0 \text{ Hz}), 126.5, 121.0 (q, J_{\text{CF}} = 3.9 \text{ Hz}), 72.8, 43.6, 40.6;

\( ^{19} \text{F-NMR} (376 \text{ MHz, CDCl}_3): \delta -62.8;

HRMS (ESI+): exact mass calculated for \([\text{M+H}]^+ (C_{18}H_{18}NF_6) \) requires \( m/z \) 362.1338, found \( m/z \) 362.1335.

1-(4-Methoxyphenyl)-\( N,N \)-dimethyl-2-phenylethanamine (15)

According to the general procedure for amide-reductive Grignard addition, \( N,N \)-dimethyl-4-methoxybenzamide (53.8 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol)
were used, work up method B was applied. Title compound was obtained as a colourless gel (64 mg, 84% yield).

IR (neat) $\nu_{\text{max}}$: 2962, 2480, 1611, 1514, 1440, 1251, 732;

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.16-7.09 (m, 3H), 7.07 (dt, $J = 8.7$, 2.0 Hz, 2H), 6.98 (d, $J = 6.8$ Hz, 2H), 6.80 (dt, $J = 8.7$, 2.0 Hz, 2H), 3.77 (s, 3H), 3.45 (dd, $J = 9.8$, 4.9 Hz, 1H), 3.32 (dd, $J = 13.2$, 4.8 Hz, 1H), 2.98 (dd, $J = 13.2$, 9.8 Hz, 1H), 2.25 (s, 6H);

$^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 158.6, 139.7, 131.6, 129.8, 129.4, 128.0, 125.8, 113.3, 72.0, 55.2, 42.9, 40.1;

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{17}$H$_{22}$NO) requires m/z 256.1696, found m/z 256.1694.

1-(4-Bromophenyl)-N,N-dimethyl-2-phenylethanamine (16)

![1-(4-Bromophenyl)-N,N-dimethyl-2-phenylethanamine](image)

According to the general procedure for amide-reductive Grignard addition, $N,N$-dimethyl-4-bromo-benzamide (68.4 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a white solid (89 mg, 97% yield).

IR (neat) $\nu_{\text{max}}$: 2956, 2775, 2461, 1590, 1491, 1453, 1075, 1039, 745, 699;

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.37 (dt, $J = 8.4$, 2.3 Hz, 2H), 7.16-7.08 (m, 3H), 7.02 (d, $J = 8.4$ Hz, 2H), 6.94 (d, $J = 6.9$ Hz, 2H), 3.46 (dd, $J = 10.0$, 4.8 Hz, 1H), 3.36 (dd, $J = 13.2$, 4.7 Hz, 1H), 2.93 (dd, $J = 13.2$, 10.0 Hz, 1H), 2.28 (s, 6H);

$^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 138.8, 138.6, 131.1, 130.5, 129.3, 126.1, 121.0, 72.3, 43.0, 39.9;

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{16}$H$_{19}$NBr) requires m/z 304.0695, found m/z 304.0693.

1-(4-Iodophenyl)-N,N-dimethyl-2-phenylethanamine (17)
According to the general procedure for amide-reductive Grignard addition, N,N-dimethyl-4-iodobenzamide (82.5 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a white solid (97 mg, 92% yield).

IR (neat) ν\textsubscript{max}: 2951, 2774, 1496, 1481, 1004, 822, 743, 698;

\textsuperscript{1}H-NMR (400 MHz, CDCl\textsubscript{3}): δ 7.57 (dt, J = 8.3, 2.2 Hz, 4H), 7.17-7.08 (m, 3H), 6.95 (dt, J = 6.6, 1.6 Hz, 4H), 6.88 (dt, J = 8.3, 1.7 Hz, 4H), 3.41 (dd, J = 9.8, 4.9 Hz, 1H), 3.33 (dd, J = 13.2, 4.9 Hz, 1H), 2.91 (dd, J = 13.2, 9.8 Hz, 1H), 2.25 (s, 6H);

\textsuperscript{13}C-NMR (100 MHz, CDCl\textsubscript{3}): δ 139.8, 139.0, 137.0, 129.4, 128.1, 126.0, 92.5, 72.4, 43.1, 40.0;

HRMS (ESI\textsuperscript{+}): exact mass calculated for [M+H]\textsuperscript{+} (C\textsubscript{16}H\textsubscript{19}NI) requires m/z 352.0557, found m/z 352.0552.

1-(4-Chlorophenyl)-N,N-dimethyl-2-phenylethanamine (18)

According to the general procedure for amide-reductive Grignard addition, N,N-dimethyl-4-chlorobenzamide (55.1 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a colourless oil (70 mg, 90% yield).

IR (neat) ν\textsubscript{max}: 2950, 2775, 1600, 1493, 1147, 1040, 828, 699;
$^1$H-NMR (400 MHz, CDCl$_3$): δ 7.22 (dt, $J = 8.4$, 1.9 Hz, 2H), 7.17-7.10 (m, 3H), 7.06 (dt, $J = 11.3$, 1.9 Hz, 2H), 6.94 (dt, $J = 6.7$, 1.6 Hz, 2H), 3.44 (dd, $J = 9.9$, 4.8 Hz, 1H), 3.34 (dd, $J = 13.2$, 4.8 Hz, 1H), 2.91 (dd, $J = 13.2$, 9.9 Hz, 1H), 2.26 (s, 6H);

$^{13}$C-NMR (100 MHz, CDCl$_3$): δ 139.1, 138.6, 132.7, 130.0, 129.4, 128.1 (2C), 126.0, 72.3, 43.1, 40.1;

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{16}$H$_{19}$NCl) requires m/z 260.1201, found m/z 260.1200.

1-(Furan-2-yl)-N,N-dimethyl-2-phenylethanamine (19)

![Chemical structure of 1-(Furan-2-yl)-N,N-dimethyl-2-phenylethanamine](image)

According to the general procedure for amide-reductive Grignard addition, N,N-dimethylfuran-2-carboxamide (41.7 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a yellowish oil (61 mg, 94% yield).

IR (neat) $\nu_{\text{max}}$: 2934, 2780, 1497, 1475, 1147, 1014, 732, 698;

$^1$H-NMR (400 MHz, CDCl$_3$): δ 7.38 (dd, $J = 1.8$, 0.7 Hz, 1H), 7.22-7.12 (m, 3H), 7.08 (d, $J = 6.8$ Hz, 2H), 6.27 (dd, $J = 3.2$, 1.8 Hz, 1H), 6.06 (dd, $J = 3.2$, 0.4 Hz, 1H), 3.79 (dd, $J = 9.3$, 5.8 Hz, 1H), 3.20-3.10 (m, 2H), 2.28 (s, 6H);

$^{13}$C-NMR (100 MHz, CDCl$_3$): δ 152.9, 141.7, 139.5, 129.1, 128.2, 126.1, 109.8, 108.9, 64.6, 42.0, 37.5;

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{14}$H$_{18}$NO) requires m/z 216.1383, found m/z 216.1384.

1-(4-Isocyanophenyl)-N,N-dimethyl-2-phenylethanamine (20)

![Chemical structure of 1-(4-Isocyanophenyl)-N,N-dimethyl-2-phenylethanamine](image)
According to the general procedure for amide-reductive Grignard addition, N,N-dimethyl-4-cyano-benzamide (52.3 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.18 mL, 2 M in THF, 0.36 mmol) were used, work up method B was applied. Title compound was obtained as a colourless gel (60 mg, 80 % yield).

IR (neat) $\nu_{\text{max}}$: 2954, 2777, 2227, 1606, 1497, 1453, 1040, 750, 699;

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.50 (dt, $J = 8.4, 1.8$ Hz, 2H), 7.21 (dt, $J = 8.3, 1.7$ Hz, 2H), 7.14-7.09 (m, 3H), 6.88 (dt, $J = 7.3, 1.9$ Hz, 2H), 3.45 (dd, $J = 9.9, 4.9$ Hz, 1H), 2.85 (dd, $J = 13.1, 9.9$ Hz, 1H), 2.26 (s, 6H);

$^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 146.5, 138.4, 131.8, 129.3, 128.2, 126.2, 119.0, 110.9, 73.0, 43.4, 40.2;

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{17}$H$_{19}$N$_2$) requires $m/z$ 251.1543, found $m/z$ 251.1542.

**Phenyl(2-(2-phenyl-1-(piperidin-1-yl)ethyl)phenyl)methanone (21)**

According to the general procedure for amide-reductive Grignard addition, (2-benzoylphenyl)(piperidin-1-yl)methanone (88.0 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.18 mL, 2 M in THF, 0.36 mmol) were used, work up method B was applied. Title compound was obtained as a colourless gel (74 mg, 67% yield).

IR (neat) $\nu_{\text{max}}$: 2932, 2853, 1663, 1449, 1288, 927, 698;

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.69 (d, $J = 7.4$ Hz, 2H), 7.54 (t, $J = 7.5$ Hz, 1H), 7.40-7.37 (m, 3H), 7.34 (td, $J = 6.8, 1.7$ Hz, 1H), 7.26-7.07 (m, 7H), 4.21 (dd, $J = 9.9, 4.4$ Hz, 1H), 3.24 (dd, $J = 14.3, 4.6$ Hz, 1H), 3.06 (dd, $J = 14.3, 9.9$ Hz, 1H), 2.42-2.40 (m, 2H), 2.29-2.26 (m, 2H), 1.18 (br, 6H);

$^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 197.5, 142.1, 140.1, 139.9, 137.8, 132.6, 130.0, 129.2, 128.9, 128.3, 128.1, 128.0, 126.0, 125.9, 65.3, 50.3, 34.3, 25.5, 24.6;

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{26}$H$_{28}$NO) requires $m/z$ 370.2165, found $m/z$ 370.2162.
1-(2-Phenyl-1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethyl)piperidine (22)

According to the general procedure for amide-reductive Grignard addition, 4-(Piperidine-1-carbonyl)phenylboronic acid pinacol ester (94.6 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.18 mL, 2 M in THF, 0.36 mmol) were used, work up method A was applied. Title compound was obtained as a colourless gel (73 mg, 62% yield).

IR (neat) ν max: 2977, 2932, 2797, 1610, 1400, 1361, 1321, 1145, 1091, 860, 662;

$^1$H-NMR (400 MHz, CDCl$_3$): δ 7.70 (d, $J = 7.8$ Hz, 2H), 7.16-7.07 (m, 5H), 7.01 (d, $J = 7.5$ Hz, 2H), 3.64 (dd, $J = 9.5, 4.9$ Hz, 1H), 3.33 (dd, $J = 13.4, 4.9$ Hz, 1H), 3.07 (dd, $J = 13.4, 9.6$ Hz, 1H), 2.42 (br, 8H), 1.58-1.53 (m, 4H), 1.33 (br, 15H);

$^{13}$C-NMR (100 MHz, CDCl$_3$): δ 142.6, 139.9, 134.3, 129.5, 128.6, 128.0, 125.8, 83.8, 72.5, 51.5, 39.1, 26.5, 25.0, 24.7;

$^{11}$B-NMR (128 MHz, CDCl$_3$): δ 31.6;

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{25}$H$_{35}$NO$_2$B) requires m/z 391.2792, found m/z 391.2775.

$\text{tert-Butyl 4-(1,2-diphenylethyl)piperazine-1-carboxylate (23)}^{20}$

According to the general procedure for amide-reductive Grignard addition, N-Benzoyl-4-$N$-Boc-piperazine (87.1 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.18 mL, 2 M in THF, 0.36 mmol) were used, work up method A was applied. Title compound was obtained as a colourless gel (81 mg, 74% yield).
 According to the general procedure for amide-reductive Grignard addition, *N*-benzoyl-L-proline methyl ester (70.0 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.18 mL, 2 M in THF, 0.36 mmol) were used, work up method B was applied. Title compound was obtained as a colourless oil (77 mg, 83% yield). After acid/base work up as referred in method B, ~85 mg of the crude product was dissolved in 2 ml of DCM at rt, following by the addition of HCl in dixone (0.13 mL, 4 M, 0.5 mmol). The result solution was slowly evaporated until small amount of 24-HCl salt was obtained as small, needle like crystal, which was suitable for X-ray characterization (CCDC 1552384, cif file was submitted separately).

\[ \alpha \]_D^25 = -15.1 (c 1.08, CHCl₃);

IR (neat) ν_max: 2976, 2847, 2361, 1732, 1453, 1195, 1168, 746, 700;

\(^1\)H-NMR (400 MHz, CDCl₃): δ 7.30-7.23 (m, 3H), 7.19-7.13 (m, 5H), 7.02 (dt, J = 6.4, 1.6 Hz, 2H), 3.64 (dd, J = 9.0, 5.7 Hz, 1H), 3.44 (br, 4H), 3.37 (dd, J = 13.2, 5.7 Hz, 1H), 3.01 (dd, J = 13.2, 9.1 Hz, 1H), 2.48 (br, 3H), 1.46 (s, 9H);

\(^13\)C-NMR (100 MHz, CDCl₃): δ 154.8, 139.5, 139.4, 129.5, 128.9, 128.1, 127.3, 126.0, 79.6, 72.0, 50.3, 39.3, 29.9, 28.5.

HRMS (ESI+): exact mass calculated for [M+H]^+ (C₂₀H₂₄NO₂) requires m/z 310.1802, found m/z 310.1802.

1-(1,2-Diphenylethyl)piperidine (25)\(^2\)
According to the general procedure for amide-reductive Grignard addition, phenyl(piperidin-1-yl)methanone (56.8 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a colourless oil (76 mg, 95% yield).

\[^1\text{H-NMR}\] (400 MHz, CDCl\(_3\)): δ 7.19-7.13 (m, 3H), 7.09-7.02 (m, 5H), 6.95 (d, \(J = 7.6\) Hz, 2H), 3.55 (dd, \(J = 9.5, 5.4\) Hz, 1H), 3.28 (d, \(J = 13.2, 5.3\) Hz, 1H), 2.97 (d, \(J = 13.2, 9.4\) Hz, 2H), 2.38 (br, 4H), 1.54-1.47 (m, 4H), 1.34-1.28 (m, 2H);

\[^{13}\text{C-NMR}\] (100 MHz, CDCl\(_3\)): δ 140.1, 139.5, 129.5, 129.0, 127.9, 127.8, 126.9, 125.7, 72.5, 51.5, 39.3, 26.5, 24.8.

1-(1-(2-Methoxyphenyl)-2-phenylethyl)piperidine (26)

According to the general procedure for amide-reductive Grignard addition, (2-methoxyphenyl)(piperidin-1-yl)methanone (65.8 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a colourless oil (59 mg, 67% yield).

IR (neat) \(\nu_{\text{max}}\): 2931, 2790, 2361, 1600, 1490, 1343, 1030, 751, 697;

\[^1\text{H-NMR}\] (400 MHz, CDCl\(_3\)): δ 7.38 (dd, \(J = 7.6, 1.7\) Hz, 1H), 7.19-7.05 (m, 6H), 6.97 (td, \(J = 7.5, 1.0\) Hz, 1H), 6.77 (dd, \(J = 8.3, 1.0\) Hz, 1H), 4.35 (dd, \(J = 9.3, 5.9\) Hz, 1H), 3.05 (s, 3H), 3.31 (dd, \(J = 13.4, 5.7\) Hz, 1H), 3.00 (dd, \(J = 13.4, 9.3\) Hz, 1H), 2.48 (brs, 4H), 1.60-1.53 (m, 4H), 1.40-1.34 (m, 2H);
$^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 158.1, 140.3, 129.5, 128.9, 128.6, 127.7, 127.6, 125.5, 120.1, 111.0, 62.6, 55.6, 51.5, 39.4, 26.6, 24.9;

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{20}$H$_{28}$NO) requires $m/z$ 296.2009, found $m/z$ 296.2007.

1-(1-(2-Fluorophenyl)-2-phenylethyl)pyrrolidine (27)

According to the general procedure for amide-reductive Grignard addition, (2-fluorophenyl)(pyrrolidin-1-yl)methanone (58.0 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a colourless oil (71 mg, 87% yield).

IR (neat) $\nu_{\text{max}}$: 2968, 2782, 1488, 1454, 1226, 1132, 757, 698;

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.47 (td, $J = 7.4, 1.9$ Hz, 1H), 7.16-7.06 (m, 5H), 6.97 (dd, $J = 7.9, 1.8$ Hz, 2H), 6.87-6.82 (m, 1H), 3.94 (dd, $J = 10.1, 4.8$ Hz, 1H), 3.39 (dd, $J = 13.2, 4.7$ Hz, 1H), 3.02 (dd, $J = 13.2, 10.1$ Hz, 1H), 2.71-2.66 (m, 2H), 2.51-2.48 (m, 2H), 1.83-1.76 (m, 4H);

$^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 162.1 (d, $J_{CF} = 245.3$ Hz), 138.8, 129.7 (d, $J_{CF} = 4.8$ Hz), 129.6, 129.4 (d, $J_{CF} = 13.5$ Hz), 128.9, 128.8, 128.3, 128.2, 128.0, 126.0, 123.9, 115.2 (d, $J_{CF} = 3.2$ Hz), 63.9, 52.7, 41.8, 23.4;

$^{19}$F-NMR (376 MHz, CDCl$_3$): $\delta$ -118.0;

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{18}$H$_{21}$NF) requires $m/z$ 270.1653, found $m/z$ 270.1650.

$N$-Benzyl-$N$-ethyl-1,2-diphenylethalamine (S28')
According to the general procedure for amide-reductive Grignard addition, N-benzyl-N-ethylbenzamide (71.8 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a colourless oil (90 mg, 95% yield).

IR (neat) $\nu_{\text{max}}$: 3026, 2967, 2800, 1494, 1452, 1072, 746, 697;

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.33-7.29 (m, 2H), 7.26-7.15 (m, 11H), 7.08 (d, $J = 8.2$ Hz, 2H), 4.01 (t, $J = 7.5$ Hz, 1H), 3.83 (d, $J = 14.3$ Hz, 1H), 3.34 (dt, $J = 14.3$, 3.8 Hz, 2H), 3.03 (d, $J = 13.7$, 7.8 Hz, 1H), 2.83-2.74 (m, 1H), 2.36-2.27 (m, 1H), 1.02 (t, $J = 7.1$ Hz, 3H);

$^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 140.9, 140.3, 140.2, 129.6, 128.9, 128.6, 128.2, 128.1, 128.0, 127.0, 126.6, 125.8, 65.1, 54.1, 43.2, 38.5, 12.9;

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{23}$H$_{26}$N) requires $m/z$ 316.2060, found $m/z$ 316.2062.

$^{N}$-Ethyl-1,2-diphenylethan-1-amine (28)$^{22}$

$N$-benzyl-$N$-ethyl-1,2-diphenylethanamime (20 mg, 0.063 mmol) and Pd/C (15.0 mg, 10 wt.%) was charged into a 25 mL flask with a septum. The flask was then vacuumed and refilled with a H$_2$ balloon, before methanol (2 mL) and ethyl acetate (2 mL) were injected. The result mixture was stirred for 2 h at room temperature. The mixture was filtrated with celite and purified by a flash column chromatography after removing the solvent under vacuum. Title compound was obtained as a colourless oil (11 mg, 71% yield).

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.38-7.25 (m, 8H), 7.19-7.17 (m, 2H), 3.93 (dd, $J = 7.9$, 6.4 Hz, 1H), 2.99-2.96 (m, 2H), 2.50-2.46 (m, 2H), 1.05 (t, $J = 7.1$ Hz, 3H);

$^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 144.0, 139.1, 129.4 (2C), 128.5, 128.4, 127.4, 127.1, 126.4, 65.0, 45.4, 42.2, 15.4.

1-Cyclohexyl-4-(1,2-diphenylethyl)piperazine (29)
According to the general procedure for amide-reductive Grignard addition, (4-cyclohexylpiperazin-1-yl)(phenyl)methanone (81.7 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a colourless gel (99 mg, 95% yield).

IR (neat) ν<sub>max</sub>: 2926, 2853, 2807, 1494, 1451, 1150, 738, 698;

<sup>1</sup>H-NMR (400 MHz, CDCl₃): δ 7.13-7.06 (m, 3H), 7.05-6.98 (m, 5H), 6.87 (dd, J = 8.4, 1.5 Hz, 2H), 3.46 (dd, J = 9.5, 4.9 Hz, 1H), 3.26 (dd, J = 13.2, 4.9 Hz, 1H), 2.89 (dd, J = 13.2, 9.6 Hz, 1H), 2.50-2.45 (br, 8H), 2.12-2.07 (m, 1H), 1.80-1.67 (m, 4H), 1.54 (d, J = 12.6 Hz, 1H), 1.15-0.98 (m, 5H);

<sup>13</sup>C-NMR (100 MHz, CDCl₃): δ 139.6, 129.4, 128.9, 127.9 (2C), 127.0, 125.7, 72.2, 63.5, 51.0, 49.4, 39.5, 29.1, 26.4, 25.9;

HRMS (ESI⁺): exact mass calculated for [M+H]<sup>+</sup> (C<sub>24</sub>H<sub>33</sub>N<sub>2</sub>) requires m/z 349.2638, found m/z 349.2636.

<sup>N</sup>,<sup>N</sup>-Dimethyl-1-phenylethanamine (30)<sup>23</sup>

According to the general procedure for amide-reductive Grignard addition, <sup>N</sup>,<sup>N</sup>-dimethyl benzoyleamide (45.0 mg, 0.3 mmol) and methylmagnesium bromide solution (0.2 mL, 3 M in Et₂O, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a colourless volatile oil (29 mg, 64% yield).

<sup>1</sup>H-NMR (400 MHz, CDCl₃): δ 7.33-7.22 (m, 5H), 3.27 (d, J = 6.7 Hz, 1H), 2.20 (s, 6H), 1.38 (d, J = 6.7 Hz, 3H);

<sup>13</sup>C-NMR (100 MHz, CDCl₃): δ 144.1, 128.3, 127.7, 127.0, 66.1, 43.4, 20.4.
\textbf{N,N-Dimethyl-1-phenylhexan-1-amine (31)}

\begin{center}
\includegraphics[width=0.2\textwidth]{structure1}
\end{center}

According to the general procedure for amide-reductive Grignard addition, \textit{N,N}-dimethyl benzoylamide (45.0 mg, 0.3 mmol) and \textit{n}-pentylmagnesium chloride solution (0.3 mL, 2 M in Et\textsubscript{2}O, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a colourless oil (54 mg, 88\% yield).

IR (neat) \textit{v}_{\text{max}}: 2957, 2930, 2853, 2469, 1459, 1169, 922, 703;

\textsuperscript{1}H-NMR (400 MHz, CDCl\textsubscript{3}): \textit{\delta} 7.33-7.30 (m, 2H), 7.26-7.21 (m, 3H), 3.16 (dd, \textit{J} = 9.5, 4.5 Hz, 1H), 2.17 (s, 6H), 1.92-1.83 (m, 1H), 1.77-1.68 (m, 1H), 1.23-1.03 (m, 6H), 0.82 (t, \textit{J} = 7.3 Hz, 3H);

\textsuperscript{13}C-NMR (100 MHz, CDCl\textsubscript{3}): \textit{\delta} 140.7, 128.7, 128.1, 127.0, 71.1, 43.0, 33.3, 32.1, 26.3, 22.7, 14.2;

HRMS (ESI\textsuperscript{+}): exact mass calculated for [M+H]\textsuperscript{+} (C\textsubscript{14}H\textsubscript{24}N) requires \textit{m}/\textit{z} 206.1903, found \textit{m}/\textit{z} 206.1901.

\textbf{N,N-Dimethyl-1-phenyl-3-propylheptan-1-amine (32)}

\begin{center}
\includegraphics[width=0.2\textwidth]{structure2}
\end{center}

\textit{dr} 1:1

According to the general procedure for amide-reductive Grignard addition, \textit{N,N}-dimethyl benzoylamide (45.0 mg, 0.3 mmol) and (2-ethylhexyl)magnesium bromide solution (0.6 mL, 1 M in Et\textsubscript{2}O, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a colourless oil (39 mg, 52\% yield).

IR (neat) \textit{v}_{\text{max}}: 2959, 2928, 2874, 2857, 2581, 2474, 1460, 922, 750, 702;

\textsuperscript{1}H-NMR (400 MHz, CDCl\textsubscript{3}): \textit{\delta} 7.35-7.21 (m, 5H), 3.32-3.26 (m, 1H), 2.17 (s, 6H), 1.78-1.73 (m, 2H), 1.36-1.02 (m, 9H), 0.91-0.73 (m, 6H);
$^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 140.1, 140.0, 128.8 (2C), 127.9, 127.1, 127.0, 68.4 (2C), 42.7, 42.6, 36.8, 36.6, 35.6, 35.3, 32.2, 28.6, 28.2, 26.4, 25.2, 23.2, 23.0, 14.2, 14.1, 10.7, 10.1;

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{18}$H$_{32}$N) requires $m/z$ 262.2529, found $m/z$ 262.2530.

$N,N$-Dimethyl-1-phenyl-2-(trimethylsilyl)ethanamine (33)$^{24}$

\[
\text{TMS} \quad \text{N} \quad \text{Me}
\]

According to the general procedure for amide-reductive Grignard addition, $N,N$-dimethyl benzoylamine (45.0 mg, 0.3 mmol) and (trimethylsilyl)methylmagnesium chloride solution (0.6 mL, 1 M in Et$_2$O, 0.6 mmol) were used, work up method A was applied. Title compound was obtained as a colourless oil (56 mg, 84% yield).

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.36-7.24 (m, 5H), 3.43 (dd, $J = 10.7, 5.2$ Hz, 1H), 2.19 (s, 6H), 1.29-1.17 (m, 2H), 0.19 (m, 9H);

$^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 140.8, 128.8, 128.0, 127.2, 67.4, 42.1, 21.7, -1.12.

$N,N$-Dimethyl-1-(p-tolyl)ethanamine (34)$^{25}$

\[
\text{Me} \quad \text{N} \quad \text{N}
\]

According to the general procedure for amide-reductive Grignard addition, $N,N,4$-trimethyl benzamide (1.01 g, 6.2 mmol) and methylmagnesium bromide solution (4.1 mL, 3 M in Et$_2$O, 12.4 mmol) were used, work up method B was applied. Title compound was obtained as a colourless oil (860 mg, 85% yield).

IR (neat) $\nu_{\text{max}}$: 2981, 2919, 2678, 1651, 1480, 1062, 826, 739, 699;

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.19 (dt, $J = 8.1, 1.9$ Hz, 2H), 7.13 (d, $J = 8.1$ Hz, 2H), 3.25 (q, $J = 6.7$ Hz, 1H), 2.34 (s, 3H), 2.19 (s, 6H), 1.37 (d, $J = 6.7$ Hz, 3H);

$^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 141.1, 136.5, 129.0, 127.6, 65.8, 43.4, 21.2, 20.4.
**N,N-Dimethyl-1-phenylprop-2-en-1-amine (35)**

![Chemical structure of N,N-Dimethyl-1-phenylprop-2-en-1-amine (35)]

According to the general procedure for amide-reductive Grignard addition, *N,N*-dimethyl benzoylamide (45.0 mg, 0.3 mmol) and vinylmagnesium bromide solution (0.6 mL, 1 M in THF, 0.6 mmol) were used, work up method B was applied. Yield 78% (nmr yield with 3,5-dibromoanisole as internal standard, 73% yield after flash column calculated according to the ratio and the mass (44 mg) : with 15% of double bond hydrogenated).

IR (neat) $\nu_{\text{max}}$: 2917, 2849, 1461, 1200, 1050, 733, 703;

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.25-7.14 (m, 5H), 5.95-5.86 (m, 1H), 5.16 (d, $J = 17.1$ Hz, 1H), 5.03 (dd, $J = 10.1$, 1.6 Hz, 1H), 3.46 (d, $J = 8.7$ Hz, 1H), 2.12 (s, 6H);

$^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 142.6, 140.4, 128.6, 127.9, 127.3, 116.2, 76.3, 43.9;

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{11}$H$_{16}$N) requires $m$/z 162.1277, found $m$/z 162.1277.

**N,N-Dimethyl-1-phenylhept-2-yn-1-amine (36)**

![Chemical structure of N,N-Dimethyl-1-phenylhept-2-yn-1-amine (36)]

According to the general procedure for amide-reductive Grignard addition, *N,N*-dimethyl benzoylamide (45.0 mg, 0.3 mmol) and hex-1-yn-1-ylmagnesium bromide solution (freshly prepared according to the procedure of alkynyl Grignard) were used, work up method B was applied. Title compound was obtained as a colourless oil (56 mg, 86% yield).

IR (neat) $\nu_{\text{max}}$: 2932, 2860, 1458, 1327, 1013, 920, 731, 698;

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.55 (d, $J = 7.5$ Hz, 2H), 7.36-7.32 (m, 2H), 7.29-7.25 (m, 1H), 4.58 (s, 1 H), 2.36 (td, $J = 7.0$, 1.9 Hz, 2H), 2.23 (s, 6H), 1.62-1.46 (m, 4H), 0.97 (t, $J = 7.3$ Hz, 3H);

$^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 139.4, 128.5, 128.1, 127.5, 88.6, 75.0, 61.9, 41.6, 31.3, 22.1, 18.6, 13.8;
HRMS (ESI\(^+\)): exact mass calculated for [M+H\(^+\)] \((C_{15}H_{22}N)\) requires \(m/z\) 216.1747, found \(m/z\) 216.1747.

1-Benzhydrylpyrrolidine (37)

\[
\begin{array}{c}
\text{\includegraphics[width=0.1\textwidth]{benzhydrylpyrrolidine}}
\end{array}
\]

According to the general procedure for amide-reductive Grignard addition, phenyl(pyrrolidin-1-yl)methanone (52.6 mg, 0.3 mmol) and phenylmagnesium bromide solution (0.6 mL, 1 M in THF, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a colourless oil (50 mg, 66% yield).

\(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.64 (d, \(J = 7.3\) Hz, 4H), 7.45 (t, \(J = 7.6\) Hz, 4H), 7.35 (t, \(J = 7.2\) Hz, 2H), 4.33 (s, 1H), 2.60 (br, 4H), 1.94 (br, 4H);

\(^{13}\)C-NMR (100 MHz, CDCl\(_3\)): \(\delta\) 144.5, 128.5, 127.6, 126.9, 76.7, 53.8, 23.7.

1-Benzhydryl-4-cinnamylpiperazine (38)

\[
\begin{array}{c}
\text{\includegraphics[width=0.1\textwidth]{benzhydryl-4-cinnamylpiperazine}}
\end{array}
\]

According to the general procedure for amide-reductive Grignard addition, (4-cinnamylpiperazin-1-yl)(phenyl)methanone (91.9 mg, 0.3 mmol) and phenylmagnesium bromide solution (0.6 mL, 1 M in THF, 0.6 mmol) were used, work up method B was applied. Title compound was obtained as a white solid (74 mg, 67% yield).

IR (neat) \(\nu_{\text{max}}\): 3025, 2959, 2805, 1598, 1492, 1450, 1135, 1029, 706, 693;

\(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.49 (d, \(J = 7.2\) Hz, 4H), 7.43 (d, \(J = 7.4\) Hz, 2H), 7.31-7.21 (m, 9H), 6.59 (d, \(J = 15.8\) Hz, 1H), 6.37-6.30 (m, 1H), 4.31 (s, 1H), 3.24 (d, \(J = 6.5\) Hz, 2H), 2.60-2.54 (br, 8H);
\[ ^{13}\text{C}-\text{NMR} \ (100 \text{ MHz, CDCl}_3) : \delta \ 142.8, 137.0, 133.1, 128.6, 128.5, 128.0, 127.5, 127.0, 126.7, 126.4, 76.3, 61.1, 53.6, 52.0; \]

HRMS (ESI+): exact mass calculated for [M+H]^+ (C_{26}H_{29}N_2) requires \( m/z \) 369.2325, found \( m/z \) 369.2323.

**1-(Phenyl(4-(trifluoromethyl)phenyl)methyl)pyrrolidine (39)**

![Structure of 1-(Phenyl(4-(trifluoromethyl)phenyl)methyl)pyrrolidine](structure.png)

According to the general procedure for amide-reductive Grignard addition, phenyl(pyrrolidin-1-yl)methanone (52.6 mg, 0.3 mmol) and (4-(trifluoromethyl)phenyl)magnesium bromide solution (freshly prepared according to the general procedure of magnesium/iodine exchange) were used, work up method B was applied. Title compound was obtained as a colourless oil (60 mg, 65% yield).

IR (neat) \( \nu_{\text{max}} \): 2970, 2790, 1619, 1417, 1323, 1162, 1122, 1066, 700;

\(^1\text{H}-\text{NMR} \ (400 \text{ MHz, CDCl}_3) : \delta \ 7.62 \ (d, J = 8.3 \text{ Hz, } 2\text{H}), 7.54 \ (d, J = 8.2 \text{ Hz, } 2\text{H}), 7.46 \ (d, J = 7.3 \text{ Hz, } 2\text{H}), 7.31 \ (t, J = 7.8 \text{ Hz, } 2\text{H}), 7.22 \ (t, J = 7.3 \text{ Hz, } 1\text{H}), 4.24 \ (s, 1\text{H}), 2.43 \ (s, 4\text{H}), 1.80 \ (s, 4\text{H}); \]

\(^{13}\text{C}-\text{NMR} \ (100 \text{ MHz, CDCl}_3) : \delta \ 148.5, 143.5, 129.3 \ (d, J_{CF} = 32 \text{ Hz}), 128.7, 127.8, 127.6, 127.3, 125.7 \ (d, J_{CF} = 271 \text{ Hz}), 125.5 \ (q, J_{CF} = 4.0 \text{ Hz}), 76.2, 53.7, 23.7; \]

\(^{19}\text{F}-\text{NMR} \ (376 \text{ MHz, CDCl}_3) : \delta \ -62.4; \]

HRMS (ESI+): exact mass calculated for [M+H]^+ (C_{18}H_{19}NF_3) requires \( m/z \) 306.1464, found \( m/z \) 306.1463.

**Ethyl 4-(piperidin-1-ylmethyl)benzoate (40)**

![Structure of Ethyl 4-(piperidin-1-ylmethyl)benzoate](structure.png)

According to the general procedure for amide-reductive Grignard addition, formylpiperidine (34 mg, 0.3 mmol) and (4-(ethoxycarbonyl)phenyl)magnesium bromide solution (freshly prepared according to the
general procedure of magnesium/iodine exchange) were used, work up method B was applied. Title compound was obtained as a colourless oil (63 mg, 85% yield).

IR (neat) $\nu_{\text{max}}$: 2935, 2853, 2793, 1717, 1612, 1272, 1095, 754, 700;

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.98 (d, $J = 8.3$ Hz, 2H), 7.39 (d, $J = 8.1$ Hz, 2H), 4.38 (q, $J = 7.1$ Hz, 2H), 3.49 (s, 2H), 2.35 (br, 4H), 1.58-1.53 (m, 4H), 1.43 (br, 2H), 1.39 (t, $J = 7.1$ Hz, 3H);

$^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 166.7, 144.3, 129.5, 129.0, 63.6, 60.9, 54.7, 26.1, 24.4, 14.5;

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{15}$H$_{22}$NO$_2$) requires $m/z$ 248.1645, found $m/z$ 248.1644.

5-Chloro-2-(piperidin-1-ylmethyl)pyrimidine (41)

According to the general procedure for amide-reductive Grignard addition, formylpiperidine (34 mg, 0.3 mmol) and (5-chloropyrimidin-2-yl)magnesium bromide solution (freshly prepared according to the general procedure of magnesium/iodine exchange) were used, work up method B was applied. Title compound was obtained as a yellowish oil (47 mg, 74% yield).

IR (neat) $\nu_{\text{max}}$: 2935, 2853, 2798, 1539, 1419, 1131, 1020, 637;

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 8.65 (s, 2H), 3.72 (s, 2H), 2.45 (br, 4H), 1.63-1.57 (m, 4H), 1.42-1.41 (m, 2H); $^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 166.0, 155.7 (2C), 129.6, 65.3, 54.9, 25.8, 24.2;

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{10}$H$_{15}$N$_3$Cl) requires $m/z$ 212.0949, found $m/z$ 212.0947.

2,4-Dichloro-5-(piperidin-1-ylmethyl)pyrimidine (42)

According to the general procedure for amide-reductive Grignard addition, formylpiperidine (34 mg, 0.3 mmol) and (2,4-dichloropyrimidin-5-yl)magnesium bromide solution (freshly prepared according to the general procedure of magnesium/iodine exchange) were used, work up method B was applied. Title compound was obtained as a yellowish oil (64 mg, 86% yield).
IR (neat) ν_{max}: 2937, 2854, 2801, 1560, 1519, 1365, 1342, 1176, 852, 737, 674;

^1^H-NMR (400 MHz, CDCl\textsubscript{3}): δ 8.63 (s, 1H), 3.51 (s, 2H), 2.41 (br, 4H), 1.59-1.56 (m, 4H), 1.46-1.43 (m, 2H);

^13^C-NMR (100 MHz, CDCl\textsubscript{3}): δ 161.9, 160.9, 158.7, 129.9, 56.8, 54.7, 26.0, 24.1;

HRMS (ESI\textsuperscript{+}): exact mass calculated for [M+H]+ (C\textsubscript{10}H\textsubscript{14}N\textsubscript{3}Cl\textsubscript{2}) requires \textit{m}/z 246.0559, found \textit{m}/z 246.0556.

(3a\textit{R},5\textit{R},6\textit{R},6a\textit{R})-5-(2,2-Dimethyl-1,3-dioxolan-4-yl)-6-((4-iodobenzyl)oxy)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxole (43)

According to the general procedure for amide-reductive Grignard addition, formylpiperidine (34 mg, 0.3 mmol) and (4-(((3a\textit{R},5\textit{R},6\textit{R},6a\textit{R})-5-(\textit{R})-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-6-yl)(oxy)methyl)phenyl)magnesium bromide solution (0.2 mmol in THF, freshly prepared according to the general procedure of magnesium/iodine exchange at rt instead of 0 °C) were used, work up method A was applied. Title compound was obtained as a white solid (41 mg, 46% yield).

IR (neat) ν_{max}: 2935, 2854, 2796, 2361, 1371, 1214, 1074, 1021, 846;

^1^H-NMR (400 MHz, CDCl\textsubscript{3}): δ 7.28 (s, 4H), 5.89 (d, J = 3.7 Hz, 1H), 4.67 (dd, J = 19.1, 11.7 Hz, 2H), 4.57 (d, J = 3.7 Hz, 1H), 4.38 (dd, J = 13.7, 6.1 Hz, 1H), 4.15-4.09 (m, 2H), 4.01-3.98 (m, 2H), 3.45 (s, 2H), 2.35 (br, 4H), 1.59-1.53 (m, 4H), 1.48 (s, 3H), 1.42 (br, 5H), 1.37 (s, 3H), 1.30 (s, 3H);

^13^C-NMR (100 MHz, CDCl\textsubscript{3}): δ 138.4, 136.3, 129.4, 127.7, 111.9, 109.1, 105.4, 82.8, 81.7, 81.4, 72.6, 72.4, 67.5, 63.7, 54.6, 27.0, 26.9, 26.4, 26.1, 25.6, 24.5;

HRMS (ESI\textsuperscript{+}): exact mass calculated for [M+H]+ (C\textsubscript{25}H\textsubscript{38}NO\textsubscript{6}) requires \textit{m}/z 448.2694, found \textit{m}/z 448.2685.
According to the general procedure for amide-reductive Grignard addition, formylpiperidine (34 mg, 0.3 mmol) and (4-(((3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)-4-piperidin-1-ylmethyl)benzoate (44) were used. Work up method A was applied. Title compound was obtained as a white solid (60 mg, 51%).

**IR (neat)** \( \nu_{\text{max}} \): 2966, 2933, 2867, 2849, 2361, 1716, 1468, 1272, 1114, 754;

**\(^1\)H-NMR (400 MHz, CDCl\(_3\))**: \( \delta \) 7.99 (d, \( J = 8.3 \) Hz, 2H), 7.39 (d, \( J = 8.3 \) Hz, 2H), 5.42 (d, \( J = 4.2 \) Hz, 1H), 4.89-4.81 (m, 1H), 3.51 (s, 2H), 2.46 (d, \( J = 7.8 \) Hz, 2H), 2.36 (br, 4H), 2.01-1.01 (m, 35H), 0.93 (d, \( J = 8.6 \) Hz, 3H), 0.88 (d, \( J = 1.7 \) Hz, 3H), 0.86 (d, \( J = 1.7 \) Hz, 3H), 0.69 (s, 3H);

**\(^{13}\)C-NMR (100 MHz, CDCl\(_3\))**: \( \delta \) 166.1, 144.2, 139.8, 129.6, 129.0, 122.9, 74.6, 63.6, 56.8, 56.3, 54.7, 50.2, 42.5, 39.9, 39.7, 38.4, 37.2, 36.8, 36.3, 36.0, 32.1, 32.0, 28.4, 28.2, 28.0, 26.1, 24.4, 24.0, 23.0, 22.7, 21.2, 19.5, 18.9, 12.0;

**HRMS (EI)**: exact mass calculated for [M+H]\(^+\) \((C_{40}H_{62}NO_2)\) requires \( m/z \) 588.4775, found \( m/z \) 588.4765.

1-(((3E,5E)-6-(Benzo[d][1,3]dioxol-5-yl)-1-phenylhexa-3,5-dien-2-yl)piperidine (45)
According to the general procedure for amide-reductive Grignard addition, Piperine (85.6 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method A was applied. Title compound was obtained as a colourless gel (101 mg, 93% yield).

IR (neat) \( \nu_{\text{max}} \): 2932, 2851, 2788, 1641, 1488, 1444, 1249, 1038, 699;

\(^1\)H-NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.18-7.15 (m, 2H), 7.09-7.06 (m, 3H), 6.82 (d, \( J = 1.7 \) Hz, 1H), 6.70-6.64 (m, 2H), 6.50 (dd, \( J = 8.1, 1.7 \) Hz, 1H), 6.23 (d, \( J = 15.6 \) Hz, 1H), 5.91-5.85 (m, 3H), 5.65 (dd, \( J = 15.2, 8.3 \) Hz, 1H), 3.08-2.98 (m, 2H), 2.66 (dd, \( J = 12.7, 9.0 \) Hz, 1H), 2.55 (m, 2H), 2.44 (m, 2H), 1.55-1.51 (m, 4H), 1.39-1.35 (m, 2H);

\(^13\)C-NMR (100 MHz, CDCl\(_3\)): \( \delta \) 148.1, 147.2, 140.0, 133.3, 132.6, 132.0, 131.2, 129.6, 128.2, 127.1, 125.9, 121.2, 108.5, 105.5, 101.2, 69.9, 50.9, 38.8, 26.6, 24.9;

HRMS (ESI+): exact mass calculated for \([M+H]^+ \) (C\(_{24}\)H\(_{28}\)NO\(_2\)) requires \( m/z \) 362.2115, found \( m/z \) 362.2112.

1-((1E,3E)-1-(Benzo[d][1,3]dioxol-5-yl)nona-1,3,8-trien-5-yl)piperidine (46)

According to the general procedure for amide-reductive Grignard addition, Piperine (200 mg, 0.7 mmol) and but-3-en-1-ylmagnesium bromide solution (1.4 mL, 1 M in THF, 1.4 mmol) were used, work up method A was applied. Title compound was obtained as a colourless gel (190 mg, 83% yield).

IR (neat) \( \nu_{\text{max}} \): 2932, 2854, 2789, 1639, 1488, 1445, 1250, 1039, 987;

\(^1\)H-NMR (400 MHz, CDCl\(_3\)): \( \delta \) 6.94 (d, \( J = 1.2 \) Hz, 1H), 6.83 (dd, \( J = 8.1, 1.0 \) Hz, 1H), 6.76 (d, \( J = 8.1 \) Hz, 1H), 6.65 (dd, \( J = 15.4, 10.3 \) Hz, 1H), 6.44 (d, \( J = 15.6 \) Hz, 1H), 6.22-6.16 (m, 1H), 5.95 (s, 2H), 5.86-5.76 (m, 1H), 5.70 (dd, \( J = 15.2, 9.1 \) Hz, 1H), 5.03-4.93 (m, 2H), 2.87-2.81 (m, 1H), 2.55 (br, 2H), 2.41 (br, 2H), 2.12-1.96 (m, 2H), 1.82-1.73 (m, 1H), 1.59-1.53 (m, 5H), 1.44-1.39 (m, 2H);

\(^13\)C-NMR (100 MHz, CDCl\(_3\)): \( \delta \) 148.2, 147.2, 138.8, 133.5, 133.3, 132.0, 131.3, 127.2, 121.2, 114.6, 108.5, 105.5, 101.2, 67.7, 50.9, 31.6, 31.0, 26.5, 24.9;

HRMS (ESI+): exact mass calculated for \([M+H]^+ \) (C\(_{21}\)H\(_{28}\)NO\(_2\)) requires \( m/z \) 326.2115, found \( m/z \) 326.2112.
1-(Benzo[d][1,3]dioxol-5-ylmethyl)-4-(1-(4-chlorophenoxy)-3-phenylpropan-2-yl)piperazine (47)

According to the general procedure for amide-reductive Grignard addition, Fipexide (116.5 mg, 0.3 mmol) and benzylmagnesium chloride solution (0.3 mL, 2 M in THF, 0.6 mmol) were used, work up method A was applied. Title compound was obtained as a colourless gel (101 mg, 73%).

IR (neat) \(\nu_{\text{max}}\): 2933, 2876, 2810, 2770, 1489, 1439, 1241, 1038, 824, 700;

\(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.13-7.10 (m, 2H), 7.06-7.03 (m, 5H), 6.71 (s, 1H), 6.60-6.58 (m, 4H), 5.78 (s, 2H), 3.81 (ddd, \(J = 22.3, 9.8, 3.6\) Hz, 2H), 3.27 (s, 2H), 2.91-2.61 (m, 7H), 2.32 (br, 4H);

\(^13\)C-NMR (100 MHz, CDCl\(_3\)): \(\delta\) 157.3, 147.7, 146.6, 139.9, 132.1, 129.3 (2C), 128.4, 126.2, 125.6, 122.4, 115.9, 109.7, 107.9, 100.9, 66.8, 65.2, 63.0, 53.6, 49.6, 34.3;

HRMS (ESI+): exact mass calculated for [M+H]\(^+\) (C\(_{27}\)H\(_{30}\)N\(_2\)O\(_3\)Cl) requires \(m/z\) 465.1940, found \(m/z\) 465.1936.

\(N\)-Benzyl-\(N\)-methyl-4-(piperidin-1-yl)but-2-yn-1-amine (48)

According to the general procedure for amide-reductive Grignard addition, formylpiperidine (34 mg, 0.3 mmol) and (3-(benzyl(methyl)amino)prop-1-yn-1-yl)magnesium bromide solution (0.45 mmol in THF, freshly prepared according to the procedure of alkynyl Grignard) were used, work up method B was applied. Title compound was obtained as a yellowish oil (42 mg, 54% yield).

IR (neat) \(\nu_{\text{max}}\): 2934, 2854, 2793, 2340, 1454, 1322, 1076, 1024, 739, 699;

\(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.33-7.28 (m, 4H), 7.26-7.22 (m, 1H), 3.56 (s, 2H), 3.32 (s, 2H), 3.31 (s, 2H), 2.52 (br, 4H), 2.31 (s, 3H), 1.65-1.59 (m, 4H), 1.43 (br, 2H);
\( ^{13}\text{C}-\text{NMR} \ (100 \text{ MHz, CDCl}_3): \delta \ 138.6, 129.3, 128.4, 127.3, 80.8, 79.6, 60.3, 53.4, 48.1, 45.5, 42.1, 26.1, 24.1; \)

HRMS (ESI+): exact mass calculated for \([\text{M+H}]^+ (\text{C}_{17}\text{H}_{25}\text{N}_2)\) requires \(m/z\) 257.2012, found \(m/z\) 257.2010.

9. References


10. NMR spectra
35
with ~15% of double bond hydrogenated